

KNEE STABILISATION STRATEGIES DURING AN ISOMETRIC WEIGHT-
BEARING FORCE-MATCHING TASK IN MALES AND FEMALES AFTER ACL
INJURY

Michael Del Bel

In partial fulfillment of the requirements for the
for the M.Sc. Degree in Human Kinetics
School of Human Kinetics
Faculty of Health Sciences
University of Ottawa

ACKNOWLEDGEMENTS

I would like to thank all of the people involved in the process of completing my Master's thesis. First, I would like to thank my family for their continuous support throughout this experience. If it were not for them, I would not have been exposed or able to take advantage of this great opportunity. I would also like to acknowledge the amazing individuals that I am privileged to call my colleagues in both Denmark and Canada. Our Danish collaborators, Drs. Tine Alkjaer, Erik B Simonsen, Michael R. Krogsgaard and their research team were instrumental in ensuring our research projects came to fruition. Their guidance, generosity, and knowledge are greatly appreciated and will not be forgotten. I am forever grateful for the participants who volunteered their time to be a part of this study.

I would like to thank the following colleagues in the Neuromuscular Rehabilitation and Research Unit at the University of Ottawa for their support and ultimately their friendship: Olivia Bayliss-Zajdman, Brigitte Potvin, Nick Romanchuk, Olivier Miguel, Luis Roberto Licón Cano, Reiko Otsuki, and Mohammad S. Shourijeh. Additionally, I would like to acknowledge Teresa Flaxman and Kenneth (Brent) Smale, whom I have the upmost amount of respect and admiration for; I will always be grateful for their friendship, mentorship, and contributions to my personal development as a researcher. Finally, if it were not for Dr. Daniel Benoit, my experience would not have been nearly as fulfilling as it was. I am extremely grateful for his continuous guidance and encouragement; he brings the best out of his students. I truly believe that I am taking much more than a degree out of my experience with Dr. Benoit, as I did not only grow academically but also personally.

I would also like to take this opportunity to acknowledge the various funding agencies that facilitated my Master's thesis. I am very thankful for the University of Ottawa and the School of

Human Kinetics for enabling me to conduct research and for the financial support during my graduate degree. In addition, I am greatly appreciative of the following contributors who were instrumental in financially supporting this research: the Canadian Institutes of Health Research, the Natural Sciences and Engineering Research Council of Canada, the Lundbeck Foundation, the Åse and Ejnar Danielsens Fund, The Danish Rheumatism Association, and the University of Copenhagen.

TABLE OF CONTENTS

LIST OF ACRONYMS, SYMBOLS, AND ABBREVIATIONS	vi
LIST OF FIGURES.....	vii
LIST OF TABLES.....	ix
GENERAL ABSTRACT	x
CHAPTER 1: INTRODUCTION.....	1
Rationale for research.....	1
CHAPTER 2: LITERATURE REVIEW.....	3
Functional role of anterior cruciate ligament	3
Risk factors associated with ACL injury mechanism.....	4
Sex-bias associated with ACL injury	5
Altered knee joint function among a ACL-deficient population	7
Functional knee joint assessment through patient-reported outcome measures	8
Knee joint stability during isometric force-matching task	10
CHAPTER 3: PURPOSE and HYPOTHESES.....	13
Purpose.....	13
Research questions and hypotheses.....	14
CHAPTER 4: GENERAL METHODOLOGY.....	17
Collaborators.....	17
Study Design.....	17
Participants.....	18
CHAPTER 5: MANUSCRIPT 1.....	19
Abstract	20
Introduction	21
Methods.....	23
<i>Participants</i>	23
<i>Consent and questionnaires</i>	23
<i>Participant preparation and equipment</i>	24
<i>Experimental protocol</i>	25
<i>Data processing</i>	27
<i>Statistical analysis</i>	28
Results.....	29
Discussion	39
<i>Limitations</i>	42
Conclusion	43
References	43
CHAPTER 6: MANUSCRIPT 2.....	48
Introduction	50
Methods.....	53
<i>Participants</i>	53
<i>Consent and questionnaires</i>	53
<i>Participant preparation and equipment</i>	53
<i>Experimental protocol</i>	54
<i>Data processing</i>	55
<i>Statistical analysis</i>	56
Results.....	57
Discussion	59
<i>Limitations</i>	62
Conclusion	62
References	63
CHAPTER 7: GENERAL DISCUSSION.....	68
REFERENCES	72

APPENDIX A – Muscle variable equations 81
APPENDIX B – Normalization of patient reported outcome measures..... 83
APPENDIX C – Results of normality calculations 84
APPENDIX D – Calculation of effect size..... 85
APPENDIX E – Subjective and functional outcome measures correlations 86

LIST OF ACRONYMS, SYMBOLS, AND ABBREVIATIONS

ϕ	Mean direction of muscle activation
ACL	Anterior cruciate ligament
ACL-d	Anterior cruciate ligament deficient
ACL-r	Anterior cruciate ligament reconstruction
ADD	Adductor muscle group
ADL	Activities of daily living
ANOVA	Analysis of Variance
BF	Biceps femoris
BMI	Body mass index
CON	Control participant (healthy)
EMG	Electromyography
EMG _i	Electromyography vector
FACL	Females with ACL deficiency
FYC	Female young controls
GM	Gluteus medius
GRF	Ground reaction forces
KOOS	Knee Osteoarthritis and injury Outcome Score
LG	Lateral gastrocnemius
MACL	Males with ACL deficiency
MANOVA	Multivariate Analysis of Variance
MG	Medial gastrocnemius
MOA	Moment arm orientation
MYC	Male young controls
MVIC	Maximum voluntary isometric contractions
OA	Osteoarthritis
PROM	Patient-reported outcome measures
QOL	Quality of life
r_s	Spearman's rho correlation coefficient
r_{es}	Effect size
S/R	Sports and recreation
SD	Standard deviation
SENIAM	Surface Electromyography for the Non-Invasive Assessment of Muscles
SI	Specificity Index
ST	Semitendinosus
TFL	Tensor fascia lata
VL	Vastus lateralis
VM	Vastus medialis
X _{EMG}	Mean magnitude of muscle activation

LIST OF FIGURES

Figure 5.1. Laboratory setup; participant standing with foot of interest in a water-ski boot, fixed to force platform while facing a projector displaying immediate feedback of GRF generated (solid circle). Participants were required to position the cursor between the target's two circles (dashed lines) by controlling the direction of GRFs in the sagittal (F_y) and frontal (F_x). The diameter of the cursor was controlled by the participant's body weight (F_z); increasing or decreasing in diameter with more or less body weight, respectively (modified from Flaxman et al., 2012).

Figure 5.2. Polar plot displaying the 12 targets at the 60% level of maximum effort. Outer numbers represent target location angle in degrees ($^{\circ}$).

Figure 5.3. Mean knee moments (Nm/kg) for FYC, MYC, FACL, and MACL groups at each target direction location ($^{\circ}$). Significant post-hoc differences between groups ($p < 0.05$) are shown at the target location: (†) represents a significant difference between FYC and FACL; (‡) represents a significant difference between MYC and MACL; (§) represents a significant difference between FACL and MACL.

Figure 5.4. Mean hip moments (Nm/kg) for FYC, MYC, FACL, and MACL groups at each target direction location ($^{\circ}$). Significant post-hoc differences between groups ($p < 0.05$) are shown at the target location: (†) represents a significant difference between FYC and FACL.

Figure 5.5. Mean EMG polar plots of RF, VL, VM, BF, and ST muscles for FYC, MYC (solid lines), FACL, and MACL (dashed lines) groups. Outer numbers represent target location angle ($^{\circ}$); inner numbers represent normalized EMG magnitude (ratio of MVIC). Significant differences between groups ($p < 0.05$) are shown at the target location: (*) represents a sex effect between FYC and MYC.

Figure 5.6. Mean EMG polar plots of TFL, LG, MG, ADD, and GM muscles for FYC, MYC (solid lines), FACL, and MACL (dashed lines) groups. Outer numbers represent target location angle ($^{\circ}$); inner numbers represent normalized EMG magnitude (ratio of MVIC). Significant differences between groups ($p < 0.05$) are shown at the target location: (†) represents a significant difference between FYC and FACL; and (‡) represents a significant difference between MYC and MACL.

Figure 5.7. Means and standard deviations of normalized muscle activation magnitudes (X_{EMG} : ratio of MVIC) of 10 muscles for FYC, MYC, FACL, and MACL groups. Significant post-hoc differences ($p < 0.05$) are shown: (*) represents a significant difference between FYC and MYC; (†) represents a significant difference between FYC and FACL; and (‡) represents a significant difference between MYC and MACL.

Figure 5.8. Means and Raleigh's R (circular variance) of muscle activation directions (ϕ : $^{\circ}$) of 10 muscles for FYC, MYC, FACL, and MACL groups. No significant differences between groups were observed. Muscles with empty bars had symmetrical activations and therefore their directional variables were not considered in analyses.

Figure 5.9. Means and standard deviations of the specificity index (SI: 0 to 1) of 10 muscles for FYC, MYC, FACL, and MACL groups. Muscles with empty bars had symmetrical activations and therefore their directional variables were not considered in analyses. Significant post-hoc

differences ($p < 0.05$) are shown: (†) represents a significant difference between FYC and FACL; and (§) represents a significant difference between FACL and MACL.

Figure 6.1. Laboratory setup for maximal force generation trials; participants stood with foot of interest in a water-ski boot, fixed to force platform while facing a projected image of immediate feedback of the inferior/superior ($\pm F_z$) component of GRF generated (grey solid bar, displayed as a percentage of their total body weight). Participants were required to generate and match half of their body weight (black solid bar) by controlling their body weight (F_z); increasing or decreasing in magnitude with more or less body weight, respectively, during the maximal effort trials (modified from Flaxman et al., 2012).

Figure E.1. Correlations between subjective and functional outcome measures for FACL participants for each maximum forces generated for the four platform channels; $-F_y$ (anterior), $+F_y$ (posterior), $-F_x$ (medial), and $+F_x$ (lateral), and the KOOS sub-scores; Symptoms (Symp), Pain, Activities of Daily Living (ADL), and Sports and Recreation (S/R).

Figure E.2. Correlations between subjective and functional outcome measures for FACL participants for each maximum forces generated for the four platform channels; $-F_y$ (anterior), $+F_y$ (posterior), $-F_x$ (medial), and $+F_x$ (lateral), and the sub-scores of the KOOS; Quality of Life (QOL), and the IKDC, Lysholm, and Tegner scores. Significant differences ($p < 0.05$) and trends toward significant differences ($p < 0.10$) are denoted with (*) and (†), respectively.

Figure E.3. Correlations between subjective and functional outcome measures for MACL participants for each maximum forces generated for the four platform channels; $-F_y$ (anterior), $+F_y$ (posterior), $-F_x$ (medial), and $+F_x$ (lateral), and the KOOS sub-scores; Symptoms (Symp), Pain, Activities of Daily Living (ADL), and Sports and Recreation (S/R). Trends towards significant differences ($p < 0.10$) are denoted with (†).

Figure E.4. Correlations between subjective and functional outcome measures for MACL participants for each maximum forces generated for the four platform channels; $-F_y$ (anterior), $+F_y$ (posterior), $-F_x$ (medial), and $+F_x$ (lateral), and the sub-scores of the KOOS; Quality of Life (QOL), and the IKDC, Lysholm, and Tegner scores. Trends towards significant differences ($p < 0.10$) are denoted with (†).

LIST OF TABLES

Table 5.1. Group means (standard deviations) for FYC, MYC, FACL, and MACL of participant demographics, mean joint angles, and mean GRFs. The mean GRFs were scaled to represent 60% of each direction's maximum elicited force produced during 100% effort trials for a successful target-match. P-values with (*) represent a significant difference between groups ($p < 0.05$).

Table 5.2. Functional muscle roles for the 10 muscles tested among the four test groups in order of muscle activation specificity. The three functional roles were identified for each muscle using symmetry of activation, X_{EMG} , ϕ , SI and the muscle activation profiles.

Table 6.1. Group mean (standard deviations) for FYC, MYC, FACL, and MACL groups for maximum generated ground reaction forces (GRFs) normalized to body weight; $-F_y$ (anterior), $+F_y$ (posterior), $-F_x$ (medial), and $+F_x$ (lateral) force platform channels, and PROMs; the five sub-groups of the KOOS, the IKDC the Lysholm scoring scale, and the Tegner assessment. P-values with (*) represent a significant difference between groups ($p < 0.05$).

Table 6.2. Post-hoc Mann-Whitney tests between FYC and FACL, and MYC and MACL with reported group medians for maximum generated ground reaction forces (GRFs) normalized to body weight; $+F_y$ (posterior) force platform channels. P-values with (*) represent a significant difference between groups ($p < 0.025$) and effect sizes were interpreted as small (± 0.1), medium (± 0.3), and large (± 0.5).

Table 6.3. Spearman's rho correlation coefficients (r_s) for FACL and MACL between each maximum generated ground reaction force (GRFs) normalized to body weight; $-F_y$ (anterior), $+F_y$ (posterior), $-F_x$ (medial), and $+F_x$ (lateral) force platform channels, and PROMs; the five sub-groups of the KOOS, the IKDC, the Lysholm scoring scale, and the Tegner assessment. P-values with (*) represent a significant difference between groups ($p < 0.05$); r_s were interpreted as weak (± 0.1), medium (± 0.3), and strong (± 0.5) relationships.

Table C.1. Kolmogorov-Smirnov (K-S) tests for assessing normality FYC of dependent variables tested: maximum generated ground reaction forces (GRFs) normalized to body weight; $-F_y$ (anterior), $+F_y$ (posterior), $-F_x$ (medial), and $+F_x$ (lateral) force platform channels, and subjective questionnaires (scores were normalized to a score out of 100); the five sub-groups of the KOOS, the IKDC the Lysholm scoring scale, and the Tegner assessment. Significant P-values ($p < 0.05$) are represented by (*) and were deemed non-normally distributed. Tests were omitted (N/A) when the reported values were constant for the participants.

GENERAL ABSTRACT

The anterior cruciate ligament (ACL) plays an important role in knee joint stability, and unfortunately is one of the most commonly injured knee joint structures. The muscles surrounding the knee are also critical for stabilising the knee joint and their activations are altered following ACL injury. Despite the fact that ACL injuries are up to 8 times more likely to occur in females compared to males, there is limited research evaluating the effects of sex on how ACL-deficient individuals adjust neuromuscular control strategies during varying loading conditions. In order to have clinicians implement optimal rehabilitation strategies for ACL-deficient males and females, it is crucial to understand the adaptive functional strategies that are taking place once an ACL injury has occurred. The purpose of this thesis was therefore to provide objective and quantitative measurements describing the functional roles of muscles surrounding the knee. This was accomplished and outlined in this thesis through two chapters in manuscript format and summarised below.

i) Sex and ACL-deficiency influence functional muscle roles during an isometric, weight-bearing, force-generation task

First, the functional roles of muscles were quantified through the assessment of muscle activations during a series of multi-directional force-production tasks in ACL-deficient males and females while weight bearing. A highly controlled, isometric, force-matching task, whereby participants modulated ground reaction forces in various combinations of sagittal and frontal plane loads was used to quantify force-generation strategies (muscle activations and functional role) of the knee joint. Mean activation magnitudes and profile patterns from 10 muscles in the lower extremity (rectus femoris, vastus lateralis, vastus medialis, biceps femoris, semitendinosus, lateral gastrocnemius, medial gastrocnemius, tensor fascia latae, adductor muscle group, and gluteus medius) were recorded using wireless electromyography (EMG) sensors. Their

activations were quantified with an orientation analysis to determine if differences in functional muscle roles existed between four groups; healthy female controls, healthy male controls, ACL-deficient females, and ACL-deficient males.

Overall, different functional muscle roles were found between groups. Healthy male controls activated their muscles the most specifically; females with ACL-deficiency activated their muscles the least specifically, while healthy female controls and males with ACL-deficiency shared similar functional muscle roles. This suggests that there was a specificity hierarchy in the ability, or efficiency, to modulate the activation of muscles about the knee joint when exposed to various directional loading conditions.

ii) Associations between subjective measures of knee dysfunction and measures of ground reaction forces in ACL-deficient males and females

Correlational relationships were evaluated between perceived knee joint function and functional capacity of the knee joint. These relationships were calculated between patient reported outcome measures (PROM) from commonly used knee assessment scoring scales maximal generated forces in the sagittal and frontal planes.

Both ACL-deficient groups had significantly lower perceived knee joint function compared to healthy controls. A trend towards significance was observed in the ability to generate maximum forces in the sagittal and frontal planes, with ACL-deficient females generating smaller maximal posterior GRFs compared to healthy females. Only two statistically significant correlations (both for ACL-deficient females) were found between maximal medial GRFs and patient reported outcome measures from the Lysholm and Tegner scoring scales. This indicates that there may be a discrepancy in the sensitivity of subjective outcome measures between sexes and their corresponding ability to generate maximum GRFs.

In conclusion, sex differences exist in subjective outcome measures and the functional strategy of neuromuscular control of the knee joint both before and after ACL-injury. The results of this thesis indicate the need for sex-specific tailoring of rehabilitation programs, thus providing an opportunity to improve the success rate of rehabilitation following ACL-injury. Moreover, sensitivity of subjective outcome measures and their relation to simple, practical, functional tasks between sexes warrants further investigations.

CHAPTER 1: INTRODUCTION

Rationale for research

An injury to the anterior cruciate ligament (ACL) is one of the most common injuries to the knee joint. Reported ACL injuries in the United States rose from 86,687 in 1994 to 129,836 in 2006 (Mall et al., 2014), with rates continuing to rise among active male and female athletes (Agel et al., 2016). Risk-factors associated with ACL injuries have been established, such as sex, however the mechanisms behind the injury are still not clearly understood (Acevedo et al., 2014; Hewett et al., 2006; LaBella et al., 2014). In recent years, there has been an emphasis in the literature on the sex differences present in biomechanical variables in relation to ACL injuries, given that females have been reported to be from 2 up to 8 times more likely to sustain a non-contact ACL injury compared to their male counterparts (Agel et al., 2005; Brophy et al., 2010; Hewett et al., 2015; Ireland 1999; Waldén et al., 2010). These injuries can be traumatic to an individual and result in long-term health consequences. It has been proposed that without an ACL, or an ACL-deficient (ACL-d) knee, there is a decrease in the mechanical stability of the joint and a deficit in sensory feedback (Krogsgaard et al., 2011). This reduction in mechanical stability and sensory feedback has been suggested to be associated with the increased likelihood (50% to 71%) of knee osteoarthritis (OA) among ACL-d individuals (Lohmander et al., 2007; Lohmander et al., 2004; Oiestad et al., 2011; Roos et al., 1995), within 5 to 20 years after the occurrence of the injury.

Each ACL injury costs approximately 17 000 USD for reconstruction surgery and rehabilitation, with total annual estimates reaching 3 billion USD for ACL injuries (Benjaminse et al., 2010; Petushek et al., 2015) and, based on data collected in 2003, the estimated cost of treating OA was 128 billion USD (Yelin et al., 2007) in the United States alone. As such, these injuries, coupled with the increased probability of knee OA, result in a substantial economic

burden on various health care sectors and cannot be ignored. Ultimately, however, the greatest burden is with the ACL injured individual who runs a significant risk of not achieving activity levels experienced prior to their injury.

When an individual sustains an ACL injury, their knee joint stability and function are typically altered and/or compromised (Krogsgaard et al., 2011): ACL-d patients display altered neuromuscular (Catalfamo et al., 2010; DeMont and Lephart, 1998; Lindström et al., 2010) and biomechanical (Button et al., 2008; Catalfamo et al., 2010; Gustavsson et al., 2006) strategies at the knee joint during various tasks (i.e. level-walking and single-leg hops). However the different neuromuscular contributors to force generation from the knee joint after an ACL injury, and how these changes may influence knee joint stability, are still unclear. Through this thesis, these gaps in understanding of how individual muscles adapt their functional role and contribution to force generation after an ACL injury were addressed. This thesis provided new information on how an ACL-d knee alters neuromuscular control over a range of highly controlled loading conditions. The results of this thesis will help to improve rehabilitation programs aimed at returning knee stability and pre-injury activity levels to this injured population.

CHAPTER 2: LITERATURE REVIEW

Functional role of anterior cruciate ligament

The anterior cruciate ligament (ACL) is an essential component in maintaining the controlled movement of a healthy knee joint in its six degrees of motion, consisting of three rotations (internal/external, valgus/varus and flexion/extension) and three translations (anterior/posterior, medial/lateral and compression/distraction) (Girgis et al., 1975; Takeda et al., 1994). The ACL also has a role in stability of the knee joint; with stability being defined as the ability maintain proper position(s) through an equalization of forces (Riemann and Lephart, 2002; Williams et al., 2001). This definition will be referred to when discussing knee stability throughout this thesis. Mechanically, the primary role of the ACL is to restrain anterior translation of the tibia, with respect to the femur, and acts as a secondary resistor to internal rotation, valgus/varus and hyperextension of the knee joint (Girgis et al., 1975; Takeda et al., 1994). The ACL is able to limit and dictate the aforementioned movements of the knee joint due to its two functional bundles, being the antero-medial band (AMB) and the postero-lateral bundle (PLB) each consisting of a balance of elastic and stiff properties (Goldblatt and Richmond, 2003; Ross and Pawlina, 2010; Sugimoto et al., 2015). In addition to its mechanical role, the ACL provides proprioception or motion sensory feedback via stress and strain mechanoreceptors embedded in the ligament's tissues that have been demonstrated to influence the activity of the surrounding muscles to aid in knee joint stabilisation (Krogsgaard et al., 2011). Therefore an injury to the ACL significantly diminishes proprioceptive feedback from the knee, which may be a major contributor to the reduction in functional stability during loading of the knee joint post ACL-injury (Borsa et al., 1997; Krogsgaard et al., 2011).

Risk factors associated with ACL injury mechanism

The underlying risk factors in the mechanism of an ACL injury are multifactorial, consisting of extrinsic and intrinsic factors. These factors include, but are not limited to: physical and/or visual perturbations, type of sport, sex, age, anatomic variations, neuromuscular deficits, biomechanical abnormalities, and hormonal balance (Acevedo et al., 2014; Hewett et al., 2006; LaBella et al., 2014).

Over the last few decades, it has been consistently reported that approximately 70% of all ACL injuries are a result of a non-contact mechanism (Hewett et al., 2006; Noyes et al., 1983; Waldén et al., 2015), whereby there is no direct contact to the individual at the time of injury. This situation implies intrinsic variables (i.e. sex and neuromuscular deficits) are playing a major factor in the resulting injury. In order to understand the exact mechanism of injury, several studies have performed video analyses examining the movement patterns of an individual at the exact time of injury (Bere et al., 2011; Boden et al., 2000; Brophy et al., 2015; Koga et al., 2010; Olsen et al., 2004; Waldén et al., 2015). These analyses considered a wide range of sports (skiing, soccer, handball, and basketball) yet found similar findings: non-contact ACL injuries arise during an athletic maneuver such as a decelerated stop, landing from a jump, or a sudden change of direction. These maneuvers put the lower extremity in a high-risk position, which includes a coupling of medial and internal rotational loads being placed on the knee joint (Hewett 2010; Kiapour et al., 2015; Quatman et al., 2014). Through our isometric, weight-bearing, force matching protocol, representations of these coupled loading conditions can be safely reproduced and analyzed, allowing a comparison of neuromuscular control strategies of healthy and injured populations.

Sex-bias associated with ACL injury

ACL injury related studies have generally incorporated a comparison between groups based on biological sex. The focus of sex comparisons stems from the consistently reported sex-bias in the incidences of ACL injuries, with females being up to 8 times more likely to sustain a non-contact ACL injury compared to males (Benjaminse et al., 2010; Brophy et al., 2015; Flaxman et al., 2014; Ford et al., 2005; Iguchi et al., 2013; McLean et al., 2004; Sigward et al., 2012). Several factors associated with this sex-bias have been discussed in the literature such as neuromuscular, biomechanical, anatomical and hormonal composition. However, the general consensus in the literature for approximately the last 15 years is that the disparity in ACL incidences between males and females arises from a combination of these factors (Arendt et al., 1999; Simon et al., 2015).

When sex is considered, differences between males and females have become apparent with females being in a high-risk position more often than their male counterparts (Beaulieu et al., 2009; Ireland, 1999). This high-risk position, often seen during side-cuts and jump-landings, entails a coupling of medial and internal rotational loading, which is when the ACL is most likely to rupture (Andrews et al., 1977) and likely contributes to the consequential sex-bias in ACL injuries.

Sex differences in neuromuscular and biomechanical strategies have been analyzed in a wide range of populations performing various maneuvers where medial and internal rotational loads are observed. Maneuvers such as a side-cut (Beaulieu et al., 2009; Bencke and Zebis, 2011; Hanson et al., 2008; Iguchi et al., 2013; Landry et al., 2009; Sigward and Powers, 2006), and a countermovement jump (Chappell et al., 2007; Cowling and Steele, 2001; Fagenbaum and Darling, 2003; Hewett et al., 2015; Holden et al., 2015; Quatman et al., 2006; Weinhandl et al.,

2015) are frequently used due to non-contact ACL injuries being most likely to occur during these tasks. Some studies using these tasks showed females are generally quadriceps-dominant (activating their quadriceps at a higher ratio compared to their hamstrings) compared to males, who typically employ a more balanced activation between their quadriceps and hamstrings (Beaulieu et al., 2009; Hanson et al., 2008; Landry et al., 2007). However, the role of the quadriceps in relation to ACL loading has been debated in the literature. It has been suggested that the quadriceps activate to protect the ACL from injury by increasing the compression of the knee joint (Hashemi et al., 2007). Other researchers have suggested that increased quadriceps activity in relation to hamstrings activity may be detrimental to the ACL, as greater anterior translation of the tibia may occur (Hanson et al., 2008; Iguchi et al., 2013; McLean et al., 2004).

In addition, common kinematics and kinetics findings are that females typically have greater peak knee valgus angles and moments, smaller peak extension moments, smaller peak knee flexion angles, and smaller peak internal rotation of the knee joint compared to their male counterparts (Beaulieu et al., 2008; Benjaminse et al., 2010; McLean et al., 2004; Pollard et al., 2004). These variables all contribute to the aforementioned high-risk position of increased ACL loading and thus put females more at risk of sustaining an ACL injury compared to males.

Taken together, it is reasonable to conclude that sex may directly influence the neuromuscular and biomechanical outputs of an individual, influencing the risk of sustaining an ACL injury. Nevertheless, the specific mechanism of an ACL injury and how sex is a major contributing factor, is still not well understood (Benjaminse et al., 2010; Sugimoto et al., 2015) and will be addressed in this study by comparing the neuromuscular control strategies of the lower extremity during various directional loading conditions between males and females among healthy and ACL-d populations.

Altered knee joint function among a ACL-deficient population

Anterior cruciate ligament-deficient (ACL-d) individuals may opt to avoid reconstruction surgery (ACL-r) and choose the conservative approach, where a surgery does not take place and there is greater emphasis on physiotherapy rehabilitation to maximize the function and stability of their ACL-d knee (Button et al., 2008; Fitzgerald et al., 2000; Marx et al., 2003).

For those who choose the conservative approach, altered neuromuscular (Alkjaer et al., 2003; Beard et al., 1996; Boerboom et al., 2001; Bulgheroni et al., 1997; Ferber et al., 2002; Knoll et al., 2004; Kvist and Gillquist, 2001; Lindström et al., 2010; Rudolph et al., 2001; Torry et al., 2000) and biomechanical (Alkjaer et al., 2003; Alkjær et al., 2011; Bohn et al., 2016; Rudolph and Snyder-Mackler, 2004) strategies will likely be employed by their ACL-d limb, compared to their pre-injury movement patterns, limiting their ability to return to pre-injury physical activity. Interestingly, none of the aforementioned studies considered sex as an independent variable in their analyses, despite females are 2 to 8 times more likely to sustain a non-contact ACL injury compared to males (Agel et al., 2005; Waldén et al., 2010). Furthermore, sex is often considered a confounding variable in biomechanical analyses of human movement in healthy populations (Bencke and Zebis, 2011; Chappell et al., 2007; Flaxman et al., 2014; Holden et al., 2015; Landry et al., 2009; Landry et al., 2007; Weinhandl et al., 2015), limiting the application of previously reported findings in ACL-d populations where sex was not an independent variable.

Differences within ACL-d populations have been found, with subgroups typically being categorized into copers and non-copers (Alkjaer et al., 2003; Chmielewski et al., 2001; Rudolph et al., 2001, 2000). Those who are able to stabilise the knee joint, without an intact ACL, during high-demanding physical activities post-injury are categorized as copers, while those who cannot

maintain knee stability during such tasks are categorized as non-copers (Rudolph et al., 2001). An analysis was conducted on the varying levels of rehabilitation success in 281 ACL-d individuals, by analyzing gait and hop movement variables more than one year post-injury (Button et al., 2008). These individuals were then classified on the basis on which of their pre-injury activities they were able to successfully return to while maintaining knee stability. It was determined that 17% of the ACL-d participants were classified as functional copers, 45% were classified as adapters, and 38% were classified as non-copers, with only 5% of tested participants returning to high-demand physical activities after rehabilitation. This demonstrates that ACL-d individuals choosing conservative rehabilitation approaches post-injury, for the majority, require further individualized treatment options in the hopes of returning to pre-injury activities by learning to adapt with new movement strategies. Thus, a gap in rehabilitation programs is present, as these programs are not being properly tailored for those who have new, adaptive neuromuscular control strategies for knee stability. To properly address this gap, a thorough understanding of altered, individual muscle contributions to force generation at the knee joint is imperative.

Functional knee joint assessment through patient-reported outcome measures

Many instruments and rating scales have been developed in an attempt to measure outcomes from a patient's perspective, however only a few methods have been evaluated for reliability, validity, and responsiveness (Wang et al., 2010). Subjective function of the knee joint is often measured using clinically administered patient-reported outcome measures (PROMs) and have traditionally been viewed as not being the most valid means of determining knee joint function, but have become more popular due to their incorporation of a patient's perceived knee joint function (Bent et al., 2009). However, many of these outcome measures lack a relevancy

between the patient reported outcome measures (PROMs) and the patient's clinical measurement of knee function, such as the Lachman and pivot-shift tests for translational and rotational laxity of the knee joint (Snyder-Mackler et al., 1997).

Common examples of PROMs are; the Knee Injury and Osteoarthritis Outcome Score (KOOS; Roos and Toksvig-Larsen, 2003), the International Knee Documentation Committee score form (IKDC; Irrgang et al., 2001), the Lysholm scoring scale (Lysholm and Gillquist, 1982), and the Tegner physical activity level assessment (Tegner and Lysholm, 1985). The KOOS and the IKDC are both often used in literature (Wang et al., 2010). They are both reliable and responsive assessments that were developed to evaluate the short- and long-term patient-relevant outcomes following an injury to the knee joint (*i.e.* ligament and meniscal tears, osteoarthritis) (Irrgang et al., 2001; Roos and Toksvig-Larsen, 2003). The Lysholm scoring scale is an evaluation of functional impairment of the knee joint with the inclusion of joint instability as a measurement (Lysholm and Gillquist, 1982). The Tegner assessment is a grading scale with emphasis on work and sport activities that was developed as a tool to compliment that functional score evaluation of the Lysholm scale (Tegner and Lysholm, 1985).

Comparisons of some of the above-mentioned PROMs in both ACL-r and non-operative (ACL-d) populations have found consistent findings of similar functional outcome measures at up to five years after injury (Frobell et al., 2013; Grindem et al., 2014; Smith et al., 2014), implying that non-operative rehabilitation of an ACL injury should be the primary treatment option (Failla et al., 2015). There has been little research in determining a relationship between subjective outcome measures and functional tasks, with the exception of single-leg hops and counter-movement jumps in patients who have undergone ACL-reconstruction (Hildebrandt et al., 2015; Hopper et al., 2002; Reid et al., 2007). It is therefore necessary to determine how

PROMs relate to a patient's actual knee joint function in an ACL-deficient population, while considering the influence of sex to aid in the guiding knee rehabilitation progression.

Knee joint stability during isometric force-matching task

A stable knee joint is critical in everyday life. When the ACL is ruptured there is a loss in proprioception and also a mechanical change in the knee joint, which reduces this stability. As mentioned, stability of the knee joint can be described as a state of homeostasis, with three factors interacting to maintain it: (i) integration of articulating geometry (*i.e.* femur, tibia), (ii) soft tissue restraints (*i.e.* ligaments, cartilage, menisci), and (iii) compressive loads applied to the joint (*i.e.* weight-bearing, muscular forces) (Riemann and Lephart, 2002; Williams et al., 2001). Among these, the main contributor to knee stability are the compressive loads applied to the joint from the muscles that cross the knee joint, which are also the only active and easily modifiable joint stabilisers.

Studies performing biomechanical analyses on the knee joint, typically involve dynamic tasks, making it difficult to isolate a muscle's function in relation to force generation and stability (Wilkie, 1949). Therefore, in order to isolate each muscle's contribution to the force generation and stability of the knee joint, it is necessary to limit the biomechanical factors such as changing joint angles and velocities while maintaining a physiologically relevant experimental design. This requirement led to the development of an isometric force-matching task by several groups (Benoit et al., 2006; Buchanan et al., 1986; Buchanan and Lloyd, 1997; Escamilla et al., 1998; Flaxman et al., 2014, 2012; Krishnan et al., 2008; Krishnan and Williams, 2009; Levin et al., 2003; Smith et al., 2012a; Wilk et al., 1996; Williams, 2004; Williams et al., 2003), each with a slight variation of the protocol used. This protocol allows for an evaluation of muscle

activation strategies used about the knee joint to support various combinations of flexion/extension and valgus/varus directional loading.

Early adaptations of the isometric force-matching protocol (Buchanan and Lloyd, 1997; Krishnan et al., 2008; Krishnan and Williams, 2009; Williams, 2004; Williams et al., 2003) were successful in limiting biomechanical parameters to muscle activations and the generated compressive forces at the knee joint, however these studies did not incorporate weight-bearing/gravitational forces. The protocol was further expanded upon by incorporating an evaluation of muscle activations at various levels of externally applied forces (Buchanan et al., 1986; Levin et al., 2003). This experimental design allowed for an assessment of the relationship between external torque and muscle activation amplitudes. However, it was only considered in a healthy population and a relationship between torque and muscle activation amplitudes has yet to be established during an isometric force-matching task for an injured population.

We have developed a weight-bearing force-matching task to evaluate functional applications of neuromuscular strategies employed by various populations. This approach is beneficial as it more closely emulates true physiological influences on loading at the knee joint, as muscles are the only dynamic joint stabilisers (Williams et al., 2001). This technique allows electromyography (EMG) data to be collected and plotted in polar coordinates, permitting comparisons of muscle activation patterns across different test cohorts (Flaxman et al., 2012; Williams et al., 2003). In order to understand the specific role of each muscle crossing the knee joint during the force-matching stability task at varying effort levels, individual muscles have been classified as moment actuators or joint stabilisers through the following variables; i) specificity index (SI – directional variation about the mean direction of activity), ii) mean direction of activation (ϕ), and iii) mean magnitude of activation (X_{EMG}) (Flaxman et al., 2012).

Analyses considering sex differences have been performed by our research group, on active, young, healthy adults with results demonstrating that healthy males and females employ different knee muscle activation strategies to generate various directional loads (Flaxman et al., 2014). Females demonstrated significantly greater muscle activations in the rectus femoris (RF), lateral gastrocnemius (LG) and tensor fascia lata (TFL) compared to their male counterparts during the isometric force-matching task while weight-bearing (Flaxman et al., 2014). Williams and colleagues (2003) considered the differences in neuromuscular control among ACL-d and healthy individuals. Through a similar isometric force-matching protocol it was determined that eight of ten muscles had lower specificity indexes (SI) in ACL-d individuals, with the vastus lateralis (VL) showing the greatest deficit in SI, compared to the activity profiles of a healthy cohort. Furthermore, ACL-d participants employed a much greater co-activation strategy during the force-matching protocol in their affected limbs when compared to their healthy limbs, suggesting that an altered neuromuscular control strategy was employed for stabilising the injured leg (Williams et al., 2003). That being said, this study involved a seated force-matching task and did not include weight-bearing conditions. The absence of weight-bearing limits the application of their findings, given that most functional tasks are performed while weight-bearing, which has been shown to alter the lower limb biomechanics (kinematics and loading) and neuromuscular activity (Escamilla et al., 1998; Wilk et al., 1996). A standing, weight-bearing, isometric, force-matching task will address this gap and will produce a more physiologically accurate dataset to determine group differences in lower limb biomechanics and neuromuscular control during various directional loading conditions between males and females among healthy and ACL-d populations.

CHAPTER 3: PURPOSE and HYPOTHESES

Purpose

With an ACL injury, there is a reduction in sensory feedback of the knee joint (Krogsgaard et al., 2011), however there is limited research considering sex when evaluating how ACL-d individuals adjust knee stabilisation strategies in varying loading conditions. In order to have clinicians implement optimal rehabilitation strategies for ACL-d males and females, it is crucial to understand the following: i) what role the individual muscles play during various directional loading at the knee joint and how this differs between a) healthy and ACL-d populations, and b) males and females, and ii) how we can improve the understanding of the relationship between a patient's perceived knee joint function and clinical functional assessments of the knee joint in ACL-d males and females. The purpose of this thesis is therefore to provide objective and quantitative measurements describing the functional roles of muscles in an ACL injured population that can be used to improve the clinical/rehabilitating management of ACL injuries among male and female patients and ultimately aid in the individuals' return to activity levels prior to injury.

To achieve this, muscle activations (and their functional role) surrounding the knee joint were examined using an isometric, weight-bearing, force-matching protocol in males and females in healthy and ACL-d populations. This approach encompassed 12 different directions of loading (30° increments), enabling the elicitation of force generation strategies at varying loading conditions. This protocol has been validated for highly controlled conditions, which are both functional and reliable (Smith et al. 2012), making it a useful and relevant research tool to quantify differences between males and females of ACL-d and healthy populations.

Research questions and hypotheses

This thesis addresses the following research questions related to investigating the differences in neuromuscular control and knee joint function present between males and females of an ACL-deficient population.

i. How does ACL-deficiency affect neuromuscular control strategies at the knee joint during an isometric, weight-bearing, force-matching task when compared to healthy controls?

i. *Hypotheses:* The ACL is a major contributor to the stabilisation of the knee joint during functional tasks while weight-bearing (Rudolph et al., 2001). With the removal of this important structure, it has been suggested that, to compensate for the loss of the ligament, altered neuromuscular and biomechanical strategies are employed by ACL-deficient individuals (Aalbersberg et al., 2009; Alkjær et al., 2011; Reed-Jones and Vallis, 2008; Shelburne et al., 2004). Based on these studies that found altered strategies in an ACL-deficient population, we hypothesized that during the isometric force-matching protocol, ACL-deficient participants would rely more on a general activation strategy of the muscles in the thigh (quadriceps and hamstring muscle groups), whereas healthy controls would have higher specificity for each muscle, depending on the loading direction (Williams et al., 2003). Furthermore, it was thought that altered joint loading strategies would be seen with ACL-deficient participants displaying lower internal knee joint moments during all loading directions (Alkjær et al., 2011).

ii. Do sex differences exist in ACL-deficient males and females in neuromuscular control of the knee joint during an isometric, weight-bearing, force-matching task?

ii. *Hypotheses:* Sex differences have been identified in the literature in protocols involving isometric force-matching tasks. Females employed a greater activation of the quadriceps muscles compared to males during knee extension trials at three different levels of peak moments, 10%, 20% and 30% during a non-weight-bearing task, whereas no differences were found between males and females for the activations of hamstrings muscles (Krishnan and Williams, 2009). During weight-bearing force-matching tasks, a significantly higher activation in the quadriceps was observed, specifically the rectus femoris, in females when compared to males in a healthy population (Flaxman et al., 2014). Thus, we hypothesized that sex and injury effects in neuromuscular activations would be present, with ACL-deficient males and females displaying overall greater muscle activations compared to their healthy counterparts and ACL-deficient females would have greater quadriceps activations compared to their healthy controls.

iii. Can maximum force generation tasks be used as a clinically relevant task to assess subjective knee function in ACL-deficient males and females?

iii. *Hypotheses:* As previously discussed, sex and ACL-deficient differences have been established. Furthermore, lower maximum ground reaction forces have been reported in an ACL-d patient's affected limb compared to their healthy limb (Dai et al., 2014). It was hypothesized that ACL-d males and females would have significantly lower outcome measures for the four PROMs and overall lower maximum ground reaction forces in both the sagittal and frontal planes. Furthermore, we expected to see strong positive correlations between maximum force generation, specifically in the sagittal plane with all subjective outcome measures in both ACL-d males and females, given that ACL-d

populations have been reported to have lower internal sagittal knee moments compared to healthy controls (Bohn et al., 2016; Rudolph and Snyder-Mackler, 2004).

CHAPTER 4: GENERAL METHODOLOGY

Collaborators

These studies are part of a large-scaled research project aimed at understanding the roles of neuromuscular patterns and biomechanical loading at the knee joint in various populations. This research project stems from a collaborative relationship between the Neuromuscular and Rehabilitation Research Unit of the University of Ottawa, Canada, and the Department of Neuroscience and Pharmacology of the University of Copenhagen, Denmark.

The data of 81 participants used in this study were collected at the University of Copenhagen by graduate students supervised by Dr. Benoit (MJ Del Bel, TS Flaxman, and KB Smale) with assistance from Drs. T Alkjaer and EB Simonsen from the University of Copenhagen. The author of this thesis, Del Bel, was responsible for conception of the two studies in this thesis and the processing and analyzing of the raw data (marker trajectories, electromyography, and force plate) from healthy and ACL-d male and female participants who performed the isometric force-matching protocol that were used in this thesis. In addition, he was responsible for drafting, editing, and finalizing the manuscripts included in this thesis.

Study Design

A two-part cross-sectional experimental study design was implemented to evaluate the differences in neuromuscular control and force-generation between healthy and ACL-d males and females during an isometric, weight-bearing force-matching protocol. This was accomplished through two different studies, which are included in this thesis. The first study consisted of determining the activations and functional role of 10 muscles in the lower extremity during various directional-loading conditions. The second study evaluated the correlational relationships between a patient's perceived knee joint function (through subjective

questionnaires) and their functional capacity of generating maximum forces in the sagittal and frontal planes during isometric conditions.

Participants

A priori power analysis in G*Power (3.1.0) software revealed that to achieve a power of 0.8, with an input effect size of 0.40 and $\alpha = 0.05$, a total sample size of 52 was required to effectively test the research hypotheses of this study based on the dependent variable of peak EMG magnitude of the vastus medialis.

Forty-seven ACL-d participants (27 males; 20 females) were recruited with the assistance of Dr. Michael Krogsgaard, from the Bispebjerg University Hospital, Copenhagen, Denmark. Of the 47 recruited participants, 38 ACL-d (21 males; 17 females) were able to complete the study's protocol with their injured limb. Participants had confirmed rupture of their ACL through MRI and/or arthroscopy. The test limb of ACL-d participants was defined as the injured limb. Thirty-four healthy control participants (17 males; 17 females) were recruited through the University of Copenhagen and the city of Copenhagen, Denmark.

CHAPTER 5: MANUSCRIPT 1

SEX AND ACL-DEFICIENCY INFLUENCE FUNCTIONAL MUSCLE ROLES DURING AN ISOMETRIC, WEIGHT-BEARING, FORCE-GENERATION TASK

Michael J Del Bel¹, Kenneth B Smale¹, Teresa E Flaxman², Tine Alkjaer³, Erik B Simonsen³,
Michael R Krogsgaard⁴, and Daniel L Benoit^{1,2}

¹ School of Human Kinetics, University of Ottawa, Canada

² School of Rehabilitation Sciences, University of Ottawa, Canada

³ Department of Neuroscience and Pharmacology, University of Copenhagen, Denmark

⁴ Section for Sports Traumatology M51, Bispebjerg-Frederiksberg Hospital, Denmark (a part of IOC Sports Medicine Copenhagen)

Keywords: neuromuscular control, ACL injury, knee stability, rehabilitation

Abstract

Background: Anterior cruciate ligament injuries are up to 8 times more likely to occur in females compared to males. Neuromuscular and biomechanical differences in ACL-deficient populations have been established during a variety of tasks, however, it remains unclear how males and females differ in neuromuscular control following injury. This study sought to determine if injury-induced changes in neuromuscular control lead to altered functional roles of the knee joint muscles between males and females.

Methods: An isometric, weight-bearing, force-matching protocol required healthy and ACL-deficient males and females to modulate ground reaction forces in various combinations of sagittal and frontal plane loads. Surface electromyography of 10 muscles in the lower extremity were normalized and displayed in polar plots. Mean activation magnitudes and patterns were quantified with an orientation analysis to determine the presence of group differences in knee neuromuscular control strategies and functional muscle roles.

Results: The classification of functional muscle roles was different between groups, with MACL and FYC sharing the same classifications. No main effects of sex or ACL injury were found for any of the muscles' mean direction of activation (ϕ). Sex and injury effects were seen in both group mean activation magnitudes and the specificity indexes (SI) of activations; i) FYC had higher magnitudes than MYC for the rectus femoris and vastus medialis, ii) FYC and MYC had higher medial gastrocnemius activation magnitudes compared to FACL and MACL, respectively, iii) FACL had lower SI values for the biceps femoris than both FYC and MACL.

Conclusion: A population-based hierarchy in muscle activation patterns used to stabilise the knee joint was discovered: healthy males demonstrated the most specified activations and the ACL-deficient females displayed the least specified activations, while healthy females and ACL-

deficient males showed similar activations. This underscores the necessity of sex-specific patient rehabilitation approaches following ACL injury.

Introduction

An injury to the anterior cruciate ligament (ACL) is one of the most common injuries to the knee joint. Reported ACL injuries in the United States rose from 86,687 in 1994 to 129,836 in 2006 (Mall et al., 2014), with rates continuing to rise among active male and female athletes (Agel et al., 2016). These injuries can be traumatic to an individual and result in long-term health consequences such as knee osteoarthritis (OA) (Lohmander et al., 2007; Roos et al., 1995), reduced activity levels, and ultimately, a reduction in quality of life (Lohmander et al., 2004). Risk-factors associated with ACL injuries have been established, such as sex and variations in neuromuscular control, however how these factors contribute to the injury mechanism is still not clearly understood (Acevedo et al., 2014; Hewett et al., 2006; LaBella et al., 2014).

When the ACL is injured, there is a reduction in the ability to stabilise the knee joint. Knee joint stability is defined as the joint's ability to remain or promptly return to proper positions through an equalization of forces, or in other words, the ability to maintain a state of positional alignment (Riemann and Lephart, 2002). The ACL contributes to dynamic knee stability by passively controlling anterior tibial translation and through its embedded mechanoreceptors. Along with other receptors in the surrounding soft tissue, these aid in joint position feedback and factor into the regulation of muscle activity surrounding the knee joint (Krogsgaard et al., 2011). Therefore, an injury to the ACL not only alters the passive mechanical resistance to anterior tibial translation, it significantly diminishes the proprioceptive feedback and causes inhibition of surrounding musculature, which has been suggested to be a major contributor to the reduction in knee function and stability post-ACL injury (Borsa et al., 1997; Krogsgaard et al., 2011).

Neuromuscular control has been extensively evaluated in an ACL-deficient population compared to healthy controls. There are consistent reports of between-group differences in movement dynamics such as less knee internal rotation (Bohn et al., 2016), less knee adduction (Alkjær et al., 2011), greater hip flexion (Rudolph and Snyder-Mackler, 2004) and smaller peak knee extension moments (Alkjaer et al., 2003) compared to their healthy counterparts. Despite these biomechanical differences, the reported neuromuscular differences between ACL injured and healthy controls is quite variable across studies (Alkjaer et al., 2003; Beard et al., 1996; Boerboom et al., 2001; Bulgheroni et al., 1997; Ferber et al., 2002; Knoll et al., 2004; Kvist and Gillquist, 2001; Lindström et al., 2010b; Rudolph et al., 2001; Torry et al., 2000). Interestingly, none of these studies considered sex as an independent variable in their analyses, despite females being 2 to 8 times more likely to sustain a non-contact ACL injury compared to males (Agel et al., 2005; Waldén et al., 2010). Sex is often considered a confounding variable in biomechanical analyses of human movement in healthy populations (Bencke and Zebis, 2011; Chappell et al., 2007; Flaxman et al., 2014; Holden et al., 2015; Landry et al., 2009; Landry et al., 2007; Weinhandl et al., 2015), therefore limiting the application of previously reported findings in ACL-deficient populations where sex was not considered.

Using a physiologically relevant, weight-bearing, force-control protocol, muscles surrounding the knee joint have been given a functional role classification (Flaxman et al., 2014; 2012). Females utilised different activation strategies during generation of forces in various combinations of directional loading, compared to males (Flaxman et al., 2014). Using the same approach, the purpose of this study was to determine if there were differences between sexes and an ACL-deficient knee with respect to knee joint neuromuscular strategies during a range of weight-bearing isometric knee joint loading conditions. It was hypothesized that both healthy

and ACL-deficient female groups would display higher quadriceps activations in all loading conditions compared to male counterparts (Flaxman et al., 2014; Krishnan et al., 2008). Furthermore, we hypothesized that all ACL-deficient participants would have lower specificity of muscle activations during all loading conditions compared to healthy controls (Williams et al., 2003).

Methods

Participants

An *a priori* power analysis in G*Power software (3.1.0) revealed that to achieve a power of 0.8, with an input effect size of 0.40 and $\alpha = 0.05$, a total sample size of 52 was required to effectively test the research hypotheses of this study based on the dependent variable of peak EMG magnitude of the vastus medialis.

Forty-seven ACL-deficient (ACL-d) participants (27 males; 20 females) were recruited and 38 ACL-d participants (21 males; 17 females) were able to complete the study's protocol with their injured limb. ACL-d participants were recruited from the Bispebjerg University Hospital, Copenhagen, Denmark. Participants had ACL rupture confirmed through MRI and/or arthroscopy. The test limb for ACL-d was defined as the injured limb. Thirty-four healthy control (CON) participants (17 males; 17 females) were recruited through the University of Copenhagen, Denmark. Eligibility criteria consisted of no history of traumatic injury and no presence of any other physical impairment. Controls were matched based on limb dominance with ACL-d. Limb dominance was determined by which leg they used to kick a soccer ball for maximal distance.

Consent and questionnaires

Testing took place in the gait laboratory at the Department of Neuroscience and Pharmacology, University of Copenhagen, Denmark. This study was approved by the local

ethics committee for the Capital Region of Denmark (De Videnskabetiske Komiteer for Region Hovedstaden, H-3-2013-126) and the University of Ottawa Research Ethics Board (H06-14-27). Participants provided informed consent and completed a series of subjective questionnaires including i) the Knee Injury and Osteoarthritis Outcome Score (KOOS; (Roos and Toksvig-Larsen, 2003), ii) the International Knee Documentation Committee (IKDC) knee form (Irrgang et al., 2001), iii) the Lysholm scoring scale (Lysholm and Gillquist, 1982), and iv) the Tegner physical activity level assessment (Tegner and Lysholm, 1985).

Participant preparation and equipment

Participant height, weight, thigh and shank lengths were recorded, followed by the preparation of the areas of the skin for placement of electromyography (EMG) electrodes. EMG of the test limb were collected for the tensor fascia lata (TFL), rectus femoris (RF), vastus lateralis (VL), vastus medialis (VM), biceps femoris (BF), semitendinosus (ST), lateral gastrocnemius (LG), medial gastrocnemius (MG), adductor muscle group (ADD), and gluteus medius (GM). Two surface EMG electrodes, in a bipolar arrangement (2DT2 Foam Dual Pre-Gelled Electrode, Multi BioSensors Inc., USA) with a 1cm inter-electrode distance, were placed over the muscle bellies using guidelines from SENIAM (Hermens et al., 2000) and DeLuca (1997). EMG were recorded with a 10 channel wireless device (MQair, Marq Medical, Farum, Denmark) and sampled at 1000 Hz, band-pass filtered at 20-500 Hz with a 6-dB/octave-filter slope.

Fifty-eight retro-reflective markers (14 mm diameter) were placed according to the HMBL cluster marker set (Mantovani and Lamontagne, 2016). Marker trajectories were sampled at 100 Hz, using a ten-camera infrared motion analysis system (Vicon, Nexus, Oxford Metrics, Oxford, UK). Ground reaction forces (GRFs) were sampled at 1000Hz from a force platform (AMTI-

OR6, Watertown, USA) and amplified with an internal gain of 1000 (MSA-6, AMTI, Watertown, USA). Marker trajectories and GRFs were recorded using the supporting software (Nexus v1.8.5, Oxford Metrics, Oxford, UK).

Experimental protocol

Familiarization of the force target-matching protocol (described below) was given prior to data collections. Maximum voluntary isometric contraction (MVIC) exercises were then performed for each muscle group. Knee extension and knee flexion exercises were performed, while seated, with the hip and knee joints at 90° and 30°, respectively, with manual resistance from the researcher. Hip extension, flexion, adduction and abduction were performed while in a standing position, with resistance being provided by a strap placed around the shank. Plantarflexion was performed, also while standing, with participants using a table to create resistance. Each MVIC exercise was held for five seconds and repeated three times, with at least 45 seconds of rest between each trial.

A reliable force target-matching protocol (Flaxman et al., 2016, 2014, 2012; Smith et al., 2012) was used to assess the participant's ability to generate isometric forces while weight-bearing. In short, participants placed their test leg in a water-ski boot (Bio, O'Brien, Redmond, WA, USA) that was fixed to a force platform with their joint flexion angles positioned at 30°, 30°, and 10° for the hip, knee, and ankle, respectively. Participants faced a screen with a projected image of a cursor and a target (Figure 5.1).

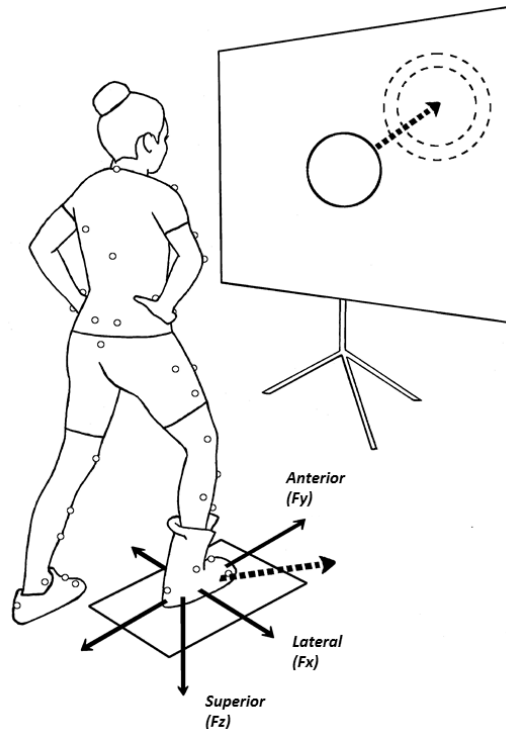


Figure 5.1. Laboratory setup; participant standing with foot of interest in water-ski boot, fixed to force platform while facing a projector displaying immediate feedback of GRF generated (solid circle). Participants were required to position the cursor between the target's two circles (dashed lines) by controlling the direction of GRFs in the sagittal (F_y) and frontal (F_x). The diameter of the cursor was controlled by the participant's body weight (F_z): increasing or decreasing in diameter with more or less body weight, respectively (modified from Flaxman et al., 2012).

The cursor provided immediate feedback of the generated GRFs in three degrees-of-motion; movements upward/downward and left/right were controlled by anterior/posterior ($\pm y$ axis) and medial/lateral ($\pm x$ axis) loads, respectively, and the diameter of the cursor was controlled by superior/inferior ($\pm z$ axis) loads. Testing consisted of a set of 12 targets that were evenly spaced by 30° in a circular arrangement of three different force effort levels (F_z) of 30%, 45% and 60% of previously recorded maximum efforts. This totalled for 36 targets, which was repeated, totalling for 72 targets appearing in a randomized order (Figure 5.2).

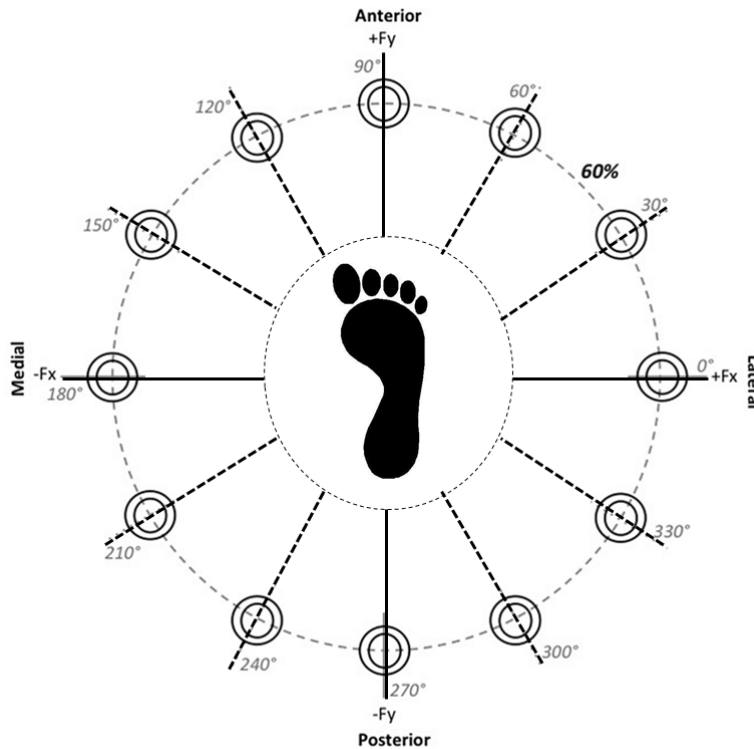


Figure 5.2. Polar plot displaying the 12 targets at the 60% level of maximum effort. Outer numbers represent target location angle in degrees ($^{\circ}$).

Once the cursor reached the target and matched for 0.5s, it was deemed successful and triggered the simultaneous collection of GRFs, EMG and marker trajectories using a custom made application in MATLAB (vR2013a, Mathworks Inc., Natick, MA, USA). Forces required to match the targets were based on previously recorded maximal GRFs recorded in the $-F_y$ (anterior), $+F_y$ (posterior), $-F_x$ (medial), and $+F_x$ (lateral) directions (Appendix A: Equation A.1).

Data processing

Marker trajectory data and GRFs were filtered with a 2nd order dual low-pass 15 Hz cut-off Butterworth filter and exported to OpenSim (v3.3, SimTK, Stanford, CA, USA). Scaling, inverse kinematics and dynamics were calculated using a reduced version of Gait2992 (Hamner et al., 2010), with knee and ankle joints being modeled as revolute joints based on (Delp et al., 1990; Seth et al., 2010) and a total of 16 degrees of freedom and 46 muscles (23 per leg).

Electromyography data were processed in a customized MATLAB application with a high-pass filter at 25 Hz with a 2nd order dual-pass Butterworth filter, full-wave rectification, and a low-pass filter at 10 Hz with 2nd order dual-pass Butterworth filter. Maximum EMG amplitudes (EMGmax) for each muscle were determined from the MVIC trials using a 50 ms moving window algorithm. EMGmax were used to normalize the force-matching trial EMG data as a ratio of MVIC. EMG data were time averaged for the duration of 0.5 seconds and ensemble averaged across the two repetitions of each target.

Statistical analysis

All statistical analyses were performed using an alpha level of 0.05, in SPSS (v22.0, IBM, Chicago, USA). All post-hoc analyses were determined *a priori* with group comparisons for significant effects of sex: FYC vs. MYC and FACL vs. MACL, and for effects of ACL injury: FYC vs. FACL and MYC vs. MACL. Only the results of the 60% GRF effort level were reported in this study, since analyses of the 30% and 45% efforts revealed the same functional muscle role results compared to the 60%, albeit at lower force and activation levels.

Tests for symmetry about the polar plot origin were performed for each muscle (Appendix A: Equation A.2) (Curray, 1956); muscles that were deemed statistically symmetrical were not considered in the evaluation of ϕ , and SI. Watson-Williams tests for circular statistics in PAST v3.11 (Hammer et al., 2001), were used to determine between-group differences in mean direction of muscle activation (ϕ ; Appendix A: Equation A.3) for each muscle. Two-way MANOVAs with a Bonferroni correction were used at each of the 12 target locations to determine significant group differences in GRFs, hip and knee joint moments. Two-way ANOVAs were used to determine group differences in participant demographics and hip and knee joint angles, variance about the mean direction of activation for each muscle (Specificity

Index: SI; Appendix A: Equation A.4) and mean magnitude of muscle activation (X_{EMG} ; Appendix A: Equation A.5). If a significant main effect of sex or ACL injury was observed, post-hoc independent t-tests were performed at each target location.

Results

Participants' age, BMI, leg dominance, leg tested, time since injury, mean joint angles, moments, and mean normalized GRFs (N/kg) required to match a target at 60% of maximum effort are presented in Table 5.1. The time since injury in ACL-d participants varied between males and females, as participants were recruited based on when they sought medical interventions for knee instability. With the exception of two male participants, all were recruited within three years of their ACL injury. FACLs had a significantly smaller +Fy (posterior) GRFs compared to the other three groups (Table 5.1).

Table 5.1. Group means (standard deviations) for FYC, MYC, FACL, and MACL of participant demographics, mean joint angles, and mean GRFs. The mean GRFs were scaled to represent 60% of each direction's maximum elicited force produced during 100% effort trials for a successful target-match. P-values with (*) represent a significant difference between groups ($p < 0.05$).

	FYC	MYC	FACL	MACL	P-value
Tested	n = 17	n = 15	n = 17	n = 21	----
Age (years)	25.29 (6.37)	28.31 (6.07)	26.25 (7.77)	30.20 (7.82)	0.13
BMI (kg/m²)	22.67 (3.36)	24.40 (2.88)	23.62 (2.47)	25.01 (3.16)	0.15
Leg Dominance					
<i>Right</i>	n = 16	n = 13	n = 10	n = 14	----
<i>Left</i>	n = 1	n = 3	n = 7	n = 7	----
Leg Tested/Injured					
<i>Dominant</i>	n = 13	n = 13	n = 11	n = 13	----
<i>Non-Dominant</i>	n = 4	n = 3	n = 6	n = 8	----
Time Since Injury (mo.)	N/A	N/A	7.27 (7.34)	20.05 (23.82)	----
Joint Angles (°)					
<i>Hip</i>	31.59 (8.07)	27.00 (11.56)	28.46 (9.93)	26.22 (6.51)	0.67
<i>Knee</i>	23.53 (8.26)	23.08 (7.34)	22.51 (9.32)	23.27 (7.95)	0.67
GRFs (N/kg)					
- <i>Fy (Anterior)</i>	1.55 (0.26)	1.48 (0.37)	1.41 (0.33)	1.42 (0.29)	0.51
+ <i>Fy (Posterior)</i>	1.16 (0.51)	1.20 (0.31)	0.83 (0.27)	1.06 (0.34)	0.03*
- <i>Fx (Medial)</i>	0.66 (0.29)	0.85 (0.22)	0.67 (0.43)	0.66 (0.36)	0.31
+ <i>Fx (Lateral)</i>	1.04 (0.40)	1.00 (0.32)	0.77 (0.30)	0.87 (0.32)	0.10

Significant differences between CON and ACL in knee joint moments were present. Post-hoc analyses revealed the effect of ACL injury was present at eleven directional loading conditions, combined between the three planes, while the effect of sex was observed at one direction in the sagittal plane (Figure 5.3). Significant differences between FYC and FACL were observed in hip joint moments at four directional loading conditions (Figure 5.4).

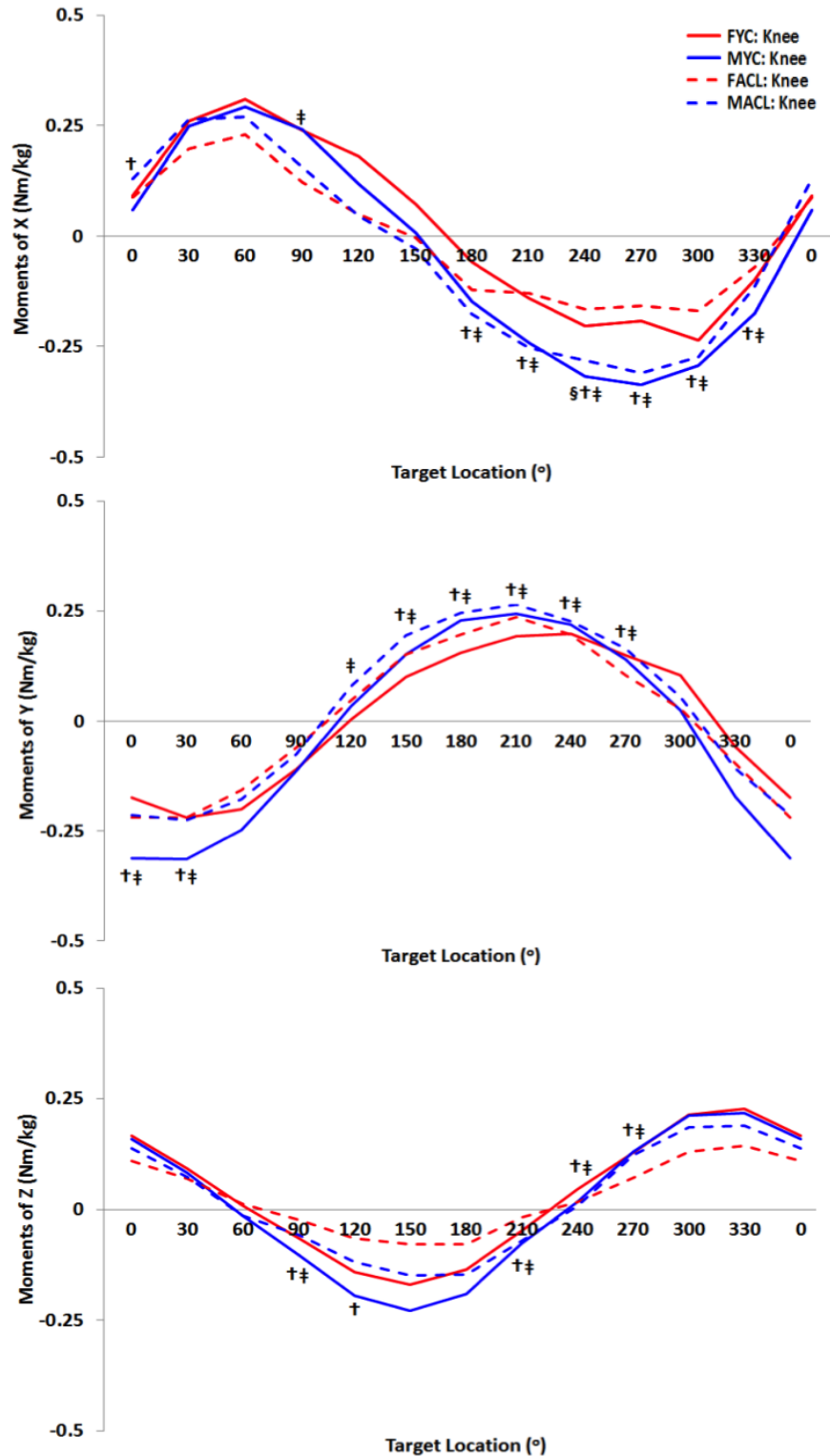


Figure 5.3. Mean knee moments (Nm/kg) for FYC, MYC, FACL, and MACL groups at each target direction location ($^{\circ}$). Significant post-hoc differences between groups ($p < 0.05$) are shown at the target location: (†) represents a significant difference between FYC and FACL; (‡) represents a significant difference between MYC and MACL; (§) represents a significant difference between FACL and MACL.

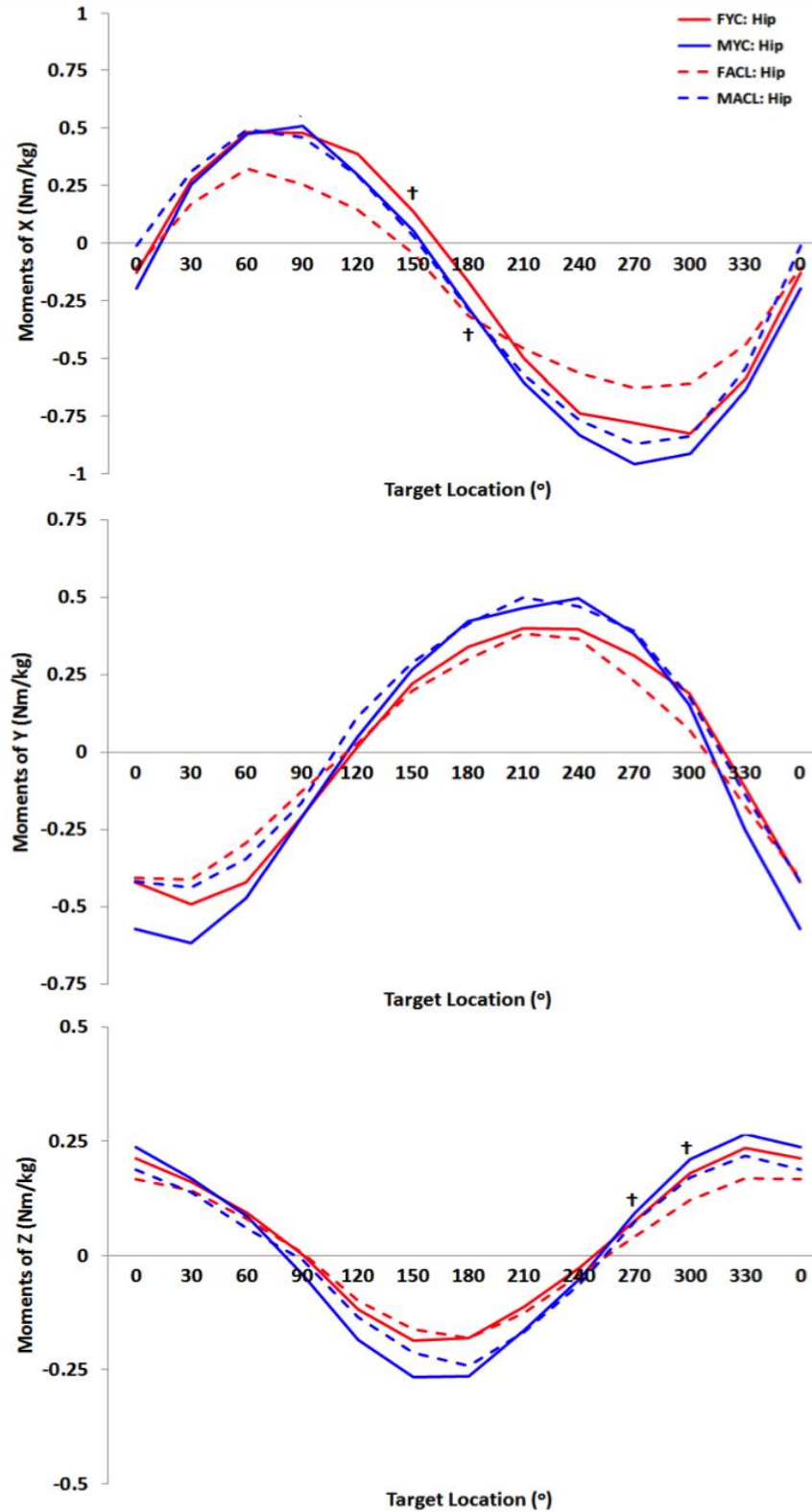


Figure 5.4. Mean hip moments (Nm/kg) for FYC, MYC, FACL, and MACL groups at each target direction location ($^{\circ}$). Significant post-hoc differences between groups ($p < 0.05$) are shown at the target location: (\dagger) represents a significant difference between FYC and FACL.

Group mean activation profiles are shown in polar plots (Figures 5.5 and 5.6). Tests for symmetrical activations revealed that asymmetrical activations were observed in all muscles for MYC, all muscles except the VL and VM for both FYC and MACL, and all muscles except the VL, VM, MG, and GM for FACL.

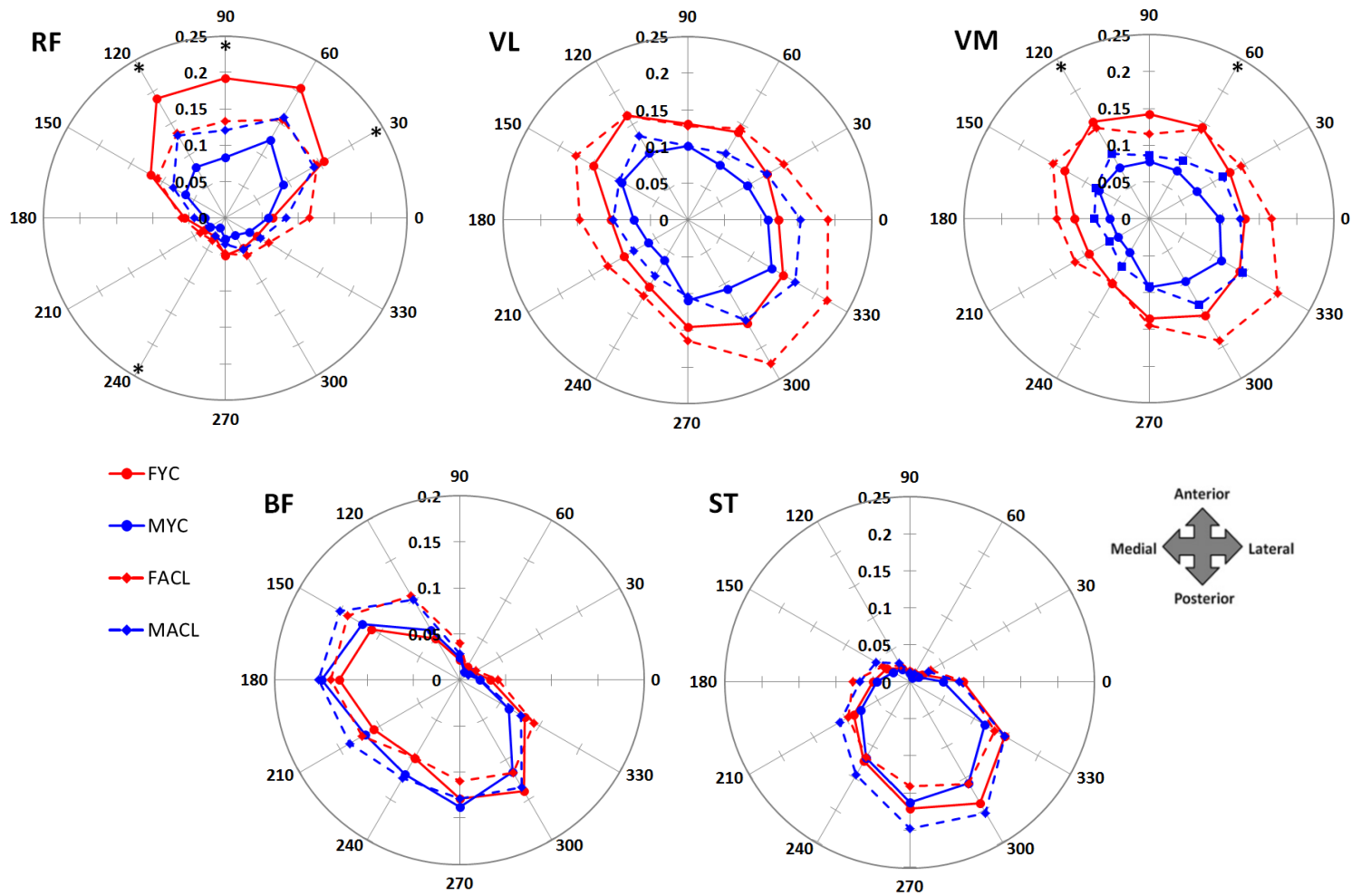


Figure 5.5. Mean EMG polar plots of RF, VL, VM, BF, and ST muscles for FYC, MYC (solid lines), FACL, and MACL (dashed lines) groups. Outer numbers represent target location angle ($^{\circ}$); inner numbers represent normalized EMG magnitude (ratio of MVIC). Significant differences between groups ($p < 0.05$) are shown at the target location: (*) represents a sex effect between FYC and MYC.

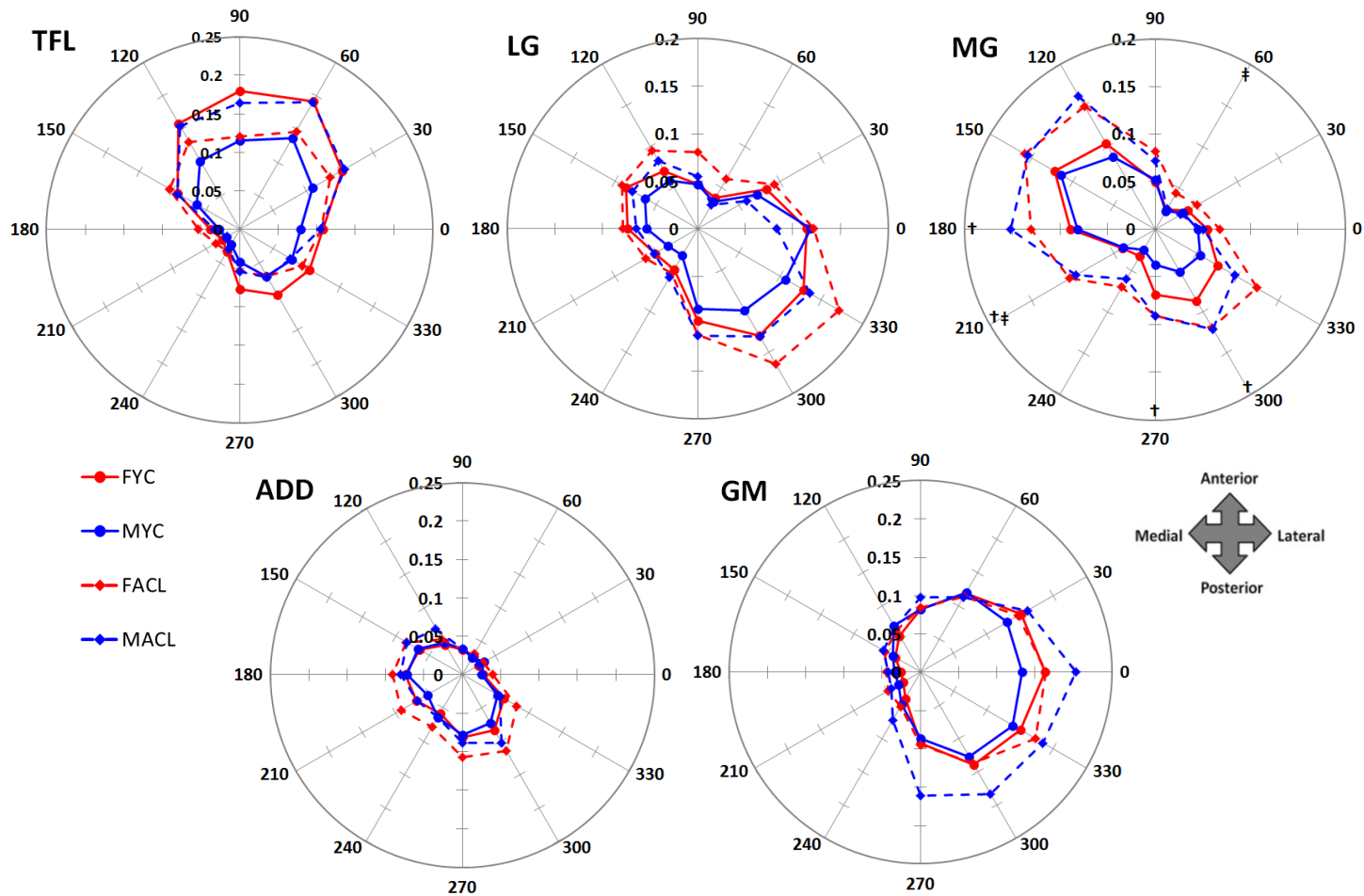


Figure 5.6. Mean EMG polar plots of TFL, LG, MG, ADD, and GM muscles for FYC, MYC (solid lines), FACL, and MACL (dashed lines) groups. Outer numbers represent target location angle ($^{\circ}$); inner numbers represent normalized EMG magnitude (ratio of MVIC). Significant differences between groups ($p < 0.05$) are shown at the target location: (†) represents a significant difference between FYC and FACL; and (‡) represents a significant difference between MYC and MACL.

Sex effects were present in the X_{EMG} for the RF ($F_{1,54}=5.63, p=0.021, \eta^2_p=0.64$), VL ($F_{1,54}=5.08, p=0.028, \eta^2_p=0.60$), and VM ($F_{1,54}=7.34, p=0.009, \eta^2_p=0.80$); and an injury effect was only seen in the MG ($F_{1,54}=11.69, p=0.001, \eta^2_p=0.92$) (Figure 5.7). Post-hoc analyses for sex revealed FYC had significantly greater X_{EMG} values compared to MYC at four loading directions for the RF ($30^\circ, p=0.023$; $90^\circ, p<0.001$; $120^\circ, p<0.001$; $240^\circ, p=0.018$) and two loading directions for the VM ($60^\circ, p=0.023$; $120^\circ, p=0.008$), while no differences were observed in any loading direction for the VL or between ACL-d groups. Post-hoc analyses for the effect of ACL injury revealed significant group differences, with FACL having greater X_{EMG} compared to FYC for the MG at two loading directions ($60^\circ, p=0.024$; $210^\circ, p=0.003$) and MACL having greater X_{EMG} compared to MYC for the MG at four loading directions ($180^\circ, p=0.016$; $210^\circ, p=0.019$; $270^\circ, p=0.001$; $300^\circ, p=0.003$).

No main effects were identified for ϕ in any of the muscles ($p>0.05$) (Figure 5.8). The effect of sex was seen in the mean SI for the BF ($F_{1,54}=14.79, p<0.001, \eta^2_p=0.97$) and ST ($F_{1,54}=4.46, p=0.039, \eta^2_p=0.55$); the effect of injury was observed in the BF ($F_{1,54}=5.45, p=0.024, \eta^2_p=0.63$) and GM ($F_{1,54}=4.43, p=0.041, \eta^2_p=0.54$) (Figure 5.9). Post-hoc analyses for sex differences revealed significant group differences with FACL having lower SI values for the BF compared to MACL ($p<0.001$) and no sex differences were observed in the ST or between FYC and MYC. Post-hoc analyses for effect of ACL injury revealed FACL had significantly lower SI values for the BF compared to FYC ($p=0.024$), while no differences were observed for the GM or between MYC and MACL.

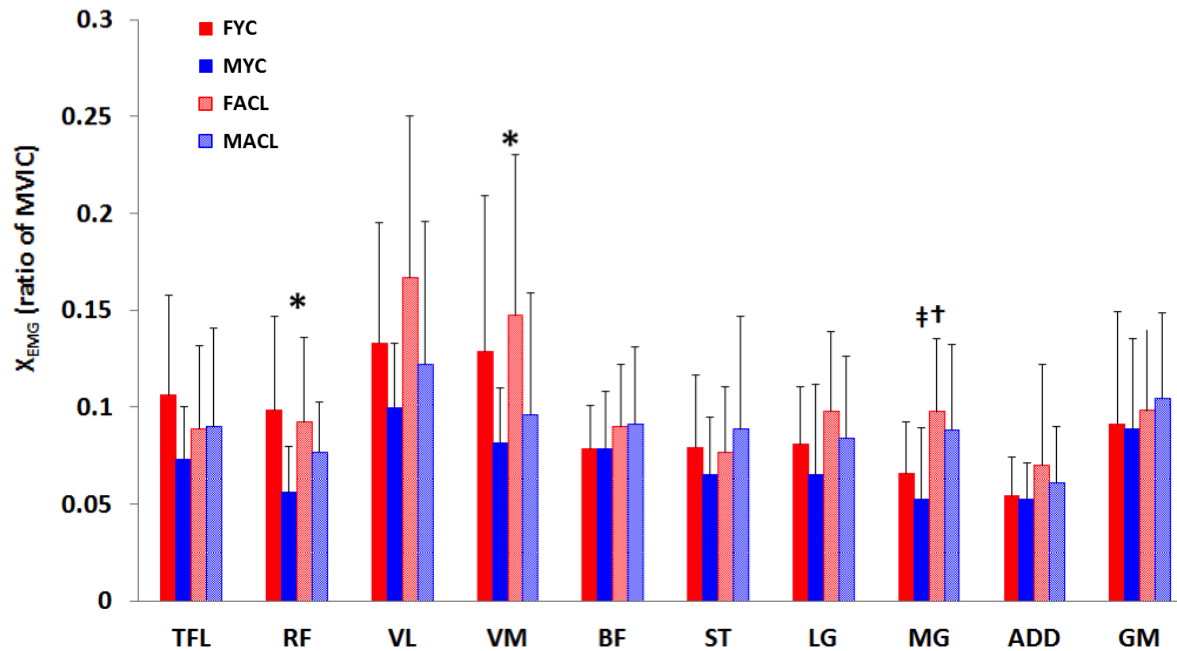


Figure 5.7. Means and standard deviations of normalized muscle activation magnitudes (X_{EMG} : ratio of MVIC) of 10 muscles for FYC, MYC, FACL, and MACL groups. Significant post-hoc differences ($p < 0.05$) are shown: (*) represents a significant difference between FYC and MYC; (†) represents a significant difference between FYC and FACL; and (‡) represents a significant difference between MYC and MACL.

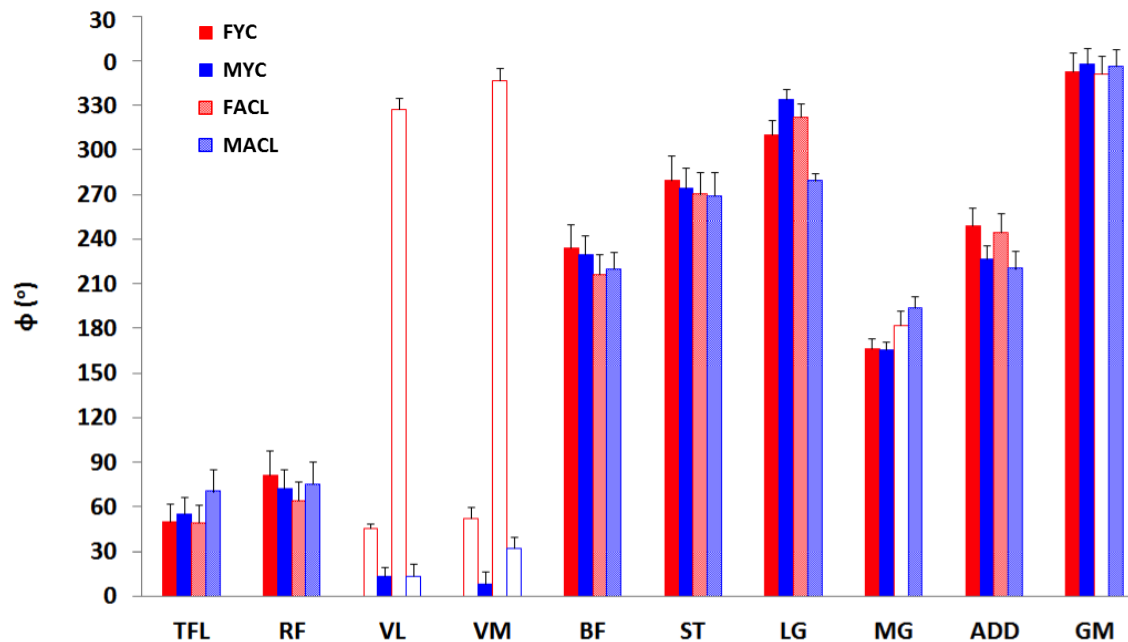


Figure 5.8. Means and Raleigh's R (circular variance) of muscle activation directions (ϕ : °) of 10 muscles for FYC, MYC, FACL, and MACL groups. No significant differences between groups were observed. Muscles with empty bars had symmetrical activations and therefore their directional variables were not considered in analyses.

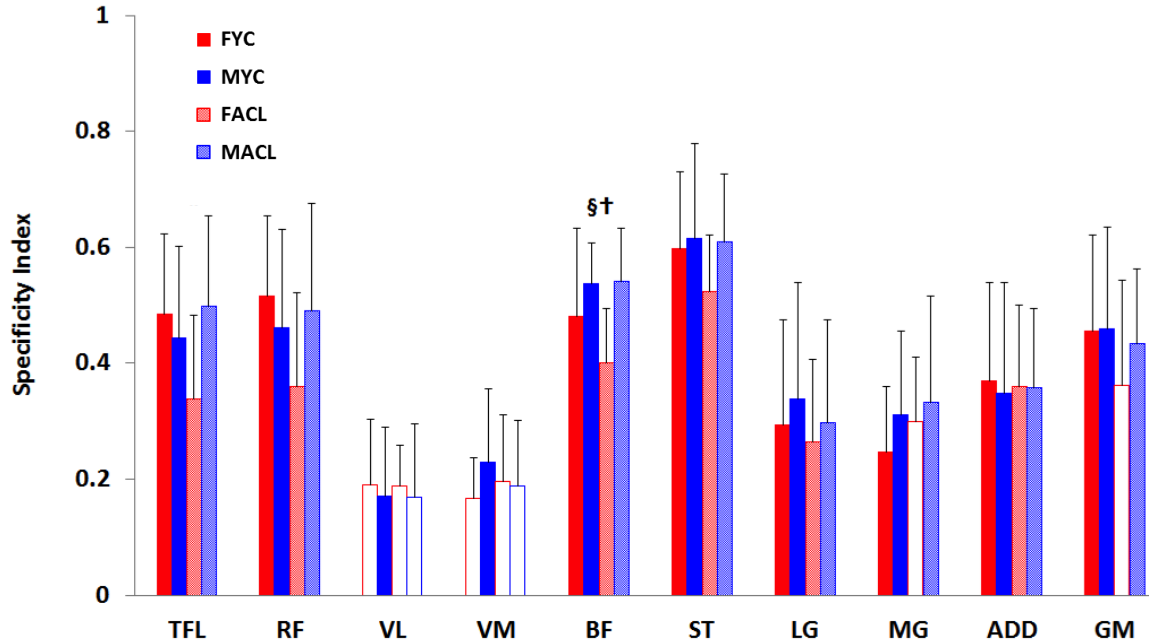


Figure 5.9. Means and standard deviations of the specificity index (SI: 0 to 1) of 10 muscles for FYC, MYC, FACL, and MACL groups. Muscles with empty bars had symmetrical activations and therefore their directional variables were not considered in analyses. Significant post-hoc differences ($p < 0.05$) are shown: (†) represents a significant difference between FYC and FACL; and (§) represents a significant difference between FACL and MACL.

Using the pattern variables of symmetry of activation about the polar plot origin, X_{EMG} , ϕ , SI and the muscle activation profiles, the muscles surrounding the knee joint were classified into 3 roles (Flaxman et al., 2012): i) *general stabiliser* (a muscle with a symmetrical activation pattern), ii) *moment actuator* (a muscle with a statistically asymmetrical activation profile opposite its reported moment arm orientation), and iii) *specific joint stabiliser* (a muscle with a statistically asymmetrical activation profile about its reported moment arm orientation). MYC and FACL groups each had a unique set of muscle roles, while FYC and MACL had the same set of muscle roles (Table 5.2).

Table 5.2. Functional muscle roles for the 10 muscles tested among the four test groups in order of muscle activation specificity. The three functional roles were identified for each muscle using symmetry of activation, X_{EMG} , ϕ , SI and the muscle activation profiles.

Muscle	MYC	FYC	MACL	FACL
TFL	<i>Moment Actuator</i>	<i>Moment Actuator</i>	<i>Moment Actuator</i>	<i>Moment Actuator</i>
RF	<i>Moment Actuator</i>	<i>Moment Actuator</i>	<i>Moment Actuator</i>	<i>Moment Actuator</i>
VL	<i>Specific Joint Stabiliser</i>	<i>General Stabiliser</i>	<i>General Stabiliser</i>	<i>General Stabiliser</i>
VM	<i>Specific Joint Stabiliser</i>	<i>General Stabiliser</i>	<i>General Stabiliser</i>	<i>General Stabiliser</i>
BF	<i>Specific Joint Stabiliser</i>	<i>Specific Joint Stabiliser</i>	<i>Specific Joint Stabiliser</i>	<i>Specific Joint Stabiliser</i>
ST	<i>Specific Joint Stabiliser</i>	<i>Specific Joint Stabiliser</i>	<i>Specific Joint Stabiliser</i>	<i>Specific Joint Stabiliser</i>
LG	<i>Moment Actuator</i>	<i>Moment Actuator</i>	<i>Moment Actuator</i>	<i>Moment Actuator</i>
MG	<i>Specific Joint Stabiliser</i>	<i>Specific Joint Stabiliser</i>	<i>Specific Joint Stabiliser</i>	<i>General Stabiliser</i>
ADD	<i>Moment Actuator</i>	<i>Moment Actuator</i>	<i>Moment Actuator</i>	<i>Moment Actuator</i>
GM	<i>Moment Actuator</i>	<i>Moment Actuator</i>	<i>Moment Actuator</i>	<i>General Stabiliser</i>

Discussion

The purpose of this study was to evaluate the effects of sex and ACL-deficiency on neuromuscular control strategies to stabilise the knee joint under multidirectional loading conditions. The protocol used was as a means to establish the relationship between muscle activations and these loads using a somewhat reductionist approach which limited confounding variables such as joint motions and velocities, thus isolating the role of each muscles in stabilisation against those loads. We also classified those muscle roles as they relate to knee stabilisation (*general stabilisers*, *specific joint stabiliser*, and *moment actuator*). It was hypothesized that differences would be elicited from both sex and ACL-d, with ACL-d contributing more to these differences. Our hypotheses were partly supported since both sex and ACL-d contributed to different functional roles being identified between groups. We found that MYC had the most specific muscle activation roles, with no muscle being a general stabiliser, while FACL used the least specific muscle activation roles, with four of ten muscles being general stabilisers. Our results indicate a hierarchy in muscle activation strategies, in terms of specificity, when stabilising the knee joint: MYC as the most specific, FYC reflecting the strategy of MACL, and FACL as the least specific.

We also found that the posteriorly directed normalized forces were significantly lower for FACLs compared to the other three groups, despite similar levels of muscle activations, implying that they are not as efficient in generating knee flexor force, perhaps as a consequence of a loss of knee joint proprioception or strength. In addition, we found smaller sagittal and transverse plane internal hip and knee joint moments, and greater moments in the frontal plane of the knee joint in the ACL-d groups at several of the loading conditions compared to their healthy controls, agreeing with previous work (Bohn et al., 2016; Rudolph and Snyder-Mackler, 2004).

Sex-related differences in neuromuscular control of the knee have been routinely cited, implying a link with increased non-contact ACL injuries among females. For example, greater RF X_{EMG} was reported among a different cohort of healthy females during the same force-matching task (Flaxman et al., 2014), while additional studies with non-weight-bearing protocols have supported our findings, with healthy females displaying greater quadriceps X_{EMG} compared to males (Krishnan et al., 2008; Krishnan and Williams, 2009). The increased activation seen in the RF and VM among healthy females compared to healthy males during several knee abduction loads has been suggested as a protective mechanism to increase compression at the knee joint and reduce ACL strain in those with knee instability (Hashemi et al., 2007). Flaxman et al. (2014) also found healthy females to have increased LG X_{EMG} compared to their male counterparts, whereas we found ACL-deficient males and females to have greater MG X_{EMG} during several knee abduction loads compared to their healthy counterparts. Similar to the quadriceps, increased gastrocnemii activity has been suggested as a protective mechanism to increase stability of the knee joint during loading (Morgan et al., 2014).

Altered neuromuscular control about the knee joint has been suggested as a compensation strategy for influential factors such as hormones (Hewett, 2000) or a ruptured ACL (Palmieri-

Smith and Thomas, 2009). The MYC group of this study used all muscles specifically, dependent on directional loads, suggesting that healthy males are able to effectively tailor their muscle activations for a given loading condition. In contrast, FACL had four of their ten muscles categorised as general stabilisers. This infers that with an injured ACL, and the consequential loss in mechanical and proprioceptive capacity, the central nervous system uses a more generalised knee stiffening strategy. These muscles could be activating in an attempt to increase compression of the knee joint thereby mitigating anterior translational forces (Hashemi et al., 2007). The FACL group relied on greater activation from the VL, VM, MG and GM when stabilising the knee joint during all loading conditions. Considering this, our results demonstrate that there appears to be a hierarchy in knee stabilisation strategies with MYC having the most adaptable knee joint stabilisation strategy and FACL having the least adaptable.

ACL-injury rehabilitation programs have been developed to focus on restoring the neuromuscular control patterns prior to the injury (Manske et al., 2012). One study determined that, after 11 years, 24% of patients treated conservatively and 45% of the surgical treated patients had developed knee OA (Kessler et al., 2008). Interestingly, there were no differences in regards to loss of ability to participate in physical activity between cohorts; however, this study did not include sex as an independent variable. Our results demonstrate differences between males and females after ACL injury and the need for sex-specific tailoring of rehabilitation programs. Considering the limited research on sex-specific intervention strategies, and our results indicating sex-specific knee stabilisation strategies, there appears to be an opportunity to improve the success rate of ACL-injury rehabilitation programs to reduce the likelihood of re-injury and early onset OA in females. Given the results of this study, the ability to specify a

muscle's activation during a task that combines loading conditions is affected when there is damage to the ACL and should be considered in developing rehabilitation interventions.

Limitations

The isometric nature of our protocol could be considered a limitation of this study with respect to the functional application of our findings. Yet, by taking a reductionist approach we have (1) isolated the task, (2) normalized the effort level, (3) required all participants to produce the same relative load combination at the knee joint, (4) identified each muscle's contribution to those loads, and (5) required participants to generate loads which were both functional and challenging. For example, not all participants were able to complete the entire set of target trials (38 of 47 ACL-d participants completed the entire protocol). Thus, while a step must be taken for the results to be transferred to dynamic tasks, we have provided a strong basis for understanding the effects of sex and ACL injury on neuromuscular control under a wide range of loading conditions. Another consideration is that while we measured muscle activations, ACL-d patients may have a strength and proprioceptive deficit compared to healthy controls which was not accounted for in this study (Krogsgaard et al., 2011; Thomas et al., 2013; Tsepis et al., 2006; Williams, 2004; Williams et al., 2005). As such, a higher level of normalized EMG cannot be directly linked to higher force generation from that muscle, since, for a given normalized task, a weaker individual would require more activation to generate the same level of force. Finally, the participant's foot was fixed in a water-ski boot throughout the duration of the force-matching protocol, to minimize foot motion on the force plate, thereby allowing participants to generate higher GRF levels. Since this limited movement of the ankle joint, the ankle joint moments were not considered in the discussion of results.

Conclusion

The results of this study indicate that males and females use differing neuromuscular control strategies to achieve the same loading conditions, and that these strategies are interacted upon by ACL injury. Our results also indicate a hierarchy in muscle activation strategies used to control the knee joint, with MYC having the most specific force production (adapting to the load generated), FYC reflecting that of the MACL participants, and FACL having the least specific force production (muscles activating regardless of load direction). This indicates the need for population-based intervention programs for management and treatment of males and females of healthy and ACL-deficient populations.

References

- Acevedo, R.J., Rivera-Vega, A., Miranda, G., Micheo, W., 2014. Anterior cruciate ligament injury: identification of risk factors and prevention strategies. *Curr. Sports Med. Rep.* 13, 186–191.
- Agel, J., Arendt, E.A., Bershadsky, B., 2005. Anterior Cruciate Ligament Injury in National Collegiate Athletic Association Basketball and Soccer A 13-Year Review. *Am. J. Sports Med.* 33, 524–531.
- Agel, J., Rockwood, T., Klossner, D., 2016. Collegiate ACL Injury Rates Across 15 Sports: National Collegiate Athletic Association Injury Surveillance System Data Update (2004-2005 Through 2012-2013). *Clin. J. Sport Med.* 26, 518–523.
- Alkjær, T., Henriksen, M., Simonsen, E.B., 2011. Different knee joint loading patterns in ACL deficient copers and non-copers during walking. *Knee Surg. Sports Traumatol. Arthrosc.* 19, 615–621.
- Alkjaer, T., Simonsen, E.B., Jørgensen, U., Dyhre-Poulsen, P., 2003. Evaluation of the walking pattern in two types of patients with anterior cruciate ligament deficiency: copers and non-copers. *Eur. J. Appl. Physiol.* 89, 301–308.
- Beard, D.J., Soundarapandian, R.S., O'Connor, J.J., Dodd, C.A.F., 1996. Gait and electromyographic analysis of anterior cruciate ligament deficient subjects. *Gait Posture* 4, 83–88.
- Bencke, J., Zebis, M.K., 2011. The influence of gender on neuromuscular pre-activity during side-cutting. *J. Electromyogr. Kinesiol.* 21, 371–375.
- Boerboom, A.L., Hof, A.L., Halbertsma, J.P., van Raaij, J.J., Schenk, W., Diercks, R.L., van Horn, J.R., 2001. Atypical hamstrings electromyographic activity as a compensatory mechanism in anterior cruciate ligament deficiency. *Knee Surg. Sports Traumatol. Arthrosc.* 9, 211–216.

- Bohn, M.B., Petersen, A.K., Nielsen, D.B., Sørensen, H., Lind, M., 2016. Three-dimensional kinematic and kinetic analysis of knee rotational stability in ACL-deficient patients during walking, running and pivoting. *J. Exp. Orthop.* 3, 27.
- Borsa, P.A., Lephart, S.M., Irrgang, J.J., Safran, M.R., Fu, F.H., 1997. The effects of joint position and direction of joint motion on proprioceptive sensibility in anterior cruciate ligament-deficient athletes. *Am. J. Sports Med.* 25, 336–340.
- Bulgheroni, P., Bulgheroni, M.V., Andrini, L., Guffanti, P., Giughello, A., 1997. Gait patterns after anterior cruciate ligament reconstruction. *Knee Surg. Sports Traumatol. Arthrosc.* 5, 14–21.
- Chappell, J.D., Creighton, R.A., Giuliani, C., Yu, B., Garrett, W.E., 2007. Kinematics and electromyography of landing preparation in vertical stop-jump: Risks for noncontact anterior cruciate ligament injury. *Am. J. Sports Med.* 35, 235–241.
- Curry, J.R., 1956. The Analysis of Two-Dimensional Orientation Data. *J. Geol.* 64, 117–131.
- Delp, S.L., Loan, J.P., Hoy, M.G., Zajac, F.E., Topp, E.L., Rosen, J.M., 1990. An interactive graphics-based model of the lower extremity to study orthopaedic surgical procedures. *IEEE Trans. Biomed. Eng.* 37, 757–767.
- DeLuca, C., 1997. The use of surface electromyography in biomechanics. *J. Appl. Biomech.* 13, 135–163.
- Ferber, R., Osternig, L.R., Woollacott, M.H., Wasielewski, N.J., Lee, J.H., 2002. Gait mechanics in chronic ACL deficiency and subsequent repair. *Clin. Biomech.* 17, 274–285.
- Flaxman, T.E., Alkjær, T., Simonsen, E.B., Krogsgaard, M.R., Benoit, D.L., 2016. Predicting the Functional Roles of Knee Joint Muscles from Internal Joint Moments. *Med. Sci. Sports Exerc.*
- Flaxman, T.E., Smith, A.J.J., Benoit, D.L., 2014. Sex-related differences in neuromuscular control: Implications for injury mechanisms or healthy stabilisation strategies? *J. Orthop. Res.* 32, 310–317.
- Flaxman, T.E., Speirs, A.D., Benoit, D.L., 2012. Joint stabilisers or moment actuators: the role of knee joint muscles while weight-bearing. *J. Biomech.* 45, 2570–2576.
- Hammer, O., Harper, D.A., Ryan, P.D., 2001. PAST: Paleontological Statistics software package for education and data analysis. *Palaeontol. Electron.* 4.
- Hamner, S.R., Seth, A., Delp, S.L., 2010. Muscle contributions to propulsion and support during running. *J. Biomech.* 43, 2709–2716.
- Hashemi, J., Chandrashekar, N., Jang, T., Karpat, F., Oseto, M., Ekwaro-Osire, S., 2007. An Alternative Mechanism of Non-contact Anterior Cruciate Ligament Injury During Jump-landing: In-vitro Simulation. *Exp. Mech.* 47, 347–354.
- Hermens, H.J., Freriks, B., Disselhorst-Klug, C., Rau, G., 2000. Development of recommendations for SEMG sensors and sensor placement procedures. *J. Electromyogr. Kinesiol.* 10, 361–374.
- Hewett, T.E., 2000. Neuromuscular and hormonal factors associated with knee injuries in female athletes. Strategies for intervention. *Sports Med. Auckl. NZ* 29, 313–327.
- Hewett, T.E., Myer, G.D., Ford, K.R., 2006. Anterior Cruciate Ligament Injuries in Female Athletes Part 1, Mechanisms and Risk Factors. *Am. J. Sports Med.* 34, 299–311.
- Holden, S., Boreham, C., Doherty, C., Wang, D., Delahunt, E., 2015. Clinical assessment of countermovement jump landing kinematics in early adolescence: Sex differences and normative values. *Clin. Biomech.* 30, 469–474.

- Irrgang, J.J., Anderson, A.F., Boland, A.L., Harner, C.D., Kurosaka, M., Neyret, P., Richmond, J.C., Shelborne, K.D., 2001. Development and Validation of the International Knee Documentation Committee Subjective Knee Form. *Am. J. Sports Med.* 29, 600–613.
- Kessler, M.A., Behrend, H., Henz, S., Stutz, G., Rukavina, A., Kuster, M.S., 2008. Function, osteoarthritis and activity after ACL-rupture: 11 years follow-up results of conservative versus reconstructive treatment. *Knee Surg. Sports Traumatol. Arthrosc.* 16, 442–448.
- Knoll, Z., Kiss, R.M., Kocsis, L., 2004. Gait adaptation in ACL deficient patients before and after anterior cruciate ligament reconstruction surgery. *J. Electromyogr. Kinesiol.* 14, 287–294.
- Krishnan, C., Huston, K., Amendola, A., Williams, G.N., 2008. Quadriceps and hamstrings muscle control in athletic males and females. *J. Orthop. Res.* 26, 800–808.
- Krishnan, C., Williams, G.N., 2009. Sex Differences in Quadriceps and Hamstrings EMG-Moment Relationships: *Med. Sci. Sports Exerc.* 41, 1653–1661.
- Krogsgaard, M.R., Fischer-Rasmussen, T., Dyhre-Poulsen, P., 2011. Absence of sensory function in the reconstructed anterior cruciate ligament. *J. Electromyogr. Kinesiol.* 21, 82–86.
- Kvist, J., Gillquist, J., 2001. Anterior positioning of tibia during motion after anterior cruciate ligament injury. *Med. Sci. Sports Exerc.* 33, 1063–1072.
- LaBella, C.R., Hennrikus, W., Hewett, T.E., 2014. Anterior cruciate ligament injuries: diagnosis, treatment, and prevention. *Pediatrics* 133, e1437-1450.
- Landry, S.C., McKean, K.A., Hubley-Kozey, C.L., Stanish, W.D., Deluzio, K.J., 2009. Gender differences exist in neuromuscular control patterns during the pre-contact and early stance phase of an unanticipated side-cut and cross-cut maneuver in 15–18 years old adolescent soccer players. *J. Electromyogr. Kinesiol.* 19, e370–e379.
- Landry, S.C., McKean, K.A., Hubley-Kozey, C.L., Stanish, W.D., Deluzio, K.J., 2007. Neuromuscular and lower limb biomechanical differences exist between male and female elite adolescent soccer players during an unanticipated run and crosscut maneuver. *Am. J. Sports Med.* 35, 1901–1911.
- Lindström, M., Felländer-Tsai, L., Wredmark, T., Henriksson, M., 2010. Adaptations of gait and muscle activation in chronic ACL deficiency. *Knee Surg. Sports Traumatol. Arthrosc.* 18, 106–114.
- Lohmander, L.S., Englund, P.M., Dahl, L.L., Roos, E.M., 2007. The long-term consequence of anterior cruciate ligament and meniscus injuries: osteoarthritis. *Am. J. Sports Med.* 35, 1756–1769.
- Lohmander, L.S., Ostenberg, A., Englund, M., Roos, H., 2004. High prevalence of knee osteoarthritis, pain, and functional limitations in female soccer players twelve years after anterior cruciate ligament injury. *Arthritis Rheum.* 50, 3145–3152.
- Lysholm, J., Gillquist, J., 1982. Evaluation of knee ligament surgery results with special emphasis on use of a scoring scale. *Am. J. Sports Med.* 10, 150–154.
- Mall, N.A., Chalmers, P.N., Moric, M., Tanaka, M.J., Cole, B.J., Bach, B.R., Paletta, G.A., 2014. Incidence and trends of anterior cruciate ligament reconstruction in the United States. *Am. J. Sports Med.* 42, 2363–2370.
- Manske, R.C., Prohaska, D., Lucas, B., 2012. Recent advances following anterior cruciate ligament reconstruction: rehabilitation perspectives. *Curr. Rev. Musculoskelet. Med.* 5, 59–71.

- Mantovani, G., Lamontagne, M., 2016. How Different Marker Sets Affect Joint Angles in Inverse Kinematics Framework. *J. Biomech. Eng.*
- Morgan, K.D., Donnelly, C.J., Reinbolt, J.A., 2014. Elevated gastrocnemius forces compensate for decreased hamstrings forces during the weight-acceptance phase of single-leg jump landing: implications for anterior cruciate ligament injury risk. *J. Biomech.* 47, 3295–3302.
- Palmieri-Smith, R.M., Thomas, A.C., 2009. A neuromuscular mechanism of posttraumatic osteoarthritis associated with ACL injury. *Exerc. Sport Sci. Rev.* 37, 147–153.
- Riemann, B.L., Lephart, S.M., 2002. The Sensorimotor System, Part I: The Physiologic Basis of Functional Joint Stability. *J. Athl. Train.* 37, 71–79.
- Roos, E.M., Toksvig-Larsen, S., 2003. Knee injury and Osteoarthritis Outcome Score (KOOS) – validation and comparison to the WOMAC in total knee replacement. *Health Qual. Life Outcomes* 1, 17.
- Roos, H., Adalberth, T., Dahlberg, L., Lohmander, L.S., 1995. Osteoarthritis of the knee after injury to the anterior cruciate ligament or meniscus: the influence of time and age. *Osteoarthritis Cartilage* 3, 261–267.
- Rudolph, K.S., Axe, M.J., Buchanan, T.S., Scholz, J.P., Snyder-Mackler, L., 2001. Dynamic stability in the anterior cruciate ligament deficient knee. *Knee Surg. Sports Traumatol. Arthrosc.* 9, 62–71.
- Rudolph, K.S., Snyder-Mackler, L., 2004. Effect of dynamic stability on a step task in ACL deficient individuals. *J. Electromyogr. Kinesiol.* 14, 565–575.
- Seth, A., Sherman, M., Eastman, P., Delp, S., 2010. Minimal formulation of joint motion for biomechanisms. *Nonlinear Dyn.* 62, 291–303.
- Smith, A.J.J., Flaxman, T.E., Speirs, A.D., Benoit, D.L., 2012. Reliability of knee joint muscle activity during weight bearing force control. *J. Electromyogr. Kinesiol.* 22, 914–922.
- Strehl, A., Eggli, S., 2007. The Value of Conservative Treatment in Ruptures of the Anterior Cruciate Ligament (ACL): *J. Trauma Inj. Infect. Crit. Care* 62, 1159–1162.
- Tegner, Y., Lysholm, J., 1985. Rating systems in the evaluation of knee ligament injuries. *Clin. Orthop.* 43–49.
- Thomas, A.C., Villwock, M., Wojtys, E.M., Palmieri-Smith, R.M., 2013. Lower extremity muscle strength after anterior cruciate ligament injury and reconstruction. *J. Athl. Train.* 48, 610–620.
- Torry, M.R., Decker, M.J., Viola, R.W., O'Connor, D.D., Richard Steadman, J., 2000. Intra-articular knee joint effusion induces quadriceps avoidance gait patterns. *Clin. Biomech.* 15, 147–159.
- Tsepis, E., Vagenas, G., Ristanis, S., Georgoulis, A.D., 2006. Thigh muscle weakness in ACL-deficient knees persists without structured rehabilitation. *Clin. Orthop.* 450, 211–218.
- Waldén, M., Hägglund, M., Werner, J., Ekstrand, J., 2010. The epidemiology of anterior cruciate ligament injury in football (soccer): a review of the literature from a gender-related perspective. *Knee Surg. Sports Traumatol. Arthrosc.* 19, 3–10.
- Weinhandl, J.T., Irmischer, B.S., Sievert, Z.A., 2015. Sex differences in unilateral landing mechanics from absolute and relative heights. *The Knee* 22, 298–303.
- Wilkie, D.R., 1949. The relation between force and velocity in human muscle. *J. Physiol.* 110, 249–280.
- Williams, G.N., 2004. Altered Quadriceps Control in People with Anterior Cruciate Ligament Deficiency. *Med. Sci. Sports Exerc.* 36, 1089–1097.

- Williams, G.N., Barrance, P.J., Snyder-Mackler, L., Axe, M.J., Buchanan, T.S., 2003. Specificity of muscle action after anterior cruciate ligament injury. *J. Orthop. Res.* 21, 1131–1137.
- Williams, G.N., Buchanan, T.S., Barrance, P.J., Axe, M.J., Snyder-Mackler, L., 2005. Quadriceps Weakness, Atrophy, and Activation Failure in Predicted Noncopers After Anterior Cruciate Ligament Injury. *Am. J. Sports Med.* 33, 402–407.
- Winter, D.A., Eng, J.A., Ishac, M.G., 1995. A review of kinetic parameters in human walking, in: *Gait Analysis: Theory and Application*. Mosby, St. Louis.
- Zysk, S.P., Refior, H.J., 2000. Operative or conservative treatment of the acutely torn anterior cruciate ligament in middle-aged patients. A follow-up study of 133 patients between the ages of 40 and 59 years. *Arch. Orthop. Trauma Surg.* 120, 59–64.

CHAPTER 6: MANUSCRIPT 2

ASSOCIATIONS BETWEEN SUBJECTIVE MEASURES OF KNEE DYSFUNCTION AND MEASURES OF GROUND REACTION FORCES IN ACL-DEFICIENT MALES AND FEMALES

Michael J Del Bel¹, Kenneth B Smale¹, Teresa E Flaxman², Tine Alkjaer³, Erik B Simonsen³,
Michael R Krogsgaard⁴, and Daniel L Benoit^{1,2}

¹ School of Human Kinetics, University of Ottawa, Canada

² School of Rehabilitation Sciences, University of Ottawa, Canada

³ Department of Neuroscience and Pharmacology, University of Copenhagen, Denmark

⁴ Section for Sports Traumatology M51, Bispebjerg-Frederiksberg Hospital, Denmark (a part of IOC Sports Medicine Copenhagen)

Keywords: ground reaction forces, sex differences, subjective knee joint function, knee rehabilitation

Abstract

Background: Subjective patient-reported outcome measures (PROMs) questionnaires are often administered by clinicians to determine knee joint function in their ACL-deficient patients.

However, it remains unclear what the relationship is between a patient's perceived joint function and their actual functional capacity. The ability to modulate ground reaction forces (GRFs) while weight bearing is critical for balance and locomotion, and thus an important component of functional capacity. This study sought to determine if relationships exist and if they differ between sexes between various PROMs and the ability to generate maximum GRFs in the sagittal and frontal planes.

Methods: An isometric, weight-bearing, force-generating task required healthy and ACL-deficient males and females to generate GRFs in the sagittal and frontal planes. Functional outcome measures included maximal anterior, posterior, medial and lateral generated GRFs, which were normalized to body weight. Subjective outcome measures included participants completing the KOOS, IKDC, Lysholm and Tegner scoring scales. Spearman's rho correlation coefficients (r_s) were calculated to evaluate the relationship between these subjective and functional outcome measures.

Results: FACL participants displayed a trend towards significance with smaller maximum posterior GRFs (1.51 N/kg, $p = 0.048$) compared to FYC (1.81 N/kg). Significantly strong correlations were determined between maximum medial GRFs and both the Lysholm ($r_s = -0.569$; $p = 0.021$) and the Tegner ($r_s = -0.814$, $p < 0.001$) scaling scores for FACL. No significantly strong correlations were found in MACL between any of the subjective and functional outcome measures.

Conclusion: Sex-dependent relationships between subjective and functional outcome measures were found with ACL-d females having a lower ability to generate posterior and medial directed forces, which was related to their lower Lysholm and Tegner scores. This difference in the sensitivity of subjective and functional outcome measures indicates that these populations should not be grouped together during studies using functional tests.

Introduction

One of the most common knee joint injuries is a non-contact anterior cruciate ligament (ACL) rupture. The rate of these injuries has continued to increase (Agel et al., 2016), with a report showing incidences rising from 86,687 in 1994 to 129,836 in 2006 in the United States alone (Mall et al., 2014). In recent years it has also been established that these injuries are more likely to occur in females, by as much as 8 times more compared to their male counterparts (Agel et al., 2005; Brophy et al., 2010; Hewett et al., 2015; Ireland, 1999; Waldén et al., 2010). An ACL injury is quite traumatic and can lead to long-term health consequences such as knee osteoarthritis (OA) and a reduced quality of life for the patient (Lohmander et al., 2007; Lohmander et al., 2004; Oiestad et al., 2011; Roos et al., 1995). Additionally, ACL injuries put a considerable economic toll on the health care system with each injury costing approximately 17 000 USD for reconstruction surgery and rehabilitation, with total annual estimates reaching 3 billion USD (Benjaminse et al., 2010; Petushek et al., 2015). Despite the increased implementation of intervention programs (Alentorn-Geli et al., 2014), these injuries remain to be a significant problem.

The ACL plays an important role in knee joint stability, defined as “the ability to maintain or promptly return to proper positions through an equalisation of forces...” (Riemann and Lephart, 2002), providing sensory feedback of the knee joint’s motion via stress and strain

mechanoreceptors embedded in the ligament's tissues (Georgoulis et al., 2001). When the ACL is ruptured there is a reduced ability to provide feedback resulting in altered neuromuscular control of the muscles surrounding the knee joint (Krogsgaard et al., 2011) and a lower capacity to generate ground reaction forces (GRFs) when weight bearing (Del Bel et al., 2017; see Chapter 5 Table 5.1). Since muscles are the only active regulators of joint stability, this leads to a reduction in the overall function of the knee joint and the ability to compensate for varying external loading conditions.

Many instruments and rating scales have been recently developed in an attempt to measure functional outcomes from a patient's perspective, with only a few methods being evaluated for reliability, validity, and responsiveness (Wang et al., 2010). Function of an ACL-deficient (ACL-d) knee joint is subjectively measured using clinically administered patient-reported outcome measures (PROMs) such as; the Knee Injury and Osteoarthritis Outcome Score (KOOS; Roos and Toksvig-Larsen, 2003), the International Knee Documentation Committee (IKDC) score form (Irrgang et al., 2001), the Lysholm scoring scale (Lysholm and Gillquist, 1982), and the Tegner physical activity level assessment (Tegner and Lysholm, 1985). Patient-reported outcome measures have traditionally not been viewed as the most valid means of determining knee joint function, but have grown in popularity as they specifically incorporate the patients' perceived knee joint function (Bent et al., 2009). However, many of these outcome measures lack a relevancy between the patient's perceived function and the patient's actual function or a clinical measurement of passive knee stability, such as the Lachman and pivot-shift tests for translational and rotational laxity of the knee joint (Snyder-Mackler et al., 1997). Comparisons of PROMs in both ACL-reconstruction (ACL-r) and non-operative (ACL-d) populations have found consistent findings of similar functional outcome measures at up to five years after injury

(Frobell et al., 2013; Grindem et al., 2014; Smith et al., 2014), implying that non-operative rehabilitation of an ACL injury should be the primary treatment option (Failla et al., 2015).

There has been little research in determining a relationship between subjective outcome measures and functional tasks, with the exception of single leg hops and counter-movement jumps in patients who have undergone ACL-r (Hildebrandt et al., 2015; Hopper et al., 2002; Reid et al., 2007). It is therefore necessary to determine how PROMs relate to a patient's actual knee joint function in an ACL-d population, while considering the influence of sex to aid in the guiding knee rehabilitation progression. Furthermore, the ability to quickly measure knee joint function in a confined area such as a clinical office would be practical. To address this, knee joint function in ACL-d males and females was quantified during a simple, weight-bearing, isometric force generation protocol (Flaxman et al., 2016, 2014, 2012; Smith et al., 2012). This quasi-static task was selected as it enabled limiting potentially confounding biomechanical variables such as joint angles and velocities (Wilkie, 1949), allowing for a controlled assessment knee function. Moreover, while the current protocol uses advanced laboratory equipment, should our results prove promising it can easily be adapted to accessible technologies.

The purpose of this study was to determine the relationships between maximum force generation in four loading directions and commonly used PROMs; the KOOS, IKDC, Lysholm and Tegner outcome measures in ACL-d males and females compared to their healthy controls. It was hypothesized that ACL-d males and females would have significantly lower outcome measures for the four PROMs and lower maximum ground reaction forces at each loading direction in their affected limb. Furthermore, we expected to see strong positive correlations between maximum force generation in the sagittal plane with the four PROMs in both ACL-d males and females, given that ACL-d populations have been reported to have lower internal

sagittal knee moments compared to healthy controls (Bohn et al., 2016; Rudolph and Snyder-Mackler, 2004).

Methods

Participants

Forty-seven ACL-d participants (27 males; 20 females) were recruited from the Bispebjerg University Hospital, Copenhagen, Denmark. Of the 47 recruited participants, 38 ACL-d (21 males; 17 females) were able to complete the study's protocol with their injured limb. Thirty-four healthy control participants (CON: 17 males; 17 females) were recruited through the University of Copenhagen, Denmark, to match as closely as possible the age, sex, activity level, and leg dominance of the injured participants. Eligibility criteria consisted of no history of traumatic injury and no presence of any other physical impairment. The dominant limb for participants was determined by which leg they used to kick a soccer ball.

Consent and questionnaires

Testing took place in the gait laboratory at the Department of Neuroscience and Pharmacology, University of Copenhagen, Denmark. This study was approved by the local ethics committee for the Capital Region of Denmark (De Videnskabssetiske Komiteer for Region Hovedstaden, H-3-2013-126) and the University of Ottawa Research Ethics Board (H06-14-27). Participants provided informed consent and completed a series of subjective questionnaires including the KOOS, IKDC, Lysholm and Tegner scoring scales.

Participant preparation and equipment

After receiving informed consent, familiarization of the force target-matching task took place. The maximum voluntary force generation trials from a reliable force target-matching protocol were used to assess differences among tested groups in their ability to generate

isometric forces while weight-bearing (Flaxman et al., 2016, 2014, 2012; Smith et al., 2012). In short, participants placed their test leg in a water-ski boot (Bio, O'Brien, Redmond, WA, USA) that was fixed to a force platform and faced a screen with a projected image of their ground reaction force (GRF) generation. The image provided immediate feedback of the magnitude of the generated GRFs in the $\pm z$ axis (inferior/superior) (Figure 6.1). GRFs were sampled at 1000Hz from a force platform (AMTI-OR6, Watertown, USA) and amplified with an internal gain of 1000 (MSA-6, AMTI, Watertown, USA), then recorded using the supporting software (Nexus v1.8.5, Oxford Metrics, Oxford, UK).

Experimental protocol

Participants were instructed to stand with their test foot in the water-ski boot (Bio, O'Brien, Redmond, WA, USA) with their joints positioned at 30° , 30° and 10° for the hip, knee, and ankle flexion, respectively, and these joint angles were maintained throughout testing. Then, a scaling trial for the force generation on the force platform was performed, with participants standing with their body weight equally distributed through each foot. Once successful, a figure with two bars appeared on the screen, with one representing half of the participant's generated GRF ($\pm F_z$) and the other providing immediate feedback of the magnitudes of the generated GRFs (Figure 6.1).

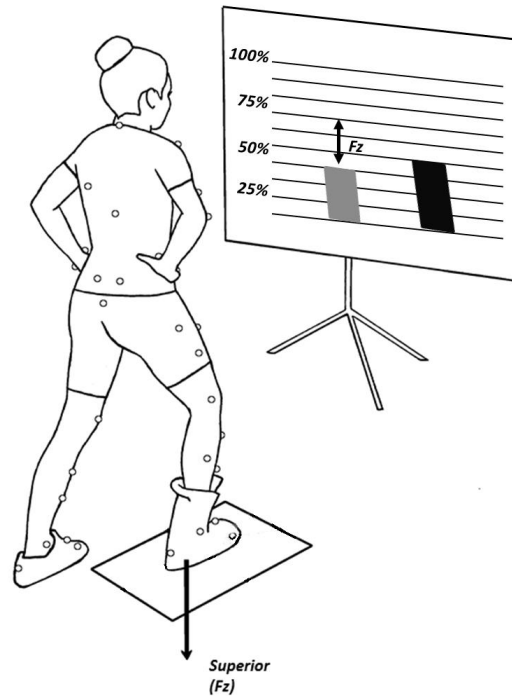


Figure 6.1. Laboratory setup for maximal force generation trials; participants stood with foot of interest in water-ski boot, fixed to force platform while facing a projected image of immediate feedback of the inferior/superior ($\pm F_z$) component of GRF generated (grey solid bar, displayed as a percentage of their total body weight). Participants were required to generate and match half of their body weight (black solid bar) by controlling their body weight (F_z); increasing or decreasing in magnitude with more or less body weight, respectively, during the maximal effort trials (modified from Flaxman et al., 2012).

By calculating the participant's normalized GRF to body weight (N/kg), a visual threshold was created as a target to match and hold for five seconds, while maintaining the above-described position. Participants then performed maximum force generation trials: they were instructed to ramp up their force generation for the first five seconds, in each of the anterior ($-F_y$), posterior ($+F_y$), medial ($-F_x$) and lateral ($+F_x$) directions, with the maximum value being recorded while they maintained half of their body weight on the test limb. Each maximal effort was repeated two times in each direction.

Data processing

Generated GRFs were filtered with a 2nd order dual low-pass 15 Hz cut-off Butterworth filter and normalized to body weight (N/kg). The four questionnaires use a Likert scale,

instructing the participants to select a number on an arbitrary scale with one end of the number range representing the lowest level of functioning and/or highest level of pain/symptoms and the opposite end of the number range representing highest level of functioning and/or lowest level of pain/symptoms. The KOOS questionnaire instructs participants to rank their knee function on a scale of 0 to 4, and has five independent sub-scores: pain, symptoms, activities of daily living (ADL), sports and recreation (S/R), and quality of life (QOL). All PROMs were normalized to a score out of 100, with 100 representing an excellent score and functional knee levels were high for visual purposes, while statistical analyses were performed on the raw scores (Appendix B).

Statistical analysis

When a dataset includes a relatively easy test where participants can achieve maximum or near-maximum scores (positive skewness), the true measurement cannot be evaluated, such as the PROM scores for CON groups of this study. This has been described as the *ceiling effect* (Wang et al., 2009) and one method to appropriately account for such an effect, is to remove the skewed data if it does not affect the interpretation of the results. Therefore, data from MYC and FYC were not included in PROM analyses.

All statistical analyses were performed in SPSS (v22.0, IBM, Chicago, USA). Normality analyses proved that non-parametric tests should be used (Appendix C). Mann-Whitney tests were used to determine differences between ACL-deficient groups for each PROM (five sub-scores of the KOOS, IKDC, Lysholm and Tegner). Kruskal-Wallis tests, with alpha levels of 0.05 for significant differences were used to determine group differences in each maximum force generated (-F_y (anterior), +F_y (posterior), -F_x (medial), and +F_x (lateral) force platform channels). If a significant effect was observed, post-hoc Mann-Whitney tests were performed with adjusted alpha levels of 0.025 for significant differences, to account for the two group comparisons, with

reported group medians and effect sizes (r_{es} : Appendix D). Effect sizes were interpreted as small (± 0.1), medium (± 0.3), and large (± 0.5) (Field, 2013). All post-hoc analyses were determined *a priori* with group comparisons (female young control: FYC, male young control: MYC, female with ACL-deficiency: FACL and male with ACL-deficiency: MACL) for significant effects of sex: FYC vs. MYC and FACL vs. MACL; and effects of ACL injury: FYC vs. FACL and MYC vs. MACL

Bivariate Spearman's rho correlation coefficients were calculated separately for each group for evaluating the strength of the individual relationships between the maximum generated forces and the PROMs. Significant ($p < 0.05$) Spearman's rho correlation coefficients (r_s) were interpreted as weak (± 0.1), medium (± 0.3), and strong (± 0.5) relationships (Field, 2013).

Results

Analysis of differences between the four groups revealed a significant main injury effect was found between CON and ACL-d groups for maximum posterior generated forces. Comparisons of PROM values between the two ACL-d groups revealed that no significant differences were present (Table 6.1).

Table 6.1. Group mean (standard deviations) for FYC, MYC, FACL, and MACL groups for maximum generated ground reaction forces (GRFs) normalized to body weight; $-F_y$ (anterior), $+F_y$ (posterior), $-F_x$ (medial), and $+F_x$ (lateral) force platform channels, and PROMs; the five sub-groups of the KOOS, the IKDC the Lysholm scoring scale, and the Tegner assessment. P-values with (*) represent a significant difference between groups ($p < 0.05$).

	FYC	MYC	FACL	MACL	P-Value	H-Value
GRFs (N/kg)						
$-F_y$	2.59 (0.44)	2.46 (0.62)	2.34 (0.55)	2.37 (0.48)	0.513	2.296
$+F_y$	1.94 (0.85)	1.99 (0.51)	1.38 (0.45)	1.76 (0.57)	0.023*	9.312
$-F_x$	1.10 (0.49)	1.42 (0.35)	1.12 (0.71)	1.09 (0.60)	0.219	4.424
$+F_x$	1.73 (0.67)	1.67 (0.54)	1.29 (0.49)	1.45 (0.53)	0.146	5.358
	FYC	MYC	FACL	MACL	P-Value	U-Value
KOOS (/100)						
<i>Symptoms</i>	N/A	N/A	79.20 (15.43)	98.21 (4.70)	0.535	157.500
<i>Pain</i>	N/A	N/A	83.01 (12.91)	99.65 (1.39)	0.636	162.500
<i>ADL</i>	N/A	N/A	91.18 (5.81)	100.0 (0.00)	0.801	170.000
<i>S/R</i>	N/A	N/A	54.41 (25.49)	99.06 (3.75)	0.791	169.500
<i>QOL</i>	N/A	N/A	43.75 (13.98)	100.0 (0.00)	0.976	177.500
IKDC (/100)	N/A	N/A	59.34 (12.13)	99.57 (1.25)	0.070	109.000
Lysholm (/100)	N/A	N/A	79.00 (16.45)	99.75 (1.00)	0.088	100.500
Tegner (/10)	N/A	N/A	3.31 (1.62)	7.19 (1.68)	0.279	142.500

Post-hoc analyses revealed there were no significant effects, but only a trend towards significance for an effect of injury between maximum posterior force generation in FYC and FACL. In addition, no significant difference was present for maximum posterior force generation between MYC and MACL (Table 6.2).

Table 6.2. Post-hoc Mann-Whitney tests between FYC and FACL, and MYC and MACL with reported group medians for maximum generated ground reaction forces (GRFs) normalized to body weight; $+F_y$ (posterior) force platform channels. P-values with (*) represent a significant difference between groups ($p < 0.025$) and effect sizes were interpreted as small (± 0.1), medium (± 0.3), and large (± 0.5).

	FYC	FACL	P-Value	U-Value	Effect size (r_{es})
GRFs (N/kg)					
$+F_y$	1.81	1.51	0.048	87.000	-0.340
	MYC	MACL	P-Value	U-Value	Effect size (r_{es})
GRFs (N/kg)					
$+F_y$	1.96	1.83	0.413	132.000	-0.136

Spearman's rho correlation coefficients (r_s) were only reported for FACL and MACL groups (Table 6.3; Appendix E, Figures E.1, E.2). Two strong significant correlations were

found for the ACL group; between medial maximum GRF and the Lysholm scoring scale ($r_s = 0.569, p = 0.021$), and the Tegner assessment ($r_s = 0.814, p < 0.001$). No significant correlations were observed for the MACL group.

Table 6.3. Spearman's rho correlation coefficients (r_s) for ACL and MACL between each maximum generated ground reaction force (GRFs) normalized to body weight; $-F_y$ (anterior), $+F_y$ (posterior), $-F_x$ (medial), and $+F_x$ (lateral) force platform channels, and PROMs; the five sub-groups of the KOOS, the IKDC, the Lysholm scoring scale, and the Tegner assessment. P-values with (*) represent a significant difference between groups ($p < 0.05$); r_s were interpreted as weak (± 0.1), medium (± 0.3), and strong (± 0.5) relationships.

	ACL				MACL			
	$-F_y$	$+F_y$	$-F_x$	$+F_x$	$-F_y$	$+F_y$	$-F_x$	$+F_x$
KOOS (/100)								
<i>Symptoms</i>	0.028	0.273	-0.188	0.199	0.208	0.246	<0.001	0.168
<i>Pain</i>	0.048	0.096	0.249	0.101	0.310	0.387	0.082	-0.091
<i>ADL</i>	0.204	0.357	-0.408	0.357	0.319	0.096	0.112	-0.041
<i>S/R</i>	0.189	0.220	0.189	0.157	0.394	0.374	0.061	0.083
<i>QOL</i>	-0.083	-0.271	-0.144	-0.214	0.202	0.134	0.192	-0.143
IKDC (/100)	0.152	0.041	0.425	0.010	0.237	0.212	-0.130	-0.245
Lysholm (/100)	0.070	0.163	0.569*	-0.010	-0.127	0.023	0.004	0.144
Tegner (/10)	0.040	0.317	0.814*	-0.192	0.109	0.033	-0.196	-0.391

Discussion

There is currently a gap in clinical rehabilitation research regarding the relationship between a patient's perceived knee joint function and their actual knee joint function. Therefore, the purpose of this study was to provide an evaluation of knee joint function in ACL-d males and females during a simple, weight-bearing, isometric force-generation task that could easily be implemented in a clinical setting. This was accomplished by investigating the relationships between maximal force generation in the sagittal and frontal planes, and four commonly used subjective outcome measures when assessing knee joint function after injury. We hypothesized that both ACL-d groups would show lower outcome measures for all questionnaires tested and maximum force generations in the sagittal plane. It was also expected that the PROMs would have a strong positive correlation with the maximum force generations in each direction, as

ACL-d patients have been reported to have lower GRF generation in their affected limb (Dai et al., 2014). Our hypotheses were partly supported by our findings since both ACL-d groups had significantly smaller outcome measures for each questionnaire, however a trend towards a significant difference in maximum GRF generation was only found in the posterior direction, with FACL generating lower normalized forces compared to FYC. Furthermore, we did not see many significant correlations between subjective outcome measures and maximum GRF generations, with the exception of strong positive correlations being observed in FACL between medial maximum GRF and both the Lysholm and Tegner scales.

Given that our results showed there were only two significant correlations in the data, it is difficult to come to any concrete conclusion. However, these findings suggest that there may be a discrepancy between the PROMS of males and females and their corresponding ability to generate maximum GRFs, specifically in the posterior and medial loading directions. Females have displayed greater vertical GRFs during single-leg hops compared to males (Harrison et al., 2011), and interestingly, this same task has been found to demonstrate a strong reliability as a functional task with subjective scores (Hooper et al., 2002). Therefore, the differences between sexes in their maximal GRF generation and the PROMs used, warrant further investigations in this and other functional tasks, while maintaining sex as an independent variable. Few statistically significant findings may have been found, due to the small sample sizes (21 MACL; 17 FACL) and high variability of the data.

After an ACL injury, patients do not uniformly respond during rehabilitation. Studies show that the majority of individuals affected by an ACL injury decrease their overall activity level (Griffin et al., 2000; Gustavsson et al., 2006; Hartigan et al., 2010). However, the perceived level of a patient's knee joint function is not consistent among patients (Irgang et al., 2001),

displaying a high variability in subjective outcome measures relating to knee joint function. Our protocol is sensitive enough to determine differences in the ability of participants to generate GRFs among patient populations with deficits in knee joint function. This corresponds with other studies that have found ACL-d patients produce lower GRFs during dynamic tasks (Bohn et al., 2016; Dai et al., 2014; Rudolph et al., 2001; Rudolph and Snyder-Mackler, 2004). As such, we believe our measures are a quantitative indicator of functional capacity.

Most questionnaires do not consider anterior/posterior stability measures of the knee joint and focus more on rotational stability of the patient. This has been suggested as a reason why there is consistently low correlations among a patient's perceived and their actual knee joint function (Neeb et al., 1997). Our study incorporated both the sagittal and frontal planes when assessing maximum force generation and found significantly strong correlations between the maximum medial GRF generation with both the Lysholm and the Tegner scoring scales. This was not surprising, given the Tegner assessment was made to compliment the Lysholm scoring scale (Tegner and Lysholm, 1985). Furthermore, these strong correlations were only seen in the FACL group, which is supported by the routinely reported sex differences in ACL injury related research (Bencke and Zebis, 2011; Chappell et al., 2007; Flaxman et al., 2014; Holden et al., 2015; Landry et al., 2009; Landry et al., 2007; Weinhandl et al., 2015). The Tegner activity level assessment provides feedback of the patient's ability to participate in activities at a range of physical demand and had a very strong relationship with the FACL's ability to generate maximum medial GRFs, which is an important component in knee stabilisation to prevent knee valgus moments (Myer et al., 2015). The Lysholm scoring scale incorporates an evaluation of joint instability as a measurement, suggesting that knee instability affects females with ACL-d more so than their male counterparts. This finding, further demonstrates that studies investigating

biomechanical differences in knee joint function in injured populations must incorporate sex as an independent variable, which is generally not the case (Alkjaer et al., 2003; Beard et al., 1996; Boerboom et al., 2001; Bulgheroni et al., 1997; Ferber et al., 2002; Knoll et al., 2004; Kvist and Gillquist, 2001; Lindström et al., 2010b; Rudolph et al., 2001; Torry et al., 2000).

Limitations

The protocol of this study considered maximal GRF generation in the sagittal and frontal planes. As previously discussed, questionnaires incorporate rotational stability assessments and our protocol did not allow for this variable to be considered functionally and thus could not be included. Also, only two trials were collected for each loading direction in order to minimize the effects of fatigue during maximum voluntary force generation. In addition, there have been deficits in strength, proprioception, and the ability to alter neural pathways (neuroplasticity) in ACL-d patients compared to healthy controls (Krogsgaard et al., 2011; Grooms et al., 2016; Thomas et al., 2013; Tsepis et al., 2006; Williams, 2004; Williams et al., 2005) which was not controlled for in this study. Lastly, not all recruited participants were able to complete the maximal force-generation task, with 38 of 47 ACL-d participants completing the protocol, reducing our sample size. Nevertheless, this study provides insight into the relationship between perceived function and functional capacity using a test that can be easily adapted to a clinical setting.

Conclusion

Using a simple approach to evaluate the relationships between subjective outcome measures and objective functional measures of the knee joint, we determined differences between males and females of ACL-d and healthy populations. There was an overall lack of correlations across all subjective and functional outcome measures of this study. These findings

suggest that maximum force generation in the sagittal and frontal planes are not strong predictors of perceived knee joint function in ACL-d participants; however the decreased ability of FACL to generate posterior and medial directed forces was related to their reduced Lysholm and Tegner scores and is worth further investigation. Finally, maximal force generation is different among ACL-d males and females, indicating that these populations should not be grouped together during non-paired studies using functional tests.

References

- Agel, J., Arendt, E.A., Bershadsky, B., 2005. Anterior Cruciate Ligament Injury in National Collegiate Athletic Association Basketball and Soccer A 13-Year Review. *Am. J. Sports Med.* 33, 524–531.
- Agel, J., Rockwood, T., Klossner, D., 2016. Collegiate ACL Injury Rates Across 15 Sports: National Collegiate Athletic Association Injury Surveillance System Data Update (2004-2005 Through 2012-2013). *Clin. J. Sport Med.* 26, 518–523.
- Alentorn-Geli, E., Mendiguchía, J., Samuelsson, K., Musahl, V., Karlsson, J., Cugat, R., Myer, G.D., 2014. Prevention of non-contact anterior cruciate ligament injuries in sports. Part II: systematic review of the effectiveness of prevention programmes in male athletes. *Knee Surg. Sports Traumatol. Arthrosc.* 22, 16–25.
- Alkjaer, T., Simonsen, E.B., Jørgensen, U., Dyhre-Poulsen, P., 2003. Evaluation of the walking pattern in two types of patients with anterior cruciate ligament deficiency: copers and non-copers. *Eur. J. Appl. Physiol.* 89, 301–308.
- Beard, D.J., Soundarapandian, R.S., O'Connor, J.J., Dodd, C.A.F., 1996. Gait and electromyographic analysis of anterior cruciate ligament deficient subjects. *Gait Posture* 4, 83–88.
- Benjaminse, A., Gokeler, A., Fleisig, G.S., Sell, T.C., Otten, B., 2010. What is the true evidence for gender-related differences during plant and cut maneuvers? A systematic review. *Knee Surg. Sports Traumatol. Arthrosc.* 19, 42–54.
- Bencke, J., Zebis, M.K., 2011. The influence of gender on neuromuscular pre-activity during side-cutting. *J. Electromyogr. Kinesiol.* 21, 371–375.
- Bent, N.P., Wright, C.C., Rushton, A.B., Batt, M.E., 2009. Selecting outcome measures in sports medicine: a guide for practitioners using the example of anterior cruciate ligament rehabilitation. *Br. J. Sports Med.* 43, 1006–1012.
- Boerboom, A.L., Hof, A.L., Halbertsma, J.P., van Raaij, J.J., Schenk, W., Diercks, R.L., van Horn, J.R., 2001. Atypical hamstrings electromyographic activity as a compensatory mechanism in anterior cruciate ligament deficiency. *Knee Surg. Sports Traumatol. Arthrosc.* 9, 211–216.
- Bohn, M.B., Petersen, A.K., Nielsen, D.B., Sørensen, H., Lind, M., 2016. Three-dimensional kinematic and kinetic analysis of knee rotational stability in ACL-deficient patients during walking, running and pivoting. *J. Exp. Orthop.* 3, 27.

- Brophy, R., Silvers, H.J., Gonzales, T., Mandelbaum, B.R., 2010. Gender influences: the role of leg dominance in ACL injury among soccer players. *Br. J. Sports Med.* 44, 694–697.
- Bulgheroni, P., Bulgheroni, M.V., Andrini, L., Guffanti, P., Giughello, A., 1997. Gait patterns after anterior cruciate ligament reconstruction. *Knee Surg. Sports Traumatol. Arthrosc.* 5, 14–21.
- Chappell, J.D., Creighton, R.A., Giuliani, C., Yu, B., Garrett, W.E., 2007. Kinematics and electromyography of landing preparation in vertical stop-jump: Risks for noncontact anterior cruciate ligament injury. *Am. J. Sports Med.* 35, 235–241.
- Dai, B., Butler, R.J., Garrett, W.E., Queen, R.M., 2014. Using ground reaction force to predict knee kinetic asymmetry following anterior cruciate ligament reconstruction. *Scand. J. Med. Sci. Sports* 24, 974–981.
- Failla, M.J., Arundale, A.J.H., Logerstedt, D.S., Snyder-Mackler, L., 2015. Controversies in Knee Rehabilitation: Anterior Cruciate Ligament Injury. *Clin. Sports Med.* 34, 301–312.
- Field, A. 2013. *Discovering statistics using IBM SPSS statistics*. 4th ed, SAGE Publications Ltd., London.
- Ferber, R., Osternig, L.R., Woollacott, M.H., Wasielewski, N.J., Lee, J.H., 2002. Gait mechanics in chronic ACL deficiency and subsequent repair. *Clin. Biomech.* 17, 274–285.
- Flaxman, T.E., Alkjær, T., Simonsen, E.B., Krogsgaard, M.R., Benoit, D.L., 2016. Predicting the Functional Roles of Knee Joint Muscles from Internal Joint Moments. *Med. Sci. Sports Exerc.* *Med. Sci. Sports Exerc.*
- Flaxman, T.E., Smith, A.J.J., Benoit, D.L., 2014. Sex-related differences in neuromuscular control: Implications for injury mechanisms or healthy stabilisation strategies? *J. Orthop. Res.* 32, 310–317.
- Flaxman, T.E., Speirs, A.D., Benoit, D.L., 2012. Joint stabilisers or moment actuators: the role of knee joint muscles while weight-bearing. *J. Biomech.* 45, 2570–2576.
- Frobell, R.B., Roos, H.P., Roos, E.M., Roemer, F.W., Ranstam, J., Lohmander, L.S., 2013. Republished research: Treatment for acute anterior cruciate ligament tear: five year outcome of randomised trial. *Br. J. Sports Med.* 47, 373–373.
- Georgoulis, A.D., Pappa, L., Moebius, U., Malamou-Mitsi, V., Pappa, S., Papageorgiou, C.O., Agnantis, N.J., Soucacos, P.N., 2001. The presence of proprioceptive mechanoreceptors in the remnants of the ruptured ACL as a possible source of re-innervation of the ACL autograft. *Knee Surg. Sports Traumatol. Arthrosc.* 9, 364–368.
- Griffin L.Y., Agel J., Albohm M.J., Arendt, E.A., Dick, R.W., Garrett, W.E., Hewett, T.E., Huston, L., Ireland, M.L., Johnson, R.J., Kibler, W.B., Lephart, S., Lewis, J.L., Lindenfeld, T.N., Mandelbaum, B.R., Marchak, P., Teitz, C.C., Wojtys, E.M. 2000. Noncontact anterior cruciate ligament injuries: risk factors and prevention strategies. *J. Am. Acad. Orthop. Surg.* 8, 141-150.
- Grindem, H., Eitzen, I., Engebretsen, L., Snyder-Mackler, L., Risberg, M.A., 2014. Nonsurgical or Surgical Treatment of ACL Injuries: Knee Function, Sports Participation, and Knee Reinjury. *J. Bone Jt. Surg. Am.* 96, 1233–1241.
- Grooms, D.R., Page, S.J., Nichols-Larsen, D.S., Chaudhari, A.M., White, S.E., Onate, J.A. 2016. Neuroplasticity associated with anterior cruciate ligament reconstruction. *J Orthop Sports Phys Ther.* 0, 1-27.

- Gustavsson, A., Neeter, C., Thomeé, P., Grävare Silbernagel, K., Augustsson, J., Thomeé, R., Karlsson, J. 2006. A test battery for evaluating hop performance in patients with an ACL injury and patients who have undergone ACL reconstruction. *Knee Surg. Sports Traumatol. Arthrosc.* 14, 778–788.
- Harrison, A.D., Ford, K.R., Myer, G.D., Hewett, T.E. 2011. Sex differences in force attenuation: a clinical assessment of single-leg hop performance on a portable force platform. *Br. J. Sports Med.* 45, 198-202.
- Hartigan, E.H., Axe, M.J., Snyder-Mackler, L. 2010. Time line for noncopers to pass return-to-sports criteria after anterior cruciate ligament reconstruction. *J. Orthop. Sports Phys. Ther.* 40, 141–154.
- Hewett, T.E., Myer, G.D., Kiefer, A.W., Ford, K.R., 2015. Longitudinal Increases in Knee Abduction Moments in Females during Adolescent Growth. *Med. Sci. Sports Exerc.* 47, 2579-2585.
- Hildebrandt, C., Müller, L., Zisch, B., Huber, R., Fink, C., Raschner, C., 2015. Functional assessments for decision-making regarding return to sports following ACL reconstruction. Part I: development of a new test battery. *Knee Surg. Sports Traumatol. Arthrosc.* 23, 1273–1281.
- Holden, S., Boreham, C., Doherty, C., Wang, D., Delahunt, E., 2015. Clinical assessment of countermovement jump landing kinematics in early adolescence: Sex differences and normative values. *Clin. Biomech.* 30, 469–474.
- Hopper, D.M., Goh, S.C., Wentworth, L.A., Chan, D.Y.K., Chau, J.H.W., Wootton, G.J., Strauss, G.R., Boyle, J.J.W., 2002. Test–retest reliability of knee rating scales and functional hop tests one year following anterior cruciate ligament reconstruction. *Phys. Ther. Sport* 3, 10–18.
- Ireland, M.L., 1999. Anterior Cruciate Ligament Injury in Female Athletes: Epidemiology. *J. Athl. Train.* 34, 150–154.
- Irrgang, J.J., Anderson, A.F., Boland, A.L., Harner, C.D., Kurosaka, M., Neyret, P., Richmond, J.C., Shelborne, K.D., 2001. Development and Validation of the International Knee Documentation Committee Subjective Knee Form. *Am. J. Sports Med.* 29, 600–613.
- Knoll, Z., Kiss, R.M., Kocsis, L., 2004. Gait adaptation in ACL deficient patients before and after anterior cruciate ligament reconstruction surgery. *J. Electromyogr. Kinesiol.* 14, 287–294.
- Krogsgaard, M.R., Fischer-Rasmussen, T., Dyhre-Poulsen, P., 2011. Absence of sensory function in the reconstructed anterior cruciate ligament. *J. Electromyogr. Kinesiol.* 21, 82–86.
- Kvist, J., Gillquist, J., 2001. Anterior positioning of tibia during motion after anterior cruciate ligament injury. *Med. Sci. Sports Exerc.* 33, 1063–1072.
- Landry, S.C., McKean, K.A., Hubley-Kozey, C.L., Stanish, W.D., Deluzio, K.J., 2009. Gender differences exist in neuromuscular control patterns during the pre-contact and early stance phase of an unanticipated side-cut and cross-cut maneuver in 15–18 years old adolescent soccer players. *J. Electromyogr. Kinesiol.* 19, e370–e379.
- Landry, S.C., McKean, K.A., Hubley-Kozey, C.L., Stanish, W.D., Deluzio, K.J., 2007. Neuromuscular and lower limb biomechanical differences exist between male and female

- elite adolescent soccer players during an unanticipated run and crosscut maneuver. *Am. J. Sports Med.* 35, 1901–1911.
- Lindström, M., Felländer-Tsai, L., Wredmark, T., Henriksson, M., 2010. Adaptations of gait and muscle activation in chronic ACL deficiency. *Knee Surg. Sports Traumatol. Arthrosc.* 18, 106–114.
- Lohmander, L.S., Englund, P.M., Dahl, L.L., Roos, E.M., 2007. The Long-term Consequence of Anterior Cruciate Ligament and Meniscus Injuries Osteoarthritis. *Am. J. Sports Med.* 35, 1756–1769.
- Lohmander, L.S., Ostenberg, A., Englund, M., Roos, H., 2004. High prevalence of knee osteoarthritis, pain, and functional limitations in female soccer players twelve years after anterior cruciate ligament injury. *Arthritis Rheum.* 50, 3145–3152.
- Lysholm, J., Gillquist, J., 1982. Evaluation of knee ligament surgery results with special emphasis on use of a scoring scale. *Am. J. Sports Med.* 10, 150–154.
- Mall, N.A., Chalmers, P.N., Moric, M., Tanaka, M.J., Cole, B.J., Bach, B.R., Paletta, G.A., 2014. Incidence and trends of anterior cruciate ligament reconstruction in the United States. *Am. J. Sports Med.* 42, 2363–2370.
- Myer, G.D., Ford, K.R., Di Stasi, S.L., Foss, K.D., Micheli, L.J., Hewett, T.E. 2015. High knee abduction moments are common risk factors for patellofemoral pain (PFP) and anterior cruciate ligament injury in girls: is PFP itself a predictor for subsequent ACL injury? *Br. J. Sports Med.* 49, 118-122.
- Neeb, T.B., Aufdemkampe, G., Wagener, J.H., Mastenbroek, L. 1997. Assessing anterior cruciate ligament injuries: the association and differential value of questionnaires, clinical tests, and functional tests. *J. Orthop. Sports Phys. Ther.* 26, 324–331.
- Oiestad, B.E., Holm, I., Engebretsen, L., Risberg, M.A., 2011. The association between radiographic knee osteoarthritis and knee symptoms, function and quality of life 10-15 years after anterior cruciate ligament reconstruction. *Br. J. Sports Med.* 45, 583–588.
- Petushek, E.J., Cokely, E.T., Ward, P., Durocher, J.J., Wallace, S.J., Myer, G.D., 2015. Injury risk estimation expertise: Assessing the ACL injury risk estimation. *Am. J. Sports Med.* 43, 1640–1647.
- Reid, A., Birmingham, T.B., Stratford, P.W., Alcock, G.K., Giffin, J.R., 2007. Hop Testing Provides a Reliable and Valid Outcome Measure During Rehabilitation After Anterior Cruciate Ligament Reconstruction. *Phys. Ther.* 87, 337–349.
- Riemann, B.L., Lephart, S.M., 2002. The Sensorimotor System, Part I: The Physiologic Basis of Functional Joint Stability. *J. Athl. Train.* 37, 71–79.
- Roos, E.M., Toksvig-Larsen, S., 2003. Knee injury and Osteoarthritis Outcome Score (KOOS) – validation and comparison to the WOMAC in total knee replacement. *Health Qual. Life Outcomes* 1, 17.
- Roos, H., Adalberth, T., Dahlberg, L., Lohmander, L.S., 1995. Osteoarthritis of the knee after injury to the anterior cruciate ligament or meniscus: the influence of time and age. *Osteoarthritis Cartilage* 3, 261–267.
- Rudolph, K.S., Axe, M.J., Buchanan, T.S., Scholz, J.P., Snyder-Mackler, L., 2001. Dynamic stability in the anterior cruciate ligament deficient knee. *Knee Surg. Sports Traumatol. Arthrosc.* 9, 62–71.

- Rudolph, K.S., Snyder-Mackler, L., 2004. Effect of dynamic stability on a step task in ACL deficient individuals. *J. Electromyogr. Kinesiol.* 14, 565–575.
- Smith, A.J.J., Flaxman, T.E., Speirs, A.D., Benoit, D.L., 2012. Reliability of knee joint muscle activity during weight bearing force control. *J. Electromyogr. Kinesiol.* 22, 914–922.
- Smith, T.O., Postle, K., Penny, F., McNamara, I., Mann, C.J.V., 2014. Is reconstruction the best management strategy for anterior cruciate ligament rupture? A systematic review and meta-analysis comparing anterior cruciate ligament reconstruction versus non-operative treatment. *Knee* 21, 462–470.
- Snyder-Mackler, L., Fitzgerald, G.K., Bartolozzi, A.R., Ciccotti, M.G., 1997. The relationship between passive joint laxity and functional outcome after anterior cruciate ligament injury. *Am. J. Sports Med.* 25, 191–195.
- Tegner, Y., Lysholm, J., 1985. Rating systems in the evaluation of knee ligament injuries. *Clin. Orthop.* 43–49.
- Torry, M.R., Decker, M.J., Viola, R.W., O'Connor, D.D., Richard Steadman, J., 2000. Intra-articular knee joint effusion induces quadriceps avoidance gait patterns. *Clin. Biomech.* 15, 147–159.
- Waldén, M., Hägglund, M., Werner, J., Ekstrand, J., 2010. The epidemiology of anterior cruciate ligament injury in football (soccer): a review of the literature from a gender-related perspective. *Knee Surg. Sports Traumatol. Arthrosc.* 19, 3–10.
- Wang, D., Jones, M.H., Khair, M.M., Miniaci, A., 2010. Patient-reported outcome measures for the knee. *J. Knee Surg.* 23, 137–151.
- Wang, L., Zhang, Z., McArdle, J.J., Salthouse, T.A., 2009. Investigating Ceiling Effects in Longitudinal Data Analysis. *Multivar. Behav. Res.* 43, 476–496.
- Weinhandl, J.T., Irmischer, B.S., Sievert, Z.A., 2015. Sex differences in unilateral landing mechanics from absolute and relative heights. *Knee* 22, 298–303.
- Wilkie, D.R., 1949. The relation between force and velocity in human muscle. *J. Physiol.* 110, 249–280.
- Williams, G.N., Chmielewski, T., Rudolph, K.S., Buchanan, T.S., Snyder-Mackler, L., 2001. Dynamic knee stability: current theory and implications for clinicians and scientists. *J. Orthop. Sports Phys. Ther.* 31, 546–566.

CHAPTER 7: GENERAL DISCUSSION

The ability to stabilise the knee joint is critical for everyday life. With an injury to the ACL, there is a loss in proprioception and also a mechanical change in the knee joint, leading to a reduction in joint stability. In an effort to maintain joint stability, an ACL-deficient (ACL-d) patient must adapt their force-generation strategies to the altered integrity of the knee. Studies show different neuromuscular (Catalfamo et al., 2010; DeMont and Lephart, 1998; Lindström et al., 2010) and biomechanical (Button, van Deursen, & Price, 2008; Catalfamo et al., 2010; Gustavsson et al., 2006) strategies used by ACL-d patients. However, after an ACL injury, patients do not uniformly respond to the implemented rehabilitation, with most not being able to return to activity levels prior to the injury (Griffin et al., 2000; Gustavsson et al., 2006; Hartigan et al., 2010). In order to have successful rehabilitation implemented for ACL-d males and females, the following needs to be taken into account: i) how an ACL rupture affects knee joint force-generation strategies, ii) how do males and females activate the individual muscles during various directional loading conditions, and iii) the relationship between a patient's perceived knee joint function and their functional capability. Furthermore, (iv) there is currently a gap in clinical rehabilitation research regarding the interaction between sex and an ACL injury with respect to knee joint neuromuscular control strategies, and the relationship between a patient's perceived knee joint function and their actual knee joint function, which also must be addressed.

The overall purpose of this thesis was to address these four issues and provide objective measures to improve clinical and rehabilitation management among males and females who have injured their ACL. The first aim was to provide objective and quantitative measurements to describe the functional roles of individual muscles in an ACL-d population. This was accomplished by using a highly controlled, weight-bearing approach to elicit force-generation

strategies at varying loading directions to further our understanding of how individual muscles objectively adapt their activation to help stabilise an ACL-d knee joint. We also classified those muscle roles as they relate to knee stabilisation (*general stabilisers*, *specific joint stabiliser*, and *moment actuator*). It was hypothesized that with a rupture to the ACL, FACL and MACL would display lower internal knee joint moments and more generalized muscle activations regardless of the loading conditions compared to their healthy counterparts. In addition, we hypothesized that sex differences would be present with females having greater activations in the quadriceps muscles. Our hypotheses were partly supported since both sex and injury effects contributed to different functional roles being identified between the four cohorts of this study. We found that MYC activated their muscles the most specifically, with no muscles being a general stabiliser, while FACL activated their muscles the least specifically, with four of ten muscles being general stabilisers. This suggests that there is a hierarchy in the specificity of muscle activation strategies for force-generation when stabilising the knee joint: MYC as the most specific, FYC reflecting the strategy of MACL, and FACL as the least specific.

The second aim of this thesis was to quantify the relationships between a patient's perceived knee joint function, through PROMs, and their functional stability after injury, through maximal force generation in the sagittal and frontal planes. It was hypothesized that ACL-d males and females would have significantly lower PROMs and lower maximum GRFs in both planes. Furthermore, we hypothesized to observe strong positive correlations between maximum GRFs in the sagittal plane with each PROM. This set of hypotheses were also partially supported by our findings, as both ACL-d groups had significantly lower perceived knee joint function compared to healthy controls. However, it was only a trend towards significance, with FACL generating smaller maximal posterior GRFs compared to their healthy counterparts. Lastly, of

the 32 correlation coefficients calculated for each FACL and MACL, two statistically significant correlations (both for FACL) were found. This indicates that there may be a discrepancy in the PROMs sensitivity between sexes and their corresponding ability to generate maximum GRFs.

As previously discussed sex-related differences in knee neuromuscular control strategies are routinely found and suggested to be linked to the increased rate of non-contact ACL injuries among females (Bencke and Zebis, 2011; Chappell et al., 2007; Flaxman et al., 2014; Holden et al., 2015; Landry et al., 2009; Landry et al., 2007; Weinhandl et al., 2015). In addition, there are many instruments and rating scales (PROMs) that are used to measure knee function from a patient's perspective, with the majority not being evaluated for the measures' reliability, validity, and responsiveness (Wang et al., 2010). Some comparisons have been performed between PROMs among ACL-d and ACL-r populations, finding similar functional outcome measures up to five years after injury (Frobell et al., 2013; Grindem et al., 2014; Smith et al., 2014). This alone suggests that non-operative rehabilitation of an ACL injury should be the primary treatment option (Failla et al., 2015), and this would require an optimal intervention strategy based on maximizing function knee joint stability. Given these knee neuromuscular control strategy differences among healthy populations and consistency among ACL-d and ACL-r PROMs, there is surprisingly limited research on sex-specific research in this domain among ACL-d populations (Alkjaer et al., 2003; Beard et al., 1996; Boerboom et al., 2001; Bulgheroni et al., 1997; Ferber et al., 2002; Knoll et al., 2004; Kvist and Gillquist, 2001; Lindström et al., 2010b; Rudolph et al., 2001; Torry et al., 2000).

We've demonstrated that sex differences in knee neuromuscular control strategies exist both before and after ACL-injury and that there is a discrepancy present between sexes in the sensitivity of commonly used PROMs, suggesting the need for sex-specific tailoring of

rehabilitation programs. Our results indicate that there is an opportunity to improve the success rate of ACL-injury rehabilitation interventions to improve function in ACL-d females. Also, as evidenced by the present gap in determining a relationship between subjective outcome measures and functional tasks, there is an opportunity to develop a functional task that can be used in a practical, clinical setting for evaluating knee stability. We believe that future rehabilitation programs for ACL-d males and females should incorporate a patient's ability to specify a muscle's activation during a combination of loading conditions, specifically medial and lateral loads, and modifications in PROMs to better resemble the functional capacity of the individual. The results of this thesis also indicate the need to tailor those exercises differently for males and females in the ACL-d populations.

REFERENCES

- Aalbersberg, S., Kingma, I., van Dieën, J.H., 2009. Hamstrings co-activation in ACL-deficient subjects during isometric whole-leg extensions. *Knee Surg. Sports Traumatol. Arthrosc.* 17, 946–955.
- Acevedo, R.J., Rivera-Vega, A., Miranda, G., Micheo, W., 2014. Anterior cruciate ligament injury: identification of risk factors and prevention strategies. *Curr. Sports Med. Rep.* 13, 186–191.
- Agel, J., Arendt, E.A., Bershadsky, B., 2005. Anterior Cruciate Ligament Injury in National Collegiate Athletic Association Basketball and Soccer A 13-Year Review. *Am. J. Sports Med.* 33, 524–531.
- Agel, J., Rockwood, T., Klossner, D., 2016. Collegiate ACL Injury Rates Across 15 Sports: National Collegiate Athletic Association Injury Surveillance System Data Update (2004-2005 Through 2012-2013). *Clin. J. Sport Med.* 26, 518–523.
- Alentorn-Geli, E., Mendiguchía, J., Samuelsson, K., Musahl, V., Karlsson, J., Cugat, R., Myer, G.D., 2014. Prevention of non-contact anterior cruciate ligament injuries in sports. Part II: systematic review of the effectiveness of prevention programmes in male athletes. *Knee Surg. Sports Traumatol. Arthrosc.* 22, 16–25.
- Alkjær, T., Henriksen, M., Simonsen, E.B., 2011. Different knee joint loading patterns in ACL deficient copers and non-copers during walking. *Knee Surg. Sports Traumatol. Arthrosc.* 19, 615–621.
- Alkjaer, T., Simonsen, E.B., Jørgensen, U., Dyhre-Poulsen, P., 2003. Evaluation of the walking pattern in two types of patients with anterior cruciate ligament deficiency: copers and non-copers. *Eur. J. Appl. Physiol.* 89, 301–308.
- Andrews, J.R., McLeod, W.D., Ward, T., Howard, K., 1977. The cutting mechanism. *Am. J. Sports Med.* 5, 111–121.
- Arendt, E.A., Agel, J., Dick, R., 1999. Anterior Cruciate Ligament Injury Patterns Among Collegiate Men and Women. *J. Athl. Train.* 34, 86–92.
- Beard, D.J., Soundarapandian, R.S., O'Connor, J.J., Dodd, C.A.F., 1996. Gait and electromyographic analysis of anterior cruciate ligament deficient subjects. *Gait Posture* 4, 83–88.
- Beaulieu, M.L., Lamontagne, M., Xu, L., 2009. Lower limb muscle activity and kinematics of an unanticipated cutting manoeuvre: a gender comparison. *Knee Surg. Sports Traumatol. Arthrosc.* 17, 968–976.
- Beaulieu, M.L., Lamontagne, M., Xu, L., 2008. Gender differences in time-frequency EMG analysis of unanticipated cutting maneuvers. *Med. Sci. Sports Exerc.* 40, 1795–1804.
- Bencke, J., Zebis, M.K., 2011. The influence of gender on neuromuscular pre-activity during side-cutting. *J. Electromyogr. Kinesiol.* 21, 371–375.
- Benjaminse, A., Gokeler, A., Fleisig, G.S., Sell, T.C., Otten, B., 2010. What is the true evidence for gender-related differences during plant and cut maneuvers? A systematic review. *Knee Surg. Sports Traumatol. Arthrosc.* 19, 42–54.
- Benoit, D.L., Ramsey, D.K., Lamontagne, M., Xu, L., Wretenberg, P., Renström, P., 2006. Effect of skin movement artifact on knee kinematics during gait and cutting motions measured in vivo. *Gait Posture* 24, 152–164.
- Bent, N.P., Wright, C.C., Rushton, A.B., Batt, M.E., 2009. Selecting outcome measures in sports medicine: a guide for practitioners using the example of anterior cruciate ligament rehabilitation. *Br. J. Sports Med.* 43, 1006–1012.

- Bere, T., Flørenes, T.W., Krosshaug, T., Koga, H., Nordsletten, L., Irving, C., Muller, E., Reid, R.C., Senner, V., Bahr, R., 2011. Mechanisms of Anterior Cruciate Ligament Injury in World Cup Alpine Skiing A Systematic Video Analysis of 20 Cases. *Am. J. Sports Med.* 39, 1421–1429.
- Boden, B.P., Dean, G.S., Feagin, J.A., Garrett, W.E., 2000. Mechanisms of anterior cruciate ligament injury. *Orthopedics* 23, 573–578.
- Boerboom, A.L., Hof, A.L., Halbertsma, J.P., van Raaij, J.J., Schenk, W., Diercks, R.L., van Horn, J.R., 2001. Atypical hamstrings electromyographic activity as a compensatory mechanism in anterior cruciate ligament deficiency. *Knee Surg. Sports Traumatol. Arthrosc.* 9, 211–216.
- Bohn, M.B., Petersen, A.K., Nielsen, D.B., Sørensen, H., Lind, M., 2016. Three-dimensional kinematic and kinetic analysis of knee rotational stability in ACL-deficient patients during walking, running and pivoting. *J. Exp. Orthop.* 3, 27.
- Borsa, P.A., Lephart, S.M., Irrgang, J.J., Safran, M.R., Fu, F.H., 1997. The effects of joint position and direction of joint motion on proprioceptive sensibility in anterior cruciate ligament-deficient athletes. *Am. J. Sports Med.* 25, 336–340.
- Brophy, R., Silvers, H.J., Gonzales, T., Mandelbaum, B.R., 2010. Gender influences: the role of leg dominance in ACL injury among soccer players. *Br. J. Sports Med.* 44, 694–697.
- Brophy, R.H., Stepan, J.G., Silvers, H.J., Mandelbaum, B.R., 2015. Defending Puts the Anterior Cruciate Ligament at Risk During Soccer: A Gender-Based Analysis. *Sports Health* 7, 244–249.
- Buchanan, T.S., Almdale, D.P., Lewis, J.L., Rymer, W.Z., 1986. Characteristics of synergic relations during isometric contractions of human elbow muscles. *J. Neurophysiol.* 56, 1225–1241.
- Buchanan, T.S., Lloyd, D.G., 1997. Muscle activation at the human knee during isometric flexion-extension and varus-valgus loads. *J. Orthop. Res.* 15, 11–17.
- Bulgheroni, P., Bulgheroni, M.V., Andriani, L., Guffanti, P., Giughello, A., 1997. Gait patterns after anterior cruciate ligament reconstruction. *Knee Surg. Sports Traumatol. Arthrosc.* 5, 14–21.
- Button, K., van Deursen, R., Price, P., 2008. Recovery in functional non-copers following anterior cruciate ligament rupture as detected by gait kinematics. *Phys. Ther. Sport* 9, 97–104.
- Catalfamo, P.F., Aguiar, G., Curi, J., Braidot, A., 2010. Anterior Cruciate Ligament Injury: Compensation during Gait using Hamstring Muscle Activity. *Open Biomed. Eng. J.* 4, 99–106.
- Chappell, J.D., Creighton, R.A., Giuliani, C., Yu, B., Garrett, W.E., 2007. Kinematics and electromyography of landing preparation in vertical stop-jump: Risks for noncontact anterior cruciate ligament injury. *Am. J. Sports Med.* 35, 235–241.
- Chimelewski, T.L., Rudolph, K.S., Fitzgerald, G.K., Axe, M.J., Snyder-Mackler, L., 2001. Biomechanical evidence supporting a differential response to acute ACL injury. *Clin. Biomech.* 16, 586–591.
- Cowling, E.J., Steele, J.R., 2001. The Effect of Upper-Limb Motion on Lower-Limb Muscle Synchrony. *J. Bone Jt. Surg Am* 83, 35–35.
- Curry, J.R., 1956. The Analysis of Two-Dimensional Orientation Data. *J. Geol.* 64, 117–131.

- Dai, B., Butler, R.J., Garrett, W.E., Queen, R.M., 2014. Using ground reaction force to predict knee kinetic asymmetry following anterior cruciate ligament reconstruction. *Scand. J. Med. Sci. Sports* 24, 974–981.
- Delp, S.L., Loan, J.P., Hoy, M.G., Zajac, F.E., Topp, E.L., Rosen, J.M., 1990. An interactive graphics-based model of the lower extremity to study orthopaedic surgical procedures. *IEEE Trans. Biomed. Eng.* 37, 757–767.
- DeLuca, C., 1997. The use of surface electromyography in biomechanics. *J. Appl. Biomech.* 13, 135–163.
- DeMont, R.G., Lephart, S.M., 1998. Muscle pre-activity among ACL-D, ACL-R, and control female subjects during various lower. *J. Athl. Train.* 33, S73.
- Dewald, J.P., Pope, P.S., Given, J.D., Buchanan, T.S., Rymer, W.Z., 1995. Abnormal muscle coactivation patterns during isometric torque generation at the elbow and shoulder in hemiparetic subjects. *Brain J. Neurol.* 118, 495–510.
- Dhillon, M.S., Bali, K., Prabhakar, S., 2011. Proprioception in anterior cruciate ligament deficient knees and its relevance in anterior cruciate ligament reconstruction. *Indian J. Orthop.* 45, 294–300.
- Escamilla, R.F., Fleisig, G.S., Zheng, N., Barrentine, S.W., Wilk, K.E., Andrews, J.R., 1998. Biomechanics of the knee during closed kinetic chain and open kinetic chain exercises. *Med. Sci. Sports Exerc.* 30, 556–569.
- Fagenbaum, R., Darling, W.G., 2003. Jump Landing Strategies in Male and Female College Athletes and the Implications of Such Strategies for Anterior Cruciate Ligament Injury. *Am. J. Sports Med.* 31, 233–240.
- Failla, M.J., Arundale, A.J.H., Logerstedt, D.S., Snyder-Mackler, L., 2015. Controversies in Knee Rehabilitation: Anterior Cruciate Ligament Injury. *Clin. Sports Med.* 34, 301–312.
- Field, A. 2013. *Discovering statistics using IBM SPSS statistics*. 4th ed, SAGE Publications Ltd., London.
- Ferber, R., Osternig, L.R., Woollacott, M.H., Wasielewski, N.J., Lee, J.H., 2002. Gait mechanics in chronic ACL deficiency and subsequent repair. *Clin. Biomech.* 17, 274–285.
- Fitzgerald, G.K., Axe, M.J., Snyder-Mackler, L., 2000. The efficacy of perturbation training in nonoperative anterior cruciate ligament rehabilitation programs for physically active individuals. *Phys. Ther.* 80, 128–151.
- Flaxman, T.E., Alkjær, T., Simonsen, E.B., Krogsgaard, M.R., Benoit, D.L., 2016. Predicting the Functional Roles of Knee Joint Muscles from Internal Joint Moments. *Med. Sci. Sports Exerc. Med. Sci. Sports Exerc.*
- Flaxman, T.E., Smith, A.J.J., Benoit, D.L., 2014. Sex-related differences in neuromuscular control: Implications for injury mechanisms or healthy stabilisation strategies? *J. Orthop. Res.* 32, 310–317.
- Flaxman, T.E., Speirs, A.D., Benoit, D.L., 2012. Joint stabilisers or moment actuators: the role of knee joint muscles while weight-bearing. *J. Biomech.* 45, 2570–2576.
- Ford, K.R., Myer, G.D., Toms, H.E., Hewett, T.E., 2005. Gender differences in the kinematics of unanticipated cutting in young athletes. *Med. Sci. Sports Exerc.* 37, 124–129.
- Frobell, R.B., Roos, H.P., Roos, E.M., Roemer, F.W., Ranstam, J., Lohmander, L.S., 2013. Republished research: Treatment for acute anterior cruciate ligament tear: five year outcome of randomised trial. *Br. J. Sports Med.* 47, 373–373.
- Georgoulis, A.D., Pappa, L., Moebius, U., Malamou-Mitsi, V., Pappa, S., Papageorgiou, C.O., Agnantis, N.J., Soucacos, P.N., 2001. The presence of proprioceptive mechanoreceptors

- in the remnants of the ruptured ACL as a possible source of re-innervation of the ACL autograft. *Knee Surg. Sports Traumatol. Arthrosc.* 9, 364–368.
- Girgis, F.G., Marshall, J.L., Monajem, A., 1975. The cruciate ligaments of the knee joint. Anatomical, functional and experimental analysis. *Clin. Orthop.* 216–231.
- Goldblatt, J.P., Richmond, J.C., 2003. Anatomy and biomechanics of the knee. *Oper. Tech. Sports Med., The Multiple Ligament Injured Knee, Part I.* 11, 172–186.
- Griffin L.Y., Agel J., Albohm M.J., Arendt, E.A., Dick, R.W., Garrett, W.E., Hewett, T.E., Huston, L., Ireland, M.L., Johnson, R.J., Kibler, W.B., Lephart, S., Lewis, J.L., Lindenfeld, T.N., Mandelbaum, B.R., Marchak, P., Teitz, C.C., Wojtys, E.M. 2000. Noncontact anterior cruciate ligament injuries: risk factors and prevention strategies. *J. Am. Acad. Orthop. Surg.* 8, 141-150.
- Grindem, H., Eitzen, I., Engebretsen, L., Snyder-Mackler, L., Risberg, M.A., 2014. Nonsurgical or Surgical Treatment of ACL Injuries: Knee Function, Sports Participation, and Knee Reinjury. *J Bone Jt. Surg Am* 96, 1233–1241.
- Grooms, D.R., Page, S.J., Nichols-Larsen, D.S., Chaudhari, A.M., White, S.E., Onate, J.A. 2016. Neuroplasticity associated with anterior cruciate ligament reconstruction. *J Orthop Sports Phys Ther.* 0, 1-27.
- Gustavsson, A., Neeter, C., Thomeé, P., Silbernagel, K.G., Augustsson, J., Thomeé, R., Karlsson, J., 2006. A test battery for evaluating hop performance in patients with an ACL injury and patients who have undergone ACL reconstruction. *Knee Surg. Sports Traumatol. Arthrosc.* 14, 778–788.
- Hammer, O., Harper, D.A., Ryan, P.D., 2001. PAST: Paleontological Statistics software package for education and data analysis. *Palaeontol. Electron.* 4.
- Hamner, S.R., Seth, A., Delp, S.L., 2010. Muscle contributions to propulsion and support during running. *J. Biomech.* 43, 2709–2716.
- Hanson, A.M., Padua, D.A., Troy Blackburn, J., Prentice, W.E., Hirth, C.J., 2008. Muscle Activation During Side-Step Cutting Maneuvers in Male and Female Soccer Athletes. *J. Athl. Train.* 43, 133–143.
- Harrison, A.D., Ford, K.R., Myer, G.D., Hewett, T.E. 2011. Sex differences in force attenuation: a clinical assessment of single-leg hop performance on a portable force platform. *Br. J. Sports Med.* 45, 198-202.
- Hartigan, E.H., Axe, M.J., Snyder-Mackler, L. 2010. Time line for noncopers to pass return-to-sports criteria after anterior cruciate ligament reconstruction. *J. Orthop. Sports Phys. Ther.* 40, 141–154.
- Hashemi, J., Chandrashekar, N., Jang, T., Karpas, F., Oseto, M., Ekwaro-Osire, S., 2007. An Alternative Mechanism of Non-contact Anterior Cruciate Ligament Injury During Jump-landing: In-vitro Simulation. *Exp. Mech.* 47, 347–354.
- Hermens, H.J., Freriks, B., Disselhorst-Klug, C., Rau, G., 2000. Development of recommendations for SEMG sensors and sensor placement procedures. *J. Electromyogr. Kinesiol.* 10, 361–374.
- Hewett, T.E., 2010. Multiple risk factors related to familial predisposition to anterior cruciate ligament injury: fraternal twin sisters with anterior cruciate ligament ruptures. *Br. J. Sports Med.* 44, 848–855.
- Hewett, T.E., 2000. Neuromuscular and hormonal factors associated with knee injuries in female athletes. Strategies for intervention. *Sports Med.* 29, 313–327.

- Hewett, T.E., Myer, G.D., Ford, K.R., 2006. Anterior Cruciate Ligament Injuries in Female Athletes Part 1, Mechanisms and Risk Factors. *Am. J. Sports Med.* 34, 299–311.
- Hewett, T.E., Myer, G.D., Kiefer, A.W., Ford, K.R., 2015. Longitudinal Increases in Knee Abduction Moments in Females during Adolescent Growth. *Med. Sci. Sports Exerc.* 47, 2579-2585.
- Hildebrandt, C., Müller, L., Zisch, B., Huber, R., Fink, C., Raschner, C., 2015. Functional assessments for decision-making regarding return to sports following ACL reconstruction. Part I: development of a new test battery. *Knee Surg. Sports Traumatol. Arthrosc.* 23, 1273–1281.
- Holden, S., Boreham, C., Doherty, C., Wang, D., Delahunt, E., 2015. Clinical assessment of countermovement jump landing kinematics in early adolescence: Sex differences and normative values. *Clin. Biomech.* 30, 469–474.
- Hopper, D.M., Goh, S.C., Wentworth, L.A., Chan, D.Y.K., Chau, J.H.W., Wootton, G.J., Strauss, G.R., Boyle, J.J.W., 2002. Test–retest reliability of knee rating scales and functional hop tests one year following anterior cruciate ligament reconstruction. *Phys. Ther. Sport* 3, 10–18.
- Iguchi, J., Tateuchi, H., Taniguchi, M., Ichihashi, N., 2013. The effect of sex and fatigue on lower limb kinematics, kinetics, and muscle activity during unanticipated side-step cutting. *Knee Surg. Sports Traumatol. Arthrosc.* 22, 41–48.
- Ireland, M.L., 1999. Anterior Cruciate Ligament Injury in Female Athletes: Epidemiology. *J. Athl. Train.* 34, 150–154.
- Irrgang, J.J., Anderson, A.F., Boland, A.L., Harner, C.D., Kurosaka, M., Neyret, P., Richmond, J.C., Shelborne, K.D., 2001. Development and Validation of the International Knee Documentation Committee Subjective Knee Form. *Am. J. Sports Med.* 29, 600–613.
- Kessler, M.A., Behrend, H., Henz, S., Stutz, G., Rukavina, A., Kuster, M.S., 2008. Function, osteoarthritis and activity after ACL-rupture: 11 years follow-up results of conservative versus reconstructive treatment. *Knee Surg. Sports Traumatol. Arthrosc.* 16, 442–448.
- Kiapour, A.M., Kiapour, A., Goel, V.K., Quatman, C.E., Wordeman, S.C., Hewett, T.E., Demetropoulos, C.K., 2015. Uni-directional coupling between tibiofemoral frontal and axial plane rotation supports valgus collapse mechanism of ACL injury. *J. Biomech.* 48, 1745–1751.
- Knoll, Z., Kiss, R.M., Kocsis, L., 2004. Gait adaptation in ACL deficient patients before and after anterior cruciate ligament reconstruction surgery. *J. Electromyogr. Kinesiol.* 14, 287–294.
- Koga, H., Nakamae, A., Shima, Y., Iwasa, J., Myklebust, G., Engebretsen, L., Bahr, R., Krosshaug, T., 2010. Mechanisms for noncontact anterior cruciate ligament injuries: knee joint kinematics in 10 injury situations from female team handball and basketball. *Am. J. Sports Med.* 38, 2218–2225.
- Krishnan, C., Huston, K., Amendola, A., Williams, G.N., 2008. Quadriceps and hamstrings muscle control in athletic males and females. *J. Orthop. Res.* 26, 800–808.
- Krishnan, C., Williams, G.N., 2009. Sex Differences in Quadriceps and Hamstrings EMG-Moment Relationships: *Med. Sci. Sports Exerc.* 41, 1653–1661.
- Krogsgaard, M.R., Fischer-Rasmussen, T., Dyhre-Poulsen, P., 2011. Absence of sensory function in the reconstructed anterior cruciate ligament. *J. Electromyogr. Kinesiol.* 21, 82–86.

- Kvist, J., Gillquist, J., 2001. Anterior positioning of tibia during motion after anterior cruciate ligament injury. *Med. Sci. Sports Exerc.* 33, 1063–1072.
- LaBella, C.R., Hennrikus, W., Hewett, T.E., 2014. Anterior cruciate ligament injuries: diagnosis, treatment, and prevention. *Pediatrics* 133, e1437-1450.
- Landry, S.C., McKean, K.A., Hubley-Kozey, C.L., Stanish, W.D., Deluzio, K.J., 2009. Gender differences exist in neuromuscular control patterns during the pre-contact and early stance phase of an unanticipated side-cut and cross-cut maneuver in 15–18 years old adolescent soccer players. *J. Electromyogr. Kinesiol.* 19, e370–e379.
- Landry, S.C., McKean, K.A., Hubley-Kozey, C.L., Stanish, W.D., Deluzio, K.J., 2007a. Neuromuscular and Lower Limb Biomechanical Differences Exist Between Male and Female Elite Adolescent Soccer Players During an Unanticipated Side-cut Maneuver. *Am. J. Sports Med.* 35, 1888–1900.
- Landry, S.C., McKean, K.A., Hubley-Kozey, C.L., Stanish, W.D., Deluzio, K.J., 2007b. Neuromuscular and lower limb biomechanical differences exist between male and female elite adolescent soccer players during an unanticipated run and crosscut maneuver. *Am. J. Sports Med.* 35, 1901–1911.
- Levin, O., Wenderoth, N., Steyvers, M., Swinnen, S.P., 2003. Directional invariance during loading-related modulations of muscle activity: evidence for motor equivalence. *Exp. Brain Res.* 148, 62–76.
- Lindström, M., Felländer-Tsai, L., Wredmark, T., Henriksson, M., 2010. Adaptations of gait and muscle activation in chronic ACL deficiency. *Knee Surg. Sports Traumatol. Arthrosc.* 18, 106–114.
- Lohmander, L.S., Englund, P.M., Dahl, L.L., Roos, E.M., 2007. The Long-term Consequence of Anterior Cruciate Ligament and Meniscus Injuries Osteoarthritis. *Am. J. Sports Med.* 35, 1756–1769.
- Lohmander, L.S., Ostenberg, A., Englund, M., Roos, H., 2004. High prevalence of knee osteoarthritis, pain, and functional limitations in female soccer players twelve years after anterior cruciate ligament injury. *Arthritis Rheum.* 50, 3145–3152.
- Lysholm, J., Gillquist, J., 1982. Evaluation of knee ligament surgery results with special emphasis on use of a scoring scale. *Am. J. Sports Med.* 10, 150–154.
- Mall, N.A., Chalmers, P.N., Moric, M., Tanaka, M.J., Cole, B.J., Bach, B.R., Paletta, G.A., 2014. Incidence and trends of anterior cruciate ligament reconstruction in the United States. *Am. J. Sports Med.* 42, 2363–2370.
- Manske, R.C., Prohaska, D., Lucas, B., 2012. Recent advances following anterior cruciate ligament reconstruction: rehabilitation perspectives. *Curr. Rev. Musculoskelet. Med.* 5, 59–71.
- Mantovani, G., Lamontagne, M., 2016. How Different Marker Sets Affect Joint Angles in Inverse Kinematics Framework. *J. Biomech. Eng.*
- Marx, R.G., Jones, E.C., Angel, M., Wickiewicz, T.L., Warren, R.F., 2003. Beliefs and attitudes of members of the American Academy of orthopaedic surgeons regarding the treatment of anterior cruciate ligament injury. *Arthrosc. J. Arthrosc. Relat. Surg.* 19, 762–770.
- McLean, S.G., Lipfert, S.W., van den Bogert, A.J., 2004. Effect of gender and defensive opponent on the biomechanics of sidestep cutting. *Med. Sci. Sports Exerc.* 36, 1008–1016.
- Morgan, K.D., Donnelly, C.J., Reinbolt, J.A., 2014. Elevated gastrocnemius forces compensate for decreased hamstrings forces during the weight-acceptance phase of single-leg jump

- landing: implications for anterior cruciate ligament injury risk. *J. Biomech.* 47, 3295–3302.
- Myer, G.D., Ford, K.R., Di Stasi, S.L., Foss, K.D., Micheli, L.J., Hewett, T.E. 2015. High knee abduction moments are common risk factors for patellofemoral pain (PFP) and anterior cruciate ligament injury in girls: is PFP itself a predictor for subsequent ACL injury? *Br. J. Sports Med.* 49, 118-122.
- Neeb, T.B., Aufdemkampe, G., Wagener, J.H., Mastenbroek, L. 1997. Assessing anterior cruciate ligament injuries: the association and differential value of questionnaires, clinical tests, and functional tests. *J. Orthop. Sports Phys. Ther.* 26, 324–331.
- Noyes, F.R., Butler, D.L., Paulos, L.E., Grood, E.S., 1983. Intra-articular cruciate reconstruction. I: Perspectives on graft strength, vascularization, and immediate motion after replacement. *Clin. Orthop.* Jan-Feb, 71–77.
- Oiestad, B.E., Holm, I., Engebretsen, L., Risberg, M.A., 2011. The association between radiographic knee osteoarthritis and knee symptoms, function and quality of life 10-15 years after anterior cruciate ligament reconstruction. *Br. J. Sports Med.* 45, 583–588.
- Olsen, O.-E., Myklebust, G., Engebretsen, L., Bahr, R., 2004. Injury mechanisms for anterior cruciate ligament injuries in team handball: a systematic video analysis. *Am. J. Sports Med.* 32, 1002–1012.
- Palmieri-Smith, R.M., Thomas, A.C., 2009. A neuromuscular mechanism of posttraumatic osteoarthritis associated with ACL injury. *Exerc. Sport Sci. Rev.* 37, 147–153.
- Petushek, E.J., Cokely, E.T., Ward, P., Durocher, J.J., Wallace, S.J., Myer, G.D., 2015. Injury risk estimation expertise: Assessing the ACL injury risk estimation. *Am. J. Sports Med.* 43, 1640–1647.
- Pollard, C.D., Davis, I.M., Hamill, J., 2004. Influence of gender on hip and knee mechanics during a randomly cued cutting maneuver. *Clin. Biomech.* 19, 1022–1031.
- Quatman, C.E., Ford, K.R., Myer, G.D., Hewett, T.E., 2006. Maturation leads to gender differences in landing force and vertical jump performance: a longitudinal study. *Am. J. Sports Med.* 34, 806–813.
- Quatman, C.E., Kiapour, A.M., Demetropoulos, C.K., Kiapour, A., Wordeman, S.C., Levine, J.W., Goel, V.K., Hewett, T.E., 2014. Preferential Loading of the ACL Compared With the MCL During Landing A Novel In Sim Approach Yields the Multiplanar Mechanism of Dynamic Valgus During ACL Injuries. *Am. J. Sports Med.* 42, 177–186.
- Reed-Jones, R.J., Vallis, L.A., 2008. Kinematics and muscular responses to a ramp descent in the ACL deficient knee. *The Knee* 15, 117–124.
- Reid, A., Birmingham, T.B., Stratford, P.W., Alcock, G.K., Giffin, J.R., 2007. Hop Testing Provides a Reliable and Valid Outcome Measure During Rehabilitation After Anterior Cruciate Ligament Reconstruction. *Phys. Ther.* 87, 337–349.
- Riemann, B.L., Lephart, S.M., 2002. The Sensorimotor System, Part I: The Physiologic Basis of Functional Joint Stability. *J. Athl. Train.* 37, 71–79.
- Roos, E.M., Toksvig-Larsen, S., 2003. Knee injury and Osteoarthritis Outcome Score (KOOS) – validation and comparison to the WOMAC in total knee replacement. *Health Qual. Life Outcomes* 1, 17.
- Roos, H., Adalberth, T., Dahlberg, L., Lohmander, L.S., 1995. Osteoarthritis of the knee after injury to the anterior cruciate ligament or meniscus: the influence of time and age. *Osteoarthritis Cartilage* 3, 261–267.

- Ross, M.H., Pawlina, W., 2010. *Histology: A Text and Atlas*, 6 edition. ed. Wolters Kluwer, Philadelphia.
- Rudolph, K.S., Axe, M.J., Buchanan, T.S., Scholz, J.P., Snyder-Mackler, L., 2001. Dynamic stability in the anterior cruciate ligament deficient knee. *Knee Surg. Sports Traumatol. Arthrosc.* 9, 62–71.
- Rudolph, K.S., Axe, M.J., Snyder-Mackler, L., 2000. Dynamic stability after ACL injury: who can hop? *Knee Surg. Sports Traumatol. Arthrosc.* 8, 262–269.
- Rudolph, K.S., Snyder-Mackler, L., 2004. Effect of dynamic stability on a step task in ACL deficient individuals. *J. Electromyogr. Kinesiol.* 14, 565–575.
- Seth, A., Sherman, M., Eastman, P., Delp, S., 2010. Minimal formulation of joint motion for biomechanisms. *Nonlinear Dyn.* 62, 291–303.
- Shelburne, K.B., Pandy, M.G., Torry, M.R., 2004. Comparison of shear forces and ligament loading in the healthy and ACL-deficient knee during gait. *J. Biomech.* 37, 313–319.
- Sigward, S.M., Pollard, C.D., Havens, K.L., Powers, C.M., 2012. The Influence of Sex and Maturation on Knee Mechanics during Side-Step Cutting. *Med. Sci. Sports Exerc.* 44, 1497–1503.
- Sigward, S.M., Powers, C.M., 2006. The influence of gender on knee kinematics, kinetics and muscle activation patterns during side-step cutting. *Clin. Biomech.* 21, 41–48.
- Simon, D., Mascarenhas, R., Saltzman, B.M., Rollins, M., Bach, B.R., MacDonald, P., 2015. The relationship between anterior cruciate ligament injury and osteoarthritis of the knee. *Adv. Orthop.* 2015, 928301.
- Smith, A.J.J., Flaxman, T.E., Speirs, A.D., Benoit, D.L., 2012. Reliability of knee joint muscle activity during weight bearing force control. *J. Electromyogr. Kinesiol.* 22, 914–922.
- Smith, T.O., Postle, K., Penny, F., McNamara, I., Mann, C.J.V., 2014. Is reconstruction the best management strategy for anterior cruciate ligament rupture? A systematic review and meta-analysis comparing anterior cruciate ligament reconstruction versus non-operative treatment. *Knee* 21, 462–470.
- Snyder-Mackler, L., Fitzgerald, G.K., Bartolozzi, A.R., Ciccotti, M.G., 1997. The relationship between passive joint laxity and functional outcome after anterior cruciate ligament injury. *Am. J. Sports Med.* 25, 191–195.
- Strehl, A., Egli, S., 2007. The Value of Conservative Treatment in Ruptures of the Anterior Cruciate Ligament (ACL): *J. Trauma Inj. Infect. Crit. Care* 62, 1159–1162.
- Sugimoto, D., Alentorn-Geli, E., Mendiguchía, J., Samuelsson, K., Karlsson, J., Myer, G.D., 2015. Biomechanical and neuromuscular characteristics of male athletes: implications for the development of anterior cruciate ligament injury prevention programs. *Sports Med.* 45, 809–822.
- Takeda, Y., Xerogeanes, J.W., Livesay, G.A., Fu, F.H., Woo, S.L., 1994. Biomechanical function of the human anterior cruciate ligament. *Arthrosc. J. Arthrosc. Relat. Surg. Off. Publ. Arthrosc. Assoc. N. Am. Int. Arthrosc. Assoc.* 10, 140–147.
- Tegner, Y., Lysholm, J., 1985. Rating systems in the evaluation of knee ligament injuries. *Clin. Orthop.* 43–49.
- Thomas, A.C., Villwock, M., Wojtys, E.M., Palmieri-Smith, R.M., 2013. Lower extremity muscle strength after anterior cruciate ligament injury and reconstruction. *J. Athl. Train.* 48, 610–620.

- Torry, M.R., Decker, M.J., Viola, R.W., O'Connor, D.D., Richard Steadman, J., 2000. Intra-articular knee joint effusion induces quadriceps avoidance gait patterns. *Clin. Biomech.* 15, 147–159.
- Tsepis, E., Vagenas, G., Ristanis, S., Georgoulis, A.D., 2006. Thigh muscle weakness in ACL-deficient knees persists without structured rehabilitation. *Clin. Orthop.* 450, 211–218.
- van Deursen, R.W., Sanchez, M.M., Ulbrecht, J.S., Cavanagh, P.R., 1998. The role of muscle spindles in ankle movement perception in human subjects with diabetic neuropathy. *Exp. Brain Res.* 120, 1–8.
- Waldén, M., Hägglund, M., Werner, J., Ekstrand, J., 2010. The epidemiology of anterior cruciate ligament injury in football (soccer): a review of the literature from a gender-related perspective. *Knee Surg. Sports Traumatol. Arthrosc.* 19, 3–10.
- Waldén, M., Krosshaug, T., Bjørneboe, J., Andersen, T.E., Faul, O., Hägglund, M., 2015. Three distinct mechanisms predominate in non-contact anterior cruciate ligament injuries in male professional football players: a systematic video analysis of 39 cases. *Br. J. Sports Med.* bjsports-2014-094573.
- Wang, D., Jones, M.H., Khair, M.M., Miniaci, A., 2010. Patient-reported outcome measures for the knee. *J. Knee Surg.* 23, 137–151.
- Wang, L., Zhang, Z., McArdle, J.J., Salthouse, T.A., 2009. Investigating Ceiling Effects in Longitudinal Data Analysis. *Multivar. Behav. Res.* 43, 476–496.
- Weinhandl, J.T., Irmischer, B.S., Sievert, Z.A., 2015. Sex differences in unilateral landing mechanics from absolute and relative heights. *Knee* 22, 298–303.
- Wilk, K.E., Escamilla, R.F., Fleisig, G.S., Barrentine, S.W., Andrews, J.R., Boyd, M.L., 1996. A comparison of tibiofemoral joint forces and electromyographic activity during open and closed kinetic chain exercises. *Am. J. Sports Med.* 24, 518–527.
- Wilkie, D.R., 1949. The relation between force and velocity in human muscle. *J. Physiol.* 110, 249–280.
- Williams, G.N., 2004. Altered Quadriceps Control in People with Anterior Cruciate Ligament Deficiency. *Med. Sci. Sports Exerc.* 36, 1089–1097.
- Williams, G.N., Barrance, P.J., Snyder-Mackler, L., Axe, M.J., Buchanan, T.S., 2003. Specificity of muscle action after anterior cruciate ligament injury. *J. Orthop. Res.* 21, 1131–1137.
- Williams, G.N., Buchanan, T.S., Barrance, P.J., Axe, M.J., Snyder-Mackler, L., 2005. Quadriceps Weakness, Atrophy, and Activation Failure in Predicted Noncopers After Anterior Cruciate Ligament Injury. *Am. J. Sports Med.* 33, 402–407.
- Williams, G.N., Chmielewski, T., Rudolph, K.S., Buchanan, T.S., Snyder-Mackler, L., 2001. Dynamic knee stability: current theory and implications for clinicians and scientists. *J. Orthop. Sports Phys. Ther.* 31, 546–566.
- Yelin, E., Murphy, L., Cisternas, M.G., Foreman, A.J., Pasta, D.J., Helmick, C.G., 2007. Medical care expenditures and earnings losses among persons with arthritis and other rheumatic conditions in 2003, and comparisons with 1997. *Arthritis Rheum.* 56, 1397–1407.
- Zysk, S.P., Refior, H.J., 2000. Operative or conservative treatment of the acutely torn anterior cruciate ligament in middle-aged patients. A follow-up study of 133 patients between the ages of 40 and 59 years. *Arch. Orthop. Trauma Surg.* 120, 59–64.

APPENDIX A – Muscle variable equations

The following calculation was used for the normalized force necessary to reach a give target, F_{target} :

Equation A.1:

$$F_{target} = \sqrt{\left[(\cos \theta \times (F_{xp} - F_{xr}) \times \%maxF)^2 + (\cos 90 - \theta \times (F_{yp} - F_{yr}) \times \%maxF)^2 \right]}$$

Where θ is the angle between the target and the + x axis, F_{xp} and F_{xr} are the peak and relaxed GRFs produced, respectively, along the \pm x axis (medial/lateral), $\%maxF$ is the perfect effort level (30%, 45% or 60%), and F_{yp} and F_{yr} are the peak and relaxed GRFs produced, respectively, along the \pm y axis (anterior/posterior).

The test for asymmetry about the polar plot origin was performed as described by Curray (1956):

Equation A.2:

$$p = e^{-L^2 n} 10^{-4}$$

Where p is the probability of a non-random asymmetry being observed, e is the base of the natural logarithm, L is the mean vector magnitude and n is the number of observations. If $p < 0.05$, then asymmetry was present, meaning that a muscle's EMG is statistically focused in one GRF direction compared to the others. If $p > 0.05$, symmetrical activation was observed, meaning that similar EMG levels were observed in all directions.

By using the arctan function on the vectors' summed in their Cartesian coordinates (x_i and y_i), the mean direction of muscle activity (ϕ) for the 12 targets was determined:

Equation A.3:

$$\phi = \tan^{-1} \left(\frac{\sum y_i}{\sum x_i} \right)$$

In order to quantify the variance, or range, of muscle activation about the mean direction of muscle activity, the specificity index (SI) was calculated. The SI was derived from the ratio of the muscle's actual resultant vector to its absolute resultant vector (Dewald et al., 1995; Williams et al., 2003). This measurement of variance was ranged between the values of 0.0 and 1.0. If a given muscle had an SI of 0.0 this indicated equal activations in all 12 target directions, in other words, its activation profile was purely symmetrical about the polar plot origin, while an SI of 1.0 indicates that a muscle was only active for one target and would therefore be completely specific in one direction of activation.

Equation A.4:

$$SI = \frac{\left[\left(\frac{\sum x_i}{n} \right)^2 + \left(\frac{\sum y_i}{n} \right)^2 \right]^{-1/2}}{\left[\left(\frac{\sum |x_i|}{n} \right)^2 + \left(\frac{\sum |y_i|}{n} \right)^2 \right]^{-1/2}}$$

Last, as a descriptor for the magnitude of each muscle's activation at a given target, the mean magnitude of muscle activity (X_{EMG}) was calculated and represented as a ratio of its MVIC value. This was performed by averaging all of the normalized EMG vectors (EMGi) for each muscle at all 12 directional loading conditions.

Equation A.5:

$$X_{EMG} = \frac{\sum EMGi}{n}$$

APPENDIX B – Normalization of patient reported outcome measures

The following conversions were made for each of the five sub-scores, Symptoms, Pain, Activities of Daily Living (ADL), Sports and Recreation (S/R), and Quality of Life (QOL), that compose the Knee and Osteoarthritis Outcome Score (KOOS). The KOOS uses a scale of 0 to 4 with 0 represented a fully functional, symptom free knee and 4 represented a non-functional, severely symptomatic knee.

Equation B.1:Symptoms

$$= 100 - \left(\frac{(Total\ Score) \times 100}{36} \right)$$

Equation B.2:Pain

$$= 100 - \left(\frac{(Total\ Score) \times 100}{36} \right)$$

Equation B.3:ADL

$$= 100 - \left(\frac{(Total\ Score) \times 100}{68} \right)$$

Equation B.4:S/R

$$= 100 - \left(\frac{(Total\ Score) \times 100}{20} \right)$$

Equation B.5:QOL

$$= 100 - \left(\frac{(Total\ Score) \times 100}{16} \right)$$

The IKDC Subjective Knee Evaluation Form has a variety of number ranges depending on the question. The final score was calculated by taking the sum of the scores for each question and then transforming the score to a scale that ranges from 0 to 100, where a score of 100 was interpreted as the patient having a fully functional and symptom free knee.

Equation B.6:IKDC Score

$$= \frac{Raw\ Score - Lowest\ Possible\ Score}{Range\ of\ Scores} \times 100$$

APPENDIX C – Results of normality calculations

Table C.1. Kolmogorov-Smirnov (K-S) tests for assessing normality of the following dependent variables tested: maximum generated ground reaction forces (GRFs) normalized to body weight; $-F_y$ (anterior), $+F_y$ (posterior), $-F_x$ (medial), and $+F_x$ (lateral) force platform channels, and subjective questionnaires (scores were normalized to a score out of 100); the five sub-groups of the KOOS, the IKDC the Lysholm scoring scale, and the Tegner assessment. Significant P-values ($p < 0.05$) are represented by (*) and were deemed non-normally distributed. Tests were omitted (N/A) when the reported values were constant for the participants.

	FYC		MYC		FACL		MACL	
	<i>K-S Value</i>	<i>P-value</i>	<i>K-S Value</i>	<i>P-value</i>	<i>K-S Value</i>	<i>P-value</i>	<i>K-S Value</i>	<i>P-value</i>
GRFs (N/kg)								
$-F_y$	0.146	>0.200	0.173	>0.200	0.138	>0.200	0.138	>0.200
$+F_y$	0.128	>0.200	0.222	0.044*	0.139	>0.200	0.116	>0.200
$-F_x$	0.160	>0.200	0.132	>0.200	0.170	>0.200	0.186	0.099
$+F_x$	0.184	0.150	0.108	>0.200	0.118	>0.200	0.156	>0.200
KOOS (/100)								
<i>Symptoms</i>	0.384	<0.001*	0.453	<0.001*	0.169	>0.200	0.160	>0.200
<i>Pain</i>	0.536	<0.001*	0.535	<0.001*	0.168	>0.200	0.239	0.008*
<i>ADL</i>	0.536	<0.001*	N/A	N/A	0.229	0.025*	0.264	0.002*
<i>S/R</i>	0.492	<0.001*	0.535	<0.001*	0.148	>0.200	0.105	>0.200
<i>QOL</i>	0.496	<0.001*	N/A	N/A	0.198	0.093	0.217	0.025*
IKDC (/100)	0.484	<0.001*	0.506	<0.001*	0.120	>0.200	0.220	0.021*
Lysholm (/100)	0.441	<0.001*	0.535	<0.001*	0.228	0.025*	0.096	>0.200
Tegner (/10)	0.163	>0.200	0.162	>0.200	0.166	>0.200	0.187	0.098

APPENDIX D – Calculation of effect size

The following calculation was made when determining the effect size (r_{es}) of a statistically significant variable from a Mann-Whitney test. The z -values were included in the SPSS outputs for each variable tested and n represents the total sample size of the test (Field, 2013).

Equation D.1:

$$r_{es} = \left(\frac{z \text{ value}}{\sqrt{n}} \right)$$

APPENDIX E – Subjective and functional outcome measures correlations

Patient reported outcome measure (PROM) scores from the five sub-scores of the KOOS, the IKDC, the Lysholm and the Tegner, were each plotted against each of the four maximum directional loading conditions, normalised to body weight (N/kg) for FACL (Figures E.1, 2) and MACL (Figures E.3, 4). Spearman's rho correlation coefficients (r_s ; weak (± 0.1), medium (± 0.3), and strong (± 0.5) relationships; Field, 2013) reported in Chapter 5, Table 5.3 (pg. 70).

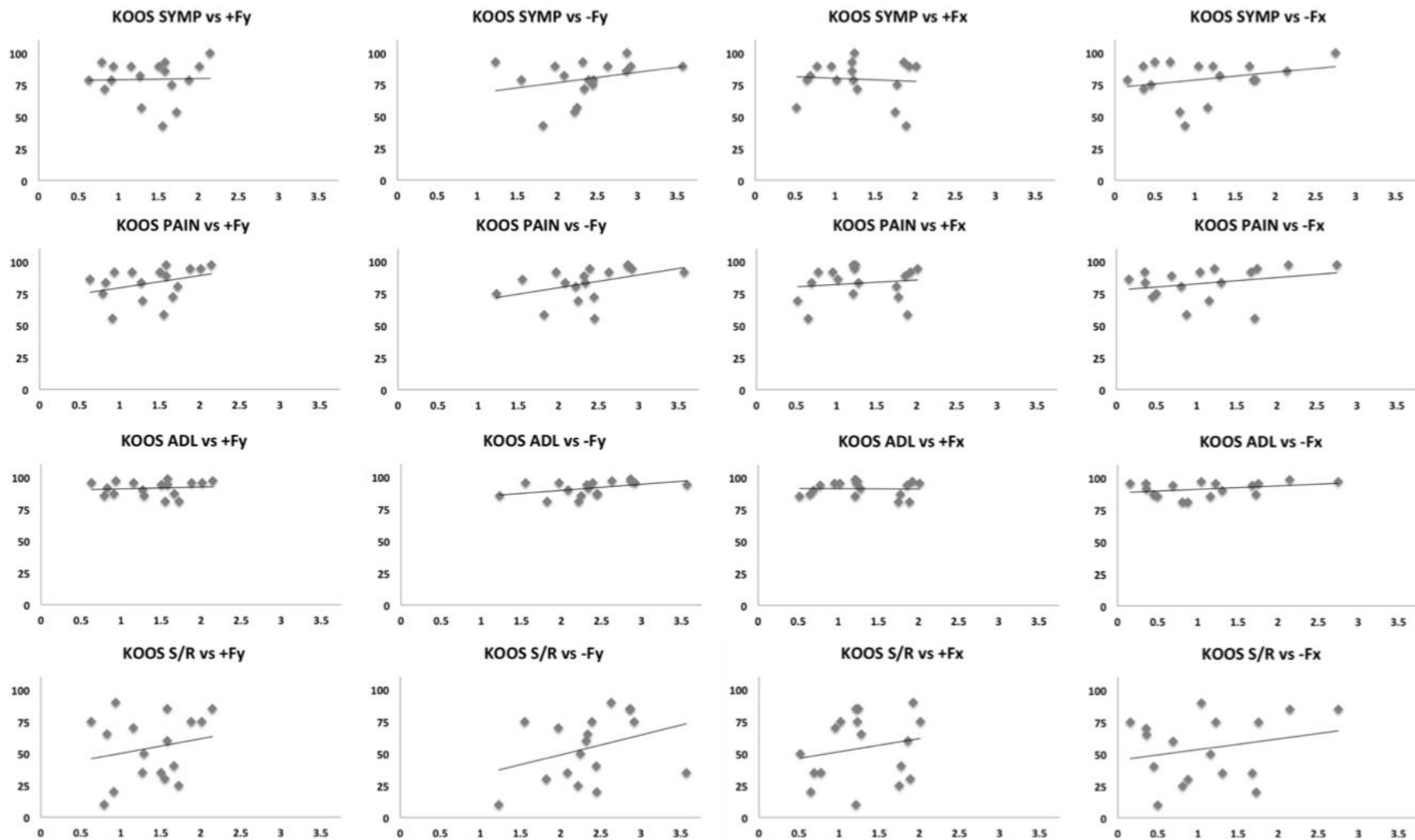


Figure E.1. Correlations between subjective and functional outcome measures for FACL participants for each maximum forces generated for the four platform channels; -F_y (anterior), +F_y (posterior), -F_x (medial), and +F_x (lateral), and the KOOS sub-scores; Symptoms (Symp), Pain, Activates of Daily Living (ADL), and Sports and Recreation (S/R).

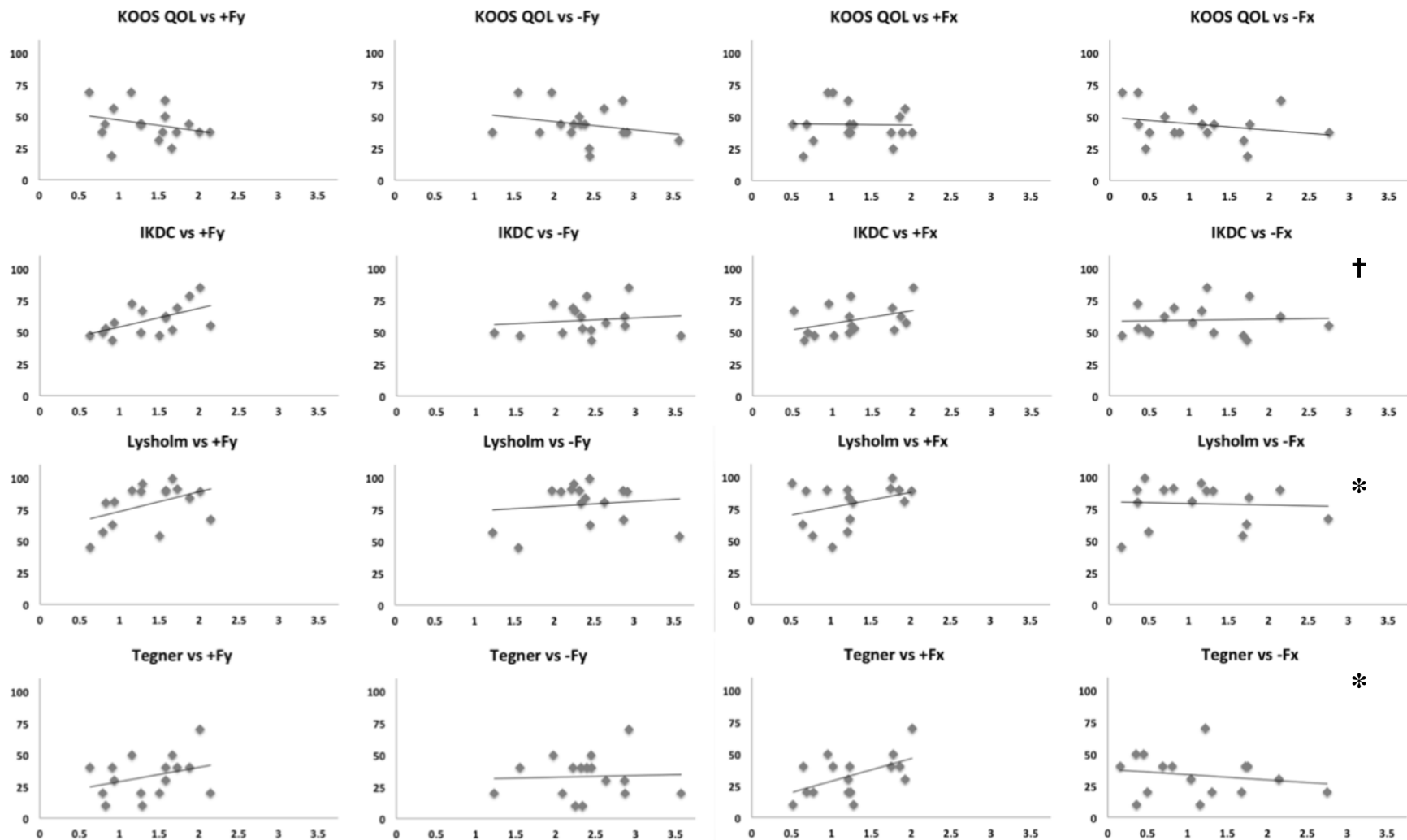


Figure E.2. Correlations between subjective and functional outcome measures for FACL participants for each maximum forces generated for the four platform channels; $-F_y$ (anterior), $+F_y$ (posterior), $-F_x$ (medial), and $+F_x$ (lateral), and the sub-scores of the KOOS; Quality of Life (QOL), and the IKDC, Lysholm, and Tegner scores. Significant differences ($p < 0.05$) and trends toward significant differences ($p < 0.10$) are denoted with (*) and (†), respectively.

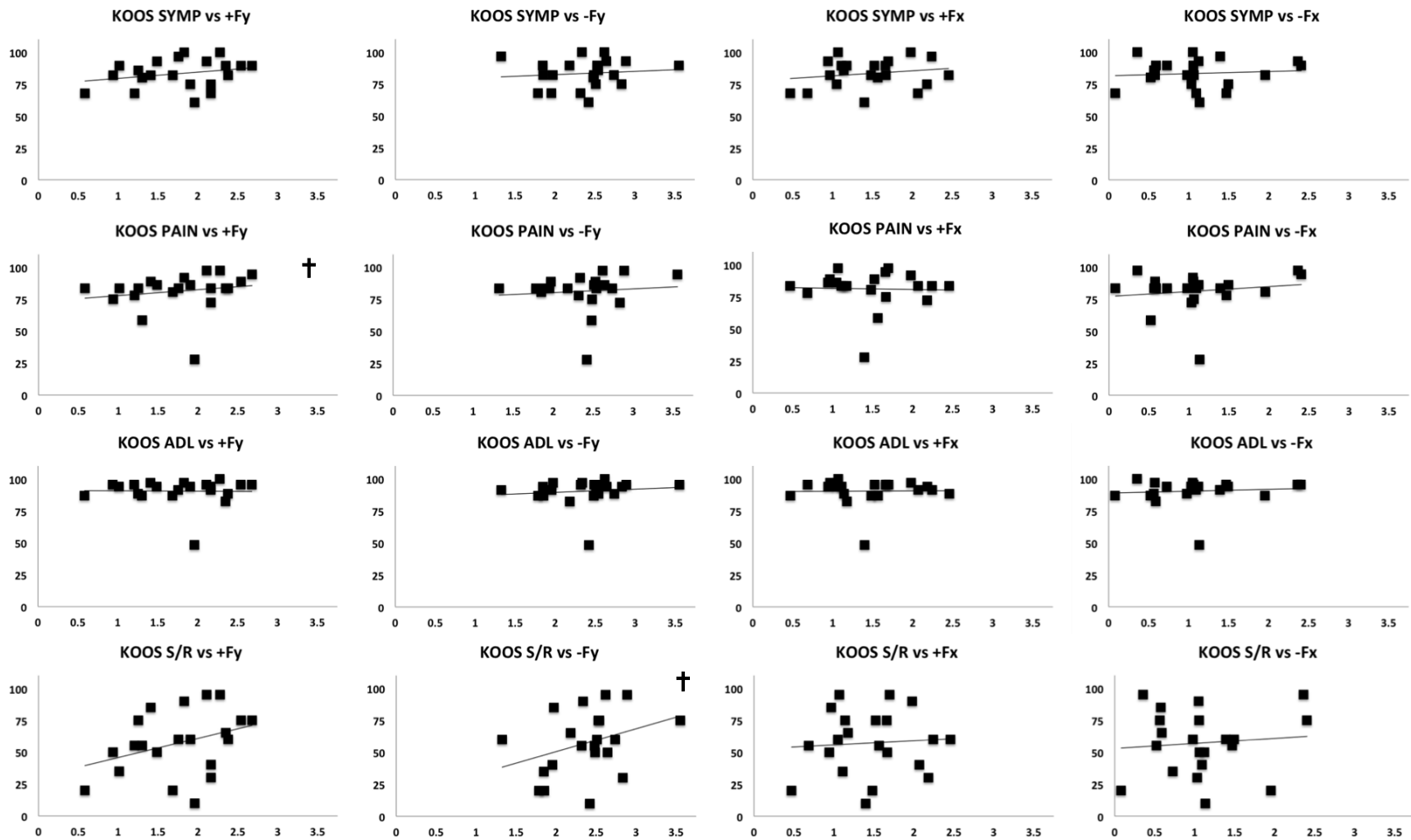


Figure E.3. Correlations between subjective and functional outcome measures for MACL participants for each maximum forces generated for the four platform channels; $-F_y$ (anterior), $+F_y$ (posterior), $-F_x$ (medial), and $+F_x$ (lateral), and the KOOS sub-scores; Symptoms (Symp), Pain, Activates of Daily Living (ADL), and Sports and Recreation (S/R). Trends towards significant differences ($p < 0.10$) are denoted with (†).

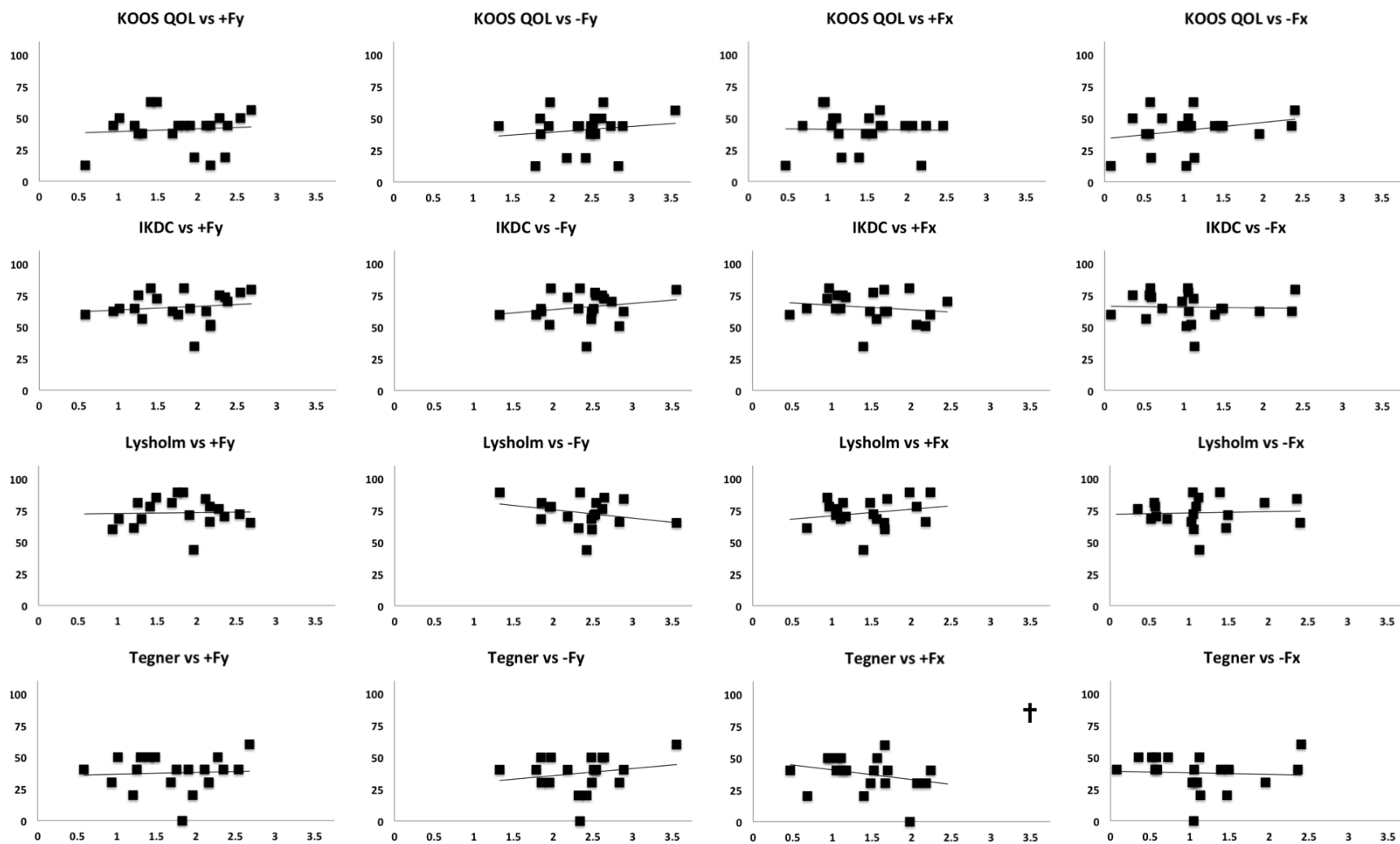


Figure E.4. Correlations between subjective and functional outcome measures for MACL participants for each maximum forces generated for the four platform channels; -F_y (anterior), +F_y (posterior), -F_x (medial), and +F_x (lateral), and the sub-scores of the KOOS; Quality of Life (QOL), and the IKDC, Lysholm, and Tegner scores. Trends towards significant differences (p < 0.10) are denoted with (†).