Muscle Dysfunction Associated With ACL Injury and Reconstruction

by

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DEDICATION PAGE

To Kristin, for inspiring this research.

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ABSTRACT

Muscle Dysfunction Associated With ACL Injury and Reconstruction

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Anterior cruciate ligament (ACL) injuries occur in over 200,000 individuals per year in the United States. Quadriceps central activation failure (CAF) is a common consequence of these knee injuries, though why it presents remains elusive. Neuromuscular impairments resulting from ACL injury may not be limited to the muscles crossing the knee joint, however, though limited data are available to confirm this. The overall goal of this dissertation is to examine the muscle dysfunction associated with ACL injury and reconstruction, possible mechanisms leading to the lingering quadriceps muscle weakness after ACL reconstruction (ACLr), and to determine the immediate impacts of this weakness on the affected individual. In the first study, I sought to establish the presence of muscle dysfunction throughout the lower extremity following ACL injury and ACLr. I found that significant quadriceps and hamstrings strength deficits were present in the injured/reconstructed limb compared to the contralateral side both pre- and post-operatively, with pre-operative injured limb strength deficits also present compared to healthy individuals. There was no hip or ankle weakness, however, compared to healthy individuals. Given the presence of quadriceps weakness following ACLr, identifying the contributing factors to this muscle weakness seemed critical. Therefore, in study two I

examined the contributions of quadriceps atrophy and CAF to persistent quadriceps strength impairments. Individuals who were six-months post-operatively following ACLr underwent quadriceps CAF and magnetic resonance imaging assessment. Results demonstrated that neither quadriceps CAF nor atrophy significantly contributed to the persistent quadriceps weakness in these individuals. Finally, I examined the effects of neuromuscular fatigue on quadriceps strength, CAF, and lower extremity biomechanics after ACLr. Individuals 7-10 months after ACLr demonstrated lower extremity biomechanics consistent with non-contact ACL injury risk prior to fatigue. Both ACLr and healthy individuals demonstrated greater quadriceps weakness and CAF following fatigue. Healthy individuals concurrently altered their biomechanics, potentially increasing their non-contact ACL injury risk. Surprisingly, ACLr subjects demonstrated similar, potentially injurious sagittal plane biomechanics pre- and post-fatigue, suggesting that reconstruction and/or rehabilitation are not sufficiently reducing the biomechanical risk factors for re-injury when individuals return to activity.

CHAPTER 1
INTRODUCTION

OVERVIEW

Over 200,000 anterior cruciate ligament (ACL) injuries occur per year in the United States.[1] As of 1999, Gotlob and colleagues[2] had estimated the annual cost of all primary surgical reconstructions of the ACL to be $2 billion.

ACL injuries not only lead to pain and disability for the injured individual, but have also been implicated in the development of post-traumatic osteoarthritis (OA). In fact, over 50% of individuals suffering an ACL tear have been demonstrated to develop OA within 5-12 years following injury, regardless of treatment strategy (i.e., surgical vs. conservative management).[3-5] In individuals opting for surgical reconstruction, specifically, it has been demonstrated that over 70% will develop OA approximately seven years post-operatively.[5]

RATIONALE

Quadriceps muscle weakness presents frequently after ACL injury and reconstruction, though how it ensues and why it persists despite otherwise successful rehabilitation remain elusive. The quadriceps are important during dynamic control of the lower extremity and, as such, quadriceps weakness may lend to altered lower limb neuromechanical control strategies. These strategies may be hazardous not only when an individual returns to activity following ACL reconstruction, but the long term effects of these altered mechanics may potentiate joint degeneration.

Previous studies examining post-operative strength deficits are limited in that they only examine quadriceps, and even hamstrings, strength. Recent evidence is emerging, though, to suggest that muscle weakness may arise elsewhere in the lower extremity following knee injury.[6] Confirming the presence of weakness within these proximal and distal muscle groups after ACL injury and reconstruction, specifically, may lend to better rehabilitation strategies.

Several studies have been undertaken examining the origin of quadriceps weakness following ACL injury[7, 8], suggesting that quadriceps atrophy and central activation failure may be key contributors to lingering weakness within this muscle group. These studies, however, examined only an ACL-injured population and did not consider individuals following ACL reconstruction. As the majority of individuals undergo surgical reconstruction of the torn ACL[9], understanding the contributors to lingering quadriceps weakness following ACL reconstruction is imperative and a critical step to countering it.

Finally, the lingering quadriceps weakness may be especially hazardous when individuals return to activity. Neuromuscular fatigue is prevalent in athletic activity and has been shown to decrease central drive to the musculature[10], with this effect being magnified in the presence of muscle weakness.[11] Understanding the response of this neurologically impaired muscle to the demands of physical activity following ACL injury and reconstruction is imperative to improving rehabilitation strategies to reduce fatigability within the musculature. Additionally, elucidating how neuromuscular fatigue influences lower extremity biomechanics following ACL reconstruction may allow for the development of strategies to counter these potentially hazardous neuromechanical consequences prior to individuals returning to activity post-operatively.

OBJECTIVE

The objective of this research was to further elucidate the effects of ACL injury and reconstruction on muscle dysfunction throughout the lower extremity. Specifically, we examined isokinetic hip, knee, and ankle muscle strength. We utilized a combination of neuromuscular and imaging assessment techniques to examine the origin of quadriceps dysfunction. And, we employed neuromuscular and biomechanical assessment techniques to explore the effects of quadriceps dysfunction under realistic movement conditions.

SIGNIFICANCE

This research may have important implications for rehabilitation following ACL reconstruction. By determining where muscle weakness exists, strategies to improve neuromuscular function with the hope of preventing re-injury and possibly OA can be implemented. Similarly, elucidating the underlying contributors to persistent quadriceps

dysfunction known to afflict ACL reconstruction patients will lend to the development of treatment strategies designed to better counter it during rehabilitation.. Lastly, by determining the need for, and incorporating fatigue-resistance training within, current rehabilitation strategies, we may be able to better protect an individual from re-injury when he/she returns to activity following ACL reconstruction.

ORGANIZATION OF THE DISSERTATION

This dissertation contains 7 chapters. Chapters 2-4 present the individual studies as full-length manuscripts prepared for publication. Chapter 2 examines strength in the musculature crossing the hip, knee, and ankle joints in the injured versus uninjured limbs of individuals pre- and post-ACL reconstruction as well as compared to healthy persons. Chapter 3 investigates the origin of persistent quadriceps dysfunction after ACL reconstruction by examining muscle atrophy (as assessed via muscle cross sectional area recorded from magnetic resonance images) and quadriceps central activation ratio determined utilizing the burst superimposition technique. Chapter 4 examines the effects of neuromuscular fatigue on quadriceps strength and central activation failure as well as the effects of fatigue on lower extremity biomechanics during dynamic landing in individuals 7-10 months after ACL reconstruction compared to healthy people. Chapter 5 provides an overall discussion of chapters 2-4. Chapter 6 contains a conclusion; Chapter 7 recommendations for future work. Chapter 8 provides a review of pertinent literature.

SPECIFIC AIM 1

To determine the presence of weakness in the lower extremity musculature following ACL injury and subsequent reconstruction.

Specifically, this study aimed to examine strength of the hip, knee, and ankle flexor and extensor musculature as well as the hip abductors/adductors to elucidate the presence of weakness within each of these muscle groups. Bilateral isokinetic muscle strength was assessed pre-operatively and 6-months post-operatively in individuals undergoing ACLr as well as healthy individuals.

Hypotheses:

Subjects would demonstrate weakness of the hip, knee, and ankle musculature. They would demonstrate this weakness in the injured compared to the uninjured limb as well as when compared to healthy persons.

Subhypothesis 1: Subjects would demonstrate hip flexor, extensor, and abductor weakness.

Subhypothesis 2: Subjects would demonstrate weakness of the quadriceps and hamstrings muscle groups.

Subhypothesis 3: Subjects would demonstrate weakness of the ankle plantar flexor and dorsiflexor musculature.

SPECIFIC AIM 2

To determine the contributors to lingering quadriceps weakness following ACLr.

Specifically, this study sought to examine muscle cross sectional area (CSA) as well as the central activation ratio (CAR) to elucidate whether quadriceps weakness manifests through peripheral or central mechanisms, respectively. Bilateral quadriceps CAR assessment and magnetic resonance imaging were performed in individuals 6-months after ACLr.

Hypotheses:

Persistent quadriceps weakness would result from a combination of CAF and muscle atrophy.

Subhypothesis 1: CAF would more strongly predict quadriceps weakness than atrophy.

Subhypothesis 2: CAF as well as quadriceps CSA would be decreased in the injured versus uninjured limbs.

SPECIFIC AIM 3

To determine whether the magnitude of quadriceps weakness and CAF was greater in patients following ACLr compared to healthy individuals. Additionally, this study sought

to determine if the magnitude of knee biomechanical changes differed between individuals after ACLr compared to healthy persons prior to and following neuromuscular fatigue.

Quadriceps isometric strength and CAF as well as sagittal and frontal plane knee joint angles and moments were measured prior to and immediately following lower extremity neuromuscular fatigue in patients who underwent ACLr and healthy persons.

Hypotheses:

Subjects would demonstrate altered kinetics and kinematics as well as greater CAF following fatigue.

Subhypothesis 1: All subjects would demonstrate greater knee extension and abduction angles/moments post-fatigue.

Subhypothesis 2: ACLr subjects would demonstrate greater CAF prior to fatigue compared to controls and will demonstrate greater biomechanical changes (increased greater knee extension and abduction angles/moments) post-fatigue compared to their healthy counterparts.

Subhypothesis 3: ACLr subjects would reach maximal fatigue faster (i.e., in less repetitions of the fatiguing exercise) than healthy individuals.

CHAPTER 2
LOWER EXTREMITY MUSCLE STRENGTH FOLLOWING ACL INJURY AND RECONSTRUCTION

ABSTRACT

Quadriceps and hamstrings muscle weakness have been demonstrated frequently following anterior cruciate ligament (ACL) injury and reconstruction. Though studied less often, evidence suggests that knee injury may precipitate weakness in the hip and ankle musculature; however, few data support this contention after ACL injury and reconstruction. Given the importance of these muscles in controlling lower extremity neuromechanics, it seems imperative to ascertain where strength deficits present so that rehabilitation strategies to combat these potential impairments can be developed and implemented. Therefore, the purpose of this study was to determine if hip flexor, extensor, abductor, and adductor, quadriceps and hamstrings, and ankle plantar and dorsiflexor weakness presented following ACL injury and reconstruction. Fourteen ACL-injured individuals underwent bilateral strength assessment pre-operatively and 6-months post-operatively. Fifteen healthy participants performed strength testing in a matched limb at a single testing session. Strength was assessed at 60°/s. Statistical analyses consisted of 2x2 (limb x time) repeated measures as well as 1x2 (limb x group) ANOVAs. Paired t-tests were used for *post hoc* analyses. The injured limb quadriceps and hamstrings were weaker compared to the uninjured limb both pre- and post-operatively ($P<0.001$). Limb by time interactions were revealed for the hamstrings ($P=0.016$) and ankle plantar flexors ($P=0.008$), with *post hoc* tests demonstrating plantar flexor weakness pre- versus post-operatively ($P=0.021$). There were no significant pre- or post-operative differences in strength between groups for any muscle tested ($P>0.05$). Weakness did not present within the hip or ankle dorsiflexor musculature, suggesting rehabilitation need not target these muscle groups. ACL rupture induced injured limb ankle plantar flexor weakness that appeared to be countered during post-operative rehabilitation. Further, our results confirmed previous reports suggesting insufficient restoration of quadriceps and hamstrings strength compared to the contralateral limb post-operatively. The quadriceps and hamstrings are important stabilizers during dynamic

activity, and weakness in these muscles could impair knee joint stability upon return to activity. As such, improving rehabilitation strategies to better target these lingering strength deficits seems imperative.

INTRODUCTION

Traumatic anterior cruciate ligament (ACL) injury occurs frequently during athletic activity, precipitating numerous immediate and long-term consequences, such as pain, disability, and, ultimately, joint degeneration.[4] Lower extremity muscle weakness, particularly in the quadriceps and hamstrings, is also commonly reported following ACL injury and reconstruction, often lingering well beyond the post-operative rehabilitation period.

Quadriceps strength deficits in the injured versus uninjured limb reportedly range from 5-30%[12-17], with hamstrings strength deficits of 9-13%[14, 17, 18] having been described. The muscle weakness following ACL reconstruction, however, seems to be more problematic in the quadriceps than the hamstrings with reports of quadriceps strength deficits persisting upwards of seven years post-operatively, while hamstring weakness frequently resolves within the first post-operative year.[12] Of additional concern is the bilateral presence of quadriceps and hamstrings muscle weakness.[14]

Less often considered is strength of the triceps surae and hip musculature. Clinical observation and emerging evidence[6] suggest, however, that strength within these muscle groups may be negatively influenced by the injury and reconstruction processes. Jaramillo and colleagues[19] reported hip flexor/extensor and abductor/adductor weakness following knee surgery, though their results were not limited to an ACL-reconstructed population. The presence of both hip flexor[6] and adductor[20] weakness have been confirmed following ACL reconstruction. Hip adductor weakness, specifically, was demonstrated following semitendinosus/gracilis (STG) autograft reconstruction, with the authors suggesting that donor site morbidity and neurological alterations may have contributed to the resultant weakness.[20]

Few studies have examined strength of the ankle joint musculature following ACL injury or reconstruction. Karanikas et al.[6] reported no differences bilaterally in isokinetic ankle

plantar flexor strength between 3-6 months or 6-12 months post-operatively; however, decreased gastrocnemius electromyographic activity has been demonstrated during gait in ACL deficient individuals as well as during landing following ACL reconstruction, findings which could be the result of muscle weakness.[21]

Considering the importance of muscle strength for controlling dynamic stability of the lower limb and that long term sequelae, such as OA, have been proposed to result from lingering muscle weakness, confirming and quantifying the presence of lower extremity muscle weakness seems imperative so that strategies to counter it can be better implemented within rehabilitation protocols. The purpose of this study, therefore, was to determine the magnitude of weakness present in the lower extremity musculature following ACL injury and subsequent reconstruction. Specifically, we sought to examine strength of the hip, knee, and ankle flexor and extensor musculature as well as the hip abductors/adductors before and after ACL reconstruction. We hypothesized that subjects would demonstrate weakness pre- and post-operatively within the 1) hip flexor, extensor, and abductor muscle groups, 2) quadriceps and hamstrings, and 3) ankle plantar flexor and dorsiflexor musculature.

METHODS

Subjects

Fourteen ACL-injured individuals (8 male, 6 female; age: 19.43±5.21years; height: 1.73±0.09m; mass: 74.03±13.61kg) and 15 control subjects (7 male, 8 female; age: 24.73±3.37years; height: 1.75±0.09m; mass: 73.25±13.48kg) were included in this study. A power analysis based on pilot data collected on ACL reconstructed individuals in our laboratory revealed that to achieve injured versus uninjured quadriceps and hamstrings isokinetic strength differences with 80% statistical power and an α-level of 0.05, thirteen subjects would be needed per group.

Potential subjects had to have sustained a complete ACL rupture during athletic activity. Individuals were excluded if they: 1) had a history of previous surgery to either knee, 2) had a previous partial ACL tear, 3) had other ligamentous damage concurrent with ACL injury, and 4) were not scheduled for ipsilateral bone patellar tendon bone (BPTB) or

STG autograft ACL reconstruction. Pregnant females were also excluded. Individuals in the healthy group were further excluded if they had a history of any lower extremity surgery or suffered a lower extremity injury in the previous six months. The rehabilitation completed by all ACL-injured subjects in this study was performed at a single outpatient clinic and was a standard rehabilitation protocol (Appendix B) initiated during the first post-operative week and concluded during the twelfth through sixteenth post-operative week, depending on the individual's progression. The Medical School Institutional Review Board at University of Michigan approved this study. All subjects provided informed consent prior to participation.

Strength Testing Procedures

ACL-injured subjects reported for testing on two occasions, pre-operatively and six months post-operatively, whereas control subjects reported for testing on a single occasion only. Strength assessments were performed bilaterally for each muscle group on an isokinetic dynamometer (Biodex System 3, Biodex Medical Systems, Shirley, New York, USA) at 60º/s and recorded using a custom-written Labview program (Labview 8.5, National Instruments, Austin, TX, USA). Three maximal voluntary concentric contractions (MVCC) were performed for each muscle group tested. The peak value over those three repetitions was normalized to subject body mass (kg) and used to quantify strength (Nm/kg). Verbal encouragement was provided throughout testing in an attempt to help elicit each subject's maximal effort. Testing order (limb and muscle group) was randomized prior to subject enrollment.

<u>Hip Strength</u>

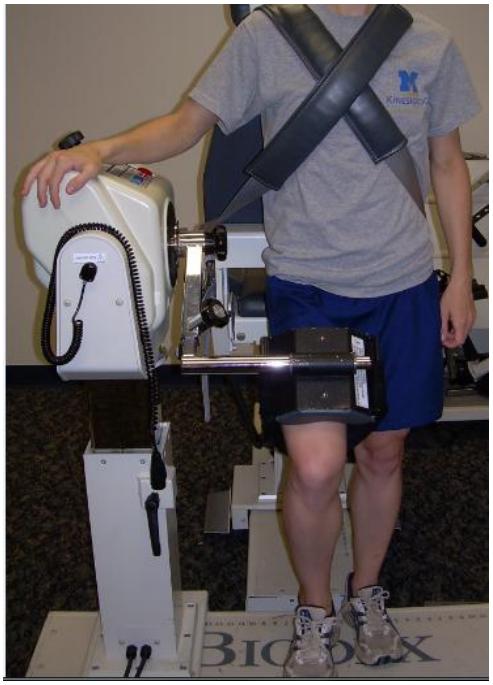


Figure 2.1. Hip flexion/extension strength testing position.

For all hip strength measurements, the mechanical axis of the dynamometer was aligned with the greater trochanter of the limb being tested, and the distal femur was strapped to the dynamometer arm. Specifically, for hip flexion/extension strength assessment, subjects stood facing away from the back of the dynamometer chair as shown in figure 2.1.[22] For hip abduction/adduction assessment, subjects were positioned side-lying on the dynamometer chair with the hip in a neutral position (Figure 2.2). Subjects were instructed to keep the trunk as still as possible and only to abduct/adduct the hip, not to rotate, flex, or extend it. The full, available range of motion was utilized for strength assessment for both muscle groups during testing. Subject positioning was monitored throughout testing by the investigator.

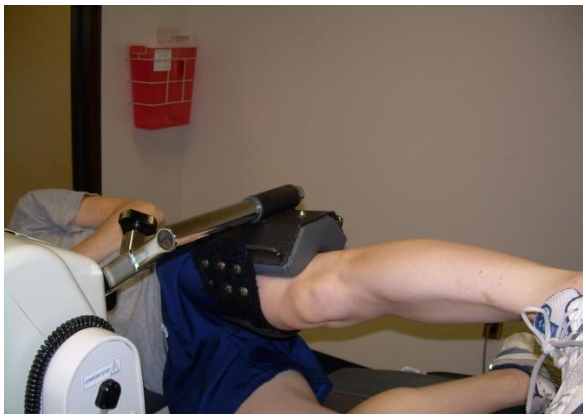


Figure 2.2. Hip abduction/adduction strength testing position.

Knee Strength

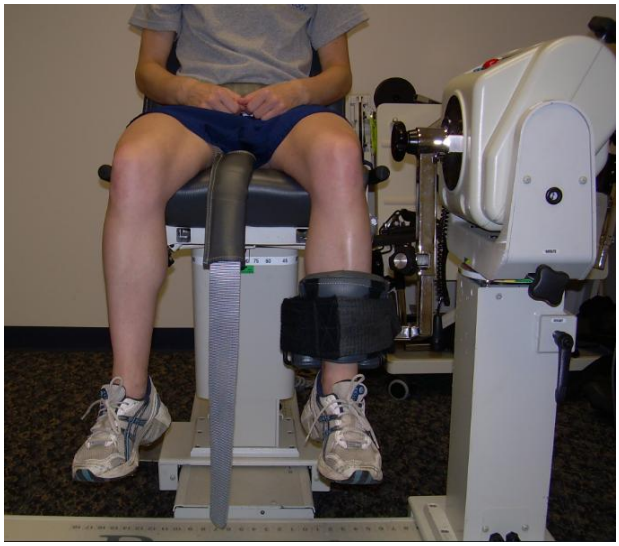


Figure 2.2. Knee extension/flexion strength testing position.

For knee flexion/extension, subjects were seated on the dynamometer chair with the hip flexed to 85°.[12] The mechanical axis of the dynamometer was aligned with the lateral aspect of the knee joint center of the test limb and the distal shank was strapped to the dynamometer arm (Figure 2.3). A stabilization strap was placed over the pelvis. Subjects were instructed to move the knee from 0-100° of flexion during testing.[12] If subjects were lacking full extension, they were instructed to move through the full, available range of motion during testing.

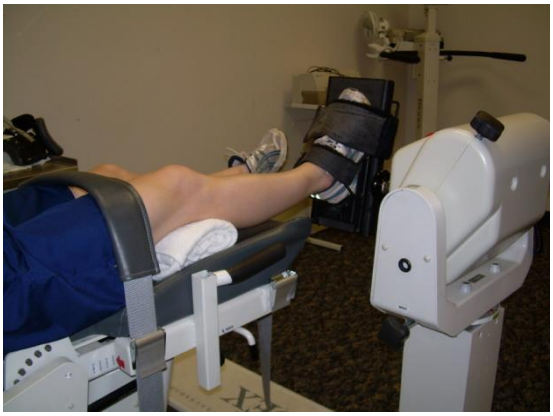


Figure 2.3. Ankle plantar flexion/dorsiflexion strength testing position.

Ankle Strength

Ankle plantar flexion and dorsiflexion strength were assessed with subjects positioned supine on the dynamometer chair with the knee flexed to approximately 15° (Figure 2.4). This position was chosen to avoid subject discomfort at full knee extension but still target the gastrocnemius muscle as much as possible. The mechanical axis of the dynamometer was aligned with the lateral malleolus of the test leg and the foot was strapped to the dynamometer's foot plate attachment. The full, available range of motion was utilized for strength assessment.

Statistical Analyses

The dependent variables used for analysis were strength (Nm/kg) of each muscle group (hip flexors and extensors, abductors and adductors; knee flexors and extensors; ankle plantar flexors and dorsiflexors) and the independent variables were limb (injured and

uninjured for the ACL-injured group or a randomly determined test limb in control subjects), group (ACL reconstructed and control), and time (pre- and post-operatively). Two x two repeated measures ANOVAs were utilized to examine the dependent variables in the ACL-injured group between limbs and over time. Additional 1x2 ANOVAs were performed to compare the dependent variables between the ACL-injured group at the pre- and post-operative time points to the control group (injured limb vs. test limb only). The *a priori* alpha level was $P \leq 0.05$. Sidak multiple comparisons procedures and paired t-tests were used for all *post hoc* analyses. Effect sizes and their associated confidence intervals were calculated in Microsoft Excel 2007 (Microsoft Corporation, Redmond, Washington) using Cohen's d.[23] Effect sizes were calculated as either $\frac{\text{ACL-injured mean-control mean}}{\text{pooled standard deviation}}$ or $\frac{\text{post-operative mean-pre-operative mean}}{\text{pooled standard deviation}}$. Effect sizes were interpreted as having small (0.2-0.5), moderate (0.51-0.8), or large (>0.81) impacts in accordance with Cohen's guidelines.[23] The Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL) version 17.0 was utilized for all other analyses.

RESULTS

Hip Strength

Statistical analyses failed to reveal a main effect for time for hip muscle strength, demonstrating that no differences were present between the pre- and post-operative time points in the ACL-injured group (flexors $P=0.09$; extensors $P=0.053$; abductors $P=0.67$; adductors $P=0.76$ [Figure 2.5]) (Table 2.1). Similarly, no main effects for limb were detected suggesting hip muscle strength was not different between limbs (flexors $P=0.94$; extensors $P=0.08$; abductors $P=0.31$; adductors $P=0.15$). Hip strength was not significantly different in the ACL-injured group compared to the control group either pre-operatively (flexors $P=0.16$; extensors $P=0.79$; abductors $P=0.59$; adductors $P=0.28$) or post-operatively (flexors $P=0.88$; extensors $P=0.2$; abductors $P=0.82$; adductors $P=0.14$).

Knee Strength

There was no time main effect for quadriceps (P=0.66) or hamstrings (P=0.85) strength (Table 2.1) (Figure 2.5) in the ACL-injured group. The ACL-injured subjects did

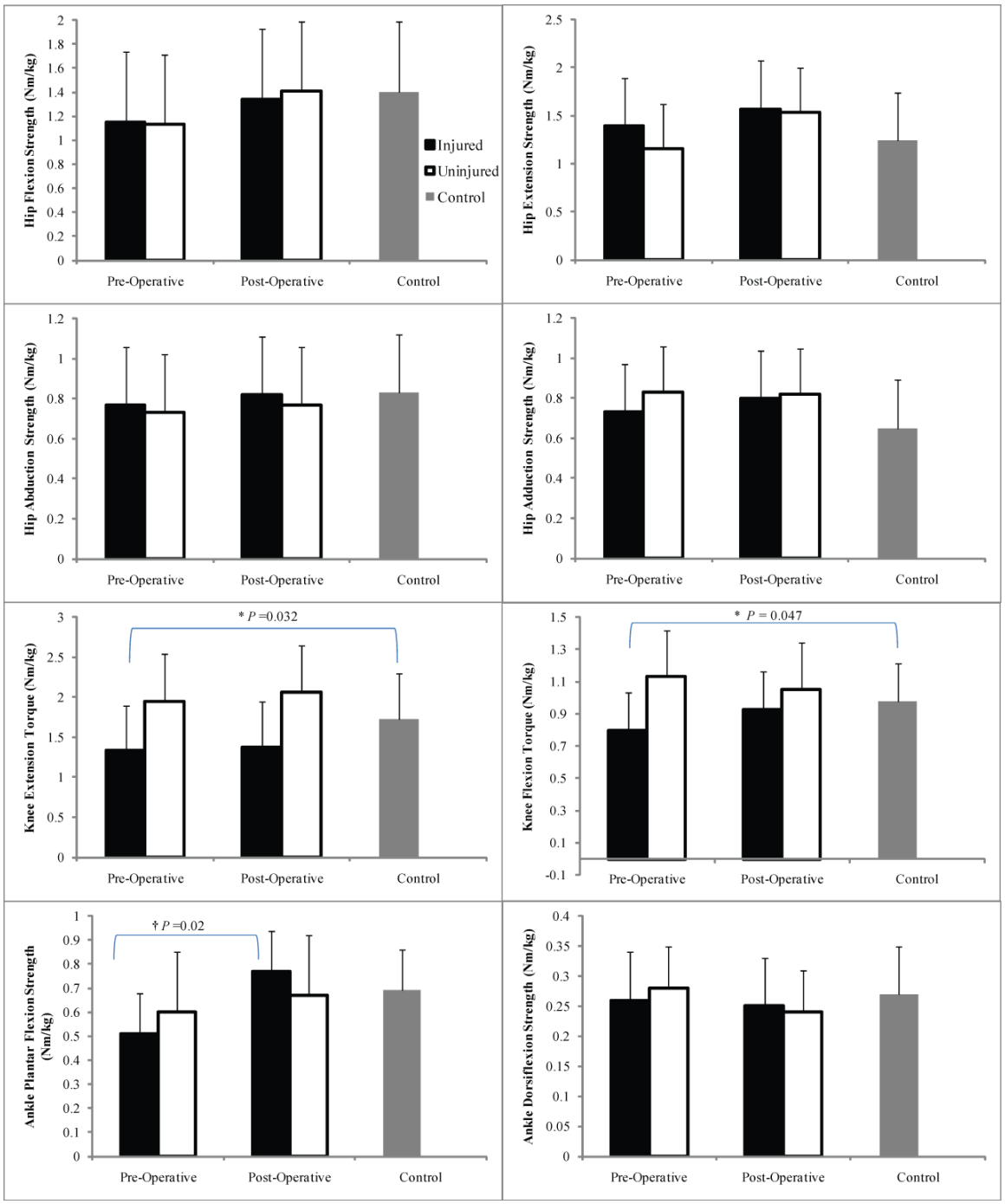


Figure 2.4. Mean ± standard deviation hip, knee, and ankle muscle strength. *Indicates significant difference between ACL-injured (pre-operative time point) and control groups. †Indicates significant difference between pre- and post-operative time points within the ACL-injured group (injured limb only).

demonstrate a significant effect of limb, with greater healthy limb quadriceps (P<0.001) and hamstrings (P<0.001) strength. Additionally, there was a significant time by limb interaction for the hamstrings (P=0.016); however, *post hoc* testing revealed the pre-operative strength was not different from that recorded post-operatively in either the injured (P=0.13) or uninjured limbs (P=0.47) There were differences in pre-operative (quadriceps P=0.032; hamstrings P=0.047) but not post-operative (quadriceps P=0.066; hamstrings P=0.62) strength in the ACL-injured group versus the control group.

Table 2.1. Hip, knee, and ankle strength data (Nm/kg) for ACL-injured and control subjects. Data are mean±standard deviation.

	ACL-Injured				Control
	Pre-Operative		Post-Operative		
	Injured	Uninjured	Injured	Uninjured	
Hip Flexion	1.15±0.29	1.13±0.33	1.34±0.59	1.41±0.58	1.40±0.59
Hip Extension	1.39±0.50	1.16±0.46	1.57±0.60	1.54±0.65	1.24±0.49
Hip Abduction	0.77±0.38	0.73±0.33	0.82±0.29	0.77±0.29	0.83±0.28
Hip Adduction	0.73±0.24	0.83±0.23	0.80±0.30	0.82±0.26	0.65±0.24
Knee Extension	1.33±0.56	1.95±.059	1.38±0.59	2.06±0.86	1.73±0.42
Knee Flexion	0.80±0.23	1.13±0.29	0.93±0.36	1.05±0.39	0.98±0.23
Ankle Plantar Flexion	0.51±017	0.60±0.25	0.77±0.29	0.67±0.21	0.69±0.36
Ankle Dorsiflexion	0.26±0.08	0.28±0.07	0.25±0.10	0.24±0.11	0.27±0.08

Ankle Strength

The ACL-injured group failed to demonstrate a time main effect for either the ankle plantar flexors (P=0.11) or dorsiflexors (P=0.33) (Table 2.1) (Figure 2.5). Further, there were no significant limb main effects for either muscle group (plantar flexors P=0.95; dorsiflexors P=0.72). Subjects in the ACL-injured group demonstrated a significant time x limb interaction for the ankle plantar flexors (P=0.008), with *post hoc* analyses revealing the injured limb plantar flexors were weaker pre- versus post-operatively (P=0.02), though no differences were noted for the uninjured limb between the pre- and post-operative time points (P=0.52). There were no differences in strength between the ACL-injured group compared to the control group pre-operatively (plantar flexors P=0.09, dorsiflexors P=0.75) or post-operatively (plantar flexors P=0.52, dorsiflexors P=0.62).

DISCUSSION

Quadriceps and hamstrings weakness are prevalent following ACL injury and subsequent reconstruction. Though clinical speculation suggests weakness also arises in the musculature crossing the hip and ankle joints, few data are available to confirm this contention. As weakness in the lower extremity musculature may dynamic lower extremity control, determining which muscles are weak is imperative so that strategies to better counter this weakness may be developed and implemented. This study sought to confirm and quantify the presence of lower extremity muscle weakness following ACL injury and reconstruction.

Hip Strength

We hypothesized that following ACL injury and reconstruction weakness would present in the hip flexors and extensors. Given that the quadriceps and the hamstrings are weak following both injury and reconstruction and that rectus femoris and hamstrings cross the hip joint, it seems likely that weakness at one joint may translate to strength deficits at the other. The absence of hip flexor weakness in the injured versus the uninjured limb in the ACL-injured group disagreed with a recent study by Karanikas et al.,[6] suggesting hip flexor strength deficits present upwards of one year after ACL reconstruction. Differences in strength assessment technique may contribute to discrepancies in our findings and those reported previously. The previous study[6] utilized a supine position, while we tested our subjects in standing, though both positions allowed for a similar anti-gravity position of the hip flexors and stabilization of the trunk. Additionally, the previously reported hip flexor strength values were not normalized to subject body mass[6]; doing so may eliminate side-to-side statistical differences in hip flexor strength. Future research seems necessary, however, to clarify the role of ACL reconstruction on hip flexor strength.

It should be noted that the ACLr group demonstrated hip flexor weakness pre-operatively versus post-operatively regardless of limb, though this relationship did not achieve statistical significance. Additionally, the effect size for this relationship was moderate, 0.60 (Table 2.2), indicating a relationship that may be clinically significant and should be investigated in future studies. As mentioned above, hip flexor weakness may be a direct result of the injury process, itself, due to the bi-articular nature of the rectus femoris and

the prevalence of quadriceps weakness following ACL injury. Hip flexor strength values were restored to levels comparable to those demonstrated in the control group post-operatively, suggesting that current rehabilitation strategies are successfully able to counter pre-operative hip flexion weakness.

Table 2.2. Effect sizes and confidence intervals for strength data.

Time Main Effects	Effect Size	Confidence Interval	
		Lower Bound	Upper Bound
Hip Flexion	0.60	0.32	0.89
Hip Extension	0.56	0.30	0.82
Hip Abduction	0.14	-0.05	0.32
Hip Adduction	0.12	-0.05	0.29
Knee Extension	0.14	-0.21	0.49
Knee Flexion	0.06	-0.12	0.24
Ankle Plantar Flexion	0.72	0.52	0.91
Ankle Dorsiflexion	-0.28	-0.32	-0.23
Limb Main Effects			
Hip Flexion	0.01	-0.07	0.08
Hip Extension	0.28	0.15	0.42
Hip Abduction	0.02	-0.07	0.10
Hip Adduction	-0.35	-0.43	-0.26
Knee Extension	-1.23	-1.48	-0.98
Knee Flexion	-0.86	-0.93	-0.79
Ankle Plantar Flexion	0.01	-0.05	0.07
Ankle Dorsiflexion	-0.07	-0.09	-0.04
ACL-injured vs. Control Pre-op			
Hip Flexion	-0.54	-0.96	-0.12
Hip Extension	0.31	-0.07	0.69
Hip Abduction	-0.19	-0.38	0.00
Hip Adduction	0.33	0.14	0.53
Knee Extension	-0.84	-1.25	-0.43
Knee Flexion	-0.78	-0.99	-0.56
Ankle Plantar Flexion	-0.65	-0.89	-0.42
Ankle Dorsiflexion	-0.12	-0.18	-0.05
ACL-injured vs. Control Post-op			
Hip Flexion	-0.01	-0.27	0.24
Hip Extension	0.60	0.25	0.95
Hip Abduction	-0.04	-0.27	0.19
Hip Adduction	0.54	0.37	0.72
Knee Extension	-0.71	-1.11	-0.31
Knee Flexion	-0.19	-0.36	-0.02
Ankle Plantar Flexion	0.24	0.04	0.44
Ankle Dorsiflexion	-0.18	-0.24	-0.12

Though not achieving statistical significance, the ACLr subjects demonstrated a trend toward a significant time main effect of the hip extensors being weaker pre-operatively

versus post-operatively regardless of the limb being tested. This result was supported by a moderate effect size of 0.56 (Table 2.2). As the hamstrings are hip extensors and hamstrings weakness is a likely consequence of the ACL injury process[24], it seems logical that hip extensor weakness could result from ACL injury. Disuse of the hip extensors during the pre-operative period may also contribute to weakness. Subjects were tested, on average, 76 days post-injury, which was sufficient time for disuse atrophy and associated muscle weakness to set in.[25] It should be noted that our hip strength testing position may have made it difficult to detect hip extensor weakness caused by the hamstrings, as subjects were instructed to maintain knee flexion while extending their hips. This is typically believed to target the gluteus maximus over the hamstrings. Future studies isolating the hamstrings during hip extensor strength testing may further elucidate the relations between ACL injury and reconstruction and hip extension strength. That hip extensor strength improved post-operatively in our subjects, however, may suggest that standard ACL rehabilitation is successfully targeting and combating hip extensor weakness.

The ACLr group also demonstrated greater hip extensor strength in the injured compared to the uninjured limb. This relationship did not reach statistical significance and the calculated effect size was small at 0.28 (Table 2.2) suggesting the relationship may not be clinically meaningful. It is possible that the testing position employed may account for these results. That our subjects were tested in standing necessitated that while testing the uninjured limb's hip extensor strength, the subject be standing on his/her injured limb. Despite sufficient stabilization provided by the researchers, it is possible the subjects felt instability in the injured knee and, thus did not put forth maximal effort. Future studies may consider utilizing different testing positions or stabilization methods.

Our subjects did not demonstrate hip abductor weakness, which was unexpected. Previous research in animal models indicates that the rectus femoris sends heteronymous neural projections to its hip synergists (i.e., sartorius)[26], suggesting that strength impairments within the rectus femoris could yield similar impairments within the hip abductors. A previous study[19] examining hip abductor strength following knee surgery did indicate weakness within this muscle group, though strength was tested in the

immediate post-operative period, making direct comparisons between this study and the previously conducted one difficult. Nonetheless, our results seem to suggest that neither ACL injury nor surgical reconstruction negatively influences strength within the hip abductor muscle group.

While we did not hypothesize that our subjects would demonstrate hip adductor weakness it is worth noting that our findings disagree with those of Hiemstra and colleagues[20] who found hip adductor strength deficits following STG autograft ACL reconstruction. Donor site morbidity likely explains the hip adductor muscle weakness in the previous study. The majority of our subjects (n =12) received BPTB autografts, however, and, as such, donor site morbidity would did not likely play a role in their hip adductor strength and may explain the differences in findings between our work and that of others.

Knee Strength

In accordance with our hypothesis, our subjects demonstrated bilateral differences in quadriceps and hamstrings strength. Specifically, our subjects demonstrated injured vs. uninjured strength deficits of 32% in the quadriceps and 21% in the hamstrings. These findings are similar to those reported previously for both quadriceps[12, 27-29]and hamstrings strength.[17, 30] The hamstrings strength deficits in our subjects also appear to differ from those reported previously, being both smaller[28] and larger[12, 29] than those reported by previous investigators. The presence of quadriceps and hamstrings weakness in the injured versus uninjured limb in our subjects seems to confirm that current rehabilitation strategies do not fully restore strength by the time that individuals return to activity. Why quadriceps and hamstrings weakness persist remains uncertain, though factors such as quadriceps activation failure[31], detraining[14], and incomplete rehabilitation[14] have been suggested to contribute. As the quadriceps and hamstrings cross the knee joint, weakness within these muscles may directly alter tibiofemoral biomechanics, possibly contributing to joint degeneration. In fact, quadriceps weakness is suggested to limit its ability to absorb energy on weight bearing, precipitating increased articular cartilage loading, which may lead to joint degeneration.[32] Further, hamstrings strength deficits at the time that individuals return to full activity may also be hazardous given that the hamstrings restrain anterior tibial translation, a known contributor to ACL injury.[33] Future studies

elucidating the underlying mechanisms behind these persistent quadriceps and hamstrings strength deficits seem warranted so that interventions to better counter them during the rehabilitation process can be developed and implemented.

That there were no differences in pre-operative compared to post-operative quadriceps and hamstrings strength in the ACL-injured group disagrees with previously reported findings[34] and seems somewhat counterintuitive. However, the surgical process likely introduces trauma to the joint beyond that of the injury process itself, which may intensify quadriceps and hamstrings weakness. Thus, while based on pre-operative testing our subjects had a 32% quadriceps strength deficit to overcome compared to their uninjured limb, it is likely that on the first post-operative day this deficit was quite a bit larger. Traditional rehabilitation often dictates that individuals are discharged from supervised care between 3-4 months post-operatively. This does not appear to be sufficient time to restore quadriceps or hamstrings strength. Retaining patients in rehabilitation (i.e., beyond 3-4 months post-operatively) may be one effective way to ensure more adequate quadriceps and hamstrings strength upon return to activity following ACL reconstruction. This may be especially beneficial for individuals in whom discharge from supervised rehabilitation and clearance for return to activity do not coincide. Additionally, the use of interventions designed to counter the underlying causes of quadriceps weakness are needed; however, successfully restoring quadriceps strength following ACL reconstruction will likely prove challenging until the underlying causes of this impairment are known and targeted treatments established. While the precise cause of quadriceps weakness following ACL reconstruction remains unknown, both central activation failure[31, 35] and atrophy[36] have been suggested to contribute. Previous research into the removal of artificially induced quadriceps muscle inhibition has suggested that the use of cryotherapy[37] and transcutaneous electrical nerve stimulation[37] may be useful adjuncts to traditional rehabilitation. Further, the use of neuromuscular electrical nerve stimulation has been explored [38, 39], though how long-lasting the strength benefits of this treatment are remain unknown. Future research into the benefits of each of these treatments within post-operative ACL rehabilitation seems warranted.

The ACL-injured subjects had weaker quadriceps and hamstrings pre-operatively compared to the control group. There was also a trend toward significant differences in post-operative quadriceps strength that was supported by a moderate (-0.71) effect size (Table 2.2), indicating quadriceps weakness is not sufficiently countered post-operatively when compared to healthy individuals. Previous research comparing strength in healthy individuals to those who have undergone ACL reconstruction is conflicting. Konishi and colleagues[18] failed to establish a difference in hamstrings torque per unit volume between the injured limb following ACL reconstruction and control subjects 12 months post-operatively. However, Hiemstra et al.[14] demonstrated differences in quadriceps and hamstrings strength between individuals an average of 40-months following ACL reconstruction and control subjects. The reason for the discrepancies in these findings is unclear, though the time since surgery could be playing a role. It would seem greater strength deficits would be expected closer to surgery when compared to controls. Rehabilitation does account for some strength gains, however, and failure to maintain these strength gains over time could lead to weakness in the years subsequent to ACL reconstruction when compared to healthy individuals. As was suggested by Hiemstra et al.[14] and has been reported previously, the presence of bilateral weakness may make the contralateral limb an inappropriate guideline for judging strength following ACL reconstruction. These authors have suggested, instead, that healthy people should serve as the barometer against which to measure strength gains.[14] However, the conflicting results demonstrated previously suggest the need for future research to clarify the relation between strength in ACL-reconstructed individuals and healthy persons.

Ankle Strength

Our subjects demonstrated significant pre-operative ankle plantar flexion weakness relative to the uninjured limb. Recently, Karanikas and colleagues[6] demonstrated that ankle plantar flexor strength was not influenced at any post-operative time point assessed in their study (3-6, 6-9, or 9-12 months post-operatively), suggesting that the restoration of plantar flexor strength may occur early during rehabilitation. That ankle plantar flexor strength improved post-operatively in our subjects, becoming nearly equivalent between the injured and uninjured limb and not differing from control subjects, agrees with these

recent findings. With the gastrocnemius crossing the knee joint, the pre-operative plantar flexor weakness in our ACL-injured subjects may have been a direct consequence of the ACL injury. Additionally, the gastrocnemius is neurally connected to the quadriceps[40, 41] and altered strength and neuromuscular activity within the quadriceps following ACL injury could potentiate gastrocnemius weakness[40, 41]. Disuse atrophy of the gastrocnemius may have further contributed to the pre-operative weakness demonstrated by our subjects. Calf girth measurements, recorded with a cloth tape measure, were not significantly different between limbs in the ACL-injured individuals in our study ($P>0.05$). However, it has been suggested that girth measurements may not be truly reflective of muscle size and/or atrophy.[42]

CONCLUSION

Injured limb quadriceps and hamstrings weakness are present six-months following ACL reconstruction. As these muscles directly contribute to safe and effective lower extremity dynamic stability when individuals return to full activity following injury, determining the precise cause of and developing more effective strategies to counter this weakness appears vital. Additionally, ankle plantar flexor weakness presented in the injured limb pre-operatively, though current rehabilitation strategies appear effective in countering this weakness following ACL reconstruction. With the exception of the trend toward hip extensor weakness pre-operatively, weakness did not present within the hip joint musculature.

CHAPTER 3
CONTRIBUTIONS OF CENTRAL ACTIVATION FAILURE AND ATROPHY TO QUADRICEPS WEAKNESS ASSOCIATED WITH ACL RECONSTRUCTION

ABSTRACT

Persistent quadriceps weakness presents after anterior cruciate ligament reconstruction (ACLr) in spite of otherwise successful rehabilitation. The precise contributors to lingering quadriceps weakness are unknown, though muscle atrophy and activation failure have been implicated. This study sought to elucidate the roles of activation failure and muscle atrophy in persistent quadriceps weakness after ACLr. Eleven individuals undergoing ACLr six months previously participated. Muscle atrophy was determined as the peak quadriceps cross sectional area (CSA) from magnetic resonance images. Quadriceps activation was assessed using the burst superimposition technique and quantified via the central activation ratio (CAR). Quadriceps strength was determined from a knee extension maximal voluntary isometric contraction (MVIC). All testing was performed bilaterally. Hierarchical linear regression analysis was performed to determine the association between quadriceps CAR and CSA and quadriceps MVIC in the injured limb. One-way ANOVAs were performed to determine if CAR, CSA, and MVIC differed between limbs. Regression analysis failed to demonstrate a significant relation between CAR and CSA and the peak MVIC following ACL reconstruction (R^2= 0.357, *P*=0.17). The CAR accounted for 27.3% (*P*=0.073) of the variance in quadriceps MVIC; subsequent inclusion of CSA accounted for the remaining 8.5% (*P*=0.335). Peak CSA (ACLr=67.04cm^2; uninjured=82.3cm^2; *P*<0.001) and the quadriceps MVIC (ACLr=1.94Nm/kg; uninjured=2.8Nm/kg; *P*=0.001) but not the CAR (ACLr=0.82; uninjured=0.86; *P*=0.16) differed between limbs. Though both quadriceps atrophy and activation failure were present in our subjects, neither quadriceps CSA nor CAR was related to MVIC. Future studies seem necessary to determine what additional factors may be associated with quadriceps MVIC so necessary modifications to current rehabilitation strategies can be made. Until quadriceps weakness is sufficiently countered during rehabilitation, individuals may be at risk for re-injury and/or joint degeneration.

INTRODUCTION

Quadriceps weakness is nearly ubiquitous following ACL injury and reconstruction. The magnitude of the reported strength deficits varies, but may be as high as 30% in the reconstructed compared to the contralateral limb 6-months post-operatively[27], a time when individuals often return to full activity. Further, this weakness been shown to persist for years after reconstruction, with deficits between limbs upwards of 20% being reported seven years post-operatively.[17]

Quadriceps weakness may have hazardous short- and long-term consequences for the injured individual. The quadriceps are important to lower limb control during dynamic activity and the presence of weakness could alter movement strategies potentiating re-injury.[43] Quadriceps weakness has also been implicated in the onset/progression of tibiofemoral osteoarthritis[32]; thus, failing to remove strength deficits may precipitate joint degeneration in these individuals. Before quadriceps strength can be effectively countered during the rehabilitation process, however, a deeper understanding of why quadriceps weakness persists is needed.

Muscle atrophy following disuse of the quadriceps and knee joint immobilization has been suggested to contribute to quadriceps weakness after ACL injury and reconstruction.[36] Quadriceps atrophy has been demonstrated following ACL reconstruction, with Konishi and colleagues[29] reporting an approximately 7% deficit in total quadriceps volume in the reconstructed versus contralateral limb in individuals between 6-12 months post-operatively. Similar magnitudes of quadriceps atrophy were reported by Lorentzon et al.[44] in people with ACL deficiency, though no relation between quadriceps atrophy and strength was identified. The authors thus concluded that muscle atrophy alone did not cause quadriceps weakness suggesting, instead, that activation failure may contribute.[44]

Central activation failure (CAF) is a common consequence of ACL injury and reconstruction, with activation deficits upwards of 15% reported two years post-operatively.[31] In individuals with radiographic tibiofemoral osteoarthritis, a population with similar magnitude quadriceps dysfunction to those following ACL injury[45, 46], CAF

was found to account for nearly twice the quadriceps strength deficit that muscle atrophy does.[45, 47] Elucidating the relationship between quadriceps muscle atrophy and CAF with lingering weakness seems imperative. Until it is known why quadriceps strength deficits persist, they cannot be effectively countered during the rehabilitation process. Thus, the purpose of this study was to determine if quadriceps atrophy and CAF contribute to persistent knee extension strength deficits in individuals six-months after ACL reconstruction. We hypothesized that persistent quadriceps dysfunction would result from a combination of CAF and muscle atrophy and that CAF would more strongly predict quadriceps dysfunction than would muscle atrophy. A secondary hypothesis was that the magnitudes of quadriceps CAF and atrophy would be greater in the injured compared with the uninjured limb.

METHODS

Subjects

Thirteen individuals were recruited to participate in this study; one was excluded after secondary screening revealed that she did not fulfill all of the study inclusion criteria. Another individual reported for magnetic resonance imaging testing but failed to report for CAF assessment. He could not be reached for follow-up and was, thus, excluded from analysis, leaving 11 individuals (4 males, 7 females; age: 20.64±6.31years; height: 1.73±0.09m; mass: 74.55±15.33kg) who underwent patellar tendon autograft ACL reconstruction six-months prior to enrollment participating in this study. A power analysis based on data examining the relation between quadriceps strength and atrophy[48] revealed the need for 12 subjects to detect 80% power with an alpha level ≤ 0.05.

Subjects reported for testing on two occasions with bilateral quadriceps muscle atrophy, in the form of muscle cross sectional area (CSA) measured at one session and strength and CAF measured at the other (average 5.73±9.60 days between testing sessions). Potential subjects were excluded if they: had a history of lower extremity surgery other than their recent ACL reconstruction, had suffered a lower extremity injury since undergoing ACL reconstruction, had current pain in either knee, underwent partial or complete meniscectomy with their ACL reconstruction, had other ligamentous damage

concurrent with their ACL injury, or had a known heart condition. Pregnant females were also excluded. This study was approved by the medical school institutional review board at the University of Michigan. All subjects provided written consent prior to participation.

Quadriceps Cross Sectional Area Assessment

Subjects were positioned supine in a magnetic resonance imaging scanner (Philips Achieva 3T Quasar Dual, Philips Electronics, Andover, MA, USA) and underwent bilateral thigh scans, with both limbs scanned simultaneously. The following parameters were utilized for the imaging protocol: repetition time 2000-3000 ms, echo time 35 ms, slice thickness 6 mm, gap between slices 6 mm, with a 364x180 matrix, and a 480x281 mm field of view.

Peak CSA for each of the four quadriceps muscles as well as total quadriceps peak CSA were evaluated. The contours of each muscle were traced in every axial image in which the muscle appeared using ImageJ software (version 1.42q, National Institutes of Health, USA) and an Intuos4 pen tablet (Wacom Technology Corporation., Vancouver, WA, USA). The sum of each muscle's CSA yielded the maximal CSA for each slice. The slice with the greatest combined CSA was used for statistical analysis.[45] All CSA measurements were performed by a single investigator with high intrarater reliability (intraclass correlation coefficient [ICC] of 0.988).

Quadriceps Strength and Central Activation Failure Assessment

Quadriceps strength was assessed during the performance of a knee extension maximal voluntary isometric contraction (MVIC) while subjects were seated on an isokinetic dynamometer (Biodex System 3, Biodex Medical Systems, Shirley, NY, USA) with the hip flexed to 85° and the knee flexed to 90°. For the MVICs, subjects were instructed to kick out as hard as they could while watching a computer monitor running a custom-written Labview (Labview 8.5, National Instruments, Austin, TX, USA) program that displayed their real-time torque output. After completion of the first MVIC, the program displayed a solid line reflecting the subject's peak torque value from the initial trial and a dashed line that was set 10% above the peak torque recorded during the initial MVIC

trial. (Figure 3.1). For all subsequent trials, subjects were encouraged to reach this target torque value denoted by the dashed line. If subjects increased their torque during any of the ensuing trials, the height of the solid and dashed lines would be adjusted appropriately. Knee extension MVICs were performed (minimum of three), with at least two minutes of rest in between each repetition, until no improvements in torque were observed by an investigator. Once each subject's knee extension torque ceased to increase any further, the peak torque value from all recorded repetitions was noted and used as a threshold value for subsequent CAF assessment.

For CAF testing, self-adhesive, stimulating electrodes (Dura-Stick II [5 cm x 9 cm] Chattanooga Group, Hixson, TN, USA) were applied proximally over the rectus femoris and distally over the vastus medialis. At the beginning of testing, the peak torque value recorded during the MVIC trials was inputted into the custom-written program. The program utilized this threshold (peak torque) value to determine whether or not it would trigger the electrical stimulator (S88 and SIU8T, GRASS Technologies, West Warwick, RI, USA) to deliver a stimulus (100 ms-long train, pulse duration: 600 μs, delivery rate: 100 pulses per second, maximal voltage: 130V). Similar to the MVIC testing, subjects were instructed to generate enough torque to reach the dashed target line displayed on the screen (i.e., a value 10% greater than their peak torque generated during MVIC testing).

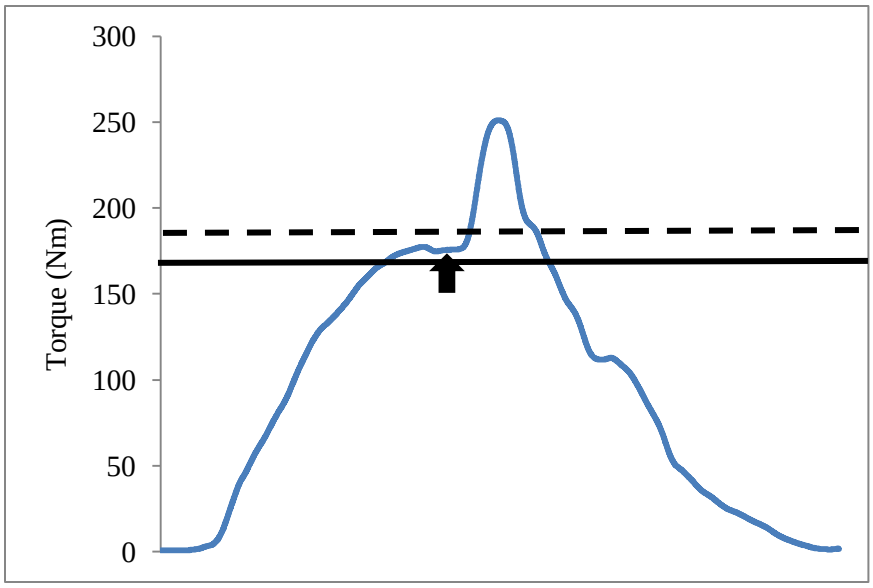


Figure 3.1. Screenshot from strength and central activation failure testing (CAF). The blue line represents the subject's real-time torque output. The solid black line corresponds to the subject's peak value from the MVIC trials and also serves as a threshold for CAF testing. Real-time torque output must cross threshold for the electrical stimulus to be delivered. The dotted line represents the subject's target value, which was set 10% above maximal strength. The black arrow corresponds to delivery of the electrical stimulus.

The custom-written program was set to deliver the stimulus once a subject's torque value reached threshold and then fell 1 Nm below their peak torque for the current trial. If a subject failed to reach the solid threshold line, the program would not deliver the stimuli, and the subject would be given two minutes of rest before the trial was repeated. The dashed target line was set so as to be unreachable for the subject; however, in the event that a subject did reach the target value, the maximal strength value (solid threshold line) was reset and CAF testing was reinitiated. Three repetitions of CAF testing were performed with two minutes of rest provided between repetitions.

Maximal strength was determined from these three CAF repetitions. The largest of the peak torque values generated immediately prior to delivery of the electrical stimulus was divided by the subject's body mass (kg) and utilized to quantity maximal strength (Nm/kg). From this same trial yielding maximal strength, CAF was quantified via the central activation ratio (CAR). To determine the CAR, the subject's peak torque generated immediately prior to the delivery of the electrical stimulus was divided by the peak torque generated as a result of the electrical stimulus.

Statistical Analyses

A hierarchical multiple regression analysis was used to determine the association between knee extension MVIC and quadriceps CAR and CSA in the injured limb, with the CAR entered into the model first. A series of 1x2 ANOVAs were performed to determine if MVIC, CSA, and CAR differed between limbs. The alpha level for all tests was set *a priori* at $P \leq 0.05$. Effect sizes (Cohen's d)[23] examining the magnitude of the between-limb difference for quadriceps strength, CSA, and CAF were calculated as the $\frac{\text{injured limb mean} - \text{uninjured limb mean}}{\text{pooled standard deviation}}$ and were determined in Microsoft Excel 2007 (Microsoft Corporation, Redmond, WA, USA). SPSS (SPSS, Chicago, IL, USA), version 17.0, was utilized for all other statistical procedures.

RESULTS

Regression analysis failed to demonstrate a significant relation between CAR and CSA and the peak MVIC following ACL reconstruction ($R^2 = 0.357$, $P=0.171$) (Figure 3.2).

When CAR was entered into the model first, it accounted for 27.3% (*P*=0.073) of the variance in quadriceps MVIC. The subsequent inclusion of CSA into the regression model accounted for the remaining 8.5% (*P*=0.335).

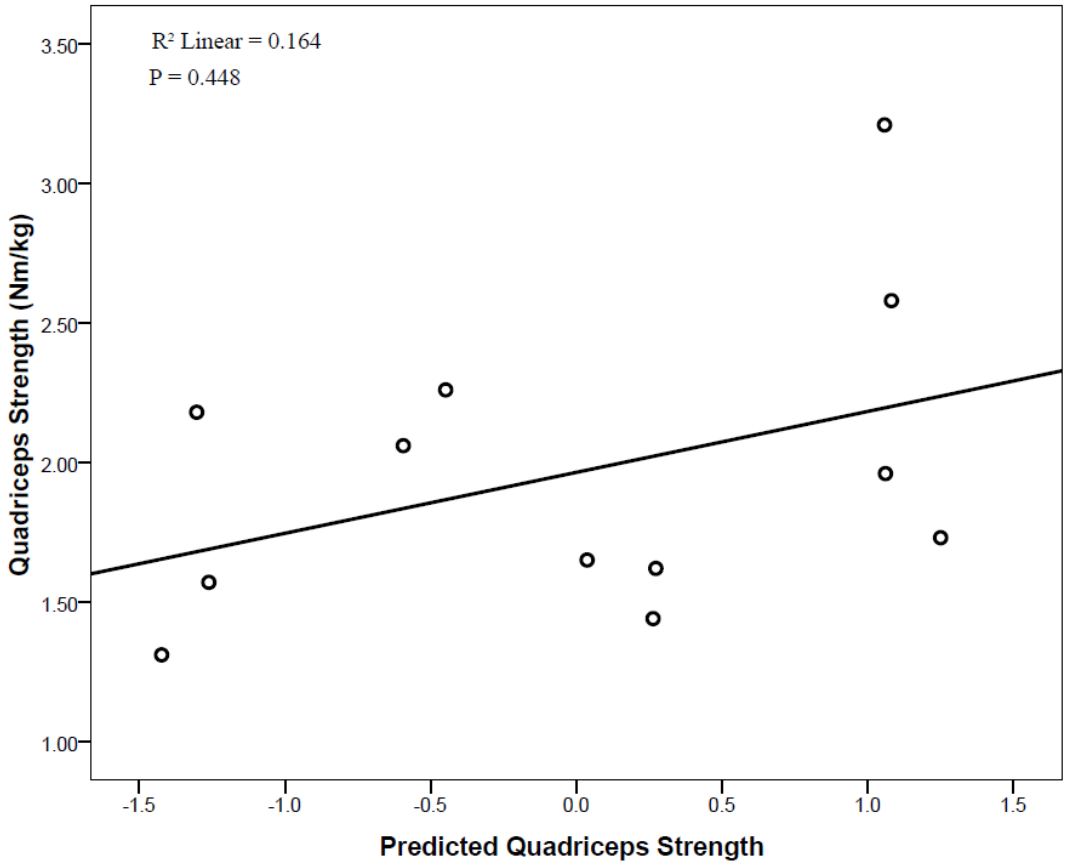


Figure 3.2. Scatter plot depicting the relation between quadriceps strength (Nm/kg) and predicted strength from hierarchical regression.

Quadriceps strength, CSA, CAR, and effect size values can be found in Table 3.1. Peak quadriceps CSA differed between limbs, with the injured limb demonstrating a significantly smaller CSA six-months post-operatively than the uninjured limb (*P* <0.001) (Figure 3.3). Knee extension MVIC also differed between limbs, with the injured limb being significantly weaker than the uninjured (*P*=0.001) limb. The CAR did not differ between limbs (*P*=0.16), though the mean values indicated CAF was present bilaterally.

Table 3.1. Quadriceps maximal voluntary isometric contraction, cross sectional area, and central activation ratio data for the injured and uninjured limbs.

	Mean±SD		P-value	Effect Size (95% CI)
	Injured Limb	Uninjured Limb		
MVIC (Nm/kg)	1.96±0.54	2.81±0.96	0.001	-0.8 (-1.16, -0.44)
CAR	0.83±0.13	0.79±0.14	0.3	0.24 (0.16, 0.32)
CSA (cm^2)	68.21±18.35	81.19±20.08	<0.001	-0.5 (-4.27, 3.28)

SD=standard deviation
CI=confidence interval

DISCUSSION

Quadriceps dysfunction is a common complication following ACL injury and reconstruction. While the precise cause of quadriceps dysfunction after ACL reconstruction remains unknown, both peripheral[36] and central[31, 35] mechanisms have been implicated. The present study sought to determine the contributions of atrophy and CAF to lingering quadriceps weakness following ACL reconstruction.

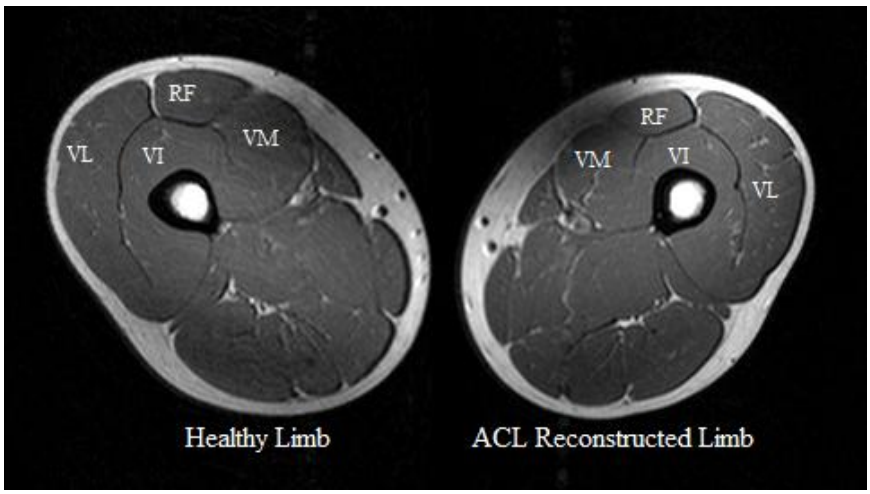


Figure 3.3. Representative magnetic resonance image demonstrating quadriceps atrophy. VL= vastus lateralis. RF= rectus femoris. VM= vastus medialis. VI= vastus intermedius.

Neither peak quadriceps CSA nor CAR were associated with knee extension MVIC six-months following ACL reconstruction, which was in disagreement with our hypothesis. While no studies to which our results can be directly compared are available, findings by Williams and colleagues[7] and Mizner et al.[45] showed that quadriceps muscle CSA and CAR contributed to strength loss in ACL deficient (non-copers) and total knee arthroplasty patients, respectively. Differences in the population studied may help to

account for discrepancies between our results and those reported previously. Additionally, recent evidence suggests the relation between CSA and CAR and volitional activity may be mediated by time since injury/surgery. Studies by both Meier et al.[49] and Petterson et al.[48] examined quadriceps atrophy and CAF in relation to strength following total knee arthroplasty. These authors reported that as patients reached and surpassed the 1-year post-operative time point, quadriceps MVIC became less associated with CAF and more associated with muscle atrophy. Thus, it seems possible that while in the early stages following ACL injury or surgery CAF is significantly associated with quadriceps strength, the same may not be true six-months post-operatively. What is associated with quadriceps strength at this time point is unclear based on the present findings and it seems that longitudinal studies within the ACL reconstructed population may be warranted to elucidate the long-term contributions of both muscle atrophy and CAF to quadriceps strength so that appropriate intervention strategies can be employed

Previous reports have suggested that both muscle morphology and architecture may mediate the relation between muscle CSA and strength, which may have contributed to our results. If our subjects demonstrated a selective atrophy of their Type II muscle fibers, this could have yielded a greater strength deficit than in the presence of more selective Type I fiber atrophy. Previous investigations of quadriceps muscle morphology, however, are conflicting. Both selective Type I[50] and Type II [51] atrophy have been demonstrated. Additionally, previous reports have suggested that no consistent morphological changes may occur (i.e., both Types I and II atrophy arise).[44, 52] Regarding muscle architecture, previous research[53, 54] suggests that fiber pennation angle may influence muscle strength and this angle may be altered by training/detraining. In fact, strength training sufficient to increase muscle CSA has been shown to increase fiber pennation angle such that the force generating capacity of the muscle improves.[53] As detraining has the opposite effect[54], it would seem that if quadriceps strength gains are not being made during rehabilitation to the point that CSA is improving, that muscle architecture may not be influencing the relation between quadriceps strength and CSA. We did not assess quadriceps muscle morphology or architecture in our study and, thus, cannot determine if selective fiber type atrophy or fiber pennation angle played a role in influencing the present outcomes.

Together, CSA and CAF explained only 16.4% of the variance in knee extension strength in our subjects, raising the question of what explains the other 83.6%. The above-mentioned factors of muscle morphology and architecture may contribute to this remaining variance in quadriceps strength, as well as the stiffness of the patellar tendon. Recent research[55], however, suggests that patellar tendon stiffness may not be directly related to quadriceps strength. While factors such as knee joint effusion and pain may contribute, our subjects did not present with side-to-side differences in knee joint effusion as measured 1 cm proximal to the superior pole of the patella with a cloth tape measure (P=0.53).[56] It remains possible that there may have been effusion present within the knee that was not detectable on clinical examination but that could have contributed to the CAF detected bilaterally. It has been demonstrated previously that only 20-30 mL of fluid is necessary to inhibit the vastus medialis[57]; however, whether this amount of effusion would be detectable with the measurement technique employed in the present study is unknown. Further, our subjects reported pain levels at only 2.36 /10 (as taken from IKDC questionnaire). Thus, it seems unlikely that either residual knee joint effusion or pain contributed substantially to the present results. Additionally, it is worth noting that the use of the burst superimposition technique to assess quadriceps central activation is not without limitations.[58, 59] This technique allows for an estimation of maximal torque production and voluntary activation without regard to descending drive to the motoneuron pool; however, what is actually contributing to the voluntary activation assessed with this measurement technique is unknown.[59] It is possible that had we utilized a different assessment technique, such as the Hoffman reflex or V-wave, our results could have been different. Future studies may benefit from the incorporation of these measurement techniques so a more complete understanding of central and descending drive to the motoneuron pool can be achieved. As this knowledge may lend to the development of more successful rehabilitation strategies, this research appears vital.

In accordance with our hypothesis, the injured limb peak quadriceps CSA was smaller than that in the uninjured limb six-months post-operatively. Compared to previous reports of healthy individuals, our subjects demonstrated smaller injured limb and similar uninjured limb quadriceps CSA[60, 61], suggesting that muscle atrophy in the ACL reconstructed limb is not sufficiently countered through post-operative rehabilitation.

Further, when compared to individuals three-months after ACL injury[7], our subjects demonstrate greater quadriceps atrophy. It is likely that the ACL reconstruction results in additional atrophy to that generated by the initial injury itself, thus resulting in greater magnitudes of quadriceps atrophy in individuals undergoing reconstruction than ACL deficient individuals. Greater post-operative atrophy has been demonstrated in the hamstrings musculature following ACL injury and subsequent semitendinosus/gracilis autograft reconstruction[62] as well as in the quadriceps following total knee arthroplasty.[45] Similar outcomes could be expected in the quadriceps following patellar tendon reconstruction, though longitudinal studies are needed to confirm this.

Possibly contributing to the quadriceps strength deficits noted in our subjects is that all of our subjects underwent ACL reconstruction using a patellar tendon autograft procedure. It has been demonstrated previously that incomplete healing of the patellar tendon is present six-months post-operatively, as indicated by increased tendon thickness and width[63] and a visually present tendon defect on MRI.[64] However, whether or not this influenced strength is inconclusive. Shelbourne and colleagues demonstrated that pre-operative patellar tendon width may influence the recovery of post-operative quadriceps strength.[65] However, it has also been demonstrated that by the sixth post-operative month, patellar tendon width no longer influences isokinetic quadriceps strength .[66] Future studies may benefit from incorporation of patellar tendon CSA to clarify the relation between patellar tendon width and quadriceps strength.

It is worth noting that hamstrings co-contraction during MVIC and, therefore, CAF, testing may have additionally contributed to quadriceps weakness in our subjects. Hamstrings co-contraction during a knee extension MVIC would counteract the moment being generated by the quadriceps, thus giving the appearance of a loss of quadriceps strength. This relation had been demonstrated previously, though the results appear conflicting. A recent report by Heiden et al.[67] noted greater hamstrings co-contraction during MVIC or CAF testing in persons with knee osteoarthritis compared to healthy persons. However, a study by Krishnan and Williams[68] demonstrated an approximately 2% increase in hamstrings activity during CAF testing, though these authors did not believe this was a clinically meaningful response. As we did not assess hamstrings

electromyography during the present study, we cannot determine if hamstrings co-contraction influenced our results.

Substantial quadriceps strength deficits were noted in our subjects. The average injured limb quadriceps strength was approximately 69% that of the uninjured limb, which is consistent with previous reports at six-months post-operatively.[12, 69, 70] This large of a strength deficit, however, may be confounded by the presence of bilateral quadriceps CAF, which may lead to an underestimate of weakness in the injured limb.[71] All of our subjects completed standard, outpatient rehabilitation, emphasizing restoration of quadriceps strength beginning during the first post-operative week and lasting for approximately four months post-operatively. It seems based on these results that traditional rehabilitation is insufficient in restoring quadriceps strength by the time individuals are released to full activity. Given that quadriceps muscle contraction is required for the execution of various dynamic movement strategies, it would seem ideal to be returning individuals to activity with as near maximal strength as possible. A study examining isolated quadriceps fatigue as a means of generating muscle weakness demonstrated reductions in the external knee extension moment, a finding consistently implicated in the non-contact ACL injury mechanism.[72] Similar results have been demonstrated following induction of an experimental knee joint effusion[73], which is known to cause quadriceps CAF.[71] Additionally, considering the importance of the quadriceps in energy absorption on weight bearing and the potential implications for joint degeneration, more complete restoration of quadriceps strength following ACL reconstruction seems imperative.

Substantial deficits in CAF were present bilaterally in our subjects (17% in the reconstructed and 21% in the contralateral limb). The magnitude of CAF in those with ACL injury varies, with some studies reporting greater[74] and others reporting smaller[7, 75] levels of activation failure than those demonstrated presently. Bilateral CAF has also been reported following ACL reconstruction, with Urbach and colleagues reporting 15% and 16% quadriceps central activation deficits in the reconstructed and contralateral limbs, respectively upwards of two years post-operatively.[35] Together, these results

suggest that central drive to the quadriceps musculature is relatively equally impaired bilaterally and that that impairment lingers six-months post-operatively.

It should be noted that the relation between quadriceps CAF and strength was close to achieving statistical significance in the present study. It is possible that this lack of significance is a result of insufficient statistical power. Future investigations could benefit from the inclusion of additional subjects.

CONCLUSION

Though the present study failed to establish an association between quadriceps CSA and CAF and knee extension MVIC, substantial deficits in all three measurements were demonstrated six-months after patellar tendon autograft ACL reconstruction, suggesting that current rehabilitation efforts are insufficient at removing these deficits. It appears that further research is necessary to determine the precise contributors to persistent quadriceps dysfunction. Until it is known why quadriceps dysfunction persists, it will be difficult to target it appropriately during rehabilitation.

CHAPTER 4
NEUROMUSCULAR FATIGUE AND QUADRICEPS INHIBITION ALTER LOWER EXTREMITY BIOMECHANICS

ABSTRACT

Quadriceps central activation failure (CAF) occurs frequently following anterior cruciate ligament reconstruction (ACLr) and lingers beyond the rehabilitation period. CAF impairs the ability to activate the quadriceps fully and has been demonstrated to alter lower extremity biomechanics. Neuromuscular fatigue similarly reduces volitional activation and neuromechanical control strategies within the affected muscle. Individuals returning to activity following ACLr likely experience both quadriceps CAF and neuromuscular fatigue, though the effects of fatigue on muscles experiencing CAF in this population are unknown. This study examined the effects of neuromuscular fatigue on CAF following ACLr. Seventeen individuals 7-10 months post-ACLr and 16 healthy, control subjects participated. Subjects had quadriceps strength and the central activation ratio (CAR) recorded pre- and post-fatigue, which was induced via sets of double-leg squats. Knee sagittal and frontal plane biomechanics were recorded while subjects performed a dynamic landing activity pre- and post-fatigue and submitted to a standard inverse dynamics analysis. Statistical analysis consisted of 2x2 (time x group) repeated measures ANOVAs. Both groups demonstrated smaller knee flexion angles (initial contact [IC]: P=0.018; peak stance [PS]: P=0.002) and moments (P<0.001) post-fatigue. Both groups also landed with less knee abduction (IC: P=0.005; PS: P=0.017) and smaller abduction moments (P=0.024) following fatigue. The ACLr group was less flexed at PS (P=0.009) and experienced a smaller flexion moment than controls regardless of fatigue state (P<0.001). Following fatigue, all subjects (ACLr and control) demonstrated significantly lower MVIC (P<0.001) and CAR (P=0.003) values. No group differences were detected for either MVIC (P=0.13) or CAR (P=0.17). Both groups demonstrated quadriceps weakness and CAF following fatigue concurrent with altered biomechanics. These biomechanical alterations may prove injurious and have been linked to non-contact ACL injury risk, confirming the need to consider fatigue-

resistance training within non-contact ACL prevention programs. Incorporation of fatigue-resistance within rehabilitation following ACLr does not seem necessary as fatigue did not worsen biomechanics in individuals after ACLr.

INTRODUCTION

Quadriceps weakness is a nearly universal consequence of anterior cruciate ligament (ACL) injury with previous reports suggesting that it may linger upwards of seven years post-operatively.[17] Central activation failure (CAF) reduces volitional activation of the affected muscle, thereby contributing to weakness. The presence of quadriceps weakness along with CAF may be detrimental to those returning to activity following ACL reconstruction (ACLr). Following experimental knee joint effusion, which is known to induce quadriceps CAF, it was found that individuals landed with a smaller knee flexion angle and a reduced external knee flexion moment.[73] These biomechanical alterations have been implicated in the non-contact ACL injury mechanism and, as such, seem potentially hazardous.

Like CAF, neuromuscular fatigue also reduces voluntary activation of the affected musculature.[76] Neuromuscular fatigue is an inevitable occurrence during athletic activity and has been demonstrated to alter lower extremity biomechanics[72, 77-79] to the point of potentially increasing ACL injury risk. Gross lower extremity neuromuscular fatigue has been reported to increase knee extension and abduction postures and moments[79, 80], all of which have been implicated in the non-contact ACL injury mechanism.

In healthy individuals, it has been demonstrated that fatigue impairs quadriceps central activation and that this effect may be magnified in the presence of muscle weakness. Stackhouse and colleagues[11] compared healthy elderly and young adults pre- and post-fatigue. Prior to fatigue, elderly adults were weaker than and had greater quadriceps CAF compared to young adults, with this difference becoming greater following fatigue.

There are few data to suggest how the quadriceps respond to neuromuscular fatigue following ACL injury/reconstruction, and those results appear conflicting. One study suggested that ACL-deficient limbs demonstrated greater magnitudes of quadriceps fatigue following sustained isometric knee extension contractions compared to the

uninvolved limb.[81] A separate study, however, suggested that the quadriceps of the ACLr limb demonstrated greater fatigue resistance than that of the uninvolved limb.[82]

With individuals returning to activity following ACLr likely experiencing both quadriceps CAF and neuromuscular fatigue, it seems imperative to understand their combined effects so that strategies to combat the potentially hazardous consequences can be developed to better protect the ACLr knee from re-injury upon return to activity. The purpose of this study, therefore, was to determine the effects of neuromuscular fatigue on lower extremity strength and biomechanics in individuals with quadriceps CAF following ACLr compared to healthy persons. We hypothesized that, following fatigue, subjects would demonstrate increased knee extension and abduction angles/moments following fatigue and that all biomechanical changes would be greater in those following ACLr than in healthy subjects. Additionally, we hypothesized that subjects in the ACLr group would demonstrate greater quadriceps weakness and CAF prior to fatigue and reach maximal fatigue faster (i.e., in less repetitions of the fatiguing exercise) than healthy subjects.

METHODS

Subjects

Seventeen individuals who underwent ACLr 7-10 months prior to enrollment (10 male, 7 female; age: 21.41±4.73 years; height: 1.75±0.08 m; mass: 76.52±11.85 kg) and 16 control (5male, 11female; age: 23.38±4.11 years; 1.71±0.08 m; mass: 68.21±10.17 kg) subjects participated in this study. For the purpose of determining a test limb for data analysis, each healthy individual was assigned to an ACLr subject according to age and activity level. The limb corresponding to the ACLr subject's reconstructed limb was designated as the control subject's matched limb and utilized in data analysis.

Potential subjects were excluded if they: had a history of lower extremity surgery other than their recent ACL reconstruction, had suffered a lower extremity injury since undergoing ACL reconstruction, had current pain in either knee, underwent meniscectomy with their ACL reconstruction, had other ligamentous damage concurrent with their ACL injury, or had a known heart condition. Pregnant females were also

excluded. Control subjects additionally could not have a history of ACL reconstruction or have suffered a lower limb injury in the previous six months. This study was approved by the medical school institutional review board at the University of Michigan. All subjects provided written consent prior to participation.

Strength and Central Activation Failure Assessment

Quadriceps strength was assessed during the performance of a knee extension maximal voluntary isometric contraction (MVIC) while subjects were seated on an isokinetic dynamometer (Biodex System 3, Biodex Medical Systems, Shirley, NY, USA) with the hip flexed to 85° and the knee flexed to 90°. For the MVICs, subjects were instructed to extend their knee as hard as they could while watching a computer screen running a custom-written program (Labview 8.5, National Instruments, Austin, TX, USA) showing their real-time torque output. Following completion of the first MVIC trial, the program displayed a solid line reflecting the subject's peak torque value from and a dashed line set 10% above the peak torque recorded from the initial MVIC. (Figure 3.1). For all subsequent trials, subjects were encouraged to reach this target torque value (dashed line). If subjects increased their torque during any of the subsequent trials, the height of the solid and dashed lines would be adjusted appropriately. Knee extension MVICs (minimum of three) were performed, with at least two minutes of rest in between each repetition, until no improvements in torque were observed by an investigator. Once each subject's knee extension torque failed to increase, the peak torque value from all recorded repetitions was noted and used as a threshold value for subsequent CAF assessment.

For CAF testing, self-adhesive, stimulating electrodes (Dura-Stick II [5 cm x 9 cm] Chattanooga Group, Hixson, TN, USA) were applied proximally over the rectus femoris and distally over the vastus medialis. At the beginning of testing, the peak torque value recorded during the MVIC trials was inputted into the computer program. The program utilized this threshold (peak torque) value to determine whether or not it would trigger the electrical stimulator (S88 and SIU8T, GRASS Technologies, West Warwick, RI, USA) to deliver a stimulus (100 ms-long train, pulse duration: 600 μs, delivery rate: 100 pulses per second, maximum voltage: 130V). Subjects were again instructed to generate enough torque to reach the dashed target line displayed on the screen (i.e., a value 10% greater

than their peak torque generated during MVIC testing). The computer program was set to deliver the stimulus once a subject's torque value reached threshold and then fell one Nm below their peak torque for the present trial. If a subject failed to reach the solid threshold line, the program would not deliver the stimulus, and the subject would be given two minutes of rest before the trial was repeated. The dashed target line was set so as to be unreachable for the subject; however, in the event that a subject did reach the target value, the maximal strength value (solid threshold line) was reset and CAF testing was reinitiated. Three repetitions of CAF testing were performed with two minutes of rest provided between repetitions.

CAF was quantified using the central activation ratio (CAR), wherein the peak torque generated immediately prior to the delivery of the electrical stimulus is divided by the peak torque generated as a result of the superimposed stimulus. Prior to the fatiguing exercise, three repetitions were performed with two minutes of rest provided between repetitions to limit the effects of fatigue on the measurement. Following the fatiguing exercise, three recordings were again captured, with only 30 seconds of rest provided. The average CAR over the three repetitions for each time point (pre- or post-fatigue) was used to quantify quadriceps CAF. Knee extension strength was also determined from these CAF repetitions. The subject's torque value generated immediately prior to delivery of the electrical stimulus was recorded and divided by participant body mass (kg). The average value over these three repetitions was utilized to quantify strength (Nm/kg). All measurements were recorded bilaterally, though only data recorded in the ACLr or matched limb in control subjects were submitted to statistical analysis.

Neuromuscular Fatigue

The fatiguing exercise consisted of sets of eight double-leg squats performed to a depth of 90° of knee flexion followed by the performance of a dynamic landing task. Verbal encouragement and feedback regarding knee joint angle were provided to subjects during the fatiguing exercise.

Subjects performed sets of squats until maximal fatigue was achieved, defined as the point at which subjects could no longer: 1) perform five consecutive repetitions to 90° of

knee flexion without assistance or 2) consistently reach the force platform during the dynamic landing task. The fatiguing exercise was also stopped if subjects reported pain in the ACL reconstructed knee. There was no limit on the number of squats a subject could perform.

Dynamic Landing Task

Dynamic landings were performed prior to fatigue, at maximal fatigue, and following the completion of each set of squats. For dynamic landings, subjects jumped forward off of both legs over a 17 cm box[83] and landed on one limb on a force platform (OR 6-7; Advanced Medical Technology, Inc, Watertown, MA) located one meter away. Immediately upon landing, subjects aggressively jumped laterally to the opposite side. The limb on which subjects landed was randomly determined using a custom-written program displayed on a computer screen in front of the subject. If the subject was to land on his/her right limb, a light was displayed on the right side of the computer screen and the subject would jump forward, land on his/her right limb on the force platform and then laterally jump to the left (Figure 4.1) Subjects practiced the dynamic landing prior to fatigue to allow adequate familiarization with the task. Three good trials, defined as the proper limb landing completely on the force platform, were analyzed pre- and post-fatigue. In the event that subjects could no longer consistently reach the force platform at maximal fatigue, the three previous dynamic landing trials were utilized as the post-fatigue landings.

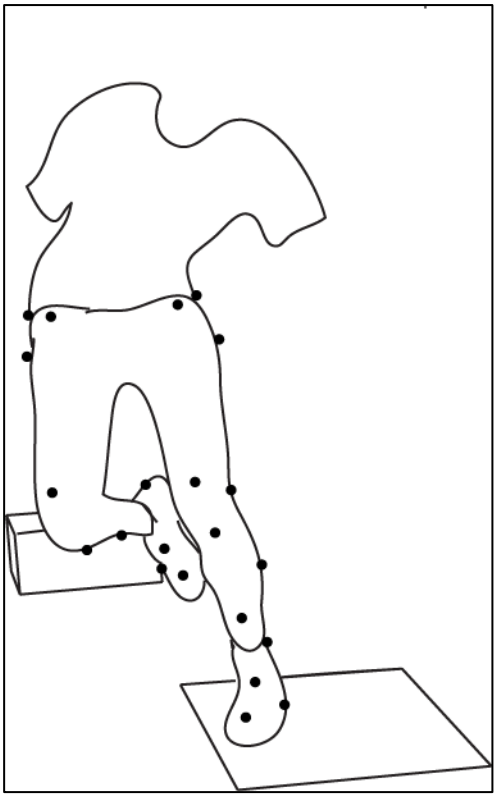


Figure 4.1. Dynamic landing task.

Biomechanical Data Collection and Analysis

Subjects were outfitted with 32 precisely attached retro-reflective markers (Figure 4.2) that were tracked via an 8-camera, high-speed (240 Hz) motion capture system (Vicon, Oxford Metrics, London, England) and from which joint rotations were quantified. An initial video recording was captured with subjects standing in a stationary position.[84] This static recording was utilized to generate a kinematic model in Visual 3D (C-Motion; Rockville, MD). The three-dimensional marker trajectories recorded during each dynamic landing trial were processed within Visual3D to solve for the respective joint rotations of each frame. Rotations were calculated utilizing a Cardan rotation sequence[85] and expressed relative to each subject's stationary position.[79] Three-dimensional ground reaction force (GRF) data were synchronized with the kinematic data and both were filtered using a zero-lag, Butterworth filter with a 12-Hz cut-off frequency[79] and submitted to standard inverse dynamics analysis within Visual 3D.[86] Kinetic outputs were normalized to subject body mass and height[86] and represented as external moments. Biomechanical data were time normalized to 100% of the stance phase for graphical purposes, with initial contact (IC) and toe-off equating to the time when the vertical GRF first exceeded and fell below 10N, respectively.[79, 80]

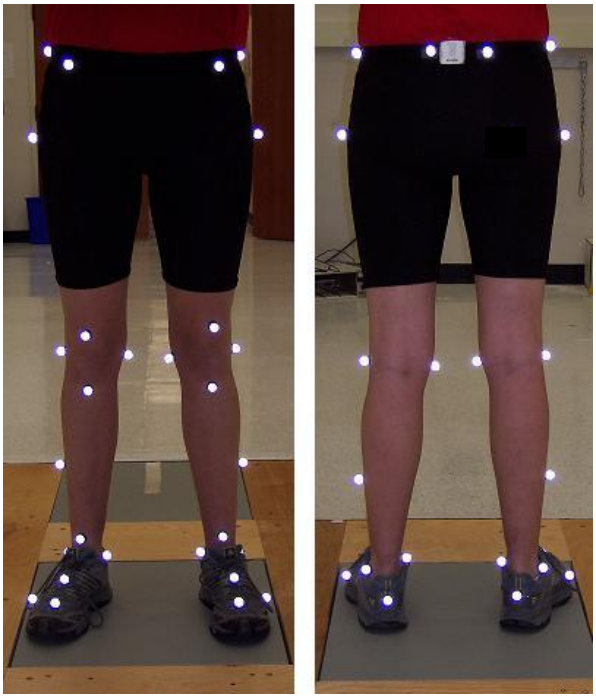


Figure 4.2. Retro-reflective marker placement for dynamic landing trials.

IC and peak stance (PS) knee joint sagittal and frontal plane rotations over the first 50% of stance were calculated for each landing trial.[80] PS joint moment data were also recorded in the sagittal and frontal planes at the knee. Data were analyzed during the first half of stance only as it is believed this is when ACL injury is most likely to occur.[87] Biomechanical data were analyzed for the ACL reconstructed limb or a matched limb in control subjects only.

Statistical Analysis

Sagittal and frontal plane knee joint angles and moments as well as CAR and MVIC were analyzed via 2x2 repeated measures ANOVAs. Each model had one within-subjects factor, fatigue state (pre- and post-fatigue) and one between-subjects factor, group (ACLr and control). An independent samples t-test was performed to determine if individuals in the ACLr group reached maximal fatigue faster than those in the control group. Sidak multiple comparisons procedures and univariate F-tests were utilized for all *post hoc* analyses. The α-level was set *a priori* at $P \leq 0.05$. Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) software version 17.0 (SPSS, Inc., Chicago, IL). Effect sizes and their associated confidence intervals were calculated using Cohen's d [23] within Microsoft Excel 2007 (Microsoft Corporation, Redmond, WA). These were calculated as either $\frac{\text{ACLr mean - control mean}}{\text{pooled standard deviation}}$ or $\frac{\text{post-fatigue mean - pre-fatigue mean}}{\text{pooled standard deviation}}$. Effect sizes were interpreted as having small (0.2-0.5), moderate (0.51-0.8), or large (>0.81) impacts in accordance with Cohen's guidelines.[23]

RESULTS

Joint Rotations

A time main effect was noted for sagittal and frontal plane knee joint angles at IC (sagittal *P*=0.018; frontal *P*=0.005) and at PS (sagittal *P*=0.002; frontal *P*=0.017) (Table 4.1). Specifically, ACLr and control subjects landed in a more extended and abducted posture when fatigued (Figure 4.3). A group main effect was also noted indicating that ACLr subjects demonstrated a significantly less flexed knee angle at PS (*P*=0.009) compared to the control subjects. No additional group main effects were noted for the remaining joint rotations (IC knee sagittal *P*=0.11; IC knee frontal *P*=0.83; PS knee frontal *P*=0.58).

Significant time by group interactions were found for knee sagittal (*P*=0.019) plane angles at PS, but not for IC angles (sagittal *P*=0.079; frontal *P*=0.097) or PS knee frontal plane angles (P=0.222). *Post hoc* analyses revealed that prior to fatigue, individuals in the ACLr group demonstrated less knee joint flexion at peak stance compared to the control

Table 4.1. .Initial contact (IC) and peak stance (PS) knee joint rotations pre- and post- fatigue. Data are mean±standard deviation.

Joint Rotations (°)	ACLr		Control	
	Pre-Fatigue	Post-Fatigue	Pre-Fatigue	Post-Fatigue
IC Knee Extension/Flexion	-10.3±5.5	-9.8±5.3	-14.3±4.3	-10.7±4.3
IC Knee Adduction/Abduction	-3.2±2.7	-2.8±3.1	-4.0±2.4	-2.4±2.5
PS Knee Extension/Flexion	-45.4±10.6	-44.1±6.1	-56.6±6.7	-48.2±10.9
PS Knee Adduction/Abduction	-12.2±6.8	-11.2±6.8	-13.6±6.8	-10.9±5.8

The rotation listed first is positive

group (P=0.001). No other significant *post hoc* results were detected (knee sagittal post-fatigue P=0.19).

Joint Moments

Significant time (P<0.001) and group (P<0.001) main effects were detected for the sagittal plane knee moment (Table 4.2). Subjects in both groups demonstrated smaller external knee flexion moments following fatigue, with the ACLr group, regardless of fatigue state, experiencing smaller moments than the control subjects (Figure 4.4). There were time (P=0.024) but not group (P=0.2) main effects for the knee frontal plane moment, suggesting that regardless of group, subjects demonstrated smaller knee abduction moments following fatigue.

Table 4.2. Knee joint moments (Nm/kg*m) pre- and post-fatigue. Data are mean±standard deviation.

Joint Moments (Nm/kg*m)	ACLr		Control	
	Pre-Fatigue	Post-Fatigue	Pre-Fatigue	Post-Fatigue
PS Knee Extension/Flexion	-1.10±0.29	-1.00±0.29	-1.74±0.24	-1.20±0.37
PS Knee Adduction/Abduction	0.29±0.15	0.28±0.18	0.43±0.19	0.31±0.16

The moment listed first is positive

A significant time by group interaction was identified for the knee sagittal plane moment (P<0.001). The ACLr group pre-fatigue had smaller external knee flexion moments than the control group (P<0.001). No statistical differences were noted between groups post-fatigue (P=0.085).

Table 4.3. Knee extension strength (Nm/kg) and quadriceps central activation ratio data. Data are mean±standard deviation.

	ACLr		Control	
	Pre-Fatigue	Post-Fatigue	Pre-Fatigue	Post-Fatigue
Knee Extension MVIC (Nm/kg)	2.03±0.57	1.58±0.46	2.63±0.92	1.61±0.54
Quadriceps CAR	0.82±0.11	0.78±0.13	0.89±0.10	0.82±0.14

Strength and Central Activation Ratio

Following fatigue, all subjects (ACLr and control) demonstrated significantly lower MVIC (P<0.001) (Figure 4.5) and CAR (P=0.003) (Figure 4.6) values (Table 4.3). No group differences were detected for either MVIC (P=0.13) or CAR (P=0.17). There was, however, a significant time by group interaction for MVIC (P=0.007) only, with *post hoc*

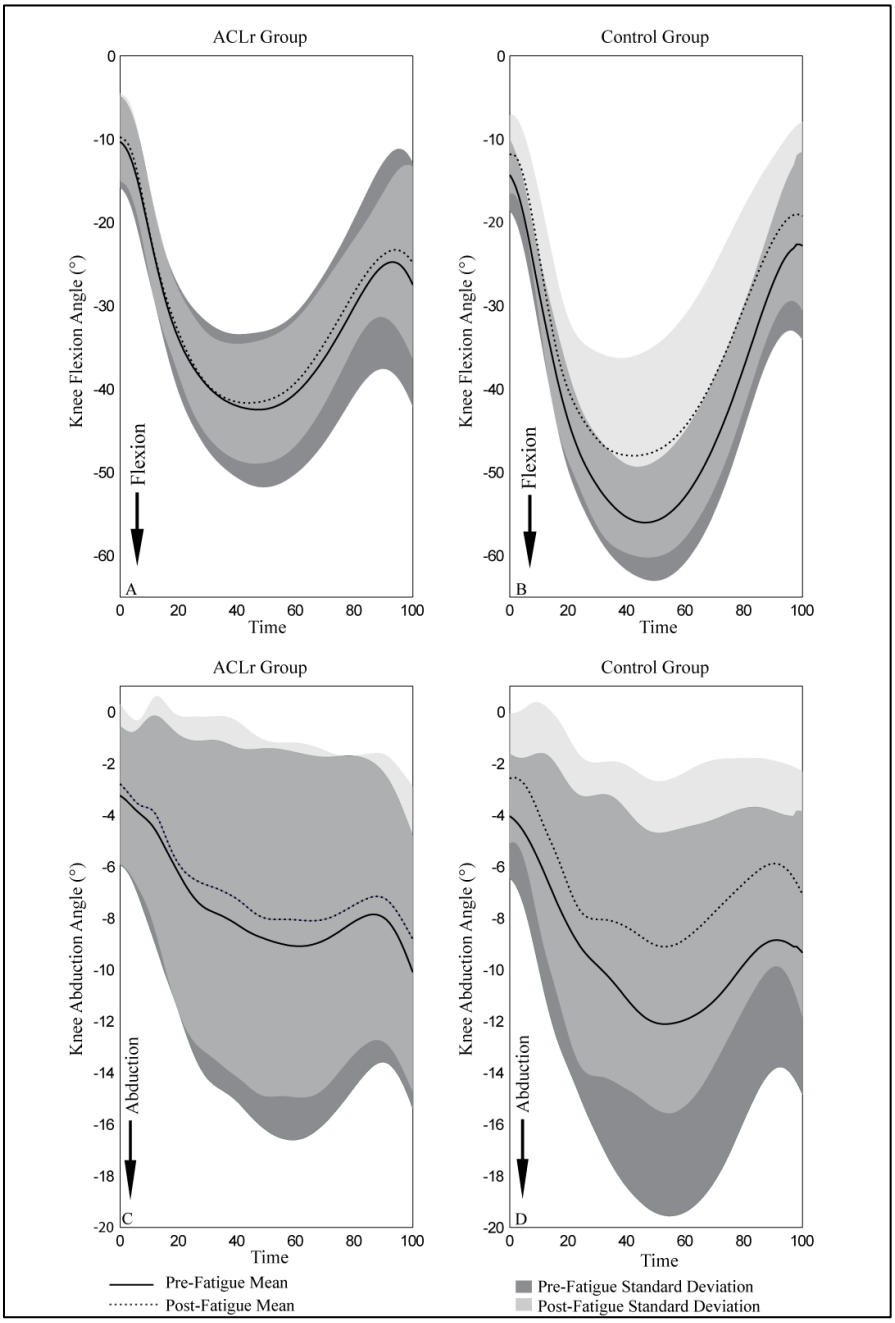


Figure 4.3. Pre- and post-fatigue joint rotations expressed as a percentage of the stance phase. A: ACLr group knee sagittal plane angle. B- control group knee sagittal plane angle. C- ACLr group knee frontal plane angle. D- Control group knee frontal plane angle.

analyses revealing that prior to fatigue, the ACLr group had significantly lower quadriceps strength than the control group (P=0.03). There were no post-fatigue differences in MVIC between groups (P=0.89).

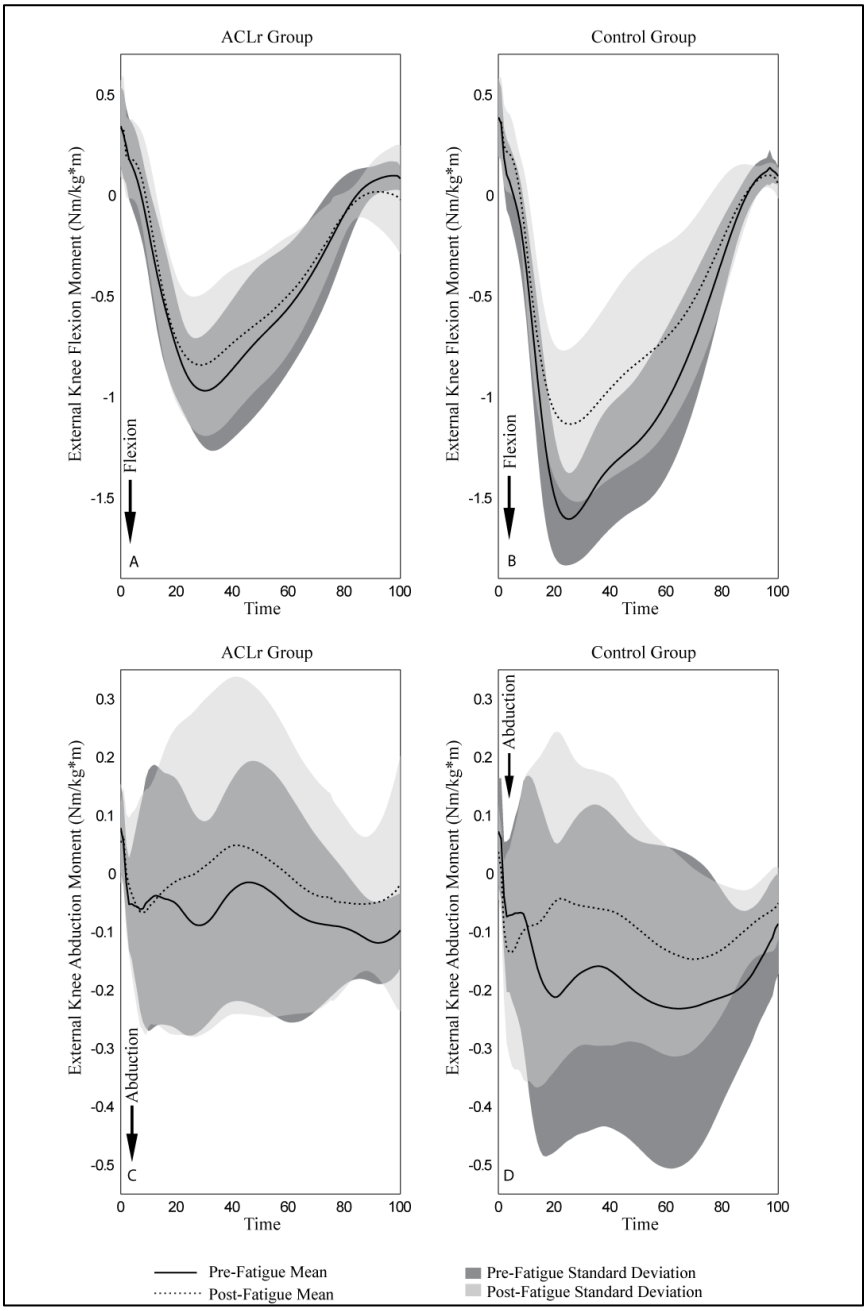


Figure 4.4. Pre- and post-fatigue joint moments expressed as a percentage of the stance phase. A: ACLr group knee sagittal plane moment. B- control group knee sagittal plane moment. C- ACLr group knee frontal plane moment. D- Control group knee frontal plane moment.

Rate of Fatigue

There was no statistical difference in the number of squats performed to reach maximal fatigue between groups (ACLr: 440.94±234.84; control: 543.13±307.67; *P*=0.29).

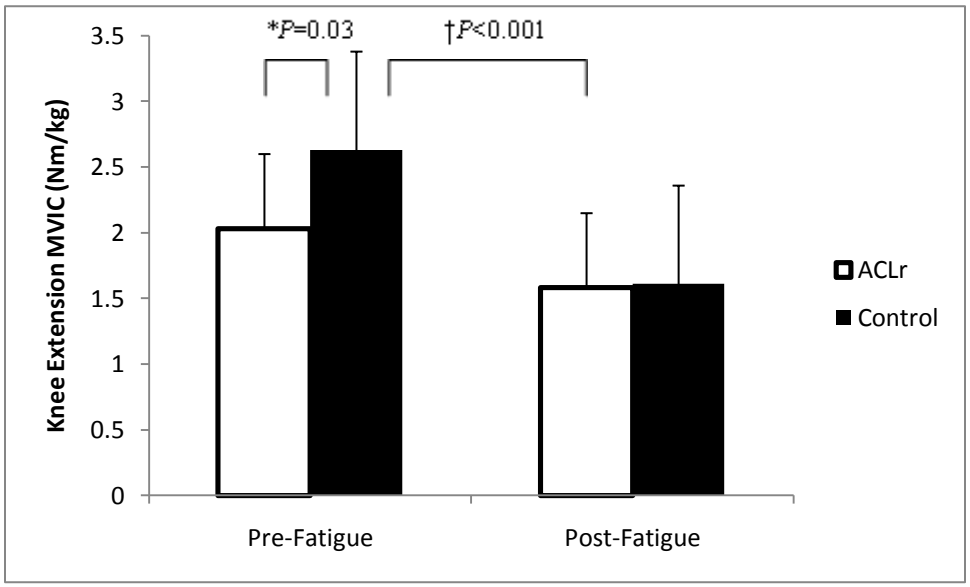


Figure 4.5. Mean±standard deviation knee extension strength (Nm/kg). * indicates significant difference between groups prior to fatigue. † indicates time main effect.

DISCUSSION

Both quadriceps CAF and neuromuscular fatigue impair volitional muscle activity, potentially yielding hazardous lower extremity biomechanics control strategies. Considering that individuals returning to sports following ACLr frequently present with quadriceps CAF and that neuromuscular fatigue is inevitable in athletic activity, understanding the cumulative effects of these two impairments seems crucial so that strategies to counter them can be better incorporated into post-operative rehabilitation. This study sought to elucidate the combined effects of quadriceps CAF and neuromuscular fatigue on lower limb biomechanics.

In accordance with our hypothesis, subjects demonstrated less knee flexion at IC and PS with concurrent reductions in the external knee flexion moment following fatigue. This sagittal plane biomechanical profile has been demonstrated previously in healthy adults following both gross lower extremity neuromuscular fatigue[79, 80] as well as following isolated quadriceps and hamstrings fatigue.[88] While maintaining a more extended knee

position may protect against collapse of the lower extremity on landing, increases in both the knee extension angle and moment have been implicated within the non-contact ACL injury mechanism.[33, 89] Thus, this adaptive strategy may be hazardous. To the best of our knowledge, this is the first study to demonstrate these altered sagittal plane biomechanics in individuals following ACLr and fatigue.

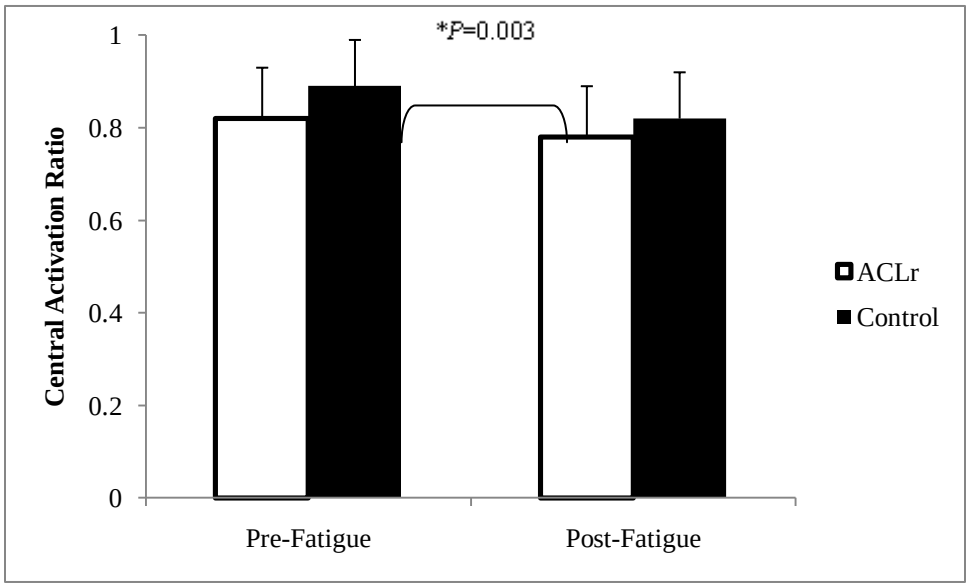


Figure 4.6. Mean±standard deviation quadriceps central activation ratio. *indicates significant time main effect.

Both ACLr and control subjects demonstrated smaller knee abduction angles and abduction moments following fatigue. Previous studies have reported increases in both the knee abduction angle[72, 77, 79, 80] and moment[79] post-fatigue as well as a lack of change in knee frontal plane biomechanics as a result of fatigue.[78] Our subjects may have developed a less aggressive landing strategy post-fatigue, one that allowed for a more neutral frontal plane knee angle during push-off. Alternatively, differences in the fatigue protocol employed between studies may account for these discrepancies. Several of these previous studies[77, 79] incorporated a change of direction task into their fatiguing exercises which may have allowed fatigue of the out of plane hip stabilizers. As the out of plane hip stabilizers aid frontal plane knee control, fatigue within these muscles may precipitate increased knee abduction.[90] Our fatiguing exercise consisted of a primarily sagittal plane motion, thus fatigue was likely limited to the quadriceps, hamstrings, and gluteus maximus muscles, thereby minimizing changes in knee frontal plane biomechanics following fatigue. Also possibly contributing to discrepancies between our findings and

those reported previously are differences in the subject population utilized, with previous studies[79, 80] utilizing division I athletes and the present study using a recreational athlete population. Previous research[91] indicates that subject skill level and training influence lower extremity neuromuscular control, which may contribute to how an individual performs a given task, and hence, affect study outcomes.

ACLr subjects demonstrated similar knee sagittal plane biomechanics regardless of fatigue state and in spite of a 22% reduction in their quadriceps strength following fatigue, suggesting that fatigue did not negatively influence sagittal plane biomechanics in the ACLr subjects to the same extent as the control group. Why this may have occurred is unclear. However, it seems that the ACLr group may have relied on a primarily hip dominant strategy[92] to decelerate the body during landing rather than one utilizing the quadriceps. This control strategy, often deemed the "quadriceps avoidance" or "knee stiffening" strategy, has been demonstrated in ACL deficient and reconstructed individuals during walking[93, 94] and may have translated to the dynamic activity employed within the present study. Relying on the hip musculature could have led to relatively unaltered sagittal plane knee biomechanics even in the presence of quadriceps fatigue. Future investigations are needed to clarify this relation between ACLr and biomechanics during activity. Alternatively, it is possible the ACLr subjects compensated using their uninjured limb during the squatting exercise, relying on the healthy limb to perform the majority of the work. This could have resulted in greater contralateral limb fatigue and, as such, relatively unchanged reconstructed limb biomechanics.

Following fatigue, both the ACLr and control groups demonstrated reductions in the CAR value, indicative of more severe CAF. Previous studies have also demonstrated reductions in central activation following fatigue, despite differences in muscle groups and fatiguing protocols employed.[95, 96] Together, these results suggest that neuromuscular fatigue, in part, is centrally mediated. Given the hazardous biomechanics demonstrated by our subjects as a result of fatigue, it seems that incorporation of training techniques to reduce the negative effects of CAF within ACL injury prevention programs may warrant consideration.

There were no differences in CAF between groups prior to fatigue, which is in conflict with our hypothesis. Several explanations for this finding are possible. First, rehabilitation may have restored some of the quadriceps CAF in the ACLr group, bringing the ACLr pre-fatigue CAR values more in line with those of the control group and contributing to the initial lack of difference in CAF. Second, the control group demonstrated an average pre-fatigue CAR of 0.89, which is below the previously accepted standard of 0.95 for fully activated in a normal, healthy individual.[97] It is possible, however, that the magnitude of the CAR in healthy individuals is lower than previously reported. Recent work indicates that voluntary activation in young, healthy individuals may be slightly lower at 94% and 90% in the stronger and weaker limbs, respectively[98]. Third, as current knee injury and pain influence CAF assessment, control subjects were carefully screened to be free of both injury and pain at the time of testing (average International Knee Documentation Committee [IKDC] score of 98.25/100), making it unlikely that these influenced the control subjects' pre-fatigue CAR values. Finally, it should be noted that when examining the effect sizes calculated for the CAR variable, both the time and group main effect values were small at -0.35 and -0.49 (Table 4.4), respectively. These values raise the question of whether or not statistically significant differences in CAR measurements between these two groups or across fatigue states are even clinically meaningful.

Table 4.4. Effect sizes for time and group main effects.

Time Main Effects	Effect Size	Confidence Interval	
		Lower Bound	Upper Bound
IC Knee Extension/Flexion Rotation	0.31	-1.35	1.97
IC Knee Adduction/Abduction Rotation	0.28	-0.41	0.98
PS Knee Extension/Flexion Rotation	0.40	-2.41	3.21
PS Knee Adduction/Abduction Rotation	0.20	-1.21	1.61
PS Knee Extension/Flexion Moment	0.78	0.68	0.87
PS Knee Adduction/Abduction Moment	0.26	0.21	0.31
Quadriceps MVIC	-0.82	-1.02	-0.63
Quadriceps CAR	-0.35	-0.39	-0.32
Group Main Effects			
IC Knee Extension/Flexion Rotation	0.57	-2.33	3.47
IC Knee Adduction/Abduction Rotation	0.07	-1.63	1.78
PS Knee Extension/Flexion Rotation	0.97	-4.38	6.33
PS Knee Adduction/Abduction Rotation	0.10	-4.01	4.20
PS Knee Extension/Flexion Moment	1.59	1.41	1.77
PS Knee Adduction/Abduction Moment	0.53	0.43	0.64
Quadriceps MVIC	-0.54	-0.94	-0.15
Quadriceps CAR	-0.49	-0.57	-0.42

Both the ACLr and control groups required a similar number of squats to reach maximal fatigue. This seems counter-intuitive considering that previous research has demonstrated that weaker muscle fatigues more quickly than stronger muscle.[11, 99] However, a previous study by Snyder-Mackler and colleagues[82] in individuals following ACLr found the quadriceps in the ACLr limb to be more fatigue-resistant than that in the contralateral limb. These authors suggested selective Type IIb fiber atrophy in the ACLr limb quadriceps may have contributed to this finding.[82] Type IIb fibers are fast twitch, non-fatigue resistant and, as such, a lower percentage of these within the quadriceps may lend to a more endurant muscle. The results of morphological studies following ACLr are conflicting, however, with studies demonstrating both selective Type I atrophy[50], selective Type II atrophy[51], as well as a relative predominance of both.[44] We did not consider quadriceps morphology within the present study and thus cannot determine if selective fiber type atrophy contributed to our findings.

It is worth noting that we included individuals who underwent both patellar tendon and semitendinosus/gracilis autograft ACLr in this study, which may have influenced our results. It is unknown whether persons who are reconstructed with different graft types respond differently to fatigue. Future studies may be needed to elucidate the potential differential responses of both graft types to neuromuscular fatigue so that graft type-specific rehabilitation strategies can be developed if necessary.

CONCLUSION

Both the ACLr and control groups demonstrated alterations in their knee joint biomechanics as well as reductions in quadriceps strength and CAR following fatigue. The worsening of sagittal and frontal plane biomechanics in the control subjects as a result of fatigue confirmed the need to perform fatigue-resistance training within ACL injury prevention modalities. That these neuromuscular and biomechanical changes were not more pronounced in the ACLr group was unexpected. Considering the important implications for re-injury, future studies seem necessary to further elucidate the effects of fatigue and CAF on lower extremity biomechanics in individuals after ACLr.

CHAPTER 5
DISCUSSION

This dissertation examined the effects of anterior cruciate ligament (ACL) injury and reconstruction on resultant lower extremity muscle weakness. In the first study, examining strength throughout the lower limb following ACL injury and reconstruction, I found that ACL injury lead to quadriceps, hamstrings, and ankle plantar flexor weakness, with the latter being sufficiently countered during post-operative rehabilitation, whereas quadriceps and hamstrings weakness were not restored six-months post-operatively. There were no hip or ankle muscle strength deficits when ACL-injured persons were compared to healthy individuals pre- or post-operatively, though differences existed for quadriceps and hamstring strength pre-operatively between ACL-injured and control individuals The results from this study suggested that improvements in current rehabilitation strategies are necessary to better target lingering quadriceps and hamstrings strength deficits.

In the second study, I examined two possible contributors to quadriceps weakness, central activation failure (CAF) and quadriceps atrophy, following ACL reconstruction (ACLr). Quadriceps CAF and atrophy were not associated with reconstructed limb strength deficits six-months post-operatively. This finding was in spite of substantial deficits in all three measurements and significant side-to-side differences in strength and atrophy. Thus, while atrophy and CAF were present six-months post-operatively, apparently other unknown factors were contributing to quadriceps strength deficits following ACLr. Elucidating these other contributors is imperative to countering quadriceps weakness within this population.

Finally, I examined the effects of quadriceps CAF and neuromuscular fatigue on knee joint biomechanics during landing. Compared to healthy people, individuals following ACLr demonstrated pre-fatigue biomechanics (reduced knee flexion angles and moments compared to controls) that may put them at risk for ACL re-injury. In addition, following fatigue both groups demonstrated potentially injurious changes in their knee joint biomechanics as well as impaired quadriceps strength and central activation. These

results corroborate that fatigue resistance training is warranted within ACL injury prevention strategies.

Collectively, these studies confirmed previous research suggesting that quadriceps weakness lingers despite rehabilitation following ACLr.[13, 17, 27] It is likely that until the contributing factors to weakness are known, attempts to fully eliminate it will prove difficult. In spite of investigating two of these possible contributing factors (CAF and atrophy) to quadriceps weakness in Chapter 3, we are currently no closer to determining the underlying causes of persistent quadriceps weakness following ACLr. As this was the first study to examine possible contributors to lingering quadriceps weakness following ACLr, no studies are available to which to compare our results directly. However, studies conducted in populations with similar quadriceps weakness suggest a clear link between CAF and atrophy and weakness, suggesting future studies need to be conducted to help confirm or refute our findings.

The inability to restore quadriceps strength may be hazardous to individuals upon return to activity following ACLr, which was confirmed in Chapter 4. ACLr subjects, presenting with initial quadriceps weakness and CAF, demonstrated pre-fatigue biomechanics that have been implicated within the non-contact ACL injury mechanism.[33, 89] These findings were consistent with those demonstrated after induction of experimental knee joint effusion[73], which can cause quadriceps CAF. Along with the control subjects, the ACLr group demonstrated potentially injurious post-fatigue knee joint biomechanics, reductions in quadriceps strength, and greater CAF. These fatigue-induced changes in biomechanics have been demonstrated in healthy people previously. This was the first study, however, to examine the effects of fatigue on biomechanics in individuals after ACLr. Our results suggested that incorporating fatigue-resistance training within current rehabilitation programs following ACLr may be necessary to aid in protecting individuals from re-injury upon return to activity post-operatively, though future studies confirming this are warranted.

STRENGTHS OF THE DISSERTATION

Collectively, these studies lend support to the body of literature suggesting a need to improve current post-operative ACL rehabilitation strategies as they relate to improving quadriceps strength. As these studies conclude, until it is known what contributes to the lingering quadriceps strength deficits presenting after ACLr, they cannot be effectively countered during rehabilitation. Chapter 3 began to provide some insight into what those contributors to muscle weakness might be, suggesting that both quadriceps CAF and atrophy accounted for a small portion of quadriceps weakness.

Chapter 4 provided direct biomechanical evidence that failure to restore quadriceps strength and central activation fully precipitates knee joint biomechanics during landing that have been implicated within the non-contact ACL injury mechanism. This suggested that the reconstruction and/or rehabilitation processes are not sufficiently reducing the biomechanical risk factors for re-injury when individuals return to activity.

LIMITATIONS OF THE DISSERTATION

Individuals undergoing both bone-patellar-tendon-bone and semitendinosus/gracilis autograft ACLr procedures were included within Chapters 2 and 4. The premise of these studies, however, was not to delineate the effects of ACL reconstruction on lower extremity muscle dysfunction by graft type.

Additionally, the strength and activation measurements employed in all three chapters were highly dependent on the subject eliciting maximal effort during testing. Despite the best efforts of the investigator and the use of visual feedback during testing, how much effort a subject put forth on a given trial was unknown.

The nature of the fatiguing exercise utilized in Chapter 4 may have limited the magnitude of the fatigue effect in the ACL reconstructed subjects. It seemed, despite constant encouragement against it, that the subjects may have compensated and utilized their contralateral limb to their advantage during the squatting exercise. It is possible that this healthy limb fatigued to a greater extent than the ACL reconstructed limb, which could have contributed to the results demonstrated by this group.

CHAPTER 6
CONCLUSION

CHAPTER 2

Findings:

1) Strength in the muscles crossing the hip and ankle joints was not different in anterior cruciate ligament (ACL)-injured individuals compared to healthy persons prior to or following surgical reconstruction.

2) Pre-operative ankle plantar flexor strength deficits were present in the injured compared to the uninjured limb.

3) Quadriceps and hamstrings strength deficits were present pre- and post-operatively in the injured versus the uninjured limb. These deficits also were present pre-operatively compared to healthy individuals

Conclusion:

Aside from the initial injury causing ankle plantar flexor weakness, strength within the hip and ankle musculature did not appear to be negatively influenced by either ACL injury or reconstruction. These results confirmed those of previous studies demonstrating the presence of quadriceps and hamstrings strength deficits in the injured/reconstructed limb pre- and post-operatively. The quadriceps and the hamstrings are important in controlling lower extremity dynamic stability. Persistent weakness within these muscle groups may lend to potentially injurious biomechanical strategies when individuals return to activity following ACL reconstruction. Thus, developing rehabilitation strategies to more effectively counter strength deficits within the quadriceps and hamstrings musculature seems imperative.

CHAPTER 3

Findings:

1) Quadriceps central activation failure (CAF) and cross sectional area (CSA) were not significantly associated with knee extension strength six-months after ACL reconstruction.

2) Peak quadriceps CSA and MVIC were significantly impaired in the injured limb six-months post-operatively compared to the uninjured limb. The CAR did not differ between limbs though the average CAR values indicated bilateral CAF was present.

Conclusion:

In spite of a lack of significant association between quadriceps CAF and CSA and knee extension strength, substantial deficits were noted in all three measurements six-months after ACL reconstruction, indicating current rehabilitation strategies are inadequate at removing these deficits.

CHAPTER 4

Findings:

1) ACL reconstructed and control subjects landed with smaller knee flexion angles and moments post-fatigue, both of which have been linked with non-contact ACL injury risk. Further, ACL reconstructed subjects had smaller knee flexion angles and moments at peak stance than controls regardless of fatigue-state.

2) Following fatigue, both groups landed with less knee abduction.

3) Both ACL reconstructed and control subjects demonstrated reductions in quadriceps strength and central activation as a result of fatigue. The ACL reconstructed subjects had greater quadriceps weakness prior to fatigue than controls.

Conclusion:

Both the ACL reconstruction and control groups demonstrated alterations in their knee joint biomechanics as well as greater quadriceps weakness and CAF following fatigue.

These hazardous post-fatigue biomechanics confirmed the need to perform fatigue-resistance training within ACL injury prevention modalities and suggested the need to explore fatigue-resistance training within rehabilitation following ACL reconstruction. The reduction in central activation concurrent with fatigue indicates that prevention strategies may benefit from improvements in central control. That these neuromuscular and biomechanical changes were not more pronounced in those undergoing ACL reconstruction was unexpected. Considering the important implications for re-injury, future studies seem necessary to further elucidate the effects of fatigue and CAF on lower extremity biomechanics in individuals after ACL reconstruction.

CHAPTER 7
RECOMMENDATIONS FOR FUTURE WORK

These dissertation studies revealed the need for future work to continue in the area of quadriceps dysfunction following ACL injury and reconstruction. Future studies need to develop better means by which to target quadriceps strength, and as demonstrated in Chapter 2 hamstrings, strength impairments post-operatively.

Until it is known why quadriceps impairments persist, it will be difficult to target them effectively during rehabilitation. Thus, future studies need to elucidate the central and/or peripheral contributors to quadriceps weakness. Several possible techniques not employed within this dissertation are the H-reflex and V-wave. The H-reflex, when normalized to maximal muscle activation (M-wave), allows for an assessment of net excitatory and inhibitory influences on alpha-motoneuron output and can provide insight into the influence of pre-synaptic inhibition of Ia afferents within quadriceps dysfunction following ACL reconstruction.[100] The V-wave, an electrophysiological variant of the H-reflex, provides an estimate of the level of descending motor drive to a muscle from supraspinal pathways in addition to reflex excitability of the motoneuron pool.[101] These measurements would allow for more precise determinants of what is contributing to central activation failure; however, these techniques are often difficult to record within the quadriceps.

There is some recent evidence to suggest following total knee arthroplasty that the relation between quadriceps CAF and atrophy and strength changes over the course of the first post-operative year. Quadriceps CAF accounts for the greatest amount of quadriceps weakness immediately after knee replacement, but as the patient approaches one-year post-operatively, this shifts towards atrophy explaining a more equal proportion of quadriceps weakness.[48, 49] Longitudinal studies may be necessary following ACL reconstruction so that phase appropriate treatment strategies can be implemented.

Incorporating fatigue-resistance training within current post-operative may be beneficial based on the results of these studies. Future work into the effects of fatigue and central activation failure on lower extremity biomechanics is necessary to elucidate what, if any,

fatigue-resistance training methods warrant inclusion within rehabilitation. These studies may benefit from not only inclusion of hip joint biomechanical data, yielding a more complete lower extremity biomechanical profile than was assessed presently, but also from a different fatiguing exercise. To eliminate the possibility of ACL reconstructed individuals compensating with their uninjured limb, it may be necessary to eliminate the healthy limb from the fatiguing exercise by switching to a unilateral squatting task. Alternatively, an isolated fatigue model as has been used previously in our lab could be employed.[88]

It may be beneficial to examine each of the above mentioned ideas in individuals undergoing either patellar tendon and semitendinosus/gracilis autograft ACL reconstruction procedures. It is known that each of these graft types impacts quadriceps and hamstrings, as well as hip adductor, strength differently, in the first 6-12 months post-operatively, though the effects of either graft type on muscle strength elsewhere in the lower extremity are unclear. Further, differential responses of individuals receiving each graft type to neuromuscular fatigue may occur. Unless these studies are undertaken, it will not be known if graft type-specific rehabilitation strategies are necessary.

CHAPTER 8
LITERATURE REVIEW

This section aims to detail the: 1) anterior cruciate ligament (ACL) injury and treatment strategies, 2) structure and function of the ACL, 3) mechanisms of muscle weakness, and 4) relation between neuromuscular fatigue and central activation.

ANTERIOR CRUCIATE LIGAMENT INJURY AND TREATMENT

The ACL is the most commonly injured knee ligament, with injuries rarely occurring in isolation, compounding an already lengthy and complicated recovery.[102] The following sections will discuss the incidence and consequences of ACL injury as well as current treatment strategies.

Anterior Cruciate Ligament Injury

ACL injuries occur at a rate of approximately 200,000 per year in the United States[1], with the majority of these occurring in individuals ages 18-45 years. Males suffer more ACL injuries annually than females; however, females are 2-8 times more likely to suffer an ACL injury when compared to males competing in similar sports (e.g.: basketball, soccer, volleyball.).[1, 103]

As of the year 2000, the estimated cost of an ACL injury (rehabilitation plus surgical reconstruction) was $17,000.[104] With approximately 50,000 ACL reconstructions (ACLr) performed annually in the United States, the cost of ACL injury is roughly $850 million.[105-107] This estimate, however, does not account for the rehabilitation costs associated with those opting for conservative treatment following injury. In addition to financial costs directly associated with injury, ACL injuries precipitate many long-term sequelae.

Post-traumatic osteoarthritis (OA) is a common consequence of ACL injury and develops in over 50% of knees approximately 5-12 years following injury.[3-5] Despite the efforts of reconstruction to restore mechanical stability to the knee, OA develops regardless of the treatment approach (operative or conservative).[4] In fact, it has been estimated that 70% of

ACL reconstructed knees will demonstrate osteoarthritic changes within seven years following reconstruction.[5]

Anterior Cruciate Ligament Injury Treatment

Following ACL injury, individuals may opt for either surgical reconstruction followed by rehabilitation or the more conservative approach of rehabilitation alone. Regardless of treatment strategy, return to full, pre-injury functional levels is often not achieved, with only 36% of ACLr[108] and 15-58% of ACL deficient[108, 109] persons returning to full activity. Further, there is a high (74%) failure rate of conservative treatment[110], with those individuals ultimately undergoing reconstruction.

A variety of ACL reconstruction procedures have been utilized, though the most commonly employed are the bone-patellar-tendon-bone (BPTB) or hamstrings autografts.[111] Numerous studies[16, 112-119] have attempted to determine which reconstructive procedure yields a superior functional outcome, though variations in surgical procedures and functional outcomes assessment make comparison between these studies difficult. The number of studies showing BPTB[115] to be superior is nearly equal to those concluding the hamstrings[112] autograft is better. Additional studies have shown surgical outcome to be equal among graft types.[16, 113, 114, 116-118]

Regardless of treatment strategy, rehabilitation is imperative following ACL injury. Two main types of rehabilitation exist, traditional and accelerated, with the ultimate goal being to restore lower extremity strength and function to pre-injury levels and delay/prevent the onset of OA. Traditional rehabilitation often returns individuals to full activity within 8-12 months following injury/reconstruction, whereas this time is reduced to roughly 4-6 months with accelerated programs.[120] Evidence demonstrating efficacy of one technique over the other is sparse, though it is suggested accelerated rehabilitation is as effective as traditional in restoring strength and function to the reconstructed limb.[121, 122]

STRUCTURE AND FUNCTION OF THE ANTERIOR CRUCIATE LIGAMENT

The ACL has both mechanical and somatosensory functions, serving as a passive stabilizer of the knee[123-125] and providing the central nervous system with information

regarding joint kinesthesia[126-130] and pain.[131] The following section will detail the mechanical and somatosensory functions of the ACL and discuss relevant anatomy.

Mechanical Function of the Anterior Cruciate Ligament

The ACL is comprised of a series of Type I collagen fibrils arranged into fascicles.[132, 133] Interspersed among the Type I collagen fibers are Types III[134, 135], IV[136], and VI[136] collagen, with Type III predominating early in ligamentization following reconstruction.[134] Also found within the structure of the ACL are water, ground substance, and elastic fibers.[133] The orientation of fascicles is location specific, with centrally located fascicles arranged in linear "waves" and those located in the periphery arranged nonlinearly, creating an accordion-like crimp to the ligament.[133, 137] As the ACL is loaded, the crimp is first straightened out, allowing low loads to be applied to the ligament without fibril damage.[133] As load increases, the fibrils become elongated and tissue stiffness increases.

Macroscopically, the ACL is comprised of two bundles, the anteromedial (AMB) and the posterolateral (PLB).[138] Because the orientation of the fibers within each bundle differs, each contributes to passive stability differently throughout the knee range of motion. In fact, a reciprocal relationship between the AMB and PLB is suggested to exist in regards to anterior tibial translation.[139] When the knee is in a more extended position, the PLB reportedly is better able to resist anterior translation.[140, 141] As the knee flexes, however, the AMB likely dominates.[140, 141]

The ACL may also serve to limit rotation about the knee joint[133], with the PLB providing greater stabilization against rotation than the AMB.[142] Much of the support for this comes from studies comparing double versus single bundle reconstruction techniques. Single bundle techniques, in essence, reconstruct only the AMB, whereas double bundle procedures reconstruct both bundles. Researchers have found that resistance to both anterior translation and combined anterior and rotary loads was greater in those undergoing double bundle reconstruction, thus supporting the contention that the PLB provides greater support to rotary loads than the AMB.[143, 144]These results, however, may reflect improper surgical techniques, where the graft is oriented more vertically (i.e. the

11 o'clock versus the 9-10 o'clock position for the right knee) and should be interpreted with caution.

The role of the ACL in frontal plane knee stability may depend on the integrity of the collateral ligaments and weightbearing status. Several studies suggest that the ACL is not a major stabilizer against knee frontal plane loading in the presence of an intact medial collateral[145-148] or lateral collateral[149] ligament. Additionally, Fleming et al.[124] have shown that the ACL does not resist abduction/adduction loads in a non-weightbearing state.

Somatosensory Function of the Anterior Cruciate Ligament

The neural structures of the ACL are located primarily in the superficial regions of the ligament near the tibial attachment.[127] The ACL receives its innervation from the posterior articular nerve, a branch of the tibial nerve. In addition, several other myelinated and unmyelinated nerve fibers are located within the ACL as well as mechanoreceptors and free nerve endings.

Mechanoreceptors comprise approximately 1% of the total area of the ACL[126] and function as transducers, converting a stimulus regarding mechanical deformation within the ligament into a neural impulse that the central nervous system (CNS) uses to interpret joint position, motion, and acceleration.[126, 150] Three classifications of mechanoreceptors have been identified in the human ACL: Ruffini endings, Pacinian corpuscles, and Golgi tendon-like organs. Ruffini endings are small (6-9 μm), low-threshold (highly sensitive), and slowly adapting mechanoreceptors that respond to changes in intra-articular pressure, static joint position, and the direction, amplitude, and velocity of joint movement.[127, 131] Pacinian corpuscles are low-threshold, rapidly adapting[127] mechanoreceptors that detect vibration[127], signal joint acceleration and deceleration[127, 128, 131, 151], and fire in response to changes in pressure.[127] Golgi tendon-like organs are large, high-threshold, slowly adapting mechanoreceptors that respond to changes in tension at the extremes of the joint's range of motion.[127]

The ACL, due to its dense mechanoreceptor population, is considered an important source of afference within the knee. Recent data supporting this suggest that a sensory-

motor arc exists between the ACL and the knee musculature.[152] Specifically, mechanical loading[152] and direct electrical stimulation[153] of the ACL increase hamstring muscle activity and decrease quadriceps activity, providing evidence for the afferent role of the ACL. It was believed initially that this reflex arc served a protective role for the ACL, activating the hamstrings to help stabilize the knee[154]; however, the latency of the reflex arc to the hamstrings (95 ms)[154] cannot activate the hamstrings quickly enough to limit anterior tibial translation. It is now suggested that the reflex arc may be involved in feed forward control during activity.[154] The neural pathway of this reflex is currently unknown, though it is believed that previous muscle contraction activates the γ-motoneuron (MN) loop.[155, 156]

When the ACL is injured, mechanoreceptors are disrupted. Mechanoreceptor regeneration following ACL injury and reconstruction remains controversial, with some research suggesting mechanoreceptors do not regenerate[157], whereas others[158, 159] suggest regeneration may occur by the eighth post-operative week. It also remains unclear whether mechanoreceptors, if able to regenerate, return to their full functional capacity. Recent studies by Ochi *et al.*[160, 161] suggest that mechanoreceptor regeneration is possible and that full function is restored by 18 months post-operatively. Lack of mechanoreceptor regeneration and/or decreased function following ACLr purportedly contribute to muscle dysfucntion[162] and diminished proprioception.[44, 163, 164] Mechanoreceptor disruption alters afference to the αMN [165], which may disrupt the reflex arc between the ACL and the knee musculature, altering or further impairing muscle activation.

Free nerve endings also contribute to the somatosensory functions of the ACL and have been identified in the cruciate ligaments.[131] Following ACL rupture, damage to joint structures (i.e. the ACL, itself) and the presence of an effusion result in stimulation of the nocioceptors. The information transmitted to the CNS from the free nerve endings is thought to contribute to muscle dysfunction.[166]

MUSCLE WEAKNESS: A CONSEQUENCE OF ANTERIOR CRUCIATE LIGAMENT INJURY AND RECONSTRUCTION

The musculature surrounding the knee joint serves a protective role for both the ACL and other structures of the joint (e.g. articular cartilage through energy absorption on weight bearing). Weakness of these muscles, however, often occurs concomitantly with ACL injury and reconstruction[13, 141, 167], contributing to altered gait mechanics and increased joint loading.[168, 169] The presence of quadriceps and hamstrings weakness has been demonstrated[12-14, 17, 27, 35, 70, 170, 171] following ACL injury and reconstruction; however, the effect of ACL injury on strength elsewhere in the lower extremity remains unclear.

Despite intensive rehabilitation efforts, quadriceps weakness is nearly universal following ACL injury, with reports of quadriceps weakness lasting upwards of one year post-operatively.[17, 70, 170] Strength deficits in the injured versus uninjured limb reportedly range from 5-30%.[12-17] Weakness has been demonstrated following both BPTB[12, 13, 17, 27, 70, 170] and hamstrings autografts.[12] Additionally, researchers have found that quadriceps strength deficits occur bilaterally.[14, 35, 171] The precise mechanism underlying quadriceps weakness is unknown, though AMI[31, 35, 171, 172] and atrophy[8] have been implicated.

Similar to the quadriceps, hamstrings weakness has also been demonstrated following both BPTB[70] and hamstrings[14, 170] autograft ACLr. Knee flexion strength deficits range from 9-13%.[14, 17, 18] Bilateral strength deficits have been reported[14], with hamstrings weakness in the reconstructed limb reportedly persisting upwards of one year post-operatively, though contralateral strength may be restored by this time point.[173] Donor site morbidity in the case of hamstring autograft reconstruction[174] and muscle atrophy[18] have been suggested as possible mechanisms contributing to hamstrings weakness.

Though little research evidence is available to support it, clinical speculation suggests that weakness of both the hip and ankle musculature also occurs following ACL injury. A study conducted by Jaramillo *et al.*[19] demonstrated hip muscle weakness— extensor, abductor, and adductor— following knee surgery. These authors, however, examined hip muscle strength following a variety of surgical procedures, limiting the applicability of their results to an ACLr population. To date, only one study[20] has examined the effects of ACLr on hip muscle strength, noting hip adductor weakness following semitendinosus/gracilis autograft reconstruction. These authors suggested donor site morbidity may contribute to weakness, though it does not likely fully explain weakness

due to the small cross sectional area of the gracilis.[20] The authors further suggested that neurological alterations may contribute to adduction weakness.[20] No studies have examined strength of the ankle joint musculature following ACL injury or reconstruction; however, decreased gastrocnemius activity has been demonstrated during gait[175] in an ACL deficient population as well as during landing[21] following ACLr, a finding which may be suggestive of muscle weakness. Additionally, clinical observation suggests atrophy presents in the calf musculature following ACLr.

Biomechanical Consequences of Muscle Weakness

Lower extremity muscle weakness following ACLr may lead to biomechanical changes during functional activity and, eventually, degenerative changes within the knee joint. Quadriceps weakness, specifically, has been linked to biomechanical adaptations, including decreased knee flexion excursion and internal knee extension moment during stance.[176, 177] The combination of these two adaptations decreases the energy absorption capability of the knee musculature on weight bearing[178], which may increase risk of degenerative joint disease.[177] Additionally, quadriceps weakness has been shown to increase the rate of knee joint loading[179], which may increase joint reaction forces[180] and further increase the risk of joint degeneration. Quadriceps weakness may also contribute to altered frontal plane knee loading, specifically increased adduction moment.[181] Considering that the quadriceps are important resistors of knee adduction moment[90, 182], quadriceps weakness could increase loads through the medial tibiofemoral compartment and possibly increase risk of OA.

Weakness of the hip musculature has also been shown to alter biomechanics, with weakness of the hip abductors increasing external knee adduction moment during weight bearing.[183] This may increase risk of medial tibiofemoral OA. When the stance limb hip abductors are weak, contralateral pelvic drop during the swing phase is increased.[184] This shifts the center of mass toward the swinging limb, causing the vertical ground reaction force vector to pass medial to the stance limb's tibiofemoral joint center, which increases forces through the medial compartment and, possibly, risk of joint degeneration.[184]

Limited attention has been paid to strength of the ankle musculature in regards to biomechanics. Computer modeling and forward dynamics analysis has demonstrated, however, that ankle plantar flexor weakness may increase hip and knee extensor work[185], which could potentially decrease hip and knee flexion angles.

MECHANISMS OF MUSCLE WEAKNESS

Muscle Atrophy

A possible explanation for weakness following ACL injury and reconstruction is disuse atrophy of the muscles of the involved limb, wherein strength deficits occur with inactivity following injury. Immobilization, in the form of bracing following ACL injury and reconstruction, can also lead to atrophy.[36]

Recent evidence suggests, however, that quadriceps atrophy cannot sufficiently explain weakness.[29, 45, 47] While not specific to an ACLr population, Mizner *et al*.[45] and Petterson *et al*.[47] found that voluntary activation failure better explains weakness than muscle atrophy.[47] Following ACLr, Konishi *et al.*[29] examined quadriceps torque per unit volume and found a reduction bilaterally compared to healthy control subjects These authors noted that reduced motor unit recruitment, specifically high-threshold motor units, in addition to muscle atrophy appear responsible for quadriceps weakness.[29]

Atrophy may explain hamstrings weakness in the injured compared to the uninjured limb 6-months post-operatively following ACLr performed with ipsilateral semitendinosus autograft.[18] At 12-months post-operatively, however, there were no differences between ACLr and healthy controls regarding hamstring muscle torque per unit volume, leading the authors to conclude that the same mechanisms underlying persistent quadriceps weakness do not explain hamstrings weakness.[18] These results directly conflict with the findings of Makihara *et al.*[186] who found that atrophy may explain hamstrings weakness upwards of 3.5 years post-operatively. These authors additionally attributed weakness to decreased length of the semitendinosus muscle fibers following graft harvest.[186] Further research into this area appears necessary to elucidate the relationship between hamstrings atrophy and strength.

Central Activation Failure and Arthrogenic Muscle Inhibition

Central activation failure (CAF) decreases volitional muscle contraction by failing to recruit all motor units or by failing to achieve maximal discharge rate from the motor units that are recruited.[187] When joint damage initiates this process, CAF is referred to as arthrogenic muscle inhibition (AMI).[188] AMI is regarded as being due, at least in part, to altered afferent feedback from a joint.[36, 189] As discussed previously, the healthy ACL houses mechanoreceptors that, under normal conditions, provide sensory feedback from the knee joint to the CNS relative to joint movement, position, and loading.[128] When the ACL ruptures, this sends an inhibitory signal to interneurons located within the CNS, causing an inhibitory MN response[190], observed as a decrease in voluntary activation of the musculature surrounding the affected joint. Altered afference may disrupt the gamma-loop, further decreasing αMN activity.[191-194] Descending inhibitory signals from the cortex may also reduce αMN excitability and minimize voluntary activation.

Following ACL rupture, the quadriceps commonly experience AMI, though the magnitude of the impairment varies among studies, with reports ranging from 8-45%.[31, 35, 75, 171, 172] Additionally, AMI has been reported in the unaffected limb following ACL injury[195, 196] and reportedly ranges from 7-26%, which is nearly equivalent to the magnitude of impairment in the injured limb in some individuals.[31, 35, 171] While studies have shown that reconstruction and rehabilitation following ACL injury reduce the severity of AMI, they do not appear to eliminate it. In fact, Urbach *et al*.[171] demonstrated bilateral AMI of 15% in the injured and 16% in the uninjured limbs, respectively, two years post-operatively.

It is believed that AMI is a natural process designed to protect the injured joint from further damage by limiting its mobility, though the effects of AMI may be more harmful than beneficial. AMI has been suggested to precipitate weakness[197] and possibly atrophy[198] of the affected limb, which may alter biomechanics, possibly initiating degenerative changes within the joint. That AMI persists beyond the rehabilitative phase suggests effective treatments to combat it have yet to be determined. Hurley and Newham[198], however, have found that strength gains are still possible in the presence of AMI, leading these authors to conclude that additional factors (i.e. altered proprioception

stemming from the neurophysiologic mechanisms of AMI) may contribute to the initiation and progression of joint degeneration.

Mechanisms of Arthrogenic Muscle Inhibition

Pre-Synaptic Inhibition

Pre-synaptic inhibition generally occurs following decreased neurotransmitter release from the pre-synaptic terminal.[199] Primary afferent depolarization (PAD) interneurons are involved in this process[200], synapsing with primary afferents containing GABA receptors. When GABAa receptors are activated, this causes an efflux of chloride ions and, therefore, PAD. PAD decreases the amplitude of the action potential, which reduces calcium influx into the pre-synaptic terminal, thereby decreasing neurotransmitter release into the synaptic cleft.[201] It has been suggested that activation of GABAb receptors directly interferes with voltage-gated calcium channels, reducing calcium influx into the pre-synaptic terminal[202]; however, the role of GABAb receptors in pre-synaptic inhibition is unclear. PAD affects Ia and Ib afferents and can be controlled by descending tracts.[200, 203, 204]

It has been demonstrated previously that pre-synaptic inhibition contributes to quadriceps AMI following induction of an experimental knee joint effusion. [205] Though the precise mechanism underlying pre-synaptic inhibition in AMI is unknown, it is suggested that GABA-ergic interneurons may be involved.[205] Increased afferent input may occur in the presence of joint effusion and GABA-ergic interneurons may serve as a gating mechanism for this increased afference, reducing excitatory input to the injured muscle.[205] This may contribute to AMI in the presence of knee joint effusion following ACL injury and reconstruction.

Reciprocal Inhibition

Reciprocal inhibition is a process wherein inhibitory Ia interneurons receive an excitatory stimulus from Ia afferents.[190] The axons of these Ia interneurons create a heterogenic synapse with the αMN of antagonistic musculature, sending an inhibitory stimulus to the

αMN. Reciprocal inhibition, therefore, ultimately results in antagonist muscle inhibition. This process may also be mediated by Renshaw cells.[206]

The precise role of reciprocal inhibition within quadriceps AMI is currently unknown; however, as Ia interneurons receive input from joint afferents[207], it is possible that a change in afference would activate the Ia interneuron, possibly contributing to AMI. Ia inhibition could reduce the efficacy of afferent transmission, decreasing efferent output, and, therefore, volitional muscle contraction.

Reciprocal inhibition has been suggested as mediating AMI in other muscles, specifically the hamstrings.[208] A study examining chronic ankle instability reported bilateral hamstrings AMI, with the authors suggesting that soleus inhibition leads to quadriceps facilitation, which they also reported. Quadriceps facilitation could, through reciprocal inhibition, cause hamstrings inhibition.[208] Considering that both the quadriceps and hamstrings send and receive neural projections to/from the ankle plantar flexor and dorsiflexor muscles[41], it seems plausible that altered Ia afferent transmission from the injured ankle could lead to altered muscle activation at the knee and that knee injury could precipitate altered ankle muscle activity. Similar neural projections that occur between the knee and ankle muscles have been shown in animals between the rectus femoris and its hip synergists (e.g. sartorius)[26], suggesting that altered afferent output following knee injury may alter activity and generate weakness of the hip musculature, though this has not been demonstrated.

Recurrent Inhibition

Recurrent inhibition results in agonist inhibition and antagonist facilitation and may be mediated by Renshaw cells. An antidromic potential from an αMN excites the Renshaw cell, which then sends an inhibitory stimulus back to the original αMN. Because Renshaw cells also synapse with Ia interneurons, inhibitory stimuli are concurrently projected to synergistic muscles.[209] It has been suggested that Renshaw cells are preferentially activated by large motoneurons, making recurrent inhibition more likely in fast-twitch, fatigable motor units.[210]

Experimental knee joint effusion has been demonstrated to cause AMI.[57, 211] Further, Renshaw cell activation has been demonstrated following experimental knee joint effusion.[212] Thus, Renshaw cells are suggested to contribute to AMI and may serve as a gating mechanism[212], controlling the efficacy of efferent drive to αMN and possibly their firing rate.[213]

Non-reciprocal Inhibition

Non-reciprocal inhibition likely originates within the Golgi tendon organ (GTO). The GTO houses Ib afferents, which synapse with Ib interneurons. These interneurons generate both excitatory and inhibitory signals, producing antagonist excitation and causing homonymous and synergistic MN inhibition.[188]

Non-reciprocal inhibition has been found to contribute to AMI. Iles *et al.*[211] induced experimental knee joint effusion and measured the magnitude of Ib inhibition at rest and during quadriceps contraction. In the presence of effusion, non-reciprocal inhibition increased compared to a non-effused state. The authors hypothesized that non-reciprocal inhibition may decrease volitional control of the injured joint, preventing further injury.[211] This decrease in volitional control may occur through stimulation of Ruffini endings in the presence of effusion.[214] Ruffini endings project an afferent stimulus to Ib interneurons, which may decrease voluntary muscle activity.[215]

Tonic Descending Inhibition

Tonic descending inhibition (TDI) is a mechanism through which the brain stem can control afferent input. TDI serves to inhibit increases in afferent information to the central nervous system.[216, 217] In the presence of joint pathology, however, spinal neurons decrease their threshold to afferent input, enhancing the effects of efferent inhibitory drive and making the spinal neurons more susceptible to peripheral feedback.[218]TDI has been implicated within AMI, and is suggested to contribute to the bilateral inhibition seen following joint injury[36] as cells within the spinal cord receive input from both the ipsilateral and contralateral limbs.[219]

Gamma-Loop Dysfunction

The gamma-loop consists of γMN activation of intrafusil fibers within the muscle spindle, which lowers the firing threshold of Ia afferents, causing αMN firing. The precise cause of gamma-loop dysfunction has yet to be determined, but two possible theories have been proposed. The first was reported by Hagbarth *et al.*[220], wherein the authors induced a partial nerve block of the deep peroneal nerve and found reduced volitional motor unit firing rates that could be countered by muscle vibration. The second mechanism is that intrafusil fibers experience fatigue similarly to extrafusil fibers. During sustained isometric contractions, it has been demonstrated that afferent firing rates decrease progressively with time and this decline is inversely proportional to EMG activity. The authors attributed decreased afferent firing to fatigue of the fusimotor system, leading to withdraw of γMN activity and disfacilitaton of the αMN.[221]

Previous studies have found that altered afferent activity, which occurs following ACL rupture, may lead to abnormal gamma efferent activity.[193, 194] In a recent series of studies by Konishi *et al.*[29, 191-194], these authors have suggested that this loss of afference following ACL injury leads to gamma-loop dysfunction and that the combined effects of altered afferent and efferent activity may explain both unilateral and bilateral quadriceps weakness following ACL injury and reconstruction. However, these authors utilized prolonged vibration of the patellar tendon, which may stimulate the GTO. As discussed previously, the GTO houses Ib afferents, which, when they synapse with Ib interneurons, mediate non-reciprocal inhibition. As non-reciprocal inhibition causes agonist inhibition (i.e. the quadriceps in the case of the patellar tendon), Ib afferent activation due to patellar tendon vibration may help to explain the quadriceps weakness demonstrated in these studies.

METHODS OF ASSESSING MUSCLE DYSFUNCTION

Muscle Atrophy Assessment

Multiple methods exist for non-invasive measurement of human skeletal muscle atrophy. Ultrasound was an early, preferred technique[222] for the assessment of superficial muscles[223]; however, due to the limited abilities of ultrasound (e.g.: poor resolution and

inability to control slice thickness)[222], computed tomography (CT) and magnetic resonance (MR) imaging have become the preferred methods.

CT scans utilize a series of x-rays to generate a soft tissue image. An x-ray beam is passed through a person to a detector located on the other side of the body segment.[224] The x-ray beam and detector move along the tissue and a series of measurements are taken with the x-ray beam at different angles.[224] These data are reconstructed to allow for the creation of an image representing the soft tissue scanned.[224] MR imaging operates on the principles of magnetic fields, wherein protons spin about an internal axis creating a magnetic dipole moment.[225] When placed in a strong magnetic field, slightly more than half of the magnetic dipoles orient with the external magnetic field.[225] The magnetic dipoles oriented with the external field are cancelled out by the dipoles oriented opposite to the external field, and an MR image is generated by the extra dipoles, the ones that have not been cancelled out.[225]

MR imaging offers several advantages to other imaging techniques for assessing muscle atrophy. Firstly, MR imaging uses non-ionizing radiation and has no known adverse physiological effects.[225] Because a series of images is required to accurately calculate muscle cross sectional area (CSA)[226], these features make MR imaging preferable. Additionally, the time required to obtain multiple MR images is less than that required to obtain multiple images using CT, allowing muscle CSA assessment in a more time and cost-effective manner.[226] Lastly, the soft tissue images obtained from MR techniques are more detailed than those obtained from CT[222] and have not been demonstrated to over-estimate muscle CSA, as often occurs with CT scans.[222, 227]

Atrophy is often quantified as either muscle volume[7, 8] or CSA.[7, 8, 44, 45] After a CT or MR image is obtained, the contours of a muscle are traced in each image in which the muscle is present[7, 8] and then submitted to a computer program which calculates volume or CSA. A study by Williams and colleagues[7] determined that both muscle volume and CSA equally predict muscle atrophy in the quadriceps. CSA has been shown to be more strongly related to quadriceps strength than volume[228] and, thus, has been suggested as an ideal measurement tool for quantifying quadriceps muscle size.[60]

Muscle Strength Assessment

Several methods exist for assessing muscle strength. Clinically, strength is typically assessed using manual muscle testing or hand held dynamometry, though both methods may be limited by the strength of the examiner. Though not always clinically accessible, isokinetic dynamometry is the gold standard. Isokinetic dynamometry allows for three types of strength assessment: isometric, concentric, and eccentric.

Isometric strength assesses a muscle's ability to produce static force.[229] This method is advantageous when the joint range of motion is limited by injury or immobilization. Isometric strength assessment, however, only indicates strength at the particular point in the range of motion where the test is occurring and, as such, is not a functional, dynamic measure.

Concentric and eccentric strength measures assess dynamic strength, with concentric being the more commonly utilized method.[230] Testing of both concentric and eccentric strength has been performed at a variety of movement velocities ranging from 30-300º/s.[231-234] It has been suggested that lower movement velocities (i.e.: 60º/s) are more useful for testing concentric strength as force output declines with increasing contraction speed..[230] Eccentric strength does not change with regards to movement velocity and is often measured at the same speed as concentric so that comparisons between the two can be made.[230]

In order to determine a force decrement following injury, a baseline (pre-injury) measurement is required. As a pre-injury measurement may be lacking, clinicians often perform a bilateral comparison. Several studies, however, have demonstrated AMI in the contralateral limb following injury.[195, 196] Thus, the contralateral limb may not be an ideal comparison. Additionally, the magnitude of the volitional muscle contraction is dependent not only on the strength of the targeted muscle, but also on factors such as pain, motivation, and agonist-antagonist co-contraction, all of which can lead to an underestimation of strength.

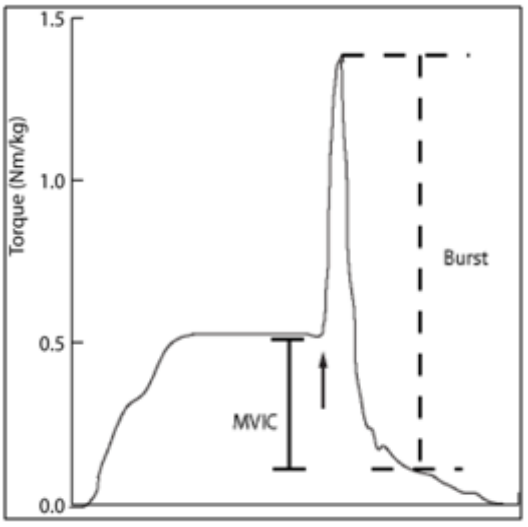
Muscle strength is often quantified by either force (N) or torque (Nm) and normalized to individual body mass so that strength can be compared across individuals. When strength

is assessed using dynamometry, torque may be the more appropriate parameter to report as the rotational strength of the muscle is what is being tested.[230]

Arthrogenic Muscle Inhibition Assessment

Burst Superimposition

The burst superimposition technique involves the application of a train of electrical stimuli during the performance of a maximum voluntary isometric contraction (MVIC). This technique indicates the level of volitional activation a person is capable of achieving versus what would be possible if no inhibition were present. When the torque signal generated by the person during MVIC is visualized, a spike in force production can be observed at the time the stimulus is delivered (Figure 1). The percent difference between this spike and the torque level immediately prior to the spike is known as a central activation ratio (CAR)[187] and is used to quantify CAF, or AMI. Because the stimulus is delivered proximal to the neuromuscular junction, Merton[235] suggested that any increase in force output following stimulation indicated that full MN pool activation had not been achieved and, thus, indicated central activation failure. As with any MVIC technique, this method requires the generation of a true maximal contraction, as submaximal contractions have been demonstrated to over-estimate CAF/AMI.[236]



CAR is calculated by the following equation (Eq. 1):

Eq. 1 $$CAR = \left(\frac{MVIC}{Superimposed\ Burst}\right) \times 100$$

where *MVIC* is the mean torque value and *Superimposed Burst* is the maximum value elicited via the electrical stimulus. Applying equation 1 yields an uncorrected CAR value, which, according to Stackhouse *et al.*[237] provides an overestimation of central activation. In a study comparing central activation at varying percentages of MVIC, it was found

that the relationship between CAR and MVIC is curvilinear, wherein CAR values are higher than their equivalent voluntary activation values.[237] For example, at 25% MVIC, a linear relationship would yield a CAR of 25; however, these authors found at 25% MVIC, the CAR value was approximately 40.[237] Thus, it was concluded that CAR over-estimates central activation, thereby underestimating AMI. The authors posit that the overestimation may be due to the duration of the train of stimuli delivered, and that full summation of force cannot be generated during the short train duration.[237]

To correct for this overestimation, an equation (Eq. 2) was developed to produce a corrected CAR value (CAR_c)[237, 238]:

Eq. 2 $$y = -0.000097x^2 + 0.019036x$$

where *y* is the CAR value obtained in equation 1. Equation 2 is solved using the quadratic formula and then divided by 100 to obtain CAR_c.

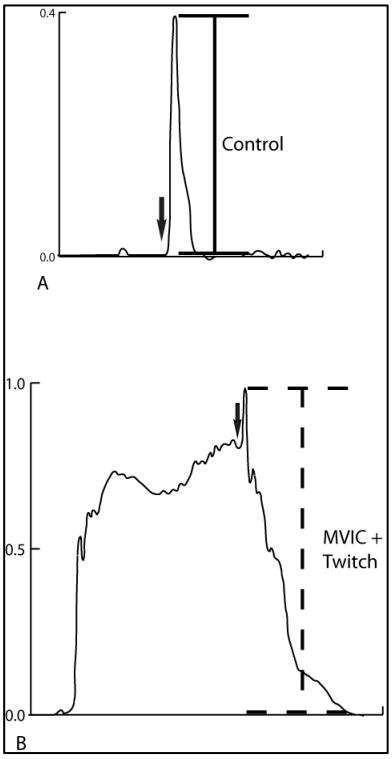


Figure 8.2. Schematic of ITT. Arrows indicate delivery of the stimulus. A) stimulus delivered at rest. B) stimulus delivered over top of an MVIC. ITT is calculated as [1-(B/A)]*100.

Interpolated Twitch Technique

In the interpolated twitch technique, an electrical pulse is superimposed on top of an MVIC, but there are two key differences between this and the burst superimposition technique. First, the electrical pulse is comprised of different parameters and is usually a singlet or a doublet of pulses rather than a train. Second, the equation used to calculate central activation is different and requires the elicitation of a resting twitch force (Figure 2) (Eq. 3)[239]:

Eq. 3

$$ITT = \left[1 - \left(\frac{superimposed\ twitch}{control\ twitch}\right)\right] \times 100$$

where *superimposed twitch* is the maximum value elicited via the electrical stimulus superimposed over

the MVIC and *control twitch* is the maximum value elicited by the twitch at rest.

Several studies have examined the efficacy of the CAR and ITT techniques as well as the number of stimuli required to accurately quantify CAF/AMI. Bampouras *et al.*[240] found that the level of activation obtained with the ITT method is similar regardless of the number of stimuli delivered. These findings directly contradict those of Lloyd *et al.*[241] and Behm *et al.*[242] who found that a train of electrical stimuli was more effective than using singlets or doublets of pulses when using the ITT method of quantification. Behm *et al.*[242] concluded that as long as a train of stimuli is delivered, both the ITT and CAR methods are equally effective at quantifying CAF/AMI.

H-reflex and M-wave

Both the Hoffman reflex (H-reflex) and M-wave are elicited when a low-intensity, percutaneous electrical stimulus is applied directly over a motor nerve[100] (Figure 3). Following Henneman's size principle[243], large diameter Ia afferent fibers are selectively recruited and action potentials generated along their axons.[244] These action potentials travel from the point of stimulation to the spinal cord, where they produce excitatory postsynaptic potentials, which, in turn, give rise to efferent potentials traveling toward the muscle. These efferent action potentials are recorded in the muscle via electromyography (EMG)

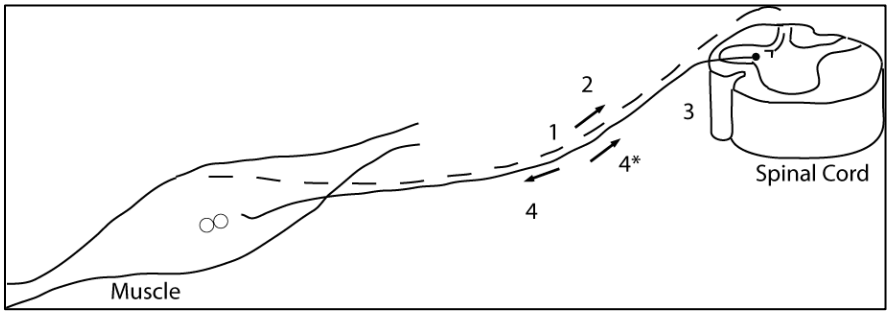


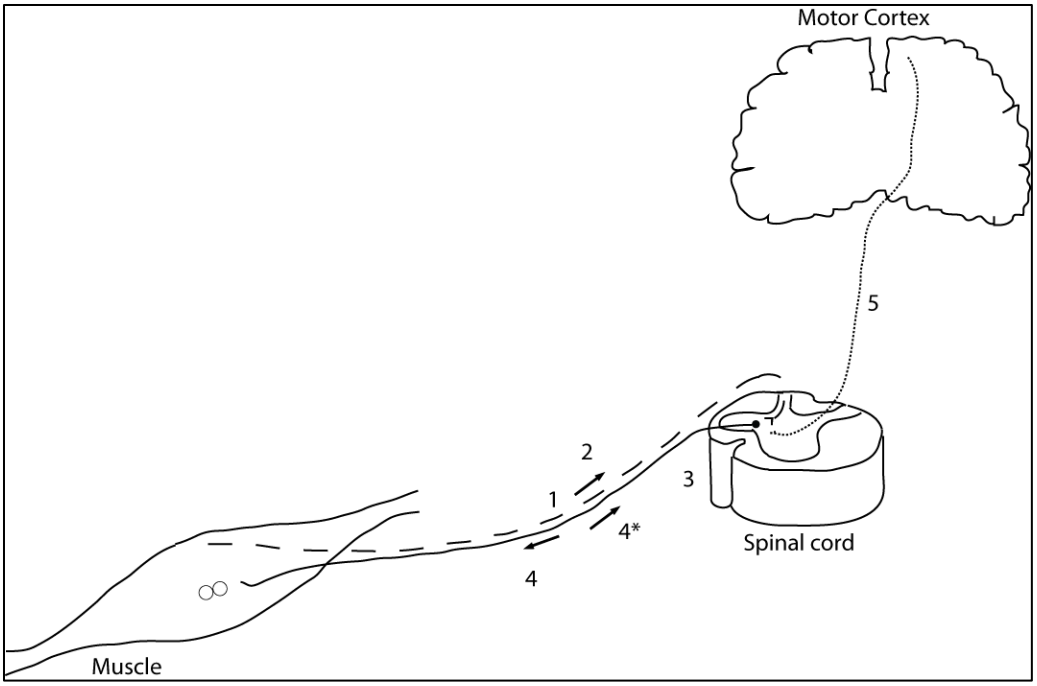
Figure 3. H-reflex and M-wave pathway. The solid line represents the αMN axon and the dashed line represents the Ia afferent axon. If a low-intensity percutaneous stimulus is delivered to a mixed nerve (1), Ia afferents are selectively recruited and action potentials within these fibers travel toward the spinal cord (2). Ia action potentials transmitted to the spinal cord synapse with interneurons and send action potentials toward the muscle belly via the αMN (3). These action potentials are recorded in the muscle belly as an H-reflex via EMG electrodes (open circles). As the stimulus intensity is increased, αMN are recruited at the point of stimulation and action potentials travel to the muscle belly where they are recorded via EMG electrodes as an M-wave(4). Action potentials generated in the αMN at the point of stimulation also travel antidromically toward the spinal cord (4*), colliding with the action potentials generated within the Ia fibers, thereby cancelling out the H-reflex signal. Modified from Aagaard, P., Simonsen, E. B., Andersen, J. L., Magnusson, P., & Dyhre-Poulsen, P. (2002). Neural adaptation to resistance training: changes in evoked V-wave and H-reflex responses. *J Appl Physiol, 92*, 2309-2318.

assessment as an H-reflex. As the intensity of the percutaneous stimulus utilized to generate an H-reflex is increased, it continues to stimulate the Ia afferents while also resulting in direct stimulation of the αMN. This direct αMN stimulation produces an M-wave that can be recorded via EMG assessment.

The peak-to-peak maximum H-reflex is representative of the portion of the MN pool capable of being excited[100], while the peak-to-peak M-wave is an estimate of maximal muscle activation.[245] The intra- and inter-session reliability have been demonstrated to be high[246] for these measurements, though they have several important limitations. The H-reflex is not recordable in all individuals and the amplitude of both measurements is sensitive to body position. It has been suggested that individuals maintain a supine body position, with the knee flexed to 15°, the arms resting at the sides with the palms facing up, and the head and eyes facing directly forward to minimize the effects of variable body position on the measurement.[247] Additionally, the H-reflex measurement is only an estimate of MN excitability and may be influenced by other factors (e.g.: presynaptic Ia inhibition, Renshaw cell activity, and Ib inhibitory interneurons) that cannot be accounted for with this measurement.[248, 249] The influence of these other factors on H-reflex amplitude may be minimized when the measurement is elicited with the muscle at rest.[248] The H-reflex technique also does not account for the influence of muscle spindle activity on MN excitability.[250] During voluntary movement, muscle spindles modulate muscle activity and, therefore, MN output.

V-wave

The V-wave is a physiological variant of the H-reflex that has been shown to reflect the level of descending, efferent, neural drive to a muscle from spinal and/or supraspinal αMNs during a voluntary muscle contraction.[101] During M-wave elicitation, action potentials produced at the point of stimulation along the αMN travel both orthodromically toward the muscle and antidromically to the spinal cord (Figure 4). Further, Ia afferents continue to be generated, producing H-reflex signals. As the antidromic potentials approach the spinal cord, they collide with the H-reflex signal traveling toward the muscle, cancelling out the H-reflex. When the percutaneous stimulus



is superimposed on an MVIC, however, the antidromic action potentials that would normally prevent the H-reflex signal from passing to the muscle are, themselves, cancelled out by the descending, orthodromic action potentials generated as a result of voluntary muscle contraction. This allows the H-reflex signal to once again pass through to the muscle[101], where the signal is then recorded as a V-wave.

Figure 4. V-wave pathway. The solid line represents the αMN axon, the dashed line represents the Ia afferent axon, and the dotted line represents the efferent axon. When a supramaximal, percutaneous stimulus is applied over a mixed nerve (1), an efferent motor response is generated due to activation of MN via descending pathways from the motor cortex (5). The efferent impulses collide with the antidromic action potentials (4*), allowing the Ia afferent signal to pass through the spinal cord to the muscle (2→3). This signal is recorded in the muscle belly via EMG electrodes (open circles) as an H-reflex. Modified from Aagaard, P., Simonsen, E. B., Andersen, J. L., Magnusson, P., & Dyhre-Poulsen, P. (2002). Neural adaptation to resistance training: changes in evoked V-wave and H-reflex responses. *J Appl Physiol, 92*, 2309-2318.

NEUROMUSCULAR FATIGUE AND CENTRAL ACTIVATION

Neuromuscular fatigue is a decrease in force-generating capability induced by exercise.[76] It is both a peripheral and a central process. Peripheral fatigue encompasses any structure distal to the neuromuscular junction[251] and is often regarded as fatigue within the muscle, itself, due to altered metabolics or muscle damage.[252] Central fatigue, which will be detailed below, occurs when the activity within spinal and supraspinal structures responsible for neural drive to a muscle is reduced.[76, 251]

Central Fatigue

Spinal Contributions

During persistent muscle contraction, input from Ia, Ib, III, and IV afferents is altered. During a sustained MVIC, Ia firing rates decline with time, ultimately reducing input to MN and decreasing force generation.[221] The role of Ib afferents remains speculative and it is believed that either decreased sensitization of Ib afferents or attenuation of their inhibitory effects occurs during fatiguing exercise. This belief stems from the fact that MN firing continues during fatigue, though at a reduced capacity. If Ib-induced non-reciprocal inhibition occurred during MVIC, MN firing in the muscle generating the contraction would not occur. The role of groups III and IV (nociceptive) afferents is unclear, though it is believed they respond to the metabolic changes that occur locally with fatigue[253, 254], which leads to an inhibitory effect on Ia afferent activity, altering αMN recruitment and decreasing voluntary force production.[221, 255]

Supraspinal Contributions

The supraspinal contribution to central fatigue comes from the motor cortex.[251] Taylor and colleagues[256] have proposed two possible mechanisms by which supraspinal fatigue may operate. First, motor cortex output decreases, possibly due to changes in corticospinal neurons or input to these neurons.[256] While changes in corticospinal neuronal activity have been demonstrated during fatigue, fatigue may also occur in the absence of these changes.[257, 258] Thus, while corticospinal neuron activity may contribute to supraspinal fatigue, it cannot fully explain it. Second, motor cortex output remains constant, but becomes less effective and MNs become less responsive to descending input, a response consistent with MN inhibition.[256]

Contributions of Fatigue to Anterior Cruciate Ligament Injury

Studying the cause of non-contact ACL injury has lead to a number of risk factors, ranging from anatomic[259] to hormonal[260, 261] and environmental.[262-264] Also emerging out of these studies have been several important biomechanical risk factors, namely what both Ireland[265] and Hewett *et al.*[266] have described as increased hip internal rotation and

adduction combined with knee extension, abduction, and external rotation postures and moments.

Neuromuscular fatigue, an essentially inevitable occurrence during athletic activity, also purportedly increases ACL injury risk.[267, 268] Lower extremity neuromuscular fatigue, specifically, has been shown to alter neuromuscular control strategy and generate lower limb postures and moments implicated within the non-contact ACL injury mechanism.[77, 78, 80, 269]

Following gross lower extremity fatigue, several alterations consistent with the aforementioned biomechanical risk factors have been reported. Specifically, fatigue leads to increases in hip internal rotation[80] and knee extension[77], abduction[77, 80, 269], and internal rotation[77, 80, 269] angles. Fatigue has also been shown to increase knee extension[78] and abduction[78, 269] moments as well as anterior tibial shear.[77, 78]

Specific adaptations linked with non-contact ACL injury risk have also been demonstrated following isolated muscle fatigue. Nyland and colleagues[72] have demonstrated that isolated quadriceps fatigue increased knee extension angle and moment.

Relationship Between Arthrogenic Muscle Inhibition and Fatigue

As discussed previously, both AMI and neuromuscular fatigue are central and peripheral processes, which ultimately lead to a decrease in voluntary muscle activation. Previous research has demonstrated that volitional control is reduced both with muscle weakness and fatigue.[10, 257]Thus, it seems the relationship between AMI and fatigue is additive, wherein fatigue would further impair central drive to the musculature.

Neuromuscular fatigue impairs not only the affected limb, but also alters the neuromuscular control strategy of the contralateral limb in unilateral fatigue.[270] The proposed mechanisms underlying this cross-over effect of fatigue may help to explain the relationship between fatigue and AMI. Group III and IV afferents are purportedly sensitive to the metabolic changes that occur locally with fatigue.[253, 254] The response of group III and IV afferents to these metabolic products leads to an inhibitory effect on Ia

afferent activity, which alters αMN recruitment and decreases voluntary force production.[221, 255]

Studies examining AMI have found that preferential atrophy may occur[36, 189], which may further explain the relationship between muscle fatigue and inhibition, though evidence regarding which phenotype is affected is conflicting. Stokes and Young[189], for example, reported that atrophy of either Type I or Type II fibers may occur. These and other authors[36], however, have also reported that an increase in type II fiber frequency occurs with AMI. Given that Type II fibers are non-fatigue resistant, this could increase muscle fatigability. Along these lines, Young[36] reported selective atrophy of Type I fibers in ACL deficient people, a population where AMI is prevalent. This selective Type I atrophy could also increase muscle fatigability. Consistent with these findings are those examining muscle phenotype and selective atrophy following ACL rupture. Both selective Type I[44, 50] and Type II[44, 51] atrophy have been reported. More research is needed into this area to determine the role of muscle phenotype changes after ACL injury and with AMI; however, it is important to consider that muscle phenotype may play a crucial role in muscle fatigability and, thus, warrants consideration as a link between fatigue and AMI.

Clinical speculation suggests that neuromuscular fatigue may be implicated in re-injury following ACLr. As discussed previously, neuromuscular fatigue may increase non-contact ACL injury risk by altering the biomechanical profile of the fatigued individual. Considering that AMI is prevalent in those returning to activity following ACLr, and that fatigue and AMI may be additive processes which are each capable of altering biomechanics, it seems that the relationship between fatigue and AMI ought to be studied. If these two processes, fatigue and AMI, are additive and the relationship can be elucidated, then better rehabilitation strategies can be developed to counter these processes and decrease the risk of re-rupture stemming from the combination of AMI and fatigue.

CONCLUSION

Knowledge regarding the neuromuscular consequences of ACL injury is limited. Elucidating the magnitude of weakness in the muscles proximal and distal to the knee, the mechanisms underlying persistent quadriceps weakness, and how fatigue impacts CAF and what the combined effects of fatigue and central activation are on neuromechanics will aid researchers and clinicians in understanding ACL injury and improving rehabilitation strategies.

APPENDIX A

IRB CONSENT FORM

UNIVERSITY OF MICHIGAN
CONSENT TO BE PART OF A RESEARCH STUDY

Information About This form

You, or your child, may be eligible to take part in a research study. This form gives you important information about the study. It describes the purpose of the study, and the risks and possible benefits of participating in the study. Parents or legal guardians who are giving permission for a child, please note: in the sections that follow the word 'you' refers to 'your child.'

Please take time to review this information carefully. After you have finished, you should talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others (for example, your friends, family, or other doctors) about your participation in this study. If you decide to take part in the study, you will be asked to sign this form. *Before you sign this form, be sure you understand what the study is about, including the risks and possible benefits to you.*

1. General Information About This Study AND the RESEARCHERS

1.1 Study title:

Neuromechanical Dysfunction Associated with ACL Injury

1.2 Company or agency sponsoring the study:

This study is funded by The University of Michigan Bone and Joint Injury Prevention & Rehabilitation Center. Additional funding is provided by the National Institutes of Health.

1.3 Names, degrees, and affiliations of the researchers conducting the study:

Riann Palmieri-Smith, PhD, ATC – University of Michigan, Division of Kinesiology
Kathryn Antle, MS – University of Michigan, Department of Orthopedics
Kimberly Becker, PT – University of Michigan, MedSport

Catherine Brandon, MD – University of Michigan, Department of Radiology
Scott McLean, PhD - University of Michigan, Division of Kinesiology
Daryl Montie, DPT, CSCS, MA – University of Michigan, MedSport
Abbey Thomas, MEd – University of Michigan, Division of Kinesiology
Ganapriya Venkatasubramanian – University of Michigan, Division of Kinesiology
Edward Wojtys, MD – University of Michigan, Department of Orthopedics
Jennifer Kreinbrink, BS – University of Michigan, Department of Orthopedics

2. PURPOSE OF THis STUDY

2.1 Study purpose:

Thigh muscle weakness often accompanies anterior cruciate ligament (ACL) injury. This study is designed to examine how thigh muscle weakness that accompanies ACL injury affects lower body positions and forces. We will also examine whether electrical stimulation therapy can improve thigh muscle strength.

3. Information About STUDY participants (SUBJECTS)

Taking part in this study is completely **voluntary**. You do not have to participate if you don't want to. You may also leave the study at any time. If you leave the study before it is finished, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled.

3.1 Who can take part in this study?

259 subjects between the ages of 14-35 will be recruited to participate. All study participants cannot have any previous history of serious knee injury (other than the current ACL tear) or surgery and cannot have a cardiac demand-type pacemaker. Furthermore, volunteers who are females and are pregnant are not eligible to participate. In addition to the criteria above, volunteers with ACL injury also cannot have any injury to any other knee ligament besides the ACL rupture and healthy volunteers cannot have any current knee pain and/or have had any lower body injury in the previous 6 months. It is very important that you accurately report your medical history.

3.2 How many people (subjects) are expected to take part in this study?

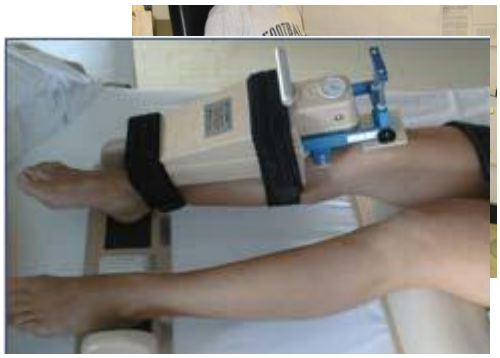
We will enroll 214 participants in this part of the study and 45 participants in another part of the study

4. information about study participation

4.1 What will happen to me in this study?

If you agree to participate in this study, you will be asked to report to the MedSport Clinic located in Domino Farms for testing. You will be asked to participate in a minimum of two testing sessions and a maximum of three testing sessions. If you are a volunteer that has torn your ACL, you will be asked to report for testing prior to your surgery, ~6 months following your surgery, and in some cases ~8 months to 1 year following your surgery. If you are a healthy, uninjured volunteer you will be asked to report for up to 3 sessions approximately 6 months apart. We will schedule these session on days/times that are convenient for you.

At the first testing session, your muscle strength, the looseness of your knee joints, and a measure of the swelling in your knees will be taken. Additionally, you will be asked to fill out a questionnaire that asks questions about your pain level and functional abilities.



Picture 2. Knee Looseness Testing

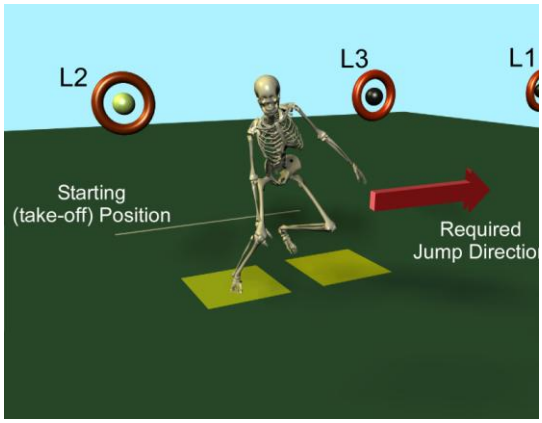
Measures of Muscle Strength: Two large pads will be placed on the front of both of your thighs and secured with bandages. Once all of the pads are attached to your leg, you will be positioned in a device that measures muscle strength. You will be asked to sit in a chair attached to the device with your knees bent (Picture 1). Once you are positioned in the device, you will be asked to kick your leg out against a pad as hard as you can. As soon as you feel comfortable with the kick, the researchers will apply a group of shocks to the skin of your thigh while you are resting. We will deliver the shocks thru the pads we attached earlier. In order to help you get use to the shocks, we will start giving them to you at a low level and will then increase the level in small amounts. We eventually need the level of the shocks to reach 150 volts each (if these shock were delivered separately they would feel like a shock of static electricity like when you walk across a carpet and touch a door knob, except a shock of static electricity can reach up to 1,000 volts) The series of 10 shocks will last less than 1 second and are delivered very close together, so you shouldn't be able to feel individual shocks. The group of shocks will allow your muscle to contract even when you are resting. These shocks may be slightly uncomfortable, the discomfort you experience in the muscle is normal. If at anytime during the procedures you feel as if the shocks are too strong and you don't want to continue, please notify the researchers immediately. Once you are comfortable with the shocks, you will again be asked to kick out as hard as

you can. Once the researchers see that you are contracting as hard as you can by watching the computer screen (usually in about 2 seconds), they will deliver the series of shocks on top of your muscle. This technique, where we deliver shocks on top of a muscle contraction, will be repeated 3 times for each leg.

Measure of looseness of your knee joint: In order to see how loose your knees are, we will place each knee into a device, one at a time. You will be asked to lay on your back and we will place a pad under both of your legs. The device will be secured to your leg, at the ankle and calf, by Velcro straps (see picture 2). Once your knee is in the device, the investigators will pull a handle on the device, which causes the shin bone to move forward. The investigators will pull on the handle 3 times for each knee.

Measure of knee swelling: We will assess how much fluid is in your knee by wrapping a cloth measuring tape around your kneecap. We will do this on both knees.

At the second and third (if applicable) testing sessions, you will repeat all of the tests done in the first session and will also be asked to complete several jump landings before and after being fatigued and 10 forward hops.



Picture 3. Jump Landing Task.

Jump Landings: The jump landing tasks will include both double and single leg take-offs. Upon landing, you will be required to quickly jump to the left, right or straight up. You will be informed in which direction to jump by a light (Picture 3). The first light (L1) is fixed to the left and in front of a force plate (similar to a scale that measures forces), If this light comes on, you will land on the left foot only and then jump to the right. A second light (L2) will be similarly positioned to the right of the force plates, and will require you to land on the right foot only and jump to the left. A third light (L3) will be placed between the two force plates. When this light comes on you will be required to land on both feet and jump straight up.

Picture 4. Forward Hop

The researchers will demonstrate the jump landings before you are asked to do it.

Following the initial jump landing trials, you will again be required to perform the above tasks, only this time while being exposed to a general fatigue protocol. Specifically, you will be asked to perform continuous sets of three single or double leg squats between the jump trials. You will alternate between squats and jumps until fatigue is reached, being defined as the point when you can no longer perform three squats in succession. You will be able to place the non-fatigued leg on a platform for stability during the single leg squats. From our previous work, we expect that you will be able to perform approximately 50 jump trials (150 squats) prior to maximum fatigue.

During all the of the jump landing you will have 28 reflective markers attached to your body, which will enable us to measure the movements of your lower body. The markers will be secured directly to the skin using adhesive tape and will not cause you any discomfort. As some markers are required to be attached to the thigh and hips, you will be asked to wear bicycle shorts and sports brassier during testing.

Forward Hops: The forward hop requires you to jump and land on a single leg. We will ask you to complete the hop for both legs. Before you hop, you will be asked to stand on the leg we are testing (picture 4), with your hands on your hips. When you are ready, you will be asked to jump forward as far as you can and stick the landing, if possible. You will be asked to hop 5 times for each leg.

Measures of brain and spinal cord output: For these tests we will obtain measures of brain and spinal cord function known as the H-reflex, M-wave, and, V-wave. To obtain the H-reflex and M-wave one small area, on both legs, will be shaved, rubbed gently with sand paper, and cleaned with isopropyl alcohol. Four round stickers (electrodes) will be applied to this area and an additional electrode will be applied to the bone on the inside of your ankle. These electrodes will be outlined with a black marker to ensure they are in the same place throughout the entire testing session. Next, you will be given a small round disc to place near your groin. A diagram will be provided to demonstrate the correct placement. Additionally, we will ask you to place a large rubber electrode on your buttocks. Several measurements will be taken while you are lying down. These measurements include a 1-millisecond shock. The intensity of this shock will vary depending on which response is being elicited. Lower intensities (50-100V) will be needed to obtain an H-reflex where higher intensities (100-200V) are needed to elicit an

M-wave. The shocks in this study feel similar to a shock of static electricity, like when you are walking across a carpet and then touch a door knob, except the voltage is much lower (A shock of static electricity can provide up to thousands of volts of electricity). To obtain the V-wave, the same technique utilized to gather the H-reflex and M-wave will be used, except that you will be asked to contract your quadriceps, by kicking out your leg, as hard as you can against resistance. The shocks will be applied atop of the quadriceps contraction.

4.2 How much of my time will be needed to take part in this study?

The first testing session will last approximately 1.5 hours, while the second and third testing session will take approximately 2.5 hours.

4.3 When will my participation in the study be over?

Most subjects will complete their part of the study within 1 year. The entire study is expected to last about 5 years.

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5. information about RISKS and benefits

5.1 What risks will I face by taking part in the study? What will the researchers do to protect me against these risks?

The known or expected risks are:

- You may experience some discomfort when the electrical shocks are applied to you skin. In order to make the shocks as comfortable as possible, large pads will be used to apply the shocks.
- You may experience muscle soreness after performing repeated muscle contractions. You will be offered ice bags following the experiment to minimize the chances of muscle soreness.
- You may suffer a joint or muscle injury during the study when performing the landing tasks. Dr. Palmieri-Smith, the lead researcher on this study, is a certified athletic trainer equipped with the knowledge to evaluate and manage musculoskeletal injuries. Thus, if an injury were to occur Dr. Palmieri-Smith would manage the condition and refer you to a physician for further evaluation.
- You may suffer a muscle or tendon injury when performing the repeated muscle contractions. Dr. Palmieri-Smith, the lead researcher on this study, is a certified athletic trainer equipped with the knowledge to evaluate and manage

musculoskeletal injuries. Thus, if an injury were to occur, Dr. Palmieri-Smith would manage the condition and refer you to a physician for further evaluation.

- There is also the potential risk of loss of confidentiality through participation in this study.
  Every effort will be made to keep your information confidential, however, this cannot be guaranteed. Some of the questions we will ask you as part of this study may make you feel uncomfortable. You may refuse to answer any of the questions and you may take a break at any time during the study. You may stop your participation in this study at any time.

- As with any research study, there may be additional risks that are unknown or unexpected.

5.2 What happens if I get hurt, become sick, or have other problems as a result of this research?

The researchers have taken steps to minimize the risks of this study. Even so, you may still have problems or side effects, even when the researchers are careful to avoid them. Please tell the researchers listed in Section 10 about any injuries, side effects, or other problems that you have during this study. You should also tell your regular doctors**.**

5.3 If I take part in this study, can I also participate in other studies?

Being in more than one research study at the same time, or even at different times, may increase the risks to you. It may also affect the results of the studies. You should not take part in more than one study without approval from the researchers involved in each study.

5.4 How could I benefit if I take part in this study? How could others benefit?

You may not receive any personal benefits from being in this study. Your participation will be of benefit to medical science.

5.5 Will the researchers tell me if they learn of new information that could change my willingness to stay in this study?

Yes, the researchers will tell you if they learn of important new information that may change your willingness to stay in this study. If new information is provided to you after

you have joined the study, it is possible that you may be asked to sign a new consent form that includes the new information.

6. Other options

6.1 If I decide not to take part in this study, what other options do I have?

Since your participation is voluntary, you may decide not to take part in the study at any time without penalty. Your only other option is not to participate.

7. ENDING THE STUDY

7.1 If I want to stop participating in the study, what should I do?

You are free to leave the study at any time. If you leave the study before it is finished, there will be no penalty to you. You will not lose any benefits to which you may otherwise be entitled. If you choose to tell the researchers why you are leaving the study, your reasons for leaving may be kept as part of the study record. If you decide to leave the study before it is finished, please tell one of the persons listed in Section 10 "Contact Information" (below).

7.2 Could there be any harm to me if I decide to leave the study before it is finished?

No harm will occur if you decide to leave the study early.

7.3 Could the researchers take me out of the study even if I want to continue to participate?

Yes. There are many reasons why the researchers may need to end your participation in the study. Some examples are:

- ✓ The researcher believes that it is not in your best interest to stay in the study.
- ✓ You become ineligible to participate.
- ✓ Your condition changes and you need treatment that is not allowed while you are taking part in the study.
- ✓ You do not follow instructions from the researchers.

- ✓ The study is suspended or canceled.

8. Financial Information

8.1 Who will pay for the costs of the study? Will I or my health plan be billed for any costs of the study?

The study will pay for research-related items or services that are provided only because you are in the study. If you are not sure what these are, see Section 4.1 above or ask the researchers for a list. If you get a bill you think is wrong, call the researchers' number listed in section 10.1.

You or your health plan will pay for all the things you would have paid for even if you were not in the study, like:

- Health care given during the study as part of your regular care
- Items or services needed to give you study drugs or devices
- Monitoring for side effects or other problems
- Treatment of complications
- Deductibles or co-pays for these items or services.

If you do not have a health plan, or if you think your health plan may not cover these costs during the study, please talk to the researchers listed in Section 10 below or call your health plan's **medical reviewer.**

By signing this form, you do not give up your right to seek payment if you are harmed as a result of being in this study.

8.2 Will I be paid or given anything for taking part in this study?

You will receive $25 for each session in which you participate. You will receive this payment in the mail approximately 4 weeks after each testing session.

8.3 Who could profit or financially benefit from the study results?

No person or organization has a financial interest in the outcome of the study.

9. confidentiality of subject records and authorization to release your protected health information

The information below describes how your privacy and the confidentiality of your research records will be protected in this study.

9.1 How will the researchers protect my privacy?

We will put the information collected about you during the study into a research record. This research record will not show your name, but will have codes entered in it, that will allow the information to be linked to you. However, we will keep your research record confidential, to the extent provided by federal, state, and local law. We will not allow anyone to see your record, other than people who have a right to see it. You will not be identified in any reports from this study.

9.2 What information about me could be seen by the researchers or by other people? Why? Who might see it?

Signing this form gives the researchers your permission to obtain, use, and share information about you for this study, and is required in order for you to take part in the study. Information about you may be obtained from any hospital, doctor, and other health care provider involved in your care, including:

- Hospital/doctor's office records, including test results (X-rays, blood tests, urine tests, etc.)
- Mental health care records (except psychotherapy notes not kept with your medical records)
- Alcohol/substance abuse treatment records
- Your AIDS/HIV status
- All records relating to your ACL injury, the treatment you have received, and your response to the treatment
- Billing information

There are many reasons why information about you may be used or seen by the researchers or others during or after this study. Examples include:

- The researchers may need the information to make sure you can take part in the study.

- The researchers may need the information to check your test results or look for side effects.

- University, Food and Drug Administration (FDA), and/or other government officials may need the information to make sure that the study is done in a safe and proper manner.

- Study sponsors or funders, or safety monitors or committees, may need the information to:
    - Make sure the study is done safely and properly
    - Learn more about side effects
    - Analyze the results of the study

- Insurance companies or other organizations may need the information in order to pay your medical bills or other costs of your participation in the study.

- The researchers may need to use the information to create a databank of information about your condition or its treatment.

- Information about your study participation may be included in your regular UMHS medical record.

- If you receive any payments for taking part in this study, the University of Michigan accounting department may need your name, address, social security number, payment amount, and related information for tax reporting purposes.

- Federal or State law may require the study team to give information to government agencies. For example, to prevent harm to you or others, or for public health reasons.

The results of this study may be published or presented at a scientific meeting. If your name and pictures will be used in any publications or presentation, the researchers will ask for your separate written permission.

9.3 What happens to information about me after the study is over or if I cancel my permission?

As a rule, the researchers will not continue to use or disclose information about you, but will keep it secure until it is destroyed. Sometimes, it may be necessary for information about you to continue to be used or disclosed, even after you have canceled your permission or the study is over. Examples of reasons for this include:

- To avoid losing study results that have already included your information
- To provide limited information for research, education, or other activities (This information would not include your name, social security number, or anything else that could let others know who you are.)
- To help University and government officials make sure that the study was conducted properly

As long as your information is kept within the University of Michigan Health System, it is protected by the Health System's privacy policies. For more information about these policies, ask for a copy of the University of Michigan Notice of Privacy Practices. This information is also available on the web at http://www.med.umich.edu/hipaa/npp.htm. Note that once your information has been shared with others as described under Question 9.2, it may no longer be protected by the privacy regulations of the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA).

9.4 When does my permission expire?

Your permission expires at the end of the study, unless you cancel it sooner. You may cancel your permission at any time by writing to the researchers listed in Section 10 "Contact Information" (below).

10. Contact Information

10.1 Who can I contact about this study?

Please contact the researchers listed below to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments
- Talk about study-related costs to you or your health plan
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished
- Express a concern about the study

Principal Investigator: Riann Palmieri-Smith, Ph.D., ATC

Mailing Address: 4745G CCRB, School of Kinesiology, University of Michigan, 401 Washtenaw Avenue, Ann Arbor, MI, 48109-2214

Telephone: 734-615-3154

You may also express a concern about a study by contacting the Institutional Review Board listed below, or by calling the University of Michigan Compliance Help Line at 1-888-296-2481.

University of Michigan Medical School Institutional Review Board (IRBMED)

Argus I

517 W. William

Ann Arbor, MI 48103-4943

Telephone: 734-763-4768

Fax: 734-615-1622

e-mail: irbmed@umich.edu

If you are concerned about a possible violation of your privacy, contact the University of Michigan Health System Privacy Officer at 1-888-296-2481.

When you call or write about a concern, please provide as much information as possible, including the name of the researcher, the IRBMED number (at the top of this form), and details about the problem. This will help University officials to look into your concern. When reporting a concern, you do not have to give your name unless you want to.

11. record of Information provided

11.1 What documents will be given to me?

Your signature in the next section means that you have received copies of all of the following documents:

- This "Consent to be Part of a Research Study" document. (*Note: In addition to the copy you receive, copies of this document will be stored in a separate confidential research file and may be entered into your regular University of Michigan medical record.)*

12. SIGNATURES

Research Subject:

I understand the information printed on this form. I have discussed this study, its risks and potential benefits, and my other choices with _____. My questions so far have been answered. I understand that if I have more questions or concerns about the study or my participation as a research subject, I may contact one of the people listed in Section 10 (above). I understand that I will receive a copy of this form at the time I sign it and later upon request. I understand that if my ability to consent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

Signature of Subject: _____ Date: _____

Name (Print legal name): _____

Patient ID:_____ Date of Birth: _____

Legal Representative (if applicable):

Signature of Person #1 Legally Authorized to Give Consent_____ Date: _____

Name (Print legal name): _____ Phone: _____

Address: _____

Check Relationship to Subject:

□Parent □Spouse □Child □Sibling □Legal Guardian □Other: _____

Signature of Person #2 Legally Authorized to Give Consent_____ Date: _____

Name (Print legal name): _____ Phone: _____

Address: _____

Check Relationship to Subject:

□Parent □Spouse □Child □Sibling □Legal Guardian □Other: _____

If this consent is for a child who is a ward of the state (for example a foster child), please tell the study team immediately. The researchers may need to contact the IRBMED.

Reason subject is unable to sign for self:

_____

Principal Investigator (or Designee):

I have given this research subject (or his/her legally authorized representative, if applicable) information about this study that I believe is accurate and complete. The subject has indicated that he or she understands the nature of the study and the risks and benefits of participating.

Name: _____ Title: _____

Signature: _____ Date of Signature: _____

APPENDIX B

DATA COLLECTION MATERIALS

COLLECTION FORMS

ACL NMES Study
Thigh and Calf Circumference/Effusion Data Collection Sheet

Participant ID #:_____ Testing Date: _____
Testing Session:_____

		Right (cm)	Left (cm)
Circumference	6 cm		
	12 cm		
	18 cm		
Effusion	Mid-patella		
	1 cm		

		Right (cm)	Left (cm)
Proximal	5 cm		
	10 cm		
	Maximum		
Distal	5 cm		
	10 cm		

Figure B.1. Circumference and effusion data collection form for aims 1-3. Testing sessions were pre-operative and/or post-operatively, as appropriate. Knee effusion and thigh circumference were recorded in the top table, calf girth in the bottom table.

ACL NMES Study
Quadriceps Activation Data Collection Sheet

Study Participant #:		Date:
Age:	Height:	Weight:

Test Session: _____

		Right		Left	
		Vol.	Burst	Vol.	Burst
Torque	1				
	2				
	3				

Test Session: _____

		Right		Left	
		Vol.	Burst	Vol.	Burst
Torque	1				
	2				
	3				

Figure B.2. Quadriceps central activation failure data collection form. Test session was post-operative (Chapter 3) or pre- or post-fatigue (Chapter 4), as appropriate.

ACL NMES Trial
Fatigue Collection Sheet

Participant #:		Date:	
Age:	Ht:		Wt:

Trial #	Side		Good/Bad	
1	R	L	Y	N
2	R	L	Y	N
3	R	L	Y	N
4	R	L	Y	N
5	R	L	Y	N
6	R	L	Y	N
7	R	L	Y	N
8	R	L	Y	N
9	R	L	Y	N
10	R	L	Y	N
11	R	L	Y	N
12	R	L	Y	N
13	R	L	Y	N
14	R	L	Y	N
15	R	L	Y	N
16	R	L	Y	N
17	R	L	Y	N
18	R	L	Y	N
19	R	L	Y	N
20	R	L	Y	N
21	R	L	Y	N
22	R	L	Y	N
23	R	L	Y	N
24	R	L	Y	N
25	R	L	Y	N
26	R	L	Y	N
27	R	L	Y	N
28	R	L	Y	N
29	R	L	Y	N
30	R	L	Y	N
31	R	L	Y	N
32	R	L	Y	N
33	R	L	Y	N
34	R	L	Y	N
35	R	L	Y	N
36	R	L	Y	N
37	R	L	Y	N
38	R	L	Y	N
39	R	L	Y	N
40	R	L	Y	N
41	R	L	Y	N
42	R	L	Y	N
43	R	L	Y	N
n^{th} trial	R	L	Y	N

Figure B.3. Data collection sheet for Chapter4 dynamic landing trials. R denotes right limb, L denotes left limb. Y was circled if the trial was good, N if the trial was bad.

SUBJECT SELF-REPORT MEASURES

2000 IKDC SUBJECTIVE KNEE EVALUATION FORM

Your Full Name_____

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

SYMPTOMS*:

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

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

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

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

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

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

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

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

   ❑Not at all
   ❑Mildly
   ❑Moderately
   ❑Very
   ❑Extremely

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

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

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

   ❑Yes ❑No

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

Page 2 – 2000 IKDC SUBJECTIVE KNEE EVALUATION FORM

SPORTS ACTIVITIES:

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

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

9. How does your knee affect your ability to:

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

FUNCTION:

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

FUNCTION PRIOR TO YOUR KNEE INJURY:

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

CURRENT FUNCTION OF YOUR KNEE:

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

Figure B.4. International Knee Documentation Committee (IKDC) Form.

Participant ID #:_____ Date:_____
Testing Session:_____

TEGNER ACTIVITY LEVEL SCALE

Please indicate in the spaces below the HIGHEST level of activity that you participated in BEFORE YOUR INJURY and the highest level you are able to participate in CURRENTLY.

BEFORE INJURY: Level_____ CURRENT: Level_____

Level 10	**Competitive sports- soccer, football, rugby (national elite)**
Level 9	**Competitive sports- soccer, football, rugby (lower divisions), ice hockey, wrestling, gymnastics, basketball**
Level 8	**Competitive sports- racquetball or bandy, squash or badminton, track and field athletics (jumping, etc.), down-hill skiing**
Level 7	**Competitive sports- tennis, running, motorcars speedway, handball** **Recreational sports- soccer, football, rugby, bandy, ice hockey, basketball, squash, racquetball, running**
Level 6	**Recreational sports- tennis and badminton, handball, racquetball, down-hill skiing, jogging at least 5 times per week**
Level 5	**Work- heavy labor (construction, etc.)** **Competitive sports- cycling, cross-country skiing,** **Recreational sports- jogging on uneven ground at least twice weekly**
Level 4	**Work- moderately heavy labor (e.g. truck driving, etc.)**
Level 3	**Work- light labor (nursing, etc.)**
Level 2	**Work- light labor** **Walking on uneven ground possible, but impossible to back pack or hike**
Level 1	**Work- sedentary (secretarial, etc.)**
Level 0	**Sick leave or disability pension because of knee problems**

Y Tegner and J Lysolm. *Rating Systems in the Evaluation of Knee Ligament Injuries.* Clinical Orthopedics and Related Research. Vol. 198: 43-49, 1985.

Figure B.5. Tegner Activity Level Scale.[271]

REHABILITATON PROTOCOL

Appendix 2

PI: Palmieri-Smith, Riann, Marin

MedSport

Name _____

Reg. # _____

Date _____

ACL AUTOGRAFT
POST-OPERATIVE PROTOCOL

This protocol has been designed as a guideline for treatment progression following anterior cruciate ligament reconstructive surgery. Specific time frames and progressions are outlined; however, treatment progressions must be individually adapted according to patient response to treatment, condition of cartilage and chondral surfaces, and recommendations by the physician.

Please contact MedSport Physical Therapy with any questions Toll Free (877)877-9333, opt. 2

PRE-OPERATIVE VISIT

1. Physical exam/surgical guidelines
2. KT 2000
3. Biodex (no effusion)
4. Review of pre-op instructions (per home program handout)

POST-OPERATIVE MD VISIT SCHEDULE (patient to be seen at MedSport)

1st post-op	discharge from hospital
2nd post-op	either 1st or 2nd week
3rd visit	4-6 weeks
4th visit	14-16 weeks
5th visit	20-24 weeks
6th visit	30-40 weeks

POST-OPERATIVE PHASE #1

INITIAL FOLLOW-UP → 1 WEEK POST-OP

GOALS

1. Full passive knee extension
2. Improve knee flexion as tolerated
3. Proper gait (heel-toe), 10% → 25% WB with crutches
4. Compliance with home program
5. Immediate identification of problem areas: pain and/or swelling, lack of extension

TREATMENT - WEEK #1

1. 1st post-op visit
   - Dressing change/wound check/DVT
   - AP & lateral x-rays
2. Evaluate ROM for extension and flexion; perform the following exercises:
   - Heel slides
   - AAROM 90-40°, PROM 40-0°

   * **Must maintain full extension passively**
3. Patellar mobilizations (all directions)
4. Flexibility exercises: hamstring and calf
5. Progressive resistive exercises (increase quad control)
   - Quad sets, with or without e-stim or biofeedback
   - Straight-leg raises
   - Hip abduction/adduction (dependent on meniscus/chondral surfaces)
   - Ankle pumps
6. Closed-chain exercises (10% → 25% WB)
   - Standing knee extensions with band
   - Bilateral mini squats
   - Standing calf raises
7. Modalities as indicated to control pain and swelling, and for muscle re-education
8. Review of ambulation
   - 10% → 25% WB, heel-toe gait pattern
9. Review of home program
   - Prone hang, if necessary
   - AAROM (flexion) in sitting
   - Supine, gravity-assisted extension
   - Heel slides
   - Exercises
     - Straight-leg raises
     - Hip abduction/adduction/extension (depending on meniscus/chondral surfaces)
     - Quad sets
     - Ankle pumps
     - Quadriceps muscle stimulation with portable home unit, 30 min, 3x/day
     - PWB mini squats
     - PWB calf raises
   - Patellar mobs
   - Icing & compressive wrap
   - Medications as prescribed by MD

*** Be alert for excessive swelling/drainage/fever/calf pain**

*** Keep sutures dry**

POST-OPERATIVE PHASE #2

2 → 6 WEEKS POST-OP (EARLY STRENGTHENING)

GOALS (by end of 4-6 weeks)

1. Maintain full extension
2. Knee flexion to 120°
3. Program and ambulation (FWB) progression determined by:
   - Muscle function
   - Normal gait pattern
   - Controlled swelling
   - Compliance of patient
4. Compliance with home program
   - Discontinue home stim unit when quad active
5. Immediate notification of problem areas:
   - Lack of extension/flexion
   - Chronic pain and/or swelling

TREATMENT - WEEK #2

1. Continue previous program
2. Suture removal (14 days)
3. Continue ROM exercises; add gentle biking (increase ROM)
4. Continue flexibility program
5. Continue progressive resistive exercises; add as tolerated:
   - Hip flexion/extension
   - Theraband hamstring (not for meniscus repair)
6. Continue closed-chain exercises (25% → 50% WB); add as tolerated:
   - Standing BAPS, PWB (supination only)
   - Leg press - 2-legged (25% → 50% WB)
   - Standing knee extensions with band above knee
   - Total Gym - PWB squats and/or calf raises
7. Ambulation 25% → 50% WB; monitor gait pattern
8. Continue with modalities as indicated
9. Compliance with home program
10. Compression sleeve if needed

TREATMENT - WEEK #3

1. Continue previous program
2. Continue flexibility program
3. Continue progressive resistive exercises; add as tolerated:
   - Hamstring curls (isotonic)
   - Isotonic hip abduction/adduction (dependent on meniscus/chondral surfaces)

4. Continue closed-chain exercises (50% → 75% WB); add as tolerated:
   - Leg press (50% → 75% WB)
   - Seated calf strengthening
   - StairMaster (50% → 75% WB)
5. Continue modalities as indicated
6. Ambulation 50% → 75% WB; monitor gait pattern
7. Compliance with home program

TREATMENT - WEEK #4

1. Continue previous program
2. Continue flexibility program
3. Continue progressive resistive exercises; add as tolerated:
   - Theraband quad exercise (90° → 40°)
4. Closed-chain exercises (75% → FWB); add as tolerated:
   - 2-legged leg press (75% → FWB)
   - 1-legged leg press or eccentric (2 up, 1 down) leg press, progress as tolerated
   - StairMaster (75% BW → FWB) and/or Versaclimber (may start seated)
5. Initiate proprioceptive/balance exercises; add as tolerated:
   - Single-leg balance progression
   - Wobble board
6. Continue modalities as indicated
7. Ambulation 75% → FWB; monitor gait pattern
8. Compliance with home program

TREATMENT - WEEK #5

1. Continue previous program
2. Continue flexibility program
3. Continue progressive resistive program as tolerated; no short arc quads, no isotonic or isokinetic knee extension
4. Continue closed-chain program to FWB; add as tolerated:
   - Forward step-ups
5. Continue proprioceptive/balance exercises; add as tolerated:
   - KAT/Rebounder
   - Steamboats (A/P only)
6. Continue modalities as indicated
7. Ambulation FWB; monitor gait pattern, determined by:
   - Muscle function
   - Normal gait pattern
   - Controlled effusion
   - Compliance of patient
8. Compliance with home program
9. Support brace as prescribed by physician, if necessary

TREATMENT - WEEK #6

1. KT 2000 performed at MedSport/physician evaluation
2. Continue previous program
3. Continue flexibility program
4. Continue progressive resistive exercise program as tolerated
5. Continue closed-chain exercise program, FWB as tolerated; add as tolerated:
   - Lateral/backward step-downs (progress step height & resistance as tolerated)
   - Single-leg partial squats
   - BAPS - FWB, full revolution with maximum to level 2
6. Continue proprioceptive/balance exercises; add as tolerated:
   - Clock squats
   - V tosses
   - Other plyoball/grid exercises
7. Continue modalities as indicated
8. Commence swimming program if available; avoid whip kick and flip turns

*** All progressions based on lack of pain and/or swelling; proper gait pattern**

POST-OPERATIVE PHASE #3
7 → 11 WEEKS POST-OP (EARLY FUNCTIONAL PROGRESSION)

GOALS

1. Attain full, active and passive ROM
2. Normal, full weight-bearing gait
3. Compliance with home program
4. Immediate identification of problem areas:
   - Lack of extension/flexion
   - Abnormal gait pattern
   - Pain and/or swelling

TREATMENT - WEEK #7

1. Progress previous exercise program as tolerated
2. Continue flexibility program
3. Continue closed-chain program; add as tolerated:
   - Fitter
   - Walking lunges
4. Ambulation FWB if no limp and no effusion
5. Compliance with home program

TREATMENT - WEEKS #8-11

1. Progress previous exercise program if tolerated
2. Continue flexibility program
3. Continue full isotonic program (3x/week); add eccentric hamstrings
4. Continue closed-chain program; add:
   - Slideboard (not for MCL sprain or meniscus repair)
   - Mini tramp (balance/functional strengthening)
5. Retro treadmill for gait improvement (1 mph), dependent on condition of joint surfaces
6. May begin walking program up to 2 miles a day (dependent on condition of joint surfaces)
   - Monitor gait/swelling
   - Must continue therapeutic exercise program
7. Compliance with home program; discuss feasibility of fitness club membership
8. Biomechanical evaluation

POST-OPERATIVE PHASE #4

12 → 15 WEEKS POST-OP (FUNCTIONAL PROGRESSION)

GOALS

1. Maintain full motion of the knee
2. Document strength/function/balance progression
3. Normal gait patterns for all functional activity
4. Compliance with home program
5. Immediate identification of problem areas:
   - Lack of active/passive motion
   - Abnormal gait pattern
   - Pain and/or swelling

TREATMENT - WEEKS #12-15

1. Continue full exercise program
2. Continue progressive resistive training, increasing weights as tolerated
3. Continue closed-chain program; add:
   - Floor work
   - Side-to-side shuffle
   - Rope jumping
4. Progress balance and proprioceptive program as tolerated
5. Add plyometric program if following criteria are met (and with MD approval):
   - Minimum 12 weeks S/P ACL surgery
   - Able to single-leg press body weight for set of 10 reps
   - "Normal" KT 2000 (less than 3 mm difference)
   - No subjective complaints of pain/discomfort with ADLs or quad exercises (press, step-down, etc.)
   - No objective signs of inflammation (i.e., swelling, palpable tenderness)
6. Compliance with home program

POST-OPERATIVE PHASE #5

16 → 19 WEEKS POST-OP (ADVANCED FUNCTIONAL PROGRESSION)

GOALS

1. Maintain full motion of the knee
2. Document strength/function/balance progression
3. First isokinetic strength test; goal:
   - Quads - 70% BW
   - Hamstrings - 50% BW
4. Normal gait pattern for all functional activities
5. Compliance with home program
6. Immediate identification of problem areas:
   - Lack of full, active and passive motion
   - Abnormal gait pattern
   - Pain and/or swelling

TREATMENT - WEEKS #16-19

1. KT 2000 performed at MedSport/physician evaluation
2. Isokinetic test performed at MedSport (after adequate warm-up):
   - 30° extension block
   - 1 set of 5 at 60°/sec
   - 1 set of 15 at 240°/sec
3. Possible functional (static) testing performed at MedSport:
   - Knee excursion
   - Balance - anteromedial balance reach
   - Sport cord single-leg squats
   - Sport cord side-to-side shuffle
   - Sport cord forward/backward jog
   - Single-leg press (goal - 10 reps at BW)
4. With passing score on isokinetic and functional tests, progress patient to:
   - Running program
   - Agilities - cariocas
   - Begin plyometrics (if criteria not previously met)
5. Continue full isotonic program
6. Continue full closed-chain program
7. Introduce sport-specific exercise program

POST-OPERATIVE PHASE #6

20 → 24 WEEKS POST-OP (SPORT-SPECIFIC TRAINING)

GOALS

1. Prepare patient for return to selected sports and activities
2. Document strength/function/balance progression
3. Isokinetic strength:
   - Quadriceps - 80-90% BW for females; 90-100% BW for males
   - Hamstrings - greater than 50% BW
4. Compliance with home program
5. Immediate identification of problem areas:
   - Lack of full motion
   - Abnormal gait pattern
   - Pain and/or swelling

TREATMENT - WEEKS #20-24

1. KT 2000 performed at MedSport/physician evaluation
2. Isokinetic test performed at MedSport
3. Functional tests (dynamic - sport-specific) performed at MedSport
4. Once goals on above isokinetic/functional tests have been achieved, progress sport-specific skills
5. Continue full exercise program
6. Continue full closed-chain program/agilities

CRITERIA TO RETURN TO FULL ACTIVITY

- Must be cleared by physician
- Quad strength – 90-100% of body weight, and/or ≤10% deficit as compared to contralateral levels
- Equivalent bilateral functional test scores
- Absence of knee pain/swelling

Figure B.6. Standard rehabilitation protocol completed by all anterior cruciate ligament injured/reconstructed subjects.

APPENDIX C

SUPPLEMENTAL DATA

AIM 1 SUPPLEMENTAL DATA

Table C.1. ACL-Injured Subject Demographic Data.

Subj. ID	Sex	Injured Limb	Age	Height (m)	Mass (kg)	Sport at Time of Injury	Mechanism of Injury*	Meniscal Damage at Injury†	Graft Type	Days from Injury to Surgery	Tegner‖ (Pre-Injury)	Tegner (Pre-Op)	Tegner (Post-Op)	IKDC# (Pre-Op)	IKDC (Post-Op)
13	M	R	16	1.71	78.84	Basketball	Did not recall	None	STG	67	7	1	9	56.32	83.91
15	F	R	14	1.74	61.23	Basketball	Non-contact	Medial	PT	30	9	2	9	45.98	97.7
16	F	L	15	1.67	81.65	Softball	Non-contact, running	Medial‡	PT	46	6	2	4	51.72	68.97
18	M	R	23	1.8	86.18	Soccer	Non-contact, cutting	Lateral‡	PT	320	7	5	5	71.26	60.92
21	F	L	15	1.85	61.23	Volleyball	Landing from hit	Medial‡	PT	48	10	1	5	11.49	85.06
22	M	L	29	1.75	77.11	Ultimate Frisbee	Non-contact, cutting	None	PT	39	10	4	4	43.68	81.61
23	F	L	27	1.57	52.16	Soccer	Non-contact, cutting	None	PT	56	5	2	7	27.59	80.46
24	F	L	19	1.84	84.37	Snowboarding	Non-contact	Lateral & Medial	PT	277	7	4	8	66.67	90.8
26	M	R	15	1.75	63.5	Soccer	Non-contact	Lateral§	PT	49	9	2	7	45.98	74.71
31	M	L	20	1.85	81.65	Soccer	Non-contact	None	PT	54	4	9	7	48.28	87.76
32	F	R	17	1.57	61.23	Gymnastics	Landing	Lateral‡	PT	39	9	4	7	52.87	81.61
34	M	L	17	1.73	61.23	Soccer	Cutting	Lateral§	PT	63	9	3	6	40.23	72.41
35	M	L	17	1.78	97.52	Football	Hit (valgus load)	No report available	STG	106	9	5	6	79.31	94.25
36	M	R	28	1.65	88.45	Basketball	Landing from jump	Lateral	PT	70	7	2	5	54.02	57.47

M= male; F= female; L= left; R= right; PT= patellar tendon; STG= semitendinosus/gracilis; IKDC= International Knee Documentation Society

* As dictated by the subject

†Meniscal damage was determined from diagnostic MRI report. ‡Indicates subject had meniscal debridement/repair concurrent with ACL reconstruction. §Indicates subject had meniscectomy concurrent with ACL reconstruction. All other subjects had no treatment of meniscal injury. ‖Tegner scale is scored from 0-10, with 10 representing participation in competitive sports at the national/elite level. #IKDC scored from 0-100, with 100 representing no pain/disability.

Table C.2. Control Subject Demographic Data.

Subject ID	Sex	Age	Height (m)	Mass (kg)	Tegner Score*	IKDC Score†
C1	F	24	1.7	64.41	10	100
C2	M	20	1.83	88.45	5	97.7
C3	F	22	1.7	61.23	9	95.4
C4	M	32	1.74	80	7	100
C5	M	22	1.88	81.65	6	100
C6	M	23	1.8	98.43	7	100
C7	F	30	1.63	48.54	9	100
C9	F	24	1.63	56.7	6	93.1
C10	F	25	1.8	86.18	6	100
C11	M	27	1.91	77.11	6	100
C12	M	25	1.78	83.91	6	94.25
C13	F	25	1.63	65.77	6	94.25
C14	F	21	1.8	70.31	7	100
C15	M	28	1.78	72.57	5	100
C16	1	23	1.68	63.5	7	100

* Tegner scale is scored from 0-10, with 10 representing participation in competitive sports at the national/elite level. †IKDC scored from 0-100, with 100 representing no pain/disability.

Table C.3. Pre-operative ACL-Injured Subject Knee Effusion and Thigh Circumference Data.

	Knee Effusion (cm)				Thigh Circumference (cm)*					
	Suprapatellar†		Mid-Patella		6 cm		12 cm		18 cm	
Subject ID	Injured	Uninjured	Injured	Uninjured	Injured	Uninjured	Injured	Uninjured	Injured	Uninjured
13	40.0	37.7	37.7	41.0	43.9	44.1	49.1	50.0	53.4	55.0
15	36.9	36.0	36.0	35.7	39.0	39.9	43.9	44.2	49.7	50.5
16	45.5	44.1	43.0	41.9	49.2	49.2	58.5	56.5	61.3	61.0
18	40.0	40.3	39.6	39.7	42.9	43.5	50.4	50.2	56.3	56.2
21	37.5	37.1	36.3	36.0	37.7	39.2	40.7	43.5	44.2	47.3
22	40.5	40.2	38.0	37.2	44.4	44.4	50.0	50.3	54.4	55.0
23	35.0	35.0	34.3	33.9	36.8	38.0	42.2	43.3	46.5	47.9
24	39.0	40.6	38.8	39.5	42.5	45.5	49.0	51.7	54.0	56.5
26	35.2	36.2	34.9	36.0	37.0	39.0	42.3	45.0	46.5	49.0
31	38.5	39.0	39.0	38.3	41.2	43.1	46.2	48.8	49.8	52.7
32	37.9	38.0	35.9	36.5	41.0	42.3	46.5	50.0	52.5	56.0
34	37.5	38.2	37.0	35.8	39.5	42.9	44.5	49.0	48.0	51.5
35	44.0	44.4	41.0	41.0	48.5	49.7	56.0	56.0	60.0	61.8
36	43.3	42.1	39.1	39.6	49.0	47.5	60.2	58.4	62.2	61.6

*Measured 6, 12, and 18 cm proximal to the superior pole of the patella with the subject in supine and the knee resting in approximately 10° of flexion on a bolster.

†Measured 1 cm proximal to the superior pole of the patella with the subject in the same position as for thigh circumference.[56]

Table C.4. Post-operative ACL-injured Subject Knee Effusion and Thigh Circumference Data.

	Knee Effusion (cm)				Thigh Circumference (cm)*					
	Suprapatellar†		Mid-Patella		6 cm		12 cm		18 cm	
Subject ID	Injured	Uninjured	Injured	Uninjured	Injured	Uninjured	Injured	Uninjured	Injured	Uninjured
13	39.8	40.3	36.8	37.5	43.3	44.9	48.8	51.9	53.7	56.2
15	36.2	37.0	35.2	35.6	39.0	41.0	44.0	45.5	49.9	51.0
16	47.0	44.0	45.0	41.3	52.4	50.0	60.3	59.0	63.0	62.0
18	38.0	37.8	38.1	38.5	40.9	41.1	48.0	48.0	54.2	52.9
21	39.0	38.7	37.6	36.7	40.0	42.0	43.5	45.4	47.5	50.4
22	39.1	40.0	37.3	37.1	43.8	43.8	50.0	50.5	52.4	54.9
23	35.0	36.2	34.0	33.5	38.0	39.0	42.5	44.0	47.0	49.7
24	48.0	41.0	48.5	39.9	42.2	45.5	49.0	52.0	53.0	56.0
26	36.7	38.5	35.8	36.4	41.5	43.0	46.0	48.5	50.5	53.2
31	39.0	38.9	39.0	38.3	42.0	43.2	48.5	49.7	52.0	53.8
32	38.0	38.0	36.4	36.0	41.6	42.9	47.5	49.0	53.0	54.0
34	39.2	39.2	36.8	36.8	42.0	43.8	47.1	49.7	50.8	53.5
35	45.3	45.3	42.0	42.0	50.5	52.0	57.4	59.1	64.5	63.4
36	43.2	43.0	39.8	40.5	49.0	48.5	57.3	58.0	63.2	64.0

*Measured 6, 12, and 18 cm proximal to the superior pole of the patella with the subject in supine and the knee resting in approximately 10° of flexion on a bolster.

†Measured 1 cm proximal to the superior pole of the patella with the subject in the same position as for thigh circumference.

Table C.5. Pre-operative ACL-injured Subject Calf Girth Data (cm).

	5 cm Proximal		10 cm Proximal		Maximum		5 cm Distal		10 cm Distal	
Subject ID	Injured	Uninjured	Injured	Uninjured	Injured	Uninjured	Injured	Uninjured	Injured	Uninjured
13	36.7	38.0	34.0	33.8	39.1	39.0	35.2	34.0	30.0	29.8
15	35.5	36.2	32.5	32.3	37.4	37.6	34.0	32.9	29.5	28.2
16	42.1	40.8	39.2	38.2	44.0	42.9	39.5	39.0	33.0	31.1
18	37.6	37.5	37.0	36.3	39.8	39.2	35.1	34.4	28.4	27.6
21	31.8	32.3	33.1	32.0	34.7	34.9	32.5	34.3	27.5	28.9
22	36.5	35.0	36.3	34.4	38.7	38.2	33.7	34.3	29.7	29.3
23	33.9	32.3	30.2	30.4	35.0	35.8	30.0	32.4	26.0	27.3
24	36.8	36.8	33.2	33.8	37.1	38.1	34.0	35.6	28.4	29.9
26	32.0	34.4	31.2	33.3	33.5	36.6	32.2	34.7	28.8	29.5
31	34.5	36.0	32.8	33.7	37.5	38.8	34.2	33.3	29.0	28.3
32	35.0	35.5	33.4	33.0	36.5	37.0	32.2	32.0	27.8	27.5
34	34.9	37.0	33.2	33.9	37.0	39.8	34.5	36.3	28.2	29.1
35	42.9	40.5	38.0	37.7	41.5	41.8	35.0	35.7	30.8	31.2
36	39.5	38.7	36.8	35.9	41.1	39.7	34.6	35.3	30.0	29.5

Measurements were taken with the subject lying in a supine position and the knee flexed so the foot was flat on the table. The distance from the lateral knee joint line to the tip of the lateral malleolus was measured. A mark was placed one-third of the way from the lateral knee joint line to the lateral malleolus to signify the spot of maximum calf girth. Measurements were recorded here, as well as 5 and 10 cm proximal and distal to this location.

Table C.6. Post-operative ACL-injured Subject Calf Girth Data (cm).

	5 cm Proximal		10 cm Proximal		Maximum		5 cm Distal		10 cm Distal	
Subject ID	Injured	Uninjured	Injured	Uninjured	Injured	Uninjured	Injured	Uninjured	Injured	Uninjured
13	36.5	38.7	34.8	35.4	39.0	39.5	36.5	34.4	31.8	30.2
15	35.2	36.5	31.8	32.5	37.0	38.2	34.5	33.5	29.6	28.5
16	44.0	42.5	41.5	38.6	43.5	43.3	38.0	38.9	31.2	32.0
18	36.7	36.8	34.4	34.2	37.4	37.8	32.3	31.9	26.5	27.2
21	36.0	35.1	33.9	33.3	36.6	37.0	33.5	35.2	28.5	31.0
22	37.2	37.0	33.8	33.0	37.4	37.8	32.7	32.5	28.3	28.4
23	34.0	34.5	29.8	31.0	35.5	36.5	31.9	32.7	26.7	27.4
24	32.5	36.9	33.8	34.0	37.5	39.0	34.9	35.3	30.0	30.2
26	34.3	35.0	32.0	33.0	37.0	38.0	34.5	35.3	28.8	30.0
31	35.4	37.2	33.0	33.3	37.2	38.5	33.1	32.7	28.1	27.8
32	35.5	36.5	33.0	33.0	36.1	36.5	32.2	31.9	27.5	27.6
34	38.4	37.6	34.4	33.9	39.0	39.7	35.0	35.5	29.0	29.4
35	43.5	42.0	39.6	39.3	44.5	43.4	37.2	37.5	33.1	32.0
36	41.2	38.7	36.5	35.6	42.0	39.5	33.2	33.8	28.9	28.5

Measurements were taken with the subject lying in supine and the knee flexed so the foot was flat on the table. The distance from the lateral knee joint line to the tip of the lateral malleolus was measured. One-third of this distance was determined and a mark 1/3 of the way from the lateral joint line to the lateral malleolus was made to signify the spot of maximum calf girth. Measurements were recorded here, as well as 5 and 10 cm proximal and distal to this location.

Table C.7. Control Subject Knee Effusion and Thigh Circumference Data.

	Knee Effusion (cm)				Thigh Circumference (cm)*					
	Suprapatellar†		Mid-Patella		6 cm		12 cm		18 cm	
Subject ID	Test Limb	Contralateral Limb	Test Limb	Contralateral Limb	Test Limb	Contralateral Limb	Test Limb	Contralateral Limb	Test Limb	Contralateral Limb
C1	37.5	36.9	36.0	35.6	41.1	40.4	47.8	46.7	53.7	53.0
C2	41.5	42.2	41.4	41.1	47.5	46.5	51.8	51.3	55.5	56.0
C3	37.0	36.5	36.2	35.8	40.5	39.9	45.1	44.9	50.0	49.0
C4	40.0	40.0	38.8	39.1	44.2	44.0	50.0	49.8	55.0	54.2
C5	35.0	34.6	34.0	34.1	39.5	38.5	44.6	43.2	48.2	47.0
C6	40.3	39.5	37.4	37.9	41.9	42.8	47.8	49.0	54.0	53.2
C7	35.0	34.6	34.0	34.1	39.5	38.5	44.6	43.2	48.2	47.0
C9	34.3	35.8	33.8	34.0	38.3	39.4	44.5	46.3	50.6	51.0
C10	43.1	42.5	40.2	40.4	48.2	47.0	52.2	51.7	57.3	57.0
C11	37.0	37.0	36.9	37.4	40.3	40.4	46.8	46.5	50.6	50.0
C12	41.0	40.5	39.0	39.1	47.3	46.8	51.9	52.7	55.8	56.5
C13	38.1	37.5	36.9	36.4	43.1	42.1	49.0	48.2	53.0	52.4
C14	39.5	39.0	38.5	37.5	42.0	41.0	45.2	44.0	49.0	48.5
C15	38.0	37.1	37.7	36.4	42.5	42.0	48.5	46.7	52.5	51.6
C16	36.6	37.8	36.5	36.3	41.5	43.5	48.5	50.5	54.4	54.5

*Measured 6, 12, and 18 cm proximal to the superior pole of the patella with the subject in supine and the knee resting in approximately 10° of flexion on a bolster.

†Measured 1 cm proximal to the superior pole of the patella with the subject in the same position as for thigh circumference.

Table C.8. Control Subject Calf Girth Measurements (cm).

	5 cm Proximal		10 cm Proximal		Maximum		5 cm Distal		10 cm Distal	
Subject ID	Test Limb	Contralateral Limb	Test Limb	Contralateral Limb	Test Limb	Contralateral Limb	Test Limb	Contralateral Limb	Test Limb	Contralateral Limb
C1	34.8	34.1	31.0	30.5	36.0	36.3	33.5	32.4	28.0	27.5
C2	39.1	39.3	35.5	36.8	37.3	34.2	31.8	29.6	27.3	26.0
C3	36.6	35.5	31.6	31.0	38.1	37.7	36.0	35.5	28.9	29.5
C4	35.2	35.2	38.6	36.8	38.6	38.0	38.5	38.5	32.0	32.2
C5	32.0	32.8	30.5	30.4	35.2	34.7	30.4	29.8	25.7	25.5
C6	36.0	36.1	34.7	35.2	38.8	38.1	35.7	35.8	31.7	31.5
C7	32.0	32.8	30.5	30.4	35.2	34.7	30.4	29.8	25.7	25.5
C9	32.0	32.8	30.5	31.7	34.4	34.8	30.6	31.2	25.4	26.8
C10	41.7	41.5	36.7	38.8	41.3	41.8	38.2	37.3	32.5	32.7
C11	35.4	35.0	31.5	31.2	37.7	37.3	34.5	35.3	28.1	29.0
C12	37.5	36.1	36.9	36.8	40.4	39.8	36.4	36.8	30.7	30.8
C13	34.1	34.4	32.9	33.0	37.9	38.2	35.2	25.7	28.5	27.8
C14	35.8	37.2	33.6	34.2	36.5	37.0	32.5	31.9	28.8	27.7
C15	36.5	35.1	33.0	32.6	37.0	36.5	33.2	31.3	28.0	26.0
C16	36.0	37.8	33.3	33.6	37.0	38.3	33.9	33.4	28.5	28.8

Measurements were taken with the subject lying in supine and the knee flexed so the foot was flat on the table. The distance from the lateral knee joint line to the tip of the lateral malleolus was measured. One-third of this distance was determined and a mark 1/3 of the way from the lateral joint line to the lateral malleolus was made to signify the spot of maximum calf girth. Measurements were recorded here, as well as 5 and 10 cm proximal and distal to this location.

Table C.9. Pre-operative ACL-injured subject strength data (Nm/kg).

	Quadriceps		Hamstrings		Ankle Plantar Flexors		Ankle Dorsiflexors		Hip Abductors		Hip Adductors		Hip Flexors		Hip Extensors	
Subj. ID	I	U	I	U	I	U	I	U	I	U	I	U	I	U	I	U
13	0.63	1.16	0.53	0.63	0.49	0.46	0.25	0.39	0.53	0.46	0.56	0.81	1.16	1.02	1.16	0.49
15	1.08	1.58	0.77	0.90	0.41	0.45	0.14	0.27	0.45	0.36	0.81	0.86	0.54	0.63	0.99	0.59
16	1.12	1.29	0.75	1.05	0.41	0.41	0.30	0.20	0.47	0.00	0.47	0.61	0.85	0.88	0.88	0.78
18	1.22	1.22	1.03	1.89	0.58	0.26	0.39	0.32	0.00	0.48	0.71	0.55	1.00	0.83	0.96	1.28
21	0.63	1.17	0.36	1.04	0.41	0.77	0.32	0.23	0.86	0.90	0.86	1.08	0.77	0.59	0.59	0.77
22	2.40	3.01	1.08	1.33	0.68	0.86	0.36	0.25	1.36	1.18	1.15	1.29	1.44	1.51	1.83	1.79
23	1.49	2.70	0.95	1.11	0.37	0.42	0.27	0.32	1.38	1.06	1.17	1.11	1.01	1.49	2.17	1.11
24	2.26	2.10	1.28	1.41	0.46	0.43	0.33	0.36	1.28	0.89	0.85	0.75	1.28	1.25	1.44	1.41
26	0.81	2.45	0.67	1.24	0.42	0.56	0.28	0.35	0.87	0.92	0.55	0.77	1.10	1.01	0.87	0.85
31	0.90	2.22	0.77	0.99	0.20	0.40	0.27	0.35	0.65	0.52	0.52	0.59	1.27	1.13	1.82	1.19
32	1.52	1.86	0.64	1.01	0.81	0.91	0.20	0.19	0.83	0.98	0.85	0.86	1.31	1.38	1.27	0.84
34	1.31	2.30	0.92	1.25	0.82	1.08	0.17	0.28	0.74	0.88	0.51	0.77	1.44	1.44	1.98	1.84
35	1.95	2.18	0.71	1.09	0.44	0.49	0.12	0.13	0.56	0.60	0.76	0.56	1.43	1.06	1.59	1.43
36	1.27	2.04	0.80	0.94	0.57	0.92	0.25	0.30	0.78	1.04	0.44	1.05	1.47	1.58	1.91	1.83

I=injured limb; U=uninjured limb

Table C.10. Post-operative ACL-injured subjects strength data (Nm/kg).

	Quadriceps		Hamstrings		Ankle Plantar Flexors		Ankle Dorsiflexors		Hip Abductors		Hip Adductors		Hip Flexors		Hip Extensors	
Subj. ID	I	U	I	U	I	U	I	U	I	U	I	U	I	U	I	U
13	1.36	2.15	0.84	1.16	0.76	0.63	0.25	0.24	0.81	0.86	0.67	0.96	1.73	1.67	1.94	1.47
15	1.56	1.86	1.03	0.84	0.87	0.66	0.18	0.14	0.72	0.50	0.76	0.81	1.06	1.02	1.56	1.52
16	1.24	1.18	0.84	0.97	0.58	0.29	0.23	0.20	0.70	0.68	0.69	0.76	1.46	1.00	1.14	1.20
18	2.28	1.81	1.10	1.00	0.93	0.77	0.38	0.31	0.75	0.69	0.96	1.00	0.76	1.11	1.32	1.39
21	1.21	1.78	0.71	0.87	0.86	0.55	0.19	0.15	0.70	0.64	1.03	0.89	1.04	1.23	1.09	1.29
22	1.90	2.93	0.99	1.13	0.65	0.83	0.24	0.30	1.08	0.95	0.95	0.97	1.62	1.38	2.14	1.54
23	1.95	3.16	1.51	1.75	1.24	1.23	0.26	0.29	1.23	1.09	1.01	0.96	1.89	2.29	2.50	2.89
24	1.38	3.10	1.38	1.30	0.58	0.60	0.32	0.31	1.05	0.88	0.92	0.92	1.41	1.51	1.83	1.62
26	1.16	2.81	1.09	1.33	0.79	0.92	0.42	0.48	1.08	1.13	1.20	0.90	1.65	1.68	1.27	1.26
31	0.77	1.27	0.72	0.88	0.90	0.61	0.32	0.29	0.86	0.81	1.03	0.88	1.13	1.13	1.83	1.68
32	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
34	2.09	2.44	1.11	1.39	1.13	0.94	0.29	0.33	0.83	0.72	0.67	0.79	2.37	2.28	1.67	2.51
35	1.46	2.18	0.73	0.99	0.65	0.54	0.24	0.19	0.78	0.73	0.56	0.61	1.40	1.63	1.68	1.60
36	0.94	2.11	0.94	1.03	0.88	0.84	0.23	0.17	0.88	1.04	0.68	1.05	2.02	1.80	2.02	1.64

I=injured limb; U=uninjured limb

Table C.11. Control subject strength data (Nm/kg).

	Quadriceps		Hamstrings		Ankle Plantar Flexors		Ankle Dorsiflexors		Hip Abductors		Hip Adductors		Hip Flexors		Hip Extensors	
Subj. ID	T	C	T	C	T	C	T	C	T	C	T	C	T	C	T	C
C1	1.41	1.46	1.05	1.00	0.60	0.70	0.23	0.26	0.92	0.85	0.62	0.75	2.83	1.93	1.49	1.01
C2	1.42	1.54	0.75	0.78	0.51	0.51	0.35	0.34	0.60	0.78	0.48	0.55	1.02	1.01	0.74	1.22
C3	2.01	2.31	1.33	1.21	1.03	1.38	0.43	0.37	0.92	0.78	0.75	0.80	1.16	1.23	1.67	1.48
C4	1.66	2.10	0.85	0.82	0.45	0.53	0.37	0.47	0.60	0.83	0.79	0.64	1.43	1.05	1.18	1.08
C5	1.99	1.40	0.93	0.82	0.15	0.18	0.11	0.14	0.66	0.39	0.75	0.49	1.31	1.22	1.29	1.34
C6	1.63	1.76	0.92	1.11	0.33	0.12	0.22	0.09	0.66	0.54	0.13	0.21	0.93	0.94	0.36	0.72
C7	2.30	2.10	1.25	1.25	1.38	0.85	0.22	0.26	1.19	1.63	1.14	1.03	1.66	1.87	1.49	1.55
C9	1.22	1.24	0.90	0.67	0.37	0.46	0.26	0.20	0.73	0.94	0.75	0.82	0.59	0.62	1.26	1.38
C10	1.72	1.96	0.85	1.04	0.70	1.05	0.16	0.21	0.89	0.68	0.31	0.38	1.41	1.43	1.59	0.21
C11	1.73	1.54	0.81	0.86	0.54	0.63	0.30	0.34	0.65	0.83	0.62	0.70	1.11	0.88	0.99	1.14
C12	2.44	2.03	1.43	1.21	0.91	1.10	0.33	0.28	0.75	0.65	0.51	0.56	1.74	1.66	1.15	1.68
C13	1.12	1.14	0.69	0.68	0.25	0.27	0.16	0.17	0.65	0.58	0.45	0.54	0.76	0.65	0.97	0.94
C14	1.41	1.51	0.90	0.81	0.75	0.78	0.26	0.25	0.90	0.96	0.87	0.86	1.89	1.17	1.71	1.35
C15	0.24	2.47	1.21	1.24	1.06	1.21	0.36	0.31	1.32	1.48	0.69	0.86	1.64	2.18	1.93	2.04
C16	1.67	1.98	0.85	0.96	0.78	0.82	0.27	0.28	1.18	1.05	0.76	0.84	1.93	1.47	1.90	1.90

T=test limb; C=contralateral limb

AIM 1 STATISTICAL OUTPUT

General Linear Model- ACL-injured vs. control at pre-op

Tests of Between-Subjects Effects

Source	Dependent Variable	Type III Sum of Squares	df	Mean Square	F	Sig.	Noncent. Parameter	Observed Power[b]
Corrected Model	pre-op injured limb knee extensor strength (Nm/kg)	1.226[a]	1	1.226	5.138	.032	5.138	.589
	pre-op injured limb knee flexor strength (Nm/kg)	.234[c]	1	.234	4.353	.047	4.353	.521
	pre-op injured limb ankle plantar flexor strength (Nm/kg)	.255[d]	1	.255	3.088	.090	3.088	.396
	pre-op injured limb ankle dorsiflexor strength (Nm/kg)	.001[e]	1	.001	.101	.754	.101	.061
	pre-op injured limb hip abductor strength (Nm/kg)	.029[f]	1	.029	.255	.618	.255	.078
	pre-op injured limb hip adductor strength (Nm/kg)	.046[g]	1	.046	.808	.377	.808	.140
	pre-op injured limb hip flexor strength (Nm/kg)	.470[h]	1	.470	2.118	.157	2.118	.289

	pre-op injured limb hip extensor strength (Nm/kg)	.164[i]	1	.164	.669	.421	.669	.124
Intercept	pre-op injured limb knee extensor strength (Nm/kg)	68.124	1	68.124	285.485	.000	285.485	1.000
	pre-op injured limb knee flexor strength (Nm/kg)	23.158	1	23.158	431.003	.000	431.003	1.000
	pre-op injured limb ankle plantar flexor strength (Nm/kg)	10.387	1	10.387	125.760	.000	125.760	1.000
	pre-op injured limb ankle dorsiflexor strength (Nm/kg)	2.040	1	2.040	328.392	.000	328.392	1.000
	pre-op injured limb hip abductor strength (Nm/kg)	18.536	1	18.536	165.512	.000	165.512	1.000
	pre-op injured limb hip adductor strength (Nm/kg)	13.776	1	13.776	244.501	.000	244.501	1.000
	pre-op injured limb hip flexor strength (Nm/kg)	47.106	1	47.106	212.165	.000	212.165	1.000
	pre-op injured limb hip extensor strength (Nm/kg)	50.063	1	50.063	203.614	.000	203.614	1.000
Group	pre-op injured limb knee extensor strength (Nm/kg)	1.226	1	1.226	5.138	.032	5.138	.589
	pre-op injured limb knee flexor strength (Nm/kg)	.234	1	.234	4.353	.047	4.353	.521
	pre-op injured limb ankle plantar flexor strength (Nm/kg)	.255	1	.255	3.088	.090	3.088	.396

	pre-op injured limb ankle dorsiflexor strength (Nm/kg)	.001	1	.001	.101	.754	.101	.061
	pre-op injured limb hip abductor strength (Nm/kg)	.029	1	.029	.255	.618	.255	.078
	pre-op injured limb hip adductor strength (Nm/kg)	.046	1	.046	.808	.377	.808	.140
	pre-op injured limb hip flexor strength (Nm/kg)	.470	1	.470	2.118	.157	2.118	.289
	pre-op injured limb hip extensor strength (Nm/kg)	.164	1	.164	.669	.421	.669	.124
Error	pre-op injured limb knee extensor strength (Nm/kg)	6.443	27	.239				
	pre-op injured limb knee flexor strength (Nm/kg)	1.451	27	.054				
	pre-op injured limb ankle plantar flexor strength (Nm/kg)	2.230	27	.083				
	pre-op injured limb ankle dorsiflexor strength (Nm/kg)	.168	27	.006				
	pre-op injured limb hip abductor strength (Nm/kg)	3.024	27	.112				
	pre-op injured limb hip adductor strength (Nm/kg)	1.521	27	.056				
	pre-op injured limb hip flexor strength (Nm/kg)	5.995	27	.222				

	pre-op injured limb hip extensor strength (Nm/kg)	6.638	27	.246				
Total	pre-op injured limb knee extensor strength (Nm/kg)	76.507	29					
	pre-op injured limb knee flexor strength (Nm/kg)	25.031	29					
	pre-op injured limb ankle plantar flexor strength (Nm/kg)	12.997	29					
	pre-op injured limb ankle dorsiflexor strength (Nm/kg)	2.213	29					
	pre-op injured limb hip abductor strength (Nm/kg)	21.660	29					
	pre-op injured limb hip adductor strength (Nm/kg)	15.305	29					
	pre-op injured limb hip flexor strength (Nm/kg)	53.953	29					
	pre-op injured limb hip extensor strength (Nm/kg)	56.727	29					
Corrected Total	pre-op injured limb knee extensor strength (Nm/kg)	7.669	28					
	pre-op injured limb knee flexor strength (Nm/kg)	1.685	28					
	pre-op injured limb ankle plantar flexor strength (Nm/kg)	2.485	28					

pre-op injured limb ankle dorsiflexor strength (Nm/kg)	.168	28					
pre-op injured limb hip abductor strength (Nm/kg)	3.052	28					
pre-op injured limb hip adductor strength (Nm/kg)	1.567	28					
pre-op injured limb hip flexor strength (Nm/kg)	6.465	28					
pre-op injured limb hip extensor strength (Nm/kg)	6.803	28					

Univariate Tests

Dependent Variable		Sum of Squares	df	Mean Square	F	Sig.	Noncent. Parameter	Observed Power[a]
pre-op injured limb knee extensor strength (Nm/kg)	Contrast	1.226	1	1.226	5.138	.032	5.138	.589
	Error	6.443	27	.239				
pre-op injured limb knee flexor strength (Nm/kg)	Contrast	.234	1	.234	4.353	.047	4.353	.521
	Error	1.451	27	.054				
pre-op injured limb ankle plantar flexor strength (Nm/kg)	Contrast	.255	1	.255	3.088	.090	3.088	.396

	Error	2.230	27	.083				
pre-op injured limb ankle dorsiflexor strength (Nm/kg)	Contrast	.001	1	.001	.101	.754	.101	.061
	Error	.168	27	.006				
pre-op injured limb hip abductor strength (Nm/kg)	Contrast	.029	1	.029	.255	.618	.255	.078
	Error	3.024	27	.112				
pre-op injured limb hip adductor strength (Nm/kg)	Contrast	.046	1	.046	.808	.377	.808	.140
	Error	1.521	27	.056				
pre-op injured limb hip flexor strength (Nm/kg)	Contrast	.470	1	.470	2.118	.157	2.118	.289
	Error	5.995	27	.222				
pre-op injured limb hip extensor strength (Nm/kg)	Contrast	.164	1	.164	.669	.421	.669	.124
	Error	6.638	27	.246				

General Linear Model- ACL-reconstructed vs. control at post-op

Tests of Between-Subjects Effects

Source	Dependent Variable	Type III Sum of Squares	df	Mean Square	F	Sig.	Noncent. Parameter	Observed Power[b]
Corrected Model	post-op injured limb knee extensor strength (Nm/kg)	.942[a]	1	.942	3.664	.066	3.664	.455
	post-op injured limb knee flexor strength	.023[c]	1	.023	.259	.615	.259	.078
	Post_Inj_Ank_PF	.047[d]	1	.047	.424	.520	.424	.096
	Post_Inj_Ank_DF	.002[e]	1	.002	.247	.623	.247	.077
	Post_Inj_Hip_Abd	.001[f]	1	.001	.013	.910	.013	.051
	Post_Inj_Hip_Add	.152[g]	1	.152	2.137	.155	2.137	.292
	Post_Inj_Hip_Flex	.000[h]	1	.000	.001	.975	.001	.050
	Post_Inj_Hip_Ext	.795[i]	1	.795	2.642	.116	2.642	.348
Intercept	post-op injured limb knee extensor strength (Nm/kg)	70.396	1	70.396	273.690	.000	273.690	1.000

	post-op injured limb knee flexor strength	26.469	1	26.469	299.772	.000	299.772	1.000
	Post_Inj_Ank_PF	15.553	1	15.553	141.733	.000	141.733	1.000
	Post_Inj_Ank_DF	1.985	1	1.985	251.248	.000	251.248	1.000
	Post_Inj_Hip_Abd	19.729	1	19.729	242.281	.000	242.281	1.000
	Post_Inj_Hip_Add	15.120	1	15.120	212.191	.000	212.191	1.000
	Post_Inj_Hip_Flex	56.707	1	56.707	162.638	.000	162.638	1.000
	Post_Inj_Hip_Ext	57.181	1	57.181	189.964	.000	189.964	1.000
Group	post-op injured limb knee extensor strength (Nm/kg)	.942	1	.942	3.664	.066	3.664	.455
	post-op injured limb knee flexor strength	.023	1	.023	.259	.615	.259	.078
	Post_Inj_Ank_PF	.047	1	.047	.424	.520	.424	.096
	Post_Inj_Ank_DF	.002	1	.002	.247	.623	.247	.077
	Post_Inj_Hip_Abd	.001	1	.001	.013	.910	.013	.051
	Post_Inj_Hip_Add	.152	1	.152	2.137	.155	2.137	.292

	Post_Inj_Hip_Flex	.000	1	.000	.001	.975	.001	.050
	Post_Inj_Hip_Ext	.795	1	.795	2.642	.116	2.642	.348
Error	post-op injured limb knee extensor strength (Nm/kg)	6.945	27	.257				
	post-op injured limb knee flexor strength	2.384	27	.088				
	Post_Inj_Ank_PF	2.963	27	.110				
	Post_Inj_Ank_DF	.213	27	.008				
	Post_Inj_Hip_Abd	2.199	27	.081				
	Post_Inj_Hip_Add	1.924	27	.071				
	Post_Inj_Hip_Flex	9.414	27	.349				
	Post_Inj_Hip_Ext	8.127	27	.301				
Total	post-op injured limb knee extensor strength (Nm/kg)	78.930	29					
	post-op injured limb knee flexor strength	28.961	29					
	Post_Inj_Ank_PF	18.522	29					

	Post_Inj_Ank_DF	2.207	29					
	Post_Inj_Hip_Abd	21.963	29					
	Post_Inj_Hip_Add	17.110	29					
	Post_Inj_Hip_Flex	66.198	29					
	Post_Inj_Hip_Ext	65.706	29					
Corrected Total	post-op injured limb knee extensor strength (Nm/kg)	7.887	28					
	post-op injured limb knee flexor strength	2.407	28					
	Post_Inj_Ank_PF	3.009	28					
	Post_Inj_Ank_DF	.215	28					
	Post_Inj_Hip_Abd	2.200	28					
	Post_Inj_Hip_Add	2.076	28					
	Post_Inj_Hip_Flex	9.414	28					
	Post_Inj_Hip_Ext	8.922	28					

Univariate Tests

Dependent Variable		Sum of Squares	df	Mean Square	F	Sig.	Noncent. Parameter	Observed Power[a]
post-op injured limb knee extensor strength (Nm/kg)	Contrast	.942	1	.942	3.664	.066	3.664	.455
	Error	6.945	27	.257				
post-op injured limb knee flexor strength	Contrast	.023	1	.023	.259	.615	.259	.078
	Error	2.384	27	.088				
Post_Inj_Ank_PF	Contrast	.047	1	.047	.424	.520	.424	.096
	Error	2.963	27	.110				
Post_Inj_Ank_DF	Contrast	.002	1	.002	.247	.623	.247	.077
	Error	.213	27	.008				
Post_Inj_Hip_Abd	Contrast	.001	1	.001	.013	.910	.013	.051
	Error	2.199	27	.081				
Post_Inj_Hip_Add	Contrast	.152	1	.152	2.137	.155	2.137	.292
	Error	1.924	27	.071				

Post_Inj_Hip_Flex	Contrast	.000	1	.000	.001	.975	.001	.050
	Error	9.414	27	.349				
Post_Inj_Hip_Ext	Contrast	.795	1	.795	2.642	.116	2.642	.348
	Error	8.127	27	.301				

Univariate Tests

Source	Measure		Type III Sum of Squares	df	Mean Square	F	Sig.	Noncent. Parameter	Observed Power[a]
time	KE	Sphericity Assumed	.087	1	.087	.199	.663	.199	.070
		Greenhouse-Geisser	.087	1.000	.087	.199	.663	.199	.070
		Huynh-Feldt	.087	1.000	.087	.199	.663	.199	.070
		Lower-bound	.087	1.000	.087	.199	.663	.199	.070
	KF	Sphericity Assumed	.004	1	.004	.036	.852	.036	.054
		Greenhouse-Geisser	.004	1.000	.004	.036	.852	.036	.054
		Huynh-Feldt	.004	1.000	.004	.036	.852	.036	.054
		Lower-bound	.004	1.000	.004	.036	.852	.036	.054
	APF	Sphericity Assumed	.401	1	.401	2.893	.113	2.893	.351
		Greenhouse-Geisser	.401	1.000	.401	2.893	.113	2.893	.351
		Huynh-Feldt	.401	1.000	.401	2.893	.113	2.893	.351
		Lower-bound	.401	1.000	.401	2.893	.113	2.893	.351
	ADF	Sphericity Assumed	.007	1	.007	1.029	.329	1.029	.156
		Greenhouse-Geisser	.007	1.000	.007	1.029	.329	1.029	.156
		Huynh-Feldt	.007	1.000	.007	1.029	.329	1.029	.156

	Lower-bound	.007	1.000	.007	1.029	.329	1.029	.156
HAb	Sphericity Assumed	.024	1	.024	.188	.671	.188	.069
	Greenhouse-Geisser	.024	1.000	.024	.188	.671	.188	.069
	Huynh-Feldt	.024	1.000	.024	.188	.671	.188	.069
	Lower-bound	.024	1.000	.024	.188	.671	.188	.069
HAd	Sphericity Assumed	.010	1	.010	.100	.757	.100	.060
	Greenhouse-Geisser	.010	1.000	.010	.100	.757	.100	.060
	Huynh-Feldt	.010	1.000	.010	.100	.757	.100	.060
	Lower-bound	.010	1.000	.010	.100	.757	.100	.060
HF	Sphericity Assumed	.978	1	.978	3.279	.093	3.279	.389
	Greenhouse-Geisser	.978	1.000	.978	3.279	.093	3.279	.389
	Huynh-Feldt	.978	1.000	.978	3.279	.093	3.279	.389
	Lower-bound	.978	1.000	.978	3.279	.093	3.279	.389

	HE	Sphericity Assumed	1.126	1	1.126	4.522	.053	4.522	.503
		Greenhouse-Geisser	1.126	1.000	1.126	4.522	.053	4.522	.503
		Huynh-Feldt	1.126	1.000	1.126	4.522	.053	4.522	.503
		Lower-bound	1.126	1.000	1.126	4.522	.053	4.522	.503
Error(time)	KE	Sphericity Assumed	5.693	13	.438				
		Greenhouse-Geisser	5.693	13.000	.438				
		Huynh-Feldt	5.693	13.000	.438				
		Lower-bound	5.693	13.000	.438				
	KF	Sphericity Assumed	1.533	13	.118				
		Greenhouse-Geisser	1.533	13.000	.118				
		Huynh-Feldt	1.533	13.000	.118				
		Lower-bound	1.533	13.000	.118				
	APF	Sphericity Assumed	1.803	13	.139				
		Greenhouse-Geisser	1.803	13.000	.139				

	Huynh-Feldt	1.803	13.000	.139				
	Lower-bound	1.803	13.000	.139				
ADF	Sphericity Assumed	.092	13	.007				
	Greenhouse-Geisser	.092	13.000	.007				
	Huynh-Feldt	.092	13.000	.007				
	Lower-bound	.092	13.000	.007				
HAb	Sphericity Assumed	1.658	13	.128				
	Greenhouse-Geisser	1.658	13.000	.128				
	Huynh-Feldt	1.658	13.000	.128				
	Lower-bound	1.658	13.000	.128				
HAd	Sphericity Assumed	1.343	13	.103				
	Greenhouse-Geisser	1.343	13.000	.103				
	Huynh-Feldt	1.343	13.000	.103				
	Lower-bound	1.343	13.000	.103				

	HF	Sphericity Assumed	3.877	13	.298				
		Greenhouse-Geisser	3.877	13.000	.298				
		Huynh-Feldt	3.877	13.000	.298				
		Lower-bound	3.877	13.000	.298				
	HE	Sphericity Assumed	3.236	13	.249				
		Greenhouse-Geisser	3.236	13.000	.249				
		Huynh-Feldt	3.236	13.000	.249				
		Lower-bound	3.236	13.000	.249				
leg	KE	Sphericity Assumed	5.896	1	5.896	25.635	.000	25.635	.997
		Greenhouse-Geisser	5.896	1.000	5.896	25.635	.000	25.635	.997
		Huynh-Feldt	5.896	1.000	5.896	25.635	.000	25.635	.997
		Lower-bound	5.896	1.000	5.896	25.635	.000	25.635	.997
	KF	Sphericity Assumed	.702	1	.702	39.395	.000	39.395	1.000
		Greenhouse-Geisser	.702	1.000	.702	39.395	.000	39.395	1.000

	Huynh-Feldt	.702	1.000	.702	39.395	.000	39.395	1.000
	Lower-bound	.702	1.000	.702	39.395	.000	39.395	1.000
APF	Sphericity Assumed	6.429E-5	1	6.429E-5	.005	.946	.005	.050
	Greenhouse-Geisser	6.429E-5	1.000	6.429E-5	.005	.946	.005	.050
	Huynh-Feldt	6.429E-5	1.000	6.429E-5	.005	.946	.005	.050
	Lower-bound	6.429E-5	1.000	6.429E-5	.005	.946	.005	.050
ADF	Sphericity Assumed	.000	1	.000	.140	.714	.140	.064
	Greenhouse-Geisser	.000	1.000	.000	.140	.714	.140	.064
	Huynh-Feldt	.000	1.000	.000	.140	.714	.140	.064
	Lower-bound	.000	1.000	.000	.140	.714	.140	.064
HAb	Sphericity Assumed	.027	1	.027	1.127	.308	1.127	.166
	Greenhouse-Geisser	.027	1.000	.027	1.127	.308	1.127	.166
	Huynh-Feldt	.027	1.000	.027	1.127	.308	1.127	.166
	Lower-bound	.027	1.000	.027	1.127	.308	1.127	.166

	HAd	Sphericity Assumed	.059	1	.059	2.334	.151	2.334	.294
		Greenhouse-Geisser	.059	1.000	.059	2.334	.151	2.334	.294
		Huynh-Feldt	.059	1.000	.059	2.334	.151	2.334	.294
		Lower-bound	.059	1.000	.059	2.334	.151	2.334	.294
	HF	Sphericity Assumed	.000	1	.000	.005	.943	.005	.051
		Greenhouse-Geisser	.000	1.000	.000	.005	.943	.005	.051
		Huynh-Feldt	.000	1.000	.000	.005	.943	.005	.051
		Lower-bound	.000	1.000	.000	.005	.943	.005	.051
	HE	Sphericity Assumed	.237	1	.237	3.712	.076	3.712	.430
		Greenhouse-Geisser	.237	1.000	.237	3.712	.076	3.712	.430
		Huynh-Feldt	.237	1.000	.237	3.712	.076	3.712	.430
		Lower-bound	.237	1.000	.237	3.712	.076	3.712	.430
Error(leg)	KE	Sphericity Assumed	2.990	13	.230				
		Greenhouse-Geisser	2.990	13.000	.230				

	Huynh-Feldt	2.990	13.000	.230				
	Lower-bound	2.990	13.000	.230				
KF	Sphericity Assumed	.232	13	.018				
	Greenhouse-Geisser	.232	13.000	.018				
	Huynh-Feldt	.232	13.000	.018				
	Lower-bound	.232	13.000	.018				
APF	Sphericity Assumed	.175	13	.013				
	Greenhouse-Geisser	.175	13.000	.013				
	Huynh-Feldt	.175	13.000	.013				
	Lower-bound	.175	13.000	.013				
ADF	Sphericity Assumed	.033	13	.003				
	Greenhouse-Geisser	.033	13.000	.003				
	Huynh-Feldt	.033	13.000	.003				
	Lower-bound	.033	13.000	.003				

HAb	Sphericity Assumed	.317	13	.024				
	Greenhouse-Geisser	.317	13.000	.024				
	Huynh-Feldt	.317	13.000	.024				
	Lower-bound	.317	13.000	.024				
HAd	Sphericity Assumed	.329	13	.025				
	Greenhouse-Geisser	.329	13.000	.025				
	Huynh-Feldt	.329	13.000	.025				
	Lower-bound	.329	13.000	.025				
HF	Sphericity Assumed	.284	13	.022				
	Greenhouse-Geisser	.284	13.000	.022				
	Huynh-Feldt	.284	13.000	.022				
	Lower-bound	.284	13.000	.022				
HE	Sphericity Assumed	.829	13	.064				
	Greenhouse-Geisser	.829	13.000	.064				

		Huynh-Feldt	.829	13.000	.064				
		Lower-bound	.829	13.000	.064				
time * leg	KE	Sphericity Assumed	.011	1	.011	.103	.754	.103	.060
		Greenhouse-Geisser	.011	1.000	.011	.103	.754	.103	.060
		Huynh-Feldt	.011	1.000	.011	.103	.754	.103	.060
		Lower-bound	.011	1.000	.011	.103	.754	.103	.060
	KF	Sphericity Assumed	.158	1	.158	7.633	.016	7.633	.724
		Greenhouse-Geisser	.158	1.000	.158	7.633	.016	7.633	.724
		Huynh-Feldt	.158	1.000	.158	7.633	.016	7.633	.724
		Lower-bound	.158	1.000	.158	7.633	.016	7.633	.724
	APF	Sphericity Assumed	.136	1	.136	9.777	.008	9.777	.824
		Greenhouse-Geisser	.136	1.000	.136	9.777	.008	9.777	.824
		Huynh-Feldt	.136	1.000	.136	9.777	.008	9.777	.824
		Lower-bound	.136	1.000	.136	9.777	.008	9.777	.824

ADF	Sphericity Assumed	.003	1	.003	1.653	.221	1.653	.222
	Greenhouse-Geisser	.003	1.000	.003	1.653	.221	1.653	.222
	Huynh-Feldt	.003	1.000	.003	1.653	.221	1.653	.222
	Lower-bound	.003	1.000	.003	1.653	.221	1.653	.222
HAb	Sphericity Assumed	.001	1	.001	.087	.773	.087	.059
	Greenhouse-Geisser	.001	1.000	.001	.087	.773	.087	.059
	Huynh-Feldt	.001	1.000	.001	.087	.773	.087	.059
	Lower-bound	.001	1.000	.001	.087	.773	.087	.059
HAd	Sphericity Assumed	.021	1	.021	1.881	.193	1.881	.246
	Greenhouse-Geisser	.021	1.000	.021	1.881	.193	1.881	.246
	Huynh-Feldt	.021	1.000	.021	1.881	.193	1.881	.246
	Lower-bound	.021	1.000	.021	1.881	.193	1.881	.246
HF	Sphericity Assumed	.004	1	.004	.152	.703	.152	.065
	Greenhouse-Geisser	.004	1.000	.004	.152	.703	.152	.065

		Huynh-Feldt	.004	1.000	.004	.152	.703	.152	.065
		Lower-bound	.004	1.000	.004	.152	.703	.152	.065
	HE	Sphericity Assumed	.148	1	.148	2.148	.167	2.148	.274
		Greenhouse-Geisser	.148	1.000	.148	2.148	.167	2.148	.274
		Huynh-Feldt	.148	1.000	.148	2.148	.167	2.148	.274
		Lower-bound	.148	1.000	.148	2.148	.167	2.148	.274
Error(time*leg)	KE	Sphericity Assumed	1.412	13	.109				
		Greenhouse-Geisser	1.412	13.000	.109				
		Huynh-Feldt	1.412	13.000	.109				
		Lower-bound	1.412	13.000	.109				
	KF	Sphericity Assumed	.268	13	.021				
		Greenhouse-Geisser	.268	13.000	.021				
		Huynh-Feldt	.268	13.000	.021				
		Lower-bound	.268	13.000	.021				

APF	Sphericity Assumed	.181	13	.014				
	Greenhouse-Geisser	.181	13.000	.014				
	Huynh-Feldt	.181	13.000	.014				
	Lower-bound	.181	13.000	.014				
ADF	Sphericity Assumed	.027	13	.002				
	Greenhouse-Geisser	.027	13.000	.002				
	Huynh-Feldt	.027	13.000	.002				
	Lower-bound	.027	13.000	.002				
HAb	Sphericity Assumed	.181	13	.014				
	Greenhouse-Geisser	.181	13.000	.014				
	Huynh-Feldt	.181	13.000	.014				
	Lower-bound	.181	13.000	.014				
HAd	Sphericity Assumed	.144	13	.011				
	Greenhouse-Geisser	.144	13.000	.011				

		Huynh-Feldt	.144	13.000	.011				
		Lower-bound	.144	13.000	.011				
	HF	Sphericity Assumed	.323	13	.025				
		Greenhouse-Geisser	.323	13.000	.025				
		Huynh-Feldt	.323	13.000	.025				
		Lower-bound	.323	13.000	.025				
	HE	Sphericity Assumed	.897	13	.069				
		Greenhouse-Geisser	.897	13.000	.069				
		Huynh-Feldt	.897	13.000	.069				
		Lower-bound	.897	13.000	.069				

General Linear Model- ACL-injured Pre-op vs. Post-op (2x2 limb x time) ANOVAs

Tests of Within-Subjects Effects

T-Test- Post-Hoc paired samples t-tests for hamstrings and ankle plantar flexors

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	pre-op injured limb knee flexor strength (Nm/kg)	.8043	14	.23530	.06289
	post-op injured limb knee flexor strength	.9279	14	.35659	.09530
Pair 2	pre-op healthy limb knee flexor strength (Nm/kg)	1.1343	14	.29244	.07816
	Post_Un_Kn_Flex	1.0457	14	.39081	.10445
Pair 3	pre-op injured limb ankle plantar flexor strength (Nm/kg)	.5050	14	.17204	.04598
	Post_Inj_Ank_PF	.7729	14	.29319	.07836
Pair 4	pre-op healthy limb ankle plantar flexor strength (Nm/kg)	.6014	14	.25331	.06770
	Post_Un_Ank_PF	.6721	14	.29720	.07943

Paired Samples Test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	pre-op injured limb knee flexor strength (Nm/kg) - post-op injured limb knee flexor strength	-.12357	.28578	.07638	-.28858	.04143	-1.618	13	.130
Pair 2	pre-op healthy limb knee flexor strength (Nm/kg) - Post_Un_Kn_Flex	.08857	.44218	.11818	-.16673	.34388	.749	13	.467
Pair 3	pre-op injured limb ankle plantar flexor strength (Nm/kg) - Post_Inj_Ank_PF	-.26786	.38485	.10286	-.49006	-.04565	-2.604	13	.022
Pair 4	pre-op healthy limb ankle plantar flexor strength (Nm/kg) - Post_Un_Ank_PF	-.07071	.39634	.10593	-.29955	.15812	-.668	13	.516

AIM 2 SUPPLEMENTAL DATA

Table C.12. Subject demographic data.

Subject ID	Sex	Injured Limb	Age	Height (m)	Mass (kg)	Sport at Time of Injury	Mechanism of Injury*	Tegner (Pre-Injury)	Tegner (at Testing)	IKDC (at Testing)	Meniscal Damage at Injury†	Days from Injury to Surgery
1	M	L	16	1.83	79.38	Football	Tackled from behind	9	8	80.46	Lateral	31
2	F	L	29	1.73	104.33	Softball	Slipped on home plate	7	4	80.46	Medial	135
4	F	L	15	1.65	59.78	Basketball	Running straight ahead	9	7	100	Medial‡	47
5	F	R	14	1.74	61.23	Basketball	Not specified/ non-contact	9	9	97.7	Medial	30
6	F	L	15	1.68	81.65	Softball	Running	7	4	68.97	Medial‡	46
7	M	L	29	1.75	77.11	Ultimate Frisbee	Cutting	10	7	81.61	None	39
8	M	L	19	1.84	84.37	Snowboarding	Not specified/ non-contact	9	8	90.8	Lateral & Medial	277
9	F	L	15	1.85	61.23	Volleyball	Landing from hit	10	5	85.06	Medial‡	48
11	F	L	27	1.57	52.16	Soccer	Cutting	5	7	80.46	None	56
12	F	L	20	1.73	70.31	Basketball	pivoting	7	5	71.26	None	222
13	M	R	28	1.65	88.45	Basketball	Landing from jump	7	5	57.47	Lateral	70
14	M	L	26	1.78	72.57	Soccer	Planting	9	9	88.51	Medial‡	320

M= male; F= female; L= left; R= right; * As dictated by the subject

†Meniscal damage was determined from each subject's diagnostic MRI report

‡ Indicates subjects had medial meniscus repair/debridement concurrent with ACL reconstruction. Other subjects received no treatment for their meniscal injuries.

Table C.13. Knee effusion and thigh circumference data.

	Knee Effusion (cm)				Thigh Circumference (cm)*					
	Suprapatellar†		Mid-Patella		6 cm		12 cm		18 cm	
Subject ID	Injured	Uninjured	Injured	Uninjured	Injured	Uninjured	Injured	Uninjured	Injured	Uninjured
1	41.6	39.8	41.8	39.7	43.8	45.5	49.2	51.2	54.8	57.2
2	44.5	50.5	47.1	42.7	54.0	52.0	60.8	59.5	65.7	64.7
4	37.5	35.6	37.1	34.2	40.0	40.3	45.5	47.2	51.4	51.8
5	36.2	35.2	37.0	35.6	39.0	41.0	44.0	45.5	49.9	51.0
6	47.0	45.0	44.0	41.3	52.4	50.0	60.3	59.0	63.0	62.0
7	39.1	37.3	40.0	37.1	43.8	43.8	50.0	50.5	52.4	54.9
8	48.0	48.5	41.0	39.9	42.2	45.5	49.0	52.0	53.0	56.0
9	39.0	37.6	38.7	36.7	40.0	42.0	43.5	45.4	47.5	50.4
11	35.0	34.0	36.2	33.5	38.0	39.0	42.5	44.0	47.0	49.7
12	41.0	37.3	40.7	38.0	43.0	44.0	48.8	50.0	54.0	54.1
13	43.2	39.8	43.0	40.5	49.0	48.5	57.3	58.0	63.2	64.0
14	45.1	36.1	40.0	37.6	36.7	48.7	42.2	37.3	45.8	36.0

*Measurements were taken 6, 12, and 18 cm proximal to the superior pole of the patella
†Measured 1 cm proximal to the superior pole of the patella with the subject in supine

Table C.14. Quadriceps strength (Nm/kg) and central activation ratio data.

	Knee Extension MVIC (Nm/kg)		Quadriceps CAR	
Subject ID	Injured	Uninjured	Injured	Uninjured
1	1.57	2.58	0.65	0.70
2	1.62	2.52	0.84	0.93
4	1.96	3.24	0.97	0.97
5	2.06	1.88	0.79	0.76
6	1.31	1.58	0.65	0.68
7	3.21	4.02	0.96	0.99
8	2.18	3.79	0.65	0.83
9	1.44	1.28	0.89	0.77
11	2.58	4.34	1.00	1.00
12	1.65	2.45	0.86	0.89
13	1.73	3.15	0.73	0.96
14	2.26	2.85	0.76	0.79

Table C.15. Quadriceps cross sectional area (cm²) data.

	Injured Limb					Uninjured Limb				
Subject ID	VL	RF	VM	VI	Quad	VL	RF	VM	VI	Quad
1	29.53	8.27	12.2	27.03	77.03	30.85	14.02	14.67	32.36	91.89
2	27.68	10.07	10.12	23.03	70.9	32.85	8.89	13.46	27.52	82.72
4	21.83	7.54	8.55	21.35	59.27	22.18	8.93	10.85	21.55	66.51
5	16.83	6.63	9.14	16.23	48.81	21.18	5.96	10.31	18.81	56.27
6	33.27	9.01	13.58	21.77	77.63	30.69	8.96	17.74	25.28	82.67
7	26.84	9	12.56	24.3	72.7	27.7	11.91	12.32	29.24	81.17
8	35.02	11.69	12.62	28.02	87.35	50.67	9.79	17.47	39.17	117.11
9	17.63	5.61	10.46	15.91	49.61	19.93	5.78	15.68	21.34	62.73
11	13.03	4.06	5.51	18	40.4	19.86	6.88	9.49	22.63	58.85
12	19.14	7.68	8.01	17.05	51.86	26.62	9.65	12.5	20.18	68.94
13	36.75	16.81	10.15	38.21	101.92	45.35	10.44	19.69	38.67	114.41
14	23.87	9.52	12.13	35.56	81.08	29.79	11.82	13.89	35.52	91.02

VL= vastus lateralis; RF= rectus femoris; VM= vastus medialis; VI= vastus intermedius; Quad= overall muscle cross sectional area (e.g., sum total of individual muscle cross sectional areas for slice with the greatest cross sectional area)

AIM 2 STATISTICAL OUTPUT

Hierarchical Regression- CAR entered first

Variables Entered/Removed[b]

Model	Variables Entered	Variables Removed	Method
1	Injured limb peak CAR across 3 trials[a]	.	Enter
2	Injured limb overall peak quad CSA across all slices[a]	.	Enter

a. All requested variables entered.

b. Dependent Variable: Injured limb peak MVIC across 3 trials (Nm/kg)

Model Summary[c]

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate	Change Statistics				
					R Square Change	F Change	df1	df2	Sig. F Change
1	.396[a]	.157	.072	.51991	.157	1.856	1	10	.203
2	.404[b]	.164	-.022	.54573	.007	.076	1	9	.789

a. Predictors: (Constant), Injured limb peak CAR across 3 trials

b. Predictors: (Constant), Injured limb peak CAR across 3 trials, Injured limb overall peak quad CSA across all slices

c. Dependent Variable: Injured limb peak MVIC across 3 trials (Nm/kg)

ANOVA[c]

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	.502	1	.502	1.856	.203[a]
	Residual	2.703	10	.270		
	Total	3.205	11			
2	Regression	.524	2	.262	.880	.448[b]
	Residual	2.680	9	.298		
	Total	3.205	11			

a. Predictors: (Constant), Injured limb peak CAR across 3 trials

b. Predictors: (Constant), Injured limb peak CAR across 3 trials, Injured limb overall peak quad CSA across all slices

c. Dependent Variable: Injured limb peak MVIC across 3 trials (Nm/kg)

Coefficients[a]

Model	Unstandardized Coefficients		Standardized Coefficients	t	Sig.
	B	Std. Error	Beta		
1 (Constant)	.557	1.044		.533	.605
Injured limb peak CAR across 3 trials	1.692	1.242	.396	1.362	.203
2 (Constant)	.240	1.586		.152	.883
Injured limb peak CAR across 3 trials	1.851	1.425	.433	1.299	.226
Injured limb overall peak quad CSA across all slices	.003	.010	.092	.276	.789

a. Dependent Variable: Injured limb peak MVIC across 3 trials (Nm/kg)

Excluded Variables[b]

Model		Beta In	t	Sig.	Partial Correlation	Collinearity Statistics: Tolerance
1	Injured limb overall peak quad CSA across all slices	.092[a]	.276	.789	.092	.837

a. Predictors in the Model: (Constant), Injured limb peak CAR across 3 trials

b. Dependent Variable: Injured limb peak MVIC across 3 trials (Nm/kg)

Residuals Statistics[a]

	Minimum	Maximum	Mean	Std. Deviation	N
Predicted Value	1.6534	2.2374	1.9642	.21832	12
Residual	-.58180	1.01468	.00000	.49363	12
Std. Predicted Value	-1.423	1.251	.000	1.000	12
Std. Residual	-1.066	1.859	.000	.905	12

a. Dependent Variable: Injured limb peak MVIC across 3 trials (Nm/kg)

General Linear Model

Within-Subjects Factors

Measure	leg	Dependent Variable
MVIC	1	Inj_MVIC
	2	Un_MVIC
CAR	1	Inj_CAR
	2	Un_CAR
QUAD	1	Inj_Quad_Comp
	2	Un_Quad_Comp

Descriptive Statistics

	Mean	Std. Deviation	N
Injured limb peak MVIC across 3 trials (Nm/kg)	1.9642	.53976	12
Un_MVIC	2.8067	.95597	12
Injured limb peak CAR across 3 trials	.8317	.12619	12
Un_CAR	.7883	.13953	12
Injured limb overall peak quad CSA across all slices	68.2133	18.35317	12
Un_Quad_Comp	81.1908	20.08139	12

Tests of Within-Subjects Effects

Univariate Tests

Source	Measure		Type III Sum of Squares	df	Mean Square	F	Sig.	Noncent. Parameter	Observed Power[a]
leg	MVIC	Sphericity Assumed	4.259	1	4.259	21.140	.001	21.140	.986
		Greenhouse-Geisser	4.259	1.000	4.259	21.140	.001	21.140	.986
		Huynh-Feldt	4.259	1.000	4.259	21.140	.001	21.140	.986
		Lower-bound	4.259	1.000	4.259	21.140	.001	21.140	.986
	CAR	Sphericity Assumed	.011	1	.011	1.175	.301	1.175	.168
		Greenhouse-Geisser	.011	1.000	.011	1.175	.301	1.175	.168
		Huynh-Feldt	.011	1.000	.011	1.175	.301	1.175	.168
		Lower-bound	.011	1.000	.011	1.175	.301	1.175	.168
	QUAD	Sphericity Assumed	1010.493	1	1010.493	45.417	.000	45.417	1.000
		Greenhouse-Geisser	1010.493	1.000	1010.493	45.417	.000	45.417	1.000
		Huynh-Feldt	1010.493	1.000	1010.493	45.417	.000	45.417	1.000

		Lower-bound	1010.493	1.000	1010.493	45.417	.000	45.417	1.000
Error(leg)	MVIC	Sphericity Assumed	2.216	11	.201				
		Greenhouse-Geisser	2.216	11.000	.201				
		Huynh-Feldt	2.216	11.000	.201				
		Lower-bound	2.216	11.000	.201				
	CAR	Sphericity Assumed	.105	11	.010				
		Greenhouse-Geisser	.105	11.000	.010				
		Huynh-Feldt	.105	11.000	.010				
		Lower-bound	.105	11.000	.010				
	QUAD	Sphericity Assumed	244.741	11	22.249				
		Greenhouse-Geisser	244.741	11.000	22.249				
		Huynh-Feldt	244.741	11.000	22.249				
		Lower-bound	244.741	11.000	22.249				

a. Computed using alpha = .05

Tests of Between-Subjects Effects

Transformed Variable:Average

Source	Measure	Type III Sum of Squares	df	Mean Square	F	Sig.	Noncent. Parameter	Observed Power[a]
Intercept	MVIC	136.565	1	136.565	136.054	.000	136.054	1.000
	CAR	15.746	1	15.746	610.111	.000	610.111	1.000
	QUAD	133929.630	1	133929.630	186.570	.000	186.570	1.000
Error	MVIC	11.041	11	1.004				
	CAR	.284	11	.026				
	QUAD	7896.370	11	717.852				

a. Computed using alpha = .05

Estimated Marginal Means

1. Grand Mean

Measure	Mean	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
MVIC	2.385	.205	1.935	2.836
CAR	.810	.033	.738	.882
QUAD	74.702	5.469	62.665	86.739

2. leg

Estimates

Measure	leg	Mean	Std. Error	95% Confidence Interval	
				Lower Bound	Upper Bound
MVIC	1	1.964	.156	1.621	2.307
	2	2.807	.276	2.199	3.414
CAR	1	.832	.036	.751	.912
	2	.788	.040	.700	.877
QUAD	1	68.213	5.298	56.552	79.874
	2	81.191	5.797	68.432	93.950

AIM 3 SUPPLEMENTAL DATA

Table C.16. ACLr subject demographic data.

Subject ID	Sex	Injured Limb	Age	Height (m)	Mass (kg)	Sport at Time of Injury	Mechanism of Injury*	Meniscal Damage at Injury†	Graft Type	Days from Injury to Surgery	Tegner‖ (Pre-Injury)	Tegner (Current)	IKDC# (Current)
1	F	R	23	1.6	74.84	sledding	put foot out to stop sled	None	PT	249	9	7	81.68
3	M	L	16	1.78	89.81	basketball	going up for layup	Medial	PT	65	10	9	65.52
4	F	L	22	1.7	77.11	skiing	turning	None	PT	93	8	8	89.66
8	M	R	26	1.75	75.92	soccer	cutting	Lateral§	PT	56	5	2	81.61
9	M	R	17	1.78	58.97	soccer	cutting	None	PT	42	9	9	n/a
10	M	R	18	1.91	83.91	football	spin move	None	PT	24	9	7	90.8
11	M	R	16	1.8	81.65	football	tackled	Lateral	PT	48	10	9	90.8
12	F	L	29	1.73	104.33	softball	stretched to beat throw	Medial	PT	135	7	4	80.46
13	M	R	27	1.7	65.77	ultimate Frisbee	cutting	None	PT	12	10	10	100
18	M	R	22	1.82	90.72	basketball	landed on someone's foot	Lateral‡	STG	196	9	5	72.41
19	M	R	26	1.8	77.11	skiing	turning	None	STG	51	7	3	55.17
20	M	L	25	1.78	67.59	soccer	cutting	None	STG	136	7	6	79.31
22	F	L	27	1.57	63.5	softball	stepped in hole running	None	STG	50	6	7	89.66
23	F	R	16	1.71	78.84	basketball	playing defense	None	STG	67	9	9	90.8
24	F	R	14	1.74	61.23	basketball	cutting	Medial	PT	29	9	9	97.7
26	M	L	21	1.85	81.65	soccer	cutting	None	STG	55	9	7	82.76
28	F	R	19	1.73	68.04	soccer	cutting	Lateral & Medial‡	PT	47	9	8	93.1

M= male; F= female; L= left; R= right; PT= patellar tendon; STG= semitendinosus/gracilis; IKDC= International Knee Documentation Society

* As dictated by the subject

†Meniscal damage was determined from diagnostic MRI report. ‡Indicates subject had meniscal debridement/repair concurrent with ACL reconstruction. §Indicates subject had meniscectomy concurrent with ACL reconstruction. All other subjects had no treatment of meniscal injury. ‖Tegner scale is scored from 0-10, with 10 representing participation in competitive sports at the national/elite level. #IKDC scored from 0-100, with 100 representing no pain/disability.

Table C.17. Control subject demographic data.

Subject ID	Sex	Age	Height (m)	Mass (kg)	Tegner Score*	IKDC Score†
C1	M	30	1.75	68.04	6	100
C2	F	19	1.7	62.14	5	94.25
C3	F	23	1.6	61.23	7	100
C5	F	20	1.7	69.4	6	94.25
C6	M	19	1.75	88.9	4	96.55
C8	F	20	1.68	72.57	5	100
C9	F	28	1.63	70.31	6	100
C10	M	27	1.91	77.11	6	100
C11	F	18	1.6	56.7	5	100
C12	M	20	1.71	61.23	7	100
C13	F	30	1.63	49.9	7	100
C14	F	23	1.7	61.23	5	98.85
C18	F	25	1.8	86.18	6	100
C19	F	21	1.8	70.31	5	100
C20	M	28	1.78	72.57	5	100
C21	F	23	1.68	63.5	7	100

* Tegner scale is scored from 0-10, with 10 representing participation in competitive sports at the national/elite level. †IKDC scored from 0-100, with 100 representing no pain/disability.

Table C.18. ACLr subject knee effusion and thigh circumference data.

	Knee Effusion (cm)				Thigh Circumference (cm)*					
	Suprapatellar†		Mid-Patella		6 cm		12 cm		18 cm	
Subject ID	Injured	Uninjured	Injured	Uninjured	Injured	Uninjured	Injured	Uninjured	Injured	Uninjured
1	41.8	38.7	39.1	42.0	45.7	46.9	53.8	53.5	57.8	56.6
3	44.5	40.8	42.2	44.3	47.3	47.8	53.4	54.5	57.5	58.6
4	44.5	40.0	40.7	43.0	48.0	47.4	54.0	55.2	61.4	61.9
8	37.4	36.0	36.5	36.5	38.8	39.8	44.8	45.6	50.5	51.1
9	34.4	34.3	35.1	33.8	36.4	37.2	41.7	42.5	46.1	46.8
10	38.8	37.9	38.9	38.5	41.5	41.0	49.0	47.8	53.4	53.0
11	41.1	38.4	38.0	40.5	46.3	47.0	55.5	55.1	60.2	59.5
12	44.5	42.7	50.5	47.1	54.0	52.0	60.8	59.5	65.7	64.7
13	36.1	36.0	35.7	36.0	40.0	39.0	47.1	47.0	51.8	52.4
18	42.5	40.5	40.5	42.9	44.9	46.2	49.2	52.0	55.5	57.0
19	39.5	37.9	37.5	40.9	40.7	43.8	45.7	50.0	50.6	54.3
20	34.0	33.4	33.0	34.0	37.0	37.7	42.1	44.4	48.0	50.3
22	43.2	40.5	41.0	44.2	46.6	48.4	54.5	55.0	59.8	60.8
23	39.8	37.5	36.8	40.3	43.3	44.9	48.8	51.9	53.7	56.2
24	36.2	35.6	35.2	37.0	39.0	41.0	44.0	45.5	49.9	51.0
26	39.0	38.3	39.0	38.9	42.0	43.2	48.5	49.7	52.0	53.8
28	38.2	40.5	56.0	38.5	41.0	54.5	44.0	46.0	50.4	52.0

*Measurements were taken 6, 12, and 18 cm proximal to the superior pole of the patella

†Measured 1 cm proximal to the superior pole of the patella with the subject in supine

Table C.19. ACLr calf girth data (cm).

	5 cm Proximal		10 cm Proximal		Maximum		5 cm Distal		10 cm Distal	
Subject ID	Injured	Uninjured	Injured	Uninjured	Injured	Uninjured	Injured	Uninjured	Injured	Uninjured
1	40.8	40.0	38.8	38.0	41.1	41.5	34.2	35.7	28.8	30.5
3	42.0	42.0	38.2	37.7	42.5	44.6	37.5	38.0	31.2	31.0
4	39.2	40.2	36.5	37.1	41.2	40.8	35.9	34.3	31.0	29.2
8	35.1	35.3	32.5	32.8	37.2	36.8	31.2	33.0	27.4	27.8
9	33.4	32.3	30.7	31.2	35.0	34.3	31.8	33.0	26.0	27.4
10	36.6	38.2	33.5	33.7	38.0	38.4	38.3	34.3	30.5	30.5
11	38.8	39.9	36.4	46.5	41.4	42.0	36.0	38.6	29.0	29.9
12	48.4	45.6	47.2	43.8	46.5	46.9	40.0	39.8	33.1	33.4
13	33.0	34.0	31.0	30.8	35.7	35.6	31.4	31.7	28.2	28.2
18	39.5	42.0	36.9	37.5	41.4	43.0	38.9	38.2	31.3	31.0
19	38.6	38.2	33.9	34.0	40.7	41.0	37.9	37.0	29.5	30.4
20	32.9	32.8	28.9	29.3	34.3	35.4	31.3	31.5	26.1	27.3
22	42.0	41.0	36.0	37.3	41.4	40.1	37.7	38.3	32.0	32.1
23	36.5	38.7	34.8	35.4	39.0	39.5	36.5	34.4	31.8	30.2
24	35.2	36.5	31.8	32.5	37.0	38.2	34.5	33.5	29.6	28.5
26	35.4	37.2	33.0	33.3	37.2	38.5	33.1	32.7	28.1	27.8
28	50.2	40.5	36.9	36.2	40.8	40.4	36.0	37.1	30.2	30.2

Measurements were taken with the subject lying in supine and the knee flexed so the foot was flat on the table. The distance from the lateral knee joint line to the tip of the lateral malleolus was measured. One-third of this distance was determined and a mark 1/3 of the way from the lateral joint line to the lateral malleolus was made to signify the spot of maximum calf girth. Measurements were recorded here, as well as 5 and 10 cm proximal and distal to this location.

Table C.20. Control subject knee effusion and thigh circumference data.

	Knee Effusion (cm)				Thigh Circumference (cm)*					
	Suprapatellar†		Mid-Patella		6 cm		12 cm		18 cm	
Subject ID	Test Limb	Contralateral Limb	Test Limb	Contralateral Limb	Test Limb	Contralateral Limb	Test Limb	Contralateral Limb	Test Limb	Contralateral Limb
C1	35.7	36.5	36.0	36.3	39.5	41.0	45.5	47.0	49.5	51.2
C2	47.5	37.4	36.4	36.7	41.0	39.5	45.2	43.9	51.0	49.2
C3	37.3	38.5	35.8	36.8	42.7	43.0	49.9	50.4	53.5	51.8
C5	40.3	40.5	37.9	39.5	45.5	46.0	53.0	52.7	56.5	56.0
C6	43.8	42.6	41.1	40.5	49.3	49.2	56.9	56.0	60.6	60.4
C8	44.0	44.4	41.0	41.2	48.7	49.0	54.1	54.4	59.7	58.2
C9	42.7	42.1	39.3	39.8	46.9	47.5	51.5	52.7	56.0	55.7
C10	37.0	37.0	36.9	37.4	40.3	40.4	46.8	46.5	50.6	50.0
C11	36.0	35.7	35.0	35.5	41.0	39.0	46.3	45.0	49.8	48.6
C12	34.1	33.8	33.6	33.3	39.0	38.5	45.5	44.3	48.1	48.3
C13	33.8	33.9	33.5	33.3	38.3	38.5	42.5	44.5	46.4	46.4
C14	38.2	37.8	36.8	36.6	42.0	41.0	45.5	44.8	51.0	50.3
C18	42.5	43.1	40.4	40.2	47.0	48.2	51.7	52.2	57.0	57.3
C19	39.5	39.0	38.5	37.5	42.0	41.0	45.2	44.0	49.0	48.5
C20	37.1	38.0	36.4	37.7	42.0	42.5	46.7	48.5	51.6	52.5
C21	36.6	37.8	36.5	36.3	41.5	43.5	48.5	50.5	54.4	54.5

*Measurements were taken 6, 12, and 18 cm proximal to the superior pole of the patella

†Measured 1 cm proximal to the superior pole of the patella with the subject in supine

Table C.21. Control subject calf girth data (cm).

	5 cm Proximal		10 cm Proximal		Maximum		5 cm Distal		10 cm Distal	
Subject ID	Test Limb	Contralateral Limb	Test Limb	Contralateral Limb	Test Limb	Contralateral Limb	Test Limb	Contralateral Limb	Test Limb	Contralateral Limb
C1	35.5	35.8	32.0	33.0	36.8	37.9	31.0	33.5	26.1	27.7
C2	34.0	34.8	33.0	32.7	33.5	32.9	29.8	28.8	24.3	24.3
C3	34.7	35.9	31.8	32.8	36.9	37.5	33.4	33.0	27.6	27.7
C5	38.0	38.6	35.2	35.5	38.3	38.0	33.1	33.0	27.0	27.1
C6	41.8	42.7	38.8	40.0	43.2	43.4	37.8	37.9	32.9	32.0
C8	43.3	44.0	39.9	38.4	42.2	43.4	38.2	38.7	33.3	33.8
C9	36.5	36.5	34.8	33.4	38.7	37.8	35.6	34.8	29.5	28.9
C10	35.4	35.0	31.5	31.2	37.7	37.3	34.5	35.3	28.1	29.0
C11	33.5	35.5	32.0	32.0	36.3	35.7	33.1	30.6	27.0	24.8
C12	32.0	32.7	32.2	30.6	35.7	35.2	31.8	29.6	27.2	25.6
C13	32.0	32.8	30.0	30.0	33.8	34.5	28.5	28.5	25.0	24.9
C14	36.6	36.0	33.9	33.0	37.9	38.0	35.8	35.4	31.1	31.0
C18	41.5	41.7	38.8	36.7	41.8	41.3	37.3	38.2	32.7	32.5
C19	35.8	37.2	33.6	34.2	36.5	37.0	32.5	31.9	28.8	27.7
C20	35.1	36.5	32.6	33.0	36.5	37.0	31.3	33.2	26.0	28.0
C21	36.0	37.8	33.3	33.6	37.0	38.3	33.9	33.4	28.5	28.8

Measurements were taken with the subject lying in supine and the knee flexed so the foot was flat on the table. The distance from the lateral knee joint line to the tip of the lateral malleolus was measured. One-third of this distance was determined and a mark 1/3 of the way from the lateral joint line to the lateral malleolus was made to signify the spot of maximum calf girth. Measurements were recorded here, as well as 5 and 10 cm proximal and distal to this location.

Table C.22. ACLr subject pre- and post-fatigue joint rotation (degrees) data.

	IC Knee Sagittal Rotation				IC Knee Frontal Rotation				PS Knee Sagittal Rotation				PS Knee Frontal Rotation			
	Pre-Fatigue		Post-Fatigue		Pre-Fatigue		Post-Fatigue		Pre-Fatigue		Post-Fatigue		Pre-Fatigue		Post-Fatigue	
Subject ID	I	U	I	U	I	U	I	U	I	U	I	U	I	U	I	U
1	-11.86	-7.66	-12.45	4.23	-2.63	-53.43	-1.91	24.64	-45.42	-11.06	-43.75	2.54	-2.63	4.21	-4.75	1.97
3	-20.75	-9.65	-5.92	6.61	-4.30	-41.44	1.44	26.42	-40.72	-7.98	-43.14	7.03	-7.16	6.61	-5.30	6.93
4	-7.49	-19.64	-11.39	4.41	-1.08	-58.22	-2.98	4.41	-47.43	-14.42	-39.15	-0.77	-11.55	-4.28	-9.55	-6.78
8	-8.08	-16.89	-3.46	-3.87	-1.51	-61.06	-0.81	-2.70	-49.71	-10.20	-48.56	-3.60	-7.77	-13.69	-5.74	-13.19
9	-15.58	-17.22	-10.60	-2.89	-3.61	-56.21	-1.98	-2.89	-54.28	-10.70	-52.22	-3.33	-13.74	-12.11	-9.97	-13.54
10	-6.83	-10.37	-8.31	-1.48	1.49	-47.01	1.19	-0.80	-36.06	-8.32	-42.37	-0.28	-5.90	-6.93	-6.27	-4.07
11	-16.43	-17.70	-18.09	-6.45	-7.49	-60.95	-5.65	-6.45	-56.88	-12.99	-50.21	-4.14	-17.64	-18.20	-14.70	-14.48
12	-10.30	-15.28	-8.93	-5.04	-4.94	-55.09	-4.38	-4.19	-36.50	-14.57	-36.31	-5.05	-7.48	-8.58	-7.49	-9.09
13	-16.59	-29.77	-19.83	-0.57	-8.00	-70.61	-9.88	-0.57	-50.66	-23.57	-53.44	1.48	-15.52	-8.83	-18.63	-6.61
18	-11.52	-12.87	-11.55	-2.23	-5.96	-65.09	-7.88	-1.95	-42.49	-12.95	-49.04	-3.37	-15.88	-11.96	-27.59	-13.13
19	-0.29	-1.30	1.47	-0.19	-3.65	-58.88	-2.43	-0.19	-22.89	3.50	-32.72	1.39	-14.51	-10.89	-15.26	-5.28
20	-12.31	0.15	-9.34	1.91	-2.51	-47.06	-1.55	1.91	-72.60	0.97	-47.02	3.91	-24.62	-19.60	-12.71	-14.17
22	-12.90	-16.16	-14.81	-3.52	-1.07	-45.40	-1.14	1.91	-37.28	-16.55	-37.07	-3.10	-7.35	-6.85	-4.42	-5.76
23	-6.02	-12.64	-10.62	-2.70	-3.40	-63.47	-4.21	-2.70	-46.23	-14.77	-49.99	-2.67	-9.02	-10.71	-8.68	-10.03
24	-12.37	-22.00	-11.48	-4.96	-5.79	-65.48	-5.13	-4.96	-48.34	-24.28	-42.32	-5.72	-23.37	-15.21	-23.75	-12.95
26	-1.40	-7.78	-3.59	-0.82	1.13	-65.29	0.72	-0.82	-40.44	-6.17	-37.22	-0.31	-8.60	-12.54	-8.41	-8.68
28	-5.00	-25.41	-6.94	-5.47	-1.88	-65.93	-0.89	-4.82	-44.44	-25.29	-44.67	-3.16	-13.77	-14.42	-7.74	-10.77

IC= initial contact; PS= peak stance

I= injured; U= uninjured

(+) rotations signify extension and abduction

Table C.23. Control subject pre- and post-fatigue joint rotation (degrees) data.

	IC Knee Sagittal Rotation				IC Knee Frontal Rotation				PS Knee Sagittal Rotation				PS Knee Frontal Rotation			
	Pre-Fatigue		Post-Fatigue		Pre-Fatigue		Post-Fatigue		Pre-Fatigue		Post-Fatigue		Pre-Fatigue		Post-Fatigue	
Subject ID	T	C	T	C	T	C	T	C	T	C	T	C	T	C	T	C
C1	-11.97	-11.06	-5.44	-9.07	-6.53	-52.93	-3.78	-6.53	-61.20	-63.43	-51.39	-52.93	-18.45	-23.00	-14.48	-10.39
C2	-13.95	-17.31	-14.28	-5.24	-3.61	-45.49	-3.53	-3.61	-53.89	-56.17	-52.47	-45.49	-16.84	-12.84	-17.67	-13.57
C3	-11.20	-16.89	-13.44	-34.63	0.94	-54.97	1.15	0.94	-45.75	-49.76	-50.27	-54.97	-13.20	-11.15	-13.89	-4.73
C5	-12.26	-12.00	-7.17	-9.37	-1.84	-42.39	-1.20	-1.84	-57.20	-49.34	-50.69	-42.39	-10.27	-9.28	-6.69	-6.79
C6	-12.40	-10.23	-18.75	-10.43	-2.65	-65.58	-1.55	-2.65	-70.26	-68.39	-74.22	-65.58	-13.83	-14.05	-10.04	-8.11
C8	-16.79	-11.36	-11.41	-14.17	-6.53	-42.42	-5.93	-6.53	-56.95	-48.11	-39.87	-42.42	-17.83	-19.07	-7.45	-13.69
C9	-23.54	-16.38	-16.85	-14.43	-2.57	-51.02	-2.57	-2.57	-55.39	-51.90	-52.04	-51.02	-8.36	-9.66	-6.05	-9.66
C10	-16.65	-20.16	-12.99	-12.73	-2.70	-48.84	-2.68	-2.70	-50.90	-50.26	-47.35	-48.84	-17.96	-10.14	-15.20	-12.86
C11	-14.42	-11.31	-11.76	-3.05	-0.95	-36.68	1.71	-0.95	-63.23	-57.15	-49.05	-36.68	-7.64	-10.58	-6.89	-3.38
C12	-16.03	-13.04	-3.05	-10.74	1.09	-58.83	1.40	1.09	-55.05	-62.60	-36.68	-58.83	-8.37	-6.82	-5.79	-6.21
C13	-22.98	-19.95	-9.84	-20.72	-6.07	-63.43	-5.05	-6.07	-69.41	-60.21	-56.88	-63.43	-7.79	-11.56	-8.05	-10.69
C14	-10.40	-7.02	-7.07	-4.40	-0.87	-43.45	-0.82	-0.87	-52.14	-40.18	-36.03	-43.45	-20.05	-16.11	-13.30	-15.41
C18	-11.94	-16.74	-6.93	-18.39	-6.50	-43.21	-6.25	-6.50	-50.32	-51.80	-36.91	-43.21	-25.67	-22.54	-18.19	-17.97
C19	-12.59	-16.48	-8.69	-19.01	-3.30	-57.66	-1.96	-3.30	-53.40	-66.68	-28.61	-57.66	-6.09	-11.79	-3.47	-14.91
C20	-6.83	-10.15	-8.58	-3.40	2.46	-49.59	2.92	2.46	-52.25	-57.21	-48.70	-49.59	-2.03	-5.14	-4.48	-7.91
C21	-14.87	-10.44	-14.18	-9.48	-1.99	-56.37	-1.99	-1.99	-58.65	-61.86	-59.28	-56.37	-23.74	-16.27	-23.18	-13.40

IC= initial contact; PS= peak stance

T=test limb; C= contralateral limb

(+) rotations signify extension and abduction

Table C.24. ACLr subjects pre- and post-fatigue external joint moments (Nm/kg*m).

	PS Knee Sagittal Moment				PS Knee Frontal Moment			
	Pre-Fatigue		Post-Fatigue		Pre-Fatigue		Post-Fatigue	
Subject ID	I	U	I	U	I	U	I	U
1	-0.80	-1.11	-0.58	0.46	-0.19	-0.27	-0.24	-0.25
3	-1.22	-0.83	-0.92	1.12	-0.14	-0.27	-0.15	-0.35
4	-1.15	-1.46	-0.84	0.57	-0.72	-0.13	-0.53	-0.18
8	-1.06	-1.62	-1.11	0.12	-0.20	-0.48	-0.14	-0.45
9	-1.49	-2.13	-1.22	0.32	-0.34	-0.17	-0.18	-0.20
10	-1.32	-1.87	-1.30	0.18	-0.11	-0.28	-0.09	-0.30
11	-1.16	-1.24	-0.93	0.19	-0.34	-0.33	-0.29	-0.31
12	-0.97	-1.46	-1.32	0.43	-0.50	-0.25	-0.34	-0.23
13	-1.64	-2.14	-1.39	0.03	-0.37	-0.60	-0.75	-0.38
18	-1.03	-1.51	-1.06	-0.01	-0.27	-0.36	-0.16	-0.64
19	-0.56	-1.56	-0.46	0.05	-0.15	-0.33	-0.13	-0.26
20	-1.21	-1.66	-1.24	0.32	-0.20	-0.22	-0.16	-0.11
22	-1.03	-2.12	-0.77	0.61	-0.23	-0.40	-0.20	-0.26
23	-1.25	-2.02	-1.30	0.16	-0.18	-0.39	-0.13	-0.22
24	-0.93	-1.97	-0.96	0.07	-0.29	-0.58	-0.48	-0.55
26	-0.57	-1.30	-0.53	0.20	-0.30	-0.31	-0.51	-0.27
28	-1.32	-2.31	-0.99	0.26	-0.45	-0.70	-0.28	-0.65

PS= peak stance

I= injured; U= uninjured

(+) moments signify extension and abduction

Table C.25. Control subjects pre- and post-fatigue external joint moments (Nm/kg*m).

	PS Knee Sagittal Moment				PS Knee Frontal Moment			
	Pre-Fatigue		Post-Fatigue		Pre-Fatigue		Post-Fatigue	
Subject ID	T	C	T	C	T	C	T	C
C1	-1.54	-1.53	0.07	-1.10	-0.61	-0.62	-0.40	-0.40
C2	-1.95	-1.86	0.06	-1.65	-0.51	-0.77	-0.37	-0.60
C3	-2.15	-2.29	0.14	-1.62	-0.31	-0.71	-0.16	-0.45
C5	-1.57	-1.40	0.29	-0.95	-0.26	-0.43	-0.15	-0.50
C6	-1.89	-1.79	0.27	-1.53	-0.45	-0.57	-0.16	-0.30
C8	-1.88	-1.10	0.08	-1.01	-0.40	-0.30	-0.45	-0.21
C9	-1.76	-1.53	0.10	-1.21	-0.34	-0.35	-0.44	-0.40
C10	-1.40	-1.38	0.20	-1.47	-0.26	-0.23	-0.21	-0.22
C11	-1.75	-1.47	0.39	-1.03	-0.07	-0.77	-0.20	-0.33
C12	-1.92	-1.73	0.09	-1.68	-0.41	-0.17	-0.43	-0.23
C13	-1.98	-1.86	0.10	-1.68	-0.62	-0.60	-0.56	-0.43
C14	-1.85	-1.63	0.06	-1.06	-0.52	-0.62	-0.30	-0.32
C18	-1.28	-1.56	0.32	-0.80	-0.79	-0.48	-0.33	-0.36
C19	-1.51	-1.50	0.03	-1.03	-0.41	-0.28	-0.15	-0.24
C20	-1.56	-1.66	0.44	-0.94	-0.16	-0.22	-0.11	-0.39
C21	-1.81	-1.88	0.20	-1.52	-0.70	-0.39	-0.59	-0.13

PS= peak stance

T= test limb; C= contralateral limb

(+) moments signify extension and abduction

Table C.26. ACLr subjects pre- and post-fatigue knee extension strength (Nm/kg) and central activation ratio data.

	Knee Extension MVIC (Nm/kg)				Quadriceps CAR			
	Pre-Fatigue		Post-Fatigue		Pre-Fatigue		Post-Fatigue	
Subject ID	Injured	Uninjured	Injured	Uninjured	Injured	Uninjured	Injured	Uninjured
1	1.47	2.27	1.50	1.72	0.75	0.89	0.76	0.85
3	1.84	2.35	1.21	1.21	0.67	0.82	0.62	0.66
4	1.85	2.03	1.09	1.11	0.80	0.77	0.67	0.58
8	2.34	3.28	1.71	2.19	0.95	0.98	0.92	0.97
9	2.37	3.17	2.09	3.01	0.97	0.95	0.96	0.95
10	2.15	3.24	2.09	1.95	0.83	0.96	0.79	0.81
11	2.68	3.03	1.98	2.73	0.95	0.92	0.92	0.90
12	1.23	2.64	1.26	2.10	0.89	0.96	0.88	0.95
13	3.10	4.25	1.96	3.17	0.85	0.95	0.77	0.87
18	1.36	2.28	1.19	1.24	0.59	0.67	0.56	0.54
19	2.06	4.15	1.46	2.43	0.86	0.89	0.74	0.77
20	2.91	2.88	2.50	1.82	0.86	0.85	0.89	0.78
22	1.93	2.39	1.14	1.30	0.83	0.83	0.75	0.71
23	1.54	1.54	1.86	1.10	0.67	0.67	0.69	0.72
24	1.48	1.48	0.80	1.15	0.75	0.68	0.69	0.66
26	1.55	3.57	1.29	1.58	0.74	0.96	0.66	0.84
28	2.67	3.60	1.75	2.27	0.99	0.99	0.99	0.91

Table C.27. Control subjects pre- and post-fatigue knee extension strength (Nm/kg) and central activation ratio data.

	Knee Extension MVIC (Nm/kg)				Quadriceps CAR			
	Pre-Fatigue		Post-Fatigue		Pre-Fatigue		Post-Fatigue	
Subject ID	Test Limb	Contralateral	Test Limb	Contralateral	Test Limb	Contralateral	Test Limb	Contralateral
C1	1.71	1.71	1.46	0.98	0.66	0.67	0.90	0.76
C2	1.52	1.80	1.09	1.44	0.72	0.80	0.68	0.74
C3	2.05	2.10	1.39	1.67	0.83	0.88	0.76	0.82
C5	2.62	2.42	0.93	1.12	0.86	0.90	0.50	0.61
C6	3.76	3.86	2.02	2.72	0.89	0.86	0.65	0.79
C8	1.81	1.82	1.30	1.27	0.93	0.99	0.96	0.95
C9	2.77	2.72	1.97	2.09	1.00	0.99	0.96	0.98
C10	3.15	3.44	2.53	2.61	0.97	0.99	0.94	0.98
C11	2.75	2.21	1.38	1.11	0.95	0.92	0.74	0.76
C12	2.11	2.21	2.15	1.98	0.82	0.82	0.84	0.96
C13	5.04	3.37	2.67	2.00	0.99	1.00	0.97	0.98
C14	2.04	2.66	1.11	1.59	0.98	0.99	0.95	0.92
C18	1.57	1.98	1.40	1.61	0.95	0.97	0.97	0.95
C19	3.12	2.84	1.55	1.19	0.90	0.90	0.79	0.67
C20	3.02	3.09	0.94	1.54	0.94	0.91	0.70	0.86
C21	3.08	3.02	1.81	2.20	0.89	0.85	0.75	0.86

AIM 3 STATISTICAL OUTPUT

General Linear Model- 2x2 Repeated Measures (Group x Time) ANOVA

Within-Subjects Factors

Measure	time	Dependent Variable
IC_KS_ROT	1	Pre_IC_Inj_KSrot
	2	Post_IC_Inj_KSrot
IC_KF_ROT	1	Pre_IC_Inj_KFrot
	2	Post_IC_Inj_KFrot
PS_KS_ROT	1	Pre_Inj_KSrot
	2	Post_Inj_KSrot
PS_KF_ROT	1	Pre_Inj_KFrot
	2	Post_Inj_KFrot
PS_KS_TRQ	1	Pre_Inj_KStrq
	2	Post_Inj_KStrq

PS_KF_TRQ	1	Pre_Inj_KFtrq
	2	Post_Inj_KFtrq
MVIC_AVG	1	Avg_MVIC
	2	Avg_MVIC_Post
CAR_AVG	1	Avg_CAR
	2	Avg_CAR_Post

Tests of Within-Subjects Effects

Univariate Tests

Source	Measure		Type III Sum of Squares	df	Mean Square	F	Sig.	Noncent. Parameter	Observed Power[a]
time	IC_KS_ROT	Sphericity Assumed	73.760	1	73.760	6.261	.018	6.261	.679
		Greenhouse-Geisser	73.760	1.000	73.760	6.261	.018	6.261	.679
		Huynh-Feldt	73.760	1.000	73.760	6.261	.018	6.261	.679
		Lower-bound	73.760	1.000	73.760	6.261	.018	6.261	.679

IC_KF_ROT	Sphericity Assumed	18.670	1	18.670	8.939	.005	8.939	.825
	Greenhouse-Geisser	18.670	1.000	18.670	8.939	.005	8.939	.825
	Huynh-Feldt	18.670	1.000	18.670	8.939	.005	8.939	.825
	Lower-bound	18.670	1.000	18.670	8.939	.005	8.939	.825
PS_KS_ROT	Sphericity Assumed	398.619	1	398.619	11.744	.002	11.744	.913
	Greenhouse-Geisser	398.619	1.000	398.619	11.744	.002	11.744	.913
	Huynh-Feldt	398.619	1.000	398.619	11.744	.002	11.744	.913
	Lower-bound	398.619	1.000	398.619	11.744	.002	11.744	.913
PS_KF_ROT	Sphericity Assumed	54.035	1	54.035	6.334	.017	6.334	.684
	Greenhouse-Geisser	54.035	1.000	54.035	6.334	.017	6.334	.684
	Huynh-Feldt	54.035	1.000	54.035	6.334	.017	6.334	.684
	Lower-bound	54.035	1.000	54.035	6.334	.017	6.334	.684
PS_KS_TRQ	Sphericity Assumed	1.706	1	1.706	44.943	.000	44.943	1.000

	Greenhouse-Geisser	1.706	1.000	1.706	44.943	.000	44.943	1.000
	Huynh-Feldt	1.706	1.000	1.706	44.943	.000	44.943	1.000
	Lower-bound	1.706	1.000	1.706	44.943	.000	44.943	1.000
PS_KF_TRQ	Sphericity Assumed	.065	1	.065	5.638	.024	5.638	.633
	Greenhouse-Geisser	.065	1.000	.065	5.638	.024	5.638	.633
	Huynh-Feldt	.065	1.000	.065	5.638	.024	5.638	.633
	Lower-bound	.065	1.000	.065	5.638	.024	5.638	.633
MVIC_AVG	Sphericity Assumed	8.981	1	8.981	54.296	.000	54.296	1.000
	Greenhouse-Geisser	8.981	1.000	8.981	54.296	.000	54.296	1.000
	Huynh-Feldt	8.981	1.000	8.981	54.296	.000	54.296	1.000
	Lower-bound	8.981	1.000	8.981	54.296	.000	54.296	1.000
CAR_AVG	Sphericity Assumed	.056	1	.056	10.517	.003	10.517	.881
	Greenhouse-Geisser	.056	1.000	.056	10.517	.003	10.517	.881

		Huynh-Feldt	.056	1.000	.056	10.517	.003	10.517	.881
		Lower-bound	.056	1.000	.056	10.517	.003	10.517	.881
time * Group	IC_KS_ROT	Sphericity Assumed	38.796	1	38.796	3.293	.079	3.293	.420
		Greenhouse-Geisser	38.796	1.000	38.796	3.293	.079	3.293	.420
		Huynh-Feldt	38.796	1.000	38.796	3.293	.079	3.293	.420
		Lower-bound	38.796	1.000	38.796	3.293	.079	3.293	.420
	IC_KF_ROT	Sphericity Assumed	6.124	1	6.124	2.932	.097	2.932	.382
		Greenhouse-Geisser	6.124	1.000	6.124	2.932	.097	2.932	.382
		Huynh-Feldt	6.124	1.000	6.124	2.932	.097	2.932	.382
		Lower-bound	6.124	1.000	6.124	2.932	.097	2.932	.382
	PS_KS_ROT	Sphericity Assumed	208.273	1	208.273	6.136	.019	6.136	.670
		Greenhouse-Geisser	208.273	1.000	208.273	6.136	.019	6.136	.670
		Huynh-Feldt	208.273	1.000	208.273	6.136	.019	6.136	.670
		Lower-bound	208.273	1.000	208.273	6.136	.019	6.136	.670

PS_KF_ROT	Sphericity Assumed	13.228	1	13.228	1.551	.222	1.551	.226
	Greenhouse-Geisser	13.228	1.000	13.228	1.551	.222	1.551	.226
	Huynh-Feldt	13.228	1.000	13.228	1.551	.222	1.551	.226
	Lower-bound	13.228	1.000	13.228	1.551	.222	1.551	.226
PS_KS_TRQ	Sphericity Assumed	.772	1	.772	20.338	.000	20.338	.992
	Greenhouse-Geisser	.772	1.000	.772	20.338	.000	20.338	.992
	Huynh-Feldt	.772	1.000	.772	20.338	.000	20.338	.992
	Lower-bound	.772	1.000	.772	20.338	.000	20.338	.992
PS_KF_TRQ	Sphericity Assumed	.041	1	.041	3.560	.069	3.560	.448
	Greenhouse-Geisser	.041	1.000	.041	3.560	.069	3.560	.448
	Huynh-Feldt	.041	1.000	.041	3.560	.069	3.560	.448
	Lower-bound	.041	1.000	.041	3.560	.069	3.560	.448
MVIC_AVG	Sphericity Assumed	1.369	1	1.369	8.273	.007	8.273	.796
	Greenhouse-Geisser	1.369	1.000	1.369	8.273	.007	8.273	.796

		Huynh-Feldt	1.369	1.000	1.369	8.273	.007	8.273	.796
		Lower-bound	1.369	1.000	1.369	8.273	.007	8.273	.796
	CAR_AVG	Sphericity Assumed	.005	1	.005	.980	.330	.980	.160
		Greenhouse-Geisser	.005	1.000	.005	.980	.330	.980	.160
		Huynh-Feldt	.005	1.000	.005	.980	.330	.980	.160
		Lower-bound	.005	1.000	.005	.980	.330	.980	.160
Error(time)	IC_KS_ROT	Sphericity Assumed	365.225	31	11.781				
		Greenhouse-Geisser	365.225	31.000	11.781				
		Huynh-Feldt	365.225	31.000	11.781				
		Lower-bound	365.225	31.000	11.781				
	IC_KF_ROT	Sphericity Assumed	64.745	31	2.089				
		Greenhouse-Geisser	64.745	31.000	2.089				
		Huynh-Feldt	64.745	31.000	2.089				
		Lower-bound	64.745	31.000	2.089				

PS_KS_ROT	Sphericity Assumed	1052.169	31	33.941				
	Greenhouse-Geisser	1052.169	31.000	33.941				
	Huynh-Feldt	1052.169	31.000	33.941				
	Lower-bound	1052.169	31.000	33.941				
PS_KF_ROT	Sphericity Assumed	264.449	31	8.531				
	Greenhouse-Geisser	264.449	31.000	8.531				
	Huynh-Feldt	264.449	31.000	8.531				
	Lower-bound	264.449	31.000	8.531				
PS_KS_TRQ	Sphericity Assumed	1.177	31	.038				
	Greenhouse-Geisser	1.177	31.000	.038				
	Huynh-Feldt	1.177	31.000	.038				
	Lower-bound	1.177	31.000	.038				
PS_KF_TRQ	Sphericity Assumed	.360	31	.012				
	Greenhouse-Geisser	.360	31.000	.012				

	Huynh-Feldt	.360	31.000	.012				
	Lower-bound	.360	31.000	.012				
MVIC_AVG	Sphericity Assumed	5.128	31	.165				
	Greenhouse-Geisser	5.128	31.000	.165				
	Huynh-Feldt	5.128	31.000	.165				
	Lower-bound	5.128	31.000	.165				
CAR_AVG	Sphericity Assumed	.166	31	.005				
	Greenhouse-Geisser	.166	31.000	.005				
	Huynh-Feldt	.166	31.000	.005				
	Lower-bound	.166	31.000	.005				

a. Computed using alpha = .05

2. Group ACLr or Control

Univariate Tests

Measure		Sum of Squares	df	Mean Square	F	Sig.	Noncent. Parameter	Observed Power[a]
IC_KS_ROT	Contrast	48.698	1	48.698	2.702	.110	2.702	.357
	Error	558.710	31	18.023				
IC_KF_ROT	Contrast	.285	1	.285	.046	.832	.046	.055
	Error	192.648	31	6.214				
PS_KS_ROT	Contrast	480.651	1	480.651	7.817	.009	7.817	.773
	Error	1906.117	31	61.488				
PS_KF_ROT	Contrast	2.860	1	2.860	.079	.780	.079	.059
	Error	1120.230	31	36.136				
PS_KS_TRQ	Contrast	1.457	1	1.457	20.762	.000	20.762	.993
	Error	2.176	31	.070				
PS_KF_TRQ	Contrast	.057	1	.057	2.360	.135	2.360	.319

	Error	.750	31	.024				
MVIC_AVG	Contrast	.809	1	.809	2.439	.128	2.439	.328
	Error	10.275	31	.331				
CAR_AVG	Contrast	.024	1	.024	2.012	.166	2.012	.280
	Error	.371	31	.012				

The F tests the effect of Group ACLr or Control. This test is based on the linearly independent pairwise comparisons among the estimated marginal means.

a. Computed using alpha = .05

3. time

4. Group ACLr or Control * time

Measure	Group ACLr or Control	time	Mean	Std. Error	95% Confidence Interval	
					Lower Bound	Upper Bound
IC_KS_ROT	ACLr	1	-10.336	1.203	-12.789	-7.884
		2	-9.755	1.169	-12.140	-7.370
	control	1	-14.301	1.240	-16.829	-11.773
		2	-10.652	1.205	-13.110	-8.194
IC_KF_ROT	ACLr	1	-3.247	.620	-4.511	-1.983
		2	-2.792	.686	-4.191	-1.394
	control	1	-4.043	.639	-5.345	-2.740
		2	-2.369	.707	-3.810	-.927
PS_KS_ROT	ACLr	1	-45.434	2.167	-49.854	-41.013
		2	-44.071	2.129	-48.413	-39.728

	control	1	-56.624	2.234	-61.181	-52.068
		2	-48.152	2.195	-52.628	-43.677
PS_KF_ROT	ACLr	1	-12.148	1.556	-15.321	-8.975
		2	-11.233	1.527	-14.348	-8.118
	control	1	-13.632	1.604	-16.903	-10.362
		2	-10.926	1.574	-14.137	-7.715
PS_KS_TRQ	ACLr	1	-1.101	.064	-1.231	-.970
		2	-.995	.080	-1.158	-.832
	control	1	-1.738	.066	-1.872	-1.603
		2	-1.199	.082	-1.368	-1.031
PS_KF_TRQ	ACLr	1	-.293	.043	-.380	-.206
		2	-.280	.041	-.365	-.195
	control	1	-.426	.044	-.516	-.337
		2	-.313	.043	-.400	-.226

MVIC_AVG	ACLr	1	2.031	.185	1.654	2.409
		2	1.581	.120	1.336	1.827
	control	1	2.632	.191	2.243	3.022
		2	1.606	.124	1.353	1.859
CAR_AVG	ACLr	1	.821	.026	.768	.873
		2	.780	.033	.713	.847
	control	1	.892	.026	.838	.947
		2	.816	.034	.748	.885

General Linear Model- Univariate ANOVAs for Post Hoc Analyses

Between-Subjects Factors

		Value Label	N
Group ACLr or Control	.00	ACLr	17
	1.00	control	16

Tests of Between-Subjects Effects

Source	Dependent Variable	Type III Sum of Squares	df	Mean Square	F	Sig.	Noncent. Parameter	Observed Power[b]
Corrected Model	pre-fatigue injured limb knee sagittal plane rotation	1032.240[a]	1	1032.240	12.926	.001	12.926	.936
	post-fatigue injured limb knee sagittal plane rotation	137.335[c]	1	137.335	1.782	.192	1.782	.253
	pre-fatigue injured limb knee sagittal plane external moment	3.344[d]	1	3.344	48.022	.000	48.022	1.000
	post-fatigue injured limb knee sagittal plane external moment	.343[e]	1	.343	3.157	.085	3.157	.406

	Avg_MVIC	2.980[f]	1	2.980	5.120	.031	5.120	.592
	Avg_MVIC_Post	.005[g]	1	.005	.021	.886	.021	.052
Intercept	pre-fatigue injured limb knee sagittal plane rotation	85851.573	1	85851.573	1075.079	.000	1075.079	1.000
	post-fatigue injured limb knee sagittal plane rotation	70102.626	1	70102.626	909.713	.000	909.713	1.000
	pre-fatigue injured limb knee sagittal plane external moment	66.391	1	66.391	953.537	.000	953.537	1.000
	post-fatigue injured limb knee sagittal plane external moment	39.700	1	39.700	365.139	.000	365.139	1.000
	Avg_MVIC	179.272	1	179.272	307.961	.000	307.961	1.000
	Avg_MVIC_Post	83.740	1	83.740	340.143	.000	340.143	1.000
Group	pre-fatigue injured limb knee sagittal plane rotation	1032.240	1	1032.240	12.926	.001	12.926	.936
	post-fatigue injured limb knee sagittal plane rotation	137.335	1	137.335	1.782	.192	1.782	.253
	pre-fatigue injured limb knee sagittal plane external moment	3.344	1	3.344	48.022	.000	48.022	1.000
	post-fatigue injured limb knee sagittal plane external moment	.343	1	.343	3.157	.085	3.157	.406

	Avg_MVIC	2.980	1	2.980	5.120	.031	5.120	.592
	Avg_MVIC_Post	.005	1	.005	.021	.886	.021	.052
Error	pre-fatigue injured limb knee sagittal plane rotation	2475.537	31	79.856				
	post-fatigue injured limb knee sagittal plane rotation	2388.866	31	77.060				
	pre-fatigue injured limb knee sagittal plane external moment	2.158	31	.070				
	post-fatigue injured limb knee sagittal plane external moment	3.371	31	.109				
	Avg_MVIC	18.046	31	.582				
	Avg_MVIC_Post	7.632	31	.246				
Total	pre-fatigue injured limb knee sagittal plane rotation	88868.149	33					
	post-fatigue injured limb knee sagittal plane rotation	72505.163	33					
	pre-fatigue injured limb knee sagittal plane external moment	71.053	33					
	post-fatigue injured limb knee sagittal plane external moment	43.227	33					

	Avg_MVIC	199.063	33					
	Avg_MVIC_Post	91.415	33					
Corrected Total	pre-fatigue injured limb knee sagittal plane rotation	3507.777	32					
	post-fatigue injured limb knee sagittal plane rotation	2526.201	32					
	pre-fatigue injured limb knee sagittal plane external moment	5.502	32					
	post-fatigue injured limb knee sagittal plane external moment	3.714	32					
	Avg_MVIC	21.026	32					
	Avg_MVIC_Post	7.637	32					

a. R Squared = .294 (Adjusted R Squared = .272)

b. Computed using alpha = .05

c. R Squared = .054 (Adjusted R Squared = .024)

d. R Squared = .608 (Adjusted R Squared = .595)

e. R Squared = .092 (Adjusted R Squared = .063)

f. R Squared = .142 (Adjusted R Squared = .114)

g. R Squared = .001 (Adjusted R Squared = -.032)

2. Group ACLr or Control

Univariate Tests

Dependent Variable		Sum of Squares	df	Mean Square	F	Sig.	Noncent. Parameter	Observed Power[a]
pre-fatigue injured limb knee sagittal plane rotation	Contrast	1032.240	1	1032.240	12.926	.001	12.926	.936
	Error	2475.537	31	79.856				
post-fatigue injured limb knee sagittal plane rotation	Contrast	137.335	1	137.335	1.782	.192	1.782	.253
	Error	2388.866	31	77.060				
pre-fatigue injured limb knee sagittal plane external moment	Contrast	3.344	1	3.344	48.022	.000	48.022	1.000
	Error	2.158	31	.070				
post-fatigue injured limb knee sagittal plane external moment	Contrast	.343	1	.343	3.157	.085	3.157	.406
	Error	3.371	31	.109				
Avg_MVIC	Contrast	2.980	1	2.980	5.120	.031	5.120	.592
	Error	18.046	31	.582				
Avg_MVIC_Post	Contrast	.005	1	.005	.021	.886	.021	.052

Error	7.632	31	.246				

The F tests the effect of Group ACLr or Control. This test is based on the linearly independent pairwise comparisons among the estimated marginal means.

a. Computed using alpha = .05

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