PREDICTING RISK FACTORS OF NON-CONTACT ANTERIOR CRUCIATE LIGAMENT INJURIES DURING SINGLE-LEG LANDING

NICHOLAS ALI

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Faculty of Health Sciences
School of Human Kinetics
University of Ottawa

Abstract

The literature suggests that body kinematics and musculoskeletal differences are major factors contributing to the high disparity in non-contact Anterior Cruciate Ligament (ACL) injury rate between genders. The literature also indicates that the incidence of non-contact ACL injury predominates during single-leg landing sports such as basketball, soccer, and handball. Despite this, there are few studies investigating kinematics or musculoskeletal differences between genders during single-leg landing from increasing vertical heights and horizontal distances. The objectives of this study are threefold: first, conduct a gap study identifying the barriers to predicting mechanisms and risk factors for non-contact ACL injury. Second, propose a new approach that can address some of the challenges encountered in some existing non-contact ACL injury study approaches. Finally, whilst determining whether or not gender differences explain the higher rate of ACL injuries among females, identify and correlate the biomechanical and musculoskeletal variables significantly impacted by gender, vertical landing height, and/or horizontal landing distance and their interactions to various ACL injury risk predictor variables during single-leg landing. Experiments using male and female subjects, inverse dynamics analysis using Visual3D, and musculoskeletal modeling simulation using AnyBody Modeling System were approaches used to explore these objectives. Salient findings from this dissertation includes but are not limited to, non-contact ACL injury that occurs during single-leg landing is mutifaceted entailing many factors that cannot be captured in any one existing ACL injury study approach. Non-contact ACL injury during single-leg landing may not be gender specific. Both vertical height and horizontal distance of landing increase the risk of non-contact ACL injury during single-leg landing. Body kinematics during single-leg landing may not be the sole determinant in attenuating ground reaction forces and consequently risk of ACL injury. The hamstring and gastrocnemius muscles were determined to strain shield the ACL while the quadriceps were found to have no significant effect on risk of ACL injury during single-leg landing.

Within the findings and limitations of this study the knowledge garnered from this research may aid in tailoring future studies so as to enable more robust non-contact ACL injury prevention protocols.

dedicated to

my father, Rasheed Mohamed, whose life and death showed me passion as well as the value of hard work. I am truly blessed to have shared the short journey we had together.

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Abbreviations

ACL	Anterior Cruciate Ligament
GRF	Ground Reaction Force
VGRF	Vertical Ground Reaction Force
PGRF	Posterior Ground Reaction Force
PTASF	Proximal Tibia Anterior Shear Force
MSM	Musculoskeletal Model
AI	Artificial Intelligence
OR	Operations Research
MDO	Multidisciplinary Design Optimization

Contents

1

Introduction

1.1 Background

High incidence of anterior cruciate ligament (ACL) injury especially among females, and frequent requirement for ACL revision surgery, remains a serious challenge for researchers. Biomechanics, video analysis, and related study approaches have somewhat elucidated how ACL injuries occur, but they are limited because they provide estimates, rather than precise measurements of the knee—and more specifically—ACL kinematics at the time of injury. Non-contact ACL injuries is defined as ACL injuries that occur without physical contact with another person or object (Boden *et al.* 2000), likely occur when many factors, forces, and extreme conditions happen simultaneously. Yet existing study approaches are limited due to their inability to simultaneously capture many of these parameters. Moreover, the mechanisms of ACL injury are complex and may involve the concurrent interaction of muscle forces, external forces, ligament forces, and joint contact forces. The effect of such interaction on ACL loading is not yet known. The interaction among muscles, bones and ligaments during an injury causing event such as single-leg landing is also unknown. Most study approaches have provided useful information to date, but could not offer a comprehensive view of ACL injury mechanisms. Moreover, non-contact ACL injury is a whole body phenomenon that is best analyzed by simultaneously addressing multiple risk factors of which neuromuscular control, joint kinematics and kinetics, as well as, external forces may be the most important.

Literature reviews (Ali and Rouhi 2010; Hewett *et al.* 2005; Quatman *et al.* 2009; Renstrom *et al.* 2008) show that much of the research on non–contact ACL injuries has focused on the effects of knee mechanics before and after ACL failure, before and after ACL reconstruction, between genders, or between ACL injured and controlled populations. Furthermore, the vast majority of studies on non-contact ACL injuries are in the context of reconstruction and surgical treatment (Bach *et al.* 1998; Fleming *et al.* 2001; Sgaglione and Schwartz 1997; Torzilli *et al.* 1994). Based on a review of the literature, it was also determined that there is a gap in knowledge on single-leg landing performed over increasing vertical heights and increasing horizontal distances (Ali *et al.* 2011a; Ali *et al.* 2011b). To fill this gap, single-leg landing experiments were conducted to investigate the effect of increasing vertical landing heights and horizontal landing distances on body kinematics and kinetics. The metrics measured and simulated were then used to identify the risk factors that predispose athletes to non-contact ACL injuries. The experimental data were then used to develop and simulate a 3D rigid body model in Visual3D. The experimental data were also used to develop, validate, and simulate a 3D full-body musculoskeletal model (MSM) of the human body in AnyBody Modeling System so as to investigate the effects of gender, vertical heights and horizontal distances on risk of non-contact ACL injury.

It is a tedious and difficult task to use a computational model on its own to study non-contact ACL injuries, given the numerous variables and constraints, many interdependencies, high dimensionality, and temporal dependencies entailed in non-contact ACL injury research. Present non-contact ACL injury study approaches lack the capabilities required to overcome such challenges. To address these challenges, new approaches are required that possess the capabilities to handle numerous variables and constraints, as well as great interdependencies, high dimensionality, and temporal dependencies. Such a method may benefit from fusing existing study approaches into a single unified environment enabling one to capture most of the problem dependent variables. As a result, this study proposes a new multifactorial study approach aimed at fusing existing non-contact

ACL injury study approaches in a single environment using an artificial intelligence (AI) technique. This multifactorial study approach can utilize the developed and validated musculoskeletal model (MSM) from this study, and then couple it with experimental studies, clinical studies, video analysis, and athlete interview studies using an AI technique. In other words, this multifactorial approach entails the fusion of data from subjects, experiments, computational modeling, video analysis, clinical studies, and athlete interviews using AI. Once validated, this proposed study approach can be a more robust approach to determine the body kinematics and kinetics at which many risk factors, forces and extreme conditions happen simultaneously to cause ACL injury. The benefit of such an approach is that it consolidates many important variables into a single environment to establish if the mechanisms and risk factors implicated to cause non-contact ACL injury are indeed mechanisms and risk factors. This approach was not developed in this thesis due to lack of resources and relevant skills sets.

To the best of the author's knowledge, no study to date has investigated gender differences during single-leg landing from varying vertical heights and horizontal distances. Further, there are no MSMs in the scholarly literature that have been developed, validated and applied to single-leg landing. As well, the majority of studies in the literature pertaining to single-leg landing do not account for the effects of whole body movement on ACL loading. In addition, to the author's best knowledge, the current literature demonstrates that there are no multifactorial study approaches aimed at fusing existing non-contact ACL injury study approaches into a single environment using an AI technique.

1.2 Research questions

This study sets out to answer the following research questions:

1. How can one go about developing a multifactorial study approach to address many of the challenges encountered in non-contact ACL injury research so as to enable a more comprehensive and accurate prediction of non-contact ACL injury mechanisms and risk factors?

2. What are the biomechanical and musculoskeletal risk factors to non-contact ACL injuries during single-leg landing from increasing vertical heights and horizontal distances?;

3. Are there biomechanical or musculoskeletal differences between genders during single-leg landing from varying vertical heights and horizontal distances that could explain the disparity in injury rate between genders?; and

4. What factors are important in attenuating the forces seen at the ACL and should be further investigated for incorporation into training regimens to enhance injury prevention protocols?

1.3 Research objectives and hypotheses

To answer the aforementioned research questions, experiments on living subjects were conducted in a gait laboratory. Furthermore, this study developed, validated and applied a MSM to better understand internal forces effect on risk of non-contact ACL injury. A robust and comprehensive multifactorial study methodology aimed at predicting mechanisms and risk factors of non-contact ACL injuries was also proposed.

The following were the major aims of this study:

1. To conduct a review of the literature to better understand the barriers to consensus and agreement on injury mechanisms and risk factors of non-contact ACL injury;
2. To conduct a review of the literature to better understand the utilization and areas of application of operation research (OR) and artificial intelligence (AI) techniques to non-contact ACL injury research;

3. To employ experimental data and rigid body modeling, examine the relationships between increasing vertical height as well as increasing horizontal distance and peak ground reaction forces (GRFs) during single-leg landing. Using these findings, determine the relationship among sagittal plane body kinematics, knee power and knee work and peak GRFs;
4. To utilize experimental data and rigid body modeling, determine whether gender differences exist in whole body kinematics and kinetics, as well as knee energetics during single-leg landings from increasing vertical heights and horizontal distances, and whether these differences explain the higher rate of injury among females.
5. To use experimental data to correlate the biomechanical variables significantly impacted by main effects and interactions of gender, vertical height and/or horizontal distance to assess the risk of non-contact ACL injury during single-leg landing;
6. To develop, validate, and present a 3D rigid body MSM of the human body for application to single-leg landings over increasing vertical height and horizontal distances;
7. To apply the MSM to experimental data to determine gender differences with respect to selected musculoskeletal variables during single-leg landing and to establish if these differences could explain the higher rate of ACL injury among females; and
8. To correlate the musculoskeletal variables significantly impacted by gender, vertical height, and/or horizontal distance main effects and interactions to risk of non-contact ACL injury.

It was hypothesized that an increase in vertical height and horizontal distance would:

1. increase both the peak VGRFs and the peak PGRFs;
2. increase knee, hip, and trunk flexion, but reduce ankle plantar flexion angle;
3. increase eccentric knee power and knee work;
4. demonstrate significantly different body kinematics, kinetics, and knee energetics between males and females; and
5. demonstrate significantly different joint reaction and muscle forces between males and females.

1.4 Rationale for this study

There are no experimental studies—similar to that employed in this study—that have investigated non-contact ACL injury during single-leg landings over increasing vertical landing heights and increasing horizontal landing distances. There are very few studies looking at the effect of increasing vertical height and horizontal distance on trunk flexion as well as knee energetics. In addition, there are no musculoskeletal modeling studies in the literature to the best of our knowledge that have been developed, validated and applied to single-leg landing. Further, information about the muscle and joint forces at the ankle, knee, and hip during single-leg landing is absent from the literature. A whole-body investigation of the body kinematics and muscle forces to attenuate large ground reaction forces resulting from increasing task demands of landing heights and distances is also absent from the literature. In addition, there are no published multifactorial study approaches like the one proposed in this study, which is aimed at coupling existing non-contact ACL injury study approaches using an AI technique to address many of the barriers to predicting non-contact ACL injury mechanisms and risk factors.

1.5 Importance of this research

One study concluded that 70% of ACL injuries emanate from non-contact events (Boden *et al.* 2000). Deceleration when landing from a jump on one leg was reportedly one of the most serious ACL injury causing actions in sports (Yu *et al.* 2002). Even though everyone is predisposed to ACL injuries, the highest incidences of ACL injuries are seen among athletes involved in sports that require pivoting and jumping such as basketball, soccer and volleyball (McLean *et al.* 2005; Myer *et al.* 2005; Olsen *et al.* 2003). Complete ACL rupture may lead to significant posttraumatic laxity, functional knee instability, and increased likelihood of osteoarthritis (Braden *et al.* 2008; Daniel and Fristschy 1994; Eastlack *et al.* 1999; Pedowitz and Popejoy 2004; Roberts *et al.* 2007; Rupp *et al.* 2001). The absolute number of ACL injuries continues to rise partly because of the growing number of people in sports, and more specifically, the increasing number of women in sports. Studies show that ACL injuries among female athletes are 2–8 times higher than in males (Harmon and Ireland 2000; Huston *et al.* 2000; Ireland 2002). One study estimated that the healthcare cost per ACL injury in the United States is approximately $17,000, with a likely similar cost in Canada (Hewett *et al.* 1996). By one estimate, Gottlob *et al.*(1999) showed that approximately 175, 000 ACL reconstruction surgeries occur every year in the United States costing annually more than US $2 billion. This number does not account for the 31% of patients who require revision surgery approximately five years after ACL reconstruction (Bach *et al.* 1998; Sgaglione and Schwartz 1997). The high number of non-contact ACL injuries and the frequent need for surgical treatment are both compelling reasons for the research undertaken in the current study.

1.6 Knee Biomechanics

It is widely recognized that tibiofemoral knee joint motions occur in three planes (sagittal, frontal, and transverse) with 6 degrees of freedom (3 rotations, 3 translations, allowing 12 directional motions) between the femoral condyles and tibial plateau (Woo, *et al.*, 2006). The knee joint can rotate in the sagittal plane by flexion and extension, in the frontal plane by abduction and adduction, and in the transverse plane by internal and external rotation. The knee joint can also translate in the sagittal plane anteriorly and posteriorly, in the frontal plane medially and laterally, and in the transverse plane by compression and distraction. While the knee can move in all 12 of these potential directions, with the exception of flexion and extension of the knee joint, most of these motions take place throughout a relatively limited range. The end range of motion is highly variable in the general population and may vary by age, pubertal status, sex, and race (Decoster, *et al.*, 1997). Excessive knee joint loading that leads to motion beyond the normal physiologic range in the sagittal, frontal or transverse planes could potentially damage the internal knee joint structures. Several studies indicate that individuals with greater knee or generalized joint laxity have an increased risk for ACL injury (Myer, *et al.*, 2008; Uhorchak *et al.*, 2003). The knee joint primarily functions as a hinge to produce flexion between the articular surfaces femoral condyles and tibial plateaus (Kapandji, 1987).

1.7 Knee Anatomy

The human knee is a large and complex joint with a surrounding osseous anatomy that includes the femur, patella, tibia, and fibula (Figure 1). These bones structurally combine to include separate articulations. These articulations have smooth articular (hyaline) cartilage with an extremely low coefficient of friction that enables the bones to move smoothly against one another. The femur and tibia are the primary weight-bearing bones at the knee. The distal femur diverges from the femoral shaft into two spherical shapes (condyles), while the proximal tibia is relatively flat. In contrast, the fibula does not bear weight at the knee joint but serves as an important surface for muscle and ligament attachments and is important for transverse plane rotational stability of the knee. The patella is embedded within the quadriceps tendon as it slides anteriorly over the femoral condyles during knee flexion. The patella serves as a fulcrum to transmit force from the quadriceps to the patellar tendon.

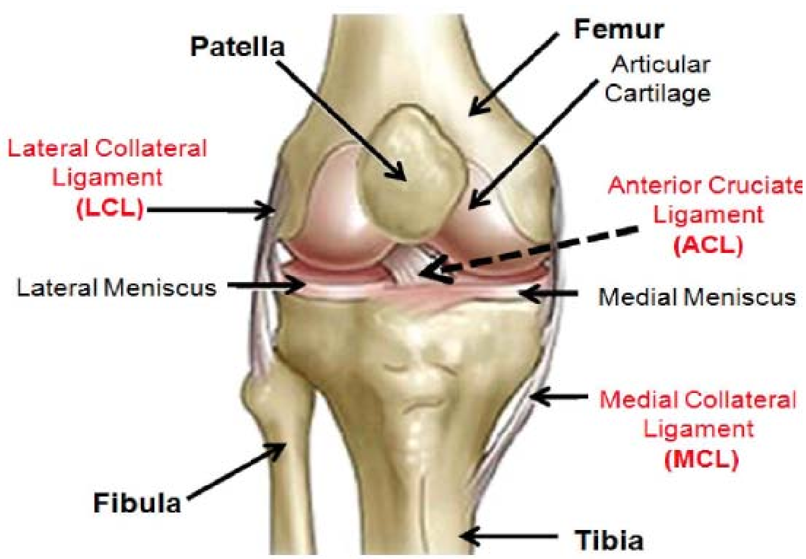

Figure 1: Anatomy of the knee joint

Numerous ligaments, or dense connective tissue bands, comprised of collagen fibers and fibroblasts, stabilize and strengthen the knee. The ligaments provide stability and help guide the joint through normal ranges of motion (Figure 1) (Woo, *et al.*, 1999). The ACL and posterior cruciate ligament (PCL) are intraarticular ligaments that criss-cross each other. The ACL is composed of two bundles: anteromedial and posterolateral. The ACL provides approximately 85% of the knee joint's total restraint to anterior tibial translation and also contributes to frontal and transverse plane knee rotation stability (Butler, *et al.*, 1980; Markolf, *et al.*, 1976). However, pure frontal (abduction-adduction) or transverse (internal-external) plane knee loading may have less of an effect on ACL strain than sagittal plane biomechanics (Fleming, *et al.*, 2001a; Grood, *et al.*, 1981). Similar to the ACL, the PCL is also composed of two bundles (anterolateral and posteromedial), passes posterior to the ACL as it arises from the posterior intercondylar area of the tibia, and attaches to the anterior part of the lateral surface of the medial femoral condyle (Woo *et al.*, 2006). The PCL primarily restrains posterior translation of the tibia relative to the femur (Amis, *et al.*, 2003; Gollehon, *et al.*, 1987). The exterior of the knee joint is made up of the medial collateral ligament (MCL) and lateral collateral ligament (LCL). The MCL is a flat band that originates from the medial femoral epicondyle and inserts medially on the tibia about 7 to 10 cm below the joint line (Beaty *et al.*, 2008). Cadaveric studies indicate that the MCL is important for restraining medial joint space opening in response to abduction loads (Matsumoto, *et al.*, 2001). At the same time, the lateral collateral ligament (LCL) extends from the lateral femoral epicondyle to the lateral surface of the fibular head. The LCL restrains knee adduction loads and help the PCL resists posterior tibial drawer (Amis *et al.*, 2003; Gollehon *et al.*, 1987).

The medial and lateral menisci are fibro-cartilage pads located intraarticularly between the femoral and tibial articulations. The menisci cushion and deepen the articular surfaces to aid joint stability, as well as help lubricate the joint (Martini and Bartholomew, 2007). The medial meniscus is larger, less circular, and less mobile than the lateral meniscus. In addition to the ligaments and menisci, the muscles that cross the knee joint also contribute to knee joint stability and function.

Skeletal muscles crossing the knee are crucial for movement production across joints, provide support to soft tissues, maintain posture, and actively increase joint stability by increasing compression across the knee joint (Martini and Bartholomew, 2007; Neumann, 2002). Although the muscles that cross the knee joint primarily contribute to knee flexion and extension, they also contribute to hip and ankle movements, since many of them also cross the adjoining hip or ankle joints. The quadriceps muscles (rectus femoris, vastus lateralis, vastus medialis, and vastus intermedius), which are important for knee extension movements, originate from the pelvis (ilium) and proximal femur. On the contrary, the hamstrings muscles (semitendinosus, semimembranosus and biceps femoris) are important for knee flexion and hip extension. The hamstrings originate from the ischial tuberosity and insert on the proximal tibia and fibula (Moore and Agur, 2002; Neumann, 2002). The gastrocnemius muscles originate from the posterior distal femur and join distally to form the Achilles tendon that inserts on the calcaneus bone of the tarsus. The gastrocnemius muscles are important for plantar flexion of the ankle; and provide joint compression and a small amount of tibial anterior shear to the knee joint (Fleming, *et al.*, 2001b; Neumann, 2002). Muscle synergy and activation patterns play an important role in both dynamic knee joint stability and neuromuscular performance of sports tasks. In particular, quadriceps, hamstrings, and gastrocnemius muscle contractions increase knee joint compression and improve knee joint stability. These muscle groups also affect the anterior shear force on the tibia and influence ACL strain (Shimokochi and Shultz, 2008). Quadriceps contractions produce anterior directed forces on the tibia at low knee flexion angles and increase ACL tensile forces (DeMorat, *et al.*, 2004). The gastrocnemius muscles may also create small anterior or posterior tibial shear forces (depending on knee flexion angle) during contractions and can affect ACL loads (Fleming *et al.*, 2001b; O'Connor, 1993). In contrast, the hamstrings are thought to resist anterior tibial shear (Solomonow, *et al.*, 1987). Co-contraction of the hamstrings and quadriceps leads to lower ACL tensile forces than isolated quadriceps forces (Draganich and Vahey, 1990; Li, *et al.*, 1999b; Solomonow *et al.*, 1987). Thus, the muscles that cross the knee joint may contribute to or protect the ACL from injury.

1.8 Anatomy of the ACL

The ACL (Figure 2) is an intraarticular ligament of the human knee joint that connects the tibia and the femur. The ACL comprises two bundles named for the location of their respective tibial attachment sites: anteromedial (AM) and posterolateral (PL) (Girgis *et al.* 1975). The average ACL length is approximately 32 mm and the average width is approximately 11 mm (Fu *et al.* 1993).

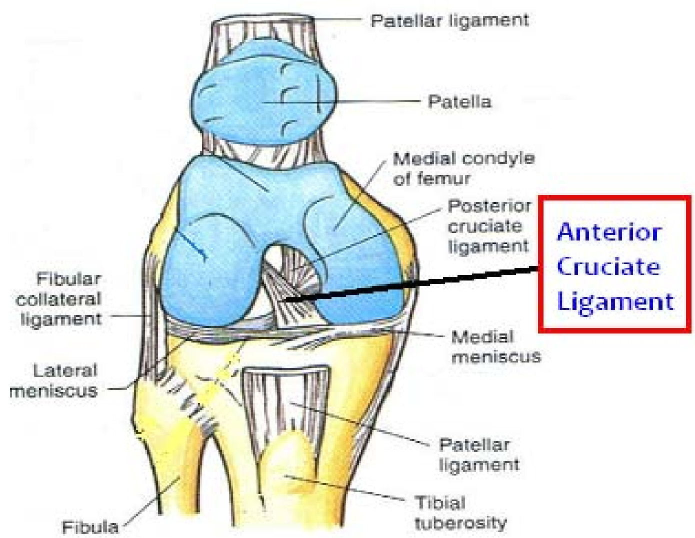

Figure 2: Human knee joint showing the major ligaments*
*Adapted from Moore and Agur 2003

1.8.1 Function and mechanical Properties of the ACL

The data demonstrating that the ACL functions to restrain anterior tibial translation (ATT) and acts as a secondary restraint to internal rotation in the non-weight-bearing knee, are well represented in the literature (Ahmed *et al.* 1987; Beynnon *et al.* 1997). Whether or not the ACL functions as a secondary restraint to tibial rotation, still remains an area for debate (Beynnon *et al.* 1997; Seering *et al.* 1980). Several studies (Butler *et al.* 1986; Woo *et al.* 1991) have estimated that the ACL has a load to failure of approximately 2160 N, a stiffness of 242 N/mm and is able to tolerate a strain of up to 20% before failure.

1.9 Non-contact ACL injury mechanisms

The mechanisms of injury to the ACL are rather complex because the injury event is quick, the injury condition is dynamic and multifactorial, and the knee is a complex joint capable of interrelated compression, translation and rotation about various axes (Hashemi *et al.* 2007). Nonetheless, many studies (Boden *et al.* 2000; FaunÃ¸ and Wulff Jakobsen 2006; Feagin Jr and Lambert 1985; Ferretti *et al.* 1992; McNair *et al.* 1990; Myklebust *et al.* 1997; Olsen *et al.* 2004; Olsen *et al.* 2003; Teitz 2001) have suggested several non-contact ACL injury mechanisms, namely, side step cutting, landing, jumping, decelerating from running without changing direction, and decelerating from running with change in direction.

Although the above studies reported valuable findings and began to establish a gender-related profile, for ACL injury they failed to report data concerning 3D kinematics and kinetics of the hip, knee and ankle joints. The coupling between hip, knee, and ankle kinematics and the link between lower extremity kinematics, external forces, and muscle forces and their effects on ACL loads requires further investigation.

1.10 Non-contact ACL injury risk factors

Even though the specific mechanisms of non-contact ACL injury are unclear, research has implicated a number of factors that increases the likelihood of non-contact ACL injuries (Figure 3). These risk factors are classified as either intrinsic (inside the body) or extrinsic (outside the body) (Harmon and Ireland 2000; Hewett *et al.* 2006). Other studies have further broken down risk factors into four areas: environmental, biomechanical, neuromuscular, and hormonal (Griffin *et al.* 2006). The identification of risk factors to non-contact ACL injuries is pivotal because such information can be used to develop prevention programs, which may reduce the risk of sustaining a non-contact

ACL injury. Among the risk factors, neuromuscular activation and muscle strength can be modified through training (Ageberg 2007; Bryant et al. 2007; Liu-Ambrose et al. 2003; Myer et al. 2007).

Studies have shown that landing with high impact forces may be a risk factor for ACL injuries (Chappell *et al.* 2002; Decker *et al.* 2003; Devita and Skelly 1992; Malinzak *et al.* 2001). These studies mostly compare lower extremity kinematics and kinetics between groups or genders, but did not actually examine the relationship among lower extremity kinematics and kinetics. More specifically, these studies suggest that increasing knee flexion at initial foot contact with the ground may decrease impact forces and knee loading during landing. It is interesting to note that the results from a later study (Yu *et al.* 2004) contradicted these findings. An *in vivo* study (Cerulli *et al.* 2003) demonstrated that for a single male subject hopping and landing on one leg, peak ACL strain occurred at peak VGRF shortly after initial contact, suggesting that perhaps peak VGRF may be a likely predictor for establishing the risk of ACL injuries.

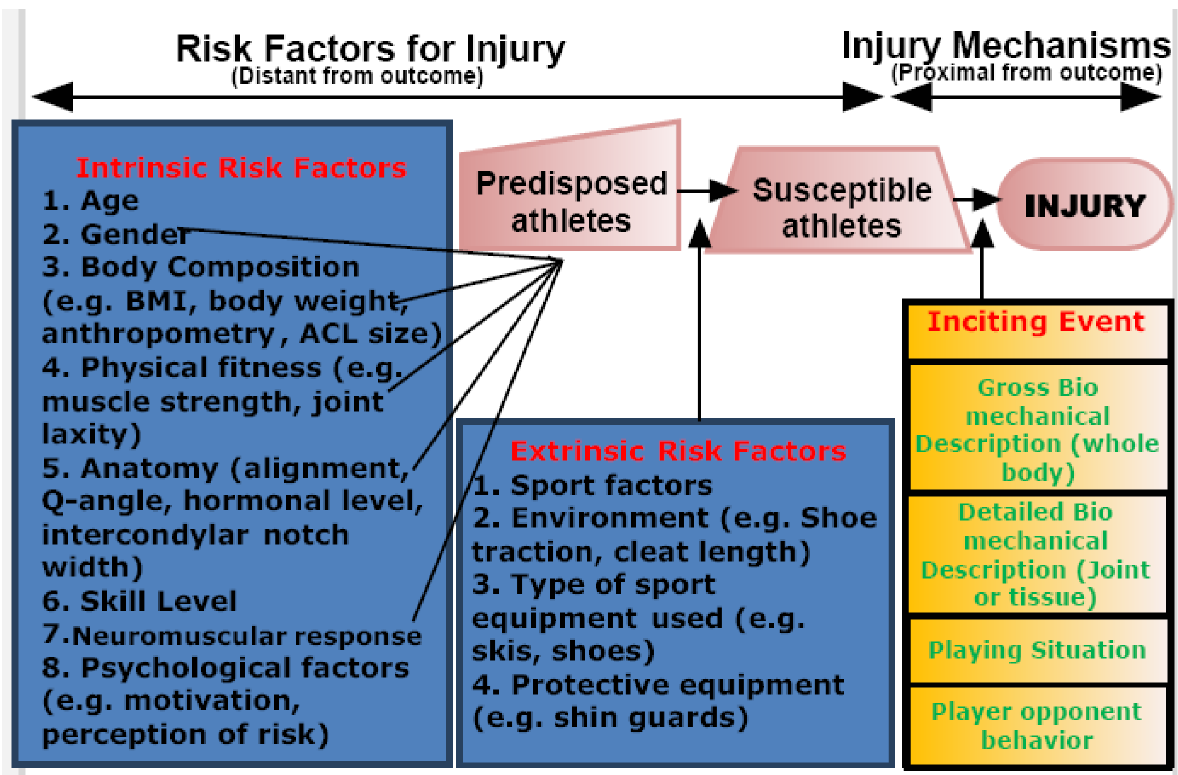

Figure 3: Risk factors implicated to cause ACL injuries*
* Adapted from Bahr and Krosshaug 2005

An epidemiological study by Hewett *et al.* (2005) investigating both genders during a two legged vertical drop landing task, reported knee valgus moment is a predictor of risk of ACL injury. However, caution should be taken when interpreting and using this study given the knee valgus moment of the nine subjects who suffered ACL injuries were 0.12 N.m/ (body weight * standing height). The average weight and height of the injured subjects were 62 kg and 1.68 m, respectively. This results in a knee valgus moment of 12.5 N.m, far too low to cause ACL injuries without the presence of large anterior shear force on the tibia as highlighted by Berns *et al.* (1992) and Fleming *et al.* (2001). Furthermore, research has demonstrated that knee valgus moment alone cannot injure the ACL when the medial collateral ligament (MCL) is intact (Bendjaballah *et al.* 1995; Mazzocca *et al.* 2003).

Although previous studies have indicated that biomechanical factors such as increased knee valgus moment, quadriceps muscle activation, and proximal tibia anterior shear force may be risk factors for non-contact ACL injuries (Chappell *et al.* 2002; Malinzak *et al.* 2001; Timothy *et al.* 2007), a recent literature review by Yu and Garett (2007) failed to find any convincing scientific evidence to support a cause and effect relationship between these proposed risk factors and non-contact ACL injuries. The lack of scientific confirmation and consensus on risk factors for non-contact ACL injury may be due to the absenceof an effective study methodology for predicting risk factors. Many of the studies above primarily addressed a single risk factor and failed to simultaneously address the multifactorial nature of non-contact ACL injuries. In other words, the host of factors contributing to ACL injuries warrants a study methodology that accounts for all of these factors at the same time, and not only examines the biomechanics associated with an individual factor, or an external or an internal risk factor in isolation (Bahr and Krosshaug 2005). Review articles can be consulted for further details on risk factors to non-contact ACL injuries (Ali and Rouhi 2010; Hewett *et al.* 2006; Huston *et al.* 2000; Ireland 1999; Quatman and Hewett 2009).

1.11 Why does this study focus only on landing?

Single-leg landing occurs frequently during many sports. Single-leg landings often occur from varying vertical heights and horizontal distances during sports. Landing from a jump can cause non-contact ACL injuries during sports (Yu *et al.* 2002). While jumping, the landing phase is more stressful for the ACL than takeoff (Chappell *et al.* 2002). In a 12 year video study looking at injuries to the ACL, Boden and co-workers (Boden *et al.* 2009) demonstrated that 21 out of the 29 subjects had ACL injuries during a single-leg landing. Moreover, at the time of the recorded maneuver 16 out of the 29 subjects' activity at ground contact, was landing from a jump on a single-leg. As well, from video analyses and interviews with athlete studies, Kirkendall and Garett Jr. (2000) showed that the vast majority of ACL injuries occur during landing when playing basketball. In one study (Paul *et al.* 2003), 91% of the patients studied had ACL injuries during sports, and almost 50% of those injuries occurred during landing events while playing sports. Furthermore, in a recent Olympic Committee Current Concepts review (Renstrom *et al.* 2008), where experts in ACL mechanics from around the world gathered, it was concluded that a likely component of an ACL injury mechanism includes most or all of the forces on a single-leg or foot, with the foot placed in front of the body, while the upper body leaning backward. Finally, single-leg landing studies can provide more functional improvements in both activities of living and sport performance because many sport movements in the competitive environment (jumps and landings) are performed on a single leg (Stålbom *et al.* 2007).

1.12 Existing study approaches used to investigate ACL injury mechanisms and risk factors

Experiment, athlete interviews, clinical studies, video analysis, and computational modeling are five different study approaches that have contributed to the understanding of ACL mechanics. A concise overview of many of these approaches, along with their strengths and weaknesses, are presented by Krosshaug *et al.* (2005). It seems that one common shortcoming of all of these approaches is their inability to simultaneously include the many factors, forces, and extreme conditions implicated as contributors to non-contact ACL injury. The multitude of intrinsic and extrinsic risk factors that come into play, and the complex interaction between these factors during non-contact ACL injury has compelled researchers to adapt a reductionist approach that focuses on a single factor or just a few factors. Clinical studies, athlete interviews, and video analysis have provided mostly qualitative data, and so are not adequate for obtaining a comprehensive understanding of injury to the ACL. However, the findings from these approaches are vital for validating quantitative study approaches. From the current literature, the two major quantitative study approaches that are employed to better understand how and why the ACL gets injured, are experimentation and computational modeling. A thorough review of the literature on the application of these two quantitative approaches to study ACL mechanics, along with their strengths and weaknesses can be found in Ali and Rouhi (2010).

1.13 Role of AI in this research

A necessary first step to a possible approach aimed at simultaneously including many of the risk factors, forces, and extreme conditions, and the complex interaction of these parameters to non-contact ACL injury research, is to determine a tool capable of combining and studying all these factors simultaneously. Conventional analytical approaches tend to be reductionist in nature. Most problems related to human health and disease is relationally complex (Quatman *et al.* 2009). Conventional analytical approaches such as regression methods are useful for identifying linear relationships, but are limited because of their inability to establish and test a web of causal relationships which may include varying weights of variables and feedback loops (Mabry *et al.* 2008). Nonetheless, reductionist approaches can be useful as they help find simple answers using simple cost effective means. However, reductionist approaches are innately problematic. The information that gets obscured or overlooked can lead to overly simplistic understandings and explanations for predicting phenomena. Some common techniques that can be used to address the limitations of existing approaches are broadly referred to as complex system modeling, or system science techniques. Complex system-based techniques embrace the integration of more powerful methodological and analytical tools such as agent-based modeling, network analysis, and dynamic systems analysis (Mabry *et al.* 2008; Wasserman and Faust 1994). These innovative methods enable investigators to simultaneously consider the dynamic interaction between and among variables at multiple levels of analysis, and the impact these factors have on the behavior of a system as a whole (Quatman *et al.* 2009). One such technique that can allow a systems approach to solve complex problems is AI. The role of AI in this study is to facilitate search and parameter identification. For the multifactorial approach proposed, AI enables one to search and determine how best to arrange (group, sequence, or assign) the controllable elements in the ACL problem definition to achieve a specified objective.

AI is required to enable one to capture the wide variability in movement patterns to cause injury, wide variability in human anthropometry, numerous design variables, design constraints, risk factors, forces and extreme conditions simultaneously entailed in non-contact ACL injury research. The author's view is that combining the five existing non-contact ACL injury study approaches using an AI technique in a single study environment may be a much more robust and comprehensive methodology to better predict the mechanisms and risk factors of non-contact ACL injury.

1.14 Role of musculoskeletal modeling in this research

Musculoskeletal models are rigid body dynamic models aimed at balancing ligament, joint contact, and muscle forces with externally applied forces to produce motion. Most musculoskeletal models are phenomelogical dynamic models that are activated by muscles and have tremendous capability in capturing muscle response during movement. These models are driven by kinematics and external forces. Two commercially available software packages that can be used to determine muscle forces are SIMM and Anybody Modeling System. Both software packages were developed based on research by Delp (Delp 1992). Some of the research groups that have used musculoskeletal modeling for ACL injury research are Scott McLean and co-workers, Marcus Pandy and co-workers, and David Lloyd and co-workers (Lloyd and Besier 2003; McLean *et al.* 2004; Pandy and Sasaki 1998; Pandy *et al.* 1997). Musculoskeletal models applied in this research are used to determine joint reaction and muscle forces during single-leg landing tasks.

1.15 Scope of this study

The purpose of this research was to identify gaps in knowledge in the area of non-contact ACL injury mechanisms and risk factors. This entailed getting familiar with the existing knowledge regarding various injury mechanisms, the associated risk factors and present injury prevention regimes. This gap in knowledge, possible reasons for this gap, and direction for future research, are presented in journal Manuscript I (Ali and Rouhi, 2010). With the gap of knowledge identified and the barriers to a better understanding of non-contact ACL injury obtained, a methodology was proposed that can resolve many of the challenges identified in Manuscript I. This proposed method suggests the coupling of many of the existing non-contact ACL injury study approaches via an AI technique. Details of this new proposed methodology are presented in journal Manuscript II (Ali et al., 2011).

Given single-leg landing was identified as an injury mechanism warranting further investigation, two manuscripts (Manuscript III and Manuscript IV) were written to report findings based on experimental studies, and biomechanical rigid body modeling in Visual 3D. The primary objective of Manuscript III (Ali et al., 2014) was to examine the effect of increasing vertical heights and horizontal distances on various sagittal plane biomechanical variables that can modulate GRFs during single-leg landing and reduce the risk of non-contact ACL injuries. This study employed seven male subjects. On the other hand, Manuscript IV (Ali et al., 2013) determined whether or not gender differences exist in body kinematics and kinetics, as well as knee energetics during single-leg landings from increasing vertical heights and horizontal distances, and whether these differences explain the higher number of non-contact ACL injuries among females. To achieve the objectives of manuscripts III and IV experiments were first conducted in a gait lab using six male and six female healthy recreational athletes performing single-leg landings from increasing vertical heights and horizontal distances, while kinematics, kinetics and EMG data were measured. The experimental data we used to develop a rigid body musculoskeletal model in Visual 3D as well as to conduct a complete Newtonian inverse dynamics analysis prior to statistical analysis. The inverse dynamics method utilized in Manuscript III and IV did not include the effect of muscles, therefore individualized MSMs were developed, validated and then applied to single-leg landing tasks to obtain a more comprehensive and accurate understanding of the changes in internal forces over increasing vertical heights and horizontal distances. The model was driven and validated using data collected from experiments. Anybody Modeling System (Anybody Technology, Aalborg, Denmark) was used to conduct the musculoskeletal modeling studies and results are presented in journal Manuscript V (Ali et. al., 2013).

In addition to the application of various study approaches applied to single-leg landing studies as captured in these journal papers, a series of findings born out of this research and construed from models developed during this research were published in the following conference proceedings:

1. Ali, N., “Key Challenges confronting biomechanists aiming to predict ACL injury mechanisms,” 32nd Conference of the Canadian Medical and Biological Engineering Society, Calgary, May 22nd 2009.

2. Ali, N., and Farah, A., “An alternative approach to better predict injury mechanisms to the ACL during non-contact events,” 22nd Canadian Congress of Applied Mechanics, Halifax, May 31st 2009.

3. Ali, N., Robertson, G., Rouhi, G., “Applicability of operations research and artificial intelligence approaches to non-contact anterior cruciate ligament injury studies,” International Society of Biomechanics in Sports, Limerick, Ireland, Sept 17th 2009.

4. Ali, N., Robertson, G., Rouhi, G., “A new approach to postural stability research using the inverted pendulum mode,” Canadian Society of Biomechanics, Kingston, Ontario, Jun 9-11th 2010.

5. Ali, N., Robertson, G., Rouhi, G., “Body kinematics during single-leg landing from varying heights and distances– implications for non-contact ACL injuries: case report”, International Society of Biomechanics in Sports, Porto, Portugal, June 28th -Jul 2nd 2011.

1.13 Thesis outline

The remaining chapters of this dissertation are outlined as follows:

Chapter 2

The barriers to a better understanding of non-contact ACL injury are presented and postulations on how to address these challenges are highlighted (Ali and Rouhi, 2010). This paper is a thorough review of the literature to expose challenges and to guide future research on non-contact ACL injury. (Manuscript I)

Chapter 3

In Chapter 3, the capabilities of operations research (OR) and artificial intelligent (AI) techniques are presented. The application of these techniques to non-contact ACL injury research is also presented and emphasized. The application of an AI technique to address many of the challenges in non-contact ACL injury research through the coupling of many disparate modalities in a single environment is presented (Ali *et al*. 2011). (Manuscript II)

Chapter 4

In Chapter 4, the findings obtained from conducting single-leg landings from increasing vertical heights and horizontal distances using male subjects are presented. The experimental data were used to develop and drive a 3D rigid body model of the human body in Visual3D whose results were then analyzed in SPSS. For this work, the effect of vertical height and horizontal distance on kinematics, kinetics and knee energetics during single-leg landing and its implications to risk of non-contact ACL injury are presented (Ali *et al*. 2014). (Manuscript III)

Chapter 5
In Chapter 5, the kinematic and kinetic gender differences during single-leg landing from increasing vertical heights and horizontal distances are presented. The significant main effects and interactions of gender, vertical height, and/or horizontal distance on various selected biomechanical variables implicated to increase the risk of non-contact ACL injury was investigated (Ali *et al*. 2013). This manuscript's central aim was to present full-body kinematics -seldom reported in the literature- so as to establish if among the biomechanical variables selected, there are any variables which can explain the higher rate of non-contact ACL injuries among females (Manuscript IV).

Chapter 6
In Chapter 6, the changes in kinematics, joint reaction forces, muscle forces, and muscle activation patterns over increasing vertical heights and horizontal distances during single-leg landing are presented. Individualized musculoskeletal models were developed, validated and applied using the Anybody Modeling System Software. The findings from these simulations are further analyzed in SPSS to establish the effect of various selected musculoskeletal variables on risk of non-contact ACL injury during single-leg landing (Ali *et al*. 2013) (Manuscript V).

Chapter 7
Chapter 7 presents general discussions and some key findings stemming from this research. Further, some future directions and concluding remarks are indicated.

Appendix A
Ethics consent form and ethical approval certificate are mandatory requirements to make this work possible and are presented in this section of the dissertation.

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Manuscript I - Barriers to Predicting the Mechanisms and Risk Factors of non-contact Anterior Cruciate Ligament Injury

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Barriers to Predicting the Mechanisms and Risk Factors of Non-Contact Anterior Cruciate Ligament Injury

Nicholas Ali[1*] Gholamreza Rouhi[2,3]

[1]School of Human Kinetics, University of Ottawa, Ottawa, Canada
[2]Department of Mechanical Engineering, University of Ottawa, Ottawa, Canada
[3]Faculty of Biomedical Engineering, Amirkabir University of Technology, Iran

[*]Corresponding author

Abstract

High incidences of non-contact anterior cruciate ligament (ACL) injury, frequent requirements for ACL reconstruction, and limited understanding of ACL mechanics have engendered considerable interest in quantifying the ACL loading mechanisms. Although some progress has been made to better understand non-contact ACL injuries, information on how and why non-contact ACL injuries occur is still largely unavailable. In other words, research is yet to yield consensus on injury mechanisms and risk factors. Biomechanics, video analysis, and related study approaches have elucidated to some extent how ACL injuries occur. However, these approaches are limited because they provide estimates, rather than precise measurements of knee - and more specifically ACL - kinematics at the time of injury. These study approaches are also limited in their inability to simultaneously capture many of the contributing factors to injury.

This paper aims at elucidating and summarizing the key challenges that confound our understanding in predicting the mechanisms and subsequently identifying risk factors of non-contact ACL injury. This work also appraise the methodological rigor of existing study approaches, review testing protocols employed in published studies, as well as presents a possible coupled approach to better understand injury mechanisms and risk factors of non-contact ACL injury. Three comprehensive electronic databases and hand search of journal papers, covering numerous full text published English articles were utilized to find studies on the association between ACL and injury mechanisms, ACL and risk factors, as well as, ACL and investigative approaches. This review unveils that new research modalities and/or coupled research methods are required to better understand how and why the ACL gets injured. Only by achieving a better understanding of ACL loading mechanisms and the associated contributing factors, one will be able to develop robust prevention strategies and exercise regimens to mitigate non-contact ACL injuries.

Keywords: Anterior cruciate ligament, non-contact ACL injury, injury mechanisms, risk factors

1. Background

A non-contact injury is defined as an injury that occurs without physical contact with another person or object [1]. Studies have demonstrated that 70 to 80% of ACL injuries occur during non-contact sporting events, which involve sudden deceleration, an abrupt change in direction, or jump landing as is common in soccer, basketball, handball, and volleyball [2-4]. Increased participation in athletic activities, especially among females, and the growing number of people in sports has resulted in an increase in the number of ACL injuries. Among athletes, females are 2-8 times more likely to sustain a non-contact ACL injury than males [5-8]. Approximately 100,000 to 175,000 ACL-related surgeries are conducted in the United States each year [9], with associated costs exceeding $2 billion. Complete ACL rupture may lead to significant posttraumatic laxity, functional knee instability, and increased likelihood of osteoarthritis [10-13]. Advances in surgical techniques and rehabilitation have resulted in ACL surgery becoming a relatively routine procedure [2].

During the 1990s, there was a paradigm shift in research focus on the ACL, from the development of more effective diagnostics and treatments to greater emphasis on identifying the mechanisms and risk factors of non-contact ACL injuries [14]. This shift was driven by the realization that only if the causal relations between applied forces and the resultant injury are understood, then appropriate programs of intervention and prevention can be designed and implemented [15]. This focus persists, but progress in this research area has been somehow patchy and somewhat slow. Nonetheless, the prevention of sport related non-contact ACL injuries today relies largely on the ability to screen at risk individuals and then modify through training the identified risk factor. Neuromuscular control strategies and muscle strength, or more specifically, proprioceptive training and hamstring strength training respectively, are among the risk factors that can be modified through training [16-18].

The goal of this work is to provide a comprehensive assessment and summary of the challenges that hinder our ability to precisely determine injury mechanisms and risk factors of non-contact ACL injury. This is a crucial task since, as an unfortunate fact, the literature lacks consensus and coherence with regards to predicting injury mechanisms and determining risk factors of non-contact ACL injuries. Understanding these challenges is also a necessary first step towards designing studies to better understand non-contact ACL injury mechanisms and the associated risk factors, as well as, subsequently enabling the development of injury prevention programs. This article also highlights the grave needs and promising opportunities to steer future research direction in non-contact ACL injury biomechanics. It focuses on one important question, that is, what is the current status in clearly predicting the mechanisms and risk factors of non-contact ACL injury?

2. Materials and Methods

This article reviewed the relevant literature on ACL injury mechanisms in the PubMed electronic database using MEDLINE (1966 to 2010), Proquest (1987 to 2010), and, Applied and Complementary Medicine Database (AMED) on Ovid (1985 to Sept. 2010). Keywords used in our search included “anterior cruciate ligament”, “ACL injuries”, “injury mechanisms”, “risk factors”, and “non-contact injuries”. A total of 813 articles were identified and reviewed. The most relevant full text English articles pertaining to ACL non-contact injuries, risk factors for ACL injuries, and study approaches to understand ACL mechanics were analyzed. Studies that captured the association of ACL and non-contact injuries, and ACL with a specific study approach were also included. Our search was supplemented by reviewing the bibliographies of retrieved articles, as well as, hand searching scholarly journals outside of the bio-fields related to this topic.

3. Challenges in identifying mechanisms and risk factors of non-contact ACL injury

The mechanism of injury to the ACL is rather complex because the injury event is quick, the injury condition is dynamic, and the knee is a complex joint capable of interrelated compression, translation and rotation about various axes [17, 19]. The mechanism of ACL injury is also complex because it involves the concurrent interaction of muscle forces, external forces, ligament forces, and joint contact forces. Several studies [2, 4, 20-26] have suggested several non-contact ACL injury mechanisms: jumping, landing, side step cutting maneuvers to name a few. Most study approaches have provided valuable information but do not offer a comprehensive view of ACL injury mechanism. The literature also reports a host of risk factors contributing to ACL injuries and as such demands the use of a method that accounts for all of these factors at the same time, and not only examine the biomechanics associated with injury or individual or external risk factors in isolation [27]. The following review articles [7, 8, 28-30] has compiled and summarized the risk factors to non contact ACL injury. So even though a recent thorough review [27] has shown that ACL injuries occur from a complex interaction of multiple risk factors, very few studies in the literature take this into account.

Fragmentation and discrepancies in the literature may be a reflection of the limitations and differences in current non-contact ACL injury study approaches which includes but not limited to, equipment used, computing power and software programs. More importantly, little is known about ligament and muscle loading and response during ACL injuries. This may be attributed to the innate difficulties associated with measuring ligament and muscle forces *in-vivo*. It is understood, based on this review, that most of the research on non-contact ACL injuries has focused on the effects of knee mechanics before and after ACL rupture, or before and after ACL reconstruction, but not on the very important aspect of precisely how and why the ACL gets injured.

Consequently, the success of any screening method relies on a precise understanding of the relationship between knee kinematics, joint geometry, external loading, neuromuscular control, ACL loading, and the associated contributing risk factors of injury. Until accurate descriptions of these relationships are available, the potential exists for all screening methods to exclude incorrectly “at risk” people from any ensuing intervention process [31, 32]. For athletes who are at higher risk, a complete understanding of injury causation needs to address the multi-factorial nature of sport injuries [33, 34]. Even though a multidisciplinary approach is recognized as a more robust study approach by some research groups [35-37] it has never been undertaken. The following section highlights some of the major impediments to furthering our understanding of non-contact ACL injury mechanisms and risk factors.

3.1 *Shortcomings and general inherent challenges of studying non-contact ACL injury*

For ethical reasons, *in-vivo* measurements of ACL loading to failure in human or animal subjects cannot be undertaken. Hence, relationships between internal forces, external loading, and ACL loading mechanism are mainly unknown due to the difficulties of measuring ligament and muscle forces *in-vivo*. Moreover, maximum kinematic changes of knee, for example, anterior tibial translation (ATT) may not necessarily correspond to maximum force in the ACL due to the concurrent interactions of multiple tissues surrounding the knee. These interactions are very difficult to capture even with the most sophisticated existing study approach. The problem is complicated further by the structural complexity of the knee and the ACL, as well as, the multiple structures that contribute to similar function. The difficulties in obtaining material property data for the hard and soft human tissues also create some limitations, especially for computational modeling studies. Other challenges include high cost of experimental studies, as well as, the difficult and sometimes impossible task of reproducing certain natural, pathological or degenerative situations *in-vitro*. In addition, there can be significant inter- and intra- subject variability during experimental testing. The following subsections elucidate specific areas where challenges and difficulties in studying non-contact ACL injury persist.

3.1.1 **Study approach do not capture muscle activation and kinematics**

Study approaches that do not include muscles may not adequately predict injury mechanisms and risk factors of non-contact ACL injury. Omitting muscles leads to inaccuracies since the forces transmitted to the ligaments and bones are dominated by the muscle forces [38]. It appears that ligaments can only play a limited role in maintaining the integrity and stability of the knee joint. In fact, it is likely that ligament rupture occurs only when muscle action fails to protect them. Muscle recruitment strategies may also be one indicator why females suffer more non-contact ACL injuries than men [39-42], and strongly points to the importance of musculo-tendon contributions in maintaining knee joint stability and integrity. Hence, if for any reason the firing pattern and the magnitude of the load by which the muscle pulls on the bones of the knee are improper, then the ACL will then have to take the brunt of the load and in some instances will rupture.

In-vivo studies [43] have concluded that ACL strain increases if there is an increase in quadriceps activity relative to hamstring activity. McConkey [44] are the first to describe eccentric quadriceps contraction as the intrinsic force responsible for ACL injury. Numerous *in-vitro* studies using defect free cadavers have also focused on the effects of increased quadriceps forces on ACL strain [45, 46] and concluded that high unopposed quadriceps forces induce ATT, and consequently increase the strain in the ACL over a specific range of knee flexion angles. One *in-vivo* study with healthy men and women (using 11 subjects) aged 21-42 years and with normal ACL [47] showed similar results. However, one *in-vitro* study using six pairs of human cadaveric knees [48] found that the quadriceps muscle force protected the ACL from injury. As well, one study demonstrated that under non-physiological loading without any ground reaction forces (GRFs), the knee locked in one position, and static quadriceps loads of 4500 N applied, ACL injury did occur [49]. The authors suggested quadriceps drawer as an injury mechanism. Hamstring muscle force applies a posterior directed force component and has been reported to strain shield the ACL by reducing ATT at large flexion angles [50]. An early study by Solomonow *et al.* [51] suggests that strength training of the hamstring muscles can help prevent damage to the intact ACL. On the other hand, a later study by Shelburne [52] demonstrated that the hamstring cannot apply large enough posterior forces to unload the ACL especially at low knee flexion angles- a position where many non-contact ACL injuries occurs. It has also been demonstrated by Simonsen *et al.* [53] that the ability of the hamstring muscles to reduce the ACL load is marginal.

The results of an *in-vivo* study by Fleming *et al.* [54] demonstrated that the gastrocnemius muscle is an antagonist to the ACL. This is in agreement with an analytical study by Pflum *et al*. [55]. On the other hand, a cadaveric study by Durselen *et al.* [56] and a theoretical investigation by Shelburne [57], both demonstrated that the contraction of the gastrocnemius muscles did not strain the ACL over the entire range of knee flexion.

The discrepancies among these studies highlight the need to determine the contribution of muscle activation and loading on ACL loading. Nonetheless, many studies clearly demonstrate that ACL loading mechanism is affected by muscle activity and that the muscles must be included in these investigations. Moreover, considering the limited strength of the ACL, active control of the knee joint depends on the balance of the resultant muscle forces.

3.1.2 **Lack of studies that include ankle and hip articulation**

The majority of non-contact ACL injury studies do not address the effects of hip and ankle kinematics and kinetics on injury. In addition, the majority of studies in the literature do not account for the effects of whole body movement on ACL loading. The inclusion of the ankle is important in non-contact ACL injury studies as it has been shown that the interaction of shoe surface interface with the ground is an important risk factor in non-contact ACL injury [24]. An increase in the coefficient of friction between the shoe and playing surface may increase the traction which can cause the foot to catch or stop inadvertently during play. Such types of events are associated with higher risk of ACL injury. By one study conducted using soccer players with varying cleat lengths, it was also shown that foot contact with the ground is an important risk factor in non-contact ACL injury [58]. Lambson *et al.* [58] also demonstrated that shoes with more cleats result in higher torsional resistance at the foot-surface interface which can result in increased risk of ACL injury. As well, muscle activity across the ankle controls the position of the foot at landing, which most likely influence the loading at the ankle [59]. Moreover, muscular activity at the ankle may influence the loads that are transferred through the ankle to the knee [59, 60]. Pflum *et al.* [55] found that the forces applied by the ground to the foot have a major impact on peak forces seen at the ACL. Another study found that when the foot was not flat, the ground reaction forces (GRFs) cannot be transmitted effectively through the bones to the ground without the actions of muscles [61]. In addition, excessive foot pronation was shown to increase the likelihood of non-contact ACL injury [62].

Inclusion of the hip articulation is also important to the understanding of how and why the ACL gets injured since hip movement is known to affect the loading on the knee [40]. Because the upper body contains over half of the total body mass, the trunk and pelvis position will have coupled effects on knee angles and resultant ACL strain. The position of the leg at the time of non-contact ACL injury displays tibial rotation, apparent knee valgus, foot pronation, and a relatively extended knee and hip [4, 14]. Muscle contraction at the hip can also affect knee loading because the hip transfers the upper body loads to the leg [6]. In addition, muscle contraction at the hip can also affect energy absorption [63, 64]. Moreover, a cadaveric study [19] and an analytical study [65] both demonstrated that if the hip movement is restricted, ATT will result and ACL injury can easily occur. Some other studies also suggested that the knee is one part of the kinetic chain and that the torso, hip, and ankle may also contribute to ACL injury [40, 66]. The importance of including the hip and ankle joints in any non-contact ACL injury study is supported by many other studies which are captured in a review article by Hewett *et al.* [30]. So, one can conclude that non-contact ACL injury is a whole body event that requires the study approach to capture the contributing effects of ankle and hip articulations on ACL loading.

3.1.3 Studies do not accurately capture knee joint geometry

Specific contours of the knee joint geometry, for example, the femoral notch [67] has been implicated as a risk factor for non-contact ACL injury. The complex geometry of the knee joint aids in stability. The femoral groove that the patella slides on, the femoral condyles resting on the tibial eminence [68] and the posteriorly sloped tibial plateau [69] are all factors that may affect loading seen at the ACL during various non-contact ACL injury mechanisms. There are many computational studies that overlook the contribution of these factors to ACL injury. In fact, Liu [70] found that articular surface geometry, ligament locations, and ligament insertion sites had a pronounced effect on the modeling outputs. Irrespective of muscular activity, Rentrom *et al.* [71] demonstrated that the ACL is subjected to an inherent increase in strain as the knee extends owing to the geometry of the articular surfaces of the knee. Despite this, many studies have not considered accurate three dimensional (3D) hard and soft tissue geometries and few have investigated the effect of geometry changes on loads seen at the ACL [72-74]. The inclusion of accurate 3D tissue geometries appears to be a crucial non-contact ACL injury study approach prerequisite. Without an objective view of these parameters in problem definition, a clear and comprehensive understanding of injury mechanisms and risk factors of non-contact ACL injury may remain elusive.

3.2 *Limitations in current non-contact ACL injury study approaches*

Experiment, athlete interviews, clinical studies, video analysis, and computational modeling are all different study approaches that have contributed to the understanding of ACL mechanics (see Figure 1). A concise overview of many of these approaches along with their strengths and weaknesses are presented by Krosshaug *et al.* [75]. It seems that one common shortcoming in all these approaches is the inability to fully capture the many factors implicated as contributors to non-contact ACL injury.

Clinical studies, athlete interviews, and video analysis has provided mostly qualitative data and so are not adequate for obtaining a comprehensive understanding of injury to the ACL. From the current literature, one can glean two main quantitative study approaches for better understanding how and why the ACL gets injured, namely, experimentation and computational modeling (highlighted in green in Figure 1). The existing quantitative study approaches shown in Figure 1 will be discussed in the context of this review.

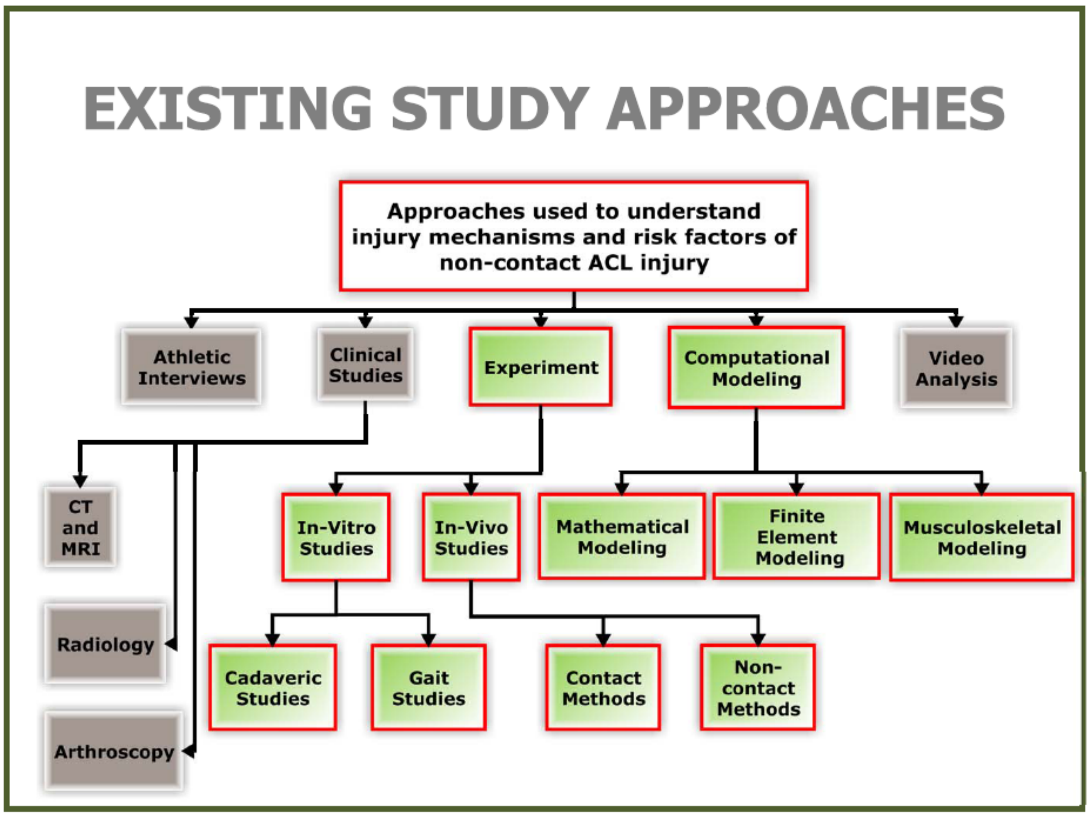

Figure 1- Existing approaches employed to better understand mechanisms and risk factors of non-contact ACL injury

3.2.1 <u>**Challenges facing the field of *in-vivo* experimentation**</u>

It can be argued that historically, research on the human musculoskeletal system was focused on empirical methods. One form of *in-vivo* testing entails the direct implantation of a transducer to subjects' tissues. These are termed contact methods and have the advantage of simultaneously including many risk factors, forces, the effects of active muscles, as well as weight-bearing loads. A significant challenge with this form of *in-vivo* testing is that it is invasive. Ethical policies controlling testing with humans make *in-vivo* testing extremely difficult. Moreover, because of the size of the sensor employed, size of the ACL, intraarticular location of the ACL and intercondylar notch, *in-vivo* studies to-date can only measure strain on the anteromedial bundle of the ACL for movements confined to the sagittal plane [76]. Measurements are restricted to linear displacement at discrete locations, knee flexion angles approximately greater than 15 degrees, and movements only in the sagittal plane [47]. In addition, many of these studies look at movements that are non-ballistic. Woo *et al.* [77] have also argued that since strain gauges and other similar type transducers are implanted into the ligament, they can alter the ligament length, and subsequently ligament force. Another complicating factor with *in-vivo* techniques is the fact that specific bands of the ligament are tensioned at different portions of the loading cycle. Another form of *in-vivo* testing includes non-contact methods. These methods do not require the implantation of a sensor into the subject's ACL. Non-contact *in-vivo* methods include, but are not limited to, the use of dynamic magnetic resonance imaging (MRI) [78], bi-plane fluoroscopy [50, 79-82] and video dimension analyzer [83] to capture tissue kinematics at various knee flexion angles. These techniques do not provide any details of the forces seen at the ACL during movement. Another, non contact method include optical techniques such as Roentgen Stereophotogrammetry [84, 85]. Various contact techniques have been used in the past to measure *in-vivo* ACL strain: implantable extensometers [47, 71, 86-91] and buckle transducers [92-97]. It may be argued that none of these techniques are truly *in-vivo* given they alter in one form or the other the way the subject moves during testing.

3.2.2 **Challenges facing the field of *in-vitro* experimentation**

In-vitro testing is conducted outside of the body typically with human subjects or post mortem human subjects (PMHS) / cadavers. The vast majority of studies investigating non-contact ACL injuries are *in-vitro* [19, 77, 98-100]. The major advantage of in-vitro testing is its utilization of biological tissue for testing. In-vitro testing also has the capability to simulate knee kinematics and muscle loads. However, *in-vitro* studies using cadavers may not accurately describe ligament function *in-vivo* since loading applied to the cadavers during experiment is different from that applied by the muscles during activity. Other challenges with *in-vitro* studies using cadavers are the inability to simulate realistic muscle activation and the difficulty in obtaining repeatable results. Furthermore, replicating an isolated ACL injury *in-vitro* is difficult, and has been achieved with only limited success [19]. This shortcoming may exist because cadaveric knee studies lack the stability and control provided by active knee musculature [101]. It is also difficult to apply large muscle forces seen during normal physical activities such as landing from a jump to in-vitro experiments using cadavers. This is partly due to the fact that many cadavers are from the elderly population. Another prevalent *in-vitro* study method is gait analysis that employs skin markers. The use of skin markers with gait studies have been shown to induce significant errors in predicting *in-vivo* ligament behavior [102-104]. Since some gait studies are conducted in the laboratory setting, there is also some level of uncertainty with respect to the ability of these tools in capturing true human response. Given the subject is aware that the camera is focused on them or their feet have to strike a force plate, it can be argued that their body response may be somewhat altered to fit the event. As a result, the data collected may not be a true representation of human motion. Despite its shortcomings, i*n-vitro* studies have the capability to provide much freedom to investigate function and behavior of the ACL. From this standpoint, it can be argued that gait analysis is the only way available today to determine the kinematics and kinetics during activity to cause non-contact ACL injury.

3.2.3 **Challenges facing the field of computational modeling**

There are mainly three approaches to computational modeling in the current literature: mathematical, finite element (FE), and musculoskeletal rigid body (RB) modeling. A computational model of the knee joint is a graphical representation of the joint anatomy that can be manipulated. Computational modeling has become popular partly because technological restrictions and ethical considerations have prevented the direct measurement of the ACL strain *in-vivo*. Many mathematical models of the human knee focus on the intact ACL. With many of these models, if injury is studied, it is done primarily by removing the effect of the ACL in the model predictions [105]. Even though mathematical models have assisted us in gaining a better understanding of the mechanics of the knee, the gross approximations and assumptions made by these models can readily be addressed with technology and information available today. Two such technologies are FE and RB modeling. Mathematical models have become less popular over recent years perhaps due to: (1) Easy access and lower cost of FE and RB modeling software; and (2) Inherent complexity and nonlinearity in the governing equations related to ACL biomechanics, and subsequently the challenges entailed in developing and verifying these models. Hefzy [106] provided an excellent review of mathematical models of the human knee joint found in the scholarly literature.

The first application of finite element analysis (FEA) to biomechanics was in orthopedics [107]. The most extensive application of FEA to knee biomechanics has been in artificial joint design and fixation. Two studies [108, 109] provided a brief review of the application of FEA to biomechanics. Andriachi *et al.* [110] was the first to develop a knee joint model for the determination of the forces using FE methods. Once verified and validated, a FE model can provide greater capabilities to answer many what if questions over mathematical models. Finite element models also have the advantage of being able to calculate parameters that are difficult to measure experimentally. The literature indicates that only a small number of FE models are used to study ACL mechanics, and none have focused on predicting mechanisms and risk factors to non-contact ACL injury (see for instance [72, 73, 111-128]).

Many of these FE studies do not report data on model verification and validation, thus limiting their use in clinical applications. Other FE studies investigating ligament mechanics in the literature modeled only the ACL [112, 129, 130]. None of these studies investigated non-contact ACL injury. Nonetheless, the challenge with FE modeling of biological tissues include the complexity of modeling material responses under loading, the level of discretization required to capture complex and intricate anatomical geometries, long computational time to converge [131], and dependence on empirical data for validation among others. Increased and affordable computing capacity and more sophisticated (nonlinear and 3D) FE software packages has allowed more realistic modeling and the application of iterative procedures to describe time-dependent biomechanical behavior. Nonetheless, this may not be enough to fully address the challenges posed by the complexity of predicting non-contact ACL injury mechanisms and risk factors.

Musculoskeletal RB modeling of the knee is based on research aimed at developing a dynamic rigid body model for balancing internal forces with externally applied forces to produce motion [132-134]. Three main approaches may be used to balance internal forces with externally applied forces for a specific motor task: inverse dynamics; forward dynamics; and optimum control theory. Erdemir *et al.* [88] provided a thorough review of these three approaches. The main advantage of musculoskeletal RB modeling is that it enables us to determine the forces in the muscles during activities implicated to cause non-contact ACL injuries. However, musculoskeletal models cannot provide details of the loads and stresses in the hard and soft tissues, like FE models can. In addition, RB musculoskeletal models can require extremely long computational time to converge to a solution and in some cases require parallel computing [135].

3.3 *Shortcomings in biomechanics field*

The literature points to some systemic challenges facing the field of biomechanics which are believed to be impeding progress and clouding a collective agreement in the understanding of mechanisms and risk factors of non-contact ACL injury. ACL biomechanics research is mostly empirical. An empirical study approach has been the main method of building the foundation of biomechanics. In fact, there is a significant gap between the advancement of empirical tools and that of analytical and numerical tools in biomechanics. It has also been recognized that there is a lack of consensus in the research community on the merit of formulating clinical recommendations based on physical and numerical model results [136]. This may exacerbate itself to much uncertainty in theories used for teaching clinical biomechanics [137]. ACL injury research is a multidisciplinary field, since one need to consult with many disciplines in a single problem. With the cross linking of certain disciplines (such as biomechanical engineering, mechano-biology, bio-infomatics, etc.), problems in non-contact ACL injury research may become more easily solvable. Such cross linking may also bring about new resources, skill sets, approaches, and outlooks to the field of biomechanics.

The following two subsections shed some light on a few shortcomings in the field of biomechanics that continues to hinder a clear understanding of the mechanisms and risk factors of non-contact ACL injury.

3.3.1 Studies Too Narrowly Focused

Based on this investigation, it is understood that the type and complexity of the research method employed depends on the question(s) posed. Many studies have pointed out that several intrinsic and extrinsic factors are responsible for non-contact ACL injuries [30, 138, 139]. Other studies have categorized risk factors into four areas: environmental, biomechanical, neuromuscular, and hormonal [40]. However, many studies focused on investigating the effects of a single risk factor by comparing intrinsic or extrinsic differences between males and females, such as Q-angle [140], intercondylar notch width [141], and hormones [142] without considering the combined effects of these and other factors implicated to cause injury. It seems that the multitude of intrinsic and extrinsic risk factors involved during sports make focusing on one factor difficult. In addition, some studies address the effects of only one muscle group on ACL rupture. It seems quite unlikely that a single risk factor or only one muscle group will be responsible for ACL injury. There are few studies, to the best of our knowledge, where a tool or methodology is employed that lends itself to simultaneously determining the effects of numerous parameters on injury mechanisms and risk factors of non-contact ACL injury. Finally, the low annual incident rate for ACL injury in the general population of 1 per 3000 people [143] – and even smaller in the athletic population – has compelled researchers aiming at pinpointing factors contributing to risk of ACL injury to adapt a reductionist approach by focusing on a single factor or few factors due to small sample size. Given this, studies to date are narrowly focused due to statistical power limitations.

3.3.2 Lack of Standardization

Combining and comparing results from separate studies that use similar research methods can be valuable, but differences in, for example, specimen type and data reporting may prevent drawing solid conclusions about the results. The challenge is these differences may exist due to the lack of guidelines on study method, instrumentation to employ, and procedures for data analysis. The dearth of standards and specifications in the field of biomechanics is believed to be one reason why dialogue among research groups and comparisons in experimental studies remains challenging, debatable, and sometimes with no solid outcome. A few attempts at standardization that have led to considerable benefits in the research community include the Visible Human Project [144], VAKHUM [145], and the standardized femur [146]. These endeavors have aided in simplifying cross validation of research results. Due to the lack of standards and specifications in study approaches, accumulating knowledge on injury mechanisms and risk factors of non-contact ACL injury is believed to be slowed. As well, many of these studies are too highly focused and are not powered to handle the contribution of multiple factors on non-contact ACL injury.

4. Towards a better understanding of risk factors to non-contact ACL injury

Non-contact ACL injury research requires the use of many modalities, data from disparate sources, and many specialized software tools [37]. A possible approach is a coupled study approach that leverages on the advantages of existing non-contact ACL injury study approaches. For a list of existing study approaches used in non-contact ACL injury research see Figure 1. Figure 2 highlights the coupled study approach proposed. This approach entails utilizing a 3D electromyography (EMG)-driven FE model of the human lower extremity fused with a RB model that is validated with experiments and existing qualitative study approaches. Starting with patient bio-data in the form of MRI and/or CT scans of the tissue of interest, a computational model is constructed. This model is then meshed in a preprocessor FE software package or standalone meshing software. The meshed model once refined constitutes the FE model that is then validated for use in non-contact ACL injury studies. The validated FE model includes all major hard and soft tissues of the lower extremity, as well as, the muscles. For model validation *in-vitro* testing in a gait lab is conducted using human subjects instrumented to collect close to injury joint kinematics, muscle activation, and GRFs. These metrics are input to a musculoskeletal RB model which can be implemented via a modeling software. The output from this analysis are the muscle kinematics specifically muscle tendon moment arms and lengths as well as muscle forces. Muscle force data, GRF data, and joint kinematics are input to the FE model and the resulting joint reaction forces and joint moments can be determined and later compared with experiment. Other key output variables from the FE model can include joint contact forces, tibial shear force, tibial displacement relative to femur and ligament forces. An Artificial intelligent (AI) tool can be used here to vary the inputs to the FE model until the output metrics are within an order of magnitude of metrics measured in experiment. If the calculated error is within a certain threshold the model can be considered validated. The model can also be modified, constrained, and loaded similarly to other FE modeling, *in-vitro*, and *in-vivo* studies in the literature and results compared to aid in model validation. As well, hard and soft tissues material property data in the literature determined using uni-axial or three point bending experiments, can aid in model validation by replicating these experiments in a virtual setting using the tissues of the FE model and comparing the results.

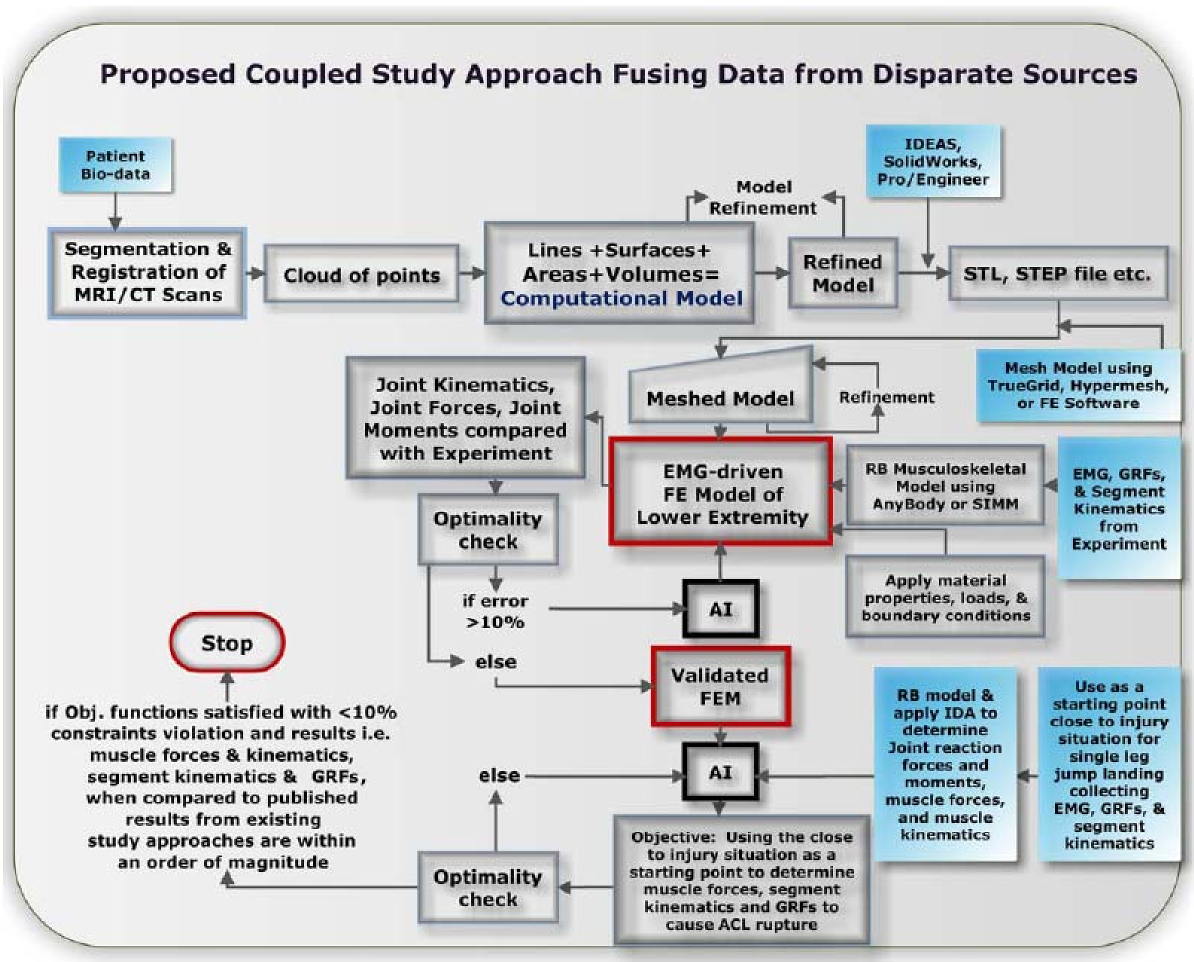

Figure 2 - Possible coupled study approach to better understand mechanisms and risk factors to non-contact ACL injury

From Figure 2 it can be gleaned that many disciplines, much hardware and software, many experts, and a high level of effort is required to execute this proposed coupled approach. Nonetheless, this approach allows for virtual experimentation which has significant implication for cost reduction through reduced equipment needs, number of subjects required for testing, and also time for testing. In addition, one of the central aims of this proposed approach is to provide an enabling tool to better capture the many variables, constraints, unknowns, uncertainty, and variability entailed in the complex problem of predicting injury mechanisms and identifying risk factors of non-contact ACL injury. This approach should also be able to simultaneously capture the interaction of multiple forces, risk factors, and other parameters that may contribute to non-contact ACL injury in a seamless automated manner. This approach should also aim to provide information that can connect the cause and effect relationships between ACL loading, injury mechanisms, and risk factors of non-contact ACL injury. There are no known quantitative body kinematic data or muscle data that precisely address position of the body at ACL injury during any injury situation. As a result, it soon becomes clear that a standalone detailed validated 3D EMG-driven FE model of the lower extremity may not be able to determine injury mechanisms and identify risk factors of non-contact ACL injury. Hence, determining the lower extremity kinematics at the time of ACL injury using computational models can be challenging. One approach to resolve this challenge may be to conduct parametric and sensitivity studies to isolate risk factors, forces, and other parameters that do not contribute to an ACL injury mechanism. This will then probably reduce the number of contributing risk factors and further allow for the elimination of others. However, apart from having no guarantee that this can be done, this approach is prone to inaccuracies. Isolating one parameter and checking for its effects on ACL strain fails to account for the influence that the isolated parameter has on other surrounding tissue, which may subsequently affect ACL loads. As a result, this approach is not preferred. Due to immense variability in data, as well as the many parameters, constraints, and unknowns incurred in a single multifaceted problem of non-contact ACL injury, a tool is needed to address such a requirement. Moreover, the numerous risk factors which are simultaneously at play during a non-contact ACL injury event, as well as, the high dimensionality, great interdependencies, and temporal dependencies demands the capabilities of some form of an optimization routine. Present non-contact ACL injury study approaches lack the capabilities required to overcome such challenges. It should be noted that classical optimization techniques such as the Newton Raphson search method cannot be applied to the problem of how and why non-contact ACL injuries occur because of the absence of a polynomial type function, and more importantly, it cannot handle many design parameters in a large domain. As an alternative, the authors believe that a stochastic or artificial intelligent (AI) technique should be employed for this purpose. The application of an AI technique to ACL injury biomechanics is relatively new, but provides an avenue to tackle problems involving many parameters, many constraints, and multiple objective functions over a large search domain. An AI technique can also be employed to orchestrate the fusion of various study approaches in a single environment as well as to facilitate search and parameter identification. Mathematical programming and the Monte Carlo method [134, 147] are the current often used optimization approaches employed to study ACL mechanics. Although both mathematical programming and Monte Carlo methods have demonstrated their usefulness and effectiveness as a research tool, there are much more advanced and robust AI techniques; namely, taboo search, simulated annealing, genetic algorithms, and artificial neural networks. For small search spaces, classical exhausted methods usually suffice; however, for larger search spaces special AI techniques must be employed.

Hence, the ability to fuse a validated EMG-driven FE model with an AI technique that allows for automatic or semi-automatic data exchange becomes imperative. This can be achieved through multidisciplinary design optimization (MDO). The author's view is that combining the five existing study approaches using an AI technique in a MDO paradigm maybe a much more robust and comprehensive methodology for predicting non-contact ACL injury mechanisms and risk factors. Multidisciplinary design optimization has recently emerged as a field of research and practice that brings together many previously disjointed disciplines and tools. Typically MDO involves many design variables, many constraints, and analysis from various contributing disciplines, where coupling between disciplines and conflicting requirements exist. This proposed MDO paradigm entails the fusion of data from patient, clinical studies, video analysis, athletic interviews, experiment, and computational modeling via an artificial intelligent (AI) technique.

A schematic outline of how this can be accomplished is shown in Figure 2. To elucidate, the validated FE model can be used to study specific non-contact ACL injury mechanisms such as deceleration when landing on one leg from a jump. The inputs to this model are measured in the gait lab and muscle kinematics determined from musculoskeletal RB modeling. An AI tool is then utilized to define a problem to determine the instance where many risk factors, many forces, and other extreme conditions happen simultaneously to cause ACL rupture. To ensure practicality, clinical studies, interviews with athletes' studies, and video analysis studies are consulted during simulation when studying the specific ACL injury causing event. Figure 2 highlights the key processes entailed in the proposed multidisciplinary approach. The authors believe that exploiting the strengths of various existing non-contact ACL injury study approaches in a combinatory manner may overshadow, yield improved information, and even negate the disadvantages encountered when each approach is employed on its own.

5. Conclusions

This review is geared towards highlighting the barriers to obtaining a better understanding of the injury mechanisms and risk factors to non-contact ACL injury. The ultimate goal of acquiring such an understanding is to improve prevention and training strategies, as well as, improve clinical diagnosis and treatment of ACL injuries. The precise mechanism of injury and combination of risk factors that endanger the ACL are not completely understood, partly because studies do not simultaneously include the effects of the muscles, accurate 3D tissue geometries, as well as, the hip, knee, and ankle articulations on ACL loading. In addition, there are many limitations with experimentation, clinical studies, and other existing study approaches when employed on their own that prohibits a comprehensive understanding of the injury mechanisms and risk factors of non-contact ACL injury. Moreover, the narrow focus of some studies and the dearth of standards and specifications in the field of biomechanics appear to have the effect of limiting progress in reinforcing our understanding of non-contact ACL injury. Given the many barriers to understanding non-contact ACL injury mechanisms and risk factors, it is presently not known which aspect of a prevention program is the key element in preventing ACL injuries, or how they work. A possible approach based on fusing existing study approaches using an AI technique in a MDO environment is proposed. The uniqueness of the proposed study is that it simultaneously captures the interaction of multiple forces and myriad of factors implicated as causes of non-contact ACL injury. As well, the proposed approach is also capable of handling numerous variables, constraints, and objective functions over a large multidimensional search space as well as great interdependencies, high dimensionality, and temporal dependencies.

Based on this review, it is evident that in spite of a significant amount of research related to non-contact ACL injury, there are still many open questions about injury mechanisms and conflicting views as to which factor contributes to risk of injury. There is a great need to develop new research methods capable of addressing the myriad of factors, high dimensionality, and great interdependencies involved in non-contact ACL injury.

Competing interest

The authors declare that they have no competing interests or external financial support.

Authors' contribution

NA was responsible for conception, writing, and revising of the manuscript, while GR was responsible for reviewing, drafting, and final approval of the manuscript.

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Manuscript II - Approaches to Non-Contact Anterior Cruciate Ligament Injury Studies: Utility of Operations Research and Artificial Intelligence

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APPROACHES TO NON-CONTACT ANTERIOR CRUCIATE LIGAMENT INJURY STUDIES: UTILITY OF OPERATIONS RESEARCH AND ARTIFICIAL INTELLIGENCE

Nicholas Ali[1], Gholamreza Rouhi[2,3], Gordon Robertson[1]

Department of Health Science, School of Human Kinetics, University of Ottawa, Ottawa, Canada[1]
Department of Mechanical Engineering, University of Ottawa, Ottawa, Canada[2]
Faculty of Biomedical Engineering, Amirkabir University of Technology, Tehran, Iran[3]

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ABSTRACT
A multidisciplinary design optimization (MDO) approach is proposed to aid in the prediction of non-contact anterior cruciate ligament (ACL) injury mechanisms and risk factors. In this investigation the need for such an approach is argued based on an exhaustive evaluation of diverse factors that cause non-contact ACL injury, and the similarly numerous and different existing study approaches that have been carried out to investigate injury. The proposed MDO approach fuses patient data and existing study approaches via an artificial intelligent (AI) technique —absent in previous biomechanics investigations—so as to offer new insights into ACL injury prevention.

Keywords: ACL injury; multidisciplinary design optimization; operations research; artificial intelligence

ÉTUDES DES APPROCHES SUR LES RUPTURES DU LIGAMENT CROISÉ ANTÉRIEUR SANS CONTACT : UTILITÉ DES RECHERCHES OPÉRATIONNELLES ET INTELLIGENCE ARTIFICIELLE

RÉSUMÉ
Une approche de conception optimale multidisciplinaire (MDO) est propose´e comme outil de pre´vision du me´canisme de rupture du ligament croise´ ante´rieur LCA et les facteurs de risque. Dans cette e´tude, le besoin d'une telle approche est discute´ sur la base d'une e´valuation exhaustive des diffe´rents facteurs qui causent les ruptures du ligament croise´ ante´rieur sans contact LCA, et plusieurs e´tudes similaires avec des approches courantes qui ont e´te´ re´alise´es pour investiguer les causes des ruptures. L'approche MDO propose´e fusionne les donne´es du patient et les approches existantes via une technique d'intelligence artificielle pour ainsi avoir de nouvelles donne´es sur la pre´vention des ruptures du LCA.

Mots-cle´s : rupture de LCA; optimisation de la conception multidisciplinaire; recherché operationnelle; intelligence artificielle.

1 INTRODUCTION

The anterior cruciate ligament (ACL) is an intra-articular ligament of the human knee joint that connects the tibia and the femur. The ACL is comprised of two bundles named after the location of their respective tibial attachment sites: anteromedial (AM) and posterolateral (PL) [1]. The average ACL length is approximately 32 mm and the average width is approximately 11 mm [2]. The primary function of the ACL is to restrain anterior tibial translation (ATT) [3]. The ACL also acts as a secondary restraint to internal tibial rotation in the non-weight-bearing knee [3, 4]. Some studies have estimated that the ACL has a load to failure of approximately 2160 N, stiffness of 242 N/mm^2 and a failure strain of up to 20% for young adults [5, 6].

ACL injuries that occur without physical contact with another person or object are referred to as non-contact ACL injuries [7]. Approximately 70% of ACL injuries occur as a result of non-contact events which amounts to an annual cost of almost one billion dollars in the United States alone [8, 9]. This does not account for the 31% of patients who require revision surgery approximately five years after ACL reconstruction [10, 11]. Even though the precise mechanisms of non-contact ACL injury are unknown, research has implicated a number of non-contact ACL injury mechanisms (see Figure 1) and risk factors [12, 13]. The identification of the mechanisms and risk factors for non-contact ACL injury is prevalent in the literature and this is partly motivated by the need to develop prevention programs and training regimes that can potentially reduce the risks of sustaining injuries. From Figure 1, it can be gleaned that non-contact ACL injury likely occurs from combined loading to the knee joint [14-17]. This suggests that non-contact ACL injury possibly occurs when many risk factors and extreme conditions happen simultaneously. Non-contact ACL injury is also a whole body phenomenon that is best analyzed by simultaneously addressing multiple risk factors of which neuromuscular control, joint kinematics and geometry, as well as, external forces that may be the most important. The five existing study approaches employed to obtain a better understanding of the mechanisms and risk factors of non-contact ACL injury are: clinical studies, interviews with athletes, video analyses, computational modeling and experimentation. Of these study methods, clinical studies, interviews with athletes and video analyses are qualitative approaches providing mostly descriptive data, and as a result, are not adequate for obtaining a comprehensive understanding of injury mechanisms to the ACL. The current literature indicates the two main quantitative approaches used to investigate ACL mechanics, namely, computational modeling and experimentation. Further details on these study approaches along with their strengths and weakness are presented by Krossburg et al. [18] and Ali et al. [19]. These study approaches cannot simultaneously capture the many contributing factors, unknowns, variabilities, uncertainties, constraints, and loading situations responsible for ACL injury. As well, these study approaches have provided valuable information but do not offer a comprehensive view of ACL injury mechanisms. Therefore, a necessary first step to a possible approach aimed at simultaneously capturing many of these parameters entailed in non-contact ACL injury research, is deciding on a solution strategy. The authors' view is that many of the challenges confronting studies aimed at reinforcing our understanding of non-contact ACL injuries may be better addressed using optimization.

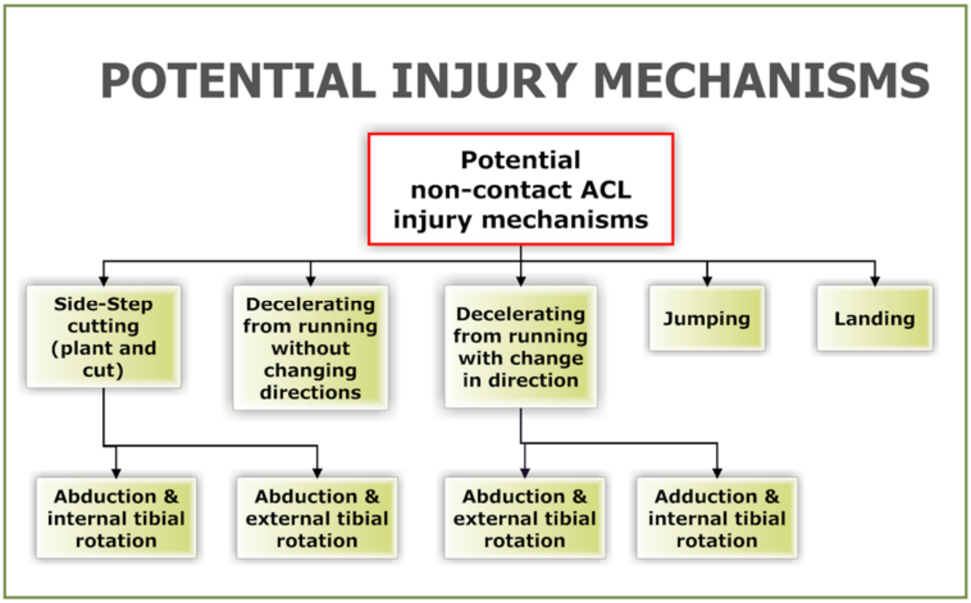

Fig 1. Possible mechanisms of non-contact ACL injury

Operations Research (OR) is a domain of optimization that applies advanced analytical methods to better facilitate decision making. Operations Research takes an interdisciplinary approach to manage and solve problems in business, industry, government, etc. Many OR methods are thought of as traditional methods of optimization, partly due to the need to have a tailored problem definition, the high computational time incurred, and the inability to handle a large search domain. Many OR techniques such as gradient-based methods cannot be applied to the problem of how and why non-contact ACL injuries occur because of the absence of a polynomial-type function, the need to obtain derivatives, and the difficulties with handling numerous design parameters and design constraints in a large search domain. Hence, from an OR perspective, there are specific problems and specific procedures for solving these problems (Table 1). It is the wording or problem definition that helps us decide which OR method to employ. Therefore, a given procedure requires certain types of attributes in the problem statement to enable us to decide which OR strategy to use to solve the problem. This has somewhat limited the range of application and robustness of OR procedures for solving complex problems.

Table 1. OR problems and corresponding solution method

Examples of OR problems	**Corresponding Procedure [20]**
Minimize some quantity subject to certain constraints being satisfied	Mathematical programming algorithms
Determine the quantity of an item (having certain demand, holding cost, and order cost)	Economic order quantity formulas
What is the earliest or latest starting time for some activity?	Network analysis algorithms
What is the expected return for a particular investment?	Expected value calculations
Determine a forecasting function based on historic data	Regression algorithms
Forecast a quantity	Forecasting functions
How many servers should be in place?	Queuing theory methods
What are the impacts of altering a system in particular ways?	Simulation algorithms

Artificial intelligence (AI) provides another domain of optimization. Artificial intelligence is the science and engineering of making intelligent machines, especially intelligent computer programs. Hence, computer systems can be imbued with behaviors that would be regarded as intelligent if witnessed in a human [20]. In addition, AI focuses on discovering new ideas and techniques which exhibit increased degrees of intelligence. The interest in optimization via AI techniques is linked to [21-25]: 1) The need to solve complex problems; 2) The system-based type of solution offered; 3) The need to handle a large multimodal search space; 4) The frequent requirements to incorporate qualitative and quantitative design variables; 5) The improved capability to locate the global optimum; and finally, 6) The improvement in the efficiency of readily available traditional methods of optimization.

Rather than presenting a historical review of the application of optimization to the biomechanics field, this paper takes a more direct approach by discussing the work in four fields: 1) Commonly used OR and AI techniques; 2) Present challenges with existing study approaches used for non-contact ACL injury research; 3) State of the art in utilizing OR and AI techniques in non-contact ACL injury research; and finally, 4) How optimization and existing non-contact ACL injury study approaches can be united to address some of the present challenges in ACL injury research.

1.1 Operations Research (OR) Optimization Techniques

The minimization or maximization of a function $f(x)$ without any constraints on x is called unconstrained optimization. Introduction of constraints into an optimization problem is called constrained optimization. This type of problem formulation is called mathematical programming. Mathematical programming can be subdivided into linear and non-linear programming. The major characteristics of linear programming (LP) are that the objective function and also its associated constraints should be linear. In addition, constraints must be expressed in terms of decision variables [26, 27]. An integer programming problem (IPP) is a LP problem in which the design variables are restricted to be non-negative integers only; otherwise, it is called non-integer programming problem. A problem that entails a quadratic objective function subjected to linear constraints is called a quadratic programming problem (QPP) [28]. To date, the range of application of mathematical programming methods is limited partly because real world problems cannot be accurately modeled by linear relationships, the input data are seldom known with accuracy, as well as the exhaustive nature of the search approach. Because of the high number of OR techniques and considering the scope of this paper, it is not feasible to discuss these techniques in depth here. Nonetheless, to garner an in depth knowledge of OR techniques as well as their capabilities and applicability, readers are encouraged to consult [26, 29, 30]. Also, specific details about unconstrained optimization methods in OR can be obtained by consulting the following references [31-36]. For further details and implementation of some commonly used constrained optimization methods of OR, the following references may also be consulted: the simplex method [29], goal programming [37], Newton-Raphson method [31], integer programming [29, 38], and the Monte-Carlo method [39-42].

1.2 Artificial Intelligence (AI) Optimization Techniques

For many practical problems encountered, the only way to be sure of finding an optimal solution is to search completely through the whole set of possible solutions. If there is a very large, but finite number of possible solutions, the idea of an exhaustive search is tempting and often quite easy to implement into a computer program. The drawback however is that this requires lengthy computational time. The time required to carry out such an exhaustive search is - although finite - far greater than is tolerable. The challenge then is to find short-cuts that will allow one to organize the search process so that it is no longer a complete search over all possible solutions, but rather it becomes an affordable search that is likely to find optimal or near optimal solutions [43]. These methods are called AI or heuristic methods. AI techniques are often applied to computationally intractable non-deterministic polynomials (NP), simply because the best (most efficient) methods we know of for solving these problems exactly (or optimally) can take an exponential amount of computational time [44]. For small search spaces, classical exhaustive OR methods such as mathematical programming usually suffice; however, for larger search spaces, special AI techniques must be employed. Some commonly used AI methods that are constantly being improved and utilized are: tabu search, simulated annealing, genetic algorithms, and artificial neural networks. Given the focus of this paper, coupled with the fact that the concepts in AI are rather complex and the field is so vast, it is not possible to explore all details of AI techniques here. Nonetheless, attempts are made to impart a flavour of these techniques in this article, and the insight they can bring to non-contact ACL injury studies. For in-depth readings on AI techniques and its applications, readers are encouraged to consult [45, 46]. Specific details on some commonly used AI techniques and its capabilities can be obtained by consulting the following references: tabu search [44, 47, 48], simulated annealing [26, 49-52], genetic algorithms [53-61], and artificial neural networks [46, 62-64].

2 PRESENT CHALLENGES WITH EXISTING APPROACHES USED FOR NON-CONTACT ACL INJURY RESEARCH

There has been much interest in quantifying ACL loading in-vivo during activity (Beynnon 1995, Pope 1991). This is motivated by the high incidence of ACL injury, lack of clear understanding of ACL mechanics, and frequent need for surgical treatment. Nonetheless, there are many challenges with existing study approaches aimed at improving our understanding of non-contact ACL injury and a brief description of some of these is highlighted below.

First and foremost, many studies have pointed out that several intrinsic and extrinsic risk factors are responsible for non-contact ACL injuries [65-67]. However, some studies address only one risk factor and investigate its effects on ACL rupture [68-70]. It seems quite unlikely that only one risk factor will be responsible for ACL injuries. It can be a reasonably surmised that a non-contact ACL injury could be multifaceted, occurring from a complex interaction of multiple risk factors and taking place when many extreme conditions happen simultaneously. Recognizing that the type of study approach used is dependent on the question posed, perhaps many research groups are compelled to focus on only one or a few risk factors, or adapt a reductionist approach to solving problems in ACL mechanics, given the limitations with existing study approaches. Secondly, many non-contact ACL injury studies are experimental. As such, they have the inherent limitations of cost, noise, low sensitivity, and difficulty of measuring stresses or strains [71, 72]. To elaborate, experimental studies whose objective are to understand non-contact ACL injuries, can be categorized as in-vivo and in-vitro. In-vivo testing is conducted with living subjects and involves the connection of a strain transducer to the ACL. Given the location and size of the ACL, in-vivo studies using strain transducers are limited to measuring strain in the AM bundle of the ACL for movement in the sagittal plane only [73]. Moreover, these studies are limited to knee flexion angles greater than 15 degrees due to potential impingement of the strain transducer with the femoral notch [16], which limits this approach ability to predict injury. Ethical standards controlling human and animal testing limit the use of in-vivo testing, given that it is invasive. In addition, the vast majority of empirical studies investigating non-contact ACL injuries are in-vitro. In-vitro testing is non-invasive and typically entails the use of human cadavers. Some major challenges with in-vitro studies using cadavers are the inability to include muscle activation and muscle forces, and the inability to obtain repeatable results. Other existing study approaches such as clinical studies, interviews with athletes and video analysis are all qualitative, and cannot provide a comprehensive understanding of non-contact ACL injury mechanisms. Finally, computational modeling approaches used to study non-contact ACL injury, specifically, mathematical [74, 75], musculoskeletal [76, 77], and finite element modeling [78-80], when employed on their own, offers a limited understanding of non-contact ACL injury mechanics. For example, musculoskeletal model can provide many details on joint kinetics, muscle activation and muscle forces, but cannot determine the load to failure of a ligament [81, 82].

An overarching challenge with all existing non-contact ACL injury study approaches is their inability to handle high variability. There is much variability in hard and soft tissue geometries due to subjects' age, race and gender, as well as, large variability in tissue material properties due to subject's age and gender, when compared to engineering structures which have mostly unvarying geometries and material properties . In addition, there are many inter- and intra-subject variabilities such as muscle activation patterns, during experiments, over which the researcher has little control. Inter-subject variabilities may be associated with the type of shoes used, surface on which task is performed, normalization method, and electrode placement [83, 84]. Intra subject variabilities may stem from technician performing experiments and can be high [85]. Moreover, non-contact ACL injuries occur from a variable number of movement patterns. Given these variabilities, in many cases it is difficult to compare the results from one study to another, due to the tremendous heterogeneity between studies. It can be argued that these variabilities partly exist because of the lack of standards and perhaps specifications for testing in the field of biomechanics.

3 STATE OF THE ART IN UTILIZING OR AND AI TECHNIQUES IN NON-CONTACT ACL INJURY RESEARCH

There has been little research on utilizing OR or AI techniques to facilitate a better understanding of non-contact ACL injuries. Studies utilizing OR techniques to deal with non-contact ACL injury is highlighted below, followed immediately by those utilizing AI techniques.

Using a 3D mathematical model, Blankevoort et al. [86] studied the articular contact surface of the knee to compare a rigid and deformable contact scenarios. The surface of the femur and tibia, as well as the ligaments and articular cartilage, were modeled. The model was developed using the work of Wisman et al. [75], but incorporated a deformable articular contact description similar to Essinger et al. [87] and An et. al. [88]. A later study by Blankvoort et al. [89] used the same mathematical model to estimate the initial strains of the ligaments of the knee joint for usage in the model since no experimental data was available. Blankvoort's research group employed an optimization scheme to estimate the initial strains since no experimental data was available. Their optimization method was based on the minimization of the difference in terms of kinematic parameters between the developed knee model and experiments via the variation of the reference strains in the ligament. The minimization scheme was based on a modified Levenberg-Marquardt algorithm (LMA) [90]. The LMA is an iterative technique used to locate the minimum in a multivariate function that is expressed as the sum of squares of non-linear real valued functions [91]. A Levenberg-Marquardt algorithm can be thought of as a combination of steepest decent and the Gauss-Newton method. This method is especially useful for problems where the initial guess is unknown and may be far from the final minimum. This method was modified by Flectcher [92] to tailor the amount of dampening use at each iteration, to improve the robustness of the algorithm through rate convergence, entrapment in local minimum, and system stability. This optimization scheme was also later utilized to estimate the reference lengths of the ligaments and stiffness of the meniscus in a finite element model study of the human knee joint by Li et al. [80]. The same study approach and optimization routine was also later used by this same research group to undertake parametric studies of knee kinematics, ligament forces, and contact pressure, in response to simulated muscle loads [93]. An analytical modeling study by Pandy et al. [94] found that hamstring co-contraction decreases the anterior shear force applied to the tibia, thereby reducing the ACL forces at small flexion angles. The authors used a non-linear programming algorithm developed by Powell [95] to solve an over-constrained system of equations via least squares optimization. Pandy's research group furthered the development of this model [81, 96] by applying this identical optimization approach and subsequently concluded that the knee is one part of a kinetic chain and that the trunk, hip, and ankle may contribute to ACL injury. Shelburne et al. [97], from the same research group as Pandy et al., also employed the same optimization approach to calculate the forces developed in the muscles and forces transmitted to the knee ligaments during squatting. Shelburne et al. [98] also developed a dynamic feature to this optimization approach to calculate muscle forces during gait. The optimization routine centered on finding the muscle excitation histories, muscle forces, and body motions subjected to an objective function geared towards minimizing metabolic energy consumed per unit distance moved. Greater details on this dynamic optimization approach used by Shelburne et al. [98] are reported in [99]. Pflum et al. [100] also from the same research group as Pandy et al., also employed this dynamic optimization method to investigate the forces transmitted to the ACL during a soft style drop landing.

McLean et al. [76, 101] used a forward dynamics musculoskeletal model of the lower extremity to study side step cutting dynamics that may cause injury to the ACL. The authors used an AI technique, specifically, simulated annealing to determine the muscle activation patterns that best replicated a subject's kinematics and kinetics [76, 101]. A Monte Carlo simulations were also performed by the authors to determine the effects of variability in neuromuscular control on peak anterior drawer force, valgus moment, and internal rotation moment [101]. Monte Carlo methods are algorithms that randomly generate and retain the best solutions before going to the next search iteration. The Monte Carlo method is used primarily in this application to evaluate the probability of random outcomes of human movement. Monte Carlo simulation is an attractive tool since it allows researchers to study and predict risk of sustaining an injury before injury occurs. To the best of our knowledge, this is the only research group that has utilized an AI technique to better understand ACL injury mechanisms. However, simulated annealing is simply mentioned by the authors, but the way the method is employed to answer the author's research question is not clear. Mclean et al. [14] also applied the identical optimization methods to examine whether sagittal plane knee loading during side step cutting could in isolation injure the ACL. As well, a recent study by the same group of researchers utilized the same approach to determine the potential for perturbations in key initial contact neuromuscular parameters to injury of the ACL [101]. Lin et al. [102] modified the model developed by McLean et al. [101] to estimate the ACL injury rate for a stop jump task. The study was geared towards validating a stochastic biomechanical model to examine the role of gender as a risk factor for non-contact ACL injury.

4 FUSING OPTIMIZATION WITH EXISTING NON-CONTACT ACL INJURY STUDY APPROACHES

Many real-world problems today involve the interaction of many disciplines, which is particularly the case in many biomechanics research projects. As a result, tying together concurrent activities involving many disciplines with an optimization technique has become popular [103-105]. More specifically, Multidisciplinary Design Optimization (MDO) has emerged as a field of research and practice that brings together many previously disjointed disciplines and tools of engineering. Multidisciplinary design optimization can be described as a technology and a methodology for the design of complex, coupled engineering systems, such as an aircraft [106]. Typically MDO involves many design variables, many constraints, and analysis from various contributing disciplines, where coupling between disciplines and conflicting requirements exist.

From a review of the literature, it does appear that research in non-contact ACL injury studies is fragmented, presented with many challenges, and limited in utilizing optimization. Many study approaches provide valuable information, but do not offer a comprehensive view of ACL injury mechanism. To address some of these challenges, we believe that a MDO methodology should be employed. The authors' approach entails combining the five existing study approaches of non-contact ACL injury studies using an AI technique in a MDO paradigm (Figure 2). Such a study approach may be a much more robust and comprehensive methodology to better predict non-contact ACL injuries [107, 108]. AI techniques are preferred over OR techniques for non-contact ACL injury studies since they do not require a mathematical function, are more robust in dealing with both qualitative and quantitative variables, enable a system-based type of approach to solving complex problems [109], and above all, share an enhanced ability to handle many design variables and constraints over a large multimodal search space [20, 110]. The AI technique is employed to orchestrate the fusion of the two quantitative study approaches in the MDO paradigm, and to facilitate search and parameter identification. In this approach, the three qualitative study approaches are used for results validation. An AI technique also enables one to capture the wide variability in movement patterns to cause injury, and in tissue material properties, numerous design variables, numerous design constraints, many risk factors, and multiple objective functions.

From Figure 2, it can be noted that many disciplines, much hardware and software, many experts, and a high level of effort are required to develop this proposed approach. As can be observed, starting with the patient bio-data in the form of MRI and/or CT scans of the joint or tissue of interest, a finite element model (FEM) was constructed. This FEM should include the major bones, joints, muscles, tendons, and ligaments of the lower extremity. Testing in a gait lab is conducted using human subjects instrumented to collect joint kinematics, muscle activation, and ground reaction forces for close to injury type motion. Some of these metrics are then supplied to a musculoskeletal rigid body modeling software package such as AnyBody. The musculoskeletal models can then be validated with electromyography (EMG) data and published data. The outputs from the musculoskeletal model are the muscle activation, muscle forces and joint kinetics. The body kinematics and external forces from experiments, as well as muscle forces and muscle kinematics from musculoskeletal modeling, will form the boundary conditions for the FEM.

The AI technique can be used to vary the inputs to the FEM until the output kinetics are within an order of magnitude of kinetics determine from inverse dynamics analysis of the musculoskeletal model. The calculated error from this exercise once within a reasonable threshold can be used as a metric to determine if the model can be considered validated. Major bones of the FEM, such as the femur, can also be modified, constrained, and loaded in an identical manner to replicate published results from three and four point bending experiments to further aid FEM validation. The validated FEM can then be used to study a specific non-contact ACL injury mechanism with the aid of the AI technique. To accomplish this, a problem is defined and formulated to determine the instance where many risk factors, many forces, and other extreme conditions happen simultaneously to cause ACL failure. The objective function can be geared towards finding the precise lower extremity kinematics that result in ACL stresses beyond its yield stress. The external forces, muscle activation, and muscle forces at this specific lower extremity kinematics should be compared to published data for the specific injury mechanism studied. As well, to ensure practicality, results in the literature from the three qualitative study approaches can be consulted and compared to results obtained from this simulation.

This MDO methodology should first be used to investigate very simple human movements for developmental and validation purposes, and then later be employed to study more complex motions such as side step cutting maneuvers.

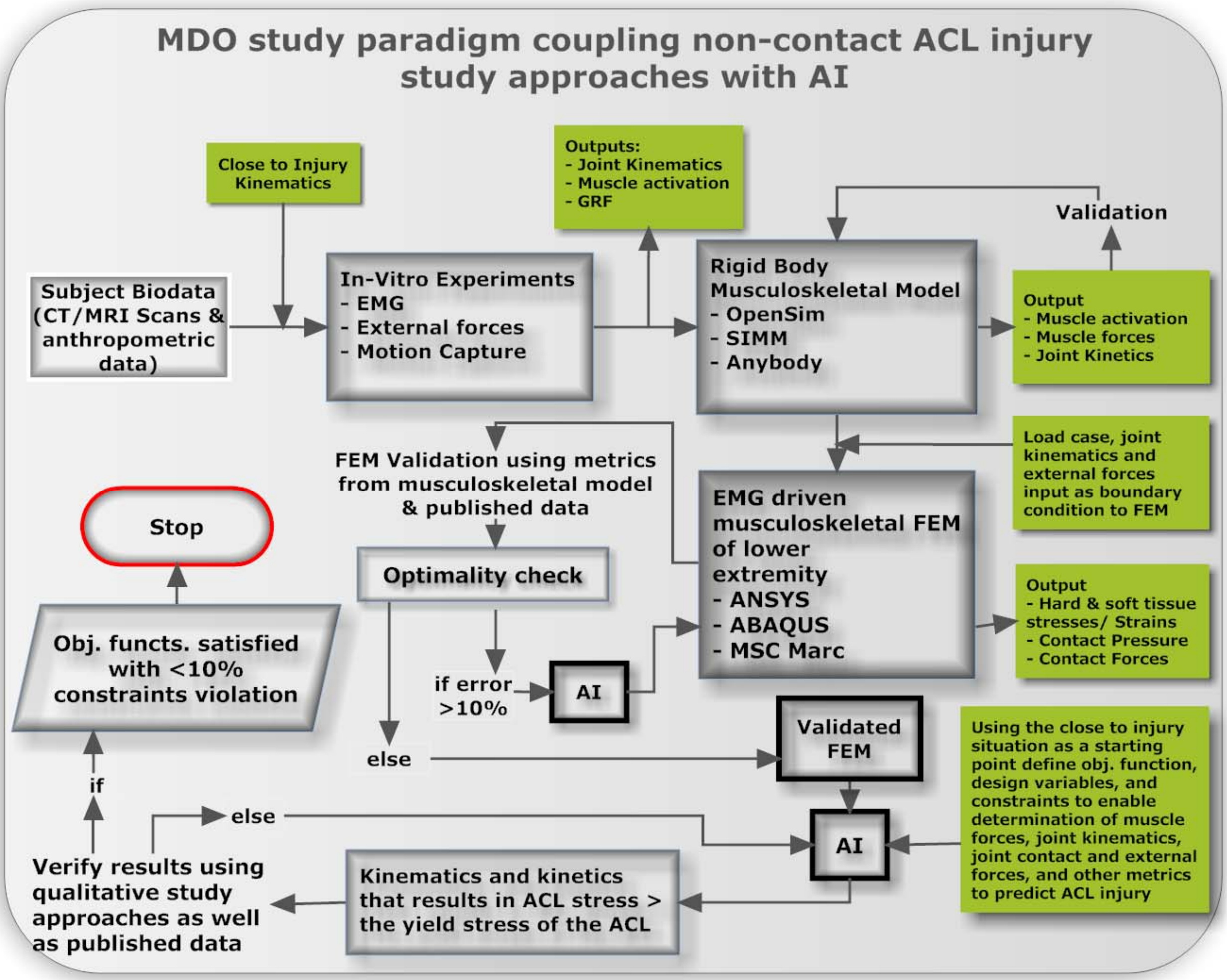

Fig. 2. A possible multidisciplinary and coupled study approach to address present challenges in non-contact ACL injury research

For each stage of this MDO paradigm, verification and validation is mandatory. For example, if a genetic algorithm is used as the optimization technique, then this technique must be verified and validated against benchmark mathematical functions. If musculoskeletal models are also employed, they too must be validated against measured EMG data and published data. This MDO methodology should allow for automatic or semiautomatic data exchange between experimental, musculoskeletal modeling, and FEM study approaches under a single software GUI. For example, data exchange algorithms and an AI technique programmed in Matlab can be used to fuse a FEM software package such as ANSYS and a musculoskeletal modeling software such as AnyBody, via batch processing. Essentially, ANSYS or AnyBody can be called up in batch mode to retrieve or send data using Matlab. This fusion should allow for dynamic data exchange between software packages. The outputs from the musculoskeletal model and finite element model can be validated with published and experimental data. This type of multidisciplinary and integrated biomechanics study paradigm is seem to be absent from the current literature.

5 SUMMARY AND CONCLUSIONS

A brief overview of the two main domains of optimization, namely, OR and AI, along with commonly used techniques within these two domains, were presented. Some of the limitations of existing non-contact ACL injury study approaches confounding our understanding of ACL mechanics were then presented. A review of the literature aimed at identifying non-contact ACL injury studies utilizing OR or AI techniques was conducted. Finally, a new approach aimed at uniting optimization with the five existing non-contact ACL injury study approaches in a MDO study paradigm was proposed.

It was shown that present challenges in non-contact ACL injury studies stem partly from the inability of existing study approaches to simultaneously capture numerous factors and parameters which are at play during ACL injury. These factors and parameters include, but are not limited to, biomechanical, environmental, anatomical and hormonal variables [111, 112]. Many studies have concluded that these factors are responsible for non-contact ACL injuries, but a large number of them have focused only on one aspect of the ACL injury mechanism, thereby failing to capture all factors at once, as well as simultaneously considering the interactions of the different parameters involved. It was also determined that there are few attempts to use either OR or AI techniques in the non-contact ACL injury research, with OR techniques being more prevalent. Furthermore, it was established that an AI technique is better suited to address present challenges in non-contact ACL injury research because of its robustness.

To address the limitations of existing non-contact ACL injury study approaches, the possibility of a coupled MDO study paradigm was proposed. This proposed approach intends to enable seamless data exchange from many existing study approaches. Another possible advantage of this approach is its possible ability to handle wide variabilities and simultaneously take into account many factors, constraints, unknowns, and uncertainties. Hence, this approach could potentially provide a tool that enables one to have a better global view of the effects of changing numerous contributing factors on non-contact ACL injury. However, this methodology is quite complex and costly and requires tools, expertise, and information from various fields of bioengineering.

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Manuscript III – Sagitall plane body kinematics and kinetics during single-leg landing from increasing vertical heights and horizontal distances: Implications for risk of non-contact ACL injury

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Body kinematics and kinetics during single-leg landing from increasing vertical heights and horizontal distances: Implications for risk of non-contact ACL injury

Nicholas Ali[1*], D.G.E. Robertson[1], and Gholamreza Rouhi[2]

[1]School of Human Kinetics, University of Ottawa, Ottawa, Canada
[2]Department of Mechanical Engineering, University of Ottawa, Ottawa, Canada

*Corresponding author, Department of Health Science, School of Human Kinetics, University of Ottawa, 125 University St., Rm 205B, Ottawa, Ontario, K1N 6N5, Canada

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Abstract

Purpose
This study identified kinematic and knee energetic variables that reduces the risk of non-contact anterior cruciate ligament (ACL) injury during single-leg landings from increasing vertical heights and horizontal distances.

Methods
Nine subjects performed single-leg landings from takeoff platforms with vertical heights of 20, 40, and 60 cm onto a force plate. Subjects also performed single-leg landings from a 40 cm high takeoff platform placed at horizontal distances of 30, 50 and 70 cm from a force plate. Kinematic and kinetic data were measured.

Results
Vertical height had a significant and positive effect on peak vertical ground reaction force (VGRF) ($p<0.001$), peak posterior ground reaction force (PGRF) ($p=0.004$), knee flexion angle ($p=0.0043$), trunk flexion angle ($p=0.03$), knee power ($p<0.001$) and knee work ($p<0.001$). There was also a significant and positive effect of horizontal distance on peak PGRF ($p<0.001$), ankle plantar flexion angle ($p=0.008$), hip flexion angle ($p=0.007$), and trunk flexion angle ($p=0.001$). At increasing vertical height, peak VGRF was significantly correlated to ankle plantar flexion and knee flexion

angles (r=–0.77, p=0.02 and r=–0.78, p=0.01, respectively). At increasing horizontal distance, peak PGRF was significantly correlated to ankle plantar flexion angle, knee power and knee work (r=–0.85, p=0.003; r=0.67, p=0.04; and r=0.73, p=0.02, respectively).

Clinical Relevance:
A better understanding of the risk factors to non-contact ACL injury during single-leg landings from increasing vertical heights and horizontal distances can aid in the design of injury prevention regimen.

1. Introduction

In a jump landing event, the landing phase is more stressful to the ACL than the takeoff phase [1]. Single-leg landing is a common athletic maneuver performed from varying vertical heights and horizontal distances during sports such as basketball, volleyball, soccer, and badminton [2]. Most non-contact ACL injuries occur during sporting activities involving single-leg landings [3]. Vertical height and horizontal distance may have different effects on landing kinematics and kinetics, thus warranting different injury prevention and training strategies. Particularly important is the ability of the body's kinematics to attenuate the GRFs during landings from a single-leg. This knowledge can provide important insights into improving our understanding of the key factors resulting in increased risk of non-contact ACL injuries during single-leg landings. As well, out-of-plane motion such as landing on a single leg with the knee abducted has been shown to result in valgus collapse, subsequently increasing the risk of ACL injury [4-7]. However, it is not clear if valgus collapse causes ACL injury or occurs as a result of the ACL being injured [4].

An *in vivo* study conducted by Cerulli et al.[8] demonstrated that during a single-leg hopping task, the peak ACL strain occurred at the same instant as peak VGRF, suggesting that peak VGRF may be a likely predictor for establishing the risk of non-contact ACL injuries. Cerulli et al. [8] obtained an average peak ACL strain of 5.47±0.28%, which may be too low to cause ACL injury during single-leg landings given two studies [9, 10] estimated that the ACL is able to tolerate strains of up to 20% before failure. Nonetheless, the *in vivo* strain to failure of the ACL during single-leg landings is unknown, and therefore relating strain values to ACL injury to date is not yet possible. However, other studies have also determined that landing with a high impact force may be a risk factor to ACL injury [1, 11-15]. In addition, a recent study by Boden et al. [16] proposed that a lack of dissipation of GRFs at landing may be a factor in ACL injury. Given this, the current study uses peak VGRF to predict risk of non-contact ACL injuries. The VGRF is defined as the reaction to the force the body exerts on the ground in the vertical direction. In addition, many studies have also reported that an increase in PGRF requires an increase in knee extensor moment for balance, and this increase in knee extensor moment is a major contributor to higher peak proximal tibia anterior shear force that likely increases ACL loading [15, 17-19]. Given this, the current study also uses peak PGRF to predict the risk of non-contact ACL injuries. The PGRF is defined as the horizontal reaction force the body exerts on the ground in the backward direction from the landing direction.

The literature has shown that single-leg landing results in increased risk of non-contact ACL injuries compared to double-leg landing [20, 21]. Pappas et al. [20] determined that single-leg landings resulted in greater risk of ACL injury compared to double-leg landings given the former led to significantly greater knee valgus, as well as, significantly lower knee flexion angles. The study by Yeow et al. [21] showed that single-leg landings produced significantly greater peak VGRF, as well as, significantly lower knee flexion angles and knee joint power compared to double-leg landings, implicating greater risk of ACL injury. There are many single-leg landing studies investigating non-contact ACL injuries [20-34]. Of these studies, many investigated single-leg landings from only one vertical height [20, 22-30, 32-34], and to the authors' best knowledge, no study has yet investigated the effect of increasing horizontal distance on single-leg landing biomechanics and further related these findings to risk of non-contact ACL injury. In addition, many single-leg landing studies investigated vertical heights lower than 30 cm, which as argued by Zhang et al. [35] is too low, and the subject's landing strategies may be completely different at greater heights. Altogether, existing single-leg landing studies have illustrated that landing technique, gender effects or fatigue may predispose athletes to ACL injury. However, it is still not clear how the body will respond in terms of kinematics and knee energetics to the effect of increasing vertical height and horizontal distance during single-leg landings. As well, in many single-leg landing studies, ankle, hip and trunk kinematics were not considered as direct contributors to risk of ACL injury. Moreover, simultaneously investigating ankle, knee, hip and trunk kinematics may be important for predicting risk of non-contact ACL injury given it has been shown that the vast majority of studies do not account for the effects of whole body movement on knee loads [36]. Pandy and Sasaki [37] and Griffin et al. [38] argued that the knee is just one part of the kinetic chain, and that the trunk, hip, and ankle may all contribute to risk of non-contact ACL injury. Though many single-leg landing studies predominately investigated knee kinematics and kinetics, further investigations are required to determine the coupling between trunk, hip, knee and ankle kinematics, and the link between these kinematic variables, knee energetics, ground reaction forces, and subsequently, risk of non-contact ACL injury.

The primary objective of this study was to identify kinematic and knee energetic variables that reduces the risk of non-contact ACL injury during single-leg landings, by examining the relationships among increasing vertical height and increasing horizontal distance, and two non-contact ACL injury risk predictor variables, namely, peak VGRF and peak PGRF. To undertake this, we first investigated the effect of increasing vertical height and horizontal distance on peak VGRF, peak PGRF, ankle, knee, hip and trunk flexion angles, as well as knee energetics during single-leg landing. Finally, this study correlated the variables significantly impacted by the main effect of vertical height or horizontal distance to two ACL injury risk predictor variables so as to assess the risk of non-contact ACL injury during single-leg landing. We hypothesized that vertical height would have a significant effect on knee flexion angle, as well as, knee power and knee work. We further hypothesized that as vertical height increased there would be a significant correlation between peak VGRF and knee flexion angle.

2. Methods

2.1. Participants

Nine male recreational athletes with mean (SD) age of 27.67 (2.56) years, heights of 1.75 (0.077) m, and masses of 78.12 (8.59) kg were recruited from the university population. None of the participants reported any musculoskeletal or ligamentous injuries to the lower extremity at the time of participation. Prior to data collection, each participant gave informed consent as stipulated by the university ethics review board. Subjects' ages and anthropometrics were recorded. The dominant leg was established as the leg used by the subject to kick a ball.

2.2. Procedure

All participants wore identical shoes (running shoe, model BY004, ASICS America Corporation, Irvine, CA) throughout data collection, so as to mitigate variability. Retro-reflective markers were placed on subjects' full-body using a customized version of the Vicon Plug-in Gait marker set via double-sided tape. The Vicon Plug-in Gait marker set was customized to include additional markers at the hip and medial aspects of the elbow, knee and ankle, as well as additional foot markers. In addition, different marker locations were also used at the proximal ends of the pelvis. A seven-camera motion capture system (Vicon MX, Oxford Metrics, UK) was used to collect the subject's kinematics at a sampling rate of 250 Hz. A force plate (Kistler type 9281B, Winterthur, Switzerland) measured GRF signals at a sampling rate of 1000 Hz. Videographic and force plate data were time synchronized. Before data collection, each subject was given enough time to warm-up and practice the single-leg landing task until comfortable. The warm-up and practice regimen was standardized to mitigate possible variability contributed by such tasks. The subjects were instructed to stand on various takeoff platforms, each having vertical heights of 20, 40, and 60 cm (termed h20, h40 and h60, respectively), which were placed 20 cm from the rear edge of the force plate. This test setup was used to investigate the effect of increasing vertical height and termed the vertical height test. A 40 cm high takeoff platform was placed at a horizontal distance of 30, 50 and 70 cm (termed d30, d50 and d70, respectively) from the rear edge of the force plate to test the effect of increasing horizontal distance, and was termed the horizontal distance test.

The subjects were instructed to stand on the takeoff platform with both arms placed on their iliac crests and with legs spaced approximately shoulder width apart. From this position, the subjects were asked to stand on their dominant leg, jump forward, and land as naturally as possible with their dominant leg only onto the force plate. Each subject performed two trials at each vertical height and horizontal distance resulting in a total of 12 trials. The order of the heights and distances of landing were randomized to reduce learning effects.

2.3. Data reduction and analysis

All marker trajectories and analog data were imported into Visual3D (C-Motion Inc. Rockville, MD) biomechanical software for rigid body modeling and inverse dynamics analysis (IDA). Cardan angles for the hip, knee, and ankle were calculated in an x (flexion-extension), y (adduction-abduction), z (internal-external rotation) sequence. In Visual3D ankle dorsiflexion is defined as positive, knee flexion as negative, hip flexion as positive, and trunk flexion as positive. Ankle angle was defined as the angle between the leg segment and foot segment. The difference between ankle joint angle when subject was standing on the takeoff platform and when peak VGRF occurred during landing was determined as the ankle flexion angle. Knee flexion angle was defined as the angle between the thigh and leg segment while hip flexion angle was defined as the angle between the thigh and pelvis segment. Trunk flexion angle was calculated as the angle between the trunk segment and a vertical line in the laboratory coordinate system. All kinematic, kinetic and knee power values were determined at the instant of peak VGRF. Kinematic data were low-pass filtered using a second-order bidirectional Butterworth filter at 6 Hz and analog data were filtered at 25 Hz. Joint kinetic data were calculated using a complete Newtonian IDA.

One trial was selected from the better of two trials for model building, data analysis, post-processing, and reporting. The better trial was determined as the one in which the participant did not remove his hands from the iliac crests during landing, did not land with both legs on the force plate, and did not lose a marker during impact with the ground. In situations where both trials did not meet these requirements, the subject repeated the task until a trial that met these requirements was obtained. Furthermore, in situations where both trials met these requirements, a trial was arbitrarily selected for post processing and data analysis. Knee joint energetics such as knee power and knee work are important indicators of energy dissipation during the landing phase. Knee power was determined by the product of knee moment and knee angular velocity over the landing phase. Knee work was then calculated as the integral of the negative portion of the knee power curve over the landing phase. The use of the negative portion of the power curve over the landing phase was based on studies [23, 39] that showed the negative power curve represents the energy dissipation by the knee extensor moment. Knee power and knee work were normalized to body mass. The landing phase was defined as 0.8 s prior to peak VGRF and 0.6 s post peak VGRF, where the time of peak VGRF was used as the second event, and 0.8 s prior and 0.6 s after peak VGRF were used as the first and third event, respectively. Kinematic data were time normalized to 100% of the landing phase (between the first and third event). Ground reaction forces were normalized to subject’s body weight in newtons (N), while knee energetics were normalized by the subject’s body mass in kilograms (kg).

2.4. Statistical Analysis

Ground reaction forces, sagittal plane body kinematics, as well as knee power and knee work were averaged across all subjects at each trial. Multiple one-way repeated-measure ANOVAs were conducted to test the effect of vertical height on all dependent variables (vertical height test). The dependent variables were peak VGRF, peak PGRF, ankle, knee, hip and trunk flexion angles, as well as, knee power and knee work. Post-hoc analyses were conducted via pairwise comparisons using dependent sample t-tests. For the vertical height test, this would result in three pairwise t-tests: h20 vs. h40, h20 vs. h60, and h40 vs. h60. The p-value for each test was Bonferroni corrected and compared to an alpha level of 0.016 (0.05/3). This ensures that the probability of committing a Type I error (rejecting the null hypothesis when it is true) will be no greater than 0.05 for the entire set of post-hoc analyses. Follow-up testing using Pearson product moment correlations (PPMCs) were also calculated to determine the relationships among the two ACL injury risk predictor variables, ankle, knee, hip and trunk flexion angles, as well as, knee power and knee work. Multiple one-way repeated-measure ANOVAs were also conducted to test the effect of horizontal distance on all dependent variables (horizontal distance test). Pairwise comparison using dependent sample t-tests were conducted for the horizontal distance test: d30 vs. d50, d30 vs. d70 and d50 vs. d70. Follow-up testing using PPMCs were also calculated to determine the relationships among the two ACL injury risk predictor variables, ankle, knee, hip and trunk flexion angles, as well as, knee power and knee work. Effect size is presented as partial η^2 (eta squared). Partial η^2 ranges between 0 and 1. These values can be interpreted using the following parameters: $0.01 \leq$ partial $\eta^2 < 0.06$ indicates a small effect, $0.06 \leq$ partial $\eta^2 < 0.14$ indicates a medium effect, and partial $\eta^2 \geq 0.14$ indicates a large effect [40]. To interpret Pearson's correlation coefficients (r), values of $|r| < 0.3$ indicates a weak correlation, $0.3 \leq |r| < 0.7$ indicates a moderate correlation and $|r| \geq 0.7$ indicates a strong correlation. Unless otherwise stated, an alpha level of 0.05 was used throughout to identify statistical significance. Statistical analyses were conducted in SPSS (Version 11.5, Chicago, IL, USA).

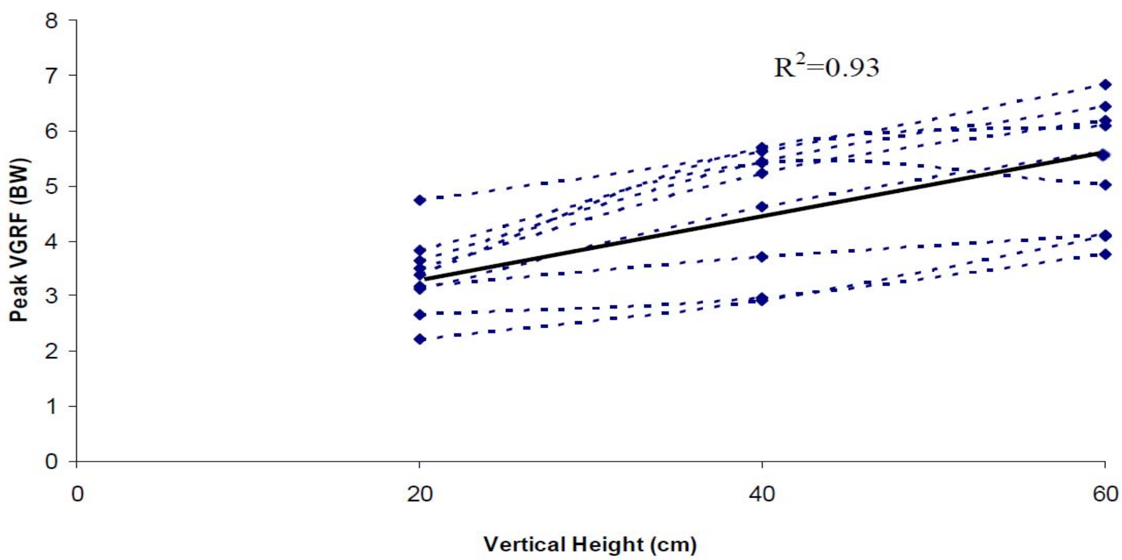
3. Results

The findings from the separate ANOVAs conducted, revealed for the vertical height test that there was a significant effect of vertical height on peak VGRF ($F(2,16)=42.41$, $p<0.001$, partial $\eta^2=0.84$, observed power=1.0). Our findings also revealed a significant effect of vertical height on peak PGRF ($F(2,16)=8.09$, $p=0.004$, partial $\eta^2=0.505$, observed power=0.91). There was also a significant effect of vertical height on knee flexion angle ($F(2,16)=3.86$, $p=0.043$, partial $\eta^2=0.33$, observed power=0.61), trunk flexion angle ($F(2,16)=12.21$, $p=0.001$, partial $\eta^2=0.60$, observed power=0.99), knee power ($F(2,16)=24.99$, $p=0.0001$, partial $\eta^2=0.76$, observed power=1.0), and knee work ($F(2,16)=64.07$, $p=0.0001$, partial $\eta^2=0.89$, observed power=1.0). Partial η^2 represents an index of strength of association between an experimental factor and the dependent variable[41]. Larger values of partial η^2 indicates a greater amount of variation accounted for by the dependent variable, to a maximum value of 1. The overall means and standard deviations of the sagittal plane body kinematics, knee power, and knee work for the vertical height test among all subjects is provided in Table 1. Figures 1a and 1b show the trends in peak VGRF and peak PGRF, respectively, during single-leg landing for all subjects as vertical height increased. From Figure 1a and 1b, one can glean that vertical height had a significant and positive effect on both peak VGRF and peak PGRF, suggesting that as vertical height increased, both the peak VGRF and peak PGRF increased. The differences in marginal means at the three vertical heights are (1.26, 0.73) and (0.07, 0.17), which represents the difference in peak VGRF and peak PGRF respectively, at landing height of 20 to 40cm and 40 to 60cm, respectively.

Table 1: The means and SDs of each dependent variable across all subjects (Vertical height test)

	Vertical Height Test		
Dependent Variable	**height=20 cm**	**height=40 cm**	**height=60 cm**
Peak VGRF (BW)	3.36±0.71	4.62±1.12	5.35±1.14
Peak HGRF (BW)	0.55±0.19	0.62±0.30	0.79±0.31
Ankle flexion (deg)	0.22±3.52	-2.11±2.44	-2.67±3.54
Knee flexion (deg)	-30.88±5.89	-32.92±3.00	-35.89±2.30
Hip flexion (deg)	23.31±7.34	19.02±5.53	21.04±6.94
Trunk flexion (deg)	13.90±3.18	12.74±2.08	16.38±3.10
Knee joint power (W/kg)	-5.05±2.95	-10.77±3.03	-15.54±4.40
Knee joint work (J/kg)	-0.86±0.36	-1.33±0.44	-1.89±0.56

A



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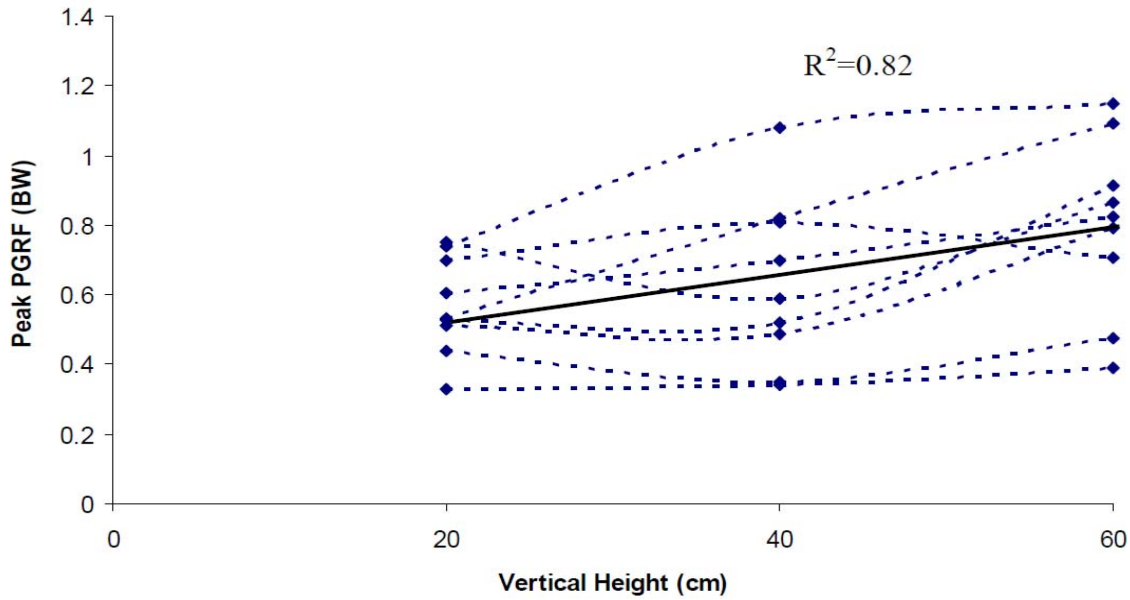

Fig. 1: A: Plot of vertical height and peak VGRF during single-leg landing for all subjects. Solid line is the average slope. B: Plot of vertical height and peak PGRF during single-leg landing for all subjects. Solid line is the average slope.

For the vertical height test, pairwise dependent sample t-tests indicated that peak VGRF was significantly lower at h20 compared to h40 ($t(8)=-5.61$, $p<0.016$), and h60 ($t(8)=-7.94$, $p<0.016$). The peak VGRF was also significantly lower at h40 compared to h60 ($t(8)=-4.20$, $p<0.016$). Peak PGRF was determined to be significantly higher at h60 compared to h20 ($t(8)=-3.50$, $p<0.016$), and h40 ($t(8)=-3.29$, $p=0.011$). There was no significant difference in peak PGRF at h20 compared to h40 ($t(8)=-1.16$, $p>0.016$). Knee flexion angle was significantly higher at h60 compared to h20 ($t(8)=2.42$, $p=0.015$). There was no significant difference in knee flexion angle at h20 compared to h40, as well as, 40 compared to h60. Trunk flexion angle was significantly higher at h60 compared to h20 ($t(8)=-3.14$, $p=0.014$) and h40, ($t(8)=-4.45$, $p=0.002$). There was no significant difference in trunk flexion angle at h20 and h40 ($t(8)=1.82$, $p>0.016$). Knee power was significantly lower at h20 compared to h40 ($t(8)=4.26$, $p=0.003$) and h60, ($t(8)=7.14$, $p<0.016$). There was no significant difference in knee power at h40 compared to h60. Results indicated that knee work was significantly lower at h20 than at h40 (t(8)=6.60, p<0.016), and also at h60, (t(8)=8.88, p<0.016). Knee work was also significantly lower at h40 compared to h60 (t(8)=7.00, p<0.016).

The PPMCs among the two ACL injury risk predictor variables and ankle, knee, hip and trunk flexion angles, as well as knee energetics for the vertical height test are reported in Table 2. From Table 2, peak VGRF was significantly and negatively correlated to ankle plantar flexion and knee flexion angle (r=–77, p=0.02 and r=–0.78, p=0.01, respectively). It is also worth noting from Table 2 that peak PGRF was significantly and negatively correlated to knee flexion angle (r=–0.72, p=0.03) as well as significantly and positively correlated to knee power (r=0.79, p=0.038).

Table 2: Pearson correlation coefficients of peak VGRF with ankle, knee, hip and trunk flexion as well as knee energetics (Vertical height test)

	Peak VGRF
Peak VGRF (BW)	
Peak PGRF (BW)	r = 0.78 (p =0.01)*
Ankle flexion (deg)	r = –0.77 (p =0.02)*
Knee flexion (deg)	r = –0.78 (p =0.01)*
Hip flexion (deg)	r = –0.14 (p =0.72)
Trunk flexion (deg)	r = –0.06 (p =0.88)
Knee joint power (W/kg)	r = 0.49 (p =0.18)
Knee joint work (J/kg)	r = 0.04 (p =0.91)

Note: * p< 0.05

Repeated-measure ANOVAs for the horizontal distance test revealed a significant effect of horizontal distance on peak PGRF (F(2,16)=28.05, p<0.0001, partial η^2=0.78, observed power=1.0), but not peak VGRF. We also determined a significant effect of horizontal distance on ankle plantar flexion angle (F(2,16)=6.70, p=0.008, partial η^2=0.46, observed power=0.85), hip flexion angle (F(2,16)=6.99, p=0.007, partial η^2=0.47, observed power=0.87), and trunk flexion angle

($F(2,16)=4.15$, $p=0.04$, partial $\eta^2=0.34$, observed power=0.65). The overall means and standard deviations of the sagittal plane body kinematics, knee power and knee work for the horizontal distance test among all subjects is provided in Table 3. Figure 2 shows the trend in peak PGRF for all subjects as horizontal distance increased. Horizontal distance of landing had a significant and positive effect on peak PGRF, suggesting as horizontal distance of landing increased peak PGRF increased (Figure 2). The difference in the marginal means at the three horizontal distances are (0.2, 0.08), which represents the difference in peak PGRF at landing distances 20 to 40cm and 40 to 60cm, respectively.

Pairwise dependent sample t-tests for the horizontal distance test revealed that peak PGRF was significantly different at all three horizontal distances tested. Peak PGRF was significantly lower at d30 compared to d50 ($t(8)=-4.29$, $p=0.003$), and at d70, ($t(8)=-6.69$, $p<0.016$). Peak PGRF was also significantly lower at d50 compared to d70 ($t(8)=-3{,}53$, $p=0.008$). Ankle plantar flexion was significantly higher at d30 compared to d70 ($t(8)=-2.84$, $p=0.015$) and d50, ($t(8)=-2.88$, $p=0.014$). There was no significant difference in ankle plantar flexion at d30 compared to d50. Hip flexion angle was significantly higher at d70 compared to d30 ($t(8)=-3.88$, $p=0.005$). There was no significant difference in hip flexion angle at d30 compared to d50, as well as, d50 compared to d70. Trunk flexion angle was significantly higher at d70 compared to d50 ($t(8)=3.96$, $p=0.004$). There was no significant difference in trunk flexion angle at d30 compared to d50, as well as, d30 compared to d70. Finally, knee work was significantly lower at d50 compared to d70 ($t(8)=-3.53$, $p=0.008$), with no other significant pairwise comparison.

The PPMCs among the two ACL injury risk predictor variables and ankle, knee, hip and trunk flexion angles, as well as, knee energetics for the horizontal distance test are reported in Table 4. Peak PGRF was significantly correlated with ankle plantar flexion angle ($r=–0.85$, $p=0.003$), knee power ($r=0.67$, $p=0.04$) and knee work ($r=0.73$, $p=0.036$). It is worth noting from Table 4 that ankle plantar flexion angle was positively and significantly correlated to knee work ($r=0.75$, $p=0.02$).

Further, from Table 4 we observed knee flexion angle was positively and significantly correlated to knee power (r=0.91, p=0.001). The time history plots of the ensemble averages of VGRF and PGRF among all subjects at each vertical height and horizontal distance tested are shown in Figure 3 and Figure 4, respectively. The time history plots of the ensemble averages of ankle, knee, hip and trunk flexion angles among all subjects at each vertical height and horizontal distance tested are shown in Figures 5a, 5b, 5c and 5d, respectively. In addition, the time history plots of the ensemble averages for knee powers among all subjects are shown in Figure 6 at each vertical height and horizontal distance tested.

Table 3: The means and SDs of each dependent variable across all subjects (Horizontal distance test).

	Horizontal Distance Test		
Dependent Variables	**distance=30 cm**	**distance=50 cm**	**distance=70 cm**
Peak VGRF (BW)	4.51±1.08	4.68±1.29	4.75±1.45
Peak HGRF (BW)	0.58±0.13	0.78±0.19	0.86±0.20
Ankle flexion (deg)	-7.97±2.80	-6.57±1.72	-5.02±1.87
Knee flexion (deg)	-40.17±4.89	-37.96±5.87	-38.38±5.55
Hip flexion (deg)	22.92±7.60	24.84±8.34	27.31±8.35
Trunk flexion (deg)	14.17±3.04	15.01±4.18	17.58±3.80
Knee joint power (W/kg)	-26.78±6.53	-27.16±6.71	-25.77±7.20
Knee joint work (J/kg)	-1.42±0.29	-1.52±0.37	-1.55±0.52

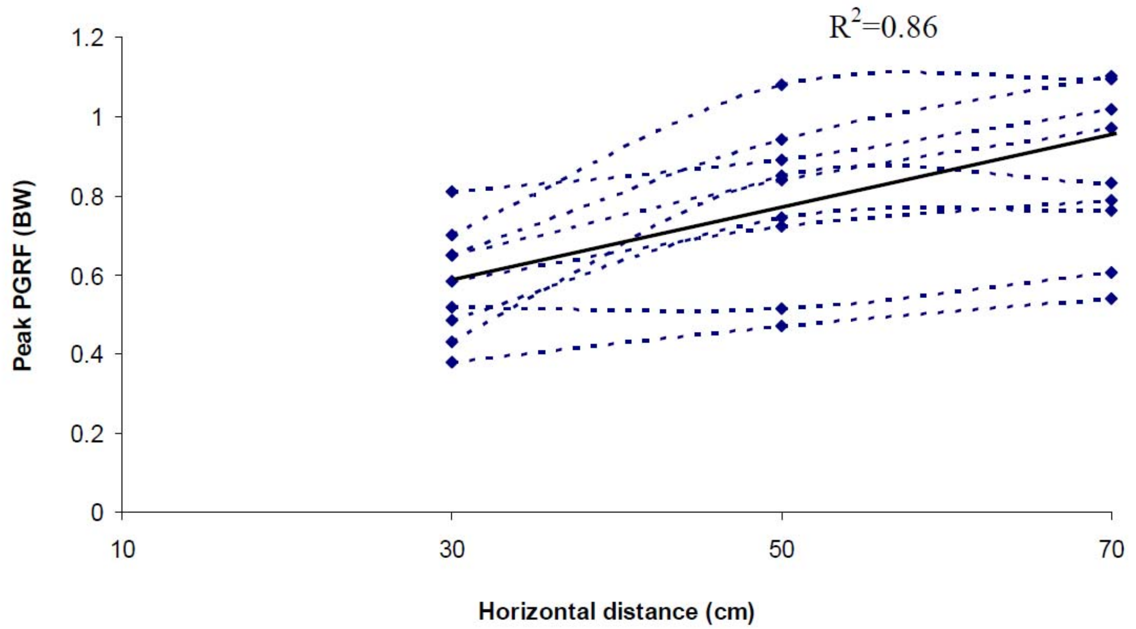

Fig. 2: Plot of horizontal distance and peak PGRF during single-leg landing for all subjects. Solid line is the average slope.

Table 4: Pearson correlation coefficients of peak PGRF with ankle, knee, hip and trunk flexion angle as well as knee energetics.

	Peak PGRF
Peak PGRF (BW)	
Peak VGRF (BW)	r = 0.67 (p =0.04)*
Ankle flexion (deg)	r = –0.85 (p =0.00)*
Knee flexion (deg)	r = –0.29 (p =0.45)
Hip flexion (deg)	r = –0.42 (p =0.26)
Trunk flexion (deg)	r = 0.54 (p =0.13)
Knee joint power (W/Kg)	r = 0.67 (p =0.04)*
Knee joint work (J/kg)	r = 0.73 (p =0.03)*

Note: * $p< 0.05$

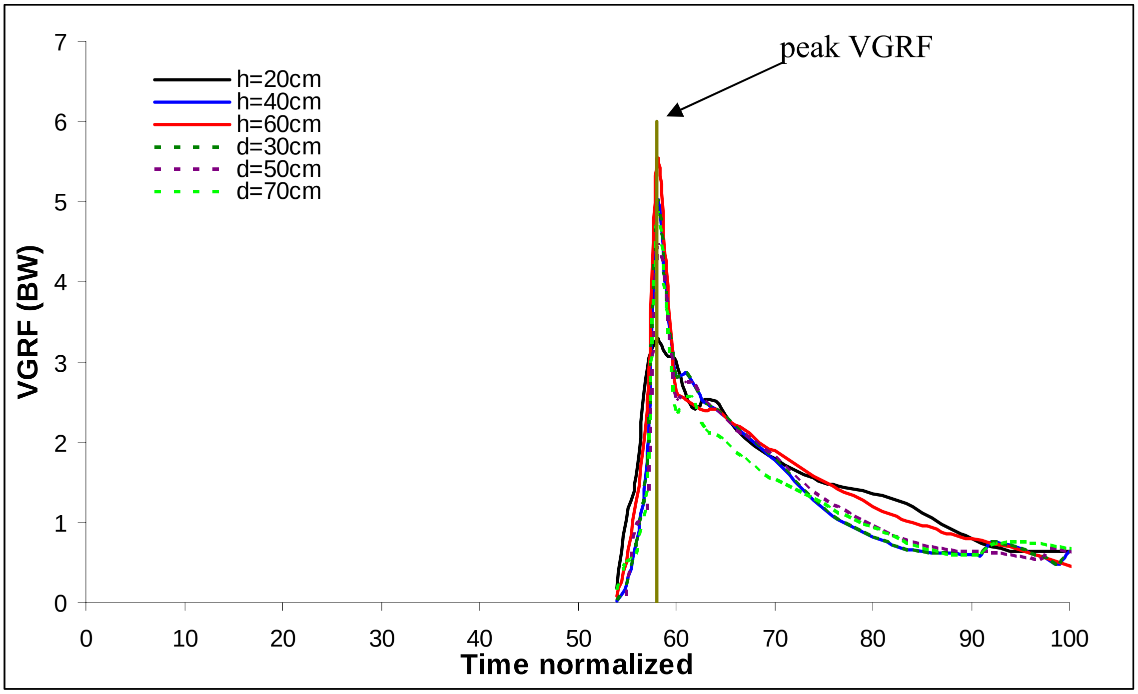

Fig. 3: Time histories of the ensemble average of VGRF at the three vertical heights and horizontal distances tested during single-leg landing among all subjects.

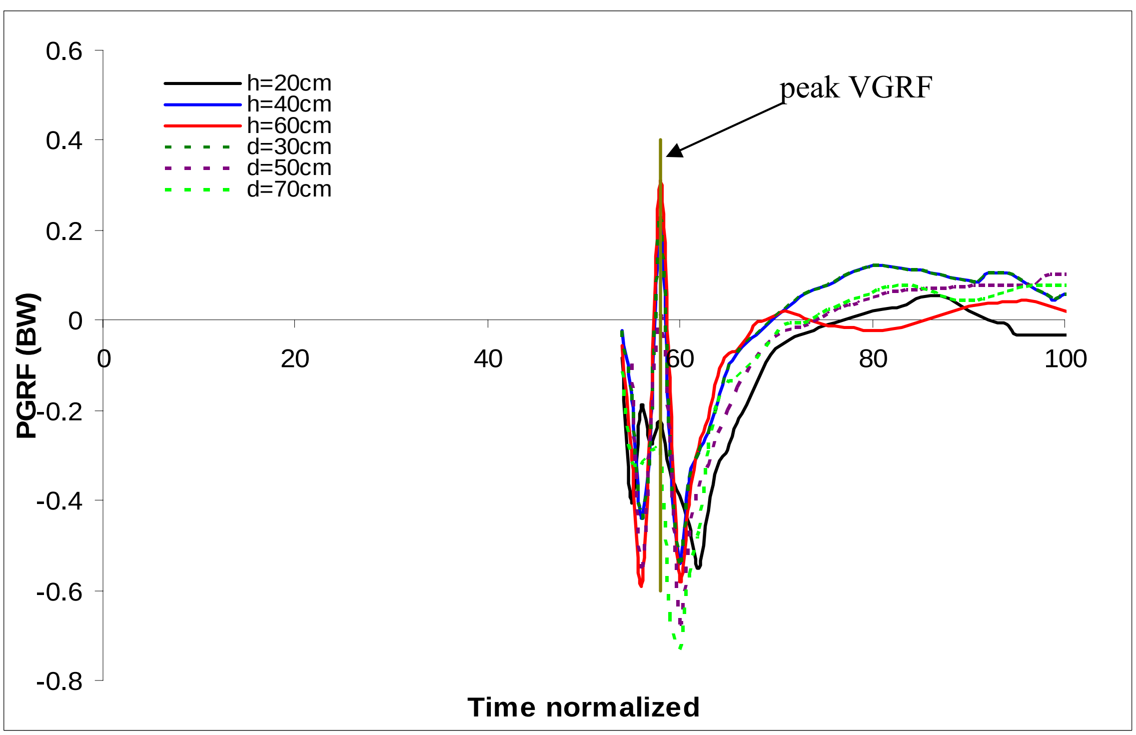

Fig. 4: Time histories of the ensemble average of PGRF at the three vertical heights and horizontal distances tested during single-leg landing among all subjects.

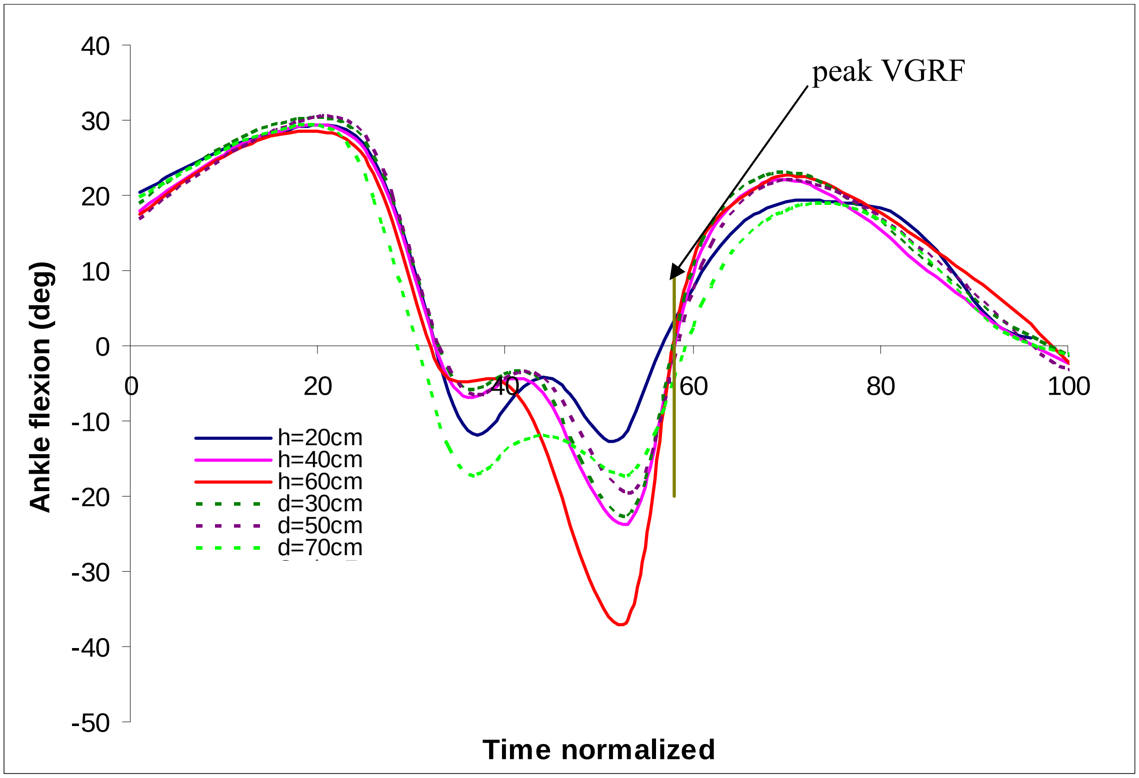

Fig. 5a: Time histories of the ensemble average of ankle flexion angles at the three vertical heights and horizontal distances tested during single-leg landing among all subjects.

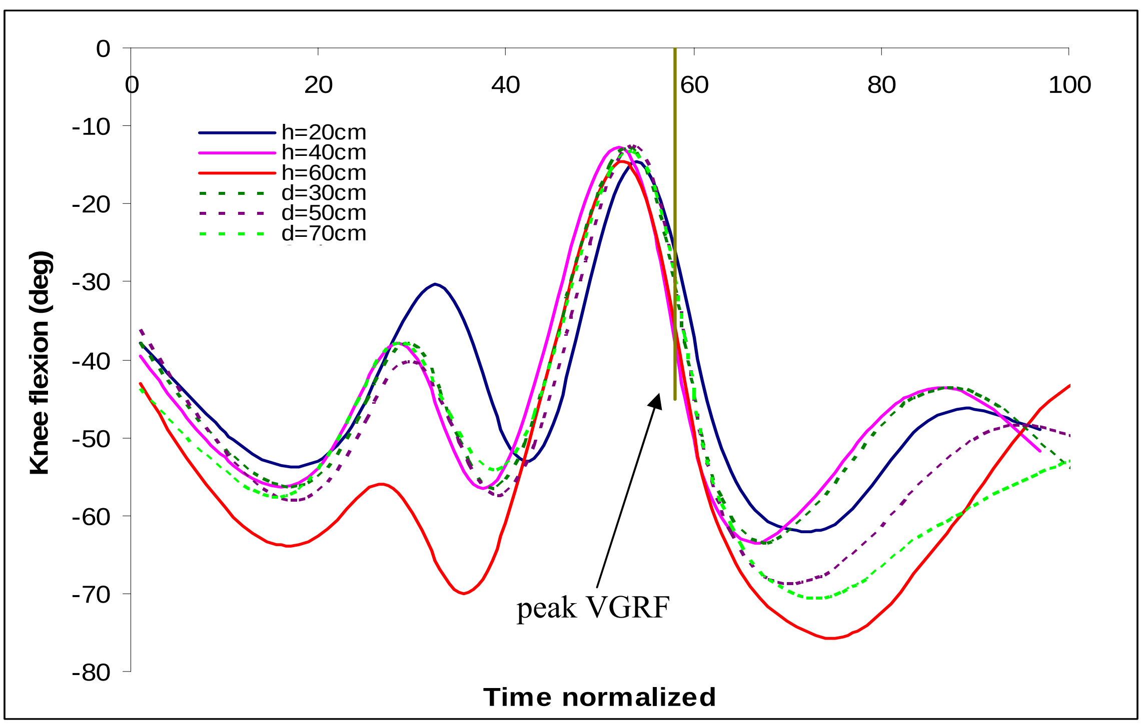

Fig. 5b: Time histories of the ensemble average of knee flexion angles at the three vertical heights and horizontal distances tested during single-leg landing among all subjects.

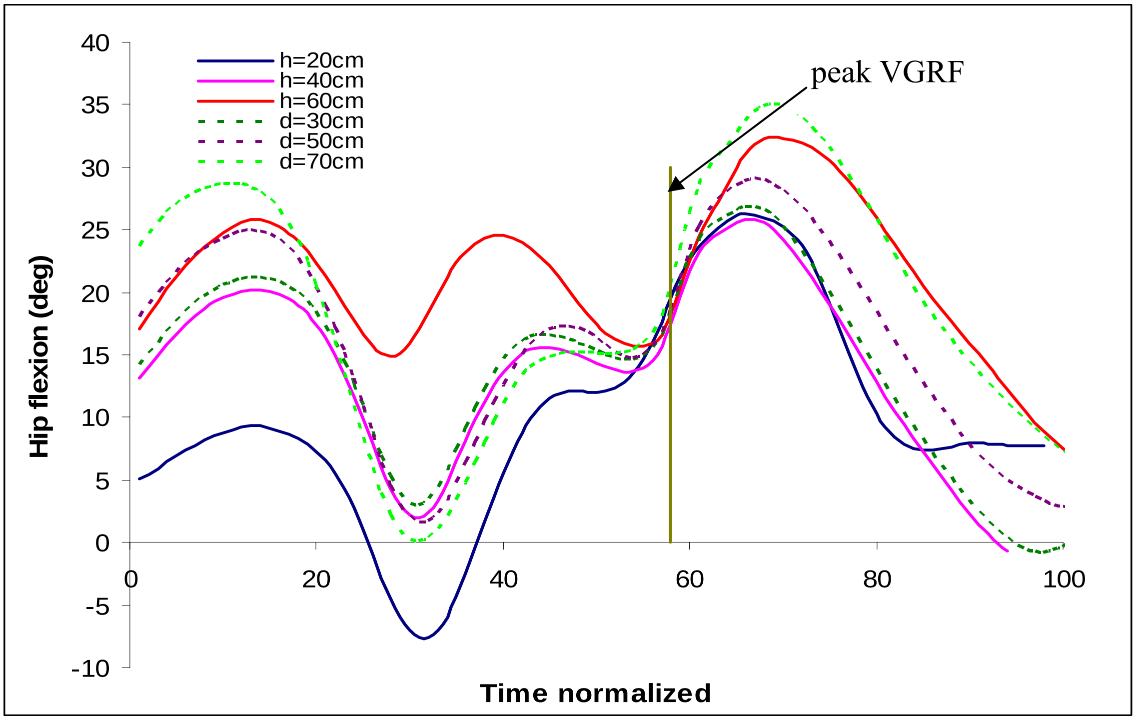

Fig. 5c: Time histories of ensemble average of hip flexion angles at the three vertical heights and horizontal distances tested during single-leg landing among all subjects.

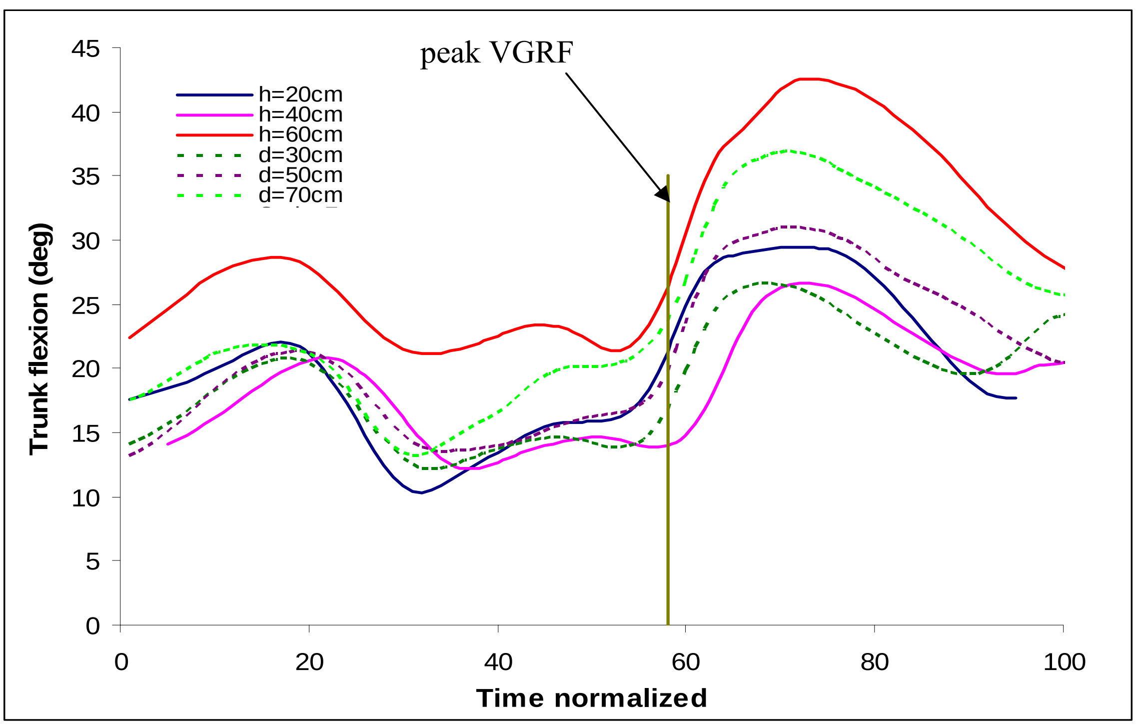

Fig. 5d: Time histories of the ensemble average of trunk flexion angles at the three vertical heights and horizontal distances tested during single-leg landing

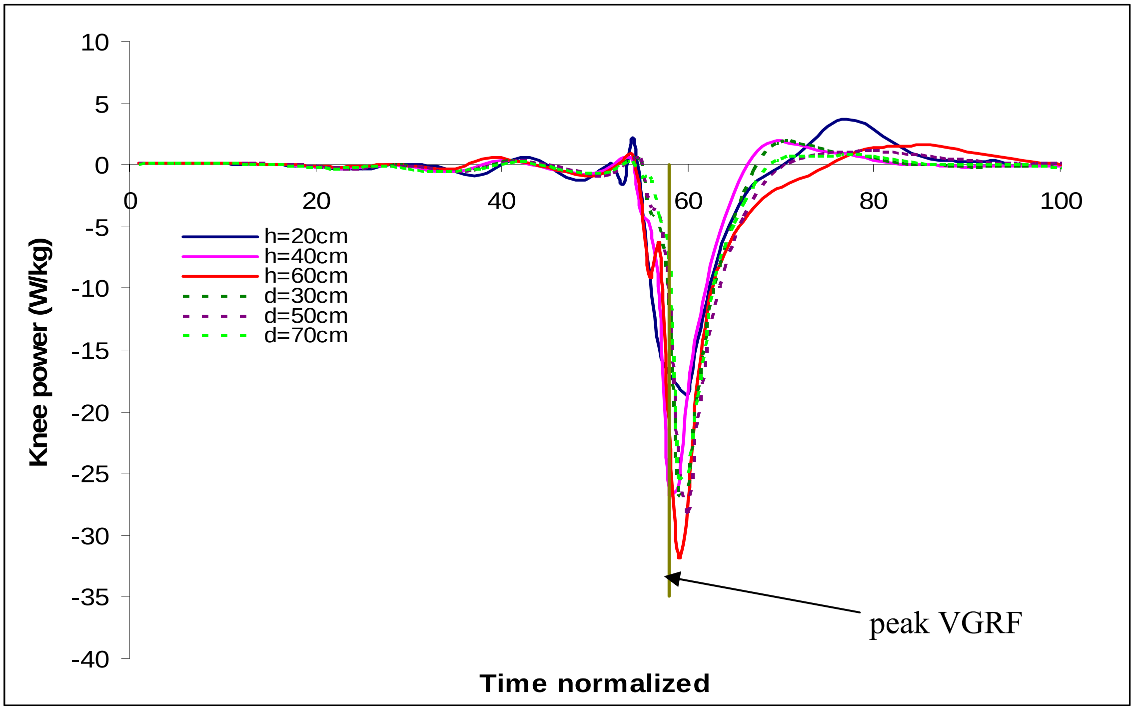

Fig. 6: Time histories of the ensemble average of knee power at the three vertical heights and horizontal distances tested during single-leg landing among all subjects.

4. Discussion and Conclusions

Investigations of how body kinematics function to attenuate impact forces during single-leg landing over increasing vertical heights and horizontal distances may provide new insights into key factors that may mitigate the risk of non-contact ACL injury. Our results showed that an increase in vertical height resulted in a significant increase in peak VGRF and peak PGRF (Table 1). Further, our results showed that an increase in horizontal distance resulted in a significant increase in peak PGRF (Table 3). The finding that an increase in vertical height resulted in increased peak VGRF, which suggests a higher risk of ACL injury, is supported by Yeow and co-workers [21]. The results of the current study also revealed that single-leg landings did not produce the characteristic bimodal VGRF curve commonly reported for double-leg landings [39, 42]. It appears that the demands of single-leg landings from the current study resulted in a rapid increase in VGRFs with a single peak (Figure 3), which is consistent with the findings by Hargrave et al.[30]. This observation is important as it elucidates the unique nature of single-leg landing studies whose findings cannot be compared with double-leg landing studies.

A study by Fagenbaum and Darling [31] showed vertical height had a significant effect on knee flexion angle, while a study by Yeow et al. [21] reported no significant effect of vertical height on knee flexion angle. The findings from the current study support the findings of Fagenbaun and Darling [31], that found greater knee flexion angles with increased vertical height (Table 1). Yeow et al. [21] may have found no significant effect of vertical height on knee flexion angle since the subjects performed both single and double-leg landings, where for the single-leg landing tasks the subjects may have landed in a manner that was protective of the ACL. Further, in the current study, subjects had larger body mass (10.92 kg greater) compared to the subjects in Yoew's et al. study [21], suggesting the task from the current study may have been more difficult and resulted in altered landing styles. Results from the current study are also consistent with previous studies that showed a significant effect of vertical height on knee power and knee work [21, 24, 43]. Vertical height had a significant effect on knee flexion angle, knee power and knee work, which corroborates our first hypothesis.

For the vertical height tests, we found ankle plantar flexion angle was significantly and negatively correlated to peak VGRF (Table 2), and this suggests that increasing ankle plantar flexion may be effective at attenuating peak VGRFs at increased vertical height during single-leg landings. This finding is supported by previous studies [16, 24, 32, 39, 44] that found the ankle plantar flexion was effective in absorbing the shock of landing. From Table 2 we also observed that knee flexion angle was significantly and negatively correlated to peak VGRF, which supports our second hypothesis. This finding is consistent with the study by Stacoff et al. (1988) who showed that knee flexion angle can be used to reduce the magnitude of the impact loads during landing. In addition, previous studies [22, 30, 33] have reported that knee flexion plays a key role in force attenuation, subsequently reducing the risk of non-contact ACL injury during single-leg landing, which is consistent with our findings. Table 2 also showed that hip and trunk flexion angles were not associated with peak VGRFs (Table 2). Given there are no single-leg landing studies investigating hip and trunk flexion angles at increasing vertical heights, we could draw no comparison.

For the horizontal distance test, there was a significant effect of horizontal distance on ankle, hip and trunk flexion angle. As well, peak PGRF was significantly and negatively correlated to ankle plantar flexion angles (Table 4). Furthermore, there was no significant correlation between peak PGRF and knee, hip or trunk flexion angle. However, both knee power and knee work were significantly and positively correlated to peak PGRF (Table 4). In addition, for the horizontal distance test we observed a significant and positive correlation between ankle plantar flexion angle and knee work, as well as, knee flexion angle and knee power (Table 4). These findings suggest that higher ankle plantar flexion and knee flexion angles promote more eccentric work by the knee extensors to dissipate impact energy; a finding supported by a double-leg landing study [11]. Given there are no known single-leg landing studies investigating the effect of increasing horizontal distance on risk of non-contact ACL injury, we could make no direct comparisons to confirm the validity of these findings.

Even though this study used a small sample size (n=9) we observed sufficiently high statistical power and significance that suggests for some of the results presented, the sample size used was adequate. This is likely because our experimental design used large differences in task demands, we used repeated-measure ANOVAs, and we employed homogenous data (height and weight matched males). While we cannot conclude (given small sample size) that the general male population would exhibit similar sagittal plane body kinematics, knee power, and knee work as reported in the current study, we were able to show that the relationships found have a strong support in terms of partial η^2 , r^2 and p values for the subjects tested. Although reasonable correlations were obtained, this study was performed in a controlled laboratory environment where subjects could plan for these tasks and as such may not be representative of maneuvers experienced during sports. Even though subjects performed at least two trials at each landing height and distance, reliability data could not be determined given only one trial was post processed and there was not enough data points for the nine subjects tested. As well, even though single-leg landings performed in the current study were sagittal plane dominant, out-of-plane movements commonly involved in sports and not captured in this study may be important contributors to the risk of non-contact ACL injury. In the present study, the single-leg landing tasks investigated entailed little out-of-plane motion and therefore it is likely that valgus loading implicated to increase the risk of non-contact ACL injury may not be influential. However, an area of future research remains single-leg landings from varying vertical height and horizontal distance that involves out-of-plane motion such as landing to the medial or lateral aspect of the knee. Furthermore, since we did not measure ACL loads during the single-leg landing tasks, the results and discussions stemming from this study are only based on what is known about the relationship between ACL loads and GRFs. Further studies addressing the aforementioned limitations, as well as accounting for the effect of gender during single-leg landings from increasing vertical heights and horizontal distances are needed to shed more light on the biomechanics of non-contact ACL injury during single-leg landing.

This study investigated the relationships among vertical heights and horizontal distances on peak GRFs, sagittal plane body kinematics, and knee energetics, as well as related these findings to risk of non-contact ACL injury during single-leg landing. Within the findings and limitations of this study, we observed that vertical height had a significant effect on peak VGRF, peak PGRF, knee flexion angle, trunk flexion angle, knee power and knee work. We also observed that horizontal distance had a significant effect on peak PGRF, as well as ankle, hip, and trunk flexion angles. Results from PPMCs showed that larger ankle plantar flexion and knee flexion angles as well as knee energetics may aid in attenuating peak VGRF and peak PGRF, which may promote more appropriate muscle firing patterns to protect the ACL.

5. Conflict of interest statement

All authors declare that there are no direct or indirect financial interests involved with the content of this paper.

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Manuscript IV - Gender, Vertical Height and Horizontal Distance Effects on Single-Leg Landing Kinematics: Implications for Risk of Non-contact ACL Injury

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Gender, Vertical Height and Horizontal Distance Effects on Single-Leg Landing Kinematics: Implications for Risk of non-contact ACL Injury

by

Nicholas Ali[1], Gholamreza Rouhi[1,2] , Gordon Robertson[1]

[1] - *School of Human Kinetics, University of Ottawa.*

[2] - *Department of Mechanical Engineering, University of Ottawa.*

There is a lack of studies investigating gender differences in whole-body kinematics during single-leg landings from increasing vertical heights and horizontal distances. This study determined the main effects and interactions of gender, vertical height, and horizontal distance on whole-body joint kinematics during single-leg landings, and established whether these findings could explain the gender disparity in non-contact anterior cruciate ligament (ACL) injury rate. Recreationally active males (n=6) and females (n=6) performed single-leg landings from a takeoff deck of vertical height of 20, 40, and 60 cm placed at a horizontal distance of 30, 50 and 70 cm from the edge of a force platform, while 3D kinematics and kinetics were simultaneously measured. It was determined that peak vertical ground reaction force (VGRF) and the ankle flexion angle exhibited significant gender differences ($p=0.028$, partial $\eta^2=0.40$ and $p=0.035$, partial $\eta^2=0.37$, respectively). Peak VGRF was significantly correlated to the ankle flexion angle ($r= -0.59$, $p=0.04$), hip flexion angle ($r= -0.74$, $p=0.006$), and trunk flexion angle ($r= -0.59$, $p=0.045$). Peak posterior ground reaction force (PGRF) was significantly correlated to the ankle flexion angle ($r= -0.56$, $p=0.035$), while peak knee abduction moment was significantly correlated to the knee flexion angle ($r= -0.64$, $p=0.03$). Rearfoot landings may explain the higher ACL injury rate among females. Higher plantar-flexed ankle, hip, and trunk flexion angles were associated with lower peak ground reaction forces, while higher knee flexion angle was associated with lower peak knee abduction moment, and these kinematics implicate reduced risk of non-contact ACL injury.

Key words: *Injury mechanism, kinematics, kinetics, ground reaction force (GRF), knee abduction moment, risk factors.*

Introduction

Most non-contact ACL injuries occur during activities involving single-leg landings (Boden et al., 2009). In a jump landing event, the landing phase is more stressful to the ACL than takeoff (Chappell et al., 2002). Single-leg landings are common tasks performed from varying vertical heights and horizontal distances during sporting events such as volleyball, basketball and soccer (Dufek and Bates, 1991). The literature informs us that single-leg and double-leg landing biomechanics are different (McNitt-Gray, 1993). Single-leg landings result in greater risk of non-contact ACL injuries compared to double-leg landings (Pappas et al., 2007; Yeow et al., 2010). There are many single-leg landing studies in the literature (Self and Paine, 2001; Lephart et al., 2002; Fagenbaum and Darling, 2003; Hargrave et al., 2003; Ford et al., 2006; Russell et al., 2006; Nagano et al., 2007; Pappas et al., 2007; Schmitz et al., 2007; Lawrence III et al., 2008; Kiriyama et al., 2009; Shimokochi et al., 2009; Yeow et al., 2010). These studies explicate factors implicated in contributing to the risk of non-contact ACL injuries, as well as, biomechanical gender differences that possibly explain the gender disparity in non-contact ACL injury rate (Fagenbaum and Darling, 2003; Ford et al., 2006; Russell et al., 2006; Nagano et al., 2007; Pappas et al., 2007; Schmitz et al., 2007; Lawrence III et al., 2008; Kiriyama et al., 2009; Shimokochi et al., 2009; Yeow et al., 2010). However, most of these studies investigated single-leg landings from only one vertical height (Self and Paine, 2001; Lephart et al., 2002; Hargrave et al., 2003; Ford et al., 2006; Russell et al., 2006; Nagano et al., 2007; Pappas et al., 2007; Schmitz et al., 2007; Lawrence III et al., 2008; Kiriyama et al., 2009; Shimokochi et al., 2009) and to the authors' best knowledge, none of these studies investigated the effect of horizontal distance on single-leg landing biomechanics. Moreover, many of these studies investigated vertical heights lower than 30 cm, which as argued by Zhang et al. (2000) is too low, and the participant's landing strategies may be completely different at higher heights. In addition, to the authors' best knowledge none of these studies investigated the interaction of gender, vertical height, and horizontal distance on single-leg landing kinematics. As well, we observed that some single-leg landing studies only report data on knee kinematics (Fagenbaum and Darling, 2003; Hargrave et al., 2003; Russell et al., 2006; Nagano et al., 2007; Pappas et al., 2007), but it may be equally important to simultaneously consider the role of ankle, knee, hip and trunk kinematics as they act in concert to modulate impact forces. Apart from the knee joint, the trunk, hip and ankle joint may also contribute to the overall shock absorption through their respective flexion motions during landing (Zhang et al., 2000).

Gender differences in whole-body joint kinematics and how these kinematics can attenuate GRFs and knee abduction moments (to mitigate the risk of non-contact ACL injury) during single-leg landings from increasing vertical heights and horizontal distances are not yet known. The current study examines the relationships between three non-contact ACL injury risk predictor variables, namely, peak vertical ground reaction force (VGRF), peak posterior ground reaction force (PGRF), and peak knee abduction moment, and various single-leg landing biomechanical variables. These three non-contact ACL injury risk predictor variables were selected for the following reasons. Firstly, an *in vivo* study demonstrated for a male subject hopping and landing on a single leg, the peak in vivo ACL strain occurred at the same instant as peak VGRF, suggesting that peak VGRF may predict the risk of non-contact ACL injury (Cerulli et al., 2003). Other studies have also determined that landing with a high impact force may pose high risk to the ACL (Chappell et al., 2002; Boden et al., 2009). Secondly, it was shown that an increase in peak PGRF requires an increase in knee extensor moment for balance, and this knee extensor moment generated by the quadriceps muscle was a major contributor to the higher proximal tibia anterior shear forces that likely increases ACL loads (Yu and Garrett, 2007). Therefore, peak PGRF may also predict the risk of non-contact ACL injury. Finally, the literature has shown that knee abduction moment may also predict the risk of non-contact ACL injury (Hewett et al., 2005). The objective of this study was twofold: first, to examine the main effects and interactions of gender, vertical height, and horizontal distance on whole-body joint kinematics during single-leg landings; and second, to correlate the biomechanical variables significantly impacted by main effects and interactions of gender, vertical height and/or horizontal distance to three non-contact ACL injury risk predictor variables. It was hypothesized that males and females would demonstrate significantly different whole-body joint kinematics, which would explain the higher incidences of non-contact ACL injury among females.

Material and Methods

Participants

Six male recreational athletes with a mean age of 24.7 ± 1.9 years, body height of 172 ± 11 cm, and body mass of 69.5 ± 8.6 kg, and six female recreational athletes with a mean age of 23.3 ± 1.86 years, body height of 170 ± 3 cm, and body mass of 66.75 ± 6.2 kg, were recruited from the university population. None of the participants reported any previous history of musculoskeletal, ligamentous or orthopaedic injuries to the lower extremity at the time of participation. A recreational athlete was defined as a participant who takes part in some form of a jump landing sport for 30 minutes a day at least 3 times a week. Prior to data collection, each participant gave informed consent as stipulated by the university's ethics review board. Participants' age and anthropometrics were recorded. The dominant leg was established as the leg used by the participant to kick a ball.

Procedures

All participants wore identical shoes (running shoe, model BY004, ASICS America Corporation, Irvine, CA) throughout data collection, so as to mitigate possible variability. Retro-reflective markers were fixed with a double-sided tape using a customized version of Vicon Plug-in Gait marker set (Figure 1). The Vicon Plug-in Gait marker set was customized to include additional markers at the hip and medial aspects of the elbow, knee and ankle as well as additional foot markers. Different marker locations were also used at the proximal ends of the pelvis. A total of 42 retro-reflective markers were used on each participant. A seven-camera motion capture system (Vicon MX, Oxford Metrics, UK) collected marker trajectories at a sampling rate of 250 Hz. A force platform (Kistler type 9281B, Winterthur, Switzerland) measured GRFs at a sampling rate of 1000 Hz. Videographic and force plate data were time synchronized. The VGRF was defined as the reaction to the force the body exerts on the ground in the vertical direction. The PGRF was defined as the horizontal reaction force the body exerts on the ground in the backward direction from landing.

Before data collection, each participant was given enough time to warm-up and practice the single-leg landing task until comfortable. The command of 'ready' was given to the participants before the start of each landing task. For each landing task all participants began in a standard take-off position by standing on a takeoff deck with hands placed on the iliac crests, legs shoulder width apart, and the toes of both feet aligned with the edge of the deck. Participants were then instructed to stand on their dominant leg, jump forward, and land as naturally as possible with their dominant foot only centered on the force plate. The participants were asked to keep their hands on their iliac crests when landing to reduce any variability from swinging arms. The participants were instructed to perform single-leg landings from takeoff decks of three different vertical heights (20, 40, and 60 cm) that were placed at three horizontal distances (30, 50 and 70 cm) from the edge of a force plate. The combination of vertical height and horizontal distance was defined as a landing configuration. The nine different landing configurations tested were h20d30, h20d50, h20d70, h40d30, h40d50, h40d70, h60d30, h60d50, and h60d70, where h represents the vertical height and d represents the horizontal distance. The number after h and d refers to the vertical height and horizontal distance, respectively, in centimeters. Each participant performed two trials at each landing configuration. The sequence of landing configurations were randomized to reduce learning effects.

Data reduction and analysis

One trial was selected from the better of two trials for model building, data analysis, and reporting. In general, each participant performed two trials at each landing configuration. The better trial was determined as the one in which the participant did not remove their hands from the iliac crests during landing, did not allow their non-dominant leg to impact the force plate during landing, or did not lose a marker during impact with the ground. At the time of peak VGRF, joint kinematics and kinetics were determined for the dominant leg. All marker trajectories and analog data were imported into Visual3D (C-Motion Inc. Rockville, MD) biomechanical software. In Visual3D, ankle dorsiflexion was defined as positive, ankle plantar flexion as negative, knee flexion as negative, hip flexion as positive, and trunk flexion as positive. The ankle flexion angle was defined as the angle between the leg segment and foot segment. The difference between the ankle flexion angle when the participant stood on the takeoff platform and when peak VGRF occurred during landing was determined as the ankle flexion angle. The knee flexion angle was defined as the angle between the thigh and leg segment, while the hip flexion angle was defined as the angle between the thigh and pelvis segment. Trunk flexion angle was calculated as the angle between the trunk segment and a vertical line in the laboratory coordinate system. Kinematic data were low-pass filtered using a second-order bidirectional Butterworth filter at 6Hz and analog data were filtered at 25Hz. Kinetic data were calculated using a Newtonian inverse dynamics analysis by Visual3D software. The ground reaction forces were normalized to body weight and knee abduction moments normalized by the product of body mass and body height.

Statistical analysis

Multiple three-way repeated-measures ANOVAs were first conducted to test the main effects and interactions of gender (males and females), vertical height (20, 40 and 60 cm) and horizontal distance (30, 50 and 70 cm) on various single-leg landing biomechanical dependent variables; namely, peak VGRF, peak PGRF, peak knee abduction moment, as well as, ankle, knee, hip and trunk flexion angle. Descriptive statistics for these biomechanical variables are presented. Follow-up tests entailed Pearson Product Moment Correlations (PPMCs) determined for variables significantly impacted by the main effects and interactions of vertical height, horizontal distance and gender. PPMCs were measured to determine the associations between the three non-contact ACL injury risk predictor variables and the biomechanical variables. The α level was set at 0.05 for statistical analyses conducted in SPSS (SPSS for Windows, Release 11.5.0).

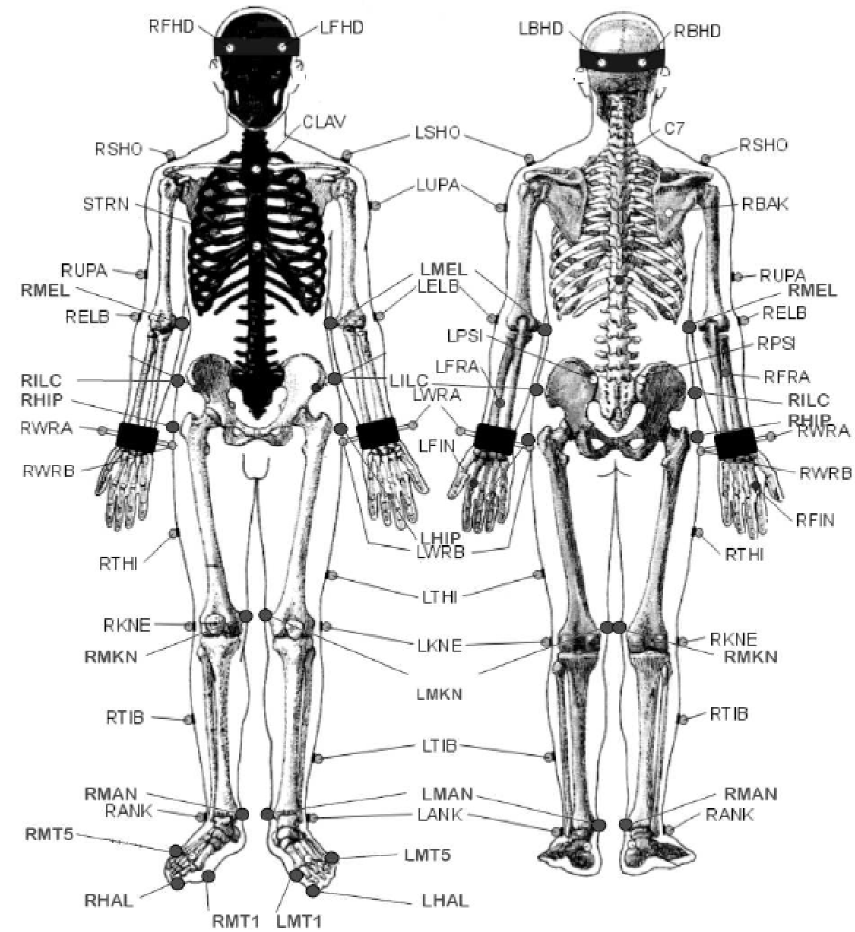

Figure 1

Customized marker set used in this study.
** Adapted from Oxford Metrics Plug-in-gait marker placement document*

Results

Figures 2a, 2b and 2c show the time histories of VGRFs, PGRFs, and knee abduction moments, respectively, during single-leg landings for a participant at the nine landing configurations tested. The key findings from the separate ANOVAs conducted are shown in Table 1. From Table 1, a significant main effect of gender with peak VGRF ($F(1,10)=6.56$, $p=0.028$, partial $\eta^2=0.40$, observed power=0.64) and with the ankle plantar/dorsiflexion angle ($F(1,10)=5.92$, $p=0.035$, partial $\eta^2=0.37$, observed power=0.60) was determined. Females had significantly lower peak VGRF and ankle plantar flexion angles compared to males (Table 2). Among the three ACL injury risk predictor variables, follow-up tests revealed peak VGRF was significantly and negatively correlated to the ankle plantar/dorsiflexion angle among males ($r=-0.80$, $p=0.048$), while no significant correlation was observed for females.

From Table 1, we also observed that there was a significant height×distance interaction with peak VGRF ($F(4, 40)=4.67$, $p=0.003$; partial $\eta^2=0.32$, observed power=0.92), hip flexion angle ($F(4, 40)=3.96$, $p=0.008$, $\eta^2=0.28$, observed power=0.87) and trunk flexion angle ($F(4, 40)=3.90$, $p=0.022$, $\eta^2=0.28$, observed power=0.86). There was a significant height×gender interaction with trunk flexion angle ($F(2, 20)=7.58$, $p=0.020$, $\eta^2=0.43$, observed power=0.91) (Table 1). Results revealed no significant distance×gender or height×distance×gender interactions for any of the biomechanical variables tested (Table 1). Results showed many significant main effects of both vertical height and horizontal distance with the biomechanical variables tested (Table 1). With the exception of peak VGRF and ankle plantar/dorsiflexion angle, given there was no significant effect of gender on any of the other dependent variables tested, the male and female data were pooled for subsequent follow-up statistical testing using PPMCs. Descriptive statistics of the biomechanical variables after pooling male and female data are presented in Table 3, while PPMCs among the three non-contact ACL injury risk predictor variables and the biomechanical variables tested are presented in Table 4. From Table 4, it can be gleaned that peak VGRF was significantly and negatively correlated to the ankle plantar/dorsiflexion angle ($r= -0.59$, $p=0.04$), hip flexion angle ($r= -0.74$, $p=0.006$), and trunk flexion angle ($r= -0.59$, $p=0.045$). We also observed that peak PGRF was significantly and negatively correlated to the ankle plantar/dorsiflexion angle ($r= -0.56$, $p=0.04$). Finally, there was a significant and negative correlation between peak knee abduction moment and the knee flexion angle ($r= -0.64$, $p=0.03$).

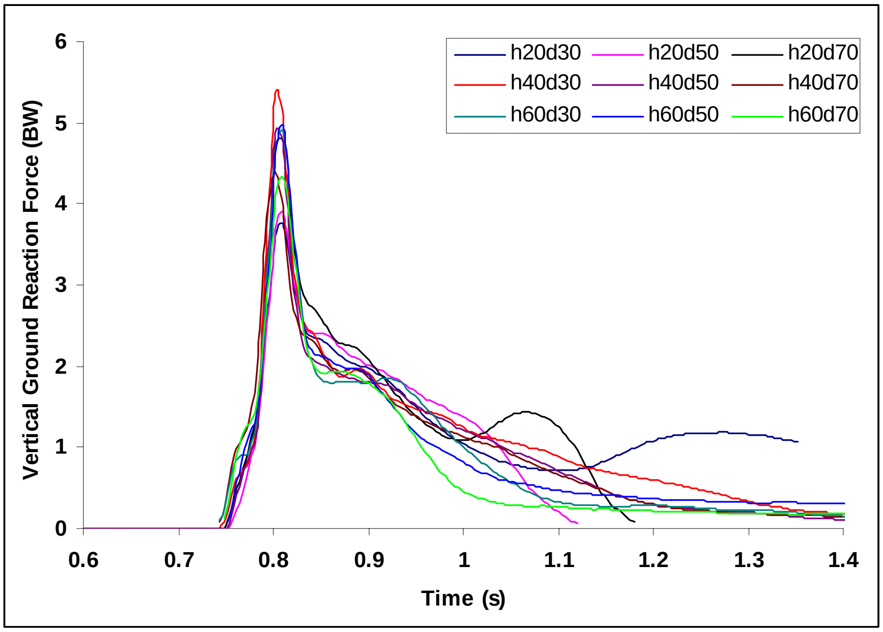

Figure 2a

Time histories of VGRFs during single-leg landings from the nine landing configurations for a participant.

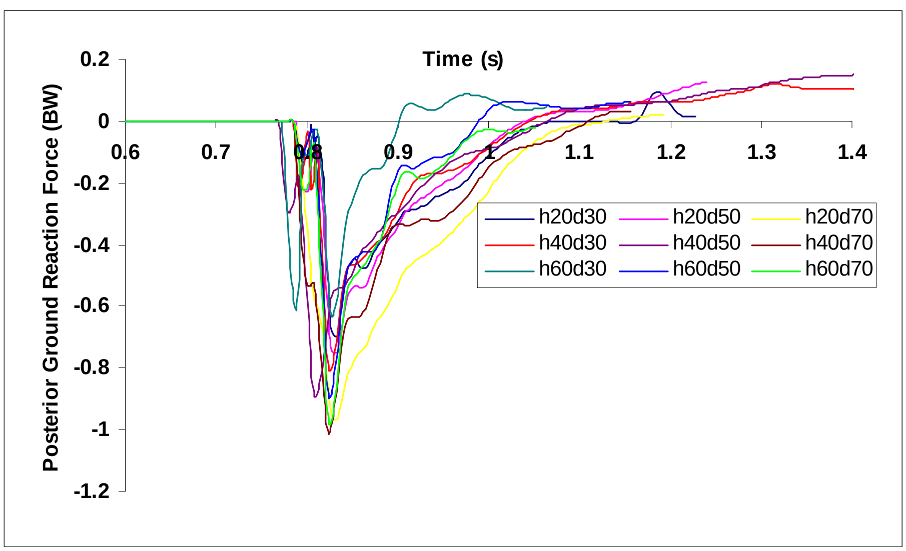

Figure 2b

Time histories of PGRFs during single-leg landings from the nine landing configurations for a participant.

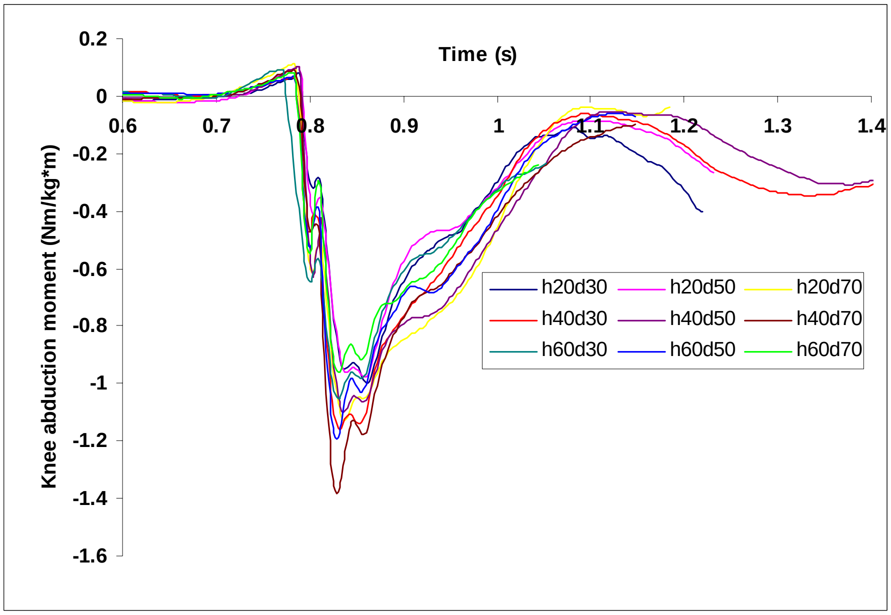

Figure 2c

Time histories of knee abduction moments during single-leg landings from the nine landing configurations for a participant.

Table 1

ANOVA summary showing interactions and main effects observed.

	Dependent Variables						
	Peak VGRF	Peak PGRF	Ankle plantar/ dorsi flexion angle	Knee flexion angle	Peak Knee abduction moment	Hip flexion angle	Trunk flexion angle
Height	0.000	0.000		0.000			0.040
Distance		0.000	0.000		0.007	0.000	
Height x Gender							0.020
Distance x Gender							
Height x Distance	0.003					0.008	0.022
Height x Distance x Gender							
Gender	0.028		0.035				

Table 2

Descriptive statistics (mean ± SD) of biomechanical variables significantly different between genders.

Dependent Variables	h20d30	h20d50	h20d70	h40d30	h40d50	h40d70	h60d30	h60d50	h60d70
Males (n=6)									
Peak VGRF (BW)	3.60±0.39	3.78±0.40	3.91±0.70	5.22±0.34	4.88±0.86	5.29±0.92	5.94±0.73	6.07±0.78	5.56±1.09
Ankle plantar/dorsi flexion angle (deg)	-1.81±5.02	0.93±5.16	2.35±6.86	-4.47±3.41	-2.17±2.16	1.22±5.64	-4.29±4.74	-0.11±3.53	-1.26±5.75
Females (n=6)									
Peak VGRF (BW)	3.00±0.29	3.28±0.38	3.46±0.44	4.51±0.24	4.38±0.34	4.63±0.69	5.62±0.75	5.06±0.55	4.89±0.50
Ankle plantar/dorsi flexion angle (deg)	0.94±5.41	2.81±1.88	7.75±6.69	0.59±3.77	5.56±6.94	6.30±9.64	0.73±4.13	3.55±3.73	7.23±3.56

Table 3

Descriptive statistics (mean ±SD) of the biomechanical dependent variables tested.

	(n=12)								
Dependent Variables	**h20d30**	**h20d50**	**h20d70**	**h40d30**	**h40d50**	**h40d70**	**h60d30**	**h60d50**	**h60d70**
Peak VGRF (BW)	3.30±0.45	3.52±0.46	3.67±0.60	4.87±0.47	4.63±0.68	4.96±0.84	5.78±0.72	5.56±0.83	5.23±0.88
Peak PGRF (BW)	-0.19±0.15	-0.28±0.21	-0.43±0.23	-0.09±0.20	-0.06±0.20	-0.24±0.18	-0.33±0.28	-0.05±0.19	-0.04±0.30
Peak knee abd. moment (N·m/kg·m)	-0.13±0.18	-0.09±0.37	-0.15±0.21	-0.11±0.19	-0.16±0.20	-0.02±0.28	-0.19±0.30	-0.16±0.17	-0.04±0.15
Ankle plantar/ dorsiflexion angle (deg)	-0.44±5.10	1.87±3.81	5.05±7.00	-1.94±4.28	1.69±6.30	3.76±7.89	-1.78±4.90	1.72±3.89	2.98±6.26
Knee flexion angle (deg)	-27.86±9.71	-27.04±9.10	-25.91±8.02	-30.44±9.70	-29.55±8.70	-29.17±9.57	-31.39±11.09	-31.67±8.10	-30.95±8.85
Hip flexion angle (deg)	21.45±11.30	20.61±10.40	22.62±10.37	20.38±11.20	22.20±10.79	24.26±10.50	17.84±14.10	25.16±10.21	24.88±9.27
Trunk flexion angle (deg)	17.63±6.80	18.1±8.42	21.53±8.45	17.94±9.10	19.61±11.45	17.87±11.00	21.88±9.30	20.52±11.40	20.18±9.60

Table 4

Bivariate Pearson's r correlations between the three ACL injury risk predictor variables and biomechanical variables significantly impacted by main effects and interactions of height and distance.

(n=12)							
Pearson's Correlation	**Peak VGRF**	**Peak PGRF**	**Peak knee abduction moment**	**Ankle plantar/dorsi flexion angle**	**Knee flexion angle**	**Hip flexion angle**	**Trunk flexion angle**
Peak VGRF (BW)	1.00	0.18	-0.05	-0.59*	0.35	-0.74**	-0.59*
Peak PGRF (BW)		1.00	-0.09	-0.56*	0.01	-0.27	0.38
Peak knee abd. moment (N.m/kg.m)			1.00	0.09	-0.64*	-0.08	0.18
Ankle plantar/dorsiflexion angle (deg)				1.00	0.12	0.58*	0.54*
Knee flexion angle (deg)					1.00	0.41	0.13
Hip flexion angle (deg)						1.00	0.45
Trunk flexion angle (deg)							1.00

Note: * $p < 0.05$; ** $p < 0.01$

Discussion

The trends determined in GRFs (Figure 2a and Figure 2b) for the single-leg landing tasks performed in the current study did not reveal the characteristic distinct bimodal GRF curve reported for double-leg landings in the literature (Dufek and Bates, 1990; Zhang et al., 2000). The single-leg landing tasks in the current study resulted in a smooth and rapid increase in GRFs with a single peak, which is consistent with the findings of Hargrave et al. (2003). As a result, the biomechanical comparison of double-leg and single-leg landing studies in the literature may be limited due to the differences exhibited by these two tasks.

Safe landing technique usually involves movements that act to dissipate high impact forces. Given that the single-leg landing tasks in the current study were sagittal plane dominant, possibly explains the lack of kinematic gender differences, and perhaps these differences become more pronounced during out-of-plane movements. Out-of-plane motion such as side-step cutting or single-leg landing to the medial or lateral aspect of the knee may entail both sagittal and non-sagittal plane loadings and perhaps pose greater risk to ACL injury. Nonetheless, we observed females landed with significantly lower peak VGRF compared to males, a finding that is not supported by two studies (Pappas et al., 2007; Schmitz et al., 2007). In the current study, females may have experienced lower VGRF because of their lower body mass compared to males, and perhaps musculoskeletal differences such as higher quadriceps-to-hamstring ratio, the latter factor not considered in this study. The reason for lower peak VGRF in females during single-leg landings has yet to be elucidated. Ankle plantar/dorsiflexion angle was the only kinematic variable that exhibited significant gender differences with females landing dorsiflexed while males predominantly plantar flexed (Table 2). This finding partly supports our hypothesis and may also partly explain why females are at greater risk of non-contact ACL injury given the literature has shown that athletes who injured their ACL had significantly less plantar flexed ankle angle (Self and Paine, 2001; Madigan and Pidcoe, 2003; Boden et al., 2009; Shimokochi et al., 2009). It has also been shown that kinematic differences at the ankle may contribute to gender differences in the ACL injury rate (Griffin et al., 2000). The results of the current study are also consistent with the literature that reported no gender differences during single-leg landings in hip flexion angles (Lephart et al., 2002; Pappas et al., 2007), and knee flexion angles (Nagano et al., 2007; Kiriyama et al., 2009). As well, the current study found a significant and negative correlation between peak VGRF and ankle flexion angle for males, a finding that is supported by the literature (Self and Paine, 2001; Madigan and Pidcoe, 2003; Boden et al., 2009; Shimokochi et al., 2009). Perhaps higher ankle plantar flexion angles permit more time to distribute the impact forces and better enable the musculature to dissipate these forces as demonstrated by McNitt-Gray (1993).

Table 4 showed that higher ankle plantar flexion, hip, and trunk flexion angles are associated with lower peak VGRF. Our finding that higher hip flexion angle was associated with lower peak VGRF is corroborated by the literature (Ball, 1999; Self and Paine, 2001). Furthermore, our findings are consistent with that of Ball (1999) who showed lower hip flexion angles pose greater risk of ACL injury; given that the quadriceps' high compensatory knee torques acting in combination with GRFs may excessively accelerate the tibia anteriorly beneath the femur. To the authors' best knowledge, no single-leg landing studies have investigated trunk flexion angles; therefore, direct comparison of our results with the literature was not possible. However, the findings from the current study are consistent with a double-leg landing study (McNitt-Gray, 1993) that showed that higher trunk flexion angle was associated with lower peak VGRF. This finding is also in general agreement with a study by Hewett's research group that recommended participants land with their chest over their knees to reduce the likelihood of non-contact ACL injury (Hewett et al., 2009). From Table 4 we also observed that lower peak knee abduction moment was associated with higher knee flexion angles, a finding that is supported by the literature (Hewett et al., 2005). Higher plantar flexed ankle, hip, and trunk flexion angles, as well as, higher knee flexion angles during single-leg landings reduce peak GRFs and the peak knee abduction moment, respectively. These kinematics implicate reduced risk of non-contact ACL injury that is corroborated by the literature (Alentorn-Geli et al., 2009).

Even though the current study used a small sample size (n=12), many significant main effects and interactions with high statistical power, as well as, medium to high Pearson correlation coefficients were observed, suggesting the sample size used was adequate. This may be attributed to our experimental design that used large differences in task demands, our application of repeated-measures ANOVAs, and employment of homogenous data (body height and body mass matched males and females). While we cannot conclude (given small sample size) that the general male or female population would exhibit whole-body kinematics as reported in the current study, we were able to show that the relationships found have a strong support in terms of partial η^2, r^2 and p values for the participants tested. In addition, even though reasonable correlations were obtained, this study was performed in a controlled laboratory environment where participants could plan for these tasks and as such, may not be representative of maneuvers experienced during sports. As well, the relatively small sample size used in the current study may have hindered our ability to detect small but significant differences among the variables tested. In addition, this study did not address the ability of the musculoskeletal system to absorb energy upon impact, even though a study (Lees, 1981) showed that muscular activity during landing can modify GRFs. Furthermore, this study did not investigate the anatomical and hormonal factors implicated to increase the risk of non-contact ACL injuries. Even though single-leg landings performed in the current study were sagittal plane dominant, out-of-plane movements commonly involved in sports and not captured in this study may be important contributors to the risk of non-contact ACL injury. Therefore, future studies should investigate the biomechanical demands of frontal and traverse plane loading during out-of-plane landings on a single leg. Additionally, this study may be limited given there is equally a limited number of studies supporting the use of peak VGRF, peak PGRF, and peak knee abduction moment as ACL injury risk predictor variables. Since we did not measure ACL loads during single-leg landings, the results and discussions stemming from the current study are based on what is known about the relationship between ACL loads and GRFs, as well as, ACL loads and knee abduction moment.

Conclusions

Within the findings and limitations of the current study, peak VGRF and ankle flexion angle were the only variables that demonstrated significant gender differences during single-leg landings from increasing vertical heights and horizontal distances. Females had significantly lower peak VGRF and the ankle plantar flexion angle during single-leg landings, in which the latter may have hindered their ability to attenuate GRFs, and may partly explain why this gender is at greater risk of non-contact ACL injury. Higher plantar flexed ankle, hip, and trunk flexion angles were associated with lower peak GRFs while higher knee flexion angle was associated with lower peak knee abduction moment. Higher values of these kinematic variables during single-leg landings suggest modulation of GRFs and knee abduction moments, which implicates reduced risk of non-contact ACL injury.

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Manuscript V - The application of musculoskeletal modelling to investigate gender bias in non-contact ACL injury rate during single-leg landings

Nicholas Ali, Michael Skipper Andersen, John Rasmussen, D.G.E Robertson, and Gholamreza Rouhi

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The Application of Musculoskeletal Modelling to investigate Gender bias in non-contact ACL injury rate during Single-leg Landings

Nicholas Ali[1*], Michael Skipper Andersen[2], John Rasmussen[2], D.G.E Robertson[1], and Gholamreza Rouhi[1,3]

[1]*School of Human Kinetics, University of Ottawa, Ottawa, Canada*

[2]*Department of Mechanical and Manufacturing Engineering, Aalborg University, Aalborg, Denmark*

[3]*Faculty of Biomedical Engineering, Amirkabir University of Technology, Tehran, Iran*

*Corresponding author, School of Human Kinetics, Faculty of Health Science, University of Ottawa, 125 University St., Ottawa, Ontario, K1N 6N5, Canada

The Application of Musculoskeletal Modeling to investigate Gender bias in non-contact ACL injury rate during Single-leg Landing

The central tenet of this study was to develop, validate and apply various individualized 3D musculoskeletal models (MSMs) of the human body for application to single-leg landings over increasing vertical heights and horizontal distances. While contributing to an understanding of whether gender differences explain the higher rate of non-contact ACL injuries among females, this study also correlated various musculoskeletal variables significantly impacted by gender, height, and/or distance and their interactions to two ACL injury risk predictor variables; peak vertical ground reaction force (VGRF) and peak proximal tibia anterior shear force (PTASF). Kinematic, kinetic, and electromyography (EMG) data of three male and three female subjects were measured. Results revealed no significant gender differences in the musculoskeletal variables tested except peak VGRF ($p=0.039$) and hip axial compressive force ($p=0.032$). The quadriceps and the gastrocnemius muscle forces had significant correlations with peak PTASF ($r=0.85$, $p<0.05$ and $r=-0.88$,$p<0.05$ respectively). Further, hamstring muscle force was significantly correlated to peak VGRF ($r=-0.90$, $p<0.05$). The ankle flexion angle was significantly correlated to peak PTASF ($r=-0.82$, $p<0.05$). Our findings indicate that, compared to males, females did not exhibit significantly different muscle forces, or ankle, knee and hip flexion angles during single-leg landings that would explain the gender bias in non-contact ACL injury rate. Our results also suggest that higher quadriceps muscle force increases the risk, while higher hamstring and gastrocnemius muscle forces and ankle flexion angle, reduce the risk of non-contact ACL injury.

Keywords: Non-contact ACL injury, muscle forces, muscle activity, joint reaction forces, proximal tibia anterior shear force.

Abbreviations:

ACL	Anterior Cruciate Ligament
ATT	Anterior Tibial Translation
MSM	Musculoskeletal model
GRFs	Ground Reaction Forces
VGRF	Vertical Ground Reaction Force
PGRF	Posterior Ground Reaction Force
PTASF	Proximal Tibia Anterior Shear Force
EMG	Electromyography
AMS	AnyBody Modeling System

1. INTRODUCTION

Single-leg landing is a common task performed from varying vertical heights and horizontal distances during sports. The literature indicates that the highest incidence of non-contact anterior cruciate ligament (ACL) injury occurs during single-leg landing in sports such as basketball, soccer and team handball. (Boden et al. 2009; Kirkendall and Garrett 2000; Paul et al. 2003; Renstrom et al. 2008) In spite of this, little is known about muscle response and loading when ACL injury occurs during single-leg landings. This may be attributed to the difficulties associated with measuring joint reaction and muscle forces *in vivo*, as well as the level of effort required to develop and simulate musculoskeletal models (MSMs).

There are many single-leg landing studies in the literature, (Fagenbaum and Darling 2003; Ford et al. 2006; Hargrave et al. 2003; Kiriyama et al. 2009; Laughlin et al. 2011; Lawrence III et al. 2008; Lephart et al. 2002; Nagano et al. 2007; Pappas et al. 2007; Russell et al. 2006; Schmitz et al. 2007; Self and Paine 2001; Shimokochi et al. 2009; Yeow et al. 2010) but none that utilizes a MSM to investigate single-leg landings over increasing vertical heights and horizontal distances. More importantly, none of these studies examined the relationships among height and distance of landing, ground reaction forces (GRFs), joint reaction forces, muscle forces, joint kinematics, and risk of non-contact ACL injury. McLean et al. (McLean et al. 2005; McLean et al. 2004; McLean et al. 2003), Shelburne and Pandy (2002) and Lloyd and Besier (2003) utilized a MSM to determine the forces in the muscles during activities implicated to cause non-contact ACL injury. For many of these studies, the aim was to determine the joint reaction or muscles forces during activities implicated to cause ACL injuries. The McLean and Lloyd studies (Lloyd and Besier 2003; McLean et al. 2005; McLean et al. 2004; McLean et al. 2003) focused on side-step cutting as a non-contact ACL injury mechanism, while the work of Pandy's research group (Anderson and Pandy 1999; Pandy and Shelburne 1997; Pflum et al. 2004; Shelburne and Pandy 1997; Shelburne and Pandy 2002) focused on double-leg landings. Even though a recent study by Laughlin *et al*.(Laughlin et al. 2011) investigated single-leg landings using MSMs, this study did not address the effect of height, distance or gender on risk of ACL injury. This study will add to the domain of studies investigating single-leg jump landings using musculoskeletal modelling.

The ability of body kinematics or lower extremity muscles to attenuate the GRFs upon landing on a single-leg may enable us to better prevent ACL injuries through improved biomechanical function. If these impact forces cannot be dissipated by joint motion or joint and muscle forces, the ACL may be forced to carry the brunt of the load, which may increase the risk of injury. By two studies (Boden et al. 2009; Podraza and White 2010) a lack of absorption of GRFs at landing may be a factor in ACL injury. In addition, an *in vivo* study (Cerulli et al. 2003) demonstrated that for a male subject hopping and landing on one leg, peak ACL strain occurred at peak VGRF, suggesting that peak VGRF may be a likely predictor of risk of non-contact ACL injuries. Other studies (Chappell et al. 2002; Madigan and Pidcoe 2003; Malinzak et al. 2001) confirmed that peak VGRF may amplify internal joint loads that may cause ACL injury if not sufficiently attenuated by the musculoskeletal system. Therefore, this study uses peak VGRF as an ACL injury risk predictor variable. Peak PTASF was also selected as an ACL injury risk predictor variable in this study given it has been shown that an increase in this force can lead to an increase in anterior tibial translation (ATT), which increases ACL loading. (DeMorat et al. 2004; Fleming et al. 2001; Withrow et al. 2006; Yu and Garrett 2007; Yu et al. 2006) Given this, for this study, a relationship between two possible non-contact ACL injury risk predictor variables, namely, peak

VGRF and peak PTASF and lower extremity joint reaction and muscle forces, as well as lower extremity kinematics was investigated.

To the authors' best knowledge, there are no *in vivo* or musculoskeletal modelling studies reporting joint reaction and muscle forces between genders during single-leg landings over increasing vertical heights and horizontal distances. The objective of this study is threefold: firstly, develop and validate 3D individualized MSMs of the human body for application to single-leg landings; secondly, determine gender differences with respect to joint reaction and muscle forces as well as lower extremity kinematics during single-leg landings; and finally, correlate the dependent variables significantly impacted by gender, vertical landing height, and horizontal landing distance main effects and interactions, to two possible non-contact ACL injury risk predictor variables. We hypothesize that females will land with significantly greater peak VGRFs compared to males. We also hypothesized that males and females would demonstrate significantly different lower extremity joint reaction and muscle forces which could explain the higher number of ACL injuries in females.

2. METHOD

2.1 Experimental procedure

Three male recreational athletes with mean (SD) age of 22.8 (1.60) years, heights of 1.80 (0.03) m, and masses of 67.28 (3.52) kg, and three female recreational athletes age of 21.6 (1.20) years, heights of 1.71 (0.02) m, and masses of 64.71 (2.33) kg, were recruited from the university population. Males and females were weight and height matched as closely as possible. None of the participants reported any musculoskeletal or ligamentous injuries to the lower extremity at the time of participation. Prior to data collection, each participant gave informed consent as stipulated by the university ethics review board. Subjects' ages, masses, and heights were recorded. The dominant leg was established as the leg used by the subject to kick a ball.

All participants wore identical shoes (running shoe, model BY004, ASICS America Corporation, Irvine, CA) throughout data collection so as to mitigate variability. Retroreflective markers were affixed with double-sided tape using a customized marker protocol as shown in Figure 1. A motion capture system (Vicon MX, Oxford Metrics, UK) consisting of seven infrared video cameras collected marker trajectories at a sampling rate of 250 Hz. A force plate (Kistler type 9281B, Winterthur, Switzerland) measured GRF data at a sampling rate of 1000 Hz. A Bortec AMT-8 EMG System (Bortec Biomedical Ltd., Calgary, Canada) measured surface electrode EMG of eight major muscles of the dominant leg (biceps femoris, vastus medialis, gastrocnemius, gluteus maximus, medial semitendinosus, tibialis anterior, soleus, and rectus femoris) at a sampling rate of 1000 Hz. Motion, force plate and EMG data were time synchronized.

Subjects began the task by standing on the landing deck with hands placed on their iliac crests, legs shoulder width apart, and the toes of both legs aligned with the edge of the elevated deck. Subjects were then instructed to stand on their dominant leg alone, jump forward, and land as naturally as possible with the dominant foot centered on the force platform. The subjects were asked to keep their hands on their iliac crests throughout the trials to reduce any variability from swinging arms. The participants were instructed to perform the task from an elevated deck of increasing vertical heights (20, 40, and 60 cm) that was placed at increasing horizontal distances (30, 50 and 70 cm) from the edge of the force platform. The nine different landing configurations (combination of landing height and distance) tested were h20d30, h20d50, h20d70, h40d30, d40d50, h40d70, h60d30, h60d50, and h60d70, where *h* represents the vertical landing height and *d* represents the horizontal landing distance. The number after *h* and *d* refers to the heights and distances, respectively, in centimeters. The sequence of landing configuration was randomized to reduce learning effects.

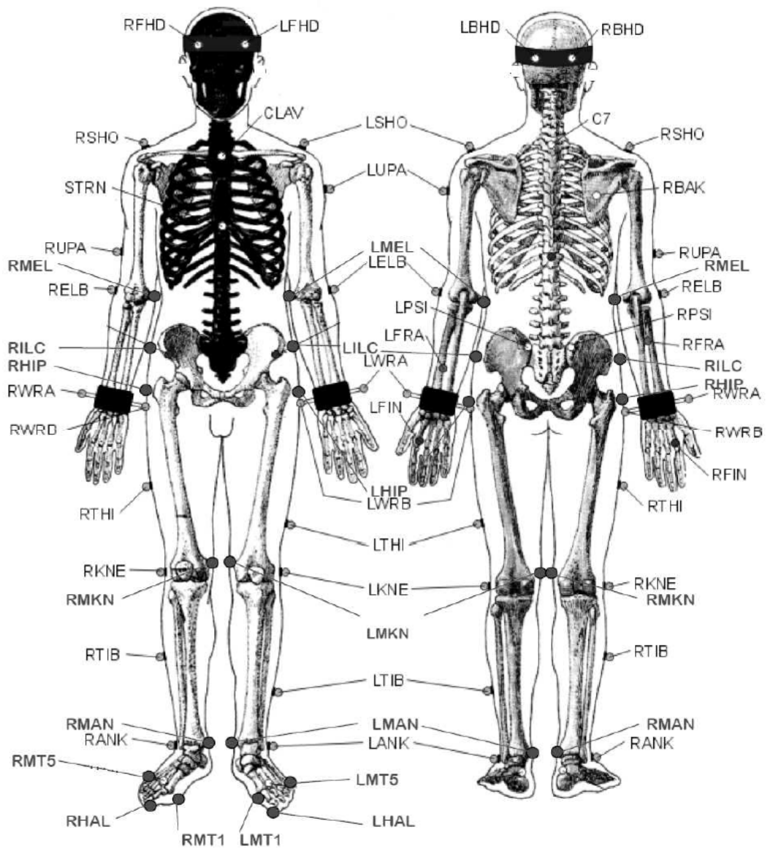


Figure 1. Customized marker set used in this study. Adapted from Oxford Metrics Plug-in-gait marker placement document

2.2 Model development and validation

The AnyBody Modeling System (AMS) software (AnyBody Technology A/S, Aalborg, Denmark) is based on inverse dynamics analysis (IDA) as well as optimization principles, and was used to develop, validate, and simulate the motion of the individualized MSMs used for this study. Inverse dynamics analysis was used to determine the unknown joint reaction and muscle forces from the known motion. Given there are more muscles than there are degrees of freedom (DOF), the redundancy posed by this muscle recruitment problem indicates that there is no unique solution, and as such, the problem is formulated as an optimization problem. In this optimization problem, the objective function is geared towards minimizing the maximum muscle activity subject to equilibrium constraints and positive muscle force constraints (i.e. muscle can only pull). This approach arguably provides more detailed information than rigid body models solved using classical

IDA that cannot calculate muscle forces and consequently cannot be used to assess joint reaction forces. Muscle inclusion is important given during motion the externally applied forces create moments about the joints that have to be balanced by muscles. Since the moment arms of muscles are much smaller than moment arms of externally applied forces, the muscles have to pull relatively more on the bones to obtain equilibrium. So the muscles' contributions to the joint reaction forces are significant and therefore rigid body models using classical IDA devoid of muscles grossly underestimates joint reaction forces. Furthermore, rigid body models using classical IDA often ignores gravity and inertia; that is, they use quasi-static assumption. Details of the mathematical and mechanical methods of the AMS software are described in the literature. (Damsgaard et al. 2006; Rasmussen et al. 2001)

The development of a MSM from the ground up is a very time consuming and complex endeavor. To mitigate these challenges, a publicly shared model repository was created by the AnyBody research group. The GaitFullBody MSM was extracted from this repository, modified for this study, individualized for each subject, validated, and then applied to the single-leg landing trials. The GaitFullBody MSM is based on an anthropometric data set from Horsman *et al.* (Horsman et al. 2007) The motion and force plate data at each landing configuration measured experimentally were used as inputs to the AMS software. The GaitFullBody model was combined with each subject's single-leg landing trials to individualize the model. More specifically, the model was scaled to fit the dimensions of the subject given the retroreflective marker positions relative to each other via an optimization routine. This optimization method simultaneously optimizes the model scaling, local marker coordinates, and model motion during a dynamic trial so as to minimize the differences between model markers and the measured marker trajectories.(Andersen et al. 2009) Once optimized kinematics were derived (determined by mean absolute error less than 0.5 between model kinematics and experimental kinematics), IDA was then performed with a min/max recruitment solver to address the redundancy challenge.(Rasmussen et al. 2001)

The GaitFullBody model included both the major upper and lower extremity joints but only the muscles of the lower extremity in order to reduce computational time. The hips were modelled as a spherical joint, the knee as a revolute joint, and ankle as a universal joint. The GaitFullBody model was actuated by a total of 70 muscles-tendon units –35 muscles on each leg. The model utilized a simple muscle model that did not consider the force-length and force-velocity relationships as well as the passive stiffness of the muscles as the Hill's muscle model does. The muscle attachment sites and geometries were scaled in accordance with a linear geometry scaling law (Eq. 1)(Rasmussen 2005):

$$s=Sp + t \tag{1}$$

where s is the scaled point, S is the scaling matrix, p is the original point, and t is the translation. A length-mass-fat scaling law was used to scale soft tissues, taking into account each subject's body weight, body height and segment lengths. For greater details on the scaling algorithm used for this study, interested readers can consult the work of Rasmussen.(Rasmussen 2005)

Validation of musculoskeletal models is a very challenging task given it is difficult and sometime impossible to measure muscle or joint reaction forces *in vivo*. As a paradox, musculoskeletal models are developed to determine these forces. To corroborate the individualized MSMs, two different approaches were taken; firstly, we compared the predicted and measured muscle activations of eight muscles. The predicted muscle activity should occur at approximately the same time as the measured muscle activity. This information is presented in an on-off timing curve (Figure 2) that shows the time when the measured (fat line) and predicted (thin lines) muscles goes above (turns on) and below (turns off) a threshold of muscle activity during a single-leg landing task. A threshold of 20% was used. A threshold of 20% was chosen to provide a reasonable number of data points to compare predicted and measured muscle activity during landing. As gleaned from Figure 2, the measured muscle activity tends to occur prior to the predicted muscle activity. This is as expected given the latency of muscles response to stimulus is not captured in the individualized MSMs. Further, at each landing configuration the predicted and measured muscle activities can be represented by a linear envelop. The average Pearson product moment correlation (PPMC) between measured and predicted muscle activity for eight muscles and across all landing configurations was 0.58 for a subject. The average PPMC for all six subjects between measured and predicted muscle activity was 0.52. The trend of the measured and predicted muscle activation curves (see sample in Figure 3) look similar but with sudden spikes in predicted data. The reason for the sudden changes in the predict muscle activation is that the inverse dynamics calculation at every time step in the AMS is completely independent of the other.

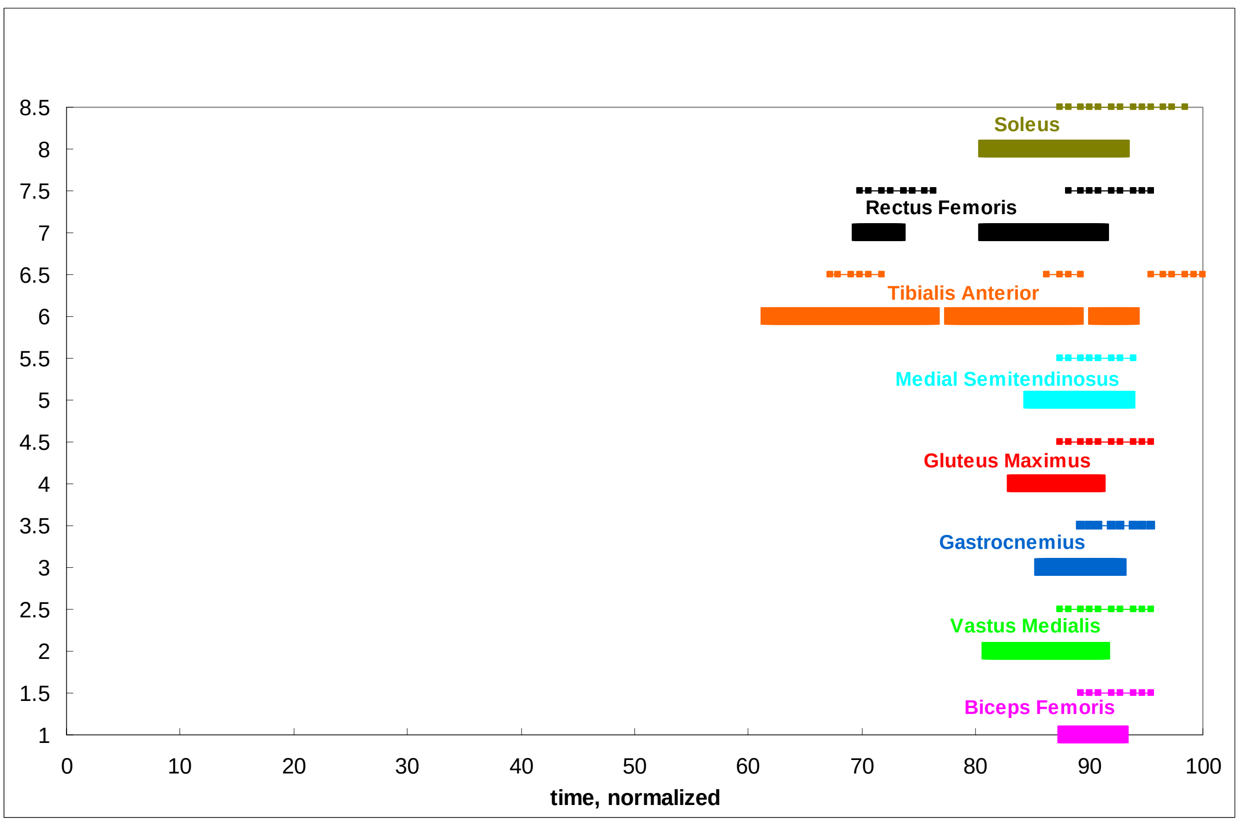


Figure 2. Measured EMG timing (fat line) compared with predicted muscle activity timing (thin line) during single-leg landing.

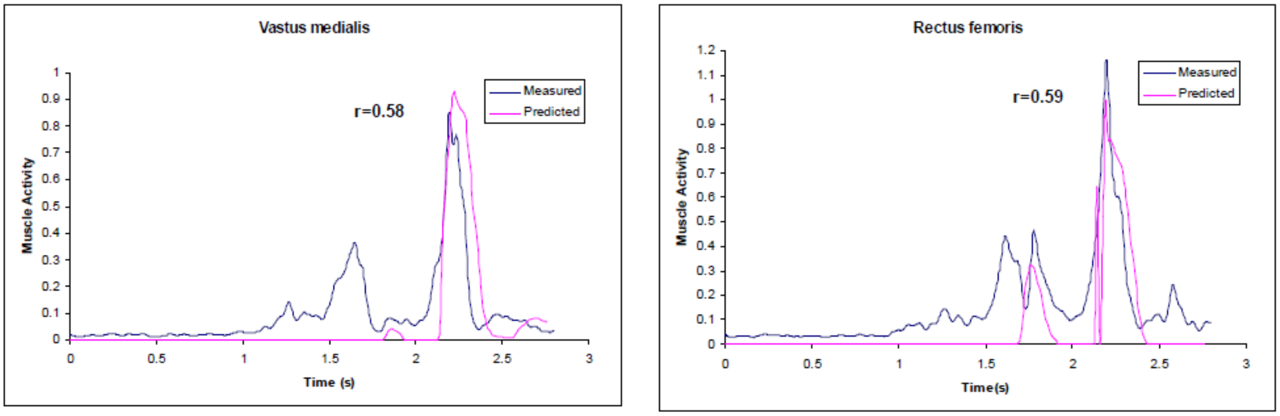


Figure 3. Sample plots showing trends in measured and predicted muscle activity for the vastus medialis and rectus femoris.

Table 1. Comparison of predicted and published *in vivo* knee joint reaction forces during walking gait. Forces are normalized to bodyweight (BW) and moments to bodyweight×body height (BW×BH).

	Predicted knee joint forces and moments by AnyBody MSM during walking gait	***In vivo* knee joint forces and moments from the literature during walking gait**
Fz (%BW) (axial direction)	376.50	223-300 (Heinlein et al. 2009; Kutzner et al. 2010); 250 (Taylor et al. 1998); 320 (Lu et al. 1997); 280 (D'Lima DD 2005; Lu et al. 1998; Taylor and Walker 2001)
Fy (%BW) (medial-lateral direction)	30.78	17-46 (Heinlein et al. 2009; Kutzner et al. 2010)
Fx (%BW) (anterior-posterior direction)	40.50	10-36 (Heinlein et al. 2009; Kutzner et al. 2010)
Mz (%BW×BH)	0.91	0.37-1.23 (Heinlein et al. 2009; Kutzner et al. 2010)
My (%BW×BH)	1.76	0.52-2.57 (Taylor and Walker 2001)

Secondly, the knee joint forces and moments measured *in vivo* from telemetered joint replacements during walking gait and reported in the literature for both males and females (D'Lima DD 2005; Heinlein et al. 2009; Kutzner et al. 2010; Lu et al. 1998; Lu et al. 1997; Taylor and Walker 2001; Taylor et al. 1998) were compared with predicted knee joint forces and moments. The authors recognize that the best way to validate the outputs from the MSMs during single-leg landings would be to compare them to *in vivo* data obtained for the identical task. To the authors' best knowledge, no *in vivo* data on the lower extremity joint forces or moments during single-leg landing exist. To aid model validation and increase confidence in our MSM model, the model was driven with walking gait data collected from the same six subjects that performed the single-leg landing tasks. The walking gait trials were conducted before the single-leg landing trials. The subjects were asked to walk along a 15m raised platform at a speed that closely matched the average speed of participants used in the literature while motion and force plate data were collected. A comparison of the predicted and *in vivo* knee joint forces and moments reported in the literature is provided in Table 1. Given our MSM predictions reported in Table 1 and recognizing variability in body anthropometry between studies (some subjects from in-vivo studies were at least 300N heavier and 10cm taller than the subjects from our population), it appears that the applied individualized MSMs tends to provide reasonable estimates of the internal knee joint moments and medial-lateral joint reaction forces while systematically overestimating the anterior-posterior and axial joint reaction forces. The latter can be controlled in the MSM by adjustment of muscle moment arms, but in the interest of reproducibility, it was elected to not pursue this option.

2.3 Model Application, data reduction and analysis

Upon completion of the validation process outlined above, simulation of the single-leg landing tasks for all subjects was conducted for the nine landing configurations using the validated MSM. An example picture of the individualized validated MSM is provided in Figure 4. Figure 4 presents a validated individualized MSM being applied at a single-leg landing configuration. The time at which peak VGRF occurred was used to determine the joint reaction and muscle forces, as well as, joint kinematics. All kinematic and force plate data were low-pass filtered using a second-order bidirectional Butterworth filter at 6 Hz and 25 Hz, respectively. These data were resampled using linear interpolation, synchronized using events, and then ensemble averaged using MatLab (The MathWorks Inc., Natick, USA). The EMG signal was first rectified and then low pass filtered at a cutoff frequency of 6 Hz using a critically–damped, zero-lag filter. The processed EMG signal was normalized to the maximum measured EMG value for that muscle over all the measurements.

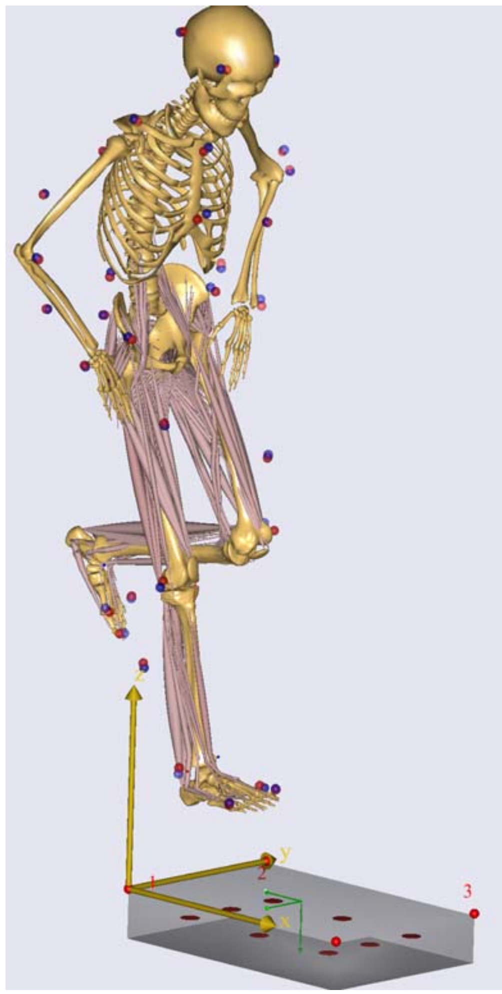


Figure 4. Validated 3D full body MSM of the human body applied to a single-leg landing task.

2.4 Statistical analysis

Multiple 3-way mixed design with repeated measures ANOVAs (2 within subject, 1 between subject) were conducted to test the main effects and interactions of three independent variables (height, distance and gender) on various musculoskeletal dependent variables. In this study, vertical height and horizontal distance were the within subject factors, gender the between subjects factor, and the dependent variables were joint reaction and muscle forces, as well as ankle, knee, and hip flexion angle. Follow up testing entailed Pearson product moment correlations (PPMCs) measured to determine the relationship between the two possible ACL injury risk predictor variables, namely peak VGRF and peak PTASF, and any of the dependent variables from ANOVA analyses significantly affected by height and distance. Statistical analyses were conducted in SPSS (SPSS for Windows, Release 11.5.0), in which a significance level of $\alpha=0.05$ was utilized.

3. RESULTS

This section presents the outputs from the musculoskeletal modelling simulations that tested the main effects and interactions of height, distance, and gender on single-leg landing. The selected outputs from the MSMs, namely, joint reaction forces, muscle forces, as well as ankle, knee and hip flexion angle are presented for the nine different landing configurations. Figure 5 shows the ensemble averages of VGRF, PGRF, and PTASF histories (Figure 5a-c for males and Figure 5d-f for females, respectively), as well as, quadriceps, hamstrings, and gastrocnemius muscle force histories (Figure 5g-i for males and Figure 5j-l for females, respectively) at the nine landing configurations.

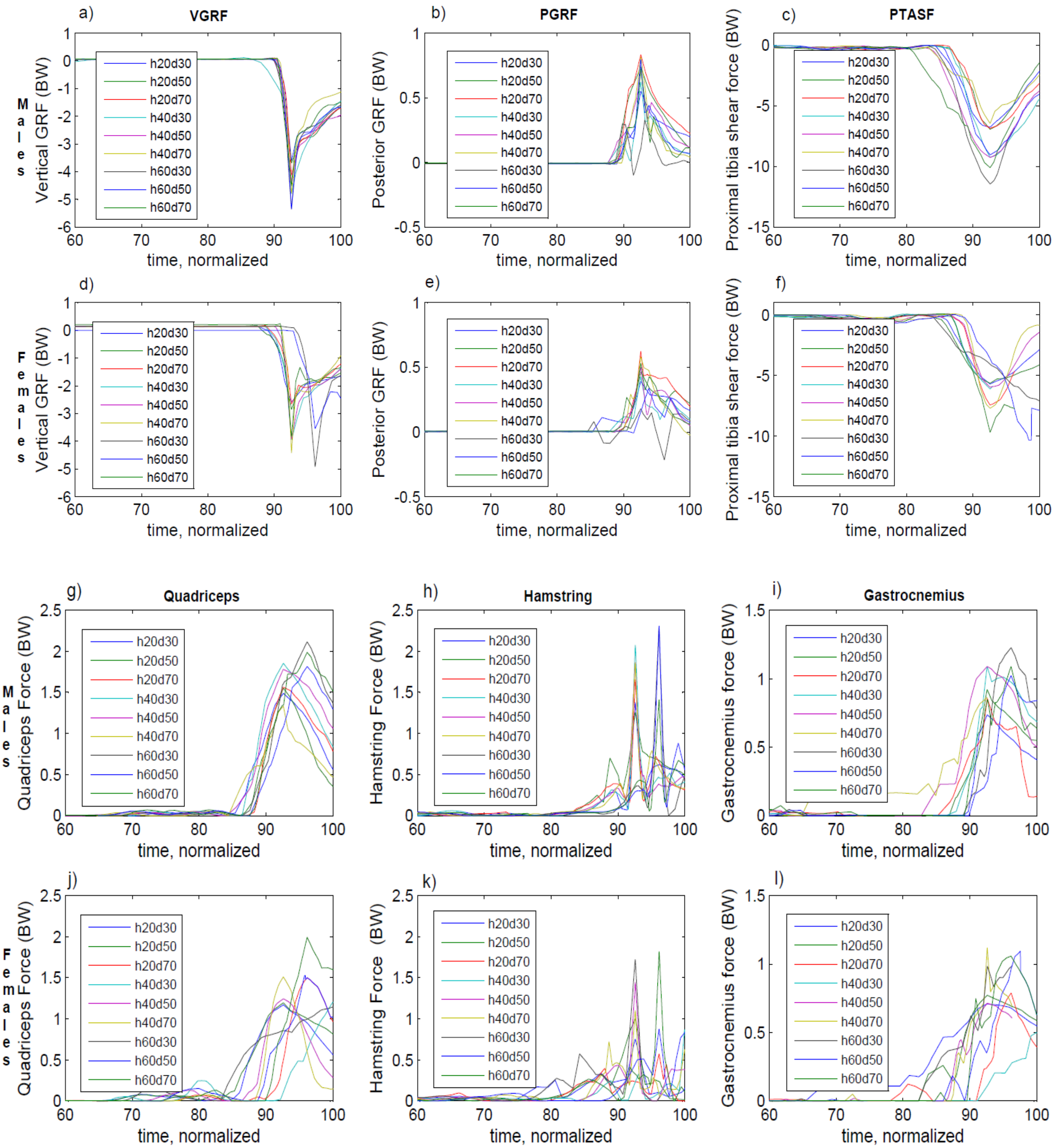


Figure 5. The ensemble averages of VGRF, PGRF, and PTASF histories as well as quadriceps, hamstring, and gastrocnemius muscle force histories during the nine single-leg landing configurations for males (first and third row, respectively) and females (second and forth row, respectively).

The key findings from the separate ANOVAs conducted are shown in Table 2. The results showed a significant main effect for gender $F(1,4)= 11.64$, $p<0.05$, partial $\eta^2=0.744$ with peak VGRF and $F(1,4)=10.515$, $p<0.05$, partial $\eta^2=0.724$ with hip axial compressive force. Here partial η^2 is a measure of effect size with the larger value indicating the more variance the effect explains in the dependent variable. Of the dependent variables studied, females had significantly lower peak VGRF and hip axial compressive forces compared to males (Table 3a and 3b).

Table 2. ANOVA summary showing interactions and main effects observed.

	Dependent Variables										
	Peak VGRF	Peak PTASF	Ankle axial Compressive force	Knee axial Compressive force	Hip axial Compressive force	Quadriceps Muscle Force	Hamstring Muscle Force	Gastrocnemius Muscle Force	Ankle Flexion Angle	Knee Flexion Angle	Hip Flexion Angle
Height	#	$		#	$	*	*	*		#	*
Distance		*							*	#	
Height x Gender											
Distance x Gender						*					
Height x Distance	*	*									
Height x Distance x Gender											
Gender	*				*						

Note:

* p<0.05; # p<0.01; $ p<0.005

TABLE 3. Descriptive statistics (mean ±SD) of risk predictor and dependent variables for males (3a) and females (3b)

3a)

	Males (n=3)								
Dependent Variables	h20d30	h20d50	h20d70	h40d30	h40d50	h40d70	h60d30	h60d50	h60d70
Peak VGRF (BW)	-3.59±0.24	-3.69±0.19	-4.11±0.47	-4.80±0.2	-4.36±0.21	-4.8±0.72	-5.37±0.62	-5.37±0.94	-4.52±0.55
Peak PTASF (BW)	-6.84±2.65	-6.99±2.23	-6.92±2.24	-9.34±3.06	-9.29±1.46	-6.47±2.47	-11.52±3.01	-9.11±2.53	-10.15±1.86
Ankle axial compressive Force (BW)	-11.53±3.18	-12.85±1.98	-12.58±1.26	-14.69±3.07	-14.02±2.47	-11.55±1.66	-14.77±3.39	-13.31±3.52	-13.38±3.08
Knee axial compressive Force (BW)	-9.44±0.49	-10.49±0.78	-10.78±1.44	-13.31±3.54	-11.35±0.41	-11.45±1.38	-14.56±2.63	-13.72±2.38	-11.81±1.45
Hip axial compressive Force (BW)	-11.36±1.05	-11.54±1.01	-11.01±0.39	-16.4±1.83	-16.17±3.06	-14.93±3.87	-18.7±4.21	-18.61±1.58	-13.24±1.19
Quadriceps muscle force (BW)	1.50±0.50	1.57±0.50	1.58±0.44	1.58±0.44	1.79±0.39	1.34±0.53	2.13±0.58	1.83±0.49	2.00±0.50
Hamstrings muscle force (BW)	1.37±0.16	1.25±0.28	1.62±0.90	2.07±0.37	1.84±0.76	1.88±0.51	2.30±0.50	2.31±0.21	1.40±0.43
Gastrocnemius muscle force (BW)	0.74±0.37	0.93±0.22	0.86±0.15	1.10±0.33	1.09±0.23	0.79±0.15	1.23±0.22	1.03±0.26	1.10±0.28
Ankle flexion angle (deg)	48.09±2.58	52.56±5.18	56.55±7.79	51.47±2.47	55.14±5.18	55.75±5.77	51.97±6.49	53.97±4.87	57.71±6.85
Knee flexion angle (deg)	54.67±4.61	54.77±2.27	59.47±6.48	60.54±0.88	67.41±10.19	72.57±8.62	71.23±8.77	74.67±11.26	80.21±10.46
Hip flexion angle (deg)	19.27±5.97	22.52±3.92	30.92±1.81	26.51±2.90	27.10±3.06	27.19±2.77	31.07±8.03	35.96±3.03	38.90±5.66

3b)

	Females (n=3)								
Dependent Variables	h20d30	h20d50	h20d70	h40d30	h40d50	h40d70	h60d30	h60d50	h60d70
Peak VGRF (BW)	-2.69±0.44	-2.97±0.35	-2.75±0.42	-4.09±0.39	-4.07±0.29	-4.59±0.49	-5.14±1.54	-4.04±0.46	-4.25±0.66
Peak PTASF (BW)	-5.90±1.70	-5.82±1.86	-7.71±1.77	-7.27±2.14	-6.48±1.83	-7.96±2.16	-9.77±2.55	-8.08±2.78	-6.45±2.55
Ankle axial compressive Force (BW)	-9.87±3.34	-9.67±2.74	-10.82±3.65	-13.36±1.50	-11.58±1.46	-13.00±1.81	-12.44±3.57	-13.20±5.14	-12.76±5.61
Knee axial compressive Force (BW)	-7.71±2.27	-7.16±2.27	-7.79±2.85	-12.09±2.49	-10.66±1.28	-10.28±0.59	-12.51±3.22	-10.20±2.21	-10.5±2.29
Hip axial compressive Force (BW)	-8.18±1.57	-9.62±1.17	-8.35±0.62	-13.80±3.91	-13.51±3.75	-11.64±0.82	-13.92±4.55	-9.68±0.71	-14.62±3.2
Quadriceps muscle force (BW)	1.21±0.31	1.23±0.44	1.55±0.36	1.24±0.56	1.28±0.37	1.56±0.41	1.22±0.86	1.53±0.34	1.93±0.74
Hamstrings muscle force (BW)	1.03±0.30	1.08±0.27	0.92±0.08	1.61±1.04	1.78±0.83	1.49±0.15	2.18±0.97	1.22±0.05	1.92±0.49
Gastrocnemius muscle force (BW)	0.77±0.31	0.80±0.28	0.82±0.28	0.69±0.24	0.74±0.28	1.16±0.06	1.19±0.36	0.92±0.14	1.10±0.42
Ankle flexion angle (deg)	49.92±5.92	48.05±6.37	53.30±6.68	50.19±12.01	51.54±8.61	53.73±6.60	50.47±8.37	50.75±8.40	51.87±1.77
Knee flexion angle (deg)	47.21±7.35	56.38±11.22	61.04±4.47	52.66±11.24	59.66±11.16	49.67±12.06	65.05±2.65	62.58±6.75	73.96±5.67
Hip flexion angle (deg)	24.38±4.14	27.68±7.34	26.99±10.27	23.70±7.64	25.25±6.12	23.86±5.15	33.78±11.65	33.80±14.09	36.27±7.91

There was a significant distance×gender interaction $F(2,8)=6.85$, $p<0.05$, partial $\eta^2=0.63$ for quadriceps muscle force. From descriptive statistics (Table 3a and 3b), the largest difference in quadriceps muscle force between genders occurred at d=30cm and d=50cm; it is these differences that are significant. It was interesting to find a significant height×distance interaction on both ACL injury risk predictor variables suggesting perhaps that horizontal distance of landing, often not considered in many studies, may be an important variable in single-leg landing biomechanics research. Results revealed no significant height×distance×gender or height×gender interactions (Table 2). ANOVA analysis also showed significant main effects of both height and distance with many musculoskeletal variables (Table 2), and descriptive statistics of these variables are shown in Table 3a and 3b. Given that, for the dependent variables tested, only two variables were significantly different between genders, the data for the male and female subjects were pooled together for subsequent statistical analysis.

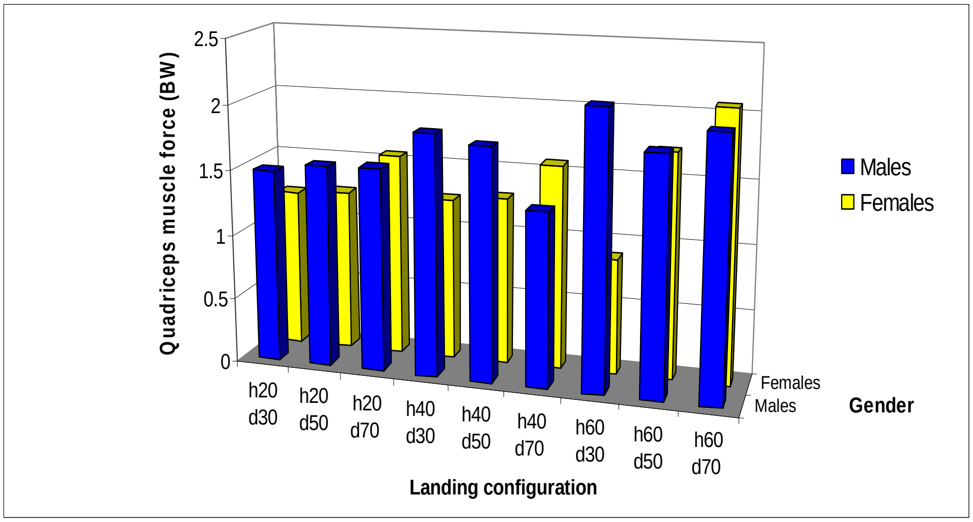
Follow up statistical testing entailed PPMCs measured to determine the relationship among ACL injury risk predictor variables and variables from ANOVA analysis significantly affected by height and distance (Table 4). From Table 4, one can glean some significant associations between the two ACL injury risk predictor variables and the variables affected by the main effects of landing height and distance. Finally, Figure 6a-c shows the normalized muscle force for males (blue) and females (yellow) for the quadriceps, hamstrings, and gastrocnemius at the nine landing configurations.

TABLE 4. The PPMCs among risk predictor variables and variables significantly affected by the main effect of height and distance.

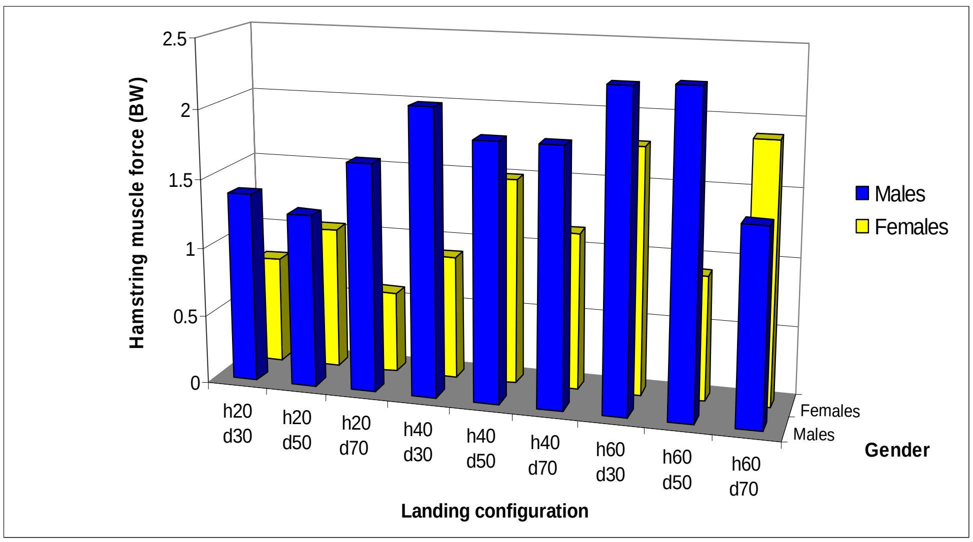
	Subjects (n=6)									
Pearson's Correlation	**Peak VGRF**	**Peak PTASF**	**Knee compressive force**	**Hip compressive force**	**Quadriceps muscle force**	**Hamstring muscle forc**	**Gastrocnemius muscle force**	**Ankle flexion**	**Knee flexion**	**Hip flexion**
Peak VGRF (BW)	1.00	0.33	0.95**	0.98**	0.23	-0.90*	0.15	0.50	-0.06	-0.27
Peak Proximal Tibia ASF (BW)		1.00	0.54	0.29	0.85*	-0.20	-0.88*	-0.82*	0.19	-0.28
Knee compressive force (BW)			1.00	0.93**	0.33	0.81**	0.34	-0.60	-0.14	-0.42
Hip compressive force (BW)				1.00	0.21	0.92*	0.11	-0.48	0.10	-0.19
Quadriceps muscle force (BW)					1.00	-0.17	0.92**	0.91**	-0.31	0.25
Hamstring muscle force (BW)						1.00	-0.25	0.11	0.08	-0.40
Gastrocnemius muscle force (BW							1.00	0.88*	-0.04	-0.08
Ankle flexion (deg)								1.00	0.32	0.13
Knee flexion (deg)									1.00	0.83*
Hip flexion (deg)										1.00

Note:
*p<0.05; **p<0.01

a)



(b)



(c)

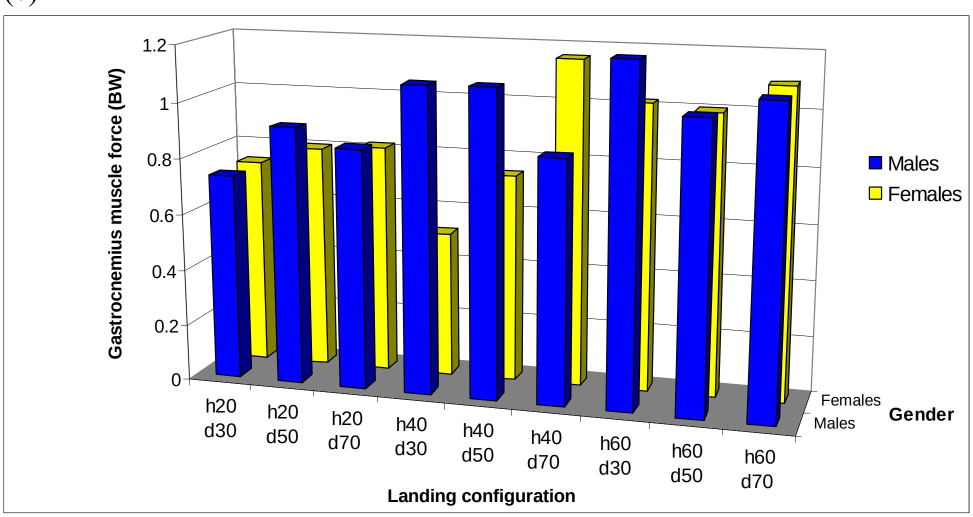


FIGURE 6. The average muscle force for males (blue) and females (yellow) at the nine single-leg landing configurations for the quadriceps (a), hamstring (b), and gastrocnemius muscle (c)

4. DISCUSSION AND CONCLUSION

To assess the risk of non-contact ACL injuries during single-leg landings, as well as to suggest prevention strategies to reduce the likelihood of injuries during such a task, it is imperative to understand the effects of increasing vertical height and horizontal distance of landing on underlying musculoskeletal variables. The literature reviewed clearly identifies the need for MSMs applied to single-leg landings.

This study showed that single-leg landings did not produce the characteristic bimodal VGRF curve commonly reported for double-leg landings.(Dufek and Bates 1990; McNitt-Gray 1993) It appears that the demands of single-leg landings from this study resulted in a rapid increase in GRFs with a single peak (Figure 4a and 4d), which is in agreement with a study by Hargrave *et al.* (Hargrave et al. 2003) This finding is important as it elucidates the unique nature of single-leg landing studies whose findings cannot be compared with double-leg landing studies.

Given this study is the first to report joint reaction and muscle forces during single-leg landing over increasing vertical heights and horizontal distances of landing, there are no studies to which direct comparisons can be drawn, so we cannot confirm that the joint reaction and muscle forces predicted by the MSMs for the various single-leg landing configurations are accurate. We found no gender differences in ankle, knee or hip flexion angle during single-leg landing. This is in agreement with earlier research that showed no difference in ankle flexion angle (Schmitz et al. 2007), knee flexion angle (Kiriyama et al. 2009; Nagano et al. 2007), or hip flexion angle (Lephart et al. 2002; Pappas et al. 2007) between genders during single-leg landings. Given that the single-leg landing tasks in this study were sagittal plane dominant, possibly explains the lack of kinematic differences between genders and these differences may become more pronounced during out-of-plane movements. It is also possible given this study was performed under controlled lab settings without the demands of a competitive sport situation that females landed in a way that was protective of their ACL. Previous studies (Devita and Skelly 1992; Zhang et al. 2000) have reported that internal and external forces at the lower extremity joints can be modulated by body kinematics. The body needs to be in a position that allows the muscles to absorb GRFs. The literature investigating single-leg landings reported females experienced higher VGRF (Pappas et al. 2007; Schmitz et al. 2007) or no difference in VGRF (Lephart et al. 2002) compared to males. This study does not support these findings and revealed females had significantly lower peak VGRF compared to males. The findings that females landed with lower peak VGRF contradicted our hypothesis. Females may have experienced lower peak VGRF upon single-leg landings because of their higher hamstring/quadriceps ratio resulting in softer landings and perhaps lower VGRF.

Further this study suggests that compared to males, females did not exhibit altered quadriceps, hamstrings, and gastrocnemius muscle force characteristics that would increase their risk of ACL injury during single-leg landing which is consistent with previous studies (Fagenbaum and Darling 2003; Pappas et al. 2007). This result did not support our hypothesis that lower extremity muscle forces would be significantly different between genders. Even though we observed significant gender differences in hip axial compressive force, the significance of this finding and its implication for sex differences in ACL injury rates remains unclear.

However, the stability to the knee joint during single-leg landing is provided by surrounding musculature. Several studies (Hewett et al. 1996; Malinzak et al. 2001; Renstrom et al. 1986; Rozzi et al. 1999) have investigated the role of ACL agonist (hamstring and gastrocnemius) and antagonist (quadriceps) on knee biomechanics. Although no statistically significant difference was observed between genders, our findings revealed that, generally speaking, muscle forces are higher in males across all landing configuration except at landing configurations using d=70 cm where males and females had approximately the same muscle force (Figure 6a-c). Further, Figure 6a-c showed that muscle forces in general were the highest for the quadriceps at low vertical landing height (h=20 cm), and highest for the hamstring at higher heights (h=40 cm and h=60 cm). Interestingly, at every height, the quadriceps muscle force increased with increasing distance for females, while this pattern did not hold for males (Figure 6a). This suggests perhaps that longer distance of landing is an important variable among females that should be considered in future single-leg landing studies. Finally, it was also found that the gastrocnemius showed the lowest muscle force of the three major muscles studied.

An early study by Lees (Lees 1981) demonstrated that muscular activity during jump landings can modify GRFs. Many single-leg landing studies in the literature investigating ACL injury do not include the effect of muscles, even though an *in vivo* study (Beynnon and Fleming 1998) demonstrated that an increase in quadriceps activity relative to hamstring activity can significantly increase ACL strain. Despite this, the effect of muscle forces on non-contact ACL injuries remains limited and controversial. To elucidate, a study by McConkey (McConkey 1986) is probably the first to describe eccentric quadriceps contraction as the intrinsic force responsible for ACL injury. Later studies have confirmed that increased quadriceps muscle activation may be a risk factor for non-contact ACL injuries (Chappell et al. 2002; Draganich and Vahey 1990; Hewett et al. 2006; Malinzak et al. 2001; Markolf et al. 2004; Timothy et al. 2007). The results reported here corroborate these findings, showing that an increase in quadriceps muscle force is associated with an increase in peak PTASF. Given that PTASF was used as an indicator of risk of ACL injury, this increase in peak PTASF may result in greater loading on the primary restraint to anterior tibial translation, the ACL.

An early study (Solomonow et al. 1989) suggested that strength training of the hamstring muscles can help prevent injury to the ACL. A number of other studies using various methodologies support this finding showing that the hamstrings can provide a counterbalancing force to protect against quadriceps induced ATT, thereby reducing the risk of ACL injury (Draganich and Vahey 1990; Liu and Maitland 2000; O'Connor 1993). Our results showed hamstring muscle force was significantly correlated to peak VGRF. Our results also revealed that hamstring muscle forces significantly correlated to both knee and hip joint axial compressive forces. These results combined together suggest that increase hamstring muscle force has the potential to reduce the peak VGRF and thereby the risk of non-contact ACL injury.

A cadaveric study (Durselen et al. 1995) and an analytical study (Shelburne and Pandy 1997) both demonstrated that contraction of the gastrocnemius muscles did not strain the ACL over the entire range of knee flexion. The results of an *in vivo* study (Fleming et al. 2001), and an analytical study (Pflum et al. 2004) both contradicted these findings by demonstrating that the gastrocnemius muscle was an antagonist to the ACL. Our results are consistent with these studies and support the notion that gastrocnemius muscle can protect the ACL.

Body kinematics can play a role in terms of its effect on non-contact ACL injury risk. Our results showed that ankle flexion angle was significantly correlated to peak PTASF. These results indicate the potential of increased ankle flexion angle to modulate peak PTASF and subsequent risk to non-contact ACL injury. This finding is in agreement with the literature that showed athletes who injured their ACL had smaller ankle flexion angles (Boden et al. 2009; Madigan and Pidcoe 2003; McNitt-Gray 1993; Self and Paine 2001; Shimokochi et al. 2009).

A limitation of this study is that the MSMs applied in this study did not include the four major knee ligaments but instead modelled the knee as a revolute joint. The literature implicates that these ligaments aid knee stability by limiting the knee’s range of motion.(Beynnon et al. 1997) Another limitation is that the human body was modelled as a rigid structure without including all the detailed deformable structures of the knee joint. This implies that the results need to be interpreted with this in mind as no damping characteristics of the human body were considered. According to a study by Gruber *et al.*,(Gruber et al. 1998) the joint moments can be very high for rigid body models compared to wobbling mass models. It can be argued that findings of this study may be limited given there is equally a limited number of studies supporting peak VGRF and peak PTASF as ACL injury risk predictor variables. A further limitation of this study is that the joint reaction and muscle forces during single-leg landings could not be directly validated. Within these limitations, this study assumes that the applied MSMs are a good starting point for estimating the joint reaction and muscle forces during single-leg landings.

Given the number of variables that can affect the ACL loads *in vivo* and the small sample size may have overlooked some significant differences, our results revealed little gender differences in the musculoskeletal variables investigated and suggests that other factors such as upper body kinematics, out-of-plane kinematics, hormones, fatigue or a combination of all these, may perhaps better explain the gender bias in non-contact ACL injury rate during single-leg landing. Perhaps the risk of non-contact ACL injury is likely multifactorial with no single causative factor being solely responsible for the increased rate. Or perhaps the lack of gender differences in lower extremity kinematics and muscle forces in this study may be attributed to other force absorbing compensatory mechanisms that were not included in this study. Therefore we conclude that factors other than those evaluated in this study needs to be considered when attempting to determine the reasons underlying the gender bias in non-contact ACL injury rate. While the findings stemming from this study requires further corroboration, its ramifications relative to single-leg landing remain tenable.

AVAILABLE FOR DOWNLOAD

The presented model can be downloaded from: http://forum.anyscript.org/.

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CONFLICT OF INTEREST STATEMENT

There are no conflicts of interest in this study from any of the authors.

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7

Summary and Future Studies

In this thesis, two separate reviews of the literature were presented and three more manuscripts based on experimental and computational modeling results were also presented. The first review paper exposed gaps in knowledge about non-contact anterior cruciate ligament (ACL) injury studies. The biomechanics literature on non-contact ACL injury, the existing study methodologies used in this domain and the existing challenges in non-contact ACL injury research, were presented to provide avenues for future research and bring a focus to this doctoral thesis (Manuscript I). Stemming from the review was the requirement to tackle one overarching concern encountered with many studies investigating non-contact ACL injuries, that is, the inability of existing methodologies to comprehensively and completely answer the research questions posed. To address this concern, the authors proposed a novel study approach that employs an AI technique and—once developed— would enable researchers to capture many of the parameters and extreme conditions simultaneously involved during non-contact ACL injuries (Manuscript II).

Stemming from the literature reviews it was determined that further investigations on single-leg landings as a non-contact ACL injury mechanism were warranted. To undertake this, experiments were designed and conducted in a gait laboratory using male and female subjects. Subjects performed single-leg landings from varying vertical heights and horizontal distances while kinematic, kinetic, and EMG data were measured. The effect of increase in vertical height and horizontal distance on single-leg landing kinematics, kinetics, and knee energetics of male subjects is reported in Manuscript III. The main effects and interactions of gender, vertical height, and horizontal distance on various single-leg landing biomechanical variables are presented in Manuscript IV. A key aim of Manuscript IV was to determine if the biomechanical variables investigated can explain the higher rates of non-contact ACL injuries among females. Finally, individualized musculoskeletal models were developed, validated and applied to single-leg landings to determine the effect of increasing vertical heights and horizontal distances on lower extremity joint and muscle forces between genders. These finding were then correlated to variables associated with risk of non-contact ACL injury. The results of this study are presented in Manuscript V.

7.1 Manuscript I

Although some progress has been made to better understand non-contact ACL injuries, information on how and why non-contact ACL injuries occur is still largely unavailable. Hence, the research community is yet to come to a consensus on injury mechanisms and risk factors of non-contact ACL injury. This paper exposes many of the challenges in understanding non-contact ACL injury to date.

It is evident that, in spite of a significant amount of research related to non-contact ACL injury, there are still many unanswered questions about injury mechanisms and conflicting views on which factors contribute to risk of injury. There is a great need to develop new research methods capable of addressing the myriad of factors, high dimensionality, and great interdependencies involved in non-contact ACL injury. This review article unveils that new research modalities and/or coupled research methods are required to better understand how and why the ACL gets injured. Only by achieving a better understanding of ACL loading mechanisms and the associated contributing factors, the scientific community will be able to develop robust prevention strategies and exercise regimens to mitigate non-contact ACL injuries.

7.2 Manuscript II

Many real-world problems today involve the interaction of many disciplines which is particularly the case in most biomechanics research projects. As a result, tying together concurrent activities from disparate disciplines that have a common objective via an optimization technique has become popular (Ali and Behdinan 2003; Kodiyalam and Sobieszczanski-Sobieski 2001; Mavris and DeLaurentis 2000).

A brief overview of the two main domains of optimization, namely, operations research (OR) and artificial intelligence (AI), along with commonly used techniques within these two domains, were introduced. Some of the limitations of existing non-contact ACL injury study approaches confounding our understanding of ACL mechanics were then presented. A review of the literature aimed at identifying non-contact ACL injury studies utilizing OR or AI techniques was conducted. Finally, a new approach aimed at uniting an AI optimization technique with the five existing non-contact ACL injury study approaches in a single unified study paradigm was proposed.

Due to the immense variability in experimental data, as well as the many parameters, constraints, and unknowns incurred in a single multifaceted problem like non-contact ACL injury, a new approach was needed to address such requirements. Moreover, the numerous risk factors which are simultaneously at play during a non-contact ACL injury, as well as, the high dimensionality, great interdependencies, and temporal dependencies, demands the capabilities of some form of an optimization routine. Existing non-contact ACL injury study approaches lack the capabilities required to overcome such challenges. It should be noted that classical optimization techniques, such as the Newton Raphson search method, cannot be applied to the problem of how and why non-contact ACL injuries occur because of the absence of a polynomial-type function. More importantly, it cannot handle many design parameters in a large domain. As an alternative, the authors believe that a stochastic or artificial intelligent (AI) technique should be employed for this purpose.

It was shown that present challenges in non-contact ACL injury studies stem partly from the inability of existing study approaches to simultaneously capture the numerous risk factors and parameters that are at play during ACL injury. These factors and parameters include, but are not limited to, biomechanical, environmental, anatomical and hormonal variables (Griffin *et al.* 2006; Renstrom *et al.* 2008). Many studies have concluded that these factors are responsible for non-contact ACL injuries, but a large number of them have focused only on one aspect of the ACL injury mechanism, thereby failing to capture all factors at once, or simultaneously considering the interactions of the different parameters involved.

To address the limitations of existing non-contact ACL injury study approaches the possibility of a multidisciplinary design optimization (MDO) study paradigm was proposed. This proposed approach intends to enable seamless data exchange from many existing study approaches. Hence, this approach could potentially provide a tool that enables one to have a better global view of the effects of changing numerous contributing factors on risk of non-contact ACL injury. However, this methodology is quite complex and costly and requires tools, expertise, and information from various fields of bioengineering, and therefore, was not undertaken.

7.3 Manuscript III

Since there were no studies investigating body kinematics, kinetics, and knee energetics during single-leg landing from both increasing vertical heights and horizontal distances, this study endeavored to address this gap in knowledge. One way to understand the effect of vertical height and horizontal distance on loading seen at the ACL is to investigate the GRFs experienced during these types of movement. Investigations of how the body kinematics can attenuate these applied forces may provide new insights into the ability of the body to reduce the loading seen at the ACL and subsequently risk of non-contact ACL injury. Based on the findings and in spite of the limitations of this study, it was observed that increasing vertical height had a significant effect on peak VGRF, peak PGRF, knee flexion angle, trunk flexion angle, knee power and knee work. We also observed that increased horizontal distance had a significant effect on peak PGRF, ankle flexion and trunk flexion angle. Our results showed that allowing larger ankle and knee flexion angles may aid in attenuating peak VGRF and peak PGRF, which may promote longer muscle firing patterns to protect the ACL.

7.4 Manuscript IV

The effect of increasing vertical height and horizontal distance on the likelihood of non-contact ACL injury during single-leg landings was compared between genders. Ankle plantar flexion was the only variable determined to explain the disparity in non-contact ACL injury rate between genders during single-leg landings. Moreover, ankle plantar flexion was the only biomechanical variable that showed a significant difference between genders. These findings are consistent with the study by Lephart *et al.* (Lephart *et al.* 2002), which showed no gender differences in hip flexion, and the study by Nagano *et al.* (Nagano *et al.* 2007), which showed no gender differences in knee flexion angle and knee abduction moment. Our results revealed that females exhibited significantly smaller plantar flexion compared to males, which offers a possible explanation for the higher number of non-contact ACL injuries among females, especially given that the literature has demonstrated that larger plantar flexion angles was correlated with the GRFs (Boden *et al.* 2009; Brophy *et al.* 2010; Madigan and Pidcoe 2003; Self and Paine 2001; Shimokochi *et al.* 2009). Further, regression analysis revealed a significant and strong correlation between peak PGRF and ankle plantar flexion angle among males and no significant correlation among females. Hence, a reduction in peak PGRF may be realized by increasing ankle plantar flexion during single-leg landings, which subsequently may reduce the risk of non-contact ACL injury. Perhaps an increase in plantar flexion permits more time to distribute the impact forces and better enables the musculature to absorb these forces, as demonstrated by the following studies (McNitt-Gray 1993; Viitasalo *et al.* 1998).

Test of within-subjects effects revealed that peak VGRF, knee internal rotational moment, hip flexion angle, and trunk flexion angle showed significant height×distance interactions, which implies that horizontal distance of landing—not accounted for in most studies—is an important variable. Our results also suggest that the knee abduction moment can be modulated by increasing trunk flexion. Given there are no single-leg landing studies to draw direct comparisons, double-leg landing studies (Blackburn and Padua 2008; McNitt-Gray 1993; Olsen *et al.* 2004) have shown that increased trunk flexion may reduce the risk of non-contact ACL injuries through reduced contraction demands of knee extensors and increase contraction demands of hip extensors. Our findings are in general agreement with recommendations of Hewett *et al.* (2006) who stated that subjects should land with their chest over their knees to reduce the likelihood of ACL injury.

Perusal of the main effects of height and distance revealed that increased knee flexion angle, hip abduction angle, knee power, knee work and horizontal distance between foot and the body COM or a decrease in vertical distance between foot and the body COM, were associated with a reduction in peak VGRF, thereby demonstrating the ability of these variables to reduce the risk of non-contact ACL injury. In addition, our results revealed that an increase in plantar flexion angle, knee flexion angle, knee power, knee work, and horizontal distance between foot and the body COM or a decrease in vertical distance between foot and the body COM were associated with a reduction in peak PGRF, and suggests reduced risk of non-contact ACL injury. No significant association was observed between knee abduction moment and the biomechanical variables tested, suggesting that knee abduction moment may be less of a predictor of risk of non-contact ACL injury compared to peak VGRF and peak PGRF for single-leg landing tasks. Due to the lack of studies examining body kinematics and kinetics over increasing heights and distances, we are unable to fully compare our results with the literature. Nonetheless, given the number of variables that can affect the ACL loads *in vivo*, our study suggests that factors other than the biomechanical variables studied, such as neuromuscular control, anatomy, or fatigue may be more involved and better explain the gender disparity in the incidences of non-contact ACL injury during single-leg landing.

7.5 Manuscript V

The literature reviewed clearly identified the need for musculoskeletal models (MSMs) applied to single-leg landings. Individualized MSMs were developed, validated, and applied to single-leg landings over increasing vertical heights and horizontal distances. The model was developed and then driven using both male and female motion capture and force plate data. There were no studies in the literature to draw direct comparisons with the findings of this study. However, results from our validation study showed reasonable agreement between measured and predicted muscle activity as well as measured *in vivo* and predicted knee joint reaction forces and moments during gait. The literature suggests that differences in lower extremity kinematics may explain the disparity in ACL injury rates; however, the results of the current study found no gender differences in ankle, knee or hip flexion angle during single-leg landings. Furthermore, our study suggests that compared to males, females did not exhibit altered quadriceps, hamstrings, and gastrocnemius muscle force characteristics that would increase their risk of ACL injury during single-leg landing. It was determined that only peak VGRF and hip axial compressive forces were significantly different between genders, with females exhibiting smaller peak VGRF and hip axial compressive forces compared to males.

Given the number of variables that can affect the ACL loads *in vivo,* the small sample size employed may have overlooked some significant differences, and the extreme demands of the landing tasks, our results revealed few gender differences in the musculoskeletal variables investigated. This suggests that other factors such as upper body kinematics, out-of-plane kinematics, hormones, training, fatigue or a combination of all these, may perhaps help to explain the gender bias in non-contact ACL injury rate during single-leg landing. Perhaps the risk of non-contact ACL injury is multifactorial, with no single causative factor being solely responsible for the increased rate. The lack of gender differences in lower extremity kinematics and muscle forces in this study might be attributed to other force absorbing compensatory mechanisms that were not included. Therefore, we conclude that factors other than those evaluated in this study need to be considered when attempting to determine the reasons underlying the gender bias in non-contact ACL injury rate.

7.6 Recommendations for future research

During this work, a number of key challenges were identified that were not addressed by other researchers. These challenges, once further developed, can help to shed more light and add scientific knowledge to non-contact ACL injury research. To further develop this work the proposed methodology in Manuscript II should be developed and combined with the validated musculoskeletal model developed in Manuscript V. This would allow one to perform experiments in a virtual environment to better inquire into kinematics and kinetics that increase the risk of non-contact ACL injury. The model can be perturbed in a virtual environment manually or iteratively via some optimization criteria to search and find the kinematics and kinetics that results in, for example, excessive peak anterior tibial shear force or excessive peak vertical ground reaction force. Once a certain threshold in these values is exceeded, within certain physiological constraints, the program would stop and the kinematics and kinetics determined. From here, the kinematics, kinetics and anatomical geometries obtained from the MSM could be used as the load case and boundary conditions in a finite element model (FEM) for analysis using software such as ANSYS. The multifactorial approach proposed in this study readily lends itself to coupling with finite element analysis (FEA) software. The benefit of doing this is to enable researchers to study localized motions of a tissue or a joint of interest, and to obtain stresses or strains within the tissue. Presently, the AnyBody Modeling System (AMS) software permits migration of tissue geometries, load cases, and boundary conditions to conduct FEA in ANSYS. There is a significant advantage of this process, as it permits one to apply physiological loads from numerous muscles at a very precise location and moment in time to a joint of interest.

Furthermore, the musculoskeletal model developed can be improved to include the four major ligaments of the knee, as well as perhaps other soft tissues around the knee joint that aid in force attenuation and knee stability. As well, the model should be applied to more out-of-plane movements to better inquire into the effects of tibial rotations and valgus/varus moments suggested by the literature to increase ACL loading.

7.7 Concluding remarks

The literature reviewed clearly identifies single-leg landing as a potentially traumatic activity that increases the risk of ACL injury during sports. To assess this injury potential and suggest motion strategies to avoid non-contact ACL injury, it is imperative to understand the effect of increasing vertical heights and horizontal distances of landing on the underlying biomechanical and musculoskeletal factors which are thought to increase the risk of injury. Hence, it is hoped that the design of experimental, biomechanical model, and musculoskeletal models developed in this research, have contributed new scientific knowledge. This study has presented experimental findings on single-leg landings never before presented in the literature. This study has also presented for the first time a validated musculoskeletal model applied to single-leg landing. This study also proposed for the first time a more comprehensive study approach which can be used to tackle many of the limitations encountered with existing non-contact ACL injury study approaches. Additional testing using a varied and larger subject population, a standardized landing protocol, as well as the application and further validation of individualized musculoskeletal models to injury causing out-of-plane movements is imperative. Further *in vivo*, *in vitro* and computer simulation studies entailing single-leg landings are also needed to corroborate our findings. Our results suggest that future studies should focus on subject-specific as opposed to gender-specific prevention programs.

A

Support Documents

A.1 Ethics Consent Form

Name of researcher:	Mr. Nicholas Ali
Name of supervisor:	Dr. Gordon Robertson Dr. Gholamreza Rouhi
Institution, Faculty, Department:	University of Ottawa, Faculty of Health Sciences, School of Human Kinetics
Telephone numbers:	613-562-5800

Title: Changes in full body kinematics and kinetics during single-leg landing over varying landing heights and distances.

I, ______________________________, agree to participate in the research conducted by Mr. Nicholas Ali of the School of Human Kinetics, Faculty of Health Sciences. The purpose of the research is to determine whole body kinematics and kinetics during the single-leg landing events.

My participation will consist of attending one session lasting approximately 2 hours. In the session, I will have to wear sports clothing and no shoes. I will have my height, weight, age and segment lengths measured. I will then have markers attached to various joint centres of my body. These markers will be attached with double-sided tape, and done in an open setting in the laboratory. In addition, EMG surface electrodes will be attached to the major muscles of my lower extremity using an adhesive tape.

I will be required to perform 1 to 3 single-leg landing at 30, 60 and 90 cm vertical heights and 30, 50 and 70 cm horizontal distance from a force platform; in total there will be 36 trials. During these trials, my landing style will be recorded on a video camera and EMG hard wired telemetry. Movie data will also be collected to aid future data analysis. Force plates will be used to determine the forces that I apply to the ground during landing. During the trials I will be filmed. If I do not wish to be videotaped, I may ask for the video not to be captured. The session will be scheduled at a time mutually agreeable by me and the principal investigator. I will be compensated for documented travel expenses (receipts for gas, bus tickets and parking).

Session date and time: ____

I have assurances from the researcher that all information I share for the study will be strictly confidential. No names will be included in any recorded or published data files. All results and data pertaining to this study will be kept in a secure area during the research process to ensure confidentiality. Video data will be stored on a secure computer in the laboratory at the University of Ottawa. Electronic data will be kept on password-protected computers at the University of Ottawa and can only be accessed by personal access code. The video data will be kept for a period of ten years or less after which they will be destroyed. The only people who will have access to the data are Mr. Ali and his research supervisor, Dr. Gordon Robertson. At no time will my individual results be made available to anyone outside the researchers except to myself upon request. The results will be written in such a way as to conceal the identity of participants. My anonymity will be guaranteed.

I agree that the videotape may be used for public viewing (example: presentation at conferences) for the purposes of research.
_____ yes _____ no

I understand before any of the trials in the testing session I will be given sufficient time to practice the single-leg landing task. I will also be given sufficient rest time between trials. Data capture will not begin until I am ready.

I understand by agreeing to participate in this research, I am helping to identify the kinematics and kinetics patterns of the lower extremity during single-leg landing. This information will be useful to assist athletes and coaches in developing training regimens and injury prevention protocols for jump landing sporting events such as basketball, volleyball, and soccer.

I am free to withdraw from the study at any time for any reason, before or during the testing session, without any negative consequences.

Please choose one of the following options:

If I choose to withdraw from the study, I want the data gathered from me until the time of withdrawal be destroyed. _____

If I choose to withdraw from the study, I accept the data gathered from me be used for the study. _____

If I have any questions with regards to the ethical conduct of this study, I may contact the Protocol Officer for Ethics in Research, University of Ottawa, Tabaret Hall, 550 Cumberland Street, Room 159, Ottawa, ON, K1N 6N5, Tel.: 562-5841, E-mail: ethics@uottawa.ca.

There are two copies of the consent form, one of which I may keep. If any questions arise during the conduct of this research project, I may contact the researcher at the numbers provided at the top of the page.

PARTICIPANT SIGNATURE: ______________________ ***DATE:*** ___________

RESEARCHER SIGNATURE: ______________________ ***DATE:*** ___________

A.2. Certificate of Ethical Approval

File Number: H08-10-07 **Date (mm/dd/yyyy):** 09/27/2010

Université d'Ottawa University of Ottawa

Bureau d'éthique et d'intégrité de la recherche Office of Research Ethics and Integrity

Ethics Approval Notice

Health Sciences and Science REB

Principal Investigator / Supervisor / Co-investigator(s) / Student(s)

First Name	Last Name	Affiliation	Role
D. Gordon E.	Robertson	Health Sciences / Human Kinetics	Supervisor
Gholamreza	Rouhi	Engineering / Mecanical Engineering	Co-Supervisor
Nicholas	Ali	Health Sciences / Human Kinetics	Student Researcher

File Number: H08-10-07

Type of Project: PhD Thesis

Title: Changes in Full Body Kinematics and Kinetics during Single-leg Landing

Approval Date (mm/dd/yyyy)	Expiry Date (mm/dd/yyyy)	Approval Type
09/27/2010	09/26/2011	Ia

(Ia: Approval, Ib: Approval for initial stage only)

Special Conditions / Comments:
N/A

550, rue Cumberland 550 Cumberland Street
Ottawa (Ontario) K1N 6N5 Canada Ottawa, Ontario K1N 6N5 Canada
(613) 562-5841 • Téléc./Fax (613) 562-5338
http://www.research.uottawa.ca/ethics/index.html
http://www.recherche.uottawa.ca/deontologie/index.html