WALKING MECHANICS, SECOND INJURY, EARLY OSTEOARTHRITIS DEVELOPMENT, AND FUNCTIONAL OUTCOMES AFTER ANTERIOR CRUCIATE LIGAMENT (ACL) RECONSTRUCTION

by

Jacob J. Capin

A dissertation submitted to the Faculty of the University of Delaware in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Biomechanics and Movement Science

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I remember vividly many conversations I had during my senior year at Christopher Newport University. The conversations would begin something like this: “If I can just get into the University of Delaware’s DPT/PhD (Doctor of Physical Therapy and Doctor of Philosophy) dual-degree program...” It feels like yesterday and a lifetime ago. Yet here I am. I am so grateful to the individuals without whom making this dream a reality would never have been possible.

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The long-term objective of this work is to improve functional outcomes and reduce second injury and early OA development after ACLR. This dissertation aimed to identify risk factors associated with second ACL injury (Aim 1) and early patellofemoral OA development (Aim 4), and to evaluate the effect of interventions (i.e., meniscus treatment and rehabilitation strategies) on a known risk factor for early tibiofemoral OA development (Aims 2 and 3) and functional outcomes (Aim 5).

Individuals after primary, unilateral ACLR were recruited. Aims 1-3 and 5 were derived from the ACL-SPORTS clinical trial, which enrolled 80 athletes who were 3-9 months after ACLR. Aim 4 was derived from the Quantitative Magnetic Resonance Imaging (QMRI) and Biomechanical Modeling study, including participants 3 and 6 months after ACLR. All participants underwent detailed biomechanical motion analyses during walking. ACL-SPORTS participants also completed comprehensive clinical and functional evaluations, and QMRI participants also underwent sagittal QMRI analyses. For Aim 5, homogenous subsets of 2 previous “gold-standard” cohorts were used for comparison to the ACL-SPORTS cohort.
The key findings of Aim 1 are that young female athletes after ACLR should delay their return to high-level sports even in the absence of gait impairments, strength deficits, and functional or clinical impairments. Aim 2 indicates that concomitant medial meniscus treatment at the time of ACLR influences walking mechanics and knee joint loading 6 months and 2 years after ACLR, potentially explaining the elevated risk for OA and informing future studies investigating tailored rehabilitation programs. Aim 3 suggests that return-to-sport training with and without perturbation training does not improve walking mechanics, but interlimb symmetry improves by 2 years after ACLR; future research should evaluate gait specific interventions. Aim 4 provides preliminary evidence of the association between walking mechanics and especially walking speed with cartilage degradation in the patellofemoral joint of individuals early after ACLR, a key preliminary step for reducing symptomatic OA. Finally, Aim 5 indicates that return-to-sport training leads to superior functional outcomes among young female athletes after ACLR.

The appendix highlights three other primary author manuscripts that are beyond the scope of the primary dissertation aims. Appendix A includes a clinical commentary, augmented by a case description, to help ice hockey players safely return to sport after ACLR. Appendix B guides clinical practice by presenting an evidence-based approach for the management of patellofemoral pain. Appendix C provides a critique, revised analysis, and re-interpretation of the results of a recent systematic review, highlighting methodological flaws in the review and demonstrating the benefit of using return-to-sport test batteries for preventing subsequent knee injuries after ACLR.
This dissertation work will guide physicians, rehabilitation specialists, and other healthcare professionals who rehabilitate the hundreds of thousands of individuals who tear their ACLs each year. This dissertation will help improve functional outcomes and reduce second ACL injury and early OA development and progression, lowering health-care costs and improving quality of life.
Chapter 1

WALKING MECHANICS, SECOND INJURY, EARLY OSTEOARTHRITIS DEVELOPMENT, AND FUNCTIONAL OUTCOMES AFTER ANTERIOR CRUCIATE LIGAMENT (ACL) RECONSTRUCTION: INTRODUCTION, RATIONALE, AND SPECIFIC AIMS

1.1 Introduction: The Problem

Anterior cruciate ligament (ACL) injury is extremely prevalent among active adolescents and young adults. Most individuals after ACL injury undergo ACL reconstruction (ACLR), one of the most common orthopedic surgeries performed in the United States. Yet despite surgery, individuals after ACLR are at greatly elevated risk for second ACL injury, early post-traumatic osteoarthritis (OA), and unsatisfactory functional outcomes. Second ACL injury to either the graft or contralateral ACL occurs in 30% of young adults who return to sport after ACLR and leads to poorer outcomes and an even greater risk for OA development. Even without second ACL injury, approximately 50% of individuals after ACLR develop OA within 5-15 years when they are still young adults. Both second ACL injury and knee OA have devastating effects, negatively impacting quality of life and creating major socioeconomic burdens for both the young adult and society at-large. Knee OA may develop in the tibiofemoral joint, the patellofemoral joint, or both. Identifying and evaluating risk factors for both tibiofemoral and patellofemoral OA are essential to designing interventions to improve long-term outcomes after ACLR. One such potential risk factor for OA is walking mechanics. Aberrant
walking mechanics six months after ACLR are a known risk factor for the eventual development of tibiofemoral OA. Whether walking mechanics early after ACLR also relate to early patellofemoral OA development is unknown. The effect of specific surgical or rehabilitation interventions on functional outcomes or walking mechanics, a known risk factor for tibiofemoral OA and suspected risk factor for patellofemoral OA and second ACL injury, are also unknowns.

The long-term objective of this work is to improve functional outcomes and reduce second injury and early OA development after ACLR. This dissertation aims to identify risk factors associated with second ACL injury (Aim 1) and early patellofemoral OA development (Aim 4), and evaluate the effect of interventions (i.e., meniscus treatment and rehabilitation strategies) on a known risk factor for early tibiofemoral OA development (Aims 2 and 3) and functional outcomes (Aim 5). This project is significant because it will help elucidate risk factors for second ACL injury and patellofemoral OA development, and evaluate treatment strategies targeting a known risk factor for early tibiofemoral OA. It will also create the foundation for future work that will develop new strategies to address suboptimal outcomes. This dissertation will inform physicians, rehabilitation specialists, and other healthcare providers to improve functional outcomes and reduce the risk of second ACL injury and early OA development after ACLR. The findings will benefit not only the many individuals after ACL injury by improving quality of life, but also reduce the economic burden on our health care system.

1.2 Overarching Scientific Premise

The overall scientific premise of this project is that changes in walking mechanics contribute to second ACL injury risk and the development of knee OA after
traumatic knee injury and that interventions such as meniscus treatment and neuromuscular training may affect functional outcomes and walking mechanics, thereby having the potential to reduce second ACL injury and OA risk and delay OA onset.

1.2.1 Scientific Premise for Aim 1: Preventing Second ACL Injuries

Compared to uninjured controls, female athletes who return to sport after ACLR are 16 times more likely to sustain an ACL injury.235 One potentially modifiable factor linked to second ACL injury is altered movement patterns.138,153,233,236,268,322 Altered lower extremity movements during a drop landing236 and impaired lower extremity coordination233 during a dynamic postural stability task predict second ACL injury in young, female athletes. Altered movement patterns during walking are associated with poor functional performance,78,105 and not meeting objective functional criteria4,121,321 places athletes at a six-fold increase in second injury risk after ACLR.121 Walking is a fundamental activity that may be assessed safely earlier after injury than more novel or sport-related tasks, and could possibly identify those at risk for second injury during rehabilitation as opposed to later in the recovery process. Aim 1 will compare walking mechanics and return-to-sport (RTS) time frames among athletes who either returned to sport without re-injury or sustained a second ACL injury. Aim 1 is significant because it will guide clinical decision-making for when (or if) it is appropriate to return to sport after ACLR.

1.2.2 Scientific Premise for Aim 2: Effect of Medial Meniscus Treatment on Walking Mechanics after ACLR.

Co-occurrence of meniscus injury with ACL rupture is common122,186,188,228,336 and may be treated non-surgically or surgically via partial meniscectomy or repair.
Regardless of how the meniscus is treated, the risk for developing knee OA, especially in the medial tibiofemoral compartment, is elevated greatly after ACLR with concomitant medial meniscal pathology compared to ACLR when both menisci are intact. Altered walking mechanics, which are associated with tibiofemoral OA development after ACLR, are often present after isolated ACLR or isolated arthroscopic partial meniscectomy. Individuals after isolated ACLR walk using smaller sagittal plane knee angles, excursions, and moments. Frontal plane knee gait mechanic alterations after ACLR, however, have been less consistently reported. Among individuals after ACLR, previous studies typically have found similar or smaller peak knee adduction moments in the surgical limb compared to the uninvolved (contralateral) limb or control limbs, but conflicting evidence exists. Among individuals after isolated arthroscopic partial meniscectomy, peak knee adduction moment and impulse increased from pre-operatively to 12 months after surgery. These findings suggest meniscectomy may lead to an opposite pattern of frontal plane kinetics and joint loading compared to what is more commonly found after ACLR. While studies investigating the effect of ACLR on gait mechanics may include individuals with meniscal pathology, the effect of concomitant meniscal pathology and surgical intervention of the meniscus has not been thoroughly investigated. Aim 2 will quantify walking mechanics and knee loading in participants after ACLR with no medial meniscal surgery, partial medial meniscectomy, or medial meniscus repair. Aim 2 will create a foundation for future work investigating targeted treatment strategies.
1.2.3 Scientific Premise for Aim 3: Effect of Neuromuscular Training on Walking Mechanics after ACLR

ACL injury is a devastating yet common injury among adolescents and young adults.\textsuperscript{15,23,28,137} Despite ACLR aimed to restore mechanical knee stability and function,\textsuperscript{198,290} movement asymmetries exist at least six months to one or more years after ACLR.\textsuperscript{46,78,105,127,129,154,253,318,320} Movement asymmetries during walking are associated with early tibiofemoral OA after ACLR,\textsuperscript{12,157,241,242,263,318} thus developing strategies to mitigate these asymmetries may be essential to preventing or delaying the progression of post-traumatic OA. Neuromuscular training programs are one proposed method for correcting movement asymmetries. Perturbation training (Figure 1.1) is a specific neuromuscular training strategy in which participants stand on an unstable surface (i.e., various rollerboard and rockerboard conditions) and respond to surface perturbations applied by the physical therapist.\textsuperscript{53,79,98,144,321} Perturbation training, when applied preoperatively to ACL-injured individuals, improves walking mechanics.\textsuperscript{53,79,129} Unfortunately, these improvements are not retained after ACLR.\textsuperscript{105,253} Postoperative interventions beyond traditional physical therapy are likely needed to restore movement patterns after ACLR given the prevalence of movement abnormalities that persist.\textsuperscript{40,105,158,173,253,264,311,318} Although previous studies show promise for the efficacy of perturbation training, the effect of postoperative perturbation training on movement patterns is unknown. Dr. Snyder-Mackler and colleagues developed the Anterior Cruciate Ligament Specialized Post-Operative Return-To-Sports (ACL-SPORTS) randomized control trial to test the effect of 10 postoperative training sessions consisting of strength, agility, plyometric, and secondary prevention exercises (SAPP) or SAPP plus perturbation (SAPP+PERT) training on walking mechanics after ACLR.\textsuperscript{321} Aim 3 will determine the longitudinal
effect of this specialized postoperative neuromuscular training program on the changes in walking mechanics of male (3a) and female (3b) athletes after primary ACLR (at 4 time points including 2 year follow-up). Aim 3 is significant because developing rehabilitation strategies to improve walking mechanics will inform physical therapist practice and improve knee health and outcomes after ACLR.

Figure 1.1. Perturbation training using a rollerboard (left) and tilt board (right).

1.2.4 Scientific Premise for Aim 4: Walking Mechanics and Patellofemoral OA

Post-traumatic patellofemoral OA exists in at least one-third of individuals 10 years after ACLR. Early signs of OA may be even more common in the patellofemoral compartment compared to the lateral or medial tibiofemoral compartments. Features of patellofemoral OA, but not tibiofemoral OA, one year after ACLR predict symptoms and quality of life two years later. Identifying potentially modifiable factors related to early patellofemoral OA development is
essential to combating this disease. One potentially modifiable factor that may be
related to OA development is walking mechanics,\textsuperscript{51,170,209,242,318} although most studies
have examined the tibiofemoral, rather than patellofemoral joint. A few studies have
investigated walking mechanics and patellofemoral OA. Altered walking mechanics
exist in those with radiographic patellofemoral OA approximately nine years after
ACLR.\textsuperscript{69} Among those with idiopathic patellofemoral OA and no history of ACLR,
walking mechanics (knee flexion moments and impulses) are correlated to
biochemical variables (i.e., T\textsubscript{1rho} and T\textsubscript{2} relaxation times) indicative of patellofemoral
joint degeneration.\textsuperscript{296} The effect of walking mechanics early after ACLR on
patellofemoral joint degradation (biochemical changes) is unknown. Aim 4 is an
exploratory aim to quantify the relationship between walking mechanics early after
ACLR and patellofemoral cartilage T\textsubscript{2} relaxation times (indicative of cartilage health)
6 months after ACLR. Aim 4 is significant because identifying early degenerative
changes and associated risk factors are integral to enable clinicians to develop
rehabilitation and secondary prevention techniques aimed at mitigating the
development and delaying early onset of symptomatic OA.

1.2.5 \textbf{Scientific Premise for Aim 5: Effect of Neuromuscular Training on
Functional Outcomes in Women after ACLR}

Functional outcomes are often worse among women compared to men after
ACL injury and ACLR. Women are less likely to return to any sport, or to preinjury
sport level, after ACL injury and ACL reconstruction (ACLR).\textsuperscript{13,35} When they do
return to sport, women are more likely than men to suffer a second ACL
injury.\textsuperscript{100,232,234,235} Moreover, female athletes have poorer functional recovery after
ACL injury\textsuperscript{143} and lower activity levels than their male counterparts, 2-6 years after
Developing and evaluating rigorous rehabilitation and return-to-sport (RTS) training programs, and comparing outcomes from these programs to those from previously successful cohorts, are essential for improving outcomes among high-level female athletes after ACL injury and ACLR. We developed the ACL-SPORTS training protocol to test the effect of 10 sessions of SAPP versus SAPP+PERT training. Previous work from Dr. Snyder-Mackler’s ACL research team found no significant or meaningful differences between SAPP versus SAPP+PERT training on strength or function among the men at pre-training, post-training, 1 year, or 2 years after ACLR, or among the women at pre-training or post-training. However, the effect of the ACL-SPORTS training program on 1- and 2-year outcomes in women is unknown. The purpose of Aim 5 is two-fold: compare the effect of SAPP versus SAPP+PERT training on the 1- and 2-year primary clinical outcomes (i.e., quadriceps strength, patient reported outcomes, and single-leg hop testing) in female athletes of the ACL-SPORTS trial; and evaluate the comparative effectiveness of 10 sessions of RTS training on clinical and functional outcomes in young female athletes 2 years after ACLR. Aim 5 is significant because it will determine optimal rehabilitation strategies for young women after ACLR, informing clinical practice and improving functional outcomes among a group at especially high risk for poor outcomes.

1.3 Significance of the Expected Research Contribution

Successful completion of this dissertation will drive forward both scientific knowledge of and treatment strategies for traumatic knee injuries. This work will inform surgeons, rehabilitation specialists, and other healthcare professionals to help improve functional outcomes and reduce second ACL injury and OA development.
after ACLR. Aim 1 will guide clinical decision-making regarding readiness for return-to-play and second ACL injury risk reduction. Aim 2 will set the stage for future work investigating targeted treatment strategies, such as the neuromuscular rehabilitation training central to Aim 3. Aim 3 will determine the effectiveness of postoperative neuromuscular training, contributing to the rehabilitation science literature developing rehabilitation strategies to optimize outcomes. Aim 4 is an exploratory aim that will help identify early risk factors for patellofemoral OA, creating a critical foundation for future work to develop ultimately rehabilitation treatments for this debilitating disease. Aim 5 will inform rehabilitation practice for young women after ACLR, improving functional outcomes among a group at especially high risk for poor outcomes. This dissertation work will move rehabilitation practice closer toward combating the high rates of second ACL injury, early OA development, and unsatisfactory functional outcomes, health concerns with immense personal and societal implications and costs. The findings may also have important implications for rehabilitating individuals who sustain other types of knee injuries or who have idiopathic OA.

1.4 Innovation

This dissertation work will be the first to use musculoskeletal modeling to assess the impact of walking mechanics on second ACL injury and early patellofemoral OA risk. Previous studies have used musculoskeletal modeling in healthy participants as well as individuals with OA, stroke, ACL deficiency, and ACLR. The project will uniquely examine walking mechanics with respect to both second ACL injury (Aim 1) and early patellofemoral OA risk (Aim 4) by estimating muscle and joint contact forces in addition to kinematics and kinetics. The ACL Lab at the University of Delaware, led by PhD
advisor, Dr. Lynn Snyder-Mackler, and co-advisor, Dr. Thomas S. Buchanan, has a well-established record of performing impactful research using this musculoskeletal modeling approach after ACL injury and reconstruction, so we are well equipped to perform these analyses.

This dissertation work will also be the first to evaluate the effect of two specific interventions, concomitant medial meniscus treatment (Aim 2) and postoperative neuromuscular and RTS training (Aims 3 and 5), on the walking mechanics (Aims 2 and 3) and functional outcomes (Aim 5) of athletes after ACLR. The project will create a foundation for future work developing targeted interventions and refining rehabilitation science, evaluating the effectiveness of a specific type of neuromuscular training, perturbation training, on both functional outcomes and walking mechanics. Previous work from Dr. Snyder-Mackler and colleagues has used perturbation training successfully after ACL injury to improve movement symmetry, but asymmetries reappear after ACLR. Additional postoperative training is likely necessary to restore movement symmetry after ACLR. The state-of-the-art clinical and research facilities, experience of the mentoring team, and publication record provide the necessary foundation to perform optimally these innovative applications, advancing rehabilitation science.

This dissertation will also innovatively investigate walking mechanics and patellofemoral OA via quantitative MRI early after ACLR (Aim 4). Few prior studies have examined walking mechanics, a likely risk factor, on patellofemoral OA; these studies have been limited to evaluating individuals with idiopathic (not post-traumatic) patellofemoral OA, semi-quantitative (not quantitative) MRI measures, and radiographic (not MRI) OA and gait 9 years after ACLR.
1.5 Specific Aims

My career goal is to optimize musculoskeletal and general health by investigating and developing non-surgical, non-pharmacological interventions that prevent or delay the development of both primary and secondary OA and other musculoskeletal pathologies. The overall objectives of this dissertation are to determine if walking mechanics influence the risk for second ACL injury and/or patellofemoral OA and if specific interventions affect walking mechanics or functional outcomes after ACLR (Figure 1.2). Innovatively applying a valid, patient-specific musculoskeletal modeling approach$^{37,193}$ will provide detailed walking mechanics, including muscle forces and knee joint loading, critical to addressing many of these research objectives through the following specific aims:

![Figure 1.2. Schematic diagram of specific aims.](image)

**Aim 1.** Compare walking mechanics and return-to-sport time frames in a matched cohort of female athletes who either returned to sport without re-injury or sustained a second ACL injury.

*Hypothesis 1.1:* Athletes who sustain second ACL injuries (ACLx2) will return to sports earlier than those who return to sport without re-injury (ACLx1).
**Hypothesis 1.2**: ACLx2 will walk using more asymmetric walking mechanics (i.e., knee kinematics, kinetics, and muscle and joint contact forces) than ACLx1.

**Aim 2.** *Quantify walking mechanics and knee loading among participants approximately 6 months (2a) and 2 years (2b) after ACLR with no medial meniscal surgery, partial medial meniscectomy, or medial meniscus repair.*

**Hypothesis 2**: There will be differences in walking mechanics and knee loading among participants 6 months (2a) and 2 years (2b) after ACLR according to the treatment of the medial meniscus at the time of ACLR.

**Aim 3.** *Determine the longitudinal effect of a specialized postoperative neuromuscular training program on the changes in walking mechanics of male (3a) and female (3b) athletes after primary ACLR.*

**Hypothesis 3.1**: Male (3.1a) and female (3.1b) athletes will walk with interlimb asymmetries in knee kinematics, kinetics, and joint contact forces at pre-training.

**Hypothesis 3.2**: Walking mechanics will improve among male (3.2a) and female (3.2b) athletes after training in both treatment groups, but more so in the SAPP+PERT versus the SAPP training group.

**Aim 4.** *Exploratory aim to define the relationship between gait mechanics early after ACLR and 6-month trochlear T2 relaxation times (higher values indicate worse cartilage health).*
**Hypothesis 4.1:** T2 relaxation times 6 months after ACLR will be higher (worse) in the involved limb compared to the uninvolved limb.

**Hypothesis 4.2:** Slower walking speeds and smaller involved limb knee excursions, moments, and muscle forces during gait would be associated with higher (worse) trochlear T2 relaxation times in the involved limb.

**Hypothesis 4.3:** Interlimb differences in gait mechanics would be negatively associated with interlimb differences in trochlear T2 relaxation times (i.e., those with smaller involved vs. uninvolved limb gait mechanics would have higher [worse] involved vs. uninvolved limb trochlear T2 relaxation times).

**Aim 5.** Compare (5.1) the effect of SAPP versus SAPP+PERT training on the 1- and 2-year primary functional outcomes in female athletes of the ACL-SPORTS trial, and (5.2) 2-year functional outcomes among women who completed the common elements of the ACL-SPORTS trial with homogenous subsets of young, high-level female athletes from two “gold-standard” comparison cohorts.

**Hypothesis 5.1:** SAPP+PERT will result in superior outcomes (i.e., quadriceps strength, patient reported outcomes, and single-leg hop testing) compared to SAPP alone among the women of the ACL-SPORTS trial.

**Hypothesis 5.2:** Female athletes who complete post-operative RTS training, compared to those who do not, will have higher functional outcomes and activity levels 2 years after ACLR.

1.6 **Summary and Positive Impact**

By using innovative applications of previously established analytic and rehabilitation techniques, this dissertation will answer important and clinically
relevant questions pertaining to second ACL injury, early OA development, and functional outcomes after ACLR. The findings will guide physicians, rehabilitation specialists, and other healthcare professionals who rehabilitate the hundreds of thousands of individuals who tear their ACLs each year. This dissertation will help improve functional outcomes and reduce second ACL injury and early OA development and progression, lowering health-care costs and improving quality of life.
Chapter 2

GAIT MECHANICS AND SECOND ACL RUPTURE: IMPLICATIONS FOR DELAYING RETURN TO SPORT

2.1 Abstract

Second anterior cruciate ligament rupture is a common and devastating injury among young women who return to sport after ACL reconstruction, but it is inadequately understood. The purpose of this study was to compare gait biomechanics and return-to-sport time frames in a matched cohort of young female athletes who, after primary ACLR, returned to sport without re-injury or sustained a second ACL injury. Approximately six months after primary reconstruction, fourteen young women (age 16 ± 2 years) involved in jumping, cutting, and pivoting sports underwent motion analysis testing after physical therapy and impairment resolution. Following objective return-to-sport clearance, seven athletes sustained a second ACL rupture within 20 months of surgery (13.4 ± 4.9 months). We matched them by age, sex, and sport-level to seven athletes who returned to sports without re-injury. Data were analyzed using a previously validated, EMG-informed, patient-specific musculoskeletal model. Compared to athletes without re-injury, athletes who sustained a second ACL injury received surgery sooner (p=0.023), had post-operative impairments resolved earlier (p=0.022), reached criterion-based return-to-sport benchmarks earlier (p=0.024), had higher body mass index (p=0.039), and walked with lower peak knee flexor muscle forces bilaterally (p=0.021). Athletes who sustained a second injury also tended to walk with larger (p=0.089) and more symmetrical peak knee flexion angles and less
co-contraction, all indicative of a more normal gait pattern. **Statement of Clinical Significance:** Delayed return-to-sport clearance even in the absence of gait or clinical impairments following primary ACL reconstruction may be necessary to mitigate second ACL injury risk in young women.

### 2.2 Introduction

Hundreds of thousands of anterior cruciate ligament (ACL) ruptures occur annually within the United States alone,\(^{118}\) with over 100,000 individuals undergoing ACL reconstruction (ACLR) each year.\(^{162,192}\) Even after reconstructive surgery, only 55% of athletes return to their pre-injury competitive level of sport.\(^{13}\) Moreover, compared to previously uninjured controls, athletes who do return to sport after ACLR are approximately 15 times more likely to sustain a second ACL injury.\(^{235}\) Younger female athletes may be at an especially high risk of second ACL injury,\(^{235,274}\) with approximately 30% sustaining a graft or contralateral ACL rupture within the first two years of returning to sport after ACLR.\(^{234,313}\) The impact and sequelae of second ACL injury are often devastating. A recent meta-analysis reported poorer knee function and a higher incidence of radiographic osteoarthritis in patients following revision versus primary ACLR.\(^{113}\) Therefore, understanding why second ACL injuries occur is a critically important research question.

The risk for second ACL injury is influenced by many factors, some of which are modifiable.\(^{153,322}\) Timing of return-to-sport (RTS) and biomechanical deficits are two potentially modifiable factors that are linked to second ACL injury risk.\(^{121,174,233–236}\) Early RTS following primary ACLR places athletes at a higher risk for graft rupture or contralateral ACL injury.\(^{121,174,234,235}\) Athletes who returned to competition within the first seven months were nearly three times more likely to sustain a second
ACL injury than those who returned after seven months, with the majority of the injuries occurring within the first month of returning to sport. A recently published study by Grindem and colleagues found that the rate of knee re-injury could be reduced by 51% for each month RTS was delayed for up to nine months post-operatively. In addition to early RTS, altered movement patterns of the trunk and lower extremities are strongly associated with primary ACL injury risk, and thus likely play a role in second injury risk as well. Notably, young athletes who sustained a second ACL injury exhibited biomechanical deficits in knee, hip, and trunk control during a drop landing task assessed after RTS clearance following primary ACLR. Athletes with impaired hip-ankle coordination in the sagittal plane may also be at greater risk for second ACL injury.

Prior studies demonstrate that athletes who perform poorly on objective performance measures six months after primary ACLR walk with larger kinematic and kinetic gait inter-limb asymmetries than those athletes who perform well. Poor functional performance is also associated with asymmetrical tibiofemoral joint loading. These studies point to a link between gait asymmetry and functional performance following ACLR; however the association between gait biomechanics and second ACL injury is unknown.

Previous studies have used musculoskeletal modeling to estimate and report muscle forces in healthy subjects as well as individuals with osteoarthritis, stroke, ACL deficiency, and ACL reconstruction. Altered tibiofemoral joint loading has implications for the development of osteoarthritis following ACL injury and reconstruction, but joint loading has not been assessed in relationship to second injury risk. The use of gait analysis, electromyography, and
musculoskeletal modeling can uniquely examine gait biomechanics and second ACL injury risk by estimating muscle and joint contact forces.

Therefore, the purpose of this study was to compare gait biomechanics and return-to-sport time frames in a matched cohort of young female athletes who, following primary ACLR and impairment resolution, returned to sport without re-injury (ACLx1) or sustained a second ACL injury (ACLx2). We hypothesized that there would be differences in RTS time frames and knee gait mechanics, muscle forces, and joint contact forces between ACLx1 and ACLx2 subjects.

2.3 Methods

2.3.1 Subjects

This study is an individual case-control study (level of evidence: 3b). This study was approved by the University of Delaware IRB, and informed consent was obtained from all subjects as well as a parent/guardian when the subject was a minor. Fourteen young female athletes (age 16.1 ± 1.7 years; range: 13-19 years) were included in this study from part of an ongoing, prospective randomized control trial with 70 subjects (30 women) currently enrolled. All subjects participated in level I or II sports (i.e., sports involving jumping, cutting, and pivoting)70,134 prior to primary ACL rupture and subsequent ACLR, and planned to return to their pre-injury sporting level. Athletes were excluded from participation if they had grade 3 concomitant ligament injury, osteochondral defects >1cm², or significant previous lower extremity injury. Following primary ACLR, all subjects underwent physical therapy and met the following criteria prior to study enrollment and motion analysis testing: minimal to no effusion,294 symmetric and full knee range of motion, ≥80% quadriceps strength limb
symmetry index, ≥12 weeks post-operative, initiation of a running progression, and ability to hop pain-free on each leg.

Following ACLR, impairment resolution, motion analysis testing, and a progressive return-to-play training program, all athletes returned to sport within the first year after ACLR. Athletes received RTS clearance when they met the following objective criteria: \( \geq 90\% \) quadriceps strength limb symmetry index, \( \geq 90\% \) limb symmetry on four single-legged hops (i.e., single, crossover, triple, and timed 6 meter), and \( \geq 90\% \) on the Knee Outcome Survey Activities of Daily Living Scale. All athletes were followed two years post-operatively. Seven athletes sustained a noncontact (N=6) or partial contact (N=1; contact to body, contralateral injury) mechanism of second ACL injury to either their ipsilateral (N=3 graft ruptures) or contralateral (N=4) knee during sport activities within the first two years post-operatively (ACLx2: 13.4 ± 4.9 months post-ACLR). We matched these subjects by sex, age, sport-level, and graft type (for those whose second injuries were graft ruptures) to seven athletes who successfully returned to their pre-injury level of sport competition within the first year of ACLR without re-injury (ACLx1). Matching was done to create a homogenous comparison group and to control for several known large independent risk factors for second ACL injury, including age and activity level. By closely controlling for sex, age, and activity level, however, we were unable to match by autograft type all ACLx2 subjects who sustained contralateral second ACL injuries. During the matching process, we prioritized sex, age, sport-level, and graft type for those whose second injuries were graft ruptures.
2.3.2 Motion Analysis Testing

Motion analysis testing occurred following impairment resolution after primary ACLR (ACLx1: 7.3 ± 1.9 months; ACLx2: 4.9 ± 1.5 months post primary ACLR; Table 2.1), which was prior to athletes receiving clearance to return to sport. Thirty-nine retroreflective markers were placed on the bilateral lower extremities and pelvis. We collected motion data during gait at 120Hz using an eight camera motion analysis system (VICON, Oxford, UK). An embedded force platform (Bertec Corporation, Columbus, OH) was used to collect kinetic data at 1080Hz. Subjects walked at a self-selected gait speed maintained throughout testing to within ±5%. Kinematic and kinetic variables were calculated via inverse dynamics using commercial software (Visual3D, C-Motion, Germantown, MD). Variables of interest included gait velocity as well as peak values during the first half of stance for the following variables: knee flexion angle (pKFA), internal knee extension moment (pKEM), knee adduction angle (pKAA), and internal knee adduction moment (pKAM). Moments were normalized to mass*height (kg*m) to allow comparisons between subjects and groups.207

2.3.3 Electromyography

Surface electromyography (EMG) data were recorded bilaterally from seven lower extremity muscles per limb (rectus femoris, medial and lateral vastii, medial and lateral hamstrings, medial and lateral gastrocnemii) at 1080Hz (MA-300 EMG System, Motion Lab Systems, Baton Rouge, LA). We prepared the skin surface by shaving and abrading the skin prior to electrode placement, which was done in accordance with previous work.101 EMG data were high-pass filtered (2nd-order Butterworth at 30Hz), rectified, and low-pass-filtered (6Hz) to create a linear
envelope. Maximal volitional isometric contractions were used to normalize EMG data in the following positions: seated with knees secured in approximately 60° of flexion for quadriceps; prone with knees secured in 30° of flexion for hamstrings; standing plantarflexion holding counter for resistance for gastrocnemii.101

2.3.4 EMG-Driven Model

All subjects’ gait data were analyzed using a validated,193 EMG-informed, musculoskeletal modeling approach previously described in detail.37,101,193 Briefly, this patient-specific modeling approach uses a Hill-type muscle fiber model. An iterative, simulated annealing process establishes optimal muscle parameters. Joint contact forces are estimated using a frontal plane moment algorithm that balances external knee adduction moments with internal knee moments (i.e., individual muscle forces x moment arms). Subsequently, three predicted walking trials per limb per subject were used for analysis. Variables of interest included knee extensor (i.e., quadriceps) muscle forces, knee flexor (i.e., combined hamstrings and gastrocnemii) muscle forces, and medial tibiofemoral joint contact force (which has larger magnitude and greater validity than lateral joint contact forces104). Specifically, we compared peak knee extensor muscle forces (pEXT) during the first half (i.e., loading phase) of stance; pEXT occurrence (stance phase normalized to 100%); knee flexor muscle forces at peak knee extension moment (FLEX @ pKEM);101 peak knee flexor muscle forces (pFLEX) during the second half of stance; pFLEX occurrence (stance phase normalized to 100%); and peak medial compartment contact force (pMCCF) during the first half of stance. Muscle and joint contact forces were normalized to each subject’s body weight and reported in body weight (BW) units, hence allowing comparison across subjects.207
2.3.5 Model Tuning

Comparing the inverse dynamics sagittal moment curve to the calibrated EMG-driven model moment curve, the model tuning coefficient of determination ($R^2$) was $0.836 \pm 0.088$ and the root mean square error (RMSE) was $6.9 \pm 3.7\%$. These statistics validate the model predictions and are similar to a previous study analyzing ACL deficient subjects.\textsuperscript{101}

2.3.6 Statistical Analysis

Statistical analyses were performed using SPSS Version 23.0 (IBM Corp, Armonk, NY) and Microsoft Excel. We utilized t-tests and Fisher’s Exact Test to compare demographics (i.e., age at surgery, body mass index, graft type) as well as time from injury to surgery, surgery to enrollment/motion analysis testing (i.e., impairment resolution), and surgery to RTS clearance ($\alpha=0.05$). We analyzed joint angles and moments, muscle forces, and medial tibiofemoral contact forces using 2x2 ANOVAs ($\alpha=0.05$) with limb (involved=limb of primary ACLR) and group (ACLx1 vs. ACLx2) as within and between group factors.

2.4 Results

2.4.1 Demographics & Timing

Athletes who sustained a second ACL injury had higher body mass index and received surgery, had impairment resolution, and met criterion-based return-to-sport clearance earlier after injury than athletes who returned to sport without second injury ($p<0.05$; Table 2.1). All athletes ($N=7$) within the ACLx2 group had hamstring autografts while there was a mixture of bone patellar-tendon bone ($N=3$) and
hamstring autografts (N=4) within the ACLx1 group. (ACLx2 athletes who sustained graft ruptures were matched by autograft type [i.e., hamstring].)

Table 2.1. Demographic characteristics and timing variables in the ACLx1 and ACLx2 groups (*p < 0.05).

<table>
<thead>
<tr>
<th>Demographic Variable</th>
<th>ACLx1</th>
<th>ACLx2</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>16.0 ± 1.7</td>
<td>16.3 ± 1.9</td>
<td>.741</td>
</tr>
<tr>
<td>Body Mass Index (kg/m(^2))</td>
<td>21.4 ± 1.8</td>
<td>24.5 ± 3.0</td>
<td>.039*</td>
</tr>
<tr>
<td>Graft Type</td>
<td>4 HS, 3 BPTB</td>
<td>7 HS, 0 BPTB</td>
<td>.192</td>
</tr>
<tr>
<td><strong>Timing Variable</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injury to Surgery (weeks)</td>
<td>6.8 ± 2.5</td>
<td>4.1 ± 1.0</td>
<td>.023*</td>
</tr>
<tr>
<td>Surgery to Meeting Criteria for Enrollment (months)</td>
<td>7.3 ± 1.9</td>
<td>4.9 ± 1.5</td>
<td>.022*</td>
</tr>
<tr>
<td>Surgery to RTS Clearance (months)</td>
<td>9.5 ± 1.9</td>
<td>6.8 ± 1.9</td>
<td>.024*</td>
</tr>
</tbody>
</table>

Abbreviation: HS: hamstring autograft; BPTB: bone patellar-tendon bone autograft; RTS: return-to-sport

2.4.2 Gait Kinematics & Kinetics

There was no significant difference in gait velocity, although a trend (p=0.063) was noted toward faster velocity in the ACLx2 group (ACLx1: 1.47 ± .16 m/s vs. ACLx2: 1.58 ± .13 m/s) with a moderate effect size\(^5\) (Cohen’s d=0.77). There was also a trend (p=0.089; Table 2.2) toward group differences in peak knee flexion angle with the ACLx2 athletes walking with larger pKFA as compared to ACLx1 in both limbs (Cohen’s d=0.69). The involved limb difference of 5.9° exceeded the minimal detectable change (MDC) of 2.9°\(^5\) while the uninvolved limb difference (2.7°) did not meet the MDC.\(^5\) ACLx2 subjects demonstrated inter-limb symmetry in pKFA.
(ACLx2 involved – uninvolved = 0.2°) while ACLx1 subjects walked with meaningful inter-limb differences in pKFA (ACLx1 involved – uninvolved = -3.0°). There were no differences in pKAA, pKEM, or pKAM (Table 2.2).

2.4.3 Muscle & Joint Contact Forces

During the loading phase (i.e., first half) of stance, moderate effect sizes were present for both peak knee extensor muscle forces (p=0.126, Cohen’s d = 0.60) and flexor muscle forces at pKEM (p=0.145, Cohen’s d=0.65), with larger knee extensor and smaller knee flexor muscles forces in ACLx2 compared to ACLx1 subjects. There was no difference between groups for the occurrence of pEXT (average: 21 ± 2% of stance, full model p=0.819) or peak medial tibiofemoral joint contact force (Table 2.2).

There was a statistically significant difference (p=0.021) in peak knee flexor muscle forces during the second half of stance regardless of limb, with ACLx2 subjects demonstrating lesser flexor forces compared to ACLx1 subjects (Table 2.2); this effect size (Cohen’s d=0.90) was large. There was a trend (p=0.080) toward lesser peak knee flexor muscle forces in the involved as compared to uninvolved limb (Figure 2.1a-d), with a moderate effect size (Cohen’s d=0.64). There was no difference in pFLEX occurrence (average: 69 ± 9% of stance, full model p=0.253), which was driven primarily by the gastrocnemii (Figure 2.2a-d).
Table 2.2 Biomechanical variables of interest between group and limb (*p<0.05; ^p<0.10).

<table>
<thead>
<tr>
<th>Variable</th>
<th>ACLx1 INV</th>
<th>ACLx1 UN</th>
<th>ACLx2 INV</th>
<th>ACLx2 UN</th>
<th>P-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>pKFA (*) (°)</td>
<td>-17.4 ± 8.0</td>
<td>-20.5 ± 5.1</td>
<td>-23.3 ± 5.1</td>
<td>-23.1 ± 6.9</td>
<td>.294</td>
</tr>
<tr>
<td>pKAA (*) (°)</td>
<td>-0.8 ± 2.3</td>
<td>0.0 ± 1.3</td>
<td>0.6 ± 3.4</td>
<td>1.0 ± 3.4</td>
<td>.647</td>
</tr>
<tr>
<td>pKEM (Nm/Kg*m)</td>
<td>0.35 ± 0.21</td>
<td>0.42 ± 0.16</td>
<td>0.43 ± 0.10</td>
<td>0.54 ± 0.18</td>
<td>.235</td>
</tr>
<tr>
<td>pKAM (Nm/Kg*m)</td>
<td>-0.23 ± 0.07</td>
<td>-0.28 ± 0.08</td>
<td>-0.29 ± 0.08</td>
<td>-0.27 ± 0.10</td>
<td>.604</td>
</tr>
<tr>
<td>pEXT (BW)</td>
<td>2.1 ± 1.0</td>
<td>2.4 ± 0.7</td>
<td>2.5 ± 0.5</td>
<td>3.0 ± 0.8</td>
<td>.210</td>
</tr>
<tr>
<td>FLEX @ pKEM (BW)</td>
<td>1.1 ± 0.6</td>
<td>1.3 ± 0.4</td>
<td>1.0 ± 0.4</td>
<td>1.0 ± 0.2</td>
<td>.452</td>
</tr>
<tr>
<td>pFLEX (BW)</td>
<td>1.8 ± 0.6</td>
<td>2.0 ± 0.7</td>
<td>1.1 ± 1.4</td>
<td>1.7 ± 0.5</td>
<td>.036*</td>
</tr>
<tr>
<td>pMCCF (BW)</td>
<td>2.9 ± 0.7</td>
<td>3.1 ± 0.6</td>
<td>3.0 ± 0.5</td>
<td>2.9 ± 0.6</td>
<td>.977</td>
</tr>
</tbody>
</table>

Abbreviations: INV=involved limb; UN=uninvolved limb; pKFA=peak knee flexion angle (negative value indicates flexion); pKAA=peak knee adduction angle (positive value indicates adduction); pKEM=peak internal knee extension moment; pKAM=peak internal knee adduction moment; pEXT=peak knee extensor muscle forces; FLEX @ pKEM=knee flexor muscle forces at pKEM; pFLEX=peak knee flexor muscle forces; pMCCF=peak medial compartment tibiofemoral contact force; BW=body weight (units)
Figure 2.1a-d. Comparison of mean extensor (EXT) and flexor (FLEX) muscle forces during stance for ACLx1 (Figures 2.1a-b) and ACLx2 (Figures 2.1c-d) subjects (whiskers are standard deviations).

Figure 2.1c. ACLx2 Involved Muscle Forces

Figure 2.1d. ACLx2 Uninvolved Muscle Forces

Figure 2.1a-d. Comparison of mean extensor (EXT) and flexor (FLEX) muscle forces during stance for ACLx1 (Figures 2.1a-b) and ACLx2 (Figures 2.1c-d) subjects (whiskers are standard deviations).
Figure 2.2a. ACLx1 Involved Flexor Muscle Forces

Figure 2.2b. ACLx1 Uninvolved Flexor Muscle Forces
Figure 2.2a-d. Contribution of the gastrocnemii versus hamstrings muscle forces to the total knee flexor (FLEX) muscle forces during stance for the ACLx1 involved (Figure 2.2a) and uninvolved (Figure 2.2b) and ACLx2 involved (Figure 2.2c) and uninvolved (Figure 2.2d) limbs.
2.5 Discussion

The purpose of this study was to investigate gait biomechanics, including modeling the muscle and joint contact forces, in a matched cohort of young female athletes after primary ACLR who either returned to sport without re-injury (ACLx1) or sustained a second ACL rupture within two years of surgery (ACLx2). We found that ACLx2 athletes received surgery more quickly after injury and met objective criteria for enrollment and RTS clearance more quickly than ACLx1 subjects. Yet despite being tested sooner after primary ACLR than ACLx1 subjects, ACLx2 subjects demonstrated a more normal gait pattern. Our findings suggest that even in the absence of clinical or gait impairments, returning to sports early after primary ACLR may place young female athletes at greater risk for second ACL injury.

The ACLx2 group demonstrated more normal gait biomechanics and symmetry than ACLx1 subjects: larger knee flexion angles, more symmetrical knee flexion angles, and less co-contraction. The inter-limb symmetry and magnitude of peak knee flexion angle of the ACLx2 athletes resembled the gait mechanics of healthy controls,\textsuperscript{180,257,258} stronger subjects after ACLR,\textsuperscript{180} and ACL-deficient subjects who have returned to pre-injury activity levels without reconstruction.\textsuperscript{257,258} ACLx2 subjects tended to walk with larger knee extensor muscle forces and smaller knee flexor muscle forces during the loading phase of gait regardless of limb; this muscle strategy is characteristic of a cyclical pattern of muscle recruitment associated with healthy control subjects and ACL-injured subjects who return to high level activities with minimal impairments.\textsuperscript{257} In contrast, during the loading phase of gait, ACLx1 subjects walked with smaller knee extensor and larger knee flexor muscle forces, which is indicative of co-contraction. ACLx1 subjects’ smaller pKFA, inter-limb pKFA asymmetry, and muscle strategies resemble subjects following ACL injury.
who have chronic knee instability, poorer function, and muscle co-contraction during gait.\textsuperscript{257}

Gait kinematics and joint contact forces may also have implications for the development of post-traumatic osteoarthritis.\textsuperscript{158,318} Ironically, the magnitudes of pKFA of the ACLx2 subjects are more consistent with subjects who do not develop radiographic osteoarthritis five years after ACLR, while the pKFA of the ACLx1 subjects is similar to those who do develop radiographic osteoarthritis.\textsuperscript{158} However, both groups walked with peak medial compartment contact forces similar in magnitude to subjects six months after ACLR who do not develop radiographic osteoarthritis by five years after ACLR.\textsuperscript{318} Neither ACLx1 nor ACLx2 subjects exhibited the medial compartment joint unloading characteristic of (a separate cohort of) subjects who develop medial compartment osteoarthritis by five years after ACLR.\textsuperscript{318} More research is needed to understand better which individuals are most at risk for the development of post-traumatic osteoarthritis and/or second ACL injury.

In light of the above, our findings suggest that earlier return-to-sport time frames—even in athletes with more normal gait mechanics—are associated with second ACL injuries. One possible explanation is that earlier resolution of impairments is linked to both better gait patterns and earlier passing of objective RTS criteria, thus enabling the “best” subjects to resume sports more quickly after ACLR, placing them at greater risk for second ACL injury. In a recently published study, Grindem and colleagues found that returning to level I\textsuperscript{70} sport prior to nine months post-ACLR and asymmetrical quadriceps strength were independent predictors of knee re-injury.\textsuperscript{121} The present study corroborates the temporal findings in a separate cohort: ACLx2 athletes returned to sport nearly three months earlier than ACLx1
athletes (6.8 vs. 9.5 months). However, all of our athletes (i.e., ACLx1 and ACLx2 subjects) returned to high level sports only after meeting stringent RTS criteria including at least 90% quadriceps limb symmetry index. Our study adds in-depth biomechanical analysis with no observed gait impairments within the ACLx2 group. Biological healing time frames may be an important consideration above and beyond both functional criteria\textsuperscript{121,150} and gait mechanics when determining RTS clearance. Even in the absence of functional or gait impairments, our data corroborate recent evidence that suggests delaying return-to-sport until at least nine months or more postoperatively may decrease second ACL injury risk.\textsuperscript{121,150}

Athletes who sustained a second ACL injury also had higher body mass index (BMI) than ACLx1 subjects. Interestingly, in a large cohort study investigating risk factors for revision ACLR, a BMI of less than 30 kg/m\textsuperscript{2} was associated with increased risk of revision surgery.\textsuperscript{191} All but one (ACLx2 subject: BMI of 30.7 kg/m\textsuperscript{2}) of our athletes had a BMI of less than 30 kg/m\textsuperscript{2}—classifying 13 of 14 subjects in this higher risk cohort. Among athletes within this high-risk cohort (i.e., BMI < 30 kg/m\textsuperscript{2}) who are returning to high level sports, our data suggest that higher, rather than lower, BMI may be associated with second injury, although more research with larger sample sizes is needed.

One factor which merits further discussion is graft type. All subjects in both groups received autografts for their primary ACLR. While all ACLx2 subjects underwent primary ACLR using a hamstring autograft, three of the ACLx1 subjects who were matched to ACLx2 subjects with contralateral second injuries had BPTB autografts. Although it may seem that these differences in graft type could influence the results\textsuperscript{166}, we expect this discrepancy to have a minimal influence on our
interpretation, for the following primary reason: the statistically significant differences in peak knee flexor muscle forces (pFLEX) occurred in the second half of stance, during which the gastrocnemii, and not the hamstrings, are contributing primarily to the total knee flexor muscle forces. For the ACLx2 group, the contribution of gastrocnemii to total knee flexor muscle forces was about 79% (involved=79%, uninvolved=79%). Similarly, for the ACLx1 group, the contribution of gastrocnemii to total knee flexor muscle forces was about 89% (involved=88%, uninvolved=90%). Also, during the first half of stance, similarities across limbs were noted: FLEX @ pKEM were similar across limbs (p=0.612) and did not interact between group and limb (p=0.694). Moreover, for ACLx2 subjects, FLEX @ pKEM were similar in both limbs (involved=0.97 body weight, uninvolved=0.99 body weight). The relative contribution of the hamstrings to the total FLEX @ pKEM was likewise similar across groups (ACLx2 involved=65%, ACLx2 uninvolved=57%; ACLx1 involved=59%, ACLx1 uninvolved=58%). Finally, all subjects in the present study were well-rehabilitated prior to study enrollment and motion analysis testing, which occurred at a time when functional regeneration of hamstrings harvested as grafts has been shown to occur.323 These findings suggest that the hamstring muscles were functioning similarly across limbs in both ACLx2 and ACLx1 subjects at this time within our cohort. Therefore, while graft type is a limitation of this study, the data suggest it had minimal influence on the results.

There are several other limitations to our study. First, the sample size is relatively small; however, we have a well-matched cohort of cases and controls in terms of age, sex, and sport. Due to all our athletes being young women, caution must be taken in generalizing the findings to men or women older than age 20. Second, our
follow-up period was limited to two years; however, re-injury risk is most common in the first seven months after ACLR 174 and increases only marginally from one to two years after RTS.234,235 Third, athletic exposures were not accounted for, thus we are unable to conclude whether or not exposure moderated second injury risk. All ACLx1 athletes did, however, return to their pre-injury competition level of sport by one year after surgery. Fourth, we analyzed subjects during gait, thus it is unclear how the results could differ if athletes were tested on more demanding sport maneuvers. Finally, muscle and joint contact forces were estimated by the musculoskeletal model, not directly measured. Direct in vivo measurement is, however, not feasible; the musculoskeletal model employed in this study is patient-specific and previously validated;37,193 and, it is the first study to investigate muscle forces and joint loading and second ACL injury risk.

The present study is also unable to answer directly why these second injuries occurred. The authors suspect that early return to high level sport is the primary modifiable reason for second injury in these athletes (as all participants met rigorous functional and performance criteria prior to RTS). This assertion is supported by recent findings by Grindem et al. in a separate cohort of subjects, indicating that early RTS greatly increases re-injury risk after ACLR.121 We suspect insufficient graft healing as the most likely explanation for ipsilateral (i.e., graft) ruptures. For both contralateral and ipsilateral injuries, biology is a plausible explanation. All subjects sustained ACL injuries once—with the majority occurring through a noncontact mechanism—suggesting they have some predispositions.36,153 They are at high risk for contralateral ruptures,153,234 and this predisposition was not altered by their rehabilitation for the first injury. Further investigation is warranted.
In conclusion, athletes who sustained a second ACL injury received primary ACLR earlier, met enrollment and RTS criteria more quickly, had higher BMI, and walked with lower knee flexor muscle forces during the second half of stance than ACLx1 athletes. Additionally, ACLx2 subjects walked with a more normal gait strategy, including larger and symmetrical peak knee flexion angles and a more refined strategy of cyclical muscle contraction patterns. Our findings are in concurrence with and add an in-depth biomechanical analysis to recent literature suggesting delaying RTS until at least nine months.\textsuperscript{121} Although there are important limitations (i.e., graft type differences, testing time-point, small sample size, case-control series design) to consider when interpreting these findings, our data provide more evidence to delay RTS clearance in young female athletes. Delaying RTS clearance after ACLR even in the absence of clinical or biomechanical gait impairments may mitigate second ACL injury risk in young female athletes.

2.6 Funding and Acknowledgments

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Chapter 3

GAIT MECHANICS AFTER ACL RECONSTRUCTION DIFFER ACCORDING TO MEDIAL MENISCAL TREATMENT

3.1 Abstract

**Background:** Knee osteoarthritis risk is high after anterior cruciate ligament reconstruction (ACLR) or arthroscopic meniscal surgery, and higher among individuals who undergo both. Although osteoarthritis development is multifactorial, altered walking mechanics may influence osteoarthritis progression. The purpose of this study was to compare gait mechanics among participants after ACLR with no medial meniscal surgery, partial medial meniscectomy, or medial meniscal repair.

**Methods:** This is a secondary analysis of data collected prospectively as part of a trial (NCT01773317). Sixty-one athletes (age 21.4±8.2 years) after primary ACLR participated when they achieved impairment resolution (5.3±1.7 months post-operatively), including minimal effusion, full range of motion, and ≥80% quadriceps strength symmetry. Participants were classified by concomitant medial meniscal status: NONE: no involvement or non-surgical management of a small, stable tear; PARTIAL: partial meniscectomy; or REPAIR: meniscus repair. Participants underwent comprehensive walking analyses. Joint contact forces were estimated using a previously-validated, EMG-driven musculoskeletal model. Variables were analyzed using a mixed-model ANOVA with group and limb comparisons (α=0.05); group differences of interlimb differences (surgical minus contralateral limb) were calculated for significant interactions.
**Results:** PARTIAL participants walked with higher peak knee adduction moment (pKAM) in the surgical versus contralateral limb compared to REPAIR (group difference of interlimb difference: 0.10 N*m/Kg*m, p=0.020) and NONE (0.06 N*m/Kg*m, p=0.037) participants. REPAIR participants walked with a smaller percentage of medial to total tibiofemoral loading in the surgical limb compared to both PARTIAL (-12%, p=0.001) and NONE (-7%, p=0.011) participants. REPAIR participants trended toward loading the medial compartment of the surgical versus contralateral limb 0.5 body-weight less than PARTIAL participants.

**Conclusions:** PARTIAL participants walked with higher pKAM and shifted loading toward the medial compartment of their surgical limb while REPAIR participants did the opposite, walking with lower pKAM and unloading their surgical versus contralateral limb. These findings may explain partially the conflicting evidence regarding pKAM after ACLR and the elevated risk for osteoarthritis (overloading versus underloading) after ACLR with concomitant medial meniscectomy or repair.

### 3.2 Introduction

An estimated 250,000 anterior cruciate ligament (ACL) ruptures occur annually within the United States. ACL ruptures typically happen during traumatic injuries, thus other knee structures are often involved. Co-occurrence of meniscus injuries with ACL rupture is especially common, exceeding 61% in individuals undergoing primary ACL reconstruction (ACLR). During or after ACLR, concomitant meniscal tears may be treated non-surgically or surgically via partial meniscectomy or repair. Regardless of how the meniscus is treated, however, the risk for developing knee osteoarthritis (OA) is elevated greatly after ACLR with concomitant meniscal pathology compared to ACLR when both menisci are
Knee OA may be especially common in the medial tibiofemoral compartment\textsuperscript{24,41}. Therefore, investigating factors associated with its development and progression is a critical step to improving treatment options and rehabilitation strategies for this debilitating disease.

While the development and progression of knee OA is multifactorial, alterations in walking gait mechanics are associated with early OA development after ACLR\textsuperscript{158,242,318} and with knee OA progression and severity\textsuperscript{12,40,94,271}. Several biomechanical variables may be of particular interest when discussing medial tibiofemoral OA development. Medial compartment tibiofemoral joint loading is likely of chief importance because it encompasses all factors contributing to compressive joint loading; moreover, medial compartment unloading during walking 6 months after ACLR is associated with radiographic knee OA 5 years post-operatively\textsuperscript{318}. Evaluating the proportion of medial compartment to total tibiofemoral joint loading is also important because it shows the degree to which joint loading is concentrated in the medial compartment versus distributed across the medial and lateral compartments. Directly measuring medial compartment or total tibiofemoral loading, however, is not feasible, thus musculoskeletal modeling approaches are necessary to estimate joint loading. Due in part to the complexity of musculoskeletal modeling, many studies are limited to using kinetic variables as surrogates for joint loading. While both sagittal and coronal plane kinetics contribute to joint loading\textsuperscript{194}, knee adduction moment is likely the most widely reported kinetic variable implicated in knee OA development.

Altered walking patterns are often present in individuals after isolated ACLR\textsuperscript{40,46,320,75,78,87,124,130,248,253,264} or isolated arthroscopic partial meniscectomy\textsuperscript{208,298}. 
Individuals after isolated ACLR walk using smaller sagittal plane knee angles, excursions, and moments\textsuperscript{46,75,124,248,264,320}. Coronal plane knee gait mechanic alterations after ACLR, however, have been less consistently reported. Among individuals after ACLR, previous studies typically have found similar\textsuperscript{308,312,316} or smaller\textsuperscript{237,312,314,338} peak knee adduction moments in the surgical limb compared to the uninvolved (contralateral) limb or control limbs, but conflicting evidence exists\textsuperscript{40}. In contrast, after isolated arthroscopic partial meniscectomy, peak knee adduction moment and impulse increased from pre-operatively to 12 months after surgery\textsuperscript{298}. These findings suggest that meniscectomy may lead to an opposite pattern of coronal plane kinetics and joint loading compared to what is more commonly found after ACLR.

While studies investigating the effect of ACLR on gait mechanics may include individuals with meniscal pathology\textsuperscript{308}, the effect of concomitant meniscal pathology and surgical intervention of the meniscus has not been thoroughly investigated. The purpose of this study was to compare knee mechanics and joint loading during level walking in participants after ACLR with no medial meniscal surgery (and minimal to no pathology), partial medial meniscectomy, or medial meniscal repair. We hypothesized that there would be differences in coronal plane gait mechanics and medial tibiofemoral compartment loading based on medial meniscal status among participants after ACLR.
3.3 Methods

3.3.1 Participants

This is a secondary analysis of data collected prospectively as part of a clinical trial (NCT01773317). Institutional review board approval was obtained. All participants provided informed consent prior to study enrollment. Data were collected at the University of Delaware (Newark, DE) between October 2011 and December 2016. Sixty-one athletes (age 21.4±8.2 years) after primary ACLR participated in this study after physical therapy and impairment resolution. Impairment resolution was operationally defined as minimal to no effusion,\textsuperscript{294} full and symmetrical knee range of motion, at least 80% quadriceps strength index, and initiation of a running progression.\textsuperscript{4,42,45,321} Individuals were excluded from participation if they: 1) did not participate regularly (>50 hours/year) in level I or II sports (i.e., sports involving jumping, cutting, and/or pivoting, such as basketball, football, baseball, or racket sports)\textsuperscript{70,134}; 2) were <3 months or >10 months after ACLR; 3) had a history of previous ACLR and/or history of serious lower extremity injury to either limb; or 4) had an osteochondral defect >1 cm\textsuperscript{2}. Participants were classified by concomitant medial meniscal pathology and intervention, based on operative report, to one of three mutually exclusive categories: NONE: no involvement or non-surgical management of a small, stable tear (N=37); PARTIAL: partial meniscectomy (N=12); or REPAIR: meniscus repair (N=12).

3.3.2 Motion Analysis Testing

Participants underwent motion analysis during over-ground walking at a self-selected speed maintained to ±5% across trials. Kinematic data were captured at 120 Hz using an 8-camera motion capture system (VICON, Oxford Metrics Limited,
London, UK) and 39 retroreflective markers and shells affixed to the bilateral lower extremities. Kinetic data were captured at 1080 Hz using an embedded force platform (Bertec Corporation, Worthington, OH); joint moments were calculated via inverse dynamics using commercial software (Visual3D, C-Motion, Germantown, MD). Surface electromyography (EMG, Motion Lab Systems, Baton Rouge, LA) were also captured bilaterally at 1080 Hz on 7 muscles per limb that cross the knee joint: medial and lateral gastrocnemii, medial and lateral hamstrings, vastus medialis, vastus lateralis, and rectus femoris. Skin preparation, electrode placement, and filtering were done according to previously published work. EMG signals were normalized to maximum values obtained during maximum volitional isometric contractions or dynamic trials (whichever was greater).

### 3.3.3 Musculoskeletal Modeling

Joint contact forces were estimated using a previously-validated, patient-specific musculoskeletal model. Anthropometric measurements were used to scale the model individually for each subject. Five walking trials per limb were used for musculoskeletal modeling. Muscle parameters were adjusted within physiological norms via simulated annealing to match the EMG-driven sagittal plane knee moment to the sagittal knee moment derived from inverse dynamics. Using these tunings, three predicted trials per limb were selected by minimizing the root mean squared error and maximizing the $R^2$ values of the two sagittal knee moment curves. A frontal plane moment balancing algorithm was used subsequently to estimate the distribution of tibiofemoral loading to the medial and lateral compartments.
3.3.4 Quadriceps Strength Testing

Quadriceps femoris strength was evaluated for each limb of every participant. Participants were seated securely in an electromechanical dynamometer (Biodex Medical Systems, Shirley, NY) with their knees flexed to 90°. Testing was performed isometrically using an electrical burst superimposition technique\textsuperscript{283,285}. The contralateral limb was tested first followed by the surgical (ACLR) limb; approximately three trials per limb were recorded. The highest volitionally achieved values for each limb were used to calculate quadriceps strength index (QI=ACLR/contralateral x 100%).

3.3.5 Variables of Interest

Primary variables of interest included peak knee adduction moment (pKAM) and peak medial compartment contact force (pMCCF). Secondary variables of interest were peak knee flexion angle (pKFA) and moment (pKFM), peak knee adduction angle (pKAA), and the percentage of medial to total joint contact force at pKFA (medial to total loading). (Medial to total loading comparisons were made at pKFA due to its correlation with peak tibiofemoral joint loads and to standardize across participants.) Moments were normalized by body mass*height while joint contact forces were normalized by body mass to allow comparisons across participants\textsuperscript{207}. Gait speed and quadriceps strength index (QI) were also compared across groups.

3.3.6 Statistical Analyses

Statistical analyses were conducted using SPSS Version 24.0 (IBM Corporation, Armonk, New York, USA). Demographic characteristics were analyzed using one-way analysis of variance (ANOVA) and Chi-Square tests of proportions. Peak variables during gait were analyzed using a 3x2 mixed-model ANOVA with
group (NONE vs. PARTIAL vs. REPAIR) and limb (surgical vs. contralateral) comparisons (α=0.05). Post-hoc t-tests were conducted using the least significant difference method; between group comparisons of interlimb differences (surgical minus contralateral limb) with 95% confidence intervals (CI) and effect sizes (Cohen’s d) were calculated for significant interactions.

3.4 Results

There were no differences among groups in demographic characteristics (Table 3.1) except for body mass index (BMI). BMI was higher in both the PARTIAL (post-hoc p=0.049) and REPAIR (post-hoc p=0.031) groups compared to the NONE group but did not differ between PARTIAL and REPAIR participants (post-hoc p=0.872). Quadriceps strength index (QI) and gait speed did not differ between groups. The vast majority of participants in each group participated in Level I sports prior to injury, and sports participation was similar across groups.

There were three biomechanical variables with statistically significant interaction effects between group (PARTIAL vs. REPAIR vs. NONE) and limb (surgical vs. contralateral). There was a group by limb interaction effect (p=0.010) for peak knee adduction moment (pKAM) characterized by differing responses between PARTIAL and REPAIR participants between their surgical (i.e., ACL reconstructed) and contralateral (i.e., uninjured) limbs (Figure 3.1). PARTIAL participants walked with significantly higher pKAM in the surgical versus contralateral limb compared to both the REPAIR and NONE groups (Table 3.2). In contrast, REPAIR participants tended to walk with relatively lower surgical versus contralateral limb pKAM compared to the NONE group.
Table 3.1 Demographic characteristics, quadriceps strength index, and gait speed according to medial meniscal treatment after ACLR

<table>
<thead>
<tr>
<th>Table 3.1. Variable</th>
<th>NONE (N=37)</th>
<th>PARTIAL (N=12)</th>
<th>REPAIR (N=12)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>19 F, 18 M</td>
<td>7 F, 5 M</td>
<td>3 F, 9 M</td>
<td>.200</td>
</tr>
<tr>
<td>Age (years)</td>
<td>21.0 ± 7.9</td>
<td>23.7 ± 11.4</td>
<td>20.3 ± 4.8</td>
<td>.539</td>
</tr>
<tr>
<td>BMI</td>
<td>24.9 ± 3.1</td>
<td>27.1 ± 3.5</td>
<td>27.4 ± 3.5</td>
<td>.034</td>
</tr>
<tr>
<td>Pre-Injury Sport Level</td>
<td>34 Level I, 3 Level II</td>
<td>10 Level I, 2 Level II</td>
<td>11 Level I, 1 Level II</td>
<td>.675</td>
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<td>Graft Type</td>
<td>9 Allo, 8 BPTB, 20 HS</td>
<td>4 Allo, 1 BPTB, 7 HS</td>
<td>2 Allo, 3 BPTB, 7 HS</td>
<td>.780</td>
</tr>
<tr>
<td>Lateral Meniscal Involvement</td>
<td>20 none, 12 partial meniscectomy, 5 repair</td>
<td>3 none, 7 partial meniscectomy, 2 repair</td>
<td>8 none, 4 partial meniscectomy, 0 repair</td>
<td>.221</td>
</tr>
<tr>
<td>Weeks after ACLR</td>
<td>24.0 ± 8.1</td>
<td>22.5 ± 5.0</td>
<td>19.0 ± 4.8</td>
<td>.114</td>
</tr>
<tr>
<td>Quadriceps Strength Index (%)</td>
<td>91.9 ± 9.6</td>
<td>93.4 ± 8.9</td>
<td>90.9 ± 6.7</td>
<td>.799</td>
</tr>
<tr>
<td>Gait Speed (m/s)</td>
<td>1.54 ± 0.12</td>
<td>1.50 ± 0.14</td>
<td>1.56 ± 0.07</td>
<td>.542</td>
</tr>
</tbody>
</table>

Abbreviations: BMI = body mass index; Level I sports involve jumping, pivoting, and hard cutting (e.g., basketball, football, soccer); Level II sports involve lateral motion but less jumping or hard cutting than level I (e.g., baseball/softball, racket sports, skiing); Allo = allograft; BPTB = bone-patellar tendon-bone autograft; HS = hamstring autograft
Figure 3.1 There was an interaction effect for peak knee adduction moment (pKAM) \( (p=0.010) \), characterized by higher surgical limb pKAM in the PARTIAL group, and lower surgical limb pKAM in the REPAIR group.

Table 3.2 Group comparisons of interlimb differences (surgical minus contralateral limb) for peak knee adduction moment according to meniscal treatment

<table>
<thead>
<tr>
<th>Table 3.2. pKAM</th>
<th>Difference</th>
<th>95% CI</th>
<th>Cohen’s d</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PARTIAL vs. REPAIR</td>
<td>0.10 N<em>m/Kg</em>m</td>
<td>0.02, 0.18</td>
<td>1.03</td>
<td>.020*</td>
</tr>
<tr>
<td>PARTIAL vs. NONE</td>
<td>0.06 N<em>m/Kg</em>m</td>
<td>0.00, 0.13</td>
<td>0.71</td>
<td>.037*</td>
</tr>
<tr>
<td>REPAIR vs. NONE</td>
<td>-0.03 N<em>m/Kg</em>m</td>
<td>-0.09, 0.02</td>
<td>0.38</td>
<td>.262</td>
</tr>
</tbody>
</table>

**Abbreviations:** CI = confidence interval, PARTIAL= partial medial meniscectomy, REPAIR = medial meniscal repair, and NONE = no medial meniscal surgery, CI = confidence interval. Positive value indicates that the group listed first walked with greater surgical versus contralateral limb pKAM compared with the second group; negative values indicate lesser relative pKAM. *Significant \( (p<0.05) \)

There was no interaction effect \( (p=0.112) \) or main effect of limb \( (p=0.259) \) for peak medial compartment contact force (pMCCF), but REPAIR participants walked with meaningful\(^{104} \) underloading in the surgical limb (Figure 3.2). There was also a pronounced difference (cohen’s d=0.99) in interlimb pMCCF loading differences:
REPAIR participants loaded their surgical versus contralateral limb medial compartment 0.5 BW (95% CI: 0.1, 1.0 BW) less than PARTIAL participants.

Figure 3.2 Peak medial compartment contact forces according to medial meniscal treatment.

There was a group by limb interaction effect (p=0.025) for the percentage of medial to total joint contact force at pKFA (medial to total loading). Similar to our findings for pKAM, REPAIR participants walked with a relatively lesser amount of medial to total loading in their surgical versus contralateral limb (Figure 3.3). In contrast, PARTIAL participants walked with a relatively greater amount of medial to total loading. REPAIR participants shifted loading away from the medial compartment of the surgical limb compared to both the PARTIAL and NONE groups (Table 3.3). PARTIAL participants tended to walk with relatively more loading distributed to the surgical limb medial compartment compared to NONE participants.
Figure 3.3 Medial to total loading at peak knee flexion angle (pKFA) differed according to medial meniscal treatment (p = 0.025)

Table 3.3 Group comparisons of interlimb differences (surgical minus contralateral limb) for medial to total loading

<table>
<thead>
<tr>
<th>Table 3.3. Medial to Total Loading</th>
<th>Difference</th>
<th>95% CI</th>
<th>Cohen’s d</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PARTIAL vs. REPAIR</td>
<td>12 %</td>
<td>5, 19</td>
<td>1.50</td>
<td>.001*</td>
</tr>
<tr>
<td>PARTIAL vs. NONE</td>
<td>5 %</td>
<td>-1, 11</td>
<td>0.58</td>
<td>.089</td>
</tr>
<tr>
<td>REPAIR vs. NONE</td>
<td>-7 %</td>
<td>-13, -2</td>
<td>0.88</td>
<td>.011*</td>
</tr>
</tbody>
</table>

Abbreviations: CI = confidence interval, PARTIAL = partial medial meniscectomy, REPAIR = medial meniscal repair, and NONE = no medial meniscal surgery, CI = confidence interval. Positive value indicates that the group listed first walked with greater surgical versus contralateral limb medial to total loading compared with the second group; negative values indicate lesser relative medial to total loading. *Significant (p<0.05).

There was a group by limb interaction effect (p=0.023) for peak knee adduction angle (pKAA; Table 3.4). PARTIAL participants walked with relatively more pKAA in the surgical versus contralateral limb compared to NONE participants.
(p=.041). There were, however, no differences between REPAIR participants and either other group.

Table 3.4 Group comparisons of interlimb differences (surgical minus contralateral limb) for peak knee adduction angle

<table>
<thead>
<tr>
<th>Table 3.4. pKAA</th>
<th>Difference</th>
<th>95% CI</th>
<th>Cohen’s d</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PARTIAL vs. REPAIR</td>
<td>1.8°</td>
<td>-2.0, 5.6</td>
<td>0.40</td>
<td>.334</td>
</tr>
<tr>
<td>PARTIAL vs. NONE</td>
<td>2.4°</td>
<td>0.1, 4.7</td>
<td>0.70</td>
<td>.041*</td>
</tr>
<tr>
<td>REPAIR vs. NONE</td>
<td>-0.6°</td>
<td>-2.9, 1.6</td>
<td>0.18</td>
<td>.582</td>
</tr>
</tbody>
</table>

Abbreviations: CI = confidence interval, PARTIAL= partial medial meniscectomy, REPAIR = medial meniscal repair, and NONE = no medial meniscal surgery, CI = confidence interval. Positive value indicates that the group listed first walked with greater surgical versus contralateral limb peak knee adduction angle (pKAA) compared with the second group; negative values indicate lesser relative pKAA. *Significant (p<0.05).

There were main effects of limb for both peak knee flexion angle (p<0.001) and peak knee flexion moment (p<0.001); however, these differences were moderated by quadriceps strength index (controlling for QI, main effect of limb p=0.637 and p=0.794, respectively). Pooling across groups, participants walked with smaller pKFA (mean interlimb difference [95% confidence interval]: -2.3° [-4.2°, -0.4°], Cohen’s d=0.43) and pKFM (-0.09 [-0.14, -0.04] N*m/Kg*m, d=0.65) in the surgical versus contralateral limb.

3.5 Discussion

The purpose of this study was to determine if meniscal status influences walking mechanics after ACLR. Our findings suggest that coronal plane gait mechanics and tibiofemoral joint loading patterns differ among patients who undergo ACLR plus medial meniscal repair compared to ACLR plus partial medial meniscectomy. Our hypothesis that there would be different loading patterns based on
meniscus status was supported, as the REPAIR group walked with smaller peak knee adduction moments (pKAM) and shifted loading away from the medial compartment of the surgical versus contralateral limb while the PARTIAL group walked with larger pKAM and shifted loading toward the medial compartment of the surgical limb. In contrast, the NONE group walked with relatively symmetrical medial compartment loading profiles.

The distinct gait strategies of PARTIAL participants and REPAIR participants may help explain their elevated risk for post-traumatic OA, but for different reasons: overloading versus underloading. While overloading has traditionally been associated with OA (as may be the case in PARTIAL participants), underloading the medial compartment (as is the case with REPAIR participants) after ACLR has been associated with future OA development. Wellsandt and colleagues found lower surgical limb loading in the medial tibiofemoral compartment among participants 6 months after ACLR who had developed radiographic OA 5 years after ACLR. Similarly, Pietrosimone et al. found that lesser biomechanical loading of the surgical versus contralateral limb 6 months after ACLR was associated with higher levels of biochemical markers indicative of harmful joint metabolism. Therefore, patients after ACLR with concomitant partial medial meniscectomy or medial meniscus repair may each benefit from different, targeted interventions to restore symmetry in the medial tibiofemoral compartment during walking. Interventions could be developed to gradually increase loading among those with combined ACLR and meniscus repair and decrease loading among those with combined ACLR and partial meniscectomy.
Our findings for both the PARTIAL and REPAIR groups, while interesting, are not surprising. Previous literature has been inconsistent reporting pKAM among participants after ACLR\textsuperscript{40,237,308,312,314,316,338}, but has not controlled for medial meniscal pathology. Peak knee adduction moment and impulse increased in the surgical versus contralateral limb from before to 12 months after arthroscopic partial meniscectomy (without ACLR)\textsuperscript{298}. Although we do not have pre-operative measures in the present study, pKAM was larger in the surgical versus contralateral limb of PARTIAL participants compared to both the REPAIR and NONE groups. In contrast, REPAIR participants not only walked with relatively lesser pKAM and medial to total loading compared to PARTIAL participants, but also walked with meaningful pMCCF underloading of the surgical versus contralateral limb. Patients undergoing meniscal repair (with or without ACLR) often have weight-bearing restrictions for upwards of 4 to 6 weeks postoperatively\textsuperscript{306} whereas arthroscopic meniscectomy rarely has weight-bearing precautions. All participants in the present study who underwent meniscal repair had protected weight-bearing restrictions ranging from non-weight bearing to weight bearing as tolerated with knee locked in full extension for 4 weeks. It is plausible that during this period of off-loading following meniscal repair, and in the subsequent months of rehabilitation, patients learn to shift loading away from the medial compartment of the surgical limb and toward the lateral compartment and/or contralateral limb. This explanation could, at least in part, justify why the REPAIR participants in the present study shifted loading away from the medial compartment of the surgical limb compared to both the PARTIAL and NONE groups.

There are some limitations to consider when evaluating and interpreting the findings of the present study. We did not control for the location of medial meniscal
pathology. Surgical decision-making regarding the selection of repair versus menisectomy is, however, based largely on the location (i.e., vascular versus avascular zone\textsuperscript{203}) and extent of the meniscal pathology, thus it is unclear whether the location or extent of the pathology, or the surgical intervention itself, had greater impact on the results. To a large degree, however, it does not matter if the cause is the initial injury or iatrogenic, as the implications for rehabilitation remain either way. We also did not control for lateral meniscal pathology, graft type, or gender; there were no differences, however, among groups on any of these variables. Moreover, by not controlling for these variables, our findings may be more generalizable to individuals after ACLR. The musculoskeletal modeling approach also comes with limitations; it estimates values that cannot be measured in vivo without a device like an instrumented knee prosthesis. The modeling approach is both patient-specific and previously validated, thus provides informative estimations of values that cannot be measured. The present study lacks long-term followup; the time-frame assessed, however, may be critical for understanding future risk of early OA development\textsuperscript{318} at a time when patients are still undergoing rehabilitation. Treatments to target gait impairments could be developed at this relatively early stage to potentially mitigate future OA risk.

In conclusion, our results suggest that concomitant medial meniscus pathology and treatment may influence walking mechanics after ACLR. Those who underwent partial medial menisectomy walked with higher pKAM and shifted loading toward the medial compartment of the surgical limb while those who had meniscal repair did the opposite, walking with lower pKAM and unloading the surgical versus contralateral limb. These findings may help to explain the conflicting evidence regarding pKAM
after ACLR and the elevated risk for osteoarthritis after ACLR with concomitant medial meniscectomy or repair.

3.6 Funding and Acknowledgments

Funding was provided by the National Institutes of Health, including the National Institute of Arthritis and Musculoskeletal and Skin Diseases, Eunice Kennedy Shriver National Institute of Child Health and Human Development, and National Institute of General Medical Sciences: R01-AR048212, R37-HD037985, R01-HD087459, P30-GM103333, U54-GM104941, and T32-HD00749. This work was also supported in part by a Promotion of Doctoral Studies (PODS)–Level I Scholarship from the Foundation for Physical Therapy (J.J.C.) and a University Doctoral Fellowship Award from the University of Delaware, Newark, Delaware (J.J.C.). Thank you to funding from the National Institutes of Health (NIAMS, NICHD, and NIGMS) and Foundation for Physical Therapy. Thank you to Martha Callahan, Angela H. Smith, and the Delaware Rehabilitation Institute for their assistance with patient recruitment. Thank you to Amelia Arundale, Kathleen Cummer, P. Michael Eckrich, Georgia Gagianas, Celeste Dix, and Naoaki Ito for their assistance with data collection and processing.

PARTIAL MEDIAL MENISCECTOMY LEADS TO ALTERED WALKING MECHANICS TWO YEARS AFTER ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION; MENISCAL REPAIR DOES NOT

4.1 Abstract

Background: Partial meniscectomy dramatically increases the risk for post-traumatic, tibiofemoral osteoarthritis after anterior cruciate ligament reconstruction (ACLR). Concomitant medial meniscus treatment influences walking mechanics early after ACLR; whether medial meniscus treatment continues to influence walking mechanics two years after ACLR is unknown.

Research Question: Does medial meniscus treatment at the time of ACLR influence walking mechanics two years after surgery?

Methods: This is a secondary analysis of prospectively collected data from a clinical trial (NCT01773317). Fifty-six athletes (age 24±8 years) with operative reports, two-year biomechanical analyses, and no second injury prior to two-year testing participated after primary ACLR. Participants were classified by concomitant medial meniscal status: no medial meniscus involvement (n=36), partial medial meniscectomy (n=9), and medial meniscus repair (n=11). Participants underwent biomechanical analyses during over-ground walking including surface electromyography; a validated musculoskeletal model estimated medial compartment tibiofemoral contact forces. Gait variables were analyzed using a 3x2 ANOVA with
group (medial meniscus treatment) and limb (involved versus uninvolved) comparisons.

**Results:** There was a main effect of group (p=.039) for peak knee flexion angle (PKFA). Participants after partial medial meniscectomy walked with clinically meaningfully smaller PKFAs in both the involved and uninvolved limbs compared to the no medial meniscus involvement group (group mean difference[95%CI]; involved: -4.9°[-8.7°,-1.0°], p=.015; uninvolved: -3.9°[-7.6°,-0.3°], p=.035) and medial meniscus repair group (involved: -5.2°[-9.9°,-0.6°], p=.029; uninvolved: -4.7°[-9.0°,-0.3°], p=.038). The partial medial meniscectomy group walked with higher (0.45 body weights) involved versus uninvolved limb medial tibiofemoral contact forces and truncated sagittal plane knee excursions. No meaningful side-to-side differences were present in either the no medial meniscus involvement or medial meniscus repair groups.

**Significance:** Aberrant gait mechanics may concentrate high forces in the antero-medial tibiofemoral cartilage among patients two years after ACLR plus partial medial meniscectomy, perhaps explaining the higher osteoarthritis rates and offering an opportunity for targeted interventions.

### 4.2 Introduction

Anterior cruciate ligament (ACL) injury rates are rising, particularly among young athletes involved in high-level sporting activities. ACL injuries, unfortunately, often occur in conjunction with injuries to other structures of the knee, with the menisci among the most commonly injured. Meniscus injuries greatly elevate the risk for post-traumatic osteoarthritis, and partial meniscectomy at the time of ACL reconstruction (ACLR) is one of the strongest predictors of future
early tibiofemoral osteoarthritis\textsuperscript{156,228}. Evaluating factors that may contribute to the development and progression of osteoarthritis after ACLR with meniscal involvement is critical to understanding the pathogenesis of post-traumatic osteoarthritis and creating targeted interventions to combat this debilitating disease.

Aberrant gait mechanics are associated with the rapid development and progression of post-traumatic osteoarthritis after ACLR, particularly in the medial tibiofemoral compartment\textsuperscript{158,263,318}. Partial medial meniscectomy may accelerate the development and progression of osteoarthritis via biomechanical changes. Medial meniscus treatment influences both walking mechanics six months after ACLR\textsuperscript{44} and downhill running mechanics two years after ACLR\textsuperscript{8}. Meniscal pathology and partial medial meniscectomy may preferentially alter frontal plane walking mechanics, especially knee adduction moments\textsuperscript{44,298}, which are associated with osteoarthritis\textsuperscript{265} and widely used as surrogates for medial compartment tibiofemoral loading. Sagittal plane asymmetries, especially lower peak knee flexion moments, are likely the most ubiquitous biomechanical asymmetries among patients in the first several years after ACLR\textsuperscript{126}, and patients with tibiofemoral osteoarthritis five years after ACLR walk using bilaterally smaller peak knee flexion angles and moments compared to their non-osteoarthritic counterparts\textsuperscript{158}. Therefore, evaluating knee kinematics, kinetics, and joint loading among individuals after ACLR with and without partial medial meniscectomy is essential to investigating the biomechanical pathway of accelerated osteoarthritis pathogenesis\textsuperscript{12}.

Quadriceps femoris weakness is also associated with osteoarthritis after ACLR. Tourville and colleagues found a significant relationship between quadriceps strength both a few months and four years after ACLR and tibiofemoral joint space
width narrowing, an early indicator of osteoarthritis\(^{300}\). Limited evidence, however, suggests concomitant meniscal involvement after ACLR may not influence quadriceps strength\(^{44,179,229,273}\) or activation\(^{179}\).

Aberrant gait mechanics and/or quadriceps weakness may mediate the relationship between ACLR plus meniscectomy and the risk for osteoarthritis. Whether medial meniscus treatment continues to influence walking mechanics two years after ACLR is unknown. Given that medial tibiofemoral osteoarthritis is more common than lateral tibiofemoral osteoarthritis\(^{24}\), and previous work suggests that medial meniscus involvement\(^{8,44}\), but not lateral meniscus involvement\(^{8}\), may be related to altered biomechanics, we evaluated the impact of medial meniscus treatment on two key factors related to tibiofemoral osteoarthritis development: gait mechanics and quadriceps strength. The purposes of this study were to compare the effect of concomitant medial meniscus treatment with ACLR on walking mechanics and, secondarily, quadriceps strength index two years after surgery. We hypothesized that patients after ACLR and concomitant partial medial meniscectomy would demonstrate altered walking mechanics, including 1) knee kinematics, 2) knee kinetics, and 3) medial tibiofemoral contact forces, relative to patients after ACLR with no medial meniscus involvement or medial meniscus repair. We also hypothesized that there would be no differences between groups in quadriceps strength index.

4.3 Materials and Methods

4.3.1 Participants

This study is a secondary analysis of data collected prospectively for a clinical trial (NCT01773317). Institutional review board approval was obtained and all
participants provided written informed consent or parental consent and patient assent if under age 18 years. Data were collected between September 2013 and August 2018 at the University of Delaware (Newark, DE). The parent trial inclusion/exclusion criteria were: regular (>50 hours/year) participant in level I or II sports (i.e., sports involving jumping, cutting, and/or pivoting) prior to ACL injury and planning to return to sport; age 13-55 years at enrollment, which occurred 3-9 months after ACLR when patients achieved impairment resolution\textsuperscript{321}; no history of previous ACLR and/or serious lower extremity injury to either limb; and no osteochondral defect >1 cm\textsuperscript{2}. For the present study, participants were included only if they had an available operative report, underwent motion analysis testing two years after ACLR, and did not sustain a second injury prior to 2-year testing. Fifty-six athletes (age: 24±8 years) met these criteria and were included in the present study. Participants were classified into three groups according to their concomitant medial meniscus status and treatment at the time of ACLR. The groups were: 1) No Medial Meniscus Involvement: no medial meniscus involvement or non-surgical management of a small, stable tear; 2) Partial Medial Meniscectomy; and 3) Medial Meniscus Repair (Table 4.1). Participants were collapsed across experimental conditions given no differences in clinical or functional outcomes or walking mechanics\textsuperscript{43,46,47} based on experimental group assignment.
Table 4.1 There were no differences across groups in demographic characteristics, activity levels, graft type, lateral meniscus involvement, gait speed, or quadriceps strength index.

<table>
<thead>
<tr>
<th>Table 4.1. Variable</th>
<th>No Medial Meniscus Involvement (N=36)</th>
<th>Partial Medial Meniscectomy (N=9)</th>
<th>Medial Meniscus Repair (N=11)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>18 F, 18 M</td>
<td>4 F, 5 M</td>
<td>2 F, 9 M</td>
<td>.174</td>
</tr>
<tr>
<td>Age (years)</td>
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<td>28 ± 12</td>
<td>23 ± 5</td>
<td>.266</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26 ± 3</td>
<td>28 ± 3</td>
<td>27 ± 3</td>
<td>.097</td>
</tr>
<tr>
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<td>33 Level I, 3 Level II</td>
<td>8 Level I, 1 Level II</td>
<td>10 Level I, 1 Level II</td>
<td>.966</td>
</tr>
<tr>
<td>2-Year Sport/Activity Level</td>
<td>28 Level I, 3 Level II, 3 Level III, 1 Level IV, 1 No Data</td>
<td>8 Level I, 1 Level II</td>
<td>10 Level I, 1 Level III</td>
<td>.860</td>
</tr>
<tr>
<td>Graft Type</td>
<td>9 Allo, 12 BPTB, 15 HS</td>
<td>4 Allo, 1 BPTB, 4 HS</td>
<td>2 Allo, 3 BPTB, 6 HS</td>
<td>.543</td>
</tr>
<tr>
<td>Lateral Meniscus Involvement</td>
<td>21 none, 10 partial meniscectomy, 5 repair</td>
<td>2 none, 5 partial meniscectomy, 2 repair</td>
<td>7 none, 4 partial meniscectomy, 0 repair</td>
<td>.216</td>
</tr>
<tr>
<td>Weeks after ACLR to 2-Year Testing</td>
<td>111 ± 15</td>
<td>111 ± 18</td>
<td>107 ± 4</td>
<td>.645</td>
</tr>
<tr>
<td>Gait Speed (m/s)</td>
<td>1.54 ± 0.11</td>
<td>1.47 ± 0.12</td>
<td>1.55 ± 0.07</td>
<td>.178</td>
</tr>
<tr>
<td>Quadriceps Strength Index (QI) at 2-years (%)*</td>
<td>102.0 ± 13.0</td>
<td>93.6 ± 11.4</td>
<td>101.9 ± 13.2</td>
<td>.210</td>
</tr>
</tbody>
</table>

Abbreviations: BMI = body mass index; Level I sports involve jumping, pivoting, and hard cutting (e.g., basketball, football, soccer); Level II sports involve lateral motion but less jumping or hard cutting than level I (e.g., baseball/softball, racket sports, skiing); Level III activities include jogging, running, swimming, and light manual work; Level IV includes activities of daily living (and no sports); Allo = allograft; BPTB = bone-patellar tendon-bone autograft; HS = hamstring autograft. *Note: one participant in the No Medial Meniscus Involvement group did not undergo quadriceps strength testing at 2-years.
4.3.2 Biomechanical Gait Analyses

All participants completed motion analyses during over-ground walking a minimum of two years (mean ± standard deviation: 2.1 ± 0.3 years) after primary ACLR according to methods described previously. Briefly, we cleaned and abraded the skin prior to placement of 7 electromyography (EMG) sensors (Motion Lab Systems, Baton Rouge, LA) per limb on the bilateral lower extremities (vastus medialis, vastus lateralis, rectus femoris, medial hamstrings, lateral hamstrings, medial gastrocnemius, and lateral gastrocnemius). Participants performed maximal volitional isometric contractions for each muscle group for EMG normalization purposes prior to placement of 39 retroreflective markers on the bilateral lower extremities. Participants walked over an embedded force platform (Bertec Corporation, Worthington, OH) at a self-selected speed (maintained within ±5%). Kinematic data were captured with an 8-camera system (VICON, Oxford Metrics Limited, London, UK) at 120 Hz while kinetic and EMG data were collected at 1080 Hz. Commercial software (Visual3D, C-Motion, Germantown, MD) was used to calculate kinematics and kinetics. A validated, EMG-informed, patient-specific musculoskeletal model was used to estimate medial compartment tibiofemoral contact force. The biomechanical variables of interest included: 1) knee kinematics: peak knee flexion angle (PKFA), knee flexion excursion during weight acceptance (i.e., initial contact to PKFA), and knee extension excursion during mid-stance (i.e., PKFA to peak knee extension angle); 2) knee kinetics: peak external knee flexion and adduction moments; and 3) peak medial compartment tibiofemoral contact forces.
4.3.3 Quadriceps Strength

We used an electromechanical dynamometer (Biodex Medical Systems, Shirley, NY) to evaluate quadriceps femoris strength. Participants completed approximately three trials per limb of maximal isometric quadriceps contractions with their knees secured at 90° flexion. A burst superimposition technique was used to ensure maximal contraction during each effort. We evaluated the uninvolved limb first followed by the involved limb, and calculated a quadriceps strength index (QI) using the highest volitionally achieved value in each, using the formula: \( QI = \frac{\text{involved limb}}{\text{uninvolved limb}} \times 100 \) (%).

4.3.4 Statistical Analyses

We compared demographic and other patient characteristics using one-way analysis of variance (ANOVA) for continuous variables and Chi-Square tests of proportions for categorical values. Biomechanical variables were analyzed using a 3x2 mixed-model ANOVA with group (No Medial Meniscus Involvement, Partial Medial Meniscectomy, and Medial Meniscus Repair) and limb (Involved and Uninvolved) comparisons. QI was compared among groups using one-way ANOVA. Statistical analyses were conducted using SPSS Version 25.0 (IBM Corporation, Armonk, New York, USA) with alpha set to 0.05 for all analyses.

4.4 Results

4.4.1 Knee Kinematics

There was a significant main effect of group \( (p=.039) \) for peak knee flexion angle (PKFA, Figure 4.1). Participants after partial medial meniscectomy walked with smaller involved limb PKFAs compared to the no medial meniscus involvement and
Participants after partial medial meniscectomy also tended to walk with smaller uninvolved limb PKFAs relative to the other two groups (post-hoc one-way ANOVA p=.071; Table 4.2b). The group differences in both the involved and uninvolved limbs among the partial medial meniscectomy patients and the other two groups exceeded the minimal clinically important difference (MCID) value of 3°79. In contrast, no statistically significant or clinically meaningful differences existed in either the involved or uninvolved limb for the no medial meniscus involvement or medial meniscus repair groups.

Figure 4.1. Peak Knee Flexion Angle

![Figure 4.1. Peak Knee Flexion Angle](image)

Figure 4.1 There was a main effect of group (p=.039), with the partial medial meniscectomy group walking with smaller peak knee flexion angles. (See Table 4.2a-b for post-hoc comparisons.)
Table 4.2a-b. Participants after partial medial meniscectomy walked with smaller involved limb peak knee flexion angles (PKFAs) compared to the no medial meniscus involvement and medial meniscus repair groups (post-hoc one-way ANOVA \( p = .039 \); Table 4.2a). Participants after partial medial meniscectomy also tended to walk with smaller uninvolved limb PKFAs relative to the other two groups (post-hoc one-way ANOVA \( p = .071 \); Table 4.2b).

<table>
<thead>
<tr>
<th>Group A</th>
<th>Group B</th>
<th>Group Mean Difference (A - B) [95% CI]</th>
<th>P-Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meniscectomy</td>
<td>No Involvement</td>
<td>-4.9° [-8.7°, -1.0°]</td>
<td>.015^</td>
</tr>
<tr>
<td>Meniscectomy</td>
<td>Repair</td>
<td>-5.2° [-9.9°, -0.6°]</td>
<td>.029^</td>
</tr>
<tr>
<td>Repair</td>
<td>No Involvement</td>
<td>0.4° [-3.2°, 4.0°]</td>
<td>.832</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group A</th>
<th>Group B</th>
<th>Group Mean Difference (A - B) [95% CI]</th>
<th>P-Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meniscectomy</td>
<td>No Involvement</td>
<td>-3.9° [-7.6°, -0.3°]</td>
<td>.035^</td>
</tr>
<tr>
<td>Meniscectomy</td>
<td>Repair</td>
<td>-4.7° [-9.0°, -0.3°]</td>
<td>.038^</td>
</tr>
<tr>
<td>Repair</td>
<td>No Involvement</td>
<td>0.7° [-2.6°, 4.1°]</td>
<td>.668</td>
</tr>
</tbody>
</table>

Abbreviations: PKFA = peak knee flexion angle; CI = confidence interval. *P-values in the table reflect the least significant difference p-value for the post-hoc comparison of Groups A and B; ^p < 0.05.

There was a main effect of limb \( (p=0.001) \) characterized by smaller involved knee flexion excursions during weight acceptance, however no group interlimb difference exceeded the MCID\(^79\) (**Figure 4.2**). There was also a main effect of limb \( (p<0.001) \) for knee extension excursion during mid-stance, however only the partial medial meniscectomy group walked with meaningfully\(^79\) smaller knee extension excursions; the other two groups walked relatively symmetrically (**Figure 4.3**).
Figure 4.2 There was a main effect of limb ($p=0.001$) for knee flexion excursion during weight acceptance, however no interlimb difference in any group exceeded the minimal clinically important difference (MCID) value of $3^\circ$. 

---

**Figure 4.2. Knee Flexion Excursion -- Weight Acceptance**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Involved</th>
<th>Uninvolved</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Medial Meniscus Involvement (n=36)</td>
<td>16.5</td>
<td>17.8</td>
</tr>
<tr>
<td>Partial Medial Meniscectomy (n=9)</td>
<td>14.0</td>
<td>16.5</td>
</tr>
<tr>
<td>Medial Meniscus Repair (n=11)</td>
<td>15.5</td>
<td>16.6</td>
</tr>
</tbody>
</table>

---

79
Figure 4.3 There was a main effect of limb (p<0.001) for knee extension excursion during mid-stance, however only the interlimb difference (4.2° less excursion in the involved limb) in the partial medial meniscectomy group was clinically meaningful.79

4.4.2 Knee Kinetics

The main effect of limb had a p-value of .080 for peak knee flexion moment, however, only the partial medial meniscectomy group interlimb difference (-0.05 [95% CI: -0.20, 0.10] N*m/kg*m; Cohen’s d effect size: -0.35) was clinically meaningful79. There were no statistically significant differences in peak knee adduction moment (interaction p = .217, limb p = .739, group p = .585). Participants in the partial medial meniscectomy group walked with higher involved limb peak knee adduction moments (mean interlimb difference [95% CI]: 0.04 [-0.07, 0.16]
N·m/kg·m; Cohen’s d effect size: 0.39) while those in the no involvement (-0.02 [-0.06, 0.03] N·m/kg·m; Cohen’s d effect size: -0.19) and repair (-0.05 [-0.13, 0.04] N·m/kg·m; Cohen’s d effect size: -0.46) groups did not.

4.4.3 Medial Compartment Tibiofemoral Contact Forces

The interaction effect had a p-value of .084 for peak medial compartment contact force (PMCCF, Figure 4.4). Participants in the partial medial meniscectomy group walked with higher involved versus uninvolved limb PMCCF (3.13 [2.70, 3.57] vs. 2.67 [2.27, 3.08] body weight [BW] units); the interlimb difference of 0.45 BW (95% CI: -0.01, 0.91 BW, p=0.053) exceeded the meaningful interlimb difference threshold of 0.4BW\textsuperscript{158}. In contrast, interlimb differences in the no medial involvement and repair groups were not meaningful\textsuperscript{158}.

4.4.4 Quadriceps Strength Index (QI)

There were no significant differences in quadriceps strength index (QI, p=.210), although the partial medial meniscectomy group had a QI that was clinically meaningfully lower than the other groups (Table 4.1, above).
Figure 4.4 There tended to be an interaction effect \((p=0.084)\) characterized by meaningfully higher involved limb peak medial compartment contact forces in the partial meniscectomy patients but not in the other groups. (Note: there were 7 subjects for which data could not be modeled.)

### 4.5 Discussion

The purposes of this study were to compare the effect of medial meniscus treatment on walking mechanics and, secondarily, QI two years after ACLR. Our hypothesis that patients after ACLR plus partial medial meniscectomy would demonstrate altered walking mechanics relative to patients after ACLR with no medial meniscus involvement or medial meniscus repair was supported. Our secondary hypothesis that there would be no differences between groups in QI was also supported statistically. All groups had mean QIs above the 90% threshold generally...
described as interlimb symmetry\textsuperscript{321}, although the clinically lower mean among the partial medial meniscectomy group warrants further discussion (below). Our key findings were that participants two years after ACLR plus partial medial meniscectomy walked with smaller involved and uninvolved limb peak knee flexion angles and exhibited meaningful gait asymmetries, including meaningfully smaller involved knee extension excursions and higher involved knee medial compartment tibiofemoral contact forces. These aberrant walking mechanics were not present among participants two years after ACLR with no medial meniscus involvement or medial meniscus repair. Our findings may help explain the greatly elevated risk of post-traumatic osteoarthritis among patients after ACLR with concomitant partial meniscectomy, and provide an area for developing targeted intervention strategies.

Our findings extend previous work that found biomechanical differences among participants according to medial meniscus pathology and treatment\textsuperscript{8,44,251,298}. Capin et al. found that patients early after ACLR with partial medial meniscectomy exhibit higher knee adduction moments in their involved (versus uninvolved) limbs compared to those after ACLR with no medial meniscus involvement and those after ACLR with medial meniscus repair\textsuperscript{44}. Akpinar and colleagues used dynamic stereo radiography to find greater anterior tibial translation during the first 10\% of stance during downhill running among those with ACLR and medial meniscus tears relative to those with isolated ACLR and those with ACLR and lateral meniscus tears two years after ACLR\textsuperscript{8}. Additionally, Thorlund et al. found, among patients after isolated arthroscopic partial medial meniscectomy, peak knee adduction moments and peak knee adduction impulses increased from before to 12 months after surgery\textsuperscript{298}; and, Ren et al., found changes in three dimensional knee kinematics and kinetics during level
walking among ACL-deficient knees with medial meniscus tears compared to those without. The present study indicates that aberrant walking mechanics persist at least two years after ACLR with partial medial meniscectomy.

Our findings contrast with previous work by Hall and colleagues, which found no differences in knee gait biomechanics between individuals after ACLR with and without concomitant meniscal pathology. The contrasting findings are likely because their study grouped all participants with meniscal pathology together, rather than accounting for the compartment of meniscal involvement and whether it was managed via partial meniscectomy or repair. Hall et al. also investigated participants over a wider range of time (12-24 months) rather than at two years post-operatively, although given previous findings that gait mechanics differ early after ACLR according to medial meniscus treatment, differences are likely to exist one year after ACLR as well.

The walking mechanics exhibited by participants after ACLR plus partial medial meniscectomy may be especially detrimental to tibiofemoral cartilage health. Andriacchi and colleagues have posited that altered kinematics, such as those common after ACLR, distribute loads to cartilage regions that may be thinner and less habituated to attenuate loading, thereby initiating or accelerating the pathogenesis of osteoarthritis. A recent study in a separate cohort of individuals five years after ACLR found that those with medial tibiofemoral radiographic osteoarthritis walked with bilaterally smaller knee flexion angles relative to those without radiographic osteoarthritis, which may have shifted the loading to the poorly conditioned anterior tibiofemoral cartilage. Khandha et al. suggested that, among patients who developed osteoarthritis five years after ACLR, the uninvolved limb PKFA may have decreased
to achieve “bad symmetry” by matching the involved limb PKFA; in contrast, among those without osteoarthritis, the involved limb PKFA may have increased to achieve “good symmetry,” matching the uninvolved limb. In the present study, patients after ACLR with partial medial meniscectomy walked using bilaterally smaller PKFAs, similar to the osteoarthritic patients in Khandha et al.’s cohort. Patients after partial medial meniscectomy in the present study also walked with truncated knee excursions and higher medial tibiofemoral joint loading. The combination of higher loads on thinner, unhabituated cartilage may be a dangerous combination that predisposes to early osteoarthritis.

The mean QI of 93.6% in the partial medial meniscectomy group was lower than in the no medial meniscus involvement (102%) or medial meniscus repair (101.9%) groups. Exploratory analyses revealed that 44.4% (4/9) of the partial meniscectomy participants failed to achieve the widely accepted symmetry index threshold of 90%, while just 14.2% (5/35) and 18.2% (2/11) of no involvement and repair participants, respectively, failed to achieve this threshold. Moreover, recent evidence suggests that 90% strength symmetry index may be insufficient for restoring function and preventing future injury, and higher values like 95%, which only the partial medial meniscectomy group did not achieve, may be more appropriate. Our findings contrast with prior work that has found no meaningful differences in quadriceps strength or activation among patients after ACLR according to concomitant meniscal involvement. These studies, however, did not account for the side of meniscus involvement, included patients with multi-ligament injuries or articular cartilage damage, or required participants to meet stringent...
criteria, including 80% QI, at the time of enrollment and quadriceps strength testing\textsuperscript{44}. Future investigations are warranted.

To the study’s merit, we used comprehensive walking analyses including electromyography and a validated musculoskeletal modeling approach\textsuperscript{37,193} to estimate medial compartment loading that cannot be measured directly in vivo. We also had a relatively homogenous cohort as we excluded for previous ACLR, concomitant grade III ligamentous injury, or osteochondral defects $>1\text{cm}^2$, although we included multiple graft types (no difference between groups). We did not use musculoskeletal imaging to evaluate for osteoarthritis or meniscus status at the 2-year gait analysis, although the higher prevalence of osteoarthritis after ACLR with partial meniscectomy is well-documented. The groups were not equal in size, although they were not different across numerous demographic characteristics. Finally, we did not control for graft type or lateral meniscus involvement, although neither differed among groups.

In summary, patients two years after ACLR with concomitant partial medial meniscectomy walked using bilaterally smaller peak knee flexion angles and exhibited gait asymmetries, especially smaller involved knee extension excursion and higher involved medial tibiofemoral joint contact forces, that were not present among participants two years after ACLR with no medial meniscus involvement or concomitant medial meniscus repair. These aberrant gait mechanics may concentrate higher forces in the antero-medial tibiofemoral cartilage\textsuperscript{12,158}, providing a plausible mechanism explaining the higher osteoarthritis rates among patients two years after ACLR plus partial medial meniscectomy. Patients after ACLR plus partial medial meniscectomy also had clinically lower quadriceps strength index. Our findings may
inform future, targeted interventions to ameliorate aberrant movement patterns among patients after ACLR and concomitant partial medial meniscectomy.

4.5.1 Statement of Clinical Significance

Aberrant gait mechanics persist two years after ACLR with partial medial meniscectomy but not in those two years after ACLR with medial meniscus repair or no medial meniscus involvement. These aberrant gait mechanics may concentrate high forces in the antero-medial tibiofemoral cartilage among patients two years after ACLR plus partial medial meniscectomy, perhaps explaining the higher osteoarthritis rates and offering an opportunity for targeted interventions.

4.6 Funding and Acknowledgments

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Chapter 5

REPORT OF THE PRIMARY OUTCOMES FOR GAIT MECHANICS IN MEN OF THE ACL-SPORTS TRIAL: SECONDARY PREVENTION WITH AND WITHOUT PERTURBATION TRAINING DOES NOT RESTORE GAIT SYMMETRY IN MEN 1 OR 2 YEARS AFTER ACL RECONSTRUCTION

5.1 Abstract

Background: Movement asymmetries during walking are common after anterior cruciate ligament (ACL) injury and reconstruction and may influence the early development of posttraumatic osteoarthritis. Preoperative neuromuscular training (like perturbation training, which is neuromuscular training requiring selective muscle activation in response to surface perturbations) improves gait asymmetries and functional outcomes among people who are ACL-deficient, but the effect of postoperative perturbation training on gait mechanics after ACL reconstruction is unknown.

Questions/purposes: Among men undergoing ACL reconstruction, we sought to compare strength, agility, and secondary prevention (SAP) treatment with SAP plus perturbation training (SAP+PERT) with respect to (1) gait mechanics; and (2) elimination of gait asymmetries 1 and 2 years after ACL reconstruction.

Methods: Forty men were randomized into a SAP group or a SAP+PERT group after ACL reconstruction and before returning to preinjury activities. Participants were required to achieve ≥ 80% quadriceps muscle strength symmetry, minimal knee effusion, full ROM, no reports of pain, and completion of a running progression (all between 3 and 9 months postoperatively) before enrollment. Of 94 potentially eligible
athletic male patients evaluated < 9 months after ACL reconstruction, 54 were excluded for prespecified reasons. Participants underwent motion analysis during overground walking at 1 and 2 years postoperatively. Variables of interest included (1) sagittal and frontal plane hip and knee angles and moments at peak knee flexion angle; (2) sagittal plane hip and knee angles and moments at peak knee extension angle; (3) sagittal plane hip and knee excursion during weight acceptance; and (4) sagittal plane hip and knee excursion during midstance. We also calculated the proportion of athletes in each group who walked with clinically meaningful interlimb asymmetry in sagittal plane hip and knee variables and compared these proportions using odds ratios. There was no differential loss to followup between groups.

**Results:** There were no differences between the SAP or SAP+PERT groups for the biomechanical gait variables. The involved limb’s knee excursion during midstance for the SAP (mean ± SD: 1 year: 15° ± 5°; 2 years: 16° ± 5°) and SAP+PERT (1 year: 16° ± 5°; 2 years: 15° ± 4°) athletes was not different between groups at 1 year (mean difference: -1°; 95% confidence interval [CI], -5° to 2°; p = 0.49) or 2 years (mean difference: 1°; 95% CI, -2° to 4°; p = 0.54). There were no differences between SAP and SAP+PERT athletes regarding the elimination of gait asymmetries, and gait asymmetries persisted to a large degree in both groups 1 and 2 years postoperatively. At 1 year, 11 of 18 SAP and 11 of 20 SAP+PERT athletes walked with truncated knee excursions during weight acceptance (odds ratio: 0.8, p = 0.70) and midstance (SAP 12 of 18, SAP+PERT 12 of 20; odds ratio: 0.8, p = 0.67), whereas at 2 years postoperatively, truncated knee excursions during weight acceptance (SAP seven of 17, SAP+PERT eight of 19; odds ratio: 1.0, p = 0.96) and midstance (SAP five of 17, SAP+PERT 11 of 19; odds ratio: 3.3, p = 0.09) remained prevalent.
**Conclusions:** We found that a comprehensive, progressive return-to-sport training program with or without perturbation was not effective at restoring interlimb symmetry among men 1 or 2 years after ACL reconstruction. Although gait asymmetries improved from 1 to 2 years postoperatively, meaningful asymmetries persisted in both groups. To restore gait symmetry after ACL reconstruction, additional interventions likely are necessary.

### 5.2 Introduction

After anterior cruciate ligament (ACL) injury, many individuals undergo reconstructive surgery to restore knee stability and function \(^{198,290}\), yet despite ACL reconstruction (ACLR), movement asymmetries exist at least 6 months to 1 year after ACLR \(^{78,105,127,129,253,318,320}\) and may persist longer \(^{253}\). Movement asymmetries during gait are associated with the development of early osteoarthritis \(^{12,318}\); thus, developing strategies to mitigate these asymmetries is an important area of research.

To improve movement asymmetries in individuals after ACL injuries, neuromuscular training programs have been suggested. One type of neuromuscular training is perturbation training \(^{53,79,98,144,321}\), which consists of external perturbations applied by a therapist while the participant stands on an unstable surface (such as a roller board or rocker board) \(^{53,98,144,321}\). Perturbation training, when applied preoperatively, improves gait asymmetries \(^{53,79,129}\). Moreover, an extended preoperative physical therapy program including perturbation training results in higher success rates and longer maintained functional status compared with control subjects with extended physical therapy but no perturbation training \(^{98}\). Unfortunately, improvements in gait asymmetry that occur from preoperative perturbation training are not retained postoperatively \(^{105,253}\). Postoperative interventions beyond traditional physical therapy
are likely needed to restore gait symmetry after ACLR given the prevalence of movement abnormalities that persist \(^{40,105,158,173,253,264,311,318}\).

Although previous studies show promise for the efficacy of perturbation training, the effect of postoperative perturbation training on movement patterns is unknown. To address this gap, we developed the Anterior Cruciate Ligament Specialized Post-Operative Return-to-Sports training protocol (ACL-SPORTS)\(^ {19,321}\) for athletes after ACLR and traditional physical therapy. The ACL-SPORTS training protocol consists of 10 progressive sessions of comprehensive strengthening, agility, and secondary prevention exercises (SAP) or this SAP protocol with the addition of perturbation training (SAP+PERT).

The purpose of this study was to evaluate the effect of two versions of the ACL-SPORTS training protocol on hip and knee gait mechanics in men 1 and 2 years after ACLR. Specifically, among men undergoing ACLR, we sought to compare SAP treatment with SAP+PERT with respect to (1) gait mechanics; and (2) elimination of gait asymmetries 1 and 2 years after ACLR.

5.3 Methods

5.3.1 Patients and Methods

A detailed description of the patients and methodology for this study may be found in Arundale et al.\(^ {19}\). Briefly, we enrolled and randomized 40 male athletes (mean age ± SD at surgery: 23 ± 7 years) after unilateral ACLR (autograft = 27, allograft = 13) when they met the following criteria for enrollment: ≥ 12 weeks after ACLR, ≥ 80% quadriceps femoris muscle strength symmetry, minimal knee effusion, full ROM, no reports of pain, and completion of a running progression\(^ {4}\). Participants were
randomized to two treatment groups: SAP group (n = 20) and SAP+PERT group (n = 20) (Figure 5.1). The SAP group received 10 training sessions (2 x/week) of ACL injury prevention exercises, agility drills, and plyometric exercises, whereas the SAP+PERT group received 10 training sessions (2 x/week) consisting of all these exercises plus perturbation training (i.e., neuromuscular training requiring selective muscle activation in response to surface perturbations applied by a physical therapist)\(^{98}\). After completing training and achieving objective return-to-sports criteria \(^{4,121,321}\) (≥ 90% quadriceps strength index, ≥ 90% limb symmetry on four single-leg hop tests\(^{226}\) and ≥ 90% score on the Knee Outcome Survey-Activities of Daily Living Scale \(^{146}\)), participants were cleared to begin a gradual, patient-specific return-to-sport progression; rehabilitation after this time was not standardized.

We analyzed participants’ walking patterns 1 and 2 years postoperatively using an eight-camera motion capture system (VICON, Oxford, UK) and embedded force platform (Bertec Corporation, Columbus, OH, USA). Thirty-nine retroreflective markers were placed on the bilateral lower extremities and pelvis before motion analysis testing. Participants then walked overground at a self-selected gait speed maintained to ± 5% across trials and time points. Kinematic data were captured at 120 Hz, whereas kinetic data were captured at 1080 Hz. Data were processed using commercial software (Visual3D; C-Motion, Germantown, MD, USA) and normalized to 100% of stance phase. Joint moments were calculated through inverse dynamics and normalized to body weight and height (Nm/Kg*m) to allow comparisons between participants\(^{207}\).

Variables of interest included (1) sagittal and frontal plane hip and knee angles and moments at peak knee flexion angle (pKFA); (2) sagittal plane hip and knee
angles and moments at peak knee extension angle (pKExtA); (3) sagittal plane hip and knee excursion during weight acceptance (i.e., pKFA – initial contact); and (4) sagittal plane hip and knee excursion during midstance (i.e., pKExtA – pKFA). Sagittal plane joint excursions during weight acceptance and midstance are of particular interest after ACLR given the role of the quadriceps muscle in eccentrically and concentrically controlling knee motion during these phases of the gait cycle.
5.3.2 Statistical Analyses

To compare the demographic characteristics of participants in each group (SAP versus SAP+PERT), we used Student’s t-tests and Pearson chi square tests of
proportions and odds ratios (Table 5.1). To compare gait biomechanical variables, we used 2 x 2 x 2 analysis of variance with three factors: (1) time (1 versus 2 years postoperatively); (2) group (SAP versus SAP+PERT); and (3) limb (uninvolved [UN] versus involved [INV]). Alpha was set at 0.05 a priori for all comparisons. We conducted post hoc t-tests and calculated mean differences (with 95% confidence intervals).

Table 5.1 Demographics and anthropometrics were similar for subjects in the SAP and SAP+PERT groups.

<table>
<thead>
<tr>
<th>Table 5.1 Demographics and Anthropometrics</th>
<th>SAP (Mean ± Standard Deviation)</th>
<th>SAP+PERT (Mean ± Standard Deviation)</th>
<th>Mean Difference (95% Confidence Interval)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at surgery (years)</td>
<td>24 ± 9</td>
<td>23 ± 6</td>
<td>0 (-4, 5)</td>
<td>0.39</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>179 ± 7</td>
<td>177 ± 7</td>
<td>2 (-2, 6)</td>
<td>0.98</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>86 ± 13</td>
<td>86 ± 10</td>
<td>0 (-7, 7)</td>
<td>0.44</td>
</tr>
<tr>
<td>Graft type</td>
<td>Autograft = 14</td>
<td>Autograft = 13</td>
<td>Odds Ratio 0.8 (0.2, 3.0)</td>
<td>1.00</td>
</tr>
<tr>
<td>Mechanism of injury</td>
<td>Contact 9</td>
<td>Contact 9</td>
<td>Odds Ratio 1.0 (0.3, 3.5)</td>
<td>1.00</td>
</tr>
<tr>
<td>Weeks from surgery to enrollment in ACL-SPORTS training protocol</td>
<td>23 ± 8</td>
<td>22 ± 7</td>
<td>1 (-4, 5)</td>
<td>0.73</td>
</tr>
</tbody>
</table>

Abbreviations: SAP = strength, agility, and secondary prevention treatment group; SAP+PERT= SAP + perturbation training group; ACL-SPORTS = ACL-Specialized Post-Operative Return-to-Sports.

We also compared interlimb differences (UN – INV) with previously established minimal clinically important difference (MCID) values to assess for meaningful interlimb asymmetries. MCID values are 3° for sagittal plane hip and knee kinematics during weight acceptance and 0.06 Nm/Kg*m and 0.04 Nm/Kg*m for
sagittal plane hip and knee kinetics, respectively, at peak knee flexion angle\textsuperscript{79}. Clinically meaningful interlimb asymmetry was defined as an absolute difference that met or exceeded the MCID\textsuperscript{79} for hip angles, moments, and excursions and knee moments. Only smaller\textsuperscript{79} involved (versus uninvolved) limb knee angles and excursions were deemed clinically meaningful given the prevalence of reduced knee flexion angles and excursions after ACLR. We computed the proportion of SAP and SAP+PERT athletes who walked with clinically meaningful interlimb asymmetry in sagittal plane hip and knee variables and compared these proportions using odds ratios.

5.3.3 Post-Hoc Power Analysis

We conducted a post hoc power analysis on our primary outcome (i.e., knee flexion angle) using the observed SDs (for peak knee flexion angle) and number of subjects per group. With 80\% power and an $\alpha$ of 0.05, we could have detected a group difference of 3.5° for knee flexion angle. The previously established MCID for peak knee is 3° \textsuperscript{79}, which is only marginally smaller than what we were powered to detect. Moreover, none of our group differences for knee flexion angles or excursions at 1 or 2 years postoperatively exceeded 2.0°: the largest measured group difference for knee flexion angles/excursions in the involved limb was 1.8° (95\% confidence interval [CI], -2.2° to 5.7°; $p = 0.37$) for pKFA 2 years postoperatively; the largest measured group difference for knee flexion angles/excursions in the uninvolved limb was -2.0° (95\% CI, -5.0° to 1.0°; $p = 0.18$) for knee excursion during midstance 1 year postoperatively.
5.4 Results

5.4.1 Gait Mechanics

There were no differences between the SAP or SAP+PERT groups for the biomechanical gait variables. Athletes walked with similar sagittal plane hip and knee angles at both 1 and 2 years postoperatively in both their involved (Table 5.2a) and uninvolved (Table 5.2b) limbs. Likewise, hip and knee excursions were similar across groups at both time points. Notably, the involved limb’s knee excursion during midstance for the SAP (mean ± SD: 1 year: 15° ± 5°; 2 years: 16° ± 5°) and SAP+PERT (1 year: 16° ± 5°; 2 years: 15° ± 4°) groups was similar between groups at both 1 year (mean difference: -1°; 95% CI, -5° to 2°; p = 0.49) and 2 years (mean difference: 1°; 95% CI, -2° to 4°; p = 0.54) postoperatively. Hip extension moments at peak knee flexion angle decreased from 1 year to 2 years postoperatively but did not differ between groups.
Table 5.2a-b Sagittal plane hip and knee angles at peak knee flexion angle did not differ between SAP and SAP+PERT groups for the involved (Table 5.2a) or uninvolved (Table 5.2b) limbs at 1 or 2 years after ACLR. Values are mean (SD) and mean group differences (95% CI).

<table>
<thead>
<tr>
<th>Table 5.2a. Involved Limb</th>
<th>Variable</th>
<th>SAP</th>
<th>SAP+PERT</th>
<th>Mean Difference</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>KFA(°) @ 1-year</td>
<td>20 (6)°</td>
<td>20 (5)°</td>
<td>0 (-3, 4)°</td>
<td>0.92</td>
<td></td>
</tr>
<tr>
<td>KFA(°) @ 2-years</td>
<td>20 (7)°</td>
<td>18 (4)°</td>
<td>2 (-2, 6)°</td>
<td>0.37</td>
<td></td>
</tr>
<tr>
<td>HFA(°) @ 1-year</td>
<td>17 (6)°</td>
<td>18 (5)°</td>
<td>-1 (-4, 2)°</td>
<td>0.55</td>
<td></td>
</tr>
<tr>
<td>HFA(°) @ 2-years</td>
<td>18 (8)°</td>
<td>17 (6)°</td>
<td>1 (-4, 6)°</td>
<td>0.63</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 5.2b. Uninvolved Limb</th>
<th>Variable</th>
<th>SAP</th>
<th>SAP+PERT</th>
<th>Mean Difference</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>KFA(°) @ 1-year</td>
<td>22 (6)°</td>
<td>24 (5)°</td>
<td>-2 (-5, 2)°</td>
<td>0.27</td>
<td></td>
</tr>
<tr>
<td>KFA(°) @ 2-years</td>
<td>22 (6)°</td>
<td>20 (6)°</td>
<td>2 (-2, 6)°</td>
<td>0.34</td>
<td></td>
</tr>
<tr>
<td>HFA(°) @ 1-year</td>
<td>17 (5)°</td>
<td>20 (5)°</td>
<td>-2 (-6, 1)°</td>
<td>0.19</td>
<td></td>
</tr>
<tr>
<td>HFA(°) @ 2-years</td>
<td>19 (7)°</td>
<td>17 (6)°</td>
<td>1 (-3, 6)°</td>
<td>0.48</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: KFA = knee flexion angle; HFA = hip flexion angle; SAP = strength, agility, and secondary prevention treatment group; SAP+PERT = SAP + perturbation training group.

5.4.2 Gait Asymmetries

There were no differences between SAP and SAP+PERT training regarding the elimination of gait asymmetries 1 or 2 years after ACLR, and gait asymmetries persisted to a large degree in both groups at both time points. The majority of both SAP and SAP+PERT athletes walked with meaningful interlimb asymmetries for sagittal plane hip and knee moments at pKFA, knee excursions during weight acceptance and midstance, and hip excursion during midstance at 1 year postoperatively, but these proportions did not differ between groups (Table 5.3a).
Likewise, the proportion of athletes who walked with clinically meaningful hip and knee angles, moments, and excursions did not differ at 2 years after ACLR (Table 5.3b).

Table 5.3a. This table displays the proportions of SAP and SAP+PERT athletes who walked with clinically meaningful interlimb asymmetries for sagittal plane hip and knee angles and moments at 1-year. Odds ratios (with 95% CI) represent the relative odds that clinically meaningful asymmetries existed in the SAP+PERT group compared to SAP group.

<table>
<thead>
<tr>
<th>Variable</th>
<th>SAP (N = 18)</th>
<th>SAP+PERT (N = 20)</th>
<th>Odds Ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HFA @ pKFA</td>
<td>5</td>
<td>9</td>
<td>2.1 (0.5, 8.3)</td>
<td>0.27</td>
</tr>
<tr>
<td>KFA @ pKFA</td>
<td>9</td>
<td>12</td>
<td>1.5 (0.4, 5.4)</td>
<td>0.54</td>
</tr>
<tr>
<td>HFM @ pKFA</td>
<td>13</td>
<td>13</td>
<td>0.7 (0.2, 2.8)</td>
<td>0.63</td>
</tr>
<tr>
<td>KFM @ pKFA</td>
<td>13</td>
<td>18</td>
<td>3.5 (0.6, 20.7)</td>
<td>0.16</td>
</tr>
<tr>
<td>Knee Excursion during WA</td>
<td>11</td>
<td>11</td>
<td>0.8 (0.2, 2.8)</td>
<td>0.70</td>
</tr>
<tr>
<td>Hip Excursion during WA</td>
<td>7</td>
<td>5</td>
<td>0.5 (0.1, 2.1)</td>
<td>0.36</td>
</tr>
<tr>
<td>Knee Excursion during MS</td>
<td>12</td>
<td>12</td>
<td>0.8 (0.2, 2.8)</td>
<td>0.67</td>
</tr>
<tr>
<td>Hip Excursion during MS</td>
<td>13</td>
<td>14</td>
<td>0.9 (0.2, 3.7)</td>
<td>0.88</td>
</tr>
</tbody>
</table>

Abbreviations: SAP = strength, agility, and secondary prevention treatment group; SAP+PERT = SAP + perturbation training group; HFA = hip flexion angle; pKFA = peak knee flexion angle; KFA = knee flexion angle; HFM = hip flexion moment; KFM = knee flexion moment; WA = weight acceptance (i.e., pKFA – initial contact); MS = midstance (i.e., peak knee extension angle – pKFA).
Table 5.3b. This table displays the proportions of SAP and SAP+PERT athletes who walked with clinically meaningful interlimb asymmetries for sagittal plane hip and knee angles and moments at 2-years. Odds ratios (with 95% CI) represent the relative odds that clinically meaningful asymmetries existed in the SAP+PERT group compared to SAP group.

<table>
<thead>
<tr>
<th>Table 5.3b Variable</th>
<th>SAP (N = 17)</th>
<th>SAP+PERT (N = 19)</th>
<th>Odds Ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HFA @ pKFA</td>
<td>7</td>
<td>4</td>
<td>0.4 (0.1, 1.7)</td>
<td>0.19</td>
</tr>
<tr>
<td>KFA @ pKFA</td>
<td>4</td>
<td>9</td>
<td>2.9 (0.7, 12.3)</td>
<td>0.14</td>
</tr>
<tr>
<td>HFM @ pKFA</td>
<td>8</td>
<td>9</td>
<td>1.0 (0.3, 3.8)</td>
<td>0.99</td>
</tr>
<tr>
<td>KFM @ pKFA</td>
<td>14</td>
<td>16</td>
<td>1.1 (0.2, 6.6)</td>
<td>0.88</td>
</tr>
<tr>
<td>Knee Excursion during WA</td>
<td>7</td>
<td>8</td>
<td>1.0 (0.3, 3.9)</td>
<td>0.96</td>
</tr>
<tr>
<td>Hip Excursion during WA</td>
<td>5</td>
<td>5</td>
<td>0.9 (0.2, 3.7)</td>
<td>0.84</td>
</tr>
<tr>
<td>Knee Excursion during MS</td>
<td>5</td>
<td>11</td>
<td>3.3 (0.8, 13.2)</td>
<td>0.09</td>
</tr>
<tr>
<td>Hip Excursion during MS</td>
<td>9</td>
<td>12</td>
<td>1.5 (0.4, 5.8)</td>
<td>0.54</td>
</tr>
</tbody>
</table>

Abbreviations: SAP = strength, agility, and secondary prevention treatment group; SAP+PERT = SAP + perturbation training group; HFA = hip flexion angle; pKFA = peak knee flexion angle; KFA = knee flexion angle; HFM = hip flexion moment; KFM = knee flexion moment; WA = weight acceptance (i.e., pKFA – initial contact); MS = midstance (i.e., peak knee extension angle – pKFA).

When comparing the interlimb difference in mean UN and INV limbs within each group, gait asymmetries existed in both SAP and SAP+PERT groups, but were more prevalent at 1 year versus 2 years postoperatively regardless of group (Table 5.4). Both groups walked with similar hip (Figure 5.2A-B) but smaller knee excursions (Figure 5.2C-D) during weight acceptance and clinically smaller hip (Figure 5.3A-B) and smaller knee (Figure 5.3C-D) excursions during midstance in the involved versus uninvolved limb. Post hoc t-tests revealed meaningful [79] interlimb mean differences at 1 year postoperatively for knee excursions during weight acceptance (SAP: UN 18° ± 3° versus INV 14° ± 4°, mean interlimb difference [95%...
CI]: 4° [1° to 7°], p = 0.004; SAP+PERT: UN 18° ± 3° versus INV 15° ± 4°, mean interlimb difference [95% CI]: 3° [1° to 5°], p = 0.007) and midstance (SAP: UN 19° ± 5° versus INV 15° ± 5°, mean interlimb difference [95% CI]: 4° [1° to 8°], p = 0.019; SAP+PERT: UN 21° ± 4° versus INV 16° ± 5°, mean interlimb difference [95% CI]: 5° [2° to 8°], p = 0.002). At 1 year postoperatively, SAP athletes walked with smaller hip excursion during midstance (SAP: UN 34° ± 6° versus INV 30° ± 6°, mean interlimb difference [95% CI]: 5° [0° to 9°], p = 0.031), whereas SAP+PERT athletes tended to walk with clinically smaller hip excursions during midstance (SAP+PERT: UN 34° ± 5° versus INV 31° ± 5°, mean interlimb difference [95% CI]: 3° [0° to 6], p = 0.065). At 2 years followup, hip and knee excursions were clinically asymmetrical for only the SAP group’s hip (UN 33° ± 6° versus INV 29° ± 5°; mean interlimb difference: 3°; 95% CI, 0° to 7°; p = 0.083) and the SAP+PERT group’s knee (UN 18° ± 4° versus INV 15° ± 4°; mean interlimb difference: 3°; 95% CI, 0° to 6°; p = 0.024) during midstance. Pooling across groups, athletes walked with smaller peak knee flexion angles in their involved versus uninvolved limbs; they also walked with smaller sagittal plane hip and knee moments in their involved versus uninvolved limbs at peak knee extension angle.
Table 5.4 Sagittal plane interlimb asymmetries (determined by the difference in the mean values of the uninvolved and involved limbs for each group) exceeding MCID values existed across both groups, as indicated by the check marks (√). Note the larger number of asymmetries that were present at 1 versus 2 years post-operatively.

<table>
<thead>
<tr>
<th>Table 5.4 Variable</th>
<th>One year</th>
<th></th>
<th>Two years</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SAP</td>
<td>SAP+PERT</td>
<td>SAP</td>
<td>SAP+PERT</td>
</tr>
<tr>
<td><strong>pFKA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hip flexion angle</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hip extension moment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Knee flexion angle</td>
<td></td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Knee extension moment</td>
<td></td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hip excursion: weight acceptance</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Knee excursion: weight acceptance</td>
<td>√</td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hip excursion: midstance</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td></td>
</tr>
<tr>
<td>Knee excursion: midstance</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
</tr>
</tbody>
</table>

MCID = minimal clinically important difference; SAP = strength, agility, and secondary prevention treatment group; SAP+PERT = SAP + perturbation training group; pKFA = peak knee flexion angle.
Figure 5.2A-D These figures display the mean sagittal plane hip (A-B) and knee (C-D) excursions during weight acceptance at 1 (A, C) and 2 (B, D) years postoperatively (whiskers are SDs). Both SAP and SAP+PERT athletes walked with meaningful smaller knee excursions during weight acceptance at 1 year postoperatively.
Figure 5.3A-D These figures display the mean sagittal plane hip (A-B) and knee (C-D) excursions during midstance at 1 (A, C) and 2 (B, D) years postoperatively (whiskers are SDs). Both SAP and SAP+PERT athletes walked with meaningful smaller hip and knee excursions during midstance at 1 year postoperatively; however, at 2 years, only SAP athletes walked with meaningfully smaller hip excursions and only SAP+PERT athletes walked with meaningfully smaller knee excursions when comparing differences in mean values.
5.5 Discussion

Movement asymmetries during walking are prevalent after ACL injury and reconstruction and may increase the risk of posttraumatic osteoarthritis (OA) early after ACLR\(^{40,318}\). Previous research has found that a specialized type of neuromuscular training (i.e., perturbation training) improves gait asymmetries and functional outcomes when applied to ACL-deficient patients\(^{53,75,79,98,129}\). However, movement asymmetries exist after ACLR even in individuals who had preoperative perturbation training and postoperative physical therapy\(^{75,129,253}\). Thus, additional training is likely needed to restore movement symmetry during gait. However, the effect of postoperative perturbation training on gait mechanics is previously unknown. Therefore, we conducted a randomized controlled trial to compare SAP with SAP+PERT training. We found no difference between SAP and SAP+PERT training on the gait mechanics or resolution of gait asymmetries in men after ACLR, and both groups walked with meaningful gait asymmetries 1 and 2 years postoperatively.

There are several limitations to consider when interpreting the results of our study. The primary limitation of this study is that we only included men in this analysis; thus, the effect of SAP and SAP+PERT training on the gait mechanics of women is unknown. We are currently recruiting our final female participants for this study and plan to analyze and report these outcomes once enrollment and testing are complete. We also did not include the pretraining and posttraining data from our male participants; thus, we do not know what their gait mechanics were before and immediately after SAP or SAP+PERT training, and the present study is unable to quantify the pre- to post changes or immediate effects of SAP versus SAP+PERT training on gait mechanics. We will analyze the pretraining and posttraining time points for both the men and women once all women have completed training.
Additionally, all participants were Level I/II (that is, jumping, cutting, and pivoting)70,134 athletes; thus, it is unknown whether our findings are applicable to less athletic populations. However, the majority of individuals who tear their ACL do so in Level I/II70,134 sports. Our findings also may not apply to individuals with severe concomitant injuries (e.g., large osteochondral defects, multiple ligament injury, previous ACL injury) given our exclusion criteria; by excluding these patients, however, we created a more homogenous cohort for randomization and analysis. We did not standardize surgical method (performed by 21 different surgeons); thus, we do not know what effect surgical technique may have had on our findings. However, because we randomized our subjects to treatment group, the findings should be more generalizable across surgical intervention. Finally, we did not analyze electromyographical data or use musculoskeletal modeling37,193 to estimate joint contact forces, which have implications for the development of OA158,318. Further analysis is warranted.

Our findings suggest that SAP+PERT training does not alter gait mechanics in men 1 or 2 years after ACLR compared with SAP training alone. Although the authors are unaware of any prior study investigating the effect of postoperative SAP versus SAP+PERT training on gait mechanics after ACLR, previous studies have investigated preoperative perturbation training on gait mechanics53,79,98,129,144. In these prior studies, changes in gait from pre- to post-intervention occurred; however, these changes were more prevalent among women, who, as compared with men and healthy control subjects, demonstrated a more impaired gait strategy (including smaller knee flexion angles75 and muscle activation imbalances144) before training53,79,129,144. In contrast to the changes seen among ACL-deficient women, ACL-deficient men
walked with similar gait patterns before and after preoperative perturbation training\textsuperscript{79}. Moreover, men who received preoperative strength training and physical therapy with or without perturbation training walked with stable and persistent truncated knee excursions pre- and post-intervention (before surgery) and 6 months after ACLR\textsuperscript{75}. Similarly, in another study by Risberg et al.\textsuperscript{252}, lower extremity biomechanics in ACL-injured patients were largely unchanged even after 20 rehabilitation sessions including neuromuscular and strength training: smaller knee excursions persisted in both walking and hopping, despite improvements in functional outcomes. Current rehabilitation programs may not be effective at changing gait, which is an automatic activity that may be resistant to change\textsuperscript{75,86,252}. Future work should investigate the pre-to post-intervention effects of SAP versus SAP+PERT training, these programs on the gait mechanics of women, and novel paradigms to improve gait mechanics after ACLR.

There were no differences between SAP and SAP+PERT groups regarding the elimination of gait asymmetries at 1 or 2 years postoperatively, and clinically meaningful asymmetries existed to a large degree in both groups at both time points. The presence of gait asymmetries among individuals after ACLR is consistent with previous work\textsuperscript{78,105,127,129,253,318,320}. Previous work has shown that limb asymmetries are prevalent in the short and medium term after ACLR\textsuperscript{78,105,127,129,253,318,320}, persist in both ACL-injured and ACL-reconstructed athletes despite rehabilitation programs including preoperative perturbation training\textsuperscript{75,79} and postoperative strengthening and neuromuscular rehabilitation\textsuperscript{252}, and may continue up to 2 years postoperatively\textsuperscript{253}. The present study corroborates these findings and underscores that limb asymmetries remain present 2 years postoperatively even among individuals who are well
rehabilitated after ACLR and have returned to sports\textsuperscript{19}. The present study adds to a growing body of rehabilitation paradigms that have not succeeded in restoring gait symmetry\textsuperscript{75,130,252}. Notably, gait asymmetries (including smaller INV versus UN limb knee flexion angles) persisted among patients after ACLR even when towing a sled or wearing a weighted vest\textsuperscript{130}. Interestingly, previous studies have typically evaluated gait mechanics in the short and medium term by comparing group means rather than the proportion of individuals who walk with clinically meaningful asymmetries, as was done in the present study. By comparing the proportions of individual athletes who walked asymmetrically (Tables 3A, 3B) with the presence of meaningful asymmetries in group means (Table 4), it is apparent that many athletes in both the SAP and SAP+PERT groups walked asymmetrically despite generally symmetric means when pooling limb data across groups. These findings suggest that meaningful asymmetries may be even more present than once thought, even among participants who were functioning at a high level. Further development of rehabilitation paradigms is likely necessary to restore gait symmetry after ACLR, but further investigation to identify an effective program is needed.

Our findings suggest that a postoperative strength, agility, and secondary prevention training program with or without perturbation training is not effective at ameliorating gait asymmetries in men 1 or 2 years after ACLR. Moreover, regardless of treatment group, meaningful interlimb asymmetries persisted during gait at both 1 and 2 years after ACLR. Interestingly, by comparing the proportion of athletes who walked with interlimb asymmetries as well as each group’s mean, our findings suggest that interlimb asymmetries may be even more ubiquitous when comparing individuals versus group means. Although impaired gait patterns may be more prevalent among
those with poorer functional and clinical performance\textsuperscript{2,78,103,318,320}, gait impairments may be present even in the absence of functional or clinical deficits\textsuperscript{141,320}. Therefore, although neither of the rehabilitation paradigms tested in the present study (SAP or SAP+PERT) restored gait symmetry or altered gait mechanics 1 or 2 years after ACLR, there may be other benefits to these programs. Previous work suggests neuromuscular training programs may be efficacious in improving functional performance and patient-reported outcomes\textsuperscript{50,201,214,252,307} and facilitating return to sport while lowering second injury risk\textsuperscript{77,138,322}. Future work should not only further investigate the functional, clinical, and biomechanical outcomes of SAP versus SAP+PERT training and compare them with outcomes of other programs and no additional training, but also explore new interventions to improve gait mechanics and ameliorate gait asymmetry in athletes after ACLR.

5.6 Funding and Acknowledgments

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Chapter 6

GAIT MECHANICS AND TIBIOFEMORAL LOADING IN MEN OF THE ACL-SPORTS RANDOMIZED CONTROL TRIAL

6.1 Abstract

The risk for post-traumatic osteoarthritis is elevated after anterior cruciate ligament reconstruction (ACLR), and may be especially high among individuals with aberrant walking mechanics, such as medial tibiofemoral joint underloading six months post-operatively. Rehabilitation training programs have been proposed as one strategy to address aberrant gait mechanics. We developed the anterior cruciate ligament specialized post-operative return-to-sports (ACL-SPORTS) randomized control trial to test the effect of 10 post-operative training sessions consisting of strength, agility, plyometric, and secondary prevention exercises (SAPP) or SAPP plus perturbation (SAPP+PERT) training on gait mechanics after ACLR. Forty male athletes (age 23 ± 7 years) after primary ACLR were randomized to SAPP or SAPP+PERT training and tested at three distinct, post-operative time points: 1) after impairment resolution (Pre-training); 2) following 10 training sessions (Post-training); and 3) two years after ACLR. Knee kinematic and kinetic variables as well as muscle and joint contact forces were calculated via inverse dynamics and a validated electromyography-informed musculoskeletal model. There were no significant improvements from Pre-training to Post-training in either intervention group. Smaller peak knee flexion angles, extension moments, extensor muscle forces, medial compartment contact forces, and tibiofemoral contact forces were present across group
and time, however the magnitude of interlimb differences were generally smaller and likely not meaningful two years post-operatively.

**Statement of Clinical Significance:** Neither SAPP nor SAPP+PERT training appears effective at altering gait mechanics in men in the short-term, however meaningful gait asymmetries mostly resolved between Post-training and two years after ACLR regardless of intervention group.

### 6.2 Introduction

Posttraumatic osteoarthritis (OA) is a major concern for individuals after anterior cruciate ligament (ACL) reconstruction (ACLR). OA prevalence after ACLR may approach or exceed 50%. One factor that may contribute to the development and progression of knee OA after ACLR is walking gait mechanics. Wellsandt and colleagues found smaller involved limb medial compartment tibiofemoral joint loading during gait six months after ACLR is associated with radiographic OA five years post-operatively. Recent findings from Pietrosimone et al. suggest lower involved limb peak vertical ground reaction forces and peak knee adduction moments during walking six months after ACLR are associated with biochemical markers (greater plasma matrix metalloproteinase-3) indicative of early joint degeneration. Gait mechanics two and five years after ACLR are also related to poorer long-term patient reported outcomes and a higher prevalence of radiographic OA, respectively. Restoring walking gait mechanics, therefore, may be a critical component of OA prevention in individuals after ACLR.

Gait mechanics after ACLR may be influenced by a number of different factors. Individuals with quadriceps muscle weakness after ACLR walk more asymmetrically, including smaller knee flexion angles and moments in their involved
limb, than both healthy controls and stronger ACL-reconstructed individuals. Quadriceps strength, however, does not fully explain knee gait asymmetries. Even individuals who restore quadriceps strength symmetry six months after ACLR still walk asymmetrically at that timepoint. Asymmetric hamstring strength is another factor that has been linked to more asymmetries during both walking and jogging two or more years after ACLR. In addition, performance on a battery of functional tests, including four single-legged hop tests, correlates to kinematic and kinetic symmetry variables during gait six months after ACLR. Taken together, these studies suggest that improving lower extremity strength, strength symmetry, and/or functional performance may improve knee symmetry during walking.

Developing interventions to address the aforementioned risk factors or to target directly the gait asymmetries themselves have been proposed. Rehabilitation programs incorporating strength and neuromuscular training programs have improved walking patterns and/or neuromuscular control strategies among individuals who are ACL-deficient (rather than ACL-reconstructed). Risberg and colleagues found improvements in knee extension moment during gait, but no changes in sagittal plane hip or knee excursions, among ACL-injured participants after 20 sessions of rehabilitation consisting of strength and neuromuscular training exercises. Hartigan and colleagues found that individuals who received pre-operative perturbation training (a specific type of neuromuscular training) plus strength training had more symmetrical knee excursions during gait compared to a group that received preoperative strength training alone. Chmielewski et al. found that perturbation training improved knee kinematics and reduced lower extremity muscle co-contraction among ACL-deficient participants. Perturbation training consists of a
series of physical therapist applied perturbations while the patient stands on an unstable surface (i.e., rollerboard or rockerboard). Patients are taught to resist these multi-directional perturbations through selective muscle activation\textsuperscript{96,98,129} rather than overpowering the movement or using a gross co-contraction strategy. Perturbation training aims to improve neuromuscular activation patterns and facilitate dynamic knee stability.\textsuperscript{53,79,98,129,144} Despite pre-operative perturbation training, gait impairments persist after ACLR\textsuperscript{105,253}, thus post-operative interventions including perturbation training may be necessary to improve gait after reconstructive surgery. We developed the anterior cruciate ligament specialized post-operative return-to-sports (ACL-SPORTS) randomized control trial to test whether or not post-operative strength training with and without the addition of perturbation training had an effect on functional measures, clinical outcomes, and walking gait mechanics.\textsuperscript{321}

Limited evidence exists on the effect of post-operative neuromuscular training after ACLR.\textsuperscript{19,46} Two recently published studies presented a portion of the primary outcomes in men of the ACL-SPORTS trial.\textsuperscript{19,46} We found no differences in these studies on clinical, functional or kinematic or kinetic gait variables among male athletes 1 and 2 years after primary ACLR who received 10 post-operative training sessions consisting of strength, agility, plyometric, and secondary prevention exercises (SAPP) or this SAPP training plus perturbation training (SAPP+PERT).\textsuperscript{19,46} These studies, however, did not examine the immediate before and after intervention effects of these two training paradigms on gait mechanics nor did they investigate at any time muscle forces or tibiofemoral joint loading, which is correlated to OA development.\textsuperscript{318} Given that perturbation training targets muscular activation patterns and, when delivered to ACL-injured individuals, reduces knee kinematic asymmetry and
inappropriate muscle co-contraction during gait, it is plausible that post-operative perturbation training could facilitate knee kinematic, kinetic, and muscle and joint contact force symmetry during gait. Evaluating medial tibiofemoral joint loading is of particular interest given the relationship between medial tibiofemoral joint loading six months to two years after ACLR and bone and cartilage health. The purpose of the present study, therefore, was to investigate tibiofemoral loading, muscle forces, and the immediate before and after intervention knee kinematics and kinetics during walking after ACLR in men of the ACL-SPORTS randomized control trial. We hypothesized that knee gait asymmetries would be present before training and improve in both groups after training. We also hypothesized that the SAPP+PERT group would demonstrate greater improvement in knee gait symmetry compared to the SAPP only group.

6.3 Methods

6.3.1 Participants

This study is a prospective, randomized control trial (level of evidence: 1). The study was performed at the University of Delaware between November 2011 and August 2016. The study was registered at clinicaltrials.gov (NCT01773317) and was approved by the University of Delaware Institutional Review Board. Informed consent was obtained from all participants as well as a parent or guardian when the participant was a minor.

Participants were eligible for enrollment if they were between 3 and 10 months after primary, unilateral ACLR and previously participated in level I or II sports (i.e., sports involving jumping, cutting, and pivoting) for at least 50 hours per year.
Participants were required to resolve all post-operative impairments, operationally defined as full and symmetric knee range of motion, minimal to no effusion, at least 80% quadriceps strength limb symmetry index, initiation of a running progression, and the ability to hop without pain on each leg. Individuals were excluded from participation if they had a previous ACLR or other severe lower extremity injury, concomitant grade III ligament (e.g., medial collateral ligament) injury, or an osteochondral defect of 1 cm² or larger. After patients completed enrollment paperwork and signed informed consents, a research administrator (MC) randomized participants to receive either SAPP or SAPP+PERT training (Figure 6.1). Participants were randomized to treatment group (SAPP vs. SAPP+PERT) using a random number generator and stratified by sex so that 20 men received SAPP training and 20 men received SAPP+PERT training. The research administrator performed scheduling only, and all physical therapist researchers who performed clinical, functional, and/or motion analysis testing were blinded to group assignment (single-blinded study). An a priori power analysis indicated that 36 men were needed to detect differences between groups in sagittal plane knee kinematics (primary outcome) based on previously established minimal clinically important differences (β = 0.20; α = 0.05, medium effect size = 0.30); we enrolled 40 participants to allow for 10% attrition.

6.3.2 Interventions

Details of the ACL-SPORTS randomized control trial have been described previously by White et al. and presented recently by Arundale et al. Briefly, all participants received 10 post-operative training sessions (approximately 2x/week) consisting of strengthening, agility, plyometric, and secondary prevention exercises (SAPP). The SAPP program included Nordic hamstrings, standing squats progressing...
to tuck jumps, drop jumps, and triple single leg hopping. Quadriceps strengthening was also performed in the clinic by participants who enrolled with a quadriceps strength index of between 80% and 90%; participants who enrolled with quadriceps strength index of 90% or greater were instructed to continue quadriceps strengthening on their own. The SAPP program also included agility drills (i.e., forward/backward running, side shuffles, cariocas, figure 8’s, circles, and 90° turns), which progressed by increasing the intensity gradually from 50% to 100% effort and incorporating sport-specific distractions, such as throwing or catching a ball. Participants in the SAPP training arm of the ACL-SPORTS randomized control trial received this training plus a sham intervention during which the athlete stood on one leg on a stable surface and performed hip flexion against a resistance band with the opposite limb. In contrast, participants in the SAPP+PERT intervention group received the same SAPP training plus 10 sessions of perturbation training. The perturbation training component lasted approximately 30 minutes per session and was delivered by a licensed physical therapist. The general progression (e.g., increasing the speed, magnitude, and/or variability of the perturbations, or adding distractions) was standardized across participants; however, rate of progression was based on participant response and distractions (e.g., ball toss/catch, kick, etc.) were tailored to each participant’s primary sport. Readers may refer to White et al. for the ACL-SPORTS trial protocol and to Chmielewski et al. for a more thorough description of perturbation training progression.

6.3.3 Motion Analysis Testing

Motion analysis testing during over ground walking occurred at three distinct, post-operative time points: 1) after impairment resolution (Pre-training); 2) following
10 training sessions (Post-training); and 3) two years post-operatively (2 years). Prior to motion capture, we first prepared for surface electromyography (EMG) electrode placement by shaving and abrading the skin with alcohol-soaked gauze to improve conductance. We then placed surface EMG electrodes (MA-300 EMG System, Motion Lab Systems, Baton Rouge, LA) on seven lower extremity muscles per limb crossing the knee joint, including the medial and lateral gastrocnemii, vasti, and hamstrings as well as the rectus femoris. We next recorded EMG during maximal volitional contractions, as described previously.\textsuperscript{45} We normalized EMG to maximal volitional isometric contractions or dynamic contractions, whichever was highest. EMG data during both normalization procedures and walking trials were collected at 1080 Hz. EMG data were high-pass filtered at 30 Hz using a 2\textsuperscript{nd} order Butterworth filter, rectified, and low-pass filtered at 6 Hz to create a linear envelope. We then affixed 39 retroreflective markers to the bilateral lower extremities and pelvis in accordance with previous work.\textsuperscript{76}

Participants walked at a self-selected gait speed maintained to within ± 5% both throughout and across all testing sessions. We collected kinematic data during gait at 120 Hz using an eight camera motion analysis system (VICON, Oxford, UK). We collected kinetic data at 1080 Hz using an embedded force platform (Bertec Corporation, Columbus, OH). We used commercial software (Visual3D, C-Motion, Germantown, MD) to calculate kinematic and kinetic variables via inverse dynamics. Kinematic and kinetic variables of interest included: peak knee flexion angle (pKFA), peak internal knee extension moment, peak knee adduction angle, and peak internal knee abduction moment. Moments were normalized by mass*height (kg*m) to allow comparisons across participants.\textsuperscript{207}
6.3.4 EMG-Driven Musculoskeletal Modeling

Walking data were also analyzed using an EMG-driven musculoskeletal modeling approach.\textsuperscript{37,101,193} This previously validated\textsuperscript{193} model uses a Hill-type muscle fiber in series with an elastic tendon, and applies an iterative, simulated annealing process to best fit a forward dynamics knee flexion moment curve to the same moment curve derived through inverse dynamics, as described above. The forward dynamics knee flexion curve is varied by allowing several muscle parameters and coefficients to vary within ± 2 standard deviations of physiological norms. This simulated annealing process is designed to minimize the root mean square error between the forward and inverse dynamics knee flexion moment curves. The process was completed for 5 walking trials per limb for each participant, at each time point. Next, each trial was predicted using the derived muscle parameters and coefficients. Three trials per limb per participant were selected by maximizing the R\textsuperscript{2} values and minimizing the root mean square error of the predicted trials. Individual muscle forces were calculated for each of the three predicted trials. Medial and lateral tibiofemoral joint contact forces were estimated using the Winby frontal plane moment algorithm.\textsuperscript{328} The total tibiofemoral joint contact force was estimated as the sum of the individual compartment contact forces. Modeling derived variables of interest included combined knee extensor (i.e., quadriceps) muscle forces at pKFA, knee flexor (i.e., combined hamstrings and gastrocnemii) muscle forces at pKFA, first peak medial tibiofemoral compartment contact force, lateral tibiofemoral compartment contact force at pKFA, and first peak total tibiofemoral contact force. Tibiofemoral joint contact forces were constrained to the first half (0-50\%) of stance due to previous work finding loading parameters during this portion of the gait cycle to be associated with knee joint
degeneration and OA development after ACLR. Muscle and joint contact forces were normalized by body weight (BW) to allow comparison across participants.

6.3.5 Statistical Analysis

A repeated measures linear mixed effects model was used to compare the effects of intervention (SAPP versus SAPP+PERT training), limb, and time for all biomechanical gait variables of interest. Three time points (Pre-training, Post-training, and 2 years) were analyzed for muscle and joint contact forces while only two time points (Pre-training and Post-training) were analyzed for kinematic and kinetic variables because we previously published one and two year outcomes for kinematic and kinetic variables (no meaningful differences between groups). Tests for significant main effects and interactions were conducted using an F-test with the Kenward-Roger approximation for the degrees of freedom to account for unbalanced groups over time due to subjects with partially observed data (Figure 6.1). Post-hoc comparisons were made for statistically significant effects (α = 0.05); Bonferroni corrections were made to account for multiple comparisons. (Post hoc p-values with Bonferroni correction were also compared to α = 0.05.) Chi-Square tests of proportions and t-tests were used to compare demographic characteristics between experimental groups (α = 0.05). Statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC), Microsoft Excel (Redmond, WA), and SPSS version 24.0 (IBM Corporation, Armonk, New York, USA).
Figure 6.1 The flow chart provides reasons for missing data at each testing session.
6.4 Results

Groups were similar for all relevant demographic and clinical variables and gait speed (Table 6.1).

Table 6.1 Demographic characteristics were similar between the SAPP and SAPP+PERT groups.

<table>
<thead>
<tr>
<th>Demographic Variable</th>
<th>SAPP Group</th>
<th>SAPP+PERT Group</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>23.5 ± 8.7</td>
<td>23.1 ± 5.8</td>
<td>.859</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.79 ± 0.07</td>
<td>1.78 ± 0.06</td>
<td>.505</td>
</tr>
<tr>
<td>Mass (kg)</td>
<td>85.3 ± 12.9</td>
<td>86.3 ± 10.0</td>
<td>.791</td>
</tr>
<tr>
<td>Body Mass Index (kg/m²)</td>
<td>26.5 ± 1.8</td>
<td>27.3 ± 2.5</td>
<td>.372</td>
</tr>
<tr>
<td>Graft Type</td>
<td>6 allograft, 5 BPTB, 9 hamstring</td>
<td>7 allograft, 3 BPTB, 10 hamstring</td>
<td>.730</td>
</tr>
<tr>
<td>Time from Surgery to Pre-training (months)</td>
<td>5.2 ± 1.8</td>
<td>5.1 ± 1.6</td>
<td>.848</td>
</tr>
<tr>
<td>Gait Speed (m/s)</td>
<td>1.54 ± 0.12</td>
<td>1.58 ± 0.11</td>
<td>.328</td>
</tr>
</tbody>
</table>

Abbreviations: SAPP: strength, agility, and secondary prevention; SAPP+PERT: strength, agility, secondary prevention plus perturbation training; allograft: soft-tissue allograft; hamstring: hamstring autograft; BPTB: bone patellar-tendon bone autograft

6.4.1 Kinematics and Kinetic Variables

There was a main effect of limb for peak knee flexion angle ($F_{1,64.1} = 10.14, p = 0.0022$; Figure 6.2). Participants walked using smaller peak knee flexion angles in the involved ($19.5 ± 5.1°$) compared to uninvolved ($22.9 ± 4.9°$) limb, regardless of group or time. The mean interlimb difference (3.5° less in the involved limb [discrepancy due to rounding]) exceeded both minimal detectable change (MDC)$^{104}$ and minimal clinically important difference (MCID)$^{79}$ values of 2.9° and 3°,
respectively. There were no detectable main effects of group or time or any interaction effects for peak knee flexion angle.

There was also a main effect of limb for peak knee extension moment ($F_{1,71.1} = 14.22, p = 0.0003$; **Figure 6.3**). Participants walked using smaller peak knee extension moments in the involved ($0.40 \pm 0.13 \text{ N}\cdot\text{m/kg}\cdot\text{m}$) compared to uninvolved ($0.50 \pm 0.13 \text{ N}\cdot\text{m/kg}\cdot\text{m}$) limb, regardless of group or time. The mean interlimb difference ($0.10 \text{ N}\cdot\text{m/kg}\cdot\text{m}$ less in the involved limb) exceeded both MDC$^{104}$ and MCID$^{79}$

![Figure 6.2 Participants walked with smaller peak knee flexion angles in the involved versus uninvolved limb regardless of group or time. There were no significant effects of group or time or any interaction effects.](image-url)
values. There were no detectable main effects of group or time or any interaction effects for peak knee extension moment.

![Peak Knee Extension Moment](image)

Figure 6.3 Participants walked using smaller peak knee extension moments in the involved compared to uninvolved limb. There were no detectable main effects of group or time or any interaction effects for peak knee extension moment.

There were no statistically significant effects for peak knee adduction angle or peak knee abduction moment. Moreover, none of the interlimb difference values for either peak knee adduction angle or abduction moment met or exceeded MDC values\textsuperscript{104}, suggesting that any observed differences were smaller than could be reasonably detected.
6.4.2 Muscle Forces

A significant main effect of limb ($F_{1,71.7} = 10.50$, $p = 0.0018$) and a significant 3-way (limb by group by time) interaction effect ($F_{4,44.8} = 3.35$, $p = 0.0175$) were present for knee extensor muscle forces at pKFA (Figure 6.4). Collapsing across group and time, participants walked with smaller knee extensor muscle forces in the involved ($2.17 \pm 0.55$ BW) compared to the uninvolved limb ($2.53 \pm 0.58$ BW). When analyzing each group more closely, however, changes occurred differently over time. At Pre-training, participants in the SAPP group walked with relatively symmetric knee extensor muscle forces ($p = 0.2977$, Bonferroni adjusted $p = 1.0$), whereas participants in the SAPP+PERT group tended to walk with smaller involved versus uninvolved limb knee extensor muscle forces at Pre-training ($p = 0.0147$, Bonferroni adjusted $p > 0.05$). At Post-training, participants in both groups walked with asymmetrically smaller involved versus uninvolved limb knee extensor muscle forces, although only the interlimb difference for the SAPP+PERT group was statistically significant after adjusting for multiple comparisons (SAPP: $p = 0.0118$, Bonferroni adjusted $p > 0.05$; SAPP+PERT: $p = 0.0003$, Bonferroni adjusted $p = 0.0231$). By 2 years, both groups walked with knee extensor muscles forces at pFKA that were not different across limbs or between groups. There were no statistically significant main effects of group or time for knee extensor muscle forces at pKFA, nor were there any two-way interaction effects detected for knee extensor muscle forces at pKFA.

There were no statistically significant differences in knee flexor muscle forces at pKFA.
Figure 6.4 Knee extensor muscle forces at peak knee flexion angle (pKFA) were smaller in the involved versus uninvolved limb at Post-training, but became relatively symmetric in both the SAPP and SAPP+PERT groups two years post-operatively. (After adjusting for multiple comparisons, only the difference between involved and uninvolved limb in the SAPP+PERT group at Post-training was statistically significant.)

6.4.3 Joint Contact Forces

There was a group by time interaction effect for peak medial compartment contact force (pMCCF: F_{2,62} = 7.76, p = 0.0010; Figure 6.5). Irrespective of limb, the SAPP group walked with lower pMCCF at Post-training (2.71 ± 0.50 BW) versus 2 years (3.03 ± 0.53 BW, Bonferroni adjusted p-value = 0.0066), while there was no detectable difference for pMCCF across time in the SAPP+PERT group. There was also a main effect of limb (F_{1,70.8} = 5.88, p = 0.0179) with lower pMCCF in the
involved (2.66 ± 0.50 BW) versus uninvolved (2.89 ± 0.49 BW) limb across group and time. This interlimb difference (0.23 BW less in the involved limb), however, was smaller than the MDC of 0.30 BW\textsuperscript{104}. Only the interlimb differences at Pre-training and Post-training in the SAPP+PERT group exceeded the MDC of 0.30 BW\textsuperscript{104}. However, the involved and uninvolved limb values at Pre-training and Post-training were similar within each intervention group (i.e., the changes between Pre-training and Post-training were similar for SAPP and SAPP+PERT), suggesting that neither SAPP nor SAPP+PERT training altered medial compartment contact force in the short term. There were no other significant main effects or interaction effects for pMCCF.

Figure 6.5 Peak medial compartment contact force increased from Pre-training and Post-training to two years post-operatively in the SAPP group only. A main effect of limb was also present, with smaller values in the involved versus uninvolved limb. Only the interlimb differences at Pre-training and Post-training in the SAPP+PERT group exceeded the MDC of 0.30 BW\textsuperscript{104}.
There was a main effect of limb ($F_{1,72.8} = 8.56, p = 0.0046$; Figure 6.6) for peak tibiofemoral joint contact force with smaller values in the involved ($3.98 \pm 0.69$ BW) compared to the uninvolved ($4.36 \pm 0.69$ BW) limb. This interlimb difference (0.38 BW less in the involved limb), however, was smaller than the MDC of 0.66 BW$^{104}$. There were no other statistically significant main effects or interaction effects for peak tibiofemoral joint contact force.

There were also no statistically significant effects for lateral compartment contact force at pKFA.

Figure 6.6 Peak tibiofemoral joint contact force was smaller in the involved versus uninvolved limb, regardless of group of time; however, the differences did not exceed the MDC of 0.66 BW$^{104}$. 

![Peak Tibiofemoral Contact Force](chart.png)
6.5 Discussion

The purpose of this study was to investigate the effect of strength, agility, plyometric, and secondary prevention (SAPP) training versus SAPP plus perturbation (SAPP+PERT) training on knee kinematic, kinetic, muscle force, and joint contact loading variables during gait in the men of the ACL-SPORTS randomized control trial. Specifically, we aimed to test the hypotheses that knee symmetry during gait would improve over time in both groups and that the SAPP+PERT intervention group would demonstrate greater improvement compared to the SAPP only group. Neither hypothesis was supported, with the exception of improved knee extensor muscle force symmetry at 2 years, but not at Post-training. The lack of change from Pre-training to Post-training across gait variables and treatment groups suggests neither SAPP nor SAPP+PERT training alters gait mechanics in the short term.

Interlimb asymmetries were present in several variables, including peak knee flexion angle, peak knee extension moment, knee extensor muscle forces at pKFA, peak medial compartment contact force, and peak tibiofemoral joint contact force. Only some of these interlimb differences, however, were likely clinically meaningful. Collapsing across group and time, interlimb differences in peak knee flexion angle and extension moments exceeded previously established MDC$^{104}$ and MCID$^{79}$ values, indicating smaller involved limb peak knee flexion angles and extension moments at both Pre-training and Post-training. This finding was not surprising given that sagittal plane kinematic and kinetic asymmetries persisted in this cohort at one year and, to a lesser degree, even two years after ACLR$^{46}$. Knee extensor muscle forces were more variable over time: smaller involved limb knee extensor muscle forces were present in both groups at Post-training, but became approximately symmetric in both groups by 2 years. To the authors’ knowledge, no MCID values exist for knee extensor muscle
forces. Pooling across group and time, interlimb differences for peak tibiofemoral joint contact force and medial compartment contact force were smaller than MDC values thus may not be meaningful clinically, but merit further discussion.

Knee loading variables were relatively symmetric in both intervention groups by two years post-operatively, which suggests favorable long-term outcomes. Interestingly, only the SAPP+PERT group walked with peak medial compartment contact force underloading at earlier time points. Underloading during this time-frame (5-7 months after ACLR) may place individuals at higher risk of radiographic knee OA 5 years post-operatively. It is unlikely that the SAPP+PERT training influenced or altered this risk, however, because underloading in the SAPP+PERT group occurred at both Pre-training and Post-training and was consistent across these two early time points. The SAPP group demonstrated more symmetrical loading at Pre-training, but also did not change significantly from Pre-training to Post-training, suggesting that neither SAPP nor SAPP+PERT training altered medial compartment tibiofemoral loading symmetry in the short-term. It is unclear, however, why the SAPP group increased medial compartment loading from Pre-training and Post-training to 2 years. Ongoing, long-term radiographic follow-up is needed to evaluate the implications of these findings as well as the effect of SAPP and SAPP+PERT training on knee joint health. Future studies may also investigate the effect of increasing joint loading on knee health, as the directionality of the relationship between joint unloading and knee degeneration after ACLR is not well established.

Frontal plane gait asymmetries were not detected in the present study, and did not change following intervention. Previous studies have reported conflicting evidence
regarding the presence and even direction of interlimb asymmetry in frontal plane gait mechanics after ACLR, although this may be due to not controlling for concomitant meniscal treatment. Therefore, it is presently unclear if, or which, participants after ACLR need interventions to address frontal plane mechanics.

Nevertheless, neither SAPP nor SAPP+PERT training appears to alter gait kinematics or kinetics in the frontal plane, at least among male athletes who, as a group, walked similarly between limbs in these variables prior to training.

Our null findings are not overly surprising. A recent systematic review and meta-analysis by Kaur et al. found that it may take an average of six years after ACLR to restore joint kinematics during gait. The failure of the ACL-SPORTS training program to restore symmetry in every knee gait biomechanical variable assessed following training, at only seven months after primary ACLR, may be unremarkable in light of the findings from Kaur and colleagues. Other post-operative rehabilitation interventions also have been unsuccessful at improving gait biomechanics in various populations. For example, Eitzen et al. found a 12-week supervised exercises therapy program did not change frontal or sagittal plane hip, knee, or ankle kinematics or kinetics in patients with hip osteoarthritis. Previous studies investigating strength and perturbation training on gait mechanics in ACL-deficient participants have found a greater response in women compared to men, who walked with similar patterns before and after training. Women may respond differently to the ACL-SPORTS training program and further investigation is needed.

One potential explanation for why the ACL-SPORTS training was largely ineffective at improving gait mechanics in male athletes is that participants were required to meet stringent inclusion criteria, including 80% quadriceps strength index,
prior to enrollment. If the study included athletes earlier after ACLR or allowed participation among athletes with significant quadriceps strength deficits (i.e., < 80% quadriceps strength index), larger interlimb gait asymmetries would likely have been present at enrollment (Pre-training). If larger asymmetries had been present initially, there would have been greater room for improvement and perhaps there would have been response to intervention. More likely, however, changing something we do continuously throughout the day like walking in late stages of rehabilitation will require more direct intervention or continuous rather than intermittent interventions.

Bioinspired technologies present exciting possibilities for future gait retraining interventions. Shull and colleagues used haptic biofeedback to train individuals with medial compartment knee OA to walk with a toe-in gait, reducing the first peak knee adduction moment. These reductions corresponded to improved symptoms and function and were maintained at one-month follow-up. Pizzolato and colleagues recently provided real-time visual biofeedback of medial tibiofemoral loading to five healthy participants; interestingly, all five participants were able to increase medial tibiofemoral loading both with and without suggestions but only three were able to decrease medial tibiofemoral loading and required suggestions in order to do so. Individualized suggestions were more effective gait retraining strategies among these participants and in 20 healthy individuals receiving vibrotactile biofeedback. Future work should investigate direct, individualized training paradigms and continuous surveillance and/or biofeedback using wearable sensors and other remote technology in individuals after ACLR.

There are several limitations to consider when interpreting the results of this study. First, we analyzed men only, thus the effect of SAPP versus SAPP+PERT
training on the gait mechanics of women is unknown. Second, we did not control for surgical factors such as surgeon or graft type, which may make our findings more generalizable, although individualized training paradigms could be considered in future studies.\textsuperscript{245,305} Third, joint contact and muscle forces were estimated rather than measured directly. The musculoskeletal modeling approach used in this study, however, has been previously validated\textsuperscript{37,193} and was applied consistently across all participants. Finally, the implications of SAPP and SAPP+PERT training on long-term knee joint health are unknown. Further investigation, including ongoing long-term radiographic follow-up and the effect of SAPP and SAPP+PERT training on gait mechanics in women, is warranted.

In conclusion, neither SAPP nor SAPP+PERT training appear effective at improving gait mechanics in male athletes in the short term. The addition of post-operative perturbation training also does not appear to alter gait mechanics, including model estimations of muscle forces and joint loading, in men after ACLR. Further analysis of the effect of ACL-SPORTS trial and other rehabilitation and gait retraining programs on gait biomechanics and long-term knee health is warranted.
6.6 Funding and Acknowledgments

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Chapter 7

GAIT MECHANICS IN WOMEN OF THE ACL-SPORTS RANDOMIZED CONTROL TRIAL: INTERLIMB SYMMETRY IMPROVES OVER TIME REGARDLESS OF TREATMENT GROUP

7.1 Abstract

Women after anterior cruciate ligament (ACL) injury and ACL reconstruction (ACLR) are more likely than men to exhibit asymmetric movement patterns, which are associated with post-traumatic osteoarthritis. We developed the ACL specialized post-operative return-to-sports (ACL-SPORTS) randomized control trial to test the effect of strength, agility, plyometric, and secondary prevention (SAPP) training with and without perturbation training (SAPP+PERT) on gait mechanics in women after ACLR. We hypothesized that movement symmetry would improve over time across both groups but more so among the SAPP+PERT group. Thirty-nine female athletes 3-9 months after primary ACLR were randomized to SAPP or SAPP+PERT training. Biomechanical testing during overground walking occurred before (Pre-training) and after (Post-training) training and one and two years post-operatively. Hip and knee kinematic and kinetic variables were compared using repeated measures ANOVA with Bonferroni corrections for post-hoc comparisons (α=0.05). There was a time by limb interaction effect (p=.028) for peak knee flexion angle (PKFA), the primary outcome which powered the study, characterized by smaller PKFA in the involved compared to uninvolved limbs across treatment groups at Pre-training, Post-training, and one year, but not two years. Similar findings occurred across sagittal plane knee excursions and
kinetics and hip extension excursion at midstance. There were no meaningful interactions involving group. Neither SAPP nor SAPP+PERT training improved walking mechanics, which persisted one but not two years after ACLR.

**Statement of Clinical Significance:** Asymmetrical movement patterns persisted long after participants achieved symmetrical strength and functional performance, suggesting more time is needed to recover fully after ACLR.

### 7.2 Introduction

Anterior cruciate ligament (ACL) injuries and ACL reconstruction (ACLR) surgeries are occurring at increasing rates, especially among young people who engage in high-level sporting activities. Young women continue to sustain ACL injuries at higher rates than young men when participating in the same sport. Women also are more likely than men to exhibit aberrant and asymmetric lower extremity movement patterns both before and after ACL injury. Aberrant and asymmetric movements may not only play a role in primary ACL injury risk, but also influence the development and progression of post-traumatic osteoarthritis. While movement asymmetries may persist years after ACLR, little is known about the effect of post-operative rehabilitation programs on movement patterns, particularly in women, after ACL.

We developed the anterior cruciate ligament specialized post-operative return-to-sports (ACL-SPORTS) randomized control trial to determine the effect of post-operative return-to-sport (RTS) rehabilitation on gait mechanics in both male and female athletes. Specifically, this randomized control trial was designed to test the effect of strength, agility, plyometric, and secondary prevention (SAPP) training with and without perturbation training (SAPP+PERT), a specific type of neuromuscular
training. The scientific premise for this study was based on evidence that rehabilitation programs incorporating both strength and neuromuscular (perturbation) training have improved movement patterns among individuals after ACL injury,\(^5\),144,252 and that the effect of post-operative rehabilitation and neuromuscular training on movement patterns was unknown.\(^321\) We recently reported our findings from the men of the ACL-SPORTS trial (as recruitment occurred more quickly among the men).\(^43\),46 Our findings suggest that, among men, there is no difference in response to SAPP versus SAPP+PERT training on walking mechanics; movement asymmetries persisted to some degree at both one and two years after ACLR, but were generally no longer clinically meaningful at two years.\(^43\),46

While the effect of post-operative rehabilitation and RTS training with or without neuromuscular training on the movement patterns of female athletes is unknown, women may respond differently than men for several reasons. Women who are ACL-deficient have shown greater improvements in movement patterns in response to strength and neuromuscular training.\(^75\),76,79,144 Women are also more likely than men to exhibit aberrant and asymmetric movement patterns after ACL injury;\(^25\),101,102,154,316 women may therefore demonstrate greater baseline movement asymmetry and thus have more room for improvement. Given that women, but not men, walk with greater movement asymmetry 6 months after ACLR compared to pre-operatively,\(^75\) differences between men and women may be exacerbated early after ACLR. Finally, our recent findings from the ACL-SPORTS cohort suggest women may take longer than men to regain quadriceps strength after ACLR,\(^18\) which could influence their walking mechanics.\(^180\)
We therefore sought to investigate knee and hip kinematics (angles and excursions) and kinetics as well as medial compartment tibiofemoral loading during walking before and after post-operative training as well as 1 and 2 years after ACLR among the women of the ACL-SPORTS randomized control trial. Our a priori hypothesis was that the women who received SAPP+PERT training, compared to SAPP alone, would exhibit greater improvements in movement symmetry (i.e., more symmetrical sagittal plane knee kinematics, the primary outcome on which the study was powered). We also hypothesized that, regardless of treatment group, movement symmetry would improve over time, especially between 1 and 2 years after ACLR, coincident with return to sport.

7.3 Methods

7.3.1 Participants

This study is a prospective, randomized control trial (level of evidence: 1), which was registered at clinicaltrials.gov (NCT01773317) and was approved by the University of Delaware Institutional Review Board. The study was performed at the University of Delaware between December 2011 and August 2018. Written informed consent was obtained from all participants; minors provided assent in addition to consent from their parent/guardian.

Female athletes after primary, unilateral ACLR were eligible for enrollment when they achieved impairment resolution, defined as full and symmetric knee range of motion, minimal to no effusion, at least 80% quadriceps strength limb symmetry index, initiation of a running progression, and the ability to hop without pain on each leg. All participants were required to meet the following inclusion/exclusion criteria:
at least 12 weeks and less than 10 months after primary, unilateral ACLR; previous participant in level I or II sports (i.e., sports involving jumping, cutting, and pivoting) for at least 50 hours per year; no history of previous ACLR or other severe lower extremity injury or surgery; no concomitant grade III knee ligament (e.g., medial collateral ligament) injury; and no osteochondral defect of 1 cm² or larger.

Participants were randomized using a random number generator and stratified by sex so that 20 women each were allocated to the SAPP and SAPP+PERT treatment groups (Figure 7.1). Randomization was performed by a research administrator (MC). All physical therapist researchers who performed data collections were blinded to group assignment (single-blinded study). Our a priori power analysis indicated that 36 women were needed to detect differences between groups in sagittal plane knee kinematics (primary outcome) based on the established minimal clinically important difference (β = 0.20; α = 0.05, medium effect size = 0.30); we enrolled 40 female athletes to allow for 10% attrition. After training, the researchers were informed that one participant may have sustained a graft rupture prior to enrollment, thus she was excluded from this study (and all analyses).
Figure 7.1 The flow chart depicts the enrollment process and testing sessions.

### 7.3.2 Interventions

We encourage readers to consult the ACL-SPORTS protocol paper, published previously by White et al.,\(^3\) as well as a recent publication by Arundale et al.,\(^1\) for additional details about the present study. We will present the general aspects of the study here only briefly. After enrollment, all participants first underwent clinical testing and motion analysis testing (described below) prior to receiving any interventions. Subsequently, participants received 10 sessions (~2x/week) of either SAPP or SAPP+PERT training. All participants in both groups received the same...
general elements of the SAPP training program, consisting of Nordic hamstrings, standing squats progressing to tuck jumps, drop jumps, triple single leg hopping, and agility drills. All participants in both groups with quadriceps strength indexes below 90% also performed quadriceps strengthening exercises in the physical therapy clinic whereas those with quadriceps strength indexes of 90% or greater continued quadriceps strengthening on their own (outside the clinic). Participants in the SAPP only group of the ACL-SPORTS randomized control trial also received a sham intervention during which the athlete stood on one leg on a stable surface and performed hip flexion against a resistance band with the opposite limb. Participants in the SAPP+PERT treatment group did not receive the sham intervention but instead received the SAPP training described above plus 10 sessions of perturbation training (~30 minutes per session). Perturbation training is a specific type of neuromuscular training designed to improve neuromuscular activation patterns and facilitate dynamic knee stability. During perturbation training, the patient stood on an unstable surface (i.e., rollerboard or rockerboard) while the physical therapist applied movements, or perturbations, to the surface. Perturbations began in a blocked manner with small movements and were progressed by increasing the speed, magnitude, direction (e.g., adding diagonals or rotations), and manner in which the perturbations were delivered (e.g., blocked progressing to random; verbal cues progressing to no verbal cues). Sport-specific distractions, such as throwing, catching, or passing a ball, were added during the later sessions. While the interventions, principles, and general progression were standardized, physical therapists were allowed clinical judgment to determine the optimal rate of progression for each individual athlete and appropriate selection of sport-specific distractions. Additional
details on perturbation training are available in the ACL-SPORTS protocol paper\textsuperscript{321} and from Chmielewski et al.\textsuperscript{53}

7.3.3 Biomechanical Testing and Variables of Interest

Biomechanical testing occurred during over-ground walking at four post-operative time points: 1) after impairment resolution and before receiving any interventions (Pre-training); 2) following 10 training sessions (Post-training); 3) one year post-operatively (1 year); and 4) two years post-operatively (2 years).

Biomechanical testing included bilateral surface electromyography (EMG) collected at 1080 Hz; electrode placement was immediately preceded by shaving and abrading the skin with alcohol-soaked gauze to improve electrode conductance. Electrodes (MA-300 EMG System, Motion Lab Systems, Baton Rouge, LA) were placed on seven lower extremity muscles crossing the knee joint on each limb: the rectus femoris, medial and lateral vasti, medial and lateral hamstrings, and medial and lateral gastrocnemius. Maximal volitional isometric contractions were performed for each muscle group\textsuperscript{45} and used for EMG normalization. EMG data were high-pass filtered at 30 Hz using a 2\textsuperscript{nd} order Butterworth filter, rectified, and low-pass filtered at 6 Hz to create a linear envelope. After placing the EMG electrodes and performing maximal volitional isometric contractions, we placed 39 retroreflective markers on the lower extremities and pelvis as previously described.\textsuperscript{76}

Participants walked across our motion analysis laboratory over an embedded force platform (Bertec Corporation, Columbus, OH) at a self-selected gait speed maintained within $\pm$ 5\% during and across all testing sessions. Kinematic data were captured at 120 Hz using an eight camera motion analysis system (VICON, Oxford, UK) whereas kinetic data were captured at 1080 Hz. We used commercial software
(Visual3D, C-Motion, Germantown, MD) to calculate kinematic and kinetic variables via inverse dynamics. All data were normalized to 100% of stance to allow temporal comparison of data across subjects. Kinetic variables were normalized by mass*height (kg*m) to allow comparisons across participants. Biomechanical variables of interest included sagittal plane hip and knee kinematics and sagittal and frontal plane hip and knee kinetics. We compared key biomechanical variables at peak knee flexion angle (PKFA). We also calculated sagittal plane hip and knee excursions during the weight acceptance and midstance phases of gait. Weight acceptance was defined as initial contact to PKFA; midstance was defined as PKFA to peak knee extension angle.

We also used a previously validated subject specific, EMG-driven musculoskeletal modeling approach to estimate medial compartment tibiofemoral joint contact forces. Described previously in detail, our model uses a hill-type muscle fiber in series with an elastic tendon. The model employs an iterative, simulated annealing process to allow muscle parameters to vary within physiological norms (± 2 standard deviations) to best fit the knee flexion moment curve derived through these EMG-derived estimations to the knee flexion moment curve derived through inverse dynamics. We performed this process for 5 walking trials per limb for each participant, at Pre-training, Post-training, and 2 years. Next, we predicted each trial (for a given limb, at a given timepoint) using the derived muscle parameters and coefficients from the other four trials. We subsequently selected the three best-fitting (highest R² and lowest root mean square) predicted trials, using the same predicted values, for each limb at each timepoint. We used the Winby frontal plane moment algorithm to estimate the medial tibiofemoral joint contact force.
Peak medial compartment contact force (PMCCF), constrained to the first 50% of stance and normalized by body weight to allow comparison across participants, was our modeling-derived variable of interest given the association between PMCCF and early knee osteoarthritis after ACLR.

7.3.4 Statistical Analysis

We used independent t-tests and chi-square tests of proportions to compare demographic characteristics between groups. We used repeated measures, mixed model analysis of variance (ANOVA) to compare all biomechanical variables of interest. Post-hoc comparisons with Bonferroni corrections for multiple comparisons were made for significant interactions or main effects of time. Differences were also compared to previously established minimum clinically important difference (MCID) values to determine whether or not statistically significantly difference values were clinically meaningful. All P values less than 0.05 were established a priori as statistically significant. Statistical analyses were performed using SPSS version 25.0 (IBM Corporation, Armonk, New York, USA).

7.4 Results

There were no differences between treatment groups for demographic characteristics, clinical variables, or gait speed among all participants (Table 7.1a). There were likewise no differences in demographics, clinical variables, or gait speed among only those 35 participants who completed biomechanical testing at all timepoints (Table 7.1b) and were used in our primary statistical analyses. There were also no statistically significant differences between the 4 participants who missed one (n=3) or two (n=1) follow-up testing sessions compared to the 35 who completed all
biomechanical testing sessions (all p > 0.05). Not every subject had data that could be modeled for reasons such as incomplete or suboptimal EMG or poor model tuning. In addition to the 4 subjects lost to follow-up as described above and depicted in Figure 1, there were 6 subjects at Pre-training, 7 subjects at Post-training, and 6 subjects at 2 years that had data that could not be modeled. There were a total of 23 (12 SAPP, 11 SAPP+PERT) women with complete modeling data at all timepoints of interest (i.e., Pre-training, Post-training, and 2 years). There were no differences in demographics of these 23 participants with complete modeling data and the remaining 16 participants with incomplete modeling data.
Table 7.1a-b Demographic characteristics did not differ between the SAPP and SAPP+PERT groups among all participants (Table 7.1a) or among only those who completed testing at all timepoints (Table 7.1b).

<table>
<thead>
<tr>
<th>Table 7.1a. Variable</th>
<th>SAPP (n=20)</th>
<th>SAPP+PERT (n=19)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at Surgery (years)</td>
<td>18.9 (5.8)</td>
<td>19.0 (8.8)</td>
<td>0.986</td>
</tr>
<tr>
<td>Gait Speed (m/s)</td>
<td>1.5 (.1)</td>
<td>1.5 (.1)</td>
<td>0.410</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.65 (.06)</td>
<td>1.65 (.08)</td>
<td>0.986</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>68.8 (10.9)</td>
<td>67.9 (14.3)</td>
<td>0.82</td>
</tr>
<tr>
<td>Body Mass Index (kg/m^2)</td>
<td>25.3 (3.3)</td>
<td>24.7 (3.9)</td>
<td>0.631</td>
</tr>
<tr>
<td>Pre-Injury Sport Level</td>
<td>19 Level I, 1 Level II</td>
<td>15 Level I, 4 Level II</td>
<td>0.182</td>
</tr>
<tr>
<td>Pre-Injury Competition Level</td>
<td>9 School Sponsored, 7 Club Level, 4 Intramural/Recreation</td>
<td>10 School Sponsored, 7 Club Level, 2 Intramural/Recreation</td>
<td>0.707</td>
</tr>
<tr>
<td>Mechanism of Injury</td>
<td>6 Contact, 14 Non-contact</td>
<td>5 Contact, 14 Non-contact</td>
<td>0.798</td>
</tr>
<tr>
<td>Graft Type</td>
<td>8 Hamstring, 8 BPTB, 4 Allograft</td>
<td>10 Hamstring, 8 BPTB, 1 Allograft</td>
<td>0.368</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 7.1b. Variable</th>
<th>SAPP (n=17)</th>
<th>SAPP+PERT (n=18)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at Surgery (years)</td>
<td>19.2 (6.2)</td>
<td>19.0 (9.1)</td>
<td>0.933</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.65 (.07)</td>
<td>1.65 (.08)</td>
<td>0.945</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>69.6 (11.7)</td>
<td>67.4 (14.5)</td>
<td>0.631</td>
</tr>
<tr>
<td>Body Mass Index (kg/m^2)</td>
<td>25.4 (3.5)</td>
<td>24.6 (4.0)</td>
<td>0.539</td>
</tr>
<tr>
<td>Gait Speed (m/s)</td>
<td>1.5 (.1)</td>
<td>1.5 (.1)</td>
<td>0.310</td>
</tr>
<tr>
<td>Pre-Injury Sport Level</td>
<td>16 Level I, 1 Level II</td>
<td>14 Level I, 4 Level II</td>
<td>0.338</td>
</tr>
<tr>
<td>Pre-Injury Competition Level</td>
<td>8 School Sponsored, 6 Club Level, 3 Intramural/Recreation</td>
<td>9 School Sponsored, 7 Club Level, 2 Intramural/Recreation</td>
<td>0.858</td>
</tr>
<tr>
<td>Mechanism of Injury</td>
<td>5 Contact, 12 Non-contact</td>
<td>4 Contact, 14 Non-contact</td>
<td>0.711</td>
</tr>
<tr>
<td>Graft Type</td>
<td>5 Hamstring, 8 BPTB, 4 Allograft</td>
<td>9 Hamstring, 8 BPTB, 1 Allograft</td>
<td>0.233</td>
</tr>
</tbody>
</table>
7.4.1 Results for Hypothesis 1: SAPP vs. SAPP+PERT Training Effect

There were no interaction or main effects involving treatment group for the primary outcome variable, peak knee flexion angle (PKFA, Figure 7.2). There were no significant 3-way interactions and no group by limb interaction effects for any variable of interest; there were, however, two significant group by time interaction effects and two main effects of group (Table 7.2). There was a group by time interaction effect for hip extension excursion during weight acceptance (Figure 7.3), however the only statistically significant post-hoc comparison was between Post-training and 2 years in the SAPP+PERT group and this difference of 1.4° was well below the MCID of 3.0°79. There were no statistically different (p ≥ .311) or clinically meaningful differences between groups at any timepoint for hip extension excursion during weight acceptance (group differences were all less than 1.1°). There was also a significant group by time interaction effect for hip extension moment at PKFA (Figure 7.4). Within the SAPP group only, there were smaller hip extension moments (collapsed across limb) at 2 years compared to any of the earlier timepoints (post-hoc Bonferroni p < .05), but no differences among any of the earlier timepoints (i.e., Pre-training, Post-training, and 1 year). There were no differences over time in the SAPP+PERT group and no differences between groups at any timepoint. While there were no interaction effects for hip abduction moment at PKFA, there were main effects of group and limb (Figure 7.5), characterized by larger values in the SAPP+PERT versus SAPP group as well as in the involved compared to uninvolved limb, regardless of time. There was also a main effect of group for internal knee extensor moment at PKFA, characterized by larger moments in the SAPP+PERT versus SAPP group collapsed across limb and time (Figure 7.6); the interaction effect of time by limb for internal knee extensor moment is described below.
Figure 7.2 There were no interaction or main effects of group for peak knee flexion angle (PKFA), the primary study outcome. There was an interaction effect of time by limb for PKFA as well as a main effect of limb for PKFA. Clinically meaningful differences were present across both groups at both Pre-training and Post-training, but not at one or two years after ACLR (bar = exceeds MCID). (Note: due to rounding, the interlimb difference in the SAPP+PERT group is 3.1° at pre-training, which exceeds the MCID of 3.0°\textsuperscript{79}, whereas the interlimb difference at one year is only 2.9°.)
Figure 7.3 There was a significant group by limb interaction effect of hip extension excursion during weight acceptance; however, no differences were clinically meaningful. (Brackets indicate the statistically significant difference between the Post-training and 2 year timepoint within the SAPP+PERT group, collapsed across limbs.)
Figure 7.4 There was a significant time by group interaction effect ($p = .022$) for hip internal extension moment at peak knee flexion angle (PKFA), characterized by smaller values at 2 years compared to any earlier timepoints in the SAPP group only (bracket denotes difference).
Figure 7.5 While there were no interaction effects for hip internal abduction moment at peak knee flexion angle (PKFA), there were main effects of group and limb, characterized by larger values in the involved compared to uninvolved limb as well as in the SAPP+PERT versus SAPP group (indicated by large bracket), regardless of time.
Figure 7.6 There was an interaction effect of time by limb for knee internal extension moment at peak knee flexion angle (PKFA), characterized by large early interlimb asymmetry that resolved across groups by two years after ACLR. Interlimb differences exceeded MCID values across both groups at Pre- and Post-training, but only in the SAPP+PERT group at one year (bar = exceeds MCID$^{79}$). There was also a main effect of group with higher knee extension moments across time and limb in the SAPP+PERT group compared to the SAPP group (indicated by the large bracket).

### 7.4.2 Results for Hypothesis 2: Effect of Time

There were time by limb interaction effects characterized by early interlimb asymmetry that resolved by 2 years for six variables of interest: peak knee flexion angle, knee flexion excursion during weight acceptance, knee extension excursion during midstance, hip extension excursion during midstance, knee internal extension moment at PKFA, and peak medial compartment contact force (Table 7.2). For peak knee flexion angle (Figure 7.2), the primary study outcome, post-hoc comparisons
with Bonferroni adjustment revealed that there were statistically significant
differences between limbs (collapsing across groups) at Pre-training, Post-training,
and 1 year (p ≤ 0.002), but not at 2 years (p = 0.161). Regardless of group, participants
walked with clinically meaningful smaller knee flexion angles in the involved
compared to uninvolved limb at Pre- and Post-training, but not at 1 or 2 years after
ACLR. There were supportive findings for sagittal plane knee moments (Figure 7.6)
and excursions during weight acceptance (Figure 7.7) and midstance (Figure 7.8).
Likewise, there was an interaction of time by limb for hip extension excursion during
midstance (Figure 7.9); post-hoc comparisons for hip extension excursion during
midstance revealed statistically significant and clinically meaningful differences
between limbs at Pre-training and Post-training (p < .001) but not at 1 year (p = .097)
or 2 years (p = .304). There was a time by limb interaction effect for peak medial
compartment contact force (Figure 7.10); while only the difference between limbs at
Post-training was statistically significant (p = .026), the minimal detectable change of
0.30 body weight (BW)\textsuperscript{104} and meaningful inter-limb difference of 0.4 BW\textsuperscript{158} were not
exceeded at Post-training (interlimb difference: - 0.27) or any other timepoint.
Figure 7.7 There was an interaction effect of time by limb for knee flexion excursion during weight acceptance, characterized by early interlimb asymmetry that resolved by one year after ACLR. Only the interlimb differences at Pre-training for the SAPP group and at Post-training for the SAPP+PERT group were clinically important (bar = exceeds MCID$^{79}$).
Figure 7.8 There was an interaction effect of time by limb for knee extension excursion during midstance, characterized by early interlimb asymmetry that resolved across groups by two years after ACLR. Interlimb differences exceeded MCID values across both groups at Pre- and Post-training, but only in the SAPP+PERT group at one year (bar = exceeds MCID).
Figure 7.9 There was an interaction effect of time by limb for hip extension excursion during midstance; clinically meaningful differences between limbs occurred across groups at both Pre-training and Post-training, but not at 1 or 2 years (bar = exceeds MCID79).

<table>
<thead>
<tr>
<th></th>
<th>Pre-Training</th>
<th>Post-Training</th>
<th>One Year</th>
<th>Two Years</th>
<th>Pre-Training</th>
<th>Post-Training</th>
<th>One Year</th>
<th>Two Years</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SAPP (n = 17)</strong></td>
<td>27.9</td>
<td>27.2</td>
<td>28.6</td>
<td>27.6</td>
<td>29.3</td>
<td>29.7</td>
<td>30.4</td>
<td>29.6</td>
</tr>
<tr>
<td><strong>SAPP+PERT (n = 18)</strong></td>
<td>32.2</td>
<td>30.9</td>
<td>30.0</td>
<td>27.7</td>
<td>33.4</td>
<td>33.1</td>
<td>32.1</td>
<td>31.0</td>
</tr>
</tbody>
</table>

Figure 9. Hip Extension Excursion During Midstance
Figure 7.10 There was a time by limb interaction for peak medial compartment contact force. While the difference between limbs at Post-training was statistically significant (p = .026), the difference (- 0.27) did not exceed the meaningful inter-limb difference threshold of 0.4 body weight (BW)\textsuperscript{158} at Post-training or any other timepoint.
Table 7.2 This table presents all p values for main effects, two-way interaction effects, and 3-way interaction effects for all biomechanical variables of interest. Values less than p = 0.05 are statistically significant, as denoted by an asterisk (*). (Abbreviation: PKFA = peak knee flexion angle.)

<table>
<thead>
<tr>
<th>Variable</th>
<th>P-Values</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Time</td>
</tr>
<tr>
<td>Peak Knee Flexion Angle</td>
<td>0.753</td>
</tr>
<tr>
<td>Knee Flexion Excursion--Weight Acceptance</td>
<td>0.023*</td>
</tr>
<tr>
<td>Knee Extension Excursion--Midstance</td>
<td>0.234</td>
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<tr>
<td>Hip Flexion Angle @PKFA</td>
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<tr>
<td>Hip Extension Excursion--Weight Acceptance</td>
<td>0.139</td>
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<td>Hip Extension Excursion--Midstance</td>
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<td>Knee Extension Moment @PKFA</td>
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<tr>
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<tr>
<td>Peak Medial Compartment Contact Force</td>
<td>0.587</td>
</tr>
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</table>
7.5 Discussion

The purpose of this study was to compare knee and hip kinematics and kinetics as well as medial compartment tibiofemoral loading during walking before and after post-operative return-to-sport training with and without perturbation as well as 1 and 2 years after ACLR among the women of the ACL-SPORTS randomized control trial. Our *a priori* hypothesis, that the women who received SAPP+PERT training, compared to SAPP alone, would exhibit greater improvements in movement symmetry, was not supported. Our second hypothesis, that movement symmetry would improve over time regardless of treatment group, was largely supported, particularly among knee sagittal plane kinematics and kinetics. Participants walked with generally symmetric gait patterns by 2 years after ACLR, but not at earlier timepoints. Our findings suggest that meaningful movement asymmetries persist during gait even after participants achieve symmetrical strength, have high functional performance, and return to sports,18 supporting the notion that more time is needed to recover after ACLR3,121 and/or task-specific training is needed to restore movement symmetry.244,245

Mounting evidence suggests recovery from ACLR does not take four to six months, as once thought, but may require one to two years or longer.3,121 Our findings support and supplement the belief that recovery takes longer, even after participants meet stringent objective criteria.4,321 The participants in the present study had resolved all impairments prior to enrollment and had a mean of 91% quadriceps strength index before training,18 yet still walked with clinically meaningful79 interlimb sagittal knee asymmetry before and after training. Movement asymmetries were not resolved globally until 2 years after ACLR, long after most participants had achieved
symmetrical strength and functional performance and returned to sports.\textsuperscript{18} These findings indicate that time and the physical challenge accompanying return to sports may be important considerations for restoring movement asymmetry, although targeted interventions may expedite this process.\textsuperscript{244,245} Future research studies examining real-time visual, auditory, and/or tactile feedback to correct aberrant movement patterns are warranted.

A few recent studies have linked early post-traumatic osteoarthritis after ACLR to aberrant walking mechanics,\textsuperscript{158,242,263,318} notably underloading of the involved limb\textsuperscript{242} and especially the medial compartment of the tibiofemoral joint.\textsuperscript{263,318} In the present study, there was a shift toward medial tibiofemoral compartment underloading of the involved versus uninvolved limb at Post-training (7 ± 2 months after ACLR) that was not present at Pre-training (6 ± 2 months after ACLR) or 2 years after ACLR. The shift in walking mechanics was accomplished through both decreased peak medial compartment contact force (PMCCF) in the involved limb and increased PMCCF in the uninvolved limb at Post-training relative to both Pre-training and 2 years. Similar findings of medial compartment underloading at Post-training also occurred among the men of the ACL-SPORTS trial\textsuperscript{43} and correspond to a potentially important change in activity patterns that occur as athletes begin to return to their sports. The early phases of rehabilitation are focused almost exclusively on the involved, surgical limb,\textsuperscript{4} but during the 10 post-operative return-to-sport training sessions, participants begin doing higher level activities on both limbs for the first time after surgery. During this return-to-sport training, participants may develop movement strategies that rely more heavily on the uninvolved limb,\textsuperscript{43,130,264,318} favoring the involved limb due to lingering deficits or lack of confidence.\textsuperscript{339}
To the study’s merit, we executed a randomized control trial with blinded assessors, minimal loss to follow-up, and comprehensive and rigorous testing at multiple timepoints using a repeated measures design. We included patients with ACLR surgeries using different graft types and performed by different surgeons, which makes our sample more heterogeneous and reflective of a clinical population but also possibly introduced variability. We did not control rehabilitation prior to enrollment in the study, but all participants met the same, rigorous enrollment criteria.\textsuperscript{4,21} Limitations include lack of pre-injury and pre-operative data. We included all female participants with complete biomechanical data in our analyses, including those women who sustained a second ACL injury. Secondary analyses excluding those with second injuries resulted in similar findings as in our primary, planned analyses. The interventions were not task-specific, thus may not be optimally designed to change movement patterns during gait,\textsuperscript{244,245} but had been shown to improve gait and neuromuscular control strategies when delivered pre-operatively.\textsuperscript{53,129,144} While the present study included only women and thus the findings may not apply to men given biomechanical differences according to sex,\textsuperscript{25,101,102,126,154,316} we previously reported similar findings in the men of the ACL-SPORTS trial,\textsuperscript{43,46} indicating that neither SAPP nor SAPP+PERT training improved gait mechanics in men or women after ACLR.

In conclusion, our findings suggest that strength, agility, plyometric, and secondary prevention (SAPP) training with and without perturbation training do not meaningfully improve walking mechanics among young female athletes.
Asymmetrical gait mechanics persist to a large degree until two years after ACLR, long after patients have achieved symmetrical strength and functional performance and have returned to sports. Our findings contribute to growing evidence suggesting full recovery after ACLR may take longer than previously thought, up to two years after ACLR.

### 7.6 Funding and Acknowledgments

Funding was provided by the Eunice Kennedy Shriver National Institute of Child Health and Human Development and National Institute of General Medical Sciences: R01-AR048212, F30-HD096830, R01-HD087459, and U54-GM104941. JJC received funding from the University of Delaware: University Doctoral Fellowship Award and University of Dissertation Fellowship Award. JJC’s work was supported in part by Promotion of Doctoral Studies (PODS) – Level I and Level II Scholarships from the Foundation for Physical Therapy. Thank you to the National Institutes of Health (NIH); Martha Callahan and the Delaware Rehabilitation Institute Research Core; Angela H. Smith and the University of Delaware Physical Therapy Clinic; and Kathleen Cummer, Amelia J. H. Arundale, P. Michael Eckrich, and Georgia Gagianas for their assistance with data collection and processing.

Chapter 8

SLOWER WALKING SPEED AND ABERRANT GAIT MECHANICS ARE ASSOCIATED WITH EARLY PATELLOFEMORAL OSTEOARTHRITIS AFTER ACL RECONSTRUCTION

8.1 Abstract

Post-traumatic patellofemoral osteoarthritis is prevalent after anterior cruciate ligament reconstruction (ACLR) and early degenerative changes may be especially common in the femoral trochlear cartilage. Determining the presence of and factors associated with early femoral trochlear cartilage degradation is a critical preliminary step in identifying those at risk for patellofemoral osteoarthritis development and designing interventions to combat the disease. Early cartilage degradation can be detected using quantitative magnetic resonance imaging (QMRI) measures, such as tissue T2 relaxation time. The purpose of this study was to 1) compare involved (ACLR) versus uninvolved (contralateral) femoral trochlear cartilage T2 relaxation times 6 months after ACLR, and 2) determine the relationship between walking mechanics 3 months after ACLR and femoral trochlear cartilage T2 relaxation times 6 months after ACLR. Thirty-five individuals after primary, unilateral ACLR participated in detailed motion analyses 3 months after ACLR and quantitative magnetic resonance imaging 6 months after ACLR. Femoral trochlear cartilage T2 relaxation times were numerically higher (worse) in the involved limb, but not statistically different than the uninvolved limb. Slower walking speed was the strongest predictor of higher (worse) femoral trochlear cartilage T2 relaxation time.
(Pearson r: -.612, p<.001). Smaller knee extension excursion (r: -.341, p=.045), knee flexion excursion (r: -.291, p=.090), and quadriceps muscle forces (r: -.245, p=.185) were also negatively associated with trochlear T2 values. This exploratory analysis indicates walking speed and gait mechanics are early predictors of post-traumatic patellofemoral osteoarthritis. **Statement of Clinical Significance:** Walking speed was by far the strongest predictor of trochlear cartilage health, suggesting slow walking speed may be an early clinical indicator of future patellofemoral osteoarthritis after ACLR.

### 8.2 Introduction

Post-traumatic patellofemoral osteoarthritis (OA) exists in at least one-third of individuals 10 years after anterior cruciate ligament reconstruction (ACLR). While many have assessed the tibiofemoral compartments for preliminary manifestations of OA development after ACLR, more recent reports suggest that early signs of OA may be more common in the patellofemoral joint compared to the lateral or medial tibiofemoral compartments. Moreover, features of patellofemoral OA, but not tibiofemoral OA, one year after ACLR predict symptoms and quality of life two years later. Identifying potentially modifiable factors related to early patellofemoral OA pathogenesis is a critical early step to develop targeted interventions and rehabilitation strategies to combat this disease.

One potentially modifiable factor that may be related to post-traumatic OA development is aberrant walking mechanics. Most studies investigating the association between walking mechanics and post-traumatic OA, however, have examined the tibiofemoral joint, rather than the patellofemoral joint. These studies have found that unloading the tibiofemoral joint, especially its medial
compartment, early after ACLR is associated with future tibiofemoral OA.\textsuperscript{242,263,266,318} One study by Culvenor et al. found that those with established, radiographic patellofemoral OA approximately nine years after ACLR walked with altered mechanics at that time.\textsuperscript{69} The altered walking mechanics may have been a result of the patellofemoral OA, rather than its cause. Among those with idiopathic patellofemoral OA and no history of ACLR, Teng et al. found that sagittal plane knee kinematics were correlated to patellofemoral joint degeneration as measured using quantitative magnetic resonance imaging (MRI) measures (i.e., $T_{1\text{rho}}$ and $T_2$ relaxation times) in both the patellar and femoral trochlear cartilage.\textsuperscript{296} Investigations performed early after ACLR using highly sensitive measures that are precursors to symptomatic or radiographic OA are needed to determine the relationship between walking mechanics early after ACLR and post-traumatic patellofemoral OA development and progression.

One highly sensitive precursor to established radiographic or clinical OA is cartilage $T_2$ relaxation time. Cartilage $T_2$ relaxation time mapping is a quantitative MRI measure that is an early indicator of semi-quantitative OA features and radiographic OA.\textsuperscript{26,27,83,296} Higher $T_2$ relaxation times indicate higher water content and greater disorganization in cartilage,\textsuperscript{296} representing cartilage pathology and early signs of joint degeneration. Cartilage $T_2$ relaxation times may detect early post-traumatic degenerative changes at a time-frame when patients are still in rehabilitation and are perhaps more amenable to change. While there are several articular cartilage regions that may be analyzed within the knee (e.g., weight-bearing femur and tibia, patella, femoral trochlea, etc.), early degenerative changes (i.e., bone marrow lesions, cartilage lesions, and osteophytes) may be most common in the femoral trochlear cartilage,\textsuperscript{64} and cartilage thinning in the femoral trochlea is common after ACLR.\textsuperscript{99}
Reduced sagittal plane knee kinematics and kinetics during walking are pervasive after ACLR and likely influence the direction and magnitude of the forces exerted on the patellofemoral cartilage during walking. Knee flexion angles and quadriceps muscle forces are correlated positively to patellofemoral joint contact force, influencing patellofemoral cartilage homeostasis, health or degeneration. Key biomechanical variables of interest include sagittal plane knee kinematics (peak knee flexion angle and knee flexion and extension excursions), sagittal plane knee kinetics (peak knee flexion moment), and quadriceps muscle forces. Walking speed, the “sixth vital sign,” is an important indicator of function that influences walking mechanics and also merits consideration as a key predictor of cartilage health.

The purpose of this study was to explore early patellofemoral OA development after ACLR by investigating the relationship between walking mechanics 3 months after ACLR and femoral trochlear cartilage T2 relaxation times 6 months after ACLR. Specifically, the study aimed to 1) compare femoral trochlear cartilage T2 relaxation times between the involved (ACLR) and uninvolved (contralateral) limb 6 months after primary, unilateral ACLR; 2) determine the relationship between (2a) walking speed and involved limb sagittal plane knee kinematics and kinetics and quadriceps muscle forces during gait 3 months after ACLR and (2b) the involved limb femoral trochlear cartilage T2 relaxation times 6 months after ACLR; and 3) determine the relationship between (3a) the interlimb differences (ILDs = involved minus uninvolved limb) in sagittal plane knee kinematics and kinetics and quadriceps muscle forces during gait 3 months after ACLR and (3b) interlimb differences in femoral trochlear T2 relaxation times 6 months after ACLR. We hypothesized that 1) trochlear T2 relaxation times would be higher (worse) in the involved limb compared to the
uninvolved limb, 2) slower walking speeds and smaller involved limb knee excursions, moments, and muscle forces would be associated with higher (worse) trochlear T2 relaxation times in the involved limb, and 3) interlimb differences in gait mechanics would be negatively associated with interlimb differences in trochlear T2 relaxation times (i.e., those with smaller involved vs. uninvolved limb gait mechanics would have higher [worse] involved vs. uninvolved limb trochlear T2 relaxation times).

8.3 Methods

8.3.1 Participants

Thirty-five participants (Table 8.1) from an ongoing, prospective cohort study (R01-HD087459) were included in this study. Participants were included only if they completed motion analysis (biomechanical) testing 3 months after ACLR and quantitative MRI acquisitions 6 months after ACLR. Participants also met the following inclusion/exclusion criteria: age 16-45 years, primary ACLR with no prior history of ACL injury or surgery to either knee, no other serious leg surgery, no concomitant grade III knee ligament sprains, no repairable meniscus injury, and no contraindications for MRI (i.e., metallic implants or components, extreme claustrophobia, pacemaker, metal in the body, aneurysm clip, or ear or eye implants).

The study was performed between June 2016 and April 2019 at the University of Delaware, which granted Institutional Review Board approval. All participants provided written informed consent; parental consent and minor assent were provided for all individuals under age 18 years at enrollment.
Table 8.1 Demographic characteristics of the participants (n = 35).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean ± Standard Deviation (SD) or Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>23 ± 7 years</td>
</tr>
<tr>
<td>Sex</td>
<td>13 women (37.1%), 22 men (62.9%)</td>
</tr>
<tr>
<td>Height</td>
<td>1.73 ± 0.09 meters</td>
</tr>
<tr>
<td>Weight</td>
<td>80 ± 14 kilograms</td>
</tr>
<tr>
<td>Graft Type</td>
<td>7 (20.0%) soft-tissue allograft, 17 (48.6%) bone-patellar tendon-bone autograft, 8 (22.9%) hamstring autograft, 3 (8.6%) other/unknown</td>
</tr>
<tr>
<td>Walking speed</td>
<td>1.57 ± .16 meters/second</td>
</tr>
</tbody>
</table>

8.3.2 Walking Mechanics

All participants completed motion analysis testing during over-ground walking approximately 3 months after ACLR. Prior to walking, electromyography (EMG) electrodes (MA-300 EMG System, Motion Lab Systems, Baton Rouge, LA) were placed on 7 muscles per lower extremity after shaving, cleaning, and abrading the skin. Participants completed maximal volitional isometric contractions (MVICs) for each muscle group (gastrocnemii, hamstrings, and quadriceps), and the highest physiological values were used for EMG normalization. EMG data were collected at 1080 Hz; EMG post-processing included a high-pass, 2nd order Butterworth filter at 30 Hz, rectification, and a low-pass filter at 6 Hz to create a linear envelope. Following EMG placement and MVICs, 39 retroreflective markers were placed on the bilateral lower extremities and pelvis. Participants then walked over an embedded force platform (Bertec Corporation, Columbus, OH) in the motion analysis laboratory while kinetics (1080 Hz) and kinematics (120 Hz) were captured using an eight camera motion analysis system (VICON, Oxford, UK). Participants walked at a self-selected speed; once participants walked at a consistent speed (typically within 5 practice
trials), only walking trials with speeds that were within ± 5% were used in the analyses.

Commercial software (Visual3D, C-Motion, Germantown, MD) was used to calculate kinematic and kinetic variables. A validated, EMG-driven, patient-specific musculoskeletal model, described previously in detail, was used to estimate quadriceps muscle forces during gait. Biomechanical data were normalized to the stance phase of gait for each participant and averaged across 3 trials per limb. Kinetic variables were normalized by mass*height (kg*m) and quadriceps muscle forces were normalized by body weight (BW).

Biomechanical variables of interest included walking speed, peak knee flexion angle (PKFA) and moment, knee flexion excursion during weight acceptance (i.e., the loading response phase of gait from initial contact to PKFA, approximately 0-25% of stance), knee extension excursion during the midstance phase of gait (occurring from PKFA to peak knee extension angle), and peak quadriceps muscle forces during gait (constrained to the first 50% of stance phase).

8.3.3 Trochlear T2 Relaxation Times

All participants also underwent supine bilateral knee imaging using a 3 Tesla, Siemens MRI scanner (Washington, D.C.) 6 months after ACLR. A 2-dimensional sagittal T2 mapping sequence using one of two sets of parameters (that were the same between limbs for each participant) was used. The scan parameters for the first nine participants were: field of view = 160 mm, slice thickness = 2 mm, repetition time (TR) = 4480 ms, and echo time (TE) = 12.5, 25, 37.5, 50, 62.5, and 75 ms. The scans parameters for the remaining 26 participants were: field of view = 150 mm, slice thickness = 3 mm, TR = 3090 ms, and TE = 10, 20, 30, 40, 50, 60, and 70 ms. The
scan parameters were changed due to an update in the software used for the MRI scanner.

T$_2$ relaxation maps were calculated using mono-exponential fitting on a pixel-by-pixel basis (3DSlicer, National Institutes of Health [NIH])\textsuperscript{1,92} after registering each knee to the individual’s uninvolved knee.\textsuperscript{344} The first echo was skipped to reduce stimulated echo artifacts.\textsuperscript{27} The entire trochlear cartilage for each knee (involved and uninvolved) of every participant was manually segmented at 3mm increments by one reader (LD). The trochlea was subdivided into medial and lateral regions of interest, with the medial trochlea defined as the deepest aspect of the trochlear sulcus and all cartilage medial to it; the lateral trochlear cartilage consisted of all trochlear cartilage lateral to the sulcus. Mean T$_2$ relaxation time values for the total, medial, and lateral trochlea were calculated using a volume-based mean. We established excellent intra-rater reliability for the total (Intraclass correlation coefficient [ICC] = .97), medial (ICC = .96), and lateral (ICC = .97) trochlear T$_2$ relaxation times.

### 8.3.4 Statistical Analyses

Paired sample t-tests were used to compare trochlear cartilage T$_2$ relaxation times (total, medial, and lateral) between the involved and uninvolved limbs of each participant. Simple linear regression was used to determine the relationship between each biomechanical predictor variable and the total trochlear T$_2$ relaxation time. Alpha was set at 0.05 for all analyses. Due to the exploratory nature of the study, no statistical adjustments were made for multiple comparisons. Statistical analyses were performed using Microsoft Excel (Redmond, WA) and SPSS version 25.0 (IBM Corporation, Armonk, New York, USA).
8.4 Results

8.4.1 Results for Hypothesis 1: Trochlear Cartilage $T_2$ Relaxation Times in the Involved vs. Uninvolved Limb

There were no differences between the involved limb and the uninvolved limb for the total, medial, or lateral femoral trochlear $T_2$ relaxation times (Table 8.2).

Table 8.2 There were no between limb differences in total, medial, or lateral trochlear $T_2$ relaxation times. (Note: Due to the volumetric-based means, the total $T_2$ relaxation time does not necessarily equal the arithmetic mean of the medial and lateral trochlear cartilage $T_2$ relaxation times.)

<table>
<thead>
<tr>
<th>Measure</th>
<th>Involved</th>
<th>Uninvolved</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Trochlear $T_2$ Relaxation Time (ms)</td>
<td>49.1 ± 3.7</td>
<td>49.0 ± 3.8</td>
<td>.897</td>
</tr>
<tr>
<td>Medial Trochlear $T_2$ Relaxation Time (ms)</td>
<td>49.1 ± 4.1</td>
<td>48.6 ± 4.7</td>
<td>.556</td>
</tr>
<tr>
<td>Lateral Trochlear $T_2$ Relaxation Time (ms)</td>
<td>49.3 ± 4.1</td>
<td>49.0 ± 4.6</td>
<td>.817</td>
</tr>
</tbody>
</table>

8.4.2 Results for Hypothesis 2: Gait Mechanics and Trochlear Cartilage $T_2$ Relaxation Times in the Involved Limb

Slower walking speed was the strongest predictor of higher (worse) femoral cartilage $T_2$ relaxation time (Figure 8.1, $p < 0.001$). Smaller knee extension excursion during midstance was also associated with higher (worse) femoral cartilage $T_2$ relaxation time (Figure 8.2, $p = 0.045$). Knee flexion excursion during weight acceptance (Figure 8.3, $p = 0.090$) and quadriceps muscle forces (Figure 8.4, $p = 0.185$) were also negatively associated with femoral cartilage $T_2$ relaxation time but did not reach statistical significance. Peak knee flexion angle (Pearson $r = -0.069$, $R^2 = 0.005$, $p = 0.694$) and peak knee flexion moment (Pearson $r = -0.102$, $R^2 = 0.01$, $p = 0.561$) were very weakly associated with femoral cartilage $T_2$ relaxation time in the same direction as the other variables of interest.
Figure 8.1. Faster self-selected walking speed at 3 months predicted healthier involved femoral trochlear cartilage (lower trochlear cartilage T2 relaxation times) 6 months after ACLR.

\[ y = -14.59x + 71.93 \]
\[ R^2 = 0.375 \]

Figure 8.2. Greater knee extension excursion at 3 months predicted healthier femoral trochlear cartilage (lower T2 relaxation times) 6 months after ACLR in the involved limb.

\[ y = -0.27x + 51.50 \]
\[ R^2 = 0.116 \]
Figure 8.3 Greater knee flexion excursion at 3 months was associated with lower (healthier) femoral trochlear cartilage $T_2$ relaxation time 6 months after ACLR in the involved limb.

Figure 8.4 Higher quadriceps muscle force during gait at 3 months was associated with lower (healthier) femoral trochlear cartilage $T_2$ relaxation time 6 months after ACLR in the involved limb. (Note: there are 30 subjects in Figure 4, as gait data could not be modeled for 5 subjects.)
8.4.3 Results for Hypothesis 3: Interlimb Differences in Gait Mechanics and Trochlear Cartilage $T_2$ Relaxation Times

There were no significant associations between interlimb differences (ILDs) in gait mechanics and ILDs in trochlear $T_2$ relaxation times (Table 8.3).

Table 8.3 Interlimb differences (ILDs) in gait mechanics were not significantly correlated to the ILDs for femoral trochlear $T_2$ relaxation times.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pearson r</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knee Flexion Excursion</td>
<td>-.066</td>
<td>.707</td>
</tr>
<tr>
<td>Knee Extension Excursion</td>
<td>-.266</td>
<td>.123</td>
</tr>
<tr>
<td>Peak Knee Flexion Angle</td>
<td>-.048</td>
<td>.784</td>
</tr>
<tr>
<td>Peak Knee Flexion Moment</td>
<td>.002</td>
<td>.993</td>
</tr>
<tr>
<td>Peak Quadriceps Muscle Forces</td>
<td>-.069</td>
<td>.714</td>
</tr>
</tbody>
</table>

8.4.4 Secondary Analysis: Gait Mechanics and Trochlear Cartilage $T_2$ Relaxation Times in the Uninvolved Limb

There was a significant correlation between walking speed and the uninvolved limb trochlear $T_2$ values (Table 8.4). A significant negative correlation was present between the uninvolved limb knee extension excursion and the uninvolved limb trochlear $T_2$ values. No other significant correlations were found between the uninvolved limb gait mechanics and uninvolved limb trochlear $T_2$ values (Table 8.4).

Table 8.4 Pearson correlations and p-values for the uninvolved limb.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pearson r</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Walking Speed</td>
<td>-.346</td>
<td>.042</td>
</tr>
<tr>
<td>Knee Flexion Excursion</td>
<td>-.243</td>
<td>.159</td>
</tr>
<tr>
<td>Knee Extension Excursion</td>
<td>-.410</td>
<td>.014</td>
</tr>
<tr>
<td>Peak Knee Flexion Angle</td>
<td>.227</td>
<td>.189</td>
</tr>
<tr>
<td>Peak Knee Flexion Moment</td>
<td>-.171</td>
<td>.325</td>
</tr>
<tr>
<td>Peak Quadriceps Muscle Forces</td>
<td>-.056</td>
<td>.766</td>
</tr>
</tbody>
</table>
8.5 Discussion

The purpose of this study was to determine the relationship between walking mechanics and early patellofemoral OA, assessed using femoral trochlear cartilage T2 relaxation times 6 months after ACLR. The first hypothesis, that trochlear T2 relaxation times would be higher (worse) in the involved limb compared to the uninvolved limb, was partially supported. The second hypothesis, that slower walking speeds and smaller involved knee excursions, moments, and muscle forces would be associated with higher (worse) trochlear T2 relaxation times in the involved limb, was generally supported. The third hypothesis, that interlimb differences in gait mechanics would be negatively associated with interlimb differences in trochlear T2 relaxation times, was not supported. Our findings suggest slower walking speed 3 months after ACLR is a strong predictor of femoral trochlear cartilage degradation 6 months after ACLR. Aberrant walking mechanics, especially truncated sagittal plane knee excursions and perhaps smaller quadriceps muscle forces, may also contribute to early patellofemoral OA. The findings of this exploratory analysis suggest slower walking speed and aberrant sagittal plane walking mechanics are related to the early development of patellofemoral OA after ACLR.

To our knowledge, this is the first study to investigate the relationship between walking mechanics and early patellofemoral OA among individuals after ACLR. While the study was exploratory in nature, our finding that walking speed was such a strong predictor of trochlear cartilage health adds to evidence supporting the use of walking speed as a functional vital sign. Self-selected walking speed has previously been associated with more severe OA among older adults with knee OA and with more severe pathology among those with articular cartilage defects. Slower walking speed has also been associated with greater serum biomarkers of cartilage breakdown.
(collagen type II cleavage product) among individuals after ACLR. Walking speed is easy to measure clinically and monitor over time. The present study suggests that evaluating walking speed during rehabilitation after ACLR may help clinicians identify patients who are at greater risk for developing patellofemoral OA.

Despite the prospective nature of the present study, cause and effect cannot be determined from this cohort study. Participants who walked more slowly 3 months after ACLR may have done so due to more severe underlying knee pathology or preclinical knee OA, although we did control for severity of initial injury and excluded people with previous or concomitant lower extremity injury/surgery. Alternatively, walking more slowly, coupled with other associated biomechanical changes, may contribute to the pathogenesis of patellofemoral OA by changing the direction and magnitude of forces acting on the patellofemoral articular cartilage. Given that lower medial tibiofemoral joint contact forces are associated with tibiofemoral OA after ACLR, it is not surprising that slower walking speeds, reduced knee excursions, and lower quadriceps muscle forces—which collectively cause lower patellofemoral joint contact forceswere associated with patellofemoral OA after ACLR. Cartilage responds to cyclic loading and may need an appropriate loading stimulus to maintain homeostasis.

While the present study is unable to determine whether slower walking drives cartilage degradation or vice versa, it does inform future study designs and clinical practice. We cannot conclude from this study that walking faster will prevent patellofemoral OA development after ACLR, but future studies could explore this idea. Our study does, however, inform who may be at high risk for subsequent patellofemoral OA: those who walked more slowly early after ACLR were more likely
to have higher trochlear cartilage $T_2$ relaxation times, a sensitive precursor to established or symptomatic OA.\textsuperscript{26,27,83,151,152,296} Simply put, while instructing patients to “walk faster” after ACLR may not prevent patellofemoral OA (and could potentially even exacerbate symptoms), clinicians may identify patients who walk more slowly as having greater risk for post-traumatic patellofemoral OA.

Our study indicates femoral trochlear cartilage $T_2$ relaxation times may be only marginally higher among individuals 6 months after ACLR. Kim et al. recently found that femoral trochlea $T_2$ relaxation times were significantly higher in the involved limb compared to the uninvolved limb among individuals who were 3 years (rather than 6 months) after ACLR.\textsuperscript{160} The study by Kim et al. also differed from the present study in that the participants were older (mean 34 years vs. mean 23 years) and the trochlear cartilage of each knee was subdivided into superficial and deep sub-regions within medial, lateral, and central trochlear cartilage regions of interest.\textsuperscript{160} The greatest between limb differences in Kim et al. were in the medial and central trochlear cartilage.\textsuperscript{160} The between limb difference in the present study were numerically higher in the medial trochalear cartilage (0.5 ms) than in the lateral trochalear cartilage (0.3 ms), although neither were statistically different. The slight majority (19/35 [54%]) of individuals in the present study had higher total trochalear $T_2$ relaxation times in the involved limb compared to the uninvolved limb, whereas the remainder did not. Cartilage degradation (detectable via $T_2$ relaxation time) may occur in only a subset of individuals 6 months after ACLR.

There are both strengths and limitations to consider when interpreting the results of this study. Strengths of the study include the acquisition of quantitative MRI and detailed biomechanical analyses, including patient-specific musculoskeletal
modeling, among all participants to address a significant and novel research question, the development of post-traumatic patellofemoral OA after ACLR. The study, however, is exploratory in nature and limited in sample size (35 participants). Only one region of interest (femoral trochlea) and one quantitative MRI variable (T2 relaxation time) were used in the present study. Future studies should examine multiple quantitative and semi-quantitative precursors to clinical OA in both the patellar and trochlear cartilage of the patellofemoral joint, in addition to long-term radiographic follow-up.

In conclusion, our findings suggest slow walking speeds, truncated knee excursions, and lower quadriceps muscle forces during gait 3 months after ACLR predicted higher (worse) femoral trochlea T2 relaxation times 6 months after ACLR. Walking speed was by far the strongest predictor of femoral trochlear cartilage health, suggesting walking speed may be an early clinical indicator of future patellofemoral OA after ACLR.

8.6 Funding and Acknowledgments

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Chapter 9

SUPERIOR 2-YEAR FUNCTIONAL OUTCOMES AMONG YOUNG FEMALE ATHLETES AFTER ACL RECONSTRUCTION IN JUST 10 RETURN-TO-SPORT SESSIONS: COMPARISON OF ACL-SPORTS RANDOMIZED CONTROL TRIAL TO DELAWARE-OSLO AND MOON COHORTS

9.1 Abstract

*Background:* Outcomes after anterior cruciate ligament reconstruction (ACLR) are not uniformly good and are worse among young female athletes. Developing better rehabilitation and return-to-sport training programs and evaluating their outcomes are essential.

*Hypotheses/Purposes:* 1) Test the effect of strength, agility, plyometric, and secondary prevention (SAPP) exercises with and without perturbation training (SAPP+PERT) on strength, hops, function, activity levels, and return-to-sport rates in young female athletes 1 and 2 years after ACLR; and 2) Compare 2-year functional outcomes and activity levels among young female athletes in the Anterior Cruciate Ligament Specialized Post-Operative Return-to-Sports (ACL-SPORTS) trial to homogeneous cohorts who completed criterion-based post-operative rehabilitation alone (Multicenter Orthopaedic Outcomes Network [MOON]) and in combination with extended pre-operative rehabilitation (Delaware-Oslo).

*Study Design:* randomized control trial and cohort study

*Methods:* 40 Level I/II female athletes were enrolled after post-operative impairment resolution, 3-9 months after primary ACLR. Participants were randomized to 10 SAPP
or SAPP+PERT sessions and tested 1 and 2 years after ACLR on quadriceps strength, hop tests, functional outcomes, and return-to-sport rates. Participants were then compared to homogeneous cohorts of young (<25 years) female athletes who completed criterion-based post-operative rehabilitation alone (MOON) and in combination with extended pre-operative rehabilitation (Delaware-Oslo) on 2-year functional outcomes.

Results: There were no significant or meaningful differences between SAPP and SAPP+PERT, so groups were collapsed for comparison to the other cohorts. At 2 years follow-up, ACL-SPORTS had the highest scores (p<0.01) on the Marx (ACL-SPORTS: 13.5±3.3, Delaware-Oslo: 12.5±2.7, MOON: 10.6±5.1), IKDC (96±7, 92±9, 84±14), KOOS-Pain (98±4, 94±9, 90±10), KOOS-Symptom (94±6, 90±9, 83±14), KOOS-ADL (100±1, 99±4, 96±7), KOOS-Sport/Recreation (94±8, 86±15, 82±17), and KOOS-Quality of Life (89±14, 78±18, 76±19). The KOOS-Sport/Recreation Patient Acceptable Symptom State threshold was achieved by 100% of ACL-SPORTS compared to 90% of Delaware-Oslo and 78% of MOON (p=.011).

Conclusion: While perturbation training provided no added benefit, 10 sessions of return-to-sport training, compared to criterion-based post-operative rehabilitation alone, yielded statistically significant and clinically meaningfully higher 2-year functional outcomes among young, high-level female athletes after ACLR.

Clinical Relevance: Return-to-sport training led to superior 2-year functional outcomes among young, high-level female athletes after ACLR and could be implemented within a group or non-clinical environment, improving outcomes without increasing rehabilitation costs.
9.2 Introduction

Recent injury surveillance data suggest that anterior cruciate ligament (ACL) injuries are occurring at alarming rates\textsuperscript{6,340} among adolescents and young adults who engage in sports involving jumping, cutting, and pivoting,\textsuperscript{70,134} and are higher among female versus male athletes in similar sports.\textsuperscript{5,6,14} Women are also less likely to return to any sport, or to preinjury sport level, after ACL injury and ACL reconstruction (ACLR).\textsuperscript{13,35} When they do return to sport, women are more likely than men to suffer a second ACL injury.\textsuperscript{100,232,234,235} Moreover, female athletes have poorer functional recovery after ACL injury\textsuperscript{143} and lower activity levels than their male counterparts, 2-6 years after ACLR.\textsuperscript{80,289} Developing and evaluating rigorous rehabilitation and return-to-sport (RTS) training programs, and comparing outcomes from these programs to those from previously successful cohorts, are essential for improving outcomes among high-level female athletes after ACL injury and ACLR.

Previous work has evaluated extended pre-operative rehabilitation and post-operative rehabilitation paradigms on outcomes among athletes after ACLR.\textsuperscript{90,91} Failla et al. found superior functional outcomes and higher RTS rates among athletes who participated in extended pre-operative rehabilitation including neuromuscular training compared to those who did not.\textsuperscript{90,91} While a recent systematic review determined there is no evidence to support a single, most appropriate rehabilitation protocol after ACLR,\textsuperscript{399} clinical practice guidelines\textsuperscript{184,185} exist and several criterion-based post-operative rehabilitation protocols\textsuperscript{4,42,150,215,335} have been proposed. Two recent articles provide quality evidence supporting the use of such criterion-based approaches to achieve objective criteria, including $\geq 90\%$ strength and hop test limb symmetry indexes, prior to returning to sport.\textsuperscript{121,172} Formal rehabilitation, however, typically ends well before athletes achieve these criteria, and athletes often receive RTS
clearance without first meeting these, or any, objective criteria.\textsuperscript{22,26} Therefore, training programs to bridge the gap between post-operative rehabilitation, the current standard of care, and achievement of objective criteria may be a critical component to improving outcomes after ACLR.

The Anterior Cruciate Ligament Specialized Post-Operative Return-to-Sports (ACL-SPORTS) training protocol was developed to fill this gap by evaluating a RTS training program designed to be completed following post-operative rehabilitation and impairment resolution, and prior to testing for clearance for unrestricted participation in sports. Specifically, the ACL-SPORTS randomized control trial was designed to test the effect of 10 sessions of strength, agility, plyometric, and secondary prevention (SAPP) exercises with and without the addition of perturbation training (SAPP+PERT).\textsuperscript{32} Among the men of the ACL-SPORTS trial, there were no significant or meaningful differences between SAPP versus SAPP+PERT training on strength, function, or gait mechanics at pre-training, post-training, 1 year, or 2 years after ACLR.\textsuperscript{18,19,43,46} Across intervention groups, however, the men did exceedingly well, including symmetric functional performance on strength and hop testing, high patient-reported outcome measures, and a 100\% RTS rate, including 95\% attaining their pre-injury level of sport by 2 years after ACLR.\textsuperscript{16,18,19} Among the women of the ACL-SPORTS trial, there were also no between group differences at pre- or post-training,\textsuperscript{18} however, the effect of the ACL-SPORTS training program on 1- and 2-year outcomes in women is unknown. The comparative effectiveness of post-operative RTS training versus criterion-based post-operative rehabilitation alone or with the addition of extended pre-operative rehabilitation is also unknown.
The purpose of the present study is two-fold. The study first sought to compare the effect of SAPP versus SAPP+PERT training on the 1- and 2-year primary clinical outcomes (i.e., quadriceps strength, patient reported outcomes, and single-leg hop testing) in female athletes of the ACL-SPORTS trial. The a priori first hypothesis was that SAPP+PERT would result in superior outcomes compared to SAPP alone. The second aim was to evaluate the comparative effectiveness of 10 sessions of RTS training on clinical and functional outcomes in young female athletes 2 years after ACLR. The hypothesis for aim 2 was that female athletes who completed post-operative RTS training, compared to those who did not, would have higher functional outcomes and activity levels 2 years after ACLR.

9.3 Materials and Methods

This study included both a prospective randomized control trial (NCT01773317) and a cohort study; IRB approval and informed consent were obtained for all participants.

9.3.1 ACL-SPORTS Participants, Methods, and Analyses

9.3.1.1 Participants – ACL-SPORTS Trial

For the ACL-SPORTS randomized control trial, 40 female athletes were enrolled, based on power calculations described previously,18,321 at the University of Delaware between December 2011 and January 2017; 2 year follow-up testing was completed by August 2018, at which time the trial ended as initially planned. Athletes were enrolled only if they were 3-9 months (mean 6±2 months) after primary ACLR and had achieved ≥80% quadriceps strength index, minimal to no knee effusion,294 full knee range of motion, and initiation of a running progression.4 (While pre-enrollment
pre-operative or post-operative] rehabilitation was not controlled, all participants underwent physical therapy and were required to meet objective clinical criteria, consistent with criterion-based rehabilitation, prior to enrollment. Patients with concomitant meniscal pathology (including repair and/or partial meniscectomy to one or both menisci at the time of ACLR) were included. Athletes were excluded if they had a previous ACL injury or lower extremity surgery to either knee, had a concomitant grade III knee ligament injury or large (>1cm²) osteochondral defect, were not age 13-55 years at enrollment, or did not participate regularly (50 hours/year) in jumping, cutting or pivoting sports prior to ACL injury. Participants completed testing before and after 10 RTS training sessions, and 1 and 2 years after ACLR, as presented in the flow diagram (Figure 9.1). Athletes who sustained a second ACL injury (graft rupture or contralateral injury) prior to follow-up testing were excluded from the analyses of strength, hop testing, and patient-reported outcomes to prevent confounding of results.
9.3.1.2 Methods – ACL-SPORTS Trial

Participants were randomized by a research administrator (MC) using a random number generator and block randomization, so that an equal number of participants would be allocated to receive SAPP and SAPP+PERT training. They subsequently completed 10 training sessions (~2x/week). Athletes in both training groups completed the common elements of the RTS training program, including
Nordic hamstrings, standing squats, drop jumps, triple (single-leg) hopping, tuck jumps, and progressive agility drills. Athletes in the SAPP+PERT group additionally completed 10 sessions of perturbation training, while athletes in the SAPP group did a sham exercise using a resistance band. Perturbation training is a specific type of neuromuscular training program where the participant stands on an unstable surface (i.e., rollerboard or rockerboard) and a physical therapist applies movements, or perturbations, to the surface; readers may consult Fitzgerald et al. and White et al. for a more thorough description of perturbation training.

Athletes were tested 1 and 2 years after primary ACLR on the primary outcome measures (SAPP versus SAPP+PERT training), knee biomechanics during walking (null findings, in press, JOR), as well as the secondary outcome measures (quadriceps strength, single-leg hop tests, patient-reported outcomes, and RTS rates). Research physical therapists (JJC, JLJ, KWC, AJHA) who were blinded to treatment group completed all testing. Isometric quadriceps strength was assessed using an isokinetic dynamometer with the knee flexed to 90° and burst superimposition. The uninvolved limb was tested first, followed by the involved limb; approximately 3 trials per limb were recorded, and the highest value for each limb was used to calculate a quadriceps strength limb symmetry index (involved limb strength/uninvolved limb strength * 100%). Participants were subsequently evaluated on 4 hop tests (single, triple, crossover, and timed 6-meter). Two trials were averaged for each limb and used to calculate a limb symmetry index (LSI) for each hop test. Participants also completed several valid and reliable patient-reported outcome measures, including the International Knee Documentation Committee Subjective Knee Evaluation Form (IKDC), Knee Injury and Osteoarthritis Outcome
Score (KOOS) subscale, Knee Outcome Survey–Activities of Daily Living Subscale (KOS-ADLS), Global Rating Score of Perceived Function, and Marx Activity Rating Scale (Marx).

Participants were asked questions at each time point about their participation in sports: 1) “Have you returned to sports or recreational activities? (Yes/No)”; and 2) “Have you returned to the same level of sports or recreational activities as before your injury? (Yes/No)”. These questions, respectively, were used to calculate RTS rates to any level and their self-reported pre-injury level of sport by 2 years (i.e., using a cumulative manner from post-training through 2 years after ACLR). Participants listed reasons for answering “No” to either RTS question.

9.3.1.3 Statistical Analyses – ACL-SPORTS Trial

Between group comparisons for quadriceps strength index, hop test LSIs, and patient-reported outcome measures 1 and 2 years after ACLR were made using mixed-measures analysis of variance (ANOVA; α=0.05). Fisher’s Exact tests compared the proportion of athletes in each group who had returned to sport by 2 years (α=0.05).

9.3.1.4 Power Calculations – ACL-SPORTS Trial

A priori power analysis calculations were based on sagittal plane knee biomechanics and indicated that 36 women were needed to detect a medium effect size (0.3) with β=0.20 and α=0.05. A secondary power analysis based on the IKDC indicated 5 participants per group would be sufficient to detect a difference in IKDC scores equivalent to the minimal clinically important difference of 11.5 (power=0.95, α=0.05, effect size of f(V)=6.44) using a 2x2 ANOVA.
9.3.2 Comparative Effectiveness of ACL-SPORTS, MOON, and Delaware-Oslo Cohorts: Participant, Methods, and Statistical Analyses

9.3.2.1 Participants – Comparative Effectiveness

This is a secondary analysis of prospectively collected data acquired through the Multicenter Orthopaedic Outcomes Network (MOON), Delaware-Oslo, and ACL-SPORTS cohorts. Data from the MOON cohort and Delaware-Oslo cohort have been published previously,\textsuperscript{90,91} and were used in the present study to evaluate RTS training compared to criterion-based post-operative rehabilitation alone (MOON cohort) and extended pre-operative rehabilitation plus criterion-based post-operative rehabilitation (Delaware-Oslo cohort). The MOON cohort provides a large database of participants after ACLR who received standardized post-operative rehabilitation\textsuperscript{335} and represents standard of care treatment for individuals after ACLR within the United States. The Delaware-Oslo cohort provides a rich dataset of individuals who received extended pre-operative rehabilitation in addition to criterion-based post-operative rehabilitation; Failla et al. found superior 2-year outcomes in the Delaware-Oslo cohort,\textsuperscript{90,91} which represents best-evidence for current rehabilitation practice.

Inclusion and exclusion criteria were applied strictly to each cohort to create homogenous comparison groups, as described below. Additionally, age was constrained to include only those age 13-24 years at enrollment (ACL-SPORTS) or time of surgery (Delaware Oslo and MOON) to focus on the young female athletes at particularly high risk for poor outcomes after ACLR.\textsuperscript{13,35,80,100,143,232,234,235,289} Inclusion criteria were: female sex; age 13-24 years at enrollment; available functional outcomes data from approximately 2 years after primary, unilateral ACLR; and participant in level I or II sport\textsuperscript{70,134} prior to index ACLR. Exclusion criteria were: previous ACL injury to either knee; symptomatic concomitant grade III knee ligament (i.e., PCL,
LCL, MCL) injury or surgery; articular cartilage defect >1 cm² or microfracture surgery; or second ACL rupture (Delaware-Oslo) or ACLR (ACL-SPORTS and MOON) to either knee prior to 2-year testing.

9.3.2.2 Methods and Measures – Comparative Effectiveness

Participants from the MOON cohort participated in a standardized, criterion-based post-operative rehabilitation alone (i.e., without extended pre-operative rehabilitation or post-operative RTS training), and represent standard of care. Participants in the Delaware-Oslo cohort participated in 10 pre-operative rehabilitation sessions consisting of progressive strengthening and neuromuscular training including perturbation training, followed by a criterion-based post-operative rehabilitation program without formal RTS training. Participants in the ACL-SPORTS cohort participated in 10 RTS training sessions consisting of strengthening, agility drills, and plyometric exercises designed to facilitate return to sports participation. Participants in each cohort completed the following patient-reported outcome measures 2 years after primary ACLR: IKDC, KOOS subscales, and Marx Activity Rating Scale.

9.3.2.3 Statistical Analyses – Comparative Effectiveness

Demographic comparisons were made between groups using one-way ANOVA and Chi-Square tests of proportions for continuous and categorical variables, respectively (α=0.05). One-way ANOVA with post-hoc comparisons between groups were used to compare scores on the IKDC, KOOS subscales, and Marx Activity Rating Scale (α=0.05). The proportion of athletes in each cohort who met the Patient Acceptable Symptom State (PASS) thresholds for the IKDC and each of the KOOS
subscales was calculated and compared among cohorts for each variable using Chi-Square tests of proportions (α=0.05).

9.4 Results

9.4.1 ACL-SPORTS Results: SAPP Versus SAPP+PERT Training

Demographic characteristics did not differ between those in the SAPP and SAPP+PERT groups (Table 9.1). There were no statistically significant or clinically meaningful differences between the SAPP and SAPP+PERT groups on any outcome measure, including quadriceps strength index, LSI on any hop test (single, crossover, triple, 6-meter timed), or any functional outcome measure (i.e., KOS-ADLS, Global Rating of Perceived Function, IKDC, any KOOS subscale, or the Marx Activity Rating Scale) (Table 9.2). All athletes (39/39, 100%) returned to sport by 2 years, including 87% (34/39) at their self-reported pre-injury level. There were no between group differences in RTS rates (SAPP: 19/20, SAPP+PERT: 15/19, p=0.182; odds ratio of returning to pre-injury sport level [95% confidence interval]: 1.2 [.9, 1.6]).
Table 9.1 Demographics did not differ between those in the SAPP and SAPP+PERT groups. Values are presented as mean (SD) for continuous variables. (Abbreviations: Allo: allograft; BPTB: bone-patellar tendon-bone autograft; Hamstring: hamstring autograft.)

<table>
<thead>
<tr>
<th>Variable</th>
<th>SAPP (n=20)</th>
<th>SAPP+PERT (n=19)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>18.9 (5.8)</td>
<td>19.0 (8.8)</td>
<td>.986</td>
</tr>
<tr>
<td>Time from Surgery to Enrollment (Weeks)</td>
<td>24.8 (7.8)</td>
<td>26.2 (8.9)</td>
<td>.621</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>68.8 (10.9)</td>
<td>67.9 (14.3)</td>
<td>.820</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.65 (.06)</td>
<td>1.65 (.08)</td>
<td>.827</td>
</tr>
<tr>
<td>BMI (kg/m^2)</td>
<td>25.3 (3.3)</td>
<td>24.7 (3.9)</td>
<td>.631</td>
</tr>
<tr>
<td>Graft Type</td>
<td>4 Allo, 8 BPTB, 8 Hamstring</td>
<td>1 Allo, 8 BPTB, 10 Hamstring</td>
<td>.368</td>
</tr>
<tr>
<td>Mechanism of Injury</td>
<td>14 non-contact, 6 contact</td>
<td>14 non-contact, 5 contact</td>
<td>.798</td>
</tr>
<tr>
<td>Pre-Injury Sport Level</td>
<td>19 Level 1, 1 Level 2</td>
<td>15 Level 1, 4 Level 2</td>
<td>.182</td>
</tr>
<tr>
<td>Concomitant Medial Meniscus Treatment</td>
<td>11 None, 4 Partial Meniscectomy, 2 Repair, 3 No Data</td>
<td>12 None, 4 Partial Meniscectomy, 1 Repair, 1 Rasping, 1 No Data</td>
<td>.671</td>
</tr>
<tr>
<td>Concomitant Lateral Meniscus Treatment</td>
<td>8 None, 7 Partial Meniscectomy, 2 Repair, 3 No Data</td>
<td>12 None, 5 Partial Meniscectomy, 1 Repair, 1 No Data</td>
<td>.486</td>
</tr>
</tbody>
</table>
Table 9.2 Quadriceps strength index, hop limb symmetry index (LSI), functional outcome measures, and the Marx Activity Rating Scale did not differ between SAPP and SAPP+PERT participants. There were no main effects of group or interaction effects of group*time; however, there were main effects of time for the 6-meter timed hop, IKDC, KOOS Pain, and KOOS Quality of Life. Values are mean (SD). Abbreviations: LSI: limb symmetry index; KOS-ADLS: Knee Outcome Survey- Activities of Daily Living; IKDC: International Knee Documentation Committee Subjective Knee Evaluation Form; KOOS: Knee Injury and Osteoarthritis Outcome Score; ADL: Activities of Daily Living; Sport/Rec: Sport and Recreation; QoL: Knee-Related Quality of Life; Marx: Marx Activity Rating Scale (Marx). (There were 13 SAPP and 13 SAPP+PERT participants for QI, 12 SAPP and 12 SAPP+PERT participants for each hop test, and 14 SAPP and 14 SAPP+PERT participants for each patient reported outcome measures who had complete data at both 1 and 2 years and who did not sustain a re-injury, and were thus included in the primary analyses [2x2 ANOVAs]).

<table>
<thead>
<tr>
<th>Variable</th>
<th>1 Year</th>
<th></th>
<th>2 Years</th>
<th></th>
<th>Interaction</th>
<th>Time</th>
<th>Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SAPP</td>
<td>SAPP+PERT</td>
<td>SAPP</td>
<td>SAPP+PERT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quadriceps Index (%)</td>
<td>94 (9)</td>
<td>100 (14)</td>
<td>101 (13)</td>
<td>102 (14)</td>
<td>.417</td>
<td>.194</td>
<td>.414</td>
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<tr>
<td>Single Hop LSI (%)</td>
<td>98 (7)</td>
<td>100 (11)</td>
<td>97 (10)</td>
<td>101 (9)</td>
<td>.616</td>
<td>.780</td>
<td>.375</td>
</tr>
<tr>
<td>Crossover Hop LSI (%)</td>
<td>99 (6)</td>
<td>97 (8)</td>
<td>101 (6)</td>
<td>97 (8)</td>
<td>.612</td>
<td>.536</td>
<td>.181</td>
</tr>
<tr>
<td>Triple Hop LSI (%)</td>
<td>101 (5)</td>
<td>97 (4)</td>
<td>100 (5)</td>
<td>99 (6)</td>
<td>.260</td>
<td>.684</td>
<td>.188</td>
</tr>
<tr>
<td>6-m Timed Hop LSI (%)</td>
<td>103 (5)</td>
<td>102 (4)</td>
<td>98 (7)</td>
<td>100 (5)</td>
<td>.313</td>
<td>.006</td>
<td>.725</td>
</tr>
<tr>
<td>KOS-ADLS</td>
<td>97 (4)</td>
<td>97 (4)</td>
<td>98 (3)</td>
<td>98 (3)</td>
<td>.888</td>
<td>.213</td>
<td>.648</td>
</tr>
<tr>
<td>Global Rating</td>
<td>94 (8)</td>
<td>94 (9)</td>
<td>98 (4)</td>
<td>97 (4)</td>
<td>.662</td>
<td>&lt;.001</td>
<td>.940</td>
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<tr>
<td>IKDC</td>
<td>92 (9)</td>
<td>92 (8)</td>
<td>97 (6)</td>
<td>95 (9)</td>
<td>.426</td>
<td>.043</td>
<td>.744</td>
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<tr>
<td>KOOS Pain</td>
<td>96 (4)</td>
<td>95 (5)</td>
<td>98 (4)</td>
<td>97 (4)</td>
<td>.901</td>
<td>.007</td>
<td>.400</td>
</tr>
<tr>
<td>KOOS Symptom</td>
<td>92 (6)</td>
<td>88 (8)</td>
<td>92 (10)</td>
<td>92 (7)</td>
<td>.177</td>
<td>.178</td>
<td>.404</td>
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<tr>
<td>KOOS ADL</td>
<td>99 (1)</td>
<td>99 (2)</td>
<td>99 (2)</td>
<td>100 (1)</td>
<td>.388</td>
<td>.388</td>
<td>.840</td>
</tr>
<tr>
<td>KOOS Sport/Rec</td>
<td>96 (9)</td>
<td>90 (10)</td>
<td>98 (4)</td>
<td>93 (9)</td>
<td>.897</td>
<td>.164</td>
<td>.081</td>
</tr>
<tr>
<td>KOOS QoL</td>
<td>78 (14)</td>
<td>80 (14)</td>
<td>88 (15)</td>
<td>89 (15)</td>
<td>.910</td>
<td>&lt;.001</td>
<td>.764</td>
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<td>Marx</td>
<td>11.7 (2.4)</td>
<td>13.0 (4.9)</td>
<td>13.9 (3.0)</td>
<td>13.2 (3.5)</td>
<td>.186</td>
<td>.109</td>
<td>.783</td>
</tr>
</tbody>
</table>
9.4.2 Comparative Effectiveness: ACL-SPORTS, Delaware-Oslo, and MOON Results

There were no differences in age, body mass index, pre-injury sport level, or medial meniscus treatment among the 3 comparison cohorts; however, there were differences across groups in time to 2-year follow-up, graft type, and lateral meniscus treatment (Table 1). There were significant differences in all outcome measures, including the Marx, IKDC, KOOS Pain, KOOS Symptoms, KOOS Activities of Daily Living, KOOS Sport and Recreation (Sport/Rec), and KOOS Knee-Related Quality of Life with the ACL-SPORTS cohort having the highest scores across every outcome (Table 2). Post-hoc comparisons revealed that ACL-SPORTS, compared to MOON, had significantly higher scores across all outcome measures (post-hoc p≤0.006); between group differences exceeded the minimal clinically important difference (MCID) values for the IKDC\textsuperscript{145} and KOOS subscales for Symptoms, Sport/Rec, and Knee-Related Quality of Life\textsuperscript{254}. ACL-SPORTS also scored significantly and meaningfully\textsuperscript{254} higher on the KOOS Knee-Related Quality of Life (post-hoc p=0.034) and tended to score higher on the KOOS Sport/Rec (post-hoc p=0.068) compared to the Delaware-Oslo cohort. The Delaware-Oslo group, compared to the MOON group, had significantly higher scores (post-hoc p≤0.035) for the IKDC, KOOS Pain, KOOS Symptoms, and KOOS Activities of Daily Living, although none of these differences exceeded MCID values\textsuperscript{145,254}. 
Table 9.3 Demographic characteristics for the comparative effectiveness study. Abbreviations: MOON: Multicenter Orthopaedic Outcomes Network; DE-Oslo: Delaware-Oslo; ACL-SPORTS: Anterior Cruciate Ligament Specialized Return-to-Sports; BMI: body mass index; BPTB: bone-patellar tendon-bone autograft. (Note: due to rounding, not all percentages total 100%.) Post-hoc comparisons within each group are denoted by superscripts, where different letters indicate p < 0.05.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cohort</th>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>P-Value</th>
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<td>Age (yrs)</td>
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<tr>
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<td>39</td>
<td>18.0</td>
<td>3.1</td>
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<tr>
<td></td>
<td>ACL-SPORTS</td>
<td>24</td>
<td>17.3</td>
<td>2.6</td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m^2)</td>
<td>MOON</td>
<td>424</td>
<td>23.3</td>
<td>4.1</td>
<td>.125</td>
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<tr>
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<td>DE-Oslo</td>
<td>39</td>
<td>22.4</td>
<td>2.8</td>
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<td></td>
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<td>24</td>
<td>24.4</td>
<td>3.6</td>
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</tr>
<tr>
<td>Time to 2-Year Followup (yrs)</td>
<td>MOON^a</td>
<td>427</td>
<td>2.4</td>
<td>0.4</td>
<td>&lt;.001</td>
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<tr>
<td></td>
<td>DE-Oslo^b</td>
<td>39</td>
<td>2.1</td>
<td>0.3</td>
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<tr>
<td></td>
<td>ACL-SPORTS^b</td>
<td>24</td>
<td>2.1</td>
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</table>

<table>
<thead>
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<th>Variable</th>
<th>Group</th>
<th>Frequency</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Graft Type</td>
<td>MOON^a</td>
<td>7% Allograft, 62% BPTB, 31% Soft-tissue Autograft</td>
<td>.003</td>
</tr>
<tr>
<td></td>
<td>DE-Oslo^b</td>
<td>10% Allograft, 31% BPTB, 59% Soft-tissue Autograft</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ACL-SPORTS^a</td>
<td>4% Allograft, 67% BPTB, 29% Soft-tissue Autograft</td>
<td></td>
</tr>
<tr>
<td>Pre-Injury Sport Level</td>
<td>MOON</td>
<td>78% Level 1, 22% Level 2</td>
<td>.187</td>
</tr>
<tr>
<td></td>
<td>DE-Oslo</td>
<td>85% Level 1, 15% Level 2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ACL-SPORTS</td>
<td>92% Level 1, 8% Level 2</td>
<td></td>
</tr>
<tr>
<td>Medial Meniscus Treatment</td>
<td>MOON</td>
<td>72% None, 8% Meniscectomy, 18% Repair, 2% Rasping/Trephination</td>
<td>.233</td>
</tr>
<tr>
<td></td>
<td>DE-Oslo</td>
<td>85% None, 3% Meniscectomy, 8% Repair, 5% Rasping/Trephination</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ACL-SPORTS</td>
<td>76% None, 10% Meniscectomy, 10% Repair, 5% Rasping/Trephination</td>
<td></td>
</tr>
<tr>
<td>Lateral Meniscus Treatment</td>
<td>MOON^a</td>
<td>65% None, 26% Meniscectomy, 9% Repair, 1% Rasping/Trephination</td>
<td>.001</td>
</tr>
<tr>
<td></td>
<td>DE-Oslo^b</td>
<td>87% None, 5% Meniscectomy, 3% Repair, 5% Rasping/Trephination</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ACL-SPORTS^a</td>
<td>57% None, 29% Meniscectomy, 14% Repair</td>
<td></td>
</tr>
</tbody>
</table>
Table 9.4 All 2-year functional outcomes differed across groups. Abbreviations: Marx: Marx Activity Rating Scale; IKDC: International Knee Documentation Committee Subjective Knee Evaluation Form; KOOS: Knee Injury and Osteoarthritis Outcome Score; ADL: Activities of Daily Living (KOOS subscale); Sport/Rec: Sport and Recreation (KOOS subscale); QoL: Knee-Related Quality of Life (KOOS subscale); DE-Oslo: Delaware-Oslo. Post-hoc comparisons within each group are denoted by superscripts, where different letters indicate p < 0.05.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cohort</th>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>ANOVA P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marx at 2 years (%)</td>
<td>MOON&lt;sup&gt;a&lt;/sup&gt;</td>
<td>431</td>
<td>10.6</td>
<td>5.1</td>
<td>.008</td>
</tr>
<tr>
<td></td>
<td>DE-Oslo&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>19</td>
<td>12.5</td>
<td>2.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ACL-SPORTS&lt;sup&gt;b&lt;/sup&gt;</td>
<td>24</td>
<td>13.5</td>
<td>3.3</td>
<td></td>
</tr>
<tr>
<td>IKDC at 2 years (%)</td>
<td>MOON&lt;sup&gt;a&lt;/sup&gt;</td>
<td>430</td>
<td>83.6</td>
<td>13.9</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>DE-Oslo&lt;sup&gt;b&lt;/sup&gt;</td>
<td>39</td>
<td>91.7</td>
<td>8.6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ACL-SPORTS&lt;sup&gt;b&lt;/sup&gt;</td>
<td>24</td>
<td>95.9</td>
<td>6.8</td>
<td></td>
</tr>
<tr>
<td>KOOS Pain at 2 years (%)</td>
<td>MOON&lt;sup&gt;a&lt;/sup&gt;</td>
<td>431</td>
<td>90.4</td>
<td>10.3</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>DE-Oslo&lt;sup&gt;b&lt;/sup&gt;</td>
<td>30</td>
<td>94.4</td>
<td>9.4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ACL-SPORTS&lt;sup&gt;b&lt;/sup&gt;</td>
<td>24</td>
<td>97.9</td>
<td>3.9</td>
<td></td>
</tr>
<tr>
<td>KOOS Symptoms at 2 years (%)</td>
<td>MOON&lt;sup&gt;a&lt;/sup&gt;</td>
<td>431</td>
<td>83.4</td>
<td>14.0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>DE-Oslo&lt;sup&gt;b&lt;/sup&gt;</td>
<td>30</td>
<td>89.6</td>
<td>9.4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ACL-SPORTS&lt;sup&gt;b&lt;/sup&gt;</td>
<td>24</td>
<td>93.5</td>
<td>6.3</td>
<td></td>
</tr>
<tr>
<td>KOOS ADL at 2 years (%)</td>
<td>MOON&lt;sup&gt;a&lt;/sup&gt;</td>
<td>430</td>
<td>95.7</td>
<td>7.1</td>
<td>.002</td>
</tr>
<tr>
<td></td>
<td>DE-Oslo&lt;sup&gt;b&lt;/sup&gt;</td>
<td>30</td>
<td>98.8</td>
<td>4.2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ACL-SPORTS&lt;sup&gt;b&lt;/sup&gt;</td>
<td>24</td>
<td>99.8</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>KOOS Sport/Rec at 2 years (%)</td>
<td>MOON&lt;sup&gt;a&lt;/sup&gt;</td>
<td>430</td>
<td>81.6</td>
<td>17.1</td>
<td>.001</td>
</tr>
<tr>
<td></td>
<td>DE-Oslo&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>30</td>
<td>86.0</td>
<td>15.4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ACL-SPORTS&lt;sup&gt;b&lt;/sup&gt;</td>
<td>24</td>
<td>94.4</td>
<td>7.6</td>
<td></td>
</tr>
<tr>
<td>KOOS QoL (%)</td>
<td>MOON&lt;sup&gt;a&lt;/sup&gt;</td>
<td>431</td>
<td>76.3</td>
<td>18.7</td>
<td>.004</td>
</tr>
<tr>
<td></td>
<td>DE-Oslo&lt;sup&gt;a&lt;/sup&gt;</td>
<td>30</td>
<td>78.3</td>
<td>17.6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ACL-SPORTS&lt;sup&gt;b&lt;/sup&gt;</td>
<td>24</td>
<td>89.1</td>
<td>13.9</td>
<td></td>
</tr>
</tbody>
</table>

There were significant differences in proportions of participants who met or exceeded (“pass”) versus fell below (“fail”) the Patient Acceptable Symptom State (PASS) scores for the IKDC, KOOS Activities of Daily Living, and KOOS.
Sport/Rec (Figure 2a-c). A lower proportion of MOON participants passed the IKDC PASS cut-off compared to participants in both the Delaware-Oslo (p=0.012) and ACL-SPORTS (p=0.038) cohorts. A lower proportion of MOON participants passed the KOOS Activities of Daily Living subscale PASS cut-off score compared to both the Delaware-Oslo (p<0.001) and ACL-SPORTS (p<0.001) cohort participants. A higher proportion of ACL-SPORTS participants passed the KOOS Sport/Rec PASS score versus the proportion of MOON participants who passed (p=0.004). There were no other statistically significant group differences.

<table>
<thead>
<tr>
<th>Group</th>
<th>Fail (%)</th>
<th>Pass (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MOON</td>
<td>22%</td>
<td>78%</td>
</tr>
<tr>
<td>DE-OSLO IKDC</td>
<td>5%</td>
<td>95%</td>
</tr>
<tr>
<td>ACL-SPORTS</td>
<td>4%</td>
<td>96%</td>
</tr>
</tbody>
</table>

Figure 9.2a The proportion of individuals who met PASS\textsuperscript{212} scores differed across groups for the IKDC (p=.003). Abbreviation: PASS: Patient Acceptable Symptom State.
Figure 9.2b The proportion of individuals who met PASS\textsuperscript{212} scores differed across groups for the KOOS Activities of Daily Living (p<.001. Abbreviation: PASS: Patient Acceptable Symptom State.

Figure 9.2c The proportion of individuals who met PASS\textsuperscript{212} scores differed across groups for the KOOS Sport and Recreation (p=0.011). Abbreviation: PASS: Patient Acceptable Symptom State.
9.5 Discussion

There were two main objectives of this study: first, to assess the primary clinical 1- and 2-year outcomes among female athletes in the ACL-SPORTS randomized control trial; and, second, to compare 2-year functional outcomes and activity levels among young female athletes who completed a formal RTS training program after ACLR to homogenous subsets of two existing “gold-standard” ACL cohorts, Delaware-Oslo and MOON. The key findings were that: 1) SAPP and SAPP+PERT training resulted in very high but comparable quadriceps strength, hop test LSI, functional outcomes, activity levels, and RTS rates 2 years after ACLR; and 2) 10 sessions of post-operative RTS training, compared to criterion-based post-operative rehabilitation alone, led to statistically significant and clinically meaningful differences in 2-year functional outcomes among young female athletes after ACLR. The first hypothesis, that the addition of perturbation training would result in superior clinical and functional outcomes, was not supported. The second hypothesis, that the addition of a structured RTS training program would improve outcomes over existing cohorts, was supported. The findings suggest that adding a post-operative RTS training program, incorporating strengthening, agilities, and plyometrics but not necessarily perturbation training, may improve functional outcomes and activity levels among young female athletes after ACLR.

The overwhelming majority of participants in the ACL-SPORTS cohort achieved the PASS thresholds for patients after ACLR, indicating a high likelihood of satisfaction with their post-operative outcomes. Muller and colleagues recently identified PASS threshold scores with sensitivity and specificity values for the IKDC and each KOOS subscale for patients 1-5 years after ACLR. The most specific measure was the IKDC, where a score of 75.9 yielded 96% specificity and 83% sensitivity, while the most sensitive measure was the KOOS Sport/Rec subscale threshold of 75.0 (88% specificity, 87% sensitivity). In the present study, 96% and
100% of participants in the ACL-SPORTS cohort achieved the thresholds for the IKDC and KOOS Sport/Rec, respectively. In contrast, 95% of Delaware-Oslo and 78% of MOON participants achieved the IKDC PASS threshold and just 90% of the Delaware-Oslo and 78% of MOON cohorts met the KOOS Sport/Rec PASS threshold. Post-operative RTS training may lead to a greater likelihood of successful outcomes among young female athletes after ACLR.

The findings provide a strong model for improving outcomes after ACLR without imposing additional rehabilitation costs, a growing concern in our health-care system.\textsuperscript{159,227,343} Given that perturbation training provided no additional benefit, the common elements of the RTS training protocol (Table 9.5), including strength, agility, and plyometric exercises, are likely the only critical components of the training regimen. These critical components include basic strength and conditioning exercises that could be performed within a group setting or under the supervision of a variety of professionals including athletic trainers and strength and conditioning coaches. They do not require a physical therapist or other rehabilitation specialist. Future studies should explore the effectiveness of delivering the strength, agility, and plyometric exercise components using different models of supervision in various settings outside the confines of a physical therapy clinic.

The ACL-SPORTS protocol also yielded exceptionally high RTS rates, far superior to those previously reported in the literature. According to a 2014 systematic review by Ardern et al., 75% of female athletes return to sport after ACLR, and just 52% of women return to their pre-injury level of sport after ACLR.\textsuperscript{13} In stark contrast, 100% (39/39) of female athletes in the ACL-SPORTS trial returned to sport by 2 years after ACLR, including 87% (34/39) at their pre-injury level of sport. Female athletes in the ACL-SPORTS cohort were required to meet stringent, objective criteria,\textsuperscript{4} including at least 90% quadriceps strength index and hop test LSI,\textsuperscript{226} in order to be
cleared by their physical therapist to return to sport. Completing the ACL-SPORTS post-operative RTS training program, which is informed by these criteria, likely facilitated the very high functional performance and RTS rates observed in the ACL-SPORTS participants.

Table 9.5 The common elements of the RTS training program were performed by all participants in the ACL-SPORTS cohort.

<table>
<thead>
<tr>
<th>Exercise</th>
<th>Sets x Reps</th>
<th>Notes/Progressions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nordic Hamstrings</td>
<td>2 x 5</td>
<td>Progress depth from 30° initially to 60° over the course of 10 sessions</td>
</tr>
<tr>
<td>Standing Squat</td>
<td>3 x 10</td>
<td>Perform bilaterally to 90° of knee flexion; add resistance band around knees after first session and progress resistance of band during later sessions; not performed during sessions 7-10 (replaced by Tuck Jumps)</td>
</tr>
<tr>
<td>Drop Jump</td>
<td>3 x 10</td>
<td>Progress height of box (10cm, 15cm, 20cm); begin taking off bilaterally and landing bilaterally, progressing to unilateral (involved limb) landing and then unilateral take-off and landing on the involved limb only over the course of 10 sessions</td>
</tr>
<tr>
<td>Triple Single-leg Hop</td>
<td>10 - 15 x 3 hops each direction for each condition</td>
<td>Sessions 1-3: 10 x 3 hops forward/backward, 10 x 3 hops side to side, over-ground Sessions 4-6: 15 x 3 hops forward/backward, 15 x 3 hops side to side, over low (~5cm) object (e.g., cup or low cone) Sessions 7-10: 15 x 3 hops forward/backward, 15 x 3 hops side to side, over higher object appropriate to athlete (e.g., 10cm cones or 15cm hurdles)</td>
</tr>
<tr>
<td>Tuck Jumps</td>
<td>2-3 x 10-30 seconds</td>
<td>Perform on sessions 7-10; progress from 2 sets of 10-20” to 3 sets of 20-30”</td>
</tr>
<tr>
<td>Agility Drills</td>
<td>3-4 drills per session</td>
<td>Progress gradually from 50% to 100% effort over the 10 training sessions; agility drills include: forward/backward running, side shuffles, carioca, figure 8 around cones, circles around cones, and 90° turns around cones</td>
</tr>
</tbody>
</table>

Strengths of the present study include that it was the first to compare (1) RTS training with and without perturbation training on medium-term outcomes in female athletes after ACLR, and (2) the addition of a supplementary, post-operative RTS training program versus criterion-based post-operative rehabilitation alone, the current
standard of care for patients after ACLR. The present study used homogenous subsets of two highly successful cohorts\textsuperscript{90,91,119} who received quality, criterion-based post-operative rehabilitation for comparison. The findings also provide a prototype for RTS training that could be implemented in a variety of settings, making its inclusion into standard of care quite feasible.

There are also limitations to consider when interpreting the results of the study. First, a cohort design was used to evaluate RTS training compared to post-operative rehabilitation alone and in combination with extended pre-operative rehabilitation, thus cause and effect cannot be determined, and there were also large differences in the numbers of participants in each cohort. Surgeons and physical therapists also varied across and within studies. Baseline differences in factors like motivation, function, or activity levels could have impacted the findings, but pre-operative data are not available for the participants of the ACL-SPORTS trial. Athletes were required to meet objective criteria prior to enrollment in the ACL-SPORTS trial, but the criteria are consistent with the criterion-based rehabilitation programs followed by the athletes in the MOON and Delaware-Oslo cohorts.\textsuperscript{4,335} The ACL-SPORTS enrollment criteria are basic clinical measures, well below those recommended or supported for RTS clearance.\textsuperscript{4,42,121,172,250,321} Moreover, only 8 of 147 (5\%) women who were screened were deemed ineligible because they were unable to resolve these impairments, thus it is unlikely that requiring patients to achieve these basic clinical milestones dramatically impacted the findings. Another consideration is that the comparative analysis included only high-level, female athletes age 13-24 years, thus the findings may not be generalizable to other individuals. The cohorts, however, were well-matched by age, pre-injury sport level, and sex, and address a subset of individuals after ACLR who are at particularly high risk for poor outcomes;\textsuperscript{13,35,80,100,143,232,234,235,289} this limitation, therefore, may also be a strength.
Additionally, there were no differences between men and women on quadriceps strength index, hop tests, or patient reported outcomes immediately following completion of the ACL-SPORTS training protocol.\textsuperscript{18} Future studies should evaluate the comparative effectiveness of post-operative RTS training in various settings using randomized control trials.

\textbf{9.6 Conclusion}

Ten sessions of post-operative RTS training, compared to criterion-based post-operative rehabilitation alone (MOON), provided clinically meaningfully higher 2-year functional outcomes among young, Level I and Level II female athletes after primary ACLR. RTS training also led to superior knee-related quality of life compared to extended pre-operative plus post-operative rehabilitation (Delaware-Oslo).

\textbf{9.7 Funding and Acknowledgments}

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10.1 Overarching Purpose

The long-term objective of this work is to improve functional outcomes and reduce second injury and early OA development after ACLR. The overall objectives of this dissertation were to determine if walking mechanics influence the risk for second ACL injury and/or patellofemoral OA and if specific interventions affect walking mechanics or functional outcomes after ACLR. This dissertation specifically aimed to identify risk factors associated with second ACL injury (Aim 1) and early patellofemoral OA development (Aim 4), and evaluate the effect of interventions (i.e., meniscus treatment and rehabilitation strategies) on a known risk factor for early tibiofemoral OA development (Aims 2 and 3) and functional outcomes (Aim 5). The dissertation provides new insights to guide clinical practice and future research (Figure 10.1).

Figure 10.1 Schematic diagram of specific aims and major results.
10.2 Aim 1 Summary

10.2.1 Aim 1 Purpose

*Compare walking mechanics and return-to-sport time frames in a matched cohort of female athletes who either returned to sport without re-injury or sustained a second ACL injury.*

10.2.2 Aim 1 Hypotheses

*Hypothesis 1.1:* Athletes who sustain second ACL injuries (ACLx2) will return to sports earlier than those who return to sport without re-injury (ACLx1).

*Hypothesis 1.2:* ACLx2 will walk using more asymmetric walking mechanics (i.e., knee kinematics, kinetics, and muscle and joint contact forces) than ACLx1.

10.2.3 Aim 1 Findings

The purpose of Aim 1 (Chapter 2) was to investigate gait biomechanics, including modeling the muscle and joint contact forces, in a matched cohort of young female athletes after primary ACLR who either returned to sport without re-injury (ACLx1) or sustained a second ACL rupture within two years of surgery (ACLx2). We found that ACLx2 athletes received surgery more quickly after injury and met objective criteria for enrollment and RTS clearance more quickly than ACLx1 subjects, supporting Hypothesis 1.1. Yet despite being tested sooner after primary ACLR than ACLx1 subjects, ACLx2 subjects demonstrated a more normal gait pattern, refuting Hypothesis 1.2. Aim 1 findings suggest delaying RTS clearance after ACLR even in the absence of clinical or biomechanical gait impairments may mitigate second ACL injury risk in young female athletes.45
10.3 Aim 2 Summary

10.3.1 Aim 2 Purpose

Quantify walking mechanics and knee loading among participants approximately 6 months (2a) and 2 years (2b) after ACLR with no medial meniscal surgery, partial medial meniscectomy, or medial meniscus repair.

10.3.2 Aim 2 Hypotheses

Hypothesis 2: There will be differences in walking mechanics and knee loading among participants 6 months (2a) and 2 years (2b) after ACLR according to the treatment of the medial meniscus at the time of ACLR.

10.3.3 Aim 2 Findings

In support of Hypothesis 2a, our results suggest that concomitant medial meniscus pathology and treatment may influence walking mechanics approximately 6 months after ACLR (Chapter 3).44 Those who underwent partial medial meniscectomy walked with higher peak knee adduction moment (pKAM) and shifted loading toward the medial compartment of the surgical limb while those who had meniscal repair did the opposite, walking with lower pKAM and unloading the surgical versus contralateral limb. These findings may help to explain the conflicting evidence regarding pKAM after ACLR and the elevated risk for osteoarthritis after ACLR with concomitant medial meniscectomy or repair.

Our findings also support Hypothesis 2b, as medial meniscus treatment continues to influence walking mechanics 2 years after ACLR (Chapter 4). Patients 2 years after ACLR with concomitant partial medial meniscectomy walked using bilaterally smaller peak knee flexion angles and exhibited gait asymmetries, especially higher peak medial tibiofemoral joint contact forces, that were not present among participants 2 years after ACLR with no medial meniscus involvement or concomitant...
medial meniscus repair. These aberrant gait mechanics may concentrate higher forces in the antero-medial tibiofemoral cartilage\textsuperscript{12,158}, providing a plausible mechanism explaining the higher osteoarthritis rates among patients 2 years after ACLR plus partial medial meniscectomy. Patients after ACLR plus partial medial meniscectomy also had clinically lower quadriceps strength index. Aim 2 findings may inform future, targeted interventions to ameliorate aberrant movement patterns among patients after ACLR and concomitant partial medial meniscectomy.

10.4 Aim 3 Summary

10.4.1 Aim 3 Purpose

Determine the longitudinal effect of a specialized postoperative neuromuscular training program on the changes in walking mechanics of male (3a) and female (3b) athletes after primary ACLR.

10.4.2 Aim 3 Hypotheses

\textit{Hypothesis 3.1}: Male (3.1a) and female (3.1b) athletes will walk with interlimb asymmetries in knee kinematics, kinetics, and joint contact forces at pre-training.

\textit{Hypothesis 3.2}: Walking mechanics will improve among male (3.2a) and female (3.2b) athletes after training in both treatment groups, but more so in the SAPP+PERT versus the SAPP training group.

10.4.3 Aim 3 Findings

Our results support Hypothesis 3.1, as both male (3.1a, Chapter 6)\textsuperscript{43} and female (3.1b Chapter 7)\textsuperscript{47} participants exhibited meaningful walking asymmetries at the pre-training time-point, which occurred approximately 5-6 months after ACLR. Our results, however, refute Hypothesis 3.2. Neither SAPP nor SAPP+PERT training was
effective at improving walking mechanics among men (3.2a, Chapter 6)\(^{43}\) or women (3.2b, Chapter 7).\(^{47}\) Walking asymmetries persisted to a large degree among both men (Chapter 5)\(^{46}\) and women (Chapter 7)\(^{47}\) at 1 year, but improved between 1 and 2 years after ACLR. Aim 3 adds to the growing body of evidence suggesting full recovery after ACLR may take longer than previously thought and indicates that gait-specific interventions may be necessary to address aberrant walking mechanics after ACLR.\(^{43,46,47}\)

10.5 Aim 4 Summary

10.5.1 Aim 4 Purpose

*Exploratory aim to define the relationship between gait mechanics early after ACLR and 6-month trochlear \(T_2\) relaxation times (higher values indicate worse cartilage health).*

10.5.2 Aim 4 Hypotheses

*Hypothesis 4.1:* \(T_2\) relaxation times 6 months after ACLR will be higher (worse) in the involved limb compared to the uninvolved limb.

*Hypothesis 4.2:* Slower walking speeds and smaller involved limb knee excursions, moments, and muscle forces during gait would be associated with higher (worse) trochlear \(T_2\) relaxation times in the involved limb.

*Hypothesis 4.3:* Interlimb differences in gait mechanics would be negatively associated with interlimb differences in trochlear \(T_2\) relaxation times (i.e., those with smaller involved vs. uninvolved limb gait mechanics would have higher [worse] involved vs. uninvolved limb trochlear \(T_2\) relaxation times).
10.5.3 Aim 4 Findings

Our findings suggest walking speed and gait mechanics 3 months after ACLR are associated with the early development of patellofemoral OA. Slower walking speeds, truncated knee excursions, and lower quadriceps muscle forces during gait 3 months after ACLR predicted higher (worse) femoral trochlea T₂ relaxation times 6 months after ACLR. Walking speed was by far the strongest predictor of femoral trochlear cartilage health, suggesting walking speed may be an early clinical indicator of future patellofemoral OA after ACLR.

10.6 Aim 5 Summary

10.6.1 Aim 5 Purpose

Compare (5.1) the effect of SAPP versus SAPP+PERT training on the 1- and 2-year primary functional outcomes in female athletes of the ACL-SPORTS trial, and (5.2) 2-year functional outcomes among women who completed the common elements of the ACL-SPORTS trial with homogenous subsets of young, high-level female athletes from two “gold-standard” comparison cohorts.

10.6.2 Aim 5 Hypotheses

Hypothesis 5.1: SAPP+PERT will result in superior outcomes (i.e., quadriceps strength, patient reported outcomes, and single-leg hop testing) compared to SAPP alone among the women of the ACL-SPORTS trial.

Hypothesis 5.2: Female athletes who complete post-operative RTS training, compared to those who do not, will have higher functional outcomes and activity levels 2 years after ACLR.
10.6.3 Aim 5 Findings

There were no differences in any outcome measures between female athletes who received SAPP+PERT training compared to those who received SAPP training alone, refuting Hypothesis 5.1. Regardless of treatment group, however, athletes who received RTS training, compared to those who did not, had higher functional outcomes and activity levels 2 years after ACLR, supporting hypothesis 5.2. The findings suggest that adding a post-operative RTS training program, incorporating strengthening, agilities, and plyometrics but not necessarily perturbation training, may improve functional outcomes and activity levels among young female athletes after ACLR.

10.7 Clinical Implications and Future Directions

This dissertation work has helped answer important and clinically relevant questions pertaining to second ACL injury, early OA development, and functional outcomes after ACLR. The findings will guide physicians, rehabilitation specialists, and other healthcare professionals who rehabilitate the many individuals who tear their ACLs each year. Our findings indicate that athletes should delay their return to high level sport, even in the absence of clinical, functional, or gait impairments (Aim 1). Meniscus treatment, particularly partial medial meniscectomy, may alter gait patterns early and 2 years after ACLR, perhaps explaining the elevated risk for OA and informing future clinical interventions and rehabilitation programs (Aim 2). Unfortunately, the rehabilitation program we evaluated, return-to-sport training with and without perturbation training, did not improve walking mechanics (Aim 3), but did result in superior clinical and functional outcomes (Aim 5). The exploratory analysis suggests walking mechanics and especially walking speed may also influence patellofemoral OA (Aim 4), providing even greater motivation for future studies to evaluate gait specific interventions following ACLR.
This dissertation will help improve functional outcomes and reduce second injury rates for individuals after traumatic knee injury. It also furthers our understanding of the mechanisms associated with rapid OA development and progression after traumatic knee injury and offers avenues for investigating future, targeted interventions. The findings from the present study and follow-up analyses will ultimately improve outcomes and quality of life among individuals after traumatic knee injury.
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Appendix A

ON-ICE RETURN-TO-HOCKEY PROGRESSION AFTER ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION

A.1 Synopsis

Limited literature exists pertaining to rehabilitation of ice hockey players seeking to return-to-sport after anterior cruciate ligament reconstruction (ACLR). The purpose of this clinical commentary is to present a criterion-based, return-to-ice hockey progression for athletes after ACLR. First, we review pertinent literature and provide previously published guidelines on general rehabilitation after ACLR. Then, we present a four-phase, on-ice skating progression with objective criteria to initiate each phase. During the early on-ice phase, the athlete is reintroduced to specific demands, including graded exposure to forward, backward, and crossover skating. In the intermediate on-ice phase, the emphasis shifts to developing power and introducing anticipated changes of direction within a controlled environment. During the late on-ice phase, the focus progresses to developing anaerobic endurance and introducing unanticipated changes of direction, but still without other players or contact. Finally, once objective return-to-sport criteria are met, non-contact team drills, outnumbered and even-numbered drills, practices, scrimmages, and games are progressively reintroduced during the return-to-sport phase. Recommendations for off-ice strength and conditioning exercises complement the on-ice progression. Additionally, we apply the return-to-hockey progression framework to a case report of a female collegiate defensive ice hockey player who returned to sport successfully.
after ACLR. This criterion-based return-to-hockey progression may guide rehabilitation specialists managing athletes returning to ice hockey after ACLR.

A.2 Introduction

Approximately 250,000 anterior cruciate ligament (ACL) injuries occur each year in the United States,\textsuperscript{118} and around 130,000 individuals undergo ACL reconstruction (ACLR).\textsuperscript{162,192} After ACLR, only 55\% of athletes return to their pre-injury competitive level of sport.\textsuperscript{13} Second ACL injury rates of 20-30\% are reported,\textsuperscript{22,234,235} with younger athletes\textsuperscript{235,272,274,313} at especially high risk for re-injury. While ACL injuries are most prevalent in jumping, cutting, and pivoting sports (e.g., basketball and soccer), they also occur in other sports.\textsuperscript{210} ACL injuries are the third most common knee injury in international ice hockey,\textsuperscript{301,302} and account for 0.7\% of all injuries in women’s collegiate ice hockey.\textsuperscript{142} Recent data from professional men’s ice hockey players indicate career length and performance are adversely affected after ACL injury and reconstruction.\textsuperscript{279} As such, determining optimal rehabilitation programs for returning athletes to sport following ACL injury and reconstruction is essential.

Limited evidence exists to guide physical therapists and other rehabilitation specialists managing hockey players returning to sport after ACLR. Tyler and McHugh suggested the importance of utilizing neuromuscular rehabilitation, particularly perturbation training, to facilitate dynamic knee stability in an Olympic women’s ice hockey player returning to sport after ACLR.\textsuperscript{303} However, a comprehensive on-ice skating progression was not described. Pierce and colleagues developed an on-ice, six-phase skating progression for a goaltender following arthroscopic hip surgery for femoracetabular impingement.\textsuperscript{240} This progression, however, did not address the specific impairments associated with ACLR nor the demands of a skating (i.e., non-goalie) ice hockey player. Additional guidance for
returning athletes to ice hockey after hip adductor strain and other injuries provide some framework and drills to facilitate the on-ice progression; however, the on-ice phases are limited and do not specifically address deficits associated with ACLR.

Return-to-sport guidelines and graded exposures exist following ACLR for other sports. Both sports-specific drills and strength and conditioning exercises are essential to comprehensive rehabilitation. Given the limited availability of ice time experienced by many non-elite athletes (e.g., high school or collegiate club athletes), designing specific on- and off-ice rehabilitation training programs may be critical for returning to sport.

The purpose of this clinical commentary, therefore, is to present and describe a criterion-based return-to-hockey progression and accompanying off-ice strength and conditioning program. Additionally, we apply the return-to-hockey progression within a brief case report of a female collegiate club ice hockey defender following ACLR. Our goal is to provide clinicians a framework—including objective clinical measures—for the successful management of ice hockey players returning to sport after ACLR.

A.3 Early Rehabilitation after ACLR

Following ACLR, impairment resolution and biological healing must occur prior to initiating a return-to-sport progression. The focus of early rehabilitation is to restore full range of motion (ROM), resolve knee effusion, normalize gait, and promote quadriceps activation and neuromuscular control. Clinical commentaries draw heavily from systematic reviews and randomized controlled trials to provide detailed, criterion-based rehabilitation programs. These programs promote early weight-bearing, restoration of ROM, resolution of effusion and gait impairments, use of resistance training exercises, and use of high-intensity electrical
stimulation to treat quadriceps strength and activation deficits.\textsuperscript{161,283,284} Progression is based on both clinical milestones and healing time frames. Readers may consult these criterion-based rehabilitation programs\textsuperscript{4,150} and the complimentary MOON guidelines\textsuperscript{335} for general ACLR rehabilitation.

Monitoring knee effusion\textsuperscript{294} and joint soreness may guide appropriate progression of activity throughout rehabilitation. Performance and progression of activities in the presence of knee effusion or joint soreness likely have deleterious effects on long-term knee health. Accordingly, we permit initiation and progression of activity only when minimal or no effusion is present and only in the absence of joint soreness. The soreness rules, initially developed for weight-training modifications after upper extremity injury,\textsuperscript{93} have since been adapted for use after ACLR.\textsuperscript{4} While we are unaware of any empirical evidence supporting the efficacy of using knee effusion or joint soreness rules, we believe following these principles is prudent given the high risk of knee osteoarthritis after ACLR.\textsuperscript{186,187,228}

In addition to quadriceps strengthening, several other lower extremity muscles merit consideration for the ice-skating athlete. The forward stride in hockey combines hip extension, abduction, and external rotation, knee extension, and plantar flexion.\textsuperscript{38,239} Quadriceps muscle torque at both 90°/sec and 210°/sec is positively correlated with ice skating speed in 11 elite women.\textsuperscript{108} Higher peak activation and prolonged activation of the hip adductor magnus (relative to other thigh muscles) occurred at faster forward skating velocities in 7 collegiate players, highlighting the importance of hip adductor strength and abductor-adductor muscle balance.\textsuperscript{49} Exercises to address these muscles include: leg press with theraband around knees, single leg squats, single leg bridge, cable column hip abduction, adduction, and flexion, knee extensions (90°- 60° knee ROM initially, progressing gradually to 90° - 0°), and heel raises.
Lateral slide board training has been shown to be a beneficial adjunct to improving quadriceps strength following ACLR. Patients who performed slide board training as part of a home exercise program had greater peak isometric knee extension torque after training and a higher maximum lateral step height after training and compared to controls. While hip muscle strength was not assessed following this training, the similarity of the lateral slide board to ice skating makes it a potentially useful component of rehabilitation for hockey players. As such, we developed a hockey-specific lateral slide board progression (Table A.1) that considers the short interval nature of ice hockey. This progression may commence when an athlete is ≥8 weeks post-operative, has full knee ROM, trace or no effusion, and can complete the activity without knee joint soreness or increased effusion.

Table A.1 The lateral slide board progression may be initiated once the athlete is ≥8 weeks after surgery, has full knee range of motion, has minimal (i.e., trace) or no effusion, and can complete the activity without pain or increase in effusion. (Note: Week number is based on when the sliding board progression is initiated, not weeks after surgery.)

<table>
<thead>
<tr>
<th>Week</th>
<th>Effort</th>
<th>Work Interval (min:sec)</th>
<th>Rest Interval (min:sec)</th>
<th>Repetitions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>25 - 50%</td>
<td>:20</td>
<td>:40</td>
<td>6-8</td>
</tr>
<tr>
<td>2</td>
<td>50 - 75%</td>
<td>:30</td>
<td>1:00</td>
<td>8-10</td>
</tr>
<tr>
<td>3</td>
<td>75 - 100%</td>
<td>:45</td>
<td>1:30</td>
<td>10-12</td>
</tr>
<tr>
<td>4</td>
<td>100%</td>
<td>1:00</td>
<td>2:00</td>
<td>12-16</td>
</tr>
</tbody>
</table>

Neuromuscular training, including perturbation training, is also an important consideration for rehabilitating hockey players after ACL injury and reconstruction. Perturbation training is a type of neuromuscular training designed to improve knee stability and function during which the athlete stands on an unstable surface (e.g., rollerboard or rockerboard) and activates lower extremity muscles in response to surface perturbations applied by the physical therapist. Once an athlete
adapts to these demands, the physical therapist progressively challenges the athlete by providing more rapid and random perturbations and incorporating sport-specific activities. Pre-operative perturbation training improves muscle activation patterns, restores inter-limb symmetry during gait, and maintains strength and function after ACLR, but there is limited evidence on post-operative perturbation training. Tyler and McHugh adapted perturbation training to hockey-specific positions (e.g., forward stride) and surfaces (e.g., slide board for lower resistance) to improve knee stability in a female Olympic ice hockey player after ACLR. This case suggests that post-operative perturbation training may be a useful component of rehabilitation after ACLR and can be modified for the demands of ice hockey.

When an athlete is ≥12 weeks after ACLR and has surgeon clearance, he or she may initiate a running progression when objective criteria are met: full and symmetrical knee ROM, trace or less effusion, and ≥80% quadriceps strength index (QI). Given limitations of using manual resistance to assess quadriceps strength, we recommend using an electromechanical dynamometer; however, using a one-repetition maximum for knee extension is an acceptable alternative. Running progression advancement is based on the soreness rules and minimal or no effusion. Slide board training may continue on days when the athlete is not running.

A.4 Return-to-Hockey Progression

The return-to-hockey on-ice progression is broken down into four broad phases: early, intermediate, late, and return-to-sport. We present the purposes, criteria, and recommendations plus sample drills to progress the athlete back to sport.
A.4.1 Early On-Ice Phase

The purpose of the early on-ice phase is to gradually expose the athlete to the specific demands of skating. We recommend that objective criteria be met prior to initiating this and each subsequent phase of the return-to-hockey progression (Table A.2). We also recommend following the soreness rules\textsuperscript{4,93} throughout rehabilitation to monitor potential symptom exacerbation and modifying accordingly.

The early on-ice phase is divided into four sub-phases (Table A.3), each at least one week in duration. Increased intensity and more challenging maneuvers are progressively introduced. For example, an athlete first uses the inside skate edges while forward skating during sub-phase A, and further incorporates this skill using C-cuts during drill sessions in sub-phase B (supplemental video 1, on-ice drills). Crossovers in both directions are introduced in a drill setting (e.g., half circles progressing to full circles). We recommend gradually increasing the total ice time during each sub-phase according to player level, while monitoring knee effusion and soreness. Initially, skating should not occur more frequently than every other day.

Off-ice rehabilitation should include continued strengthening and running as well as initiation of agility drills 2-3x/week. Developing muscle strength and hypertrophy are the primary focus in this phase of the strengthening program to provide a base to develop power in subsequent phases. If strength deficits persist (i.e., the involved limb strength is <90\% of the uninvolved limb), an athlete may perform an additional set with the involved limb. Off-ice agility drills (Table A.4) may commence at this time, gradually progressing in intensity. Drop jumps with proper form and landing technique should be completed\textsuperscript{321} prior to initiating higher level jumping drills (e.g., tuck jumps, split-squat plyometric jumps). The athlete should continue to perform the running progression (on alternate days as the on-ice skating progressing) using the soreness rules to guide progress. Continued lateral slide board training may
complement on-ice skating, particularly if ice-time is limited. An ACL brace may be worn during running, agility drills, and (early) on-ice skating. While limited and conflicting evidence exists regarding the efficacy of wearing an ACL brace,\textsuperscript{72,112,168,200,293} many physicians prescribe its use for at least 9-12 months post-ACLR,\textsuperscript{72,112} thus acclimating to wearing it is essential for some athletes. The ACL brace presents a unique challenge to the rehabilitating hockey player, who is unable to wear it and traditional padding (i.e., shin pads) simultaneously. Therefore, we recommend on-ice use of an ACL brace only when prescribed by the physician.
Table A.2 General guiding principles for on-ice hockey progression.

<table>
<thead>
<tr>
<th>Phase</th>
<th>Purpose</th>
<th>Criteria for Initiating Phase</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early On-Ice</td>
<td>Gradually expose the athlete to the specific demands of skating</td>
<td>≥16 weeks after (primary) ACLR and physician clearance</td>
<td>Follow the soreness rules&lt;sup&gt;4,93&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Trace or less effusion</td>
<td>Stick is optional</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Full knee ROM</td>
<td>No more often than every other day</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥80% QI</td>
<td>Each sub-phase should last ≥1 week</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Running progression&lt;sup&gt;4&lt;/sup&gt; level 4&lt;sup&gt;*&lt;/sup&gt; without increase in knee effusion or soreness</td>
<td>and be performed ≥2x prior to progression to the next sub-phase</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Stick is optional</td>
<td>Off-ice strengthening (&lt;table A.4&gt;) 2-3x/week: muscle strength and hypertrophy emphasis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intermediate</td>
<td>Develop power and initiate anticipated changes of direction</td>
<td>≥20 weeks after (primary) ACLR and physician clearance</td>
<td>Stick recommended</td>
</tr>
<tr>
<td>On-Ice Phase</td>
<td></td>
<td>Completion of early phase without increase in effusion or soreness</td>
<td>Once able to complete drills in this phase with proper form,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥85% QI</td>
<td>incorporate puck handling, then passing and eventually shooting</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥75% LSI on all 4 hop tests</td>
<td>Complete off-ice strengthening and agility program (&lt;table A.4&gt;)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Late On-Ice</td>
<td>Develop anaerobic endurance and initiate unanticipated changes of</td>
<td>≥6 months after (primary) ACLR and physician clearance</td>
<td>Complete off-ice strengthening, agility, and power exercise program (&lt;table A.4&gt;)</td>
</tr>
<tr>
<td>Phase</td>
<td>direction without contact</td>
<td>Completion of intermediate phase for ≥2-4 weeks without an increase in effusion or soreness</td>
<td>Progress on-ice drills to incorporate unanticipated changes in direction, slap shots and one-timers</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Running interval training&lt;sup&gt;304&lt;/sup&gt;</td>
</tr>
<tr>
<td>Return-to-Sport</td>
<td>Return to non-contact and contact drills, scrimmages, and games</td>
<td>≥9 months after (primary) ACLR and physician clearance</td>
<td>Initiate noncontact drills with teammates first, progressing to outnumbered situations, even-numbered</td>
</tr>
<tr>
<td>Phase</td>
<td></td>
<td>≥90% QI</td>
<td>situations, scrimmages, and finally games</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥90% Hip strength LSI for hip extension, external rotation, abduction, and adduction</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥90% LSI on all 4 hop tests</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>≥90% KOS-ADLS</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥90% Global Rating</td>
<td></td>
</tr>
</tbody>
</table>

<sup>*</sup> Level 4 Running Progression:<sup>4</sup> alternate jogging 700 meters and walking 100 meters for 3.2 kilometers (2 miles)

Abbreviations: ROM=range of motion (knee flexion and extension); QI=quadriceps strength index; ACLR=anterior cruciate ligament reconstruction; LSI=limb symmetry index (involved/uninvolved); KOS-ADLS=Knee Outcome Survey-Activities of Daily Living Scale<sup>146</sup>
Table A.3 Representative on-ice activities and drills during the early, intermediate, late, and return-to-sport phases of the on-ice skating progression (*supplemental video 1, on-ice drills*). The drills are not meant to be all-encompassing but rather provide a framework for appropriate progression. (*Complete Early Phase on empty ice.)

<table>
<thead>
<tr>
<th>Early*</th>
<th>Intermediate</th>
<th>Late</th>
<th>Return-to-Sport</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sub-phase A:</td>
<td>Transitions and form:</td>
<td>Anaerobic training with direction changes:</td>
<td>Non-contact team drills (e.g., passing drills, dump-ins, shooting drills, etc.)</td>
</tr>
<tr>
<td>Forward skating: 25% effort with hockey turns (i.e., no crossovers)</td>
<td>Between blue-lines transitions—pivoting forward/backward</td>
<td>Between blue-line sprinting “Suicide” sprints</td>
<td>Outnumbered situations: 3 vs. 1, 2 vs. 1, 3 vs. 2</td>
</tr>
<tr>
<td>E.g., 8-10 x 60-90” skating with 20-30” rest (alternating direction each interval)</td>
<td>Half ice→full ice transition drills</td>
<td></td>
<td>Progress to 1 vs. 1 and corner drills</td>
</tr>
<tr>
<td>Drills: none</td>
<td>Transition Circles—always facing one end of the ice</td>
<td>Agilities: Crossovers with stops</td>
<td>Progress to full participation in team practice</td>
</tr>
<tr>
<td>Duration: ≤20 minutes total</td>
<td>Tight circles around cones/dots</td>
<td>Crossovers with sprints and stops</td>
<td>Progress to scrimmages</td>
</tr>
<tr>
<td></td>
<td>Use both inside/outside edges</td>
<td>Iron cross drill</td>
<td>Progress to games</td>
</tr>
<tr>
<td></td>
<td>Forwards/ backwards/ pivoting</td>
<td>Reaction drills</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Power: Power strides with pauses (forward and backward)</td>
<td>Quick starts and stops</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Increase depth and power</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Resisted partner pull drill</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sub-phase B:</td>
<td>Puck Skills: Incorporate puck-handling with drills as athlete progresses (e.g., circles, figure 8 drill, puck-handling around cones, etc.)</td>
<td>Puck Skills: Passing Drills with Coach</td>
<td></td>
</tr>
<tr>
<td>Forward skating: 50% effort with hockey turns</td>
<td>Introduce submaximal wrist and snap shots (e.g., circles with shot at end)</td>
<td>Break out routes</td>
<td></td>
</tr>
<tr>
<td>Backwards skating: 25% effort</td>
<td></td>
<td>Passing while skating forward/backward</td>
<td></td>
</tr>
<tr>
<td>Drills: Single, double, and alternating C-cuts (forward and backward); Half circles with crossovers at 25-50% effort</td>
<td></td>
<td>Shuttle passing</td>
<td></td>
</tr>
<tr>
<td>Duration: 30 minutes total</td>
<td></td>
<td>Neutral zone regroup routes</td>
<td></td>
</tr>
<tr>
<td>Sub-phase C:</td>
<td></td>
<td>Shooting Drills with Coach</td>
<td></td>
</tr>
<tr>
<td>Forward skating: 75% effort</td>
<td></td>
<td>Give and Go’s—corner, half-wall, blue line</td>
<td></td>
</tr>
<tr>
<td>Backwards skating and crossovers: 50% effort</td>
<td></td>
<td>Catch and shoot</td>
<td></td>
</tr>
<tr>
<td>Drills: Full circles at 50-75% effort; 3 stride starts; Figure 8 drill; Incorporate puck-handling</td>
<td></td>
<td>Slap shots</td>
<td></td>
</tr>
<tr>
<td>Duration: 30-45 minutes total</td>
<td></td>
<td>One-timers</td>
<td></td>
</tr>
<tr>
<td>Sub-phase D:</td>
<td></td>
<td>Blue line push/drag</td>
<td></td>
</tr>
<tr>
<td>Forward skating: 75-90% effort</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Backwards skating and crossovers: 50-75% effort</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drills: 1 leg endurance drill; Increase effort with figure 8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration: 30-60 minutes total</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table A.4 Off-ice strength and conditioning program (*supplemental video 2*, agility drills and skater jumps).

| Strength | Agility (2-3x/week) | Power | Endurance & Speed:
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Triple Threat physio ball series (<strong>FIGURE 1</strong>)</td>
<td>Agility Drills/Agility Ladder: high knees, butt kicks, side shuffles, carioca, etc.</td>
<td>Skater jumps</td>
<td>Track Intervals: 200 meter run at 90-100% effort with 200 meter recovery jog (8-12 intervals)</td>
</tr>
<tr>
<td>Single leg squat or split-squat</td>
<td>Lateral line hops</td>
<td>Tuck jumps</td>
<td>Sprint Intervals: 4-6 sets of 6x30 meter sprints at max effort starting every 30 seconds with 2 minutes rest intervals between each set</td>
</tr>
<tr>
<td>Stride-length lunges (<strong>FIGURE 2</strong>)</td>
<td>Jump Rope: two feet, one foot, double jumps, forward/backward, side-to-side, etc.</td>
<td>Split-squat plyometric jumps</td>
<td></td>
</tr>
<tr>
<td>Single leg Romanian Deadlifts or Nordic Hamstrings</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single leg heel raises</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hip adduction, abduction, and flexion at cable column</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Core stability: planks, side planks, planks with alternating leg lifts, single-leg bridges</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*During the early phase, develop strength (e.g., 3-4 sets of 8-12 reps). During the intermediate, late, and return-to-sport phases, emphasize power (e.g., 4-5 sets of 4-6 reps).

†Gradually progress from 50% to 100% effort over about 10 sessions per soreness rules.

‡Start with 2-3 sets of 8-10 reps and progress to 3-4 sets of 10-15 reps with increased intensity; 30”-60” rest intervals.

§Start with 15-20” intervals with 15” rest, progressing to 30” to 45” intervals with 10-15” rest.
A.4.2 Intermediate On-Ice Phase

Athletes may concurrently perform the off-ice strength and conditioning program targeting strength, agility, power, and endurance (Table A.4). This program (2-3x/week) complements the on-ice progression and provides sample exercises addressing the specific demands of hockey, including core stability (e.g., planks, side-planks, and triple-threat physio-ball series [Figure A.1a-f]), squats, stride-length lunges (Figure A.2), agilities, and plyometrics. Additionally, once the athlete is able to run three miles without knee symptoms, running interval training may commence, particularly if on-ice availability is limited.
Figure A.1a-f The Triple Threat physio ball series consists of straight leg hip extensions [(a) start and (b) end position], hamstring curls [(c) start and (d) end position], and flexed knee hip extensions [(e) start and (f) end position].
Figure A.2 Stride-length lunges combine the skating stride with a lunge position (note the wider stance and externally rotated left limb). A barbell, dumbbells, or medicine ball may be added for resistance.

A.4.3 Late On-Ice Phase

The purpose of the late on-ice phase is to improve anaerobic endurance and introduce unanticipated changes of direction without contact. During the late phase, progressively challenging drills such as blue line sprinting and “suicide” sprints are introduced to target anaerobic endurance. Unanticipated changes of direction—dictated by visual or audio stimuli—require the athlete to react and respond in a manner resembling competition. Passing and shooting drills progress in complexity to further simulate these unanticipated changes in direction. Shooting drills progress to incorporate slapshots and “one-timers” (i.e., shooting the puck without stopping it first). We recommend ≥2-4 weeks in this phase prior to initiating team drills or contact situations, which begin in the return-to-sport phase. However, if the athlete has
progressed quickly through the phases up to this point, he or she should remain in the late phase and not progress to the return-to-sport phase until being ≥9 months post-operative. Our recommendation to delay return-to-sport clearance until ≥9 months after primary ACLR is based on evidence from Grindem and colleagues, who found a 51% increase in re-injury risk for each month an athlete returned to sport before nine months post-operatively.121 Recent evidence from a separate cohort of athletes after ACLR further supports delaying return-to-sport clearance until ≥9 months post-operatively even in the absence of clinical or biomechanical gait impairments.45 Further delay (i.e., ≥10-12 months post-op) is likely warranted for allografts or revision surgeries due to higher risk of graft rupture in allograft (versus autograft) ACLR220,310,334 and poorer outcomes and higher risk of re-injury in revision (versus primary) ACLR.113,334

A.4.4 Return-to-Sport Phase

Once objective criteria are met (Table A.2), athletes may begin the return-to-sport phase, during which they gradually return to team drills, practices, and games. During this final phase, athletes first participate in noncontact team drills (e.g., passing drills, shooting drills, unopposed break-out drills). Outnumbered situations (i.e., three vs. one and two vs. one) are the first “live” drills for the athlete to initiate, with the rehabilitating player in either the majority or minority group, depending on position (i.e., offense vs. defense). While this may be counterintuitive to those unfamiliar with hockey, outnumbered drills have inherently less risk for contact, thus are initiated first. Next, graded exposure to contact continues through one-on-one and corner drills. An athlete next participates in full practice followed by scrimmages and finally games. Progression through the return-to-sport phase should take ≥4-6 weeks, although individual differences (e.g., longer time periods for allograft reconstruction150 or
younger athletes must be considered. Successful completion of each step within this phase should occur before unrestricted return-to-sport clearance.

### A.4.5 Case Description and Application

Informed consent was obtained from the patient, and her rights were protected. An 18-year-old female collegiate club ice hockey player sustained a left ACL injury after falling approximately 3 meters (10 feet) rock climbing. The patient was diagnosed via magnetic resonance imaging and physical exam with a full-thickness ACL rupture, medial and lateral meniscal tears, and a partial lateral collateral ligament sprain. The patient underwent ACLR (Bone Patellar-Tendon Bone), medial meniscal repair, and partial lateral meniscectomy 2 weeks after injury. The patient received post-operative physical therapy according to current concepts for ACLR rehabilitation. Timeframes were slightly prolonged in part due to the concomitant meniscal involvement and the patient’s initial toe-touch-weight-bearing status. Approximately 4.5 months post-ACLR, she met the criteria to begin running. The patient began the running progression and a strengthening program, including lateral slide board exercises, to perform on her own while away on summer break with periodic check-ins (1-2x/month). Progress was delayed due to limited time and intermittent gym access. Approximately 7 months post-operatively, the patient could run 2 miles symptom-free while maintaining full ROM and minimal effusion. At this time, she initiated 10 sessions (2x/week) of strengthening, agility, and neuromuscular training.

Following the first of these sessions and without increase in soreness or effusion, the patient began the early phase of the on-ice skating progression. She progressed through the early sub-phases while concurrently completing 10 strengthening, agility, and neuromuscular training sessions. During the early on-ice phase, the athlete skated on an open ice rink wearing her ACL brace; she did not carry
her stick initially. She had no increase in knee joint soreness, pain, or effusion following her first time on the ice, although she did experience muscle soreness the next day. The athlete began doing crossovers during the second week of skating, which led to a mild increase in knee soreness the following day, thus leading to at least one day off and no increase in intensity or level as per the soreness rules.\(^4,93\) The athlete was performing three stride starts and skating for a total of 40 minutes by the end of her third week back on the ice, and added her stick and puck with drills by the fourth week, during which she logged 45 minutes on-ice per session. Throughout the early on-ice phase, she skated approximately 2x/week, which was limited by ice availability. She continued running, but did not progress beyond jogging two miles due to motivation.

Approximately 8.5 months post-ACLR (5-6 weeks after beginning to skate), we reassessed her lower extremity strength and functional symmetry and patient-report outcomes (Table A.5). The athlete initiated on-ice transitions drills and power drills. Additionally, she began the off-ice strength program and additional hip strengthening exercises (given deficits in adduction and abduction), including hip adduction and abduction cable column exercises.

After approximately one month of progressing through the intermediate phase (9.5 months post-ACLR) and completing off-ice strength and conditioning, the athlete returned for follow-up testing. Noting improvements in inter-limb hip strength symmetry and progression through the intermediate phase without increase in effusion or soreness, we cleared her to initiate the late on-ice phase. Her on-ice sessions focused on addressing persistent challenges, including lateral crossovers, outside edge stopping, shooting and stabilizing shots on her involved limb, tight turns, fakes (i.e., “dekes”), and unanticipated movements. Drill emphases during this time included various reaction drills, stepping-up and crossing-over to alternate sides (e.g., Iron
Cross drill), and dragging the puck into slapshots (given persistent challenge stabilizing with her involved limb during the shooting motion).

Approximately 11 months after ACLR, the athlete achieved all criteria to initiate the return-to-sport phase. At this time, she initiated non-contact team drills followed by out-numbered and then even-numbered situations. After one month, she was participating fully in practices. She played her first game approximately 13 months after ACLR. The athlete’s initial return to play was in a recreational league since it was the collegiate hockey off-season. During the following collegiate hockey season, she returned to her previous competitive level of sport. At 22 months post-operatively, she continued to play without re-injury and completed several outcome measures (Table A.5). Her Knee Injury and Osteoarthritis Outcome Score255 subscale scores are similar to or higher than Delaware-Oslo ACL Cohort and Multicenter Orthopaedic Outcomes Network (MOON) scores among subjects two years after ACLR.91
Table A.5 Case example of the objective measures obtained prior to initiating each phase; note that most, but not all, criteria were met as the formal hockey progression was developed alongside and after this athlete progressed through rehabilitation.

<table>
<thead>
<tr>
<th>Timeframe</th>
<th>Phase/Time</th>
<th>Selected Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>7 months post-op</td>
<td>Early</td>
<td>- Effusion: trace</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- ROM: full</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Pain: minimal to none (0-1/10 on numeric pain rating scale)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Level 5 of running progression (i.e., jogging 2 miles)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Quad Strength Index: 88%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- KOS-ADLS: 80%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Global Rating: 70%</td>
</tr>
<tr>
<td>8.5 months post-op</td>
<td>Intermediate</td>
<td>- Quad Strength Index: 97%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Hip Strength LSI: Flexion: 98%, Extension: 94%, Abduction: 84% Adduction: 67%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Hop Testing LSI, braced: Single hop: 75%, Crossover hop: 84%, Triple hop: 82%, Timed hop: 77%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- KOS-ADLS: 87%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Global Rating: 85%</td>
</tr>
<tr>
<td>9.5 months post-op</td>
<td>Late</td>
<td>- Hip Strength LSI: Flexion: 100%, Extension: 98%, Abduction: 96%, Adduction: 80%, External rotation: 81%, Internal rotation: 91%</td>
</tr>
<tr>
<td>11 months post-op</td>
<td>Return-to-Sport Phase</td>
<td>- Quad Strength Index: 94%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Hop Testing LSI, braced: Single hop: 97%, Crossover hop: 104%, Triple hop: 102%, Timed hop: 108%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- KOS-ADLS: 93%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Global Rating: 95%</td>
</tr>
<tr>
<td>22 months post-op</td>
<td>Follow-up Outcome Measures</td>
<td>- KOS-ADLS: 96%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Global Rating: 99%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- KOS-Sport: 87%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- KOOS composite score: 94%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- KOOS subscale scores: Symptoms/Stiffness: 93%, Pain: 94%, Activities of Daily Living: 100%, Sport/Recreation: 75%, Quality of Life: 75%</td>
</tr>
</tbody>
</table>

Abbreviations: ROM=range of motion (knee flexion and extension); KOS-ADLS=Knee Outcome Survey—Activities of Daily Living Scale; LSI=limb symmetry index (involved/uninvolved); KOS-Sport=Knee Outcome Survey—Sports Activity Scale; KOOS=Knee Injury and Osteoarthritis Outcome Score
A.4.6 Discussion

To our knowledge, this is the first article to describe a criterion-based on-ice skating progression for hockey players seeking to return-to-sport following ACLR. The return-to-hockey progression gradually exposes athletes to sport-specific demands using time- and criterion-based guidelines. Over the course of the four-phase progression, athletes acclimatize to skating, integrate anticipated and unanticipated changes of direction, and receive graded exposure to team drills, contact situations, practice, and ultimately games. The phases of the on-ice skating progression are accompanied by an off-ice strength and conditioning program to be performed with the latter phases of the on-ice progression. The return-to-hockey progression may provide clinicians with a criterion-based framework to guide ice hockey players back to sport following ACLR.

Our recommendations for return-to-sport criteria are based on previous literature utilizing a criterion-based approach, which has been validated recently. We also include the consideration of hip strength, which is essential to the ice hockey player. Notably, hip adductor strength is critical to the forward stride, and hip extension and external rotation are essential to propulsion. We suggest that an athlete have at least 90% hip strength symmetry based on other objective criterion-based approaches using 90% symmetry in other lower extremity muscle groups after ACLR. While hopping is not commonly performed during ice hockey, hop testing is used as an objective measure to evaluate functional limb symmetry after ACL injury or reconstruction, thus supporting its inclusion.

There are limitations to this clinical commentary, most notably that the return-to-hockey progression has not been rigorously tested. It is based on the best evidence from a variety of sources, but is still only expert opinion. Consequently, the implications of the return-to-hockey progression on future knee injury risk and long-
term function, including the risk for knee osteoarthritis, are unknown. However, in the absence of higher-level evidence, we believe this return-to-hockey progression may be a useful tool to guide clinicians. The case study—which was the impetus in developing the progression—illustrates how an athlete may progress safely through the program and return to competitive sport successfully. While the case study athlete had co-morbidities and other factors that complicated her rehabilitation process, her 22-month outcomes compared favorably to recently published data from large cohorts.91 It is likely that athletes with isolated ACL injuries could initiate the early on-ice phase sooner (i.e., ≥16 weeks versus 7 months post-operatively) and complete the entire program earlier. Nevertheless, even for the uncomplicated athlete, we recommend not initiating the return-to-sport phase until at least 9 months post-operatively due to increased risk of re-injury for returning to sport before this time-frame, even in the absence of impairments.45,121 Finally, while the program was designed specifically for the athlete after ACLR, many aspects of the return-to-hockey progression could apply to athletes returning to hockey after other knee injuries (e.g., MCL sprains), just with different time-frames based on severity of injury and healing time.

A.4.7 Acknowledgments

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THE CURRENT MANAGEMENT OF PATIENTS WITH PATELLOFEMORAL PAIN FROM THE PHYSICAL THERAPIST’S PERSPECTIVE

B.1 Abstract

Patellofemoral pain is a common diagnosis that includes an amalgam of conditions that are typically non-traumatic in origin and result in peripatellar and/or retropatellar knee pain. The purpose of this review is to provide an overview of the physical therapist’s management, including the evaluation and treatment, of the patient with patellofemoral pain. A thorough history is critical for appropriately diagnosing and optimally managing patellofemoral pain; the history should include the date of symptom onset, mechanism of injury and/or antecedent events, location and quality of pain, exacerbating and alleviating symptoms, relevant past medical history, occupational demands, recreational activities, footwear, and patient goals. Physical examination should identify the patient’s specific impairments, assessing range of motion, muscle length, effusion, resisted isometrics, strength, balance and postural control, special tests, movement quality, palpation, function, and patient reported outcome measures. Objective assessments should guide treatment, progression, and clinical decision-making. The rehabilitation program should be individually tailored, addressing the patient’s specific impairments and functional limitations and achieving the patient’s goals. Exercise therapy, including hip, knee, and core strengthening as well as stretching and aerobic exercise, are central to the successful management of patellofemoral pain. Other complimentary treatments may include patellofemoral and tibiofemoral joint mobilizations, patellofemoral taping, neuromuscular training, and
gait retraining. Appropriate progression of interventions should consider objective evaluations (e.g., effusion, soreness rules), systematic increases in loading, and the chronicity of symptoms. Although short-term changes or reductions in movement often are necessary in a protective capacity, the persistence of altered movement is a key characteristic of chronic pain, which may be managed in part through emphasis on function over symptoms, graded exposure, patient education, and perhaps referral. Patellofemoral pain etiology is largely movement related and a comprehensive conservative treatment using movement can be successful.

**B.2 Introduction**

Patellofemoral pain is exceedingly common. Annual prevalence for patellofemoral pain approaches 23% in the general population and is approximately 29% among adolescents, with female athletes being at particularly high risk. Participation in recreationally running or military training, both of which may lead to high patellofemoral joint contact forces, is associated with an especially high incidence of patellofemoral pain. Persistent symptoms are common and 57% of individuals with patellofemoral pain report unfavorable outcomes five to eight years after their initial diagnosis. As such, it is important for individuals with patellofemoral pain to receive optimal rehabilitation with the goal of achieving positive short- and long-term outcomes and preventing the transition from a transient, acute episode into a recurrent, chronic problem.

The purpose of this review is to provide an overview of the physical therapist’s management, including the evaluation and treatment, of the patient with patellofemoral pain. We begin with a brief overview of symptom onset, then discuss the importance of considering the complexities of the painful experience when rehabilitating individuals with patellofemoral pain, particularly among those with episodic or recalcitrant symptoms. We then present our rehabilitation approach for a
systematic physical therapy examination including a thorough subjective history and objective clinical, functional, and patient-reported outcome measures. Finally, we present a comprehensive treatment approach that draws heavily from recently published literature and clinical trials.

B.3 Symptom Onset

Patellofemoral pain, or anterior knee pain, is an amalgam of conditions that are typically non-traumatic in origin and result in peripatellar and/or retropatellar knee pain. A number of structures in and around the patellofemoral and tibiofemoral joints, such as the synovium or infrapatellar fat pad, may individually or collectively contribute to patellofemoral pain. The patellofemoral articular cartilage itself, however, is not painful when probed directly sans anesthesia, likely due to its lack of free nerve endings. While a variety of factors may also contribute to symptom onset, disruption of tissue homeostasis via acute injury or repetitive overloading (i.e. high-frequency moderate loading or an isolated very high loading event) may exceed tissue homeostasis, or the envelope of function, for a given structure(s) and lead to pathology and pain. Conservative management may initially promote relative rest and avoidance of activities that exacerbate the patient’s pain while attempting to limit loss of muscle strength, range of motion, or function. Patellofemoral pain, however, often persists for months or even years, requiring a more complex rehabilitation approach.

B.4 The Complex Pain Experience

Throughout the successful management of patellofemoral pain and especially when symptoms are chronic in nature, rehabilitation specialists must appreciate the complexity of the pain experience. In his 2016 Maley Lecture, physical therapist and pain science researcher Steven George, PT, PhD, calls for a shift in physical
therapist education, research, and clinical practice from the traditional direct link among pain, nociception, and injury to a more inclusive biopsychosocial model that incorporates pain with movement. Healthcare professionals must consider not only the patient’s underlying knee pathology (e.g., structural abnormalities, muscle dysfunction) but also the patient’s psychological distress and pain neurophysiology when evaluating the clinical pain experience. In chronic musculoskeletal conditions, as can often become the case with patellofemoral pain, symptoms may outlive their usefulness; although no clear definition exists, chronic pain is generally described as pain that lasts “beyond the body’s usual healing time” and is typically three months or greater. Clinicians must recognize the difference between acute (protective) pain and chronic pain, which may limit function and inhibit progress. Encouraging regular movement and exercise within the pain-free envelope of function and, when appropriate, such as in the chronic case, even beyond the pain-free range, may be necessary to optimize function in patients with patellofemoral pain. In such cases, graded exposure may help maximize function even in the absence of full symptom resolution.

Conscientious monitoring and progression of interventions and other activities throughout rehabilitation is thus essential to achieving optimal outcomes. The remainder of this review article will delineate strategies for conducting a thorough evaluation and creating an appropriate, progressive, and individualized treatment approach for patellofemoral pain.
B.5 Evaluation

B.5.1 History

A thorough history is critical for appropriately diagnosing \(^7^1\) and optimally managing patellofemoral pain \(^3^1^9\). While one may accurately identify the relatively young, active woman with atraumatic onset of anterior knee pain as the most likely candidate, men and women of all activity levels across a wide age range may develop patellofemoral pain \(^6^1\). The rehabilitation specialist should ask the patient to identify the date of symptom onset, mechanism of injury and/or antecedent events, location and quality of pain, exacerbating and alleviating symptoms, relevant past medical history including prior lower extremity and low back symptoms, diagnostic imaging, occupational demands, recreational activities, footwear including use of orthotics, and patient goals (Table B.1). Pertinent past medical history may include not only previous knee symptoms but also ankle, hip, and lumbar pain, as radiculopathy from the spine to the knee is possible. Referred knee pain may be present due to hip pathology, such as osteoarthritis or predominantly pediatric conditions like slipped capital femoral epiphysis \(^1^3^2, ^1^3^5\), thus subjective questioning and physical examination should consider the hip, particularly when the practitioner is unable to provoke the patient’s symptoms during a thorough, targeted knee evaluation. Gradual and even insidious onset of anterior knee pain are common in patellofemoral pain whereas acute onset of knee pain secondary to a traumatic event merits further evaluation of the integrity of the knee ligaments, tendons, menisci, and bone. Clinicians should refer their patients to an appropriate specialist if they suspect serious pathology (e.g., fracture or osteomyelitis) or non-musculoskeletal origin (e.g., cancer or infection) due to the presence of red flags (i.e., fever, unremitting night pain, or increased
temperature and swelling around the knee; or, among adolescents or children, a leg length discrepancy, limp, and limited hip range of motion possibly indicative of Perthes disease or a slipped capital femoral epiphysis) \(^6\). Physician referral is also warranted in the case of unremitting or worsening symptoms despite appropriate physical therapy and activity modification.

**B.5.2 Clinical Examination**

Physical examination should incorporate a variety of measures including range of motion (ROM), muscle length, effusion, resisted isometrics, strength, balance and postural control, movement quality assessments, special tests, palpation, functional evaluation, and patient reported outcome measures. Objective assessments should guide treatment, progression, and clinical decision-making. An individualized rehabilitation program that addresses the patient’s specific impairments and functional limitations is regarded as best practice \(^6\).
Table B.1 A thorough patient history should include the following questions.

<table>
<thead>
<tr>
<th>Questions</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of onset</td>
<td></td>
</tr>
<tr>
<td>Mechanism of injury (traumatic vs. atraumatic):</td>
<td></td>
</tr>
<tr>
<td>If atraumatic, sudden or gradual onset? What factors led to symptoms</td>
<td>If traumatic, consider and evaluate thoroughly for alternative</td>
</tr>
<tr>
<td>(i.e., any changes in activity</td>
<td>diagnoses including ligament</td>
</tr>
<tr>
<td>level, exercise, footwear, stress levels, sleep habits,</td>
<td>sprain, meniscus tear, fracture, etc.</td>
</tr>
<tr>
<td>diet or body mass)?</td>
<td></td>
</tr>
<tr>
<td>If traumatic, describe event in detail including presence of swelling</td>
<td></td>
</tr>
<tr>
<td>and time to swelling onset.</td>
<td></td>
</tr>
<tr>
<td>Chief complaint (location and quality of pain):</td>
<td></td>
</tr>
<tr>
<td>Exacerbating factors (e.g., stair descent, squatting)?</td>
<td></td>
</tr>
<tr>
<td>Alleviating factors (e.g., ice, heat, rest, stretching)?</td>
<td></td>
</tr>
<tr>
<td>Are other symptom(s) present?</td>
<td>If true giving way episodes are present, consider ligament exam; if</td>
</tr>
<tr>
<td>If yes, any giving way/buckling,</td>
<td>locking is present, consider</td>
</tr>
<tr>
<td>Diagnostic tests and imaging</td>
<td></td>
</tr>
<tr>
<td>Relevant past medical history (e.g., previous lower extremity injury,</td>
<td>If history of back pain or unable to elicit symptoms during targeted</td>
</tr>
<tr>
<td>previous back pain with or without radiculopathy)</td>
<td>knee evaluation, perform lumbar and spinal radiculopathy examination.</td>
</tr>
<tr>
<td></td>
<td>Consider also the hip joint as a source of knee pain, particularly in</td>
</tr>
<tr>
<td></td>
<td>the child \textsuperscript{132,135} or older adult.</td>
</tr>
<tr>
<td>Has the patient received any prior treatment? If so, describe in detail.</td>
<td></td>
</tr>
<tr>
<td>What are the patient’s occupational demands?</td>
<td></td>
</tr>
<tr>
<td>What recreational activities does the patient typically engage in?</td>
<td></td>
</tr>
<tr>
<td>Are these activities limited? If so, how?</td>
<td></td>
</tr>
<tr>
<td>Describe footwear and orthotic use</td>
<td>Examine footwear and orthotics for wear and irregularities.</td>
</tr>
<tr>
<td>Goals for rehabilitation</td>
<td></td>
</tr>
</tbody>
</table>
B.5.3 Range of Motion (ROM) and Muscle Length Testing

ROM of the knee as well as the ankle and hip should be assessed. The physical therapist should evaluate at a minimum both active and passive ROM measurements of tibiofemoral flexion and extension, talocrural dorsiflexion, and femoroacetabular extension, internal and external rotation, and flexion; other motions (e.g., hip abduction and adduction) or joints (e.g., subtalar eversion and inversion and lumbar flexion and extension) may also be considered.

Muscle length testing is also an important consideration as soft tissue tightness (i.e., limited flexibility) is prevalent in individuals with patellofemoral pain and may contribute to symptoms. Evaluation of the rectus femoris, hip flexors (1- and 2-joint muscles), tensor fascia lata and iliotibial band, hamstrings, gastrocnemius, and soleus should be performed.

B.5.4 Effusion

Knee joint effusion can easily be evaluated using the stroke test (Table B.2). The stroke test is a reliable grading scale that assesses the presence of intracapsular swelling. While effusion is not often present, mild effusion can occur among individuals with patellofemoral pain; significant effusion is likely indicative of more serious pathology (e.g., ligament rupture, meniscus tear, fracture) and merits further evaluation. Effusion monitoring may help determine appropriate clinical progression. Increased effusion can indicate when rehabilitation has exceeded the patient’s current envelope of function and thus rehabilitation exercises or activity should be reduced or not progressed further. Tracking or asking the patient about outside activities is critical in determining whether or not the prescribed exercises or home exercise program contributed to an exacerbation of effusion and/or other symptoms or whether other factors are more likely culpable. For example, asking a student about
activities such as walking around school or campus or attending a party may be pertinent. The use of activity trackers to monitor movement outside of therapy is becoming increasingly possible and should be considered as a more accurate way to quantify activity and joint loading.


<table>
<thead>
<tr>
<th>Grade</th>
<th>Test Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zero</td>
<td>No wave produced on downstroke</td>
</tr>
<tr>
<td>Trace</td>
<td>Small wave on medial side with downstroke</td>
</tr>
<tr>
<td>1+</td>
<td>Larger bulge on medial side with downstroke</td>
</tr>
<tr>
<td>2+</td>
<td>Effusion spontaneously returns to medial side after upstroke (no downstroke necessary)</td>
</tr>
<tr>
<td>3+</td>
<td>So much fluid that it is not possible to move the effusion out of the medial aspect of the knee</td>
</tr>
</tbody>
</table>

### B.5.5 Resisted Isometrics

Resisted isometrics at various angles of knee flexion may be used during the early portions of the clinical examination to determine what type of structure(s) is most likely involved. A finding of “strong and painful” with resisted isometric knee extension is most likely to support the diagnosis of patellofemoral pain, although weakness is also possible, particularly in the acute phase (pain-mediated) or in long-standing, chronic cases. The clinician should evaluate resisted isometrics at multiple angles of knee flexion to see if there is a range that is more or less painful for the individual patient. The clinician may use these findings to inform subsequent strength evaluations as well as treatment, selecting ranges of motion that are least provocative.
to the patient to improve muscle strength and activation while avoiding exacerbation of symptoms.

**B.5.6 Strength**

Strength assessments should evaluate not only the muscles crossing the knee joint but also the surrounding hip and ankle musculature. Knee extensor and hip extensor, abductor, and external rotator muscle strength and activation are of utmost importance given their roles in dynamically controlling hip and knee motion and the association of patellofemoral pain with weakness of these muscles, although cause and effect are unknown. Interestingly, Kindel and Challis found that patients with patellofemoral pain have weaker hip extensors and poorer neuromuscular control with the knee flexed but not extended compared to healthy controls, suggesting knee position may be important when evaluating hip musculature. A thorough evaluation should also include strength of the core muscles, knee flexors, ankle plantarflexors and dorsiflexors, and hip flexors, internal rotators, and adductors.

Given the strength of the lower extremity muscles, clinicians should evaluate lower extremity muscle, particularly quadriceps, strength using an electromechanical dynamometer when possible. When an electromechanical dynamometer is not available, one-rep max testing on knee extension machine for quadriceps strength or hand-held dynamometer secured with a strap are acceptable alternatives, although they overestimate strength of the involved quadriceps. Electrical burst superimposition may be used to evaluate quadriceps muscle activation (i.e., inhibition), but requires relatively expensive equipment that is unavailable to many clinicians. In contrast to the usual order, we recommend that clinicians test the (most) involved limb first to determine the angle of knee flexion that is pain-free or least provocative; the clinician can subsequently evaluate the contralateral limb in the same position. Clinicians may also use patellar taping (see below) to facilitate strength evaluation,
enabling some patients to complete testing with less or no pain. While we most often use a limb symmetry index (i.e., involved limb strength / uninvolved limb strength * 100 [%]) for comparison, patellofemoral pain is often a bilateral condition thus clinicians should interpret limb symmetry indexes with caution. Additional evaluation using manual muscle testing of the hip and knee muscles may provide additional insight, especially in the case of bilateral weakness.
Figure B.1 Quadriceps strength may be evaluated isometrically using an electromechanical dynamometer during with an electrical burst superimposition technique\textsuperscript{285} to assess muscle activation. Clinicians may evaluate the (most) involved limb first to determine the angle of knee flexion that is pain-free or least provocative and subsequently evaluate the contralateral limb at the same angle of knee flexion for comparison. Patellar taping may be used to alleviate pain.
B.5.7  Balance and Postural Control

Balance and postural control may be impaired in patients with patellofemoral pain compared to healthy controls\textsuperscript{211,219,230} during a variety of tasks including dynamic standing balance\textsuperscript{219}, postural stability during a stepping up and down task \textsuperscript{211}, and stair climbing\textsuperscript{230}. Static balance during single leg stance is also impaired on the involved compared to uninvolved limb among women with patellofemoral pain\textsuperscript{54}. Fatigue of the hip abductors and to a lesser degree the knee extensors is associated with greater balance instability during dynamic standing balance\textsuperscript{219}. Patients with patellofemoral pain may also exhibit especially poor postural control with their eyes closed\textsuperscript{341}. In light of these findings, it is important to assess both static balance with eyes opened and closed as well as dynamic balance on both the (most) involved and contralateral limb. To assess static balance, we evaluate single leg stance, which can be progressed in difficulty by having the patient stand on an unstable surface such as a foam pad; document the time to error and/or number of errors in a given time (e.g., 30 seconds). Dynamic balance may be assessed using the reliable Star Excursion Balance Test\textsuperscript{117,164}.

B.5.8  Movement Assessments

Clinicians should consider a variety of movement quality assessments concordant with the patient’s complaints and activity limitations given that aberrant mechanics and neuromuscular activation patterns are often present in individuals with patellofemoral pain \textsuperscript{218,223,224,260,324,326,327}. The position of dynamic knee valgus, characterized by hip adduction and internal rotation, may be associated with patellofemoral pain \textsuperscript{57,218,324,327}, thus clinicians should pay particular attention for these aberrant mechanics. Clinicians should consider evaluating multi-joint lower extremity movements including but not limited to double and single leg squatting, drop jump.
landing, hopping, walking, stair ascent and descent, and running. Identification of movement impairments may guide not only targeted strengthening but also and perhaps more importantly neuromuscular activation exercises and movement retraining.\textsuperscript{110,111,218,327}

\subsection*{B.5.9 Step Test}

We recommend using a modification of the previously described step test (Figure B.2). The step test involves standing on a 15 centimeter block with hands on hips and using the involved limb to “slowly” and “smoothly” eccentrically lower the body until the contralateral heel touches the floor\textsuperscript{221(p73)}. A positive result is reproduction of the patient’s patellofemoral pain; a positive finding is prevalent in 74\% (57 of 77) of individuals with patellofemoral pain\textsuperscript{269} and has a modest positive likelihood ratio of 2.34\textsuperscript{221}. In the authors’ clinical experience, we modify the test by recording the angle at which pain first occur and asking the patient to rate the pain on an 11-point numeric pain rating scale. If the test is positive, we often evaluate the patient again on the modified step test after applying patellar taping (described below) to determine whether or not patellar taping provides immediate relief of symptoms and may therefore be beneficial in facilitating increased function in the short-term.
Individuals with patellofemoral pain often have pain in or around the patella that may be reproduced with palpation. Clinicians should also palpate other nearby structures, such as the patellar and quadriceps tendons, to rule out other sources of anterior knee pain. For example, reproduction of pain with palpation of the patellar tendon may indicate patellar tendinopathy; pain at the distal pole of the patella in adolescents may indicate Sinding-Larsen-Johansson Syndrome \(^{238}\), and swelling and point tenderness around the tibial tuberosity in adolescents may indicate Osgood-Schlatter Disease \(^{61,238}\).

**B.5.10 Palpation**

Functional testing may evaluate tasks that are important to the patient and are currently limited. Examples of functional testing include the stair climb test, sit to
stand test, and 6-minute walk test. Performance as well as symptoms should be documented.

**B.5.12 Objective Measures for Evaluation, Treatment Progression, and Clinical Decision-Making**

Evaluation, treatment progression, and clinical decision-making like discharge and return-to-sport clearance should be based as much as possible on objective measures while simultaneously considering the patient’s needs and goals. As mentioned above, an increase in or the presence of new effusion indicates that the activity has exceeded the current envelope of function and should not be progressed further. Clinicians may also use the soreness rules (Table B.3), initially developed by Fees et al. 93 and later adapted to the lower extremity by Adams et al. 4, to monitor appropriate progression of activities. (While avoiding pain and symptom exacerbation is critical during the early management of acute patellofemoral pain, clinicians may set a threshold of acceptable symptoms [e.g., 5/10 on numeric pain rating scale] for individuals with chronic patellofemoral pain, focusing on increasing function rather than complete avoidance of symptoms.) Successful completion of a running progression (Table B.4) 4 should be pre-requisite to initiating higher level activities.

Valid and reliable patient reported outcome measures should be completed at initial evaluation and periodically throughout rehabilitation to monitor progress and inform rehabilitation. The Visual Analog Scale for usual pain or worst pain and the Kujala Anterior Knee Pain Scale 169 are reliable, valid, and responsive in individuals with patellofemoral pain 60; the Kujala Anterior Knee Pains Scale is also valid and reliable in adolescent female athletes with anterior knee pain 147.

Throughout the rehabilitation process, the clinicians must appreciate the impact of psychological factors (e.g., kinesiophobia) 261 and other factors (e.g., stress, sleep) on pain, particularly when a patient reports a transient increase in symptoms. Anxiety,
depression, catastrophizing, and kinesiophobia may be present in individuals with patellofemoral pain and correlate with higher pain ratings and reduced physical function\textsuperscript{190}; appropriate referral or consultation may be beneficial. Stress levels\textsuperscript{231} and sleep duration\textsuperscript{85} also influence pain; for example, too much (> 9 hours) or too little (< 6 hours) sleep the previous night is associated with greater pain the following day\textsuperscript{85}. Asking and educating patients about these factors is important when determining whether to progress, maintain, or reduce interventions.

Table B.3 The soreness rules provide clinicians with a guideline to monitor symptoms and evaluate progression throughout rehabilitation\textsuperscript{4,93}. Reproduced with permission from Michael J. Axe, MD.

<table>
<thead>
<tr>
<th>Soreness Rules</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Criterion</strong></td>
<td><strong>Action</strong></td>
</tr>
<tr>
<td>Soreness during warm-up that continues</td>
<td>2 days off, drop down 1 level</td>
</tr>
<tr>
<td>Soreness during warm-up that goes away</td>
<td>Stay at level that led to soreness</td>
</tr>
<tr>
<td>Soreness during warm-up that goes away but redevelops during session</td>
<td>2 days off, drop down 1 level</td>
</tr>
<tr>
<td>Soreness the day after lifting (not muscle soreness)</td>
<td>1 day off, do not advance program to the next level</td>
</tr>
<tr>
<td>No soreness</td>
<td>Advance 1 level per week or as instructed by healthcare professional</td>
</tr>
</tbody>
</table>
Table B.4 A running progression may facilitate gradual resumption of loading; progression should occur only in the absence of increased effusion or pain and on nonconsecutive days. Reproduced with permission from Tara Manal, PT, DPT, FAPTA, University of Delaware Physical Therapy Clinic.

<table>
<thead>
<tr>
<th>Level</th>
<th>Treadmill</th>
<th>Track</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level 1</td>
<td>0.1-mi walk/0.1-mi jog, repeat 10 times</td>
<td>Jog straights/walk curves (2 mi)</td>
</tr>
<tr>
<td>Level 2</td>
<td>Alternate 0.1-mi walk/0.2-mi jog (2 mi)</td>
<td>Jog straights/jog 1 curve every other lap (2 mi)</td>
</tr>
<tr>
<td>Level 3</td>
<td>Alternate 0.1-mi walk/0.3-mi jog (2 mi)</td>
<td>Jog straights/jog 1 curve every lap (2 mi)</td>
</tr>
<tr>
<td>Level 4</td>
<td>Alternate 0.1-mi walk/0.4-mi jog (2 mi)</td>
<td>Jog 1.75 laps/walk curve (2 mi)</td>
</tr>
<tr>
<td>Level 5</td>
<td>Jog full 2 mi</td>
<td>Jog all laps (2 mi)</td>
</tr>
<tr>
<td>Level 6</td>
<td>Increase workout to 2.5 mi</td>
<td>Increase workout to 2.5 mi</td>
</tr>
<tr>
<td>Level 7</td>
<td>Increase workout to 3 mi</td>
<td>Increase workout to 3 mi</td>
</tr>
<tr>
<td>Level 8</td>
<td>Alternate between running/jogging every 0.25 mi</td>
<td>Increase speed on straights/jog curves</td>
</tr>
</tbody>
</table>

* Progress to next level when patient is able to perform activity for 2 mi without increased effusion or pain. Perform no more than 4 times in 1 week and no more frequently than every other day. Do not progress more than 2 levels in a 7-day period. Conversion: 1 mi = 1.6 km.

B.6 Treatment

Patients with patellofemoral pain present with a wide variety of underlying pathophysiology and associated impairments. It is thus imperative to individually assess each patient to identify and subsequently address his or her impairments, functional limitations, and activity restrictions. Management of patellofemoral pain should consist of an individualized, multi-modal approach with exercise therapy as the hallmark of the plan.
According to the 2016 consensus statement from the International Patellofemoral Pain Research Committee, exercise therapy is the “treatment of choice” for individuals with patellofemoral pain. High-quality evidence supports exercise therapy to improve pain and function in the short-, medium-, and long-term; exercise was the only intervention that received such a high recommendation.

Exercise therapy should include both hip and knee strengthening using both open (non-weight-bearing) and closed (weight-bearing) kinetic chain exercises. Open kinetic chain exercises include straight leg raises (progress by adding ankle weights), short arc quadriceps strengthening, knee extensions, side-lying hip abduction straight leg raise, and clamshells. Closed kinetic chain exercises include wall sits, double- and single-leg squats, lateral step-downs, and leg press. Strengthening of the core and ankle musculature should be included if the patient exhibits deficits or imbalances in these areas.

Appropriate selection of open and closed chain strengthening exercises should consider the patellofemoral joint contact forces in each mode. Steinkamp et al. found that comparison of patellofemoral joint contact forces during closed (i.e., body weight squat) and open (i.e., 9 kg weighted boot) kinetic chain exercises resulted in relatively less patellofemoral contact force in the closed kinetic chain condition in less than 48° knee flexion and relatively less patellofemoral contact force in the open kinetic chain condition in more than 48° knee flexion. Similar findings have been more recently produced by Powers et al., who added that patellofemoral joint contact force was less during quadriceps strengthening using a constant resistance knee extension machine compared to squatting at angles greater than approximately 45°. Therefore, particularly during the early stages of rehabilitation, patients may benefit from...
performing open kinetic chain exercises in deeper ranges of knee flexion (e.g., 50° - 90°) and closed kinetic chain exercises in shallower ranges (e.g., 0° - 45°) 247.

Throughout the rehabilitation process, clinicians should design appropriate exercises that maximize muscle strength while minimizing symptom exacerbation, using the soreness rules (Table B.3) to guide progression. A recent study by van Rossom and colleagues provides peak and mean patellofemoral joint contact forces during gait plus nine functional exercises and may serve as a guide for appropriately and gradually progressing loading during rehabilitation 256. While initially during the acute stage of rehabilitation a clinician may strive to perform only exercises that are pain-free, the goal of completely eliminating movement-related pain in the chronic condition may be not only unrealistic but also a disservice to the patient’s recovery 107. In such cases, setting an acceptable threshold of symptoms based on the patient’s presentation may be appropriate.

Stretching is another important component of rehabilitation, as individuals with patellofemoral pain often have limited range of motion, particularly around the hip 125 and knee and perhaps also the ankle 331. Treatments should address the specific ROM and muscle length restrictions identified during the evaluation and may include the quadriceps, hip flexors, hamstrings, tensor fascia lata/iliotibial band, gastrocnemius, and/or soleus.

**B.6.2 Joint Mobilizations**

Joint mobilizations may be effective in improving pain and function among individuals with patellofemoral pain when joint mobilizations are directed at the knee (i.e., patellofemoral and tibiofemoral joint) and combined with a comprehensive treatment approach including exercise 148. A case study by Lantz et al. highlights the potential benefit of tibiofemoral mobilizations in an individual with chronic patellofemoral pain 177.
B.6.3 Patellofemoral Taping

Conflicting evidence exists regarding the efficacy of patellofemoral taping \( ^{9,59,84,140,183} \). We recommend using taping in conjunction with a multi-modal, comprehensive treatment plan if taping alleviates pain during exercises in rehabilitation and/or functional activities. Clinicians should evaluate the immediate effectiveness of patellofemoral taping within an individual by assessing a functional task pre- and post-taping that is specific to that patient’s symptoms; if pain is alleviated then taping may help the patient complete functional activities and exercises which may in turn facilitate recovery. While we recommend first evaluating medial patellar glide therapeutic taping \(^{62}\), placebo taping plus exercise may be similarly beneficial to therapeutic tension taping plus exercise \(^{183}\). The use of patellar taping in isolation is not recommended \(^{9,56,59,61–63,183}\).

B.6.4 Neuromuscular Electrical Stimulation (NMES)

A 2017 Cochrane Review by Martimbianco et al. found limited, low-quality regarding the effect of neuromuscular electrical stimulation (NMES) for the treatment of patellofemoral pain \(^{196}\). The review concluded that very low-quality evidence suggests NMES reduces pain at the end of treatment (3 to 12 weeks) but the improvement may not be clinically relevant given the small magnitude of change (1.63 out of 10 on the visual analog scale). The authors found even less support for NMES on strength or function, concluding that “insufficient and inconclusive evidence” exists for the effect of NMES on treating individuals with patellofemoral pain \(^{196(p2)}\). While one pilot study has found no statistically significant differences between 38 athletes (19 per group) who completed physiotherapy or physiotherapy plus electrical stimulation, limitations including study design, follow-up, and stimulation parameters limit its applicability \(^{30}\). Given the dose response relationship between electrical
stimulation intensity and quadriceps femoris muscle torque\textsuperscript{284}, we recommend using higher NMES intensity levels to facilitate muscular strength and activation development. A 2010 systematic review on NMES on quadriceps strength in individuals after anterior cruciate ligament reconstruction found that NMES combined with exercise is more effective than exercise alone at improving quadriceps muscle strength\textsuperscript{161}. We therefore recommend using NMES in conjunction with a comprehensive rehabilitation program in individuals who have patellofemoral pain and deficits in quadriceps strength and/or activation. We recommend the following parameters: 10.2 x 12.7 cm pads on the vastus medialis and proximal vastus lateralis muscles; 15 electrically elicited, isometric contractions of the quadriceps at about 65° knee flexion (or the most comfortable position for the patient), 75 bursts per second; 10” on, 50” off, 2” ramp; and the maximum tolerated intensity that elicits at least 50% maximum volitional isometric contraction\textsuperscript{4,284}.

### B.6.5 Neuromuscular Training

Neuromuscular activation deficits are common in individuals with patellofemoral pain, especially in the hip abductors and external rotators, knee extensors, and core musculature\textsuperscript{57,218,260,324,327}. Evaluating movements during functional tasks (described above) is essential to identifying and treating neuromuscular activation deficits. Strengthening alone seldom changes mechanics\textsuperscript{286}, thus task-specific movement retraining is likely necessary\textsuperscript{34,218,325,327}. Use of resistance tubing bands may promote activity of specific muscle groups; for example, using resistance tubing bands around the knees during a squat may facilitate hip abduction and external rotation. NMES may facilitate neuromuscular training, as improvements in kinematics and muscle activity have been observed in a small group (N = 15) of women with patellofemoral pain\textsuperscript{110}.
Running mechanics and gait retraining in patients with patellofemoral pain have received significant attention likely due in part to the high incidence of patellofemoral pain among runners \(^{281}\). Running mechanics are often altered in individuals with patellofemoral pain and young women may be especially prone to altered mechanics such as excessive hip adduction and internal rotation leading to dynamic knee valgus \(^{223–225,326,327}\). Gait retraining may be considered in individuals with patellofemoral pain who have aberrant running mechanics and should address the specific deficits in the individual \(^{326}\). Sagittal plane trunk mechanics \(^{295}\) and footwear (as described by the Minimalist Index) \(^{88}\) are related to patellofemoral joint stress during running, thus should also be considered during gait analysis and running retraining; forward trunk lean \(^{295}\) and more minimalist shoes \(^{88}\) are associated with reduced patellofemoral joint stress. A systematic review by Agresta and Brown found the use of real-time auditory and visual feedback in conjunction with therapeutic exercise to be effective in improving lower extremity kinematics in runners with patellofemoral, although no single method of feedback was deemed superior \(^{7}\).

### B.6.6 Activity Modification and Gradual Loading

During the acute phase, activity modification characterized by relative rest is likely appropriate to allow healing to occur. Reintegration of loading, however, must be implemented and should be done in a systematic way to gradually increase and restore the envelope of function. Chen et al. evaluated patellofemoral joint reaction forces in using an MRI-informed subject-specific three-dimensional model, finding that, among the four tasks evaluated, patellofemoral joint reaction forces were highest during running (58.2 N/kg-body weight [bwt]), followed by stair ascent (33.9 N/kg-bwt), stair descent (27.9 N/kg-bwt), and walking (10.1 N/kg-bwt) \(^{52}\). In light of these findings, it may be inappropriate for an individual with acute patellofemoral pain to run if stair descent is painful, although individual evaluation and clinical judgment
should be considered. Recently, van Rossom et al. added to Chen’s findings by evaluating peak and mean patellofemoral joint contact forces during ten functional tasks; peak patellofemoral joint contact forces were lowest during gait and progressively higher in sit down, stand up, squat, forward lunge, stair ascent, stair descent, single leg hop weight acceptance phase, sideward lunge, and single leg hop push-off phase.\textsuperscript{256}

**B.6.7 Other Interventions**

Numerous other interventions have been proposed as adjuvants or stand-alone treatments for individuals with patellofemoral pain and may be considered as part of a comprehensive plan of care if impairments warrant or symptoms have been intractable to the more evidence-based approaches outlined above. Foot orthotics may be beneficial in reducing pain and improving function.\textsuperscript{61} Dry needling does not appear to provide any additional benefit when added to a multi-modal treatment approach including manual therapy and strengthening exercise compared to manual therapy and strengthening exercise alone.\textsuperscript{89}

**B.6.8 Appropriate Progression and Discharge**

Rehabilitation should be progressive and rooted in objective clinical findings. Monitoring effusion and soreness should occur throughout rehabilitation and guide progression. Use of gradual, return-to-activity training protocols, such as the running progression (Table B.4)\textsuperscript{4}, may facilitate appropriate progression and aid clinical decision-making.

Discharge from physical therapy should occur when the patient has achieved his or her goals and is equipped to transition to self-management or management by an athletic trainer, strength and conditioning coach, or personal trainer if available. Patient education is thus critical at this time-point and throughout the rehabilitation
process; the patient should know what exercises to perform and how to progress activity while adhering to basic principles such as the soreness rules. Although research on return-to-sport criteria in patients with patellofemoral pain is lacking, we recommend athletes should achieve limb symmetry index scores of 90% of greater for quadriceps strength and all four hop tests (single, crossover, triple, and 6 meter timed) prior to resuming full participation; limb symmetry indexes, however, have limitations particularly in individuals with bilateral involvement thus should be interpreted with caution.

**B.7 Conclusions**

Early, appropriate rehabilitation may be critical to preventing poor outcomes and optimizing function for individuals with patellofemoral pain. We strongly recommend exercise therapy, including hip and knee strengthening and stretching, to improve short-, medium-, and long-term outcomes in individuals with patellofemoral pain. A multi-modal, individually tailored rehabilitation program should be designed to target the patient’s specific impairments and functional limitations identified during the evaluation. Treatments may include open- and closed-chain exercises, strengthening, stretching, aerobic exercise, patellofemoral and tibiofemoral mobilizations, patellar taping, high-intensity NMES, neuromuscular training, and gait retraining. Although short-term changes or reductions in movement often are necessary in a protective capacity, the persistence of altered movement is a key characteristic of chronic pain. Patellofemoral pain etiology is largely movement related and a comprehensive conservative treatment using movement can be successful.
NOTE: This is the accepted version of the following article, reproduced with permission from *Annals of Joint*: Capin JJ, Snyder-Mackler L. The current management of patients with patellofemoral pain from the physical therapist’s perspective. *Ann Jt*. 2018;3(40). doi:10.21037/aoj.2018.04.11.
Appendix C

KEEP CALM AND CARRY ON TESTING—A SUBSTANTIVE REANALYSIS AND CRITIQUE OF “WHAT IS THE EVIDENCE FOR AND VALIDITY OF RETURN-TO-SPORT TESTING AFTER ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION SURGERY? A SYSEMATIC REVIEW AND META-ANALYSIS”

C.1 Introduction

Clinicians rely on rigorous systematic reviews to guide practice. We therefore suspect many clinicians will note the results of the 2019 systematic review and meta-analysis by Webster and Hewett, “What is the Evidence for and Validity of Return-to-Sport Testing after Anterior Cruciate Ligament Reconstruction Surgery? A Systematic Review and Meta-Analysis.” We agree that it is important to evaluate the association between return-to-sport (RTS) test batteries and outcomes after anterior cruciate ligament (ACL) reconstruction. The third review question in Webster and Hewett (2019) is particularly pertinent: “Is passing RTS test batteries associated with reduced rates of subsequent knee injury (all knee injuries and ACL injury)?” We are authors of several of the original data papers cited in the systematic review and we are concerned about the study methodology and its conclusions. We highlight major problems with including 2 studies and present revised analyses that demonstrate the impact these studies had on the conclusions.

C.2 Methodological Concerns

First, we question the validity of pooling studies with substantial clinical and methodological diversity. The meta-analysis combined studies where only some athletes returned to sport and studies where all, or mostly all, returned to
sport\textsuperscript{114,121,172}; studies with skeletally immature patients\textsuperscript{114} and studies with elite athletes\textsuperscript{172}; and studies where substantially different RTS test batteries were used. Our second concern is that Webster and Hewett\textsuperscript{315} did not assess risk of bias, a fundamental precept of systematic review methodology clearly stated in the PRISMA reporting guideline.\textsuperscript{139,205,291} Assessment of study quality (as performed by Webster and Hewett\textsuperscript{315}) does not quantify risk of bias.\textsuperscript{33} A risk of bias assessment identifies factors within studies that can skew results, and these factors must be considered carefully in the decision to pool data and in the conclusion. Important bias domains for review questions 2 and 3 include (i) study participation, (ii) study attrition, (iii) methods used to ascertain RTS pass status, (iv) outcome (subsequent injury), (v) confounding, and (vi) statistical analysis and reporting.\textsuperscript{133}

**C.3 How Two Studies Designed to Assess Different Research Constructs Impacted Contralateral ACL Injury Results**

We believe that Webster and Hewett’s report of 235\% greater risk of contralateral ACL injury among those who passed RTS criteria\textsuperscript{315} is an artefact of including 2 studies that were not designed to answer the same research question as the 3 other studies in the systematic review. In the studies by Sousa et al.\textsuperscript{287} and Wellsandt et al.\textsuperscript{317}, the RTS test results were used to determine when athletes were cleared to return to sport. Early return to sport is among the strongest risk factors for reinjury\textsuperscript{45,121,150,174}, and delaying return to sport in those who initially fail RTS testing is likely to protect them from reinjury. In these 2 studies\textsuperscript{287,317}, reinjuries were reported irrespective of whether the patients returned to sport after RTS testing. The 3 other studies\textsuperscript{114,121,172} in the systematic review represented athletes who returned to sport even if they failed RTS tests (all patients returned to sport in the studies by Kyritsis et al.\textsuperscript{172} and Grindem et al.\textsuperscript{121}, and 39 of 42 patients returned to sport in Graziano et al.\textsuperscript{114}). These patients returned to sport either because of nonadherence to the protocol
or because the RTS test battery was not used for sports clearance in the sample. We contend that the clinically relevant question of whether patients should pass RTS tests prior to return to sport cannot be informed by studies where return to sport was delayed if the patient failed the RTS tests. Pooling these studies in a meta-analysis is therefore inappropriate.

In the study by Sousa et al., confounding may also play a large role and is clearly highlighted in the paper’s conclusion. Patients who passed RTS criteria in their study were younger, had higher preinjury and follow-up activity levels, and returned to sport earlier. Young age, high activity levels, and early return to sport are very strong risk factors for second ACL injury; we expect higher injury rates in the ‘passed RTS criteria’ group than in the older ‘failed RTS criteria’ group who participated in less knee-demanding sports and had delayed return to sport. The majority (9/16) of the contralateral ACL injuries reported in Webster and Hewett were derived from the Sousa et al. study, which was the only individual study that showed a higher rate of contralateral ACL injuries in the group that passed RTS tests. This single study accounted for 77% of the weighting for the contralateral ACL injury meta-analysis and heavily influenced the conclusions drawn by Webster and Hewett.

Four of the remaining 7 contralateral ACL injuries among the athletes who passed RTS testing in the meta-analysis were derived from the study by Wellsandt et al. This study was designed to evaluate estimated pre-injury capacity (EPIC) levels as alternatives to limb symmetry indexes, not the association between the established RTS criteria and second ACL injuries. Patients in this study only received RTS clearance after they passed RTS testing, either 6 months after ACLR (the test point reported by Wellsandt et al.) or at a later time-point after completing additional rehabilitation. Having no contralateral ACL injuries among those who ‘failed’ the RTS
test battery 6 months after surgery was not surprising as these patients did not return to sport at that time. Instead, athletes who failed the RTS tests continued rehabilitation and were scheduled for a new test at a later time. This prevents a meaningful comparison because no one in this specific sample returned to sport until they passed RTS criteria. As authors, we acknowledge that this information is not explicitly stated in the paper. Had we known the data would be used for another purpose than the original paper, we would have clarified to avoid this misinterpretation.

C.4 Revised Analysis and Interpretation of Results

Here we demonstrate how conclusions change when the two studies287,317 with critically different study designs are excluded from the meta-analysis.

1. In the meta-analysis for any knee injury, Sousa et al.287 and Wellsandt et al.317 were excluded by Webster and Hewett, so their analysis remains unchanged. Passing RTS test batteries is associated with 72% lower risk of further knee injury (i.e., ACL injury and other knee injuries, 95% confidence interval [CI]: 6-96 % lower risk, \( p = .09 \)).315

2. Webster and Hewett315 reported no significant association (\( p = .68 \)) between successfully passing the RTS test and having a lower rate of subsequent ACL injury (i.e., graft rupture and/or contralateral ACL injury). However, after excluding the studies by Sousa et al.287 and Wellsandt et al.317, those athletes who passed the RTS criteria had 75% lower odds (95% CI: 46% to 88% lower odds) of any ACL injury than those who failed (\( p<0.01 \), Figure C.1).

3. Webster and Hewett315 found that those who passed RTS criteria had a 60% lower risk for ACL graft rupture (95% CI: 31% - 77%, \( p = .003 \)). By excluding the inappropriate studies,287,317 and pooling remaining
data, there is **78% lower odds of graft rupture in those who passed RTS criteria compared to those who failed** (95% CI: 52% to 90% lower odds, p<0.01, Figure C.2).

4. By excluding the studies by Sousa et al. and Wellsandt et al.,287,317 there are only 4 contralateral ACL ruptures left for analysis (among those who passed or failed RTS criteria). **These numbers are too low to say whether or not passing RTS criteria influences risk of contralateral ACL rupture.**

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**Table C.1**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Passed RTS criteria</th>
<th>Not passed RTS criteria</th>
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<th>Odds Ratio</th>
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<td>18</td>
<td>9</td>
<td>55</td>
</tr>
<tr>
<td>Kyrtti 2016</td>
<td>12</td>
<td>116</td>
<td>14</td>
<td>42</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>17</td>
<td>171</td>
<td>101</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.00; Chi² = 0.15, df = 2 (p = 0.93); I² = 0%
Test for overall effect: Z = 3.51 (p = 0.0004)

---

**Figure C.1** Re-analysis showing the risk for any second ACL injury among those who pass versus fail RTS criteria. Abbreviations: RTS, Return-to-Sport; M-H, Mantel-Haenszel; OR, odds ratio.

---

**Table C.2**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Passed RTS criteria</th>
<th>Not passed RTS criteria</th>
<th>Odds Ratio</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
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<td>Events</td>
<td>Total</td>
</tr>
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<td>37</td>
<td>1</td>
<td>4</td>
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<td>18</td>
<td>8</td>
<td>55</td>
</tr>
<tr>
<td>Kyrtti 2016</td>
<td>12</td>
<td>116</td>
<td>14</td>
<td>42</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>14</td>
<td>171</td>
<td>101</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.00; Chi² = 0.11, df = 2 (p = 0.95); I² = 0%
Test for overall effect: Z = 3.73 (p = 0.0002)

---

**Figure C.2** Re-analysis showing the risk for an ACL graft rupture among those who pass versus fail RTS criteria. Abbreviations: RTS, Return-to-Sport; M-H, Mantel-Haenszel; OR, odds ratio.
C.5 Conclusion

Our reanalysis omits 2 studies\textsuperscript{287,317} with designs that addressed a different research construct than the remaining 3 and/or have a high risk of bias. We found that compared with patients who fail RTS tests prior to return to sport, athletes who pass RTS test batteries have (i) a lower risk of (any) knee reinjury, (ii) a lower risk of any second ACL injury, and (iii) a lower risk of ACL graft rupture; (iv) no conclusions regarding contralateral ACL injury risk can be drawn due to insufficient data.

More evidence is needed to refine RTS test batteries to provide greater certainty in their ability to facilitate successful RTS. Future meta-analyses should critically evaluate the study design of each potential contributing paper and include a risk of bias assessment. Meta-analyses should also consider the impact of sparse-data bias\textsuperscript{116} and avoid the Firth penalization when events are 0, as this method can change the direction of the reported association.\textsuperscript{115,195}

In future studies, authors should report and/or control for sport level and athletic exposure. Researchers should aim to rigorously evaluate (i) which tests can help clinicians help athletes return to play successfully, (ii) the optimal values for cut-off scores, and (iii) alternatives to limb symmetry indexes. Importantly, all studies to date are observational, and there is a need for interventional designs (e.g., pragmatic trials or site randomization). Such studies will improve clinicians’ understanding of RTS test batteries and, with appropriate implementation, should reduce secondary knee and ACL injuries.

Clinicians should not fear an increased risk of contralateral ACL injuries on the basis of the current literature, but continue to use RTS test batteries (and appropriate time-frames) to support RTS decision-making.
C.6 Acknowledgments

Thank you to Dr. Mohammad Ali Mansournia, MD, MPH, PhD, for his critical review of our work, and for his helpful suggestions.

Appendix D

INSTITUTIONAL REVIEW BOARD (IRB) DOCUMENTS FOR AIMS 1, 2, 3, AND 5
D.1 IRB Initial Approval Letter for Aims 1, 2, 3, and 5

DATE: March 18, 2011

TO: Lynn Snyder-Mackler, PT, ScD, FAPTA
FROM: University of Delaware IRB

STUDY TITLE: [225014-1] Can Neuromuscular Training Alter Movement Patterns? (Renewal Period)

SUBMISSION TYPE: New Project

ACTION: APPROVED
APPROVAL DATE: March 18, 2011
EXPIRATION DATE: March 15, 2012
REVIEW TYPE: Full Committee Review

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

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

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

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

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

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

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

Based on the risks, this project requires Continuing Review by this office on an annual basis. Please use the appropriate renewal forms for this procedure.
D.2 IRB Continuing Review Approval Letter for Aims 1, 2, 3, and 5

DATE: February 22, 2018

TO: Lynn Snyder-Mackler, PT, ScD, FAPTA
FROM: University of Delaware IRB

STUDY TITLE: [225014-16] Can Neuromuscular Training Alter Movement Patterns? (Renewal Period)

SUBMISSION TYPE: Continuing Review/Progress Report

ACTION: APPROVED

APPROVAL DATE: February 21, 2018

EXPIRATION DATE: March 14, 2019

REVIEW TYPE: Full Committee Review

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

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

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

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

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

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

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

Based on the risks, this project requires Continuing Review by this office on an annual basis. Please use the appropriate renewal forms for this procedure.
D.3 IRB Stamped Informed Consent for Aims 1, 2, 3, and 5

**UNIVERSITY OF DELAWARE**
DEPARTMENT OF PHYSICAL THERAPY
INFORMED CONSENT FORM

**Study Title:** Can Neuromuscular Training Alter Movement Patterns? (Renewal Period), Experiment 2 (Aim 3), new randomized controlled trial.

**Principal Investigators:** Lynn Snyder-Mackler, ScD, PT

**Co-investigators:** Thomas Buchanan, PhD, Kurt Manal, PhD, David Legerstet, PT, MPT, PhD, Michael J. Axe, MD, Amelia Arundale, PT, DPT, PhD, Ryan Zarzycki, PT, DPT, PhD, Jacob Capin, PT, DPT, MS, Jessica Johnson, PT, DPT, Celeste Dix, PT, DPT, MS, Angela H. Smith, PT, DPT, Patrick O'Rourke, PT, DPT

**PURPOSE AND BACKGROUND**

You are being asked to participate in a study that will investigate the effect of post-operative rehabilitation on the movement patterns and functional abilities in patients who have had a complete anterior cruciate ligament (ACL) rupture. You have been referred to this study because you have completed a functional screening examination and have decided to undergo ACL reconstruction. Participation in this research study is voluntary. Your treatment will not be affected by whether or not you participate and you may withdraw from the study at any time without penalty. This program will include treatment activities we currently use in our clinic to treat patients with ACL injury. Your surgeon and physical therapist have agreed that this treatment regimen and all of the testing procedures included in the study are acceptable. Your surgeon has agreed that the tests are being conducted at appropriate intervals following your surgery. In addition to the physical therapy treatment, the study includes strength testing and analysis of your knee movement during walking. There will be a total of four (4) testing sessions: 1) pre-intervention, 2) immediately after completing intervention, 3) 12 months after surgery, and 4) 24 months after surgery. This research study will involve approximately eighty (80) subjects with ACL injury between the ages of 13-55 years. Persons of all sexes, races, and ethnic origins may serve as subjects for this study.

A description of each procedure and the approximate time it takes for each test and the study procedure are outlined below.
PROCEDURES

ACL Functional Test

Functional testing will take place in the Physical Therapy Clinic at the University of Delaware, 540 S. College Ave, Newark, DE, 19713 and will last approximately 1 hour. Testing will be performed pre-intervention, immediately after intervention and 12 and 24 months after surgery. This is commonly done at the University of Delaware Physical Therapy Clinic as part of the post-operative ACL rehabilitation protocol.

Strength Testing

The test will measure the strength of the quadriceps muscle on the front of your thigh. You will be seated in a dynamometer, a device that resists your kicking motion, and measures how much force your muscle can exert. Set adhesive electrodes will be attached to the front of your thigh, and you will be asked to kick as hard as you can against the arm of the dynamometer. An electrical stimulus will be activated while you are kicking, to fully contract your muscle. During the electrical stimulus you may feel a cramp in your muscles, like a "Charlie Horse", lasting less than a second. Each test will require a series of practice and recorded contractions. Trials will be repeated (up to a maximum of 4 trials) until a maximum contraction is achieved for both legs.

Hop Testing

A series of four (4) single leg hop tests (Diagram 1) will be performed once the swelling in your knee has resolved and you demonstrate good thigh muscle strength. The tests are performed in the order seen in Diagram 1. You are required to wear a standard off-the-shelf knee brace on your injured knee during this portion of the testing.

Two practice trials will precede each of the hop tests before the recorded testing begins. You can put your other leg down at any time to prevent yourself from losing your balance. However, only the two trials in which you are able to 'stick the landing' on one foot will be counted towards your scores. This series of hop tests will be performed on both legs.

Subject's Initials

Diagram 1. Four (4) hop tests as part of the functional test protocol.
Questionnaires

Following strength and hop testing, you will be asked to complete a test packet which includes questions about your injury, past and current functional status, and perceived functional capabilities. If you are unable to complete the strength and hop testing for any reason, you will still be asked to complete the test packet so that we may get as much information about the current status of your knee as possible.

Motion Analysis Testing

All subjects will be asked to perform motion analysis testing, which will take place in the Motion Analysis Laboratory at the University of Delaware, Department of Physical Therapy, 540 S. College Ave, Newark, DE, 19713. Motion analysis testing will take place pre-intervention, immediately after intervention, 12 and 24 months after your ACL surgery.

Motion Analysis

Markers will be affixed to your skin and sneakers on both legs using adhesive skin tape. Shells with markers on them will be placed on your pelvis, thighs and calves and will be held in place with elastic wraps. These markers will allow the cameras to track your leg positions.

Muscle Activity

Electrodes, taped to your skin, will be used to record the electrical activity of your muscles. After all electrodes have been placed, you will perform a maximum contraction of each muscle, with straps applied to your ankles to provide resistance. Nine electrodes will be secured to each leg and then plugged into a small (6” x 4” x 3”) transmitter box that will be attached to the back of a vest with Velcro. The transmitter sends the signal to the computer so we can determine when the muscles are contracting during the activities. These measurements will also be taken during the walking trials of the motion analysis testing. The electrodes will be removed at the conclusion of the testing session.

Walking Trials

Immediately following the initial muscle activity testing, you will be asked to perform several walking trials in our laboratory. Walking trials will give us information about the way your hips, knees, and ankles move while you walk. You will be asked to perform 7 trials of walking at a comfortable, self-selected speed, although additional trials may be required to obtain enough data. While you are walking, a computer records the 3 dimensional motions of your hips, knees, and ankles. The entire motion analysis session will last approximately two (2) hours.
Physical Therapy

Twelve weeks after surgery, and when you have sufficient thigh muscle strength, you will be randomized into one of two different treatment groups, both of which incorporate higher level, progressive activities, including running and agility training. Ten sessions will be scheduled two to five times weekly, depending on your time constraints and your ability to progress with therapy.

Risks/Discomfort

You may experience discomfort from the removal of tape holding markers and EMG electrodes in place. Subjects with ACL injury could experience a loss of balance during testing, however your other leg is free to touch down to provide support and prevent loss of balance. The strength testing can be associated with local muscle soreness and fatigue. Following the testing, your muscles may feel as if you have exercised vigorously.

Benefits

The benefits include comprehensive testing sessions and post-operative physical therapy. All physical therapy sessions will be administered by a licensed physical therapist. The results of this study may help us improve the way we treat patients with ACL injury. Out-of-pocket expenses related to postoperative physical therapy treatment sessions, specifically your co-pay, will be covered by this grant. Medications, medical devices (e.g. braces) and other nonphysical therapy expenses are not covered.

Compensation

You will be paid an honorarium of $100 for the motion analysis testing and functional testing to compensate you for travel expenses and the time involved.

Confidentiality and records

Only the investigators, you and your physician will have access to the data. All of your data will be de-identified for the purposes of data management and processing. Neither your name nor any identifying information will be used in publication or presentation resulting from this study. A statistical report, which may include slides or photographs which will not identify you, may be disclosed in a scientific paper. Data will be archived indefinitely and may be used for secondary analysis of scientific and clinical questions that arise from this research.
Study Title: Can Neuromuscular Training Alter Movement Patterns? (Renewal Period), Experiment 2 (Aim 3), new randomized controlled trial.

Principal Investigators: Lynn Snyder-Mackler, ScD, PT

Co-investigators: Thomas Buchanan, PhD, Kurt Manal, PhD, David Logerstedt, PT, MPT, PhD, Michael J. Axe, MD, Amelia Arundale, PT, DPT, PhD, Ryan Zarzecni, PT, DPT, PhD, Jacob Caplin, PT, DPT, MS, Jessica Johnson, PT, DPT, Celeste Dix, PT, DPT, MS, Angela H. Smith, PT, DPT, Patrick O’Rourke, PT, DPT

Subject’s Statement:
I have read this consent/assent form and have discussed the procedure described above with a principal investigator. I have been given the opportunity to ask questions regarding this study, and they have been answered to my satisfaction.

If you are injured during research procedures, you will be offered first aid at no cost to you. If you need additional medical treatment, the cost of this treatment will be your responsibility or that of your third-party payer (for example, your health insurance). By signing this document you are not waiving any rights that you may have if injury was the result of negligence of the university or its investigators.

I have been fully informed of the above described procedures, with its possible risks and benefits, and I hereby consent/assent (for those under 18 years of age) to the procedures set forth above.

If I am under 18 years of age, I understand that parental or guardian consent is required. My parent or guardian has printed and signed his/her name below.

______________________________  ______________________________  ______________
Subject’s Name                Subject’s Signature           Date

______________________________  ______________________________  ______________
Parent/Guardian’s Name        Parent/Guardian’s Signature  Date

______________________________  ______________________________
Lynn Snyder-Mackler, Principal Investigator   Date

If you have any questions concerning the rights of individuals who agree to participate in research, you may contact the Institutional Review Board (302-8312137). The Institutional Review Board is created for the protection of human subjects involved in research conducted at the University of Delaware.

Further questions regarding this study may be addressed to:
Lynn Snyder-Mackler, ScD, PT
Physical Therapy Department, (302) 831-3613

Page 5 of 5

Subject’s Initials
D.4  IRB Closure/Final Report Letter for Aims 1, 2, 3, and 5

DATE:  March 21, 2019

TO:  Lynn Snyder-Mackler, PT, ScD, FAPTA
FROM:  University of Delaware IRB (HUMANS)

STUDY TITLE:  [225014-17] Can Neuromuscular Training Alter Movement Patterns? (Renewal Period)

SUBMISSION TYPE:  Closure/Final Report

ACTION:  CLOSED

EFFECTIVE DATE:  March 21, 2019

The University of Delaware IRB has CLOSED this project. No further action on submission 225014-17 is required at this time.

Please remember that in compliance with 45 CFR 46, all records associated with this project, including data and consent forms, must be retained for three (3) years from the closure date. Records must be retained in a manner consistent with your approved protocol.

If you leave the University of Delaware prior to the end of the retention requirement, study records must remain at the University. If you need assistance arranging for the secure storage of the records, the IRB office is able to assist you. If you have any questions, please contact Renee Stewart at (302) 831-2137 or stewartr@udel.edu. Please include your study title and reference number in all correspondence with this office.
Appendix E

INSTITUTIONAL REVIEW BOARD (IRB) DOCUMENTS FOR AIM 4
E.1 IRB Approval Letter for Aim 4

DATE: March 23, 2016

TO: Thomas Buchanan, PhD
FROM: University of Delaware IRB

STUDY TITLE: [888724-1] Understanding the role of unloading in the knee in osteoarthritis (OA) following anterior cruciate ligament reconstruction (ACLR).

SUBMISSION TYPE: New Project

ACTION: APPROVED

APPROVAL DATE: March 23, 2016
EXPIRATION DATE: March 15, 2017
REVIEW TYPE: Full Committee Review

*Subpart D Determination 45 CFR 46.404

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

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

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

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

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

Please report all NON-COMPLIANCE issues or COMPLAINTS regarding this study to this office.
E.2 IRB Continuing Review Approval Letter for Aim 4

DATE: March 4, 2019

TO: Thomas Buchanan, PhD
FROM: University of Delaware IRB

STUDY TITLE: [868724-10] Understanding the role of unloading in the knee in osteoarthritis (OA) following anterior cruciate ligament reconstruction (ACLR).

SUBMISSION TYPE: Continuing Review/Progress Report

ACTION: APPROVED
APPROVAL DATE: March 4, 2019
EXPIRATION DATE: March 15, 2020
REVIEW TYPE: Expedited Review
REVIEW CATEGORY: Expedited review category # (9)

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

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

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

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

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

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

Please note that all research records must be retained for a minimum of three years.
E.3 IRB Stamped Informed Consent Forms for Aim 4

INFORMED CONSENT/ASSENT/PARENTAL PERMISSION TO PARTICIPATE IN RESEARCH

Title of Project: Understanding the role of unloading in the knee in osteoarthritis (OA) following anterior cruciate ligament reconstruction (ACLR)

Principal Investigator(s): Dr. Thomas S. Buchanan

You or your child are being invited to participate in a research study. This consent form tells you about the study including its purpose, what you will be asked to do if you decide to take part, and the risks and benefits of being in the study. Please read the information below and ask us any questions you may have before you decide whether or not you want to participate as a volunteer or parent.

Participation is voluntary for you or your child and you can refuse to participate or withdraw at any time without penalty or loss of benefits to which you are otherwise entitled. If you decide to participate, you will be asked to sign this form and a copy will be given to you to keep for your reference.

WHAT IS THE PURPOSE OF THIS STUDY?

The purpose of this research study is understand the role of unloading in the knee in osteoarthritis (OA) following anterior cruciate ligament reconstruction (ACLR) surgery.

Though ACLR restores knee stability, it does not fully address abnormal knee movement and knee loading patterns, i.e. abnormal walking patterns where the ACLR knee is unloaded compared to the other non-surgical knee. Abnormal walking patterns are believed to be a mechanism leading to knee osteoarthritis (OA). Knee OA is a condition wherein the load bearing region of the knee, the cartilage, undergoes degradation. Reliable identification of knee OA requires the use of radiographs, commonly known as X-rays.

Motion analysis testing is the most common method used to analyze walking patterns. Motion analysis testing comprises of non-invasive walking experiments, often including surface electromyography (non-invasive muscle signal recording) to estimate muscle coordination patterns and force production.

In addition to walking patterns, biological and chemical changes (biochemical changes) in knee cartilage are also believed to affect the progression of OA. An imaging method, known as quantitative magnetic resonance imaging (MRI) allows for non-invasive estimation of these changes in knee cartilage. Quantitative MRI is being increasingly used over the past two decades. However, estimates of biochemical changes in knee cartilage, specific to an ACLR population, are not yet readily available in literature. It is also not known how these changes are related to walking patterns. Finally, changes in knee geometry, which can be studied using standard MRI, are also known to affect the progression of knee OA.

With that background, the purpose of this research project is to study changes in walking patterns and biochemical properties of knee cartilage after ACLR. Knee geometry measurements and OA related changes will also be evaluated. 75 subjects will be recruited 3 months after ACLR. Testing will be conducted for each subject at the following time points after ACLR:

Participant’s Initials ________
- 3, 6, and 24 months

Motion analysis testing will be used to assess walking patterns. Quantitative MRI will be used to estimate biochemical changes in knee cartilage, while standard MRI will be used to construct a geometric representation of the knee. Finally, the presence/absence of knee OA and progression of OA will be verified using radiographs.

In addition, 30 subjects, in the same age groups as ACLR subjects, but with no history of knee injury will also be recruited, to allow for comparison against subjects with ACLR. Control subjects will only be required to complete motion analysis testing and imaging (quantitative and standard MRI), similar to subjects with ACLR, and at one time point only, i.e. immediately after recruitment.

The ultimate goal of this research project is to use a mathematical model to reveal conditions that can affect the knee cartilage negatively, and result in knee OA. We also hope that an improved understanding of these conditions will eventually contribute to preventative therapeutic protocols.

WHY ARE YOU OR YOUR CHILD BEING ASKED TO PARTICIPATE?

We are asking you or your child to be in the study because you or your child has undergone ACLR approximately three months ago, and can be part of the ACLR group, or because you have no history of knee injury, and can be part of the control group. The age range for participation, for both groups, is between 16 and 45 years.

Exclusion criteria for ACLR group:

You could be excluded from volunteering for the study if you have sustained major leg injury, have undergone major leg surgery that requires serious medical management (i.e. fracture or re-injury), or an ACL injury/repair prior to the most recent procedure in either knee. You could also be excluded if you sustained major tears to other knee ligaments, or repairable meniscus injuries.

Exclusion criteria for control group:

You could be excluded from volunteering for the study if you have sustained major leg injury, have undergone major leg surgery that requires serious medical management (i.e. fracture), knee ligament injuries or knee meniscus injuries.

Exclusion criteria common to both ACLR and control groups:

You could be excluded if you have any condition that prevents you from walking, or laying still on your back.

Additionally, the conditions listed below, if met, will be grounds for exclusion because of standard precautions for imaging. Pregnancy is not a contraindication to MRI of the knee, but our scans may be taken by community providers who screen for and do not perform MRI on pregnant women when it is not medically necessary.
• Joint replacement with metallic parts
• Surgical procedure that includes metallic components
• Extreme claustrophobia (fear of small, closed spaces)
• Pacemaker (a medical implant in the heart)
• Metal in the body (implants, screws, plates, shrapnel, etc.)
• Aneurysm clips (clips used to treat bulging blood vessels)
• Ear or Eye Implants

WHAT WILL YOU BE ASKED TO DO?

If you or your child want to participate, the information below lists the location and details about the study. All the procedures are non-invasive, i.e. nothing will be inserted in the body, and rather, components will be attached to the surface of the body, when required.

Motion analysis testing will be conducted at STAR campus at the University of Delaware (540 S College Avenue, Newark DE 19713).

MRI will be conducted at either of the following locations:
- University of Delaware’s Center for Biomedical or Brain Imaging, located at 75 East Delaware Avenu, Newark DE 19716, OR
- Diagnostic Imaging Associates, located at L-6 Omega Drive, Newark DE 19713, OR
- Best Open MRI-Abbey Medical Center, 1 Centurian Drive, Suite 107, Newark DE 19713

Finally, radiography (x-ray imaging) will take place at either of the following locations:
- Diagnostic Imaging Associates, located at L-6 Omega Drive, Newark DE 19713, OR
- Go-Care at Abbey Medical Center, 1 Centurian Drive, Suite 106, Newark DE 19713, OR
- First State Orthopedics (4745 Ogletown Stanton Rd #225, Newark, DE 19713) OR

The information below provides a description of what the testing sessions will include.

Study questionnaire

Relevant time points: 3, 6 and 24 months
You or your child will fill out a survey form that will be used to capture information related to injury and functional capabilities. This will enable us to get information about the current status of the knee. It generally takes an average of 5 minutes for the survey form to be filled out.

**Motion analysis testing**

**Relevant time points: 3, 6 and 24 months**

Surface electrodes taped to your (or your child’s) skin will be used to record the electrical activity of your muscles (electromyography). After all electrodes have been placed, you will perform a maximum contraction of each muscle (i.e. applying maximum effort that is comfortable), with straps applied to your ankles to provide resistance. Nine electrodes will be secured to each leg and then plugged into a small (6” x 4” x 3”) transmitter box that will be attached to the back of a vest with Velcro. The transmitter sends the signal to the computer so we can determine when the muscles are contracting during the activities. These measurements will also be taken during the walking trials of motion analysis testing.

Markers will be attached to your skin and sneakers on both legs using adhesive skin tape. Shells with markers on them will be placed on your pelvis, thighs and calves and will be held in place with elastic wraps. These markers will allow the cameras to track your leg positions. You will be asked to perform several walking trials in our laboratory. Walking trials will give us information about the way your hips, knees, and ankles move while you walk. You will be asked to perform 7 trials of walking at a comfortable, self-selected speed, although additional trials may be required to obtain enough data. During the trials, you will also walk over a force plate that is embedded in the floor. The force plate enables collection of loading data during walking.

The electrodes and markers will be removed at the end of the testing session. Motion analysis testing is a safe, non-invasive process. The entire testing session will last approximately two (2) hours.

**Quantitative and Standard MRI**

**Relevant time points: 3, 6 and 24 months**

This study involves measuring anatomy and estimating biochemical properties of the knee using magnetic resonance imaging (MRI).

You (or your child) will be required to lie completely still on the scanner bed that will slide into the center (bore) of the MRI scanner. A knee coil will be placed around each leg alternately, to measure the signal emitted from the knee. Pillows and other cushions may be used to make you more comfortable. Several scans will be taken and you will be required to remain still on the table for about 5-10 minutes at a time. You will be given periodic breaks in which they will be able to relax but will be asked to remain on the scanner bed for the duration of the session, which should last about 45-50 minutes. Another similar MRI session will also be conducted, which can be on the same day, or a different day, depending on your preference.
You (or your child) will be able to communicate with us via a built-in intercom. You will also be holding an emergency bulb that you can squeeze at any time to let us know you want to come out of the MRI scanner. If at any time you feel uncomfortable or unwilling to continue, no matter what the reason, you can request to immediately stop the study, and the operator will remove you from the scanner. All scans will be conducted by a certified MRI Technologist or other experienced personnel with relevant safety training.

These scans will provide information regarding biochemical and geometrical knee properties.

**This is not a clinical evaluation**

The images of the knee collected in this study are not intended to reveal illness, in part because this research protocol is not designed for clinical diagnosis. The images will not be routinely examined by a clinical radiologist. The personnel at the MRI Center are not qualified to medically evaluate these images. However, if, in the course of collecting images, we have any concerns, we may show scans to a clinical radiologist, who may suggest that you (or your child) obtain further diagnostic tests. Do not rely on this research MRI to detect or screen for abnormalities.

At our discretion, you may view their images and receive digital copies of them. These images will show the inside of the knee and you should be aware of the potential distress or discomfort that may occur by viewing these type of images.

**Radiographs**

**Relevant time points:** 3 and 24 months

Standing x-rays will be taken with the knee slightly bent. These x-rays will allow a radiologist to verify the presence or absence of OA, and to determine knee joint space width (JSW) measurements. This takes 5-10 minutes to be completed.

Radiographs at the 3 month time point will be useful for establishing a baseline, while radiographs at the 24 month time point will be useful to verify the presence/absence of knee OA, and OA progression. These x-rays will be locked in a cabinet for research purposes only.

If you (or your child) are part of the control group (i.e., no history of knee injury), you will only be required to complete motion analysis testing and imaging (quantitative and standard MRI), similar to subjects with ACLR, and at one time point only, i.e. immediately after recruitment.

**WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS? (WHAT ARE THE POSSIBLE BAD THINGS ABOUT THIS RESEARCH?)**

A few things about this study that could make a volunteer uncomfortable are listed below.

**Motion analysis testing**

Participant’s Initials ______
All motion analysis testing procedures involve a simple walking task that has been standardized at the University of Delaware. The risk of re-injury for the ACL-reconstructed population within the first 5 years after ACLR is approximately 5%. Of the hundreds of tests performed on ACLR individuals at the University of Delaware, no one has torn their surgical graft during testing. At the end of motion analysis testing, you may experience discomfort from the removal of tape holding markers and electrodes in place.

Quantitative and Standard MRI

MRI is an imaging technique that uses radio waves and magnetic fields to produce images of internal structures in the body. It is commonly used in hospitals. Unlike X-rays, the MRI does not use any ionizing radiation, and it does not use radioactivity, so there are no radiation related risks from having an MRI scan. Below there is a description of MRI related risks and what is being done to reduce any possible risks associated with them:

Metal: The MRI scanner produces a constant strong magnetic field, which may cause any metal implants, clips, or implanted medical devices within the body to shift position or malfunction. You (or your child) will not be allowed to participate in this study if you have any implanted metal, clips or devices. You will be screened to make sure that it is safe for you to enter a strong magnetic field. Please provide us with as much information as you can, for example, if you had surgery in the past, so that we may decide whether it is safe for you to be a participant. Metallic objects brought into the MRI environment can become hazardous projectiles and can also interfere with the data quality. To minimize this risk, metal earrings, other piercings, necklaces and any other metal in contact with your body will be removed prior to the study. You will also be asked to remove all items from your pockets, including coins, electronics (including cell phones and hearing aids) and wallets. You will also be asked to remove belts with metal buckles, and may be asked to change into a gown that we will provide if your clothing contains significant metal, including metal underwear bras.

Pregnancy: Exposure to MRI scanning might be harmful to an unborn child. Although there are no established guidelines at this time regarding MRI and pregnancy, you (or your child) should be informed that there is a possibility of a yet undiscovered pregnancy related risk. If you know or suspect you may be pregnant or if you do not want to expose yourself to this risk, you will be excluded from participating in this study.

Inner ear damage: MRI scanning produces loud noises that can cause damage to the inner ear if appropriate hearing protection is not used. Earplugs and/or headphones will be provided to protect your (or your child’s) ears.

Claustrophobia: When you (or your child) is inside the MRI scanner, the “bore” of the scanner will surround the knee that is being scanned. You will be positioned so that their knee is centered in the bore of the scanner. If you feel anxious in confined spaces, you may not want to participate. If you are unsure, you can try a “mock” scanner when available, to evaluate the comfort level with the enclosed space of the

Participant’s Initials _________
magnet bore. If you decide to participate and begin to feel claustrophobic, you will be able to tell us via the intercom or the squeeze ball and we will discontinue the study immediately.

**Burns:** In rare cases, contact with the MRI transmitting and receiving coil, conductive materials such as wires or other metallic objects, or skin-to-skin contact that forms conductive loops may result in excessive heating and burns during the experiment. The operators of the MRI scanner will take steps, such as using foam pads when necessary, to minimize this risk. Tattoos with metallic inks can also potentially cause burns. In addition, you (or your child) are requested to let the MRI operator know immediately if you experience any heating or burning sensations during a scan. The scanning session will be stopped as soon as you tell the operator.

**Nerve or muscle stimulation:** While the scanner is operating, there is a small chance that the rapidly changing magnetic fields could cause a slight tingling sensation or a muscle twitch, usually felt in the upper arms or torso. While these sensations may be startling, they are not dangerous or a health risk, and they have no lasting consequences. The sensations should stop when the scan ends. Because these sensations may nevertheless be distracting or even possibly uncomfortable, you (or your child) will be able to squeeze the signal bulb to alert the scanner operator if you feel tingling or muscle twitching, and we will immediately stop the scan. You will then have the opportunity to choose to withdraw from the study or to continue.

**Other Risks:** Besides the risks listed above, there are no other known risks from the magnetic field or radio waves at this time. Although MRI scanning has been used for more than 20 years, long-term effects are unknown.

**Radiography**

This research study involves exposure to radiation from a standard radiograph (x-ray). This radiation exposure is not necessary for your medical care and is for research purposes only. At each time point that the radiograph is obtained, the total amount of radiation that you will receive in this study is about 0.12 mSv (milli-Sievert) and is approximately equivalent to a uniform whole-body exposure of 15 days of exposure to natural background radiation. This use involves minimal risk per National Institutes of Health guidelines, and is necessary to obtain the research information desired. To reduce exposure, you (or your child) will wear a lead apron to cover the rest of your body while the x-rays of your leg are captured.

**WHAT IF YOU OR YOUR CHILD ARE INJURED DURING PARTICIPATION IN THE STUDY?**

If you or your child are injured during research procedures, you will be offered first aid at no cost to you. If additional medical treatment is needed, the cost of this treatment will be your responsibility or that of your third-party payer (for example, your health insurance). By signing this document, you are not waiving any rights that you may have if injury was the result of negligence of the university or its investigators.

**WHAT ARE THE POTENTIAL BENEFITS? (WHAT ARE THE POTENTIAL GOOD THINGS ABOUT THIS RESEARCH?)**

Participant's Initials ________
The proposed motion analysis testing procedure aims to study walking patterns after ACLR, and the change in these patterns over time. The data collected will be used to propose a mechanism for OA, and distinguish between abnormal versus normal walking patterns. A link between abnormal patterns and OA has not yet been established and validated. Hence, the proposed motion analysis testing procedure, by itself, cannot identify OA, and as such, no direct benefit to you is expected.

Similarly, the proposed MRI imaging procedure only aims to estimate biochemical properties of the knee cartilage, which has not yet been shown to predict OA. These properties will be used in a mathematical model to reveal conditions that can affect the knee cartilage negatively, and may result in knee OA. The proposed MRI imaging procedure, by itself, cannot predict OA, and as such, no direct benefit to you is expected.

However, we do hope that an improved understanding of the effect of the study measurements will provide information about knee OA in an ACLR population, and contribute to preventative therapeutic protocols in the future.

**NEW INFORMATION THAT COULD AFFECT YOUR PARTICIPATION:**

During the course of this study, we may learn new information that could be important to you. This may include information that could cause you to change your mind about participating in the study. We will notify you as soon as possible if any new information becomes available.

**HOW WILL CONFIDENTIALITY BE MAINTAINED? (WHO MAY KNOW WHO PARTICIPATED IN THIS RESEARCH?)**

No one other than the investigators will know that you or your child were in this study. If we tell other people about the research, we will not use names.

More details for adult participants and for parents/guardians of adolescent participants are provided below.

All information obtained during the study will be held in strict confidence to the fullest extent possible by law. In no case will personal identifiable information be shared with any other individuals or groups without your expressed written consent. Your (or your child’s) images will be stored on secured computer servers and will be archived indefinitely. Non-identifiable images of your scans may be used for teaching purposes, be presented at meetings, published, and also shared in databases accessible to other researchers for further research and educational purposes. Your names or other identifying information will not be used in any publication or teaching materials without your specific permission.

Identities will be kept confidential by coding them with a subject identification number stored on a password protected computer. Only the investigators and research coordinator will have access to that file on the secure server.

All data will be electronically encrypted and archived indefinitely for comparative analyses of scientific and clinical questions related to the ACL injury, surgery and knee OA. All research findings will be compared to

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Participant’s Initials _________
knee cartilage properties, knee loading patterns and knee movement patterns reported via peer-reviewed academic journals and conferences that emphasize outcomes after ACLR.

While rare, an accidental breach of confidentiality is a risk. Should an accidental breach of confidentiality occur, the event will be reported to the institutional review board (IRB) immediately, and appropriate follow up steps will be taken based on IRB recommendations.

HIPAA AUTHORIZATION

State and federal privacy laws protect your PHI. These laws say that, in most cases, your health care provider can release your PHI for the purpose of conducting research only if you give permission by signing an Authorization.

The research team would like and appreciate access to your PHI, specifically regarding any knee injury and/or surgery, to make the study as complete as possible; however, if you do not sign this Authorization, you may still participate in the research study.

Who May Disclose and Who may Use and/or Receive my PHI?

By signing this document, you are hereby permitting your physicians, medical care providers, and UD’s physical therapy clinic to disclose the PHI described in this Authorization to the research team involved in this project, the study sponsor and its employees, the Institutional Review Board (IRB) and other regulatory agencies responsible for overseeing research.

Once your PHI is shared with these persons, you understand that the PHI may no longer be protected by federal or state privacy laws.

What PHI Will Be Disclosed and Used, and for What Purpose?

The following PHI may be disclosed to, collected by, used by, and shared with those listed above.

Operative report (about an operation) and Physical therapy records.

This only pertains to medical records related to your ACL injury and surgery.

This Authorization will expire at the conclusion of the research study. You may cancel this Authorization at any time before, during, or after your participation in this study by giving a written request with your signature on it to the Principal Investigator at buchanan@udel.edu. If you cancel this Authorization, your PHI obtained before that date may still be used for this research study.

I hereby authorize the disclosure and use of my Personal Health Information

_________________________________________   ______________
Signature of Patient or Authorized Representative Date

Participant’s Initials
Printed Name of Person Signing: __________________________

Relationship to Patient: _______________________________

WILL THERE BE ANY COSTS TO YOU FOR PARTICIPATING IN THIS RESEARCH?

There are no costs associated with participating in the study.

WILL YOU RECEIVE ANY COMPENSATION FOR PARTICIPATION?

Participants will be compensated 50 USD for motion analysis testing, 50 USD for qMRI, and 50 USD for a radiograph (x-ray). Thus, there will be a total of 150 USD compensation associated with each time point, i.e. 3, 6 and 24 month time points.

DO YOU HAVE TO TAKE PART IN THIS STUDY? (CAN YOU CHANGE YOUR MIND ABOUT BEING IN THE STUDY?)

You do not have to say yes. Taking part in this research study is up to you or your child. If you choose to take part, you can change your mind and stop at any time. If, at any time, you decide to stop, please let us know by telling one of the researchers.

If you are a student volunteer and decide not to take part in this research, your choice will not affect your grades or your relationship with your classmates and your teachers.

We may ask you to stop participating if any leg injury that requires serious medical management (i.e. fracture or re-injury) has occurred before the testing session.

WHO SHOULD YOU CALL IF YOU HAVE QUESTIONS OR CONCERNS?

If you have any questions about this study, please contact the Principal Investigator, Dr. Thomas S Buchanan at buchanan@udel.edu or (302) 831-2410.

If you have any questions or concerns about your rights as a research participant, you may contact the University of Delaware Institutional Review Board at hsrb-research@udel.edu or (302) 831-2137.
For adult participants (at least 18 years old):

Your signature below means that: 1) you are at least 18 years old; 2) you have read and understand the information given in this form; 3) you have asked any questions you have about the research and those questions have been answered to your satisfaction; 4) you accept the terms in the form and volunteer to participate in the study. You will be given a copy of this form to keep.

Printed Name of Participant  Signature of Participant  Date

For adolescent participants (less than 18 years old):

If you want to participate, and we have answered all of your questions about it, please sign below.

Printed Name of Participant  Signature of Participant  Date

For parents/guardians of adolescent participants (less than 18 years old):

You are making a decision whether or not to have your child participate in this study. Your signature indicates that you have read the information provided above and decided to allow your child to participate.

Printed Name of Parent/Guardian  Signature of Parent/Guardian  Date

Person Obtaining Consent  Person Obtaining Consent  Date
(PRIN TED NAME)  (SIGNATURE)

OPTIONAL CONSENT TO BE CONTACTED FOR FUTURE STUDIES:

Do we have your permission to contact you regarding participation in future studies? Please write your initials next to your preferred choice.

_______ YES  ________ NO

Participant’s Initials ________
Appendix F

PERMISSIONS
F.1 Permission to Use Papers Published in *Journal of Orthopaedic Research* (Chapter 2, Chapter 6, and Chapter 7)

“Contributors may use the articles in…other works such as theses.” (Wiley, 2019)


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To me

5:44 AM (2 hours ago)

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Should you require any further information, please do not hesitate to contact me.

Kind regards,

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From: Jacob Capin <capin@udel.edu>
Sent: 06 June 2019 16:40
To: Wiley Global Permissions <permissions@wiley.com>
Subject: Permission to use accepted versions of manuscripts published in JOR for use in my PhD thesis/dissertation

Hello,

According to the information available online (https://authorservices.wiley.com/author-resources/Journal-Authors/licensing/licensing-info-faqs.html), I may use the accepted version of the manuscript in my PhD thesis without any special permission, correct?

Here are the publications of reference (of which I am an author):


Thank you,

Jacob

---

Jacob J. Capin, PT, DPT, MS
BIONG PhD Candidate
Research and Teaching Assistant
University of Delaware
USA Triathlon Level I Certified Coach
ORCID: 0000-0002-0013-5809
66e-5d-2616
F.2 Permission to Use Paper Published in *Journal of Bone & Joint Surgery* (Chapter 3)

“Permission from The Journal of Bone and Joint Surgery, Inc. (JBJS) is not required for the following uses—if you are an author of the article, and JBJS is clearly identified as the copyright holder and the use is entirely non-commercial, you may… use your article in an academic dissertation required to obtain an academic degree.” (JBJS, 2019)


F.3 Permission to Use Paper Published in *Clinical Orthopaedic & Related Research* (Chapter 5)

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F.4  Permission to Use Paper Published in *Orthopaedic Journal of Sports Medicine* (Chapter 8)

Briars, Colleen

to me

Jacob,

Yes, you are more than welcome to do so. Please let me know if you have any further questions.

Best Wishes,
Colleen

Colleen Briars, ELS
AOSSM Director of Journal Publishing
OJSM Editorial & Production Manager
a. 9400 Higgins Road Suite 300, Rosemont, IL 60018
e. colleen@aossm.org  w. sportmed.org
p. 847-292-4900
h. 8 am - 4 pm

From: Jacob Capin <capin@udel.edu>
Sent: Wednesday, June 5, 2019 1:46 PM
To: Briars, Colleen <colleen@aossm.org>
Subject: Permission to use the accepted OJSM manuscript in my PhD thesis/dissertation

Hi Colleen,

May I use the accepted version of the following OJSM article in my PhD thesis/dissertation?

MS ID#: OJSM/2019/040519
MS TITLE: Superior 2-Year Functional Outcomes Among Young Female Athletes After ACL Reconstruction in Just 10 Return-to-Sport Training Sessions. Comparison of ACL-SPORTS Randomized Control Trial to Delaware-Oslo and MOON Cohorts

Please let me know if these is any specific permission request that I need.

Thank you,
Jacob

Jacob J. Capin, PT, DPT, MS
BIOMS PhD Candidate
Research and Teaching Assistant
University of Delaware
USA Triathlon Level I Certified Coach
ORCID: https://orcid.org/0000-0001-6381-5700
804-832-1818
F.5  Permission to Use Paper Published in *Journal of Orthopaedic & Sports Physical Therapy* (Appendix A)

---Original Message---
From: Jacob Capin <capin@udel.edu>
Sent: Wednesday, June 05, 2019 2:44 PM
To: Corey Parker <coreyparker@jospt.org>
Subject: Permission to use JOSPT publication in PhD thesis/dissertation

Hi Corey,

May I use the accepted version of the following JOSPT publication in my PhD thesis/dissertation?


Thank you,

Jacob

---

Jacob J. Capin, PT, DPT, MS

BIOMS PhD Candidate
Research and Teaching Assistant
University of Delaware
USA Triathlon Level I Certified Coach
ORCID: [https://orcid.org/0000-0001-9361-3700](https://orcid.org/0000-0001-9361-3700)
804-832-1616
F.6 Permission to Use Paper Published in Annals of Joint (Appendix B)

Permission form

Requestor Information:
Name: Jacob John Capin
Affiliation: University of Delaware
Address: 540 South College Ave, 210-Z, STAR Campus, Newark, DE 19713
Email: capin@udel.edu

What Publication Material Would You Like To Use/Adapt?
DOI: 10.21037/aoj.2018.04.11
Authors: Jacob J Capin, Lynn Snyder-Mackler
Article Title: The current management of patients with patellofemoral pain from the physical thera
Title of Publication: Annals of Joint
Page Numbers of Article: 1-14
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I, Jacob Capin, am requesting permission to use the accepted version of the manuscript in my PhD

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Date: 6/12/2019

Signature (Requestor):
Signature (Copyright holder):
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production bjsem (sent by tjobson@bmj.com) to me

Hi Jacob,

I've checked and this will be fine.

Hoping to get the revised proof to you by tomorrow morning.

Kind regards

Teresa

Teresa Jobson
Production Editor

On Wed, 5 Jun 2019 at 20:41, Jacob Capin <capin@udel.edu> wrote:

Hi Teresa,

May I use the accepted version of the following RJSM editorial in my PhD thesis/dissertation (giving appropriate credit/citation and including the doi)?


Thank you,

Jacob

---

Jacob J. Capin, PT, DPT, MS
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ORCID: https://orcid.org/0000-0001-3361-3700
904-932-1016