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Timing sequence of multi-planar knee kinematics revealed by physiologic cadaveric simulation of landing: Implications for ACL injury mechanism

Ata M. Kiapour [a,b], Carmen E. Quatman [c,d], Vijay K. Goel [b], Samuel C. Wordeman [c,e], Timothy E. Hewett [c,d,e,f], Constantine K. Demetropoulos [g,*]

[a] Sports Medicine Research Laboratory, Department of Orthopaedic Surgery, Boston Children's Hospital, Harvard Medical School, Boston, MA, United States
[b] Engineering Center for Orthopaedic Research Excellence (ECORE), Departments of Orthopaedics and Bioengineering, University of Toledo, Toledo, OH, United States
[c] Sports Health and Performance Institute, The Ohio State University, Columbus, OH, United States
[d] Department of Orthopaedic Surgery, The Ohio State University, Columbus, OH, United States
[e] Department of Biomedical Engineering, The Ohio State University, Columbus, OH, United States
[f] Departments of Physiology and Cell Biology, Family Medicine and the School of Health and Rehabilitation Sciences, The Ohio State University, Columbus, OH, United States
[g] Biomechanics & Injury Mitigation Systems, Research & Exploratory Development Department, The Johns Hopkins University Applied Physics Laboratory, Laurel, MD, United States

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ABSTRACT

Background: Challenges in accurate, *in vivo* quantification of multi-planar knee kinematics and relevant timing sequence during high-risk injurious tasks pose challenges in understanding the relative contributions of joint loads in non-contact injury mechanisms. Biomechanical testing on human cadaveric tissue, if properly designed, offers a practical means to evaluate joint biomechanics and injury mechanisms. This study seeks to investigate the detailed interactions between tibiofemoral joint multi-planar kinematics and anterior cruciate ligament strain in a cadaveric model of landing using a validated physiologic drop-stand apparatus.
Methods: Sixteen instrumented cadaveric legs, mean 45(SD 7) years (*8 female and 8 male*) were tested. Event timing sequence, change in tibiofemoral kinematics (position, angular velocity and linear acceleration) and change in anterior cruciate ligament strain were quantified.
Findings: The proposed cadaveric model demonstrated similar tibiofemoral kinematics/kinetics as reported measurements obtained from *in vivo* studies. While knee flexion, anterior tibial translation, knee abduction and increased anterior cruciate ligament strain initiated and reached maximum values almost simultaneously, internal tibial rotation initiated and peaked significantly later ($P < 0.015$ for all comparisons). Further, internal tibial rotation reached mean 1.8(SD 2.5)°, almost 63% of its maximum value, at the time that peak anterior cruciate ligament strain occurred, while both anterior tibial translation and knee abduction had already reached their peaks.
Interpretation: Together, these findings indicate that although internal tibial rotation contributes to increased anterior cruciate ligament strain, it is secondary to knee abduction and anterior tibial translation in its effect on anterior cruciate ligament strain and potential risk of injury.

1. Introduction

Over 125,000 anterior cruciate ligament (ACL) injuries occur annually in the United States (Kim et al., 2011), mainly affecting the young athletic population. Non-contact injuries are reported to be the predominant mechanism of ACL injury (>70% of ACL injuries) (Griffin et al., 2000; Henrichs, 2004). These injuries often occur during landing with high ground reaction forces, muscle forces and segmental inertia (Boden et al., 2000; Olsen et al., 2004). Injury prevention strategies are an appealing option to avoid long-term joint instability, pain, and early development of osteoarthritis associated with ACL injury (Agel et al., 2005; Arendt and Dick, 1995; Hewett et al., 1999; Malone et al., 1993), as well as potential loss of sports participation (Maquirriain and Megey, 2006; van Lent et al., 1994) and high costs associated with surgical reconstruction (de Loes et al., 2000).

Noncontact ACL injury mechanisms are multi-planar in nature, involving tibiofemoral joint articulation in all three anatomical planes (Kiapour, 2013; Koga et al., 2010; Quatman et al., 2010). Despite considerable efforts to characterize ACL injury mechanisms (Agel et al., 2005; Arendt and Dick, 1995; Boden et al., 2000; Chappell et al., 2002; Decker et al., 2003; Ford et al., 2003; Griffin et al., 2000; Hewett et al., 1999, 2005; Joseph et al., 2011; Kiapour et al., 2013a,b; Koga et al., 2010; Krosshaug et al., 2007; Malone et al., 1993; Moran and Marshall, 2006; Olsen et al., 2004), the relative contribution of each loading axis in the

* Corresponding author at: Biomechanics & Injury Mitigation Systems, Research & Exploratory Development Department, The Johns Hopkins University Applied Physics Laboratory, 11100 Johns Hopkins Rd, Mail Stop: MP2-N143, Laurel, MD 20723, United States.
E-mail address: constantine.demetropoulos@jhuapl.edu (C.K. Demetropoulos).

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multi-axial (multi-planar) injury mechanism during landing is unclear. Due to the high-rate dynamic environment of injurious events, precise *in vivo* measurements of tibiofemoral joint six-degrees of freedom kinematics, its interaction with ACL tension and the associated timing sequence remain a challenge.

While clinical studies ultimately represent the gold standard for the evaluation of ACL injuries, studies of cadaveric biomechanics (*ex vivo*) under controlled laboratory conditions complement and often precede such work. Biomechanical testing of human cadaveric tissue offers a practical means for the investigation of various disorders, and can evaluate associated conservative and non-conservative treatments. *Ex vivo* techniques serve to enhance our knowledge of joint biomechanics and ligament functions, and generate direct measurements of mechanical parameters (i.e. force and strain) that are challenging, if not impossible to obtain *in vivo*. Further, these techniques provide a standard framework in which to conduct robust parametric studies.

Over the past three decades, extensive efforts have been undertaken to study ACL biomechanics utilizing *ex vivo* approaches (Bach and Hull, 1998; Berns et al., 1992; Butler et al., 1980; Csintalan et al., 2006; DeMorat et al., 2004; Draganich and Vahey, 1990; Durselen et al., 1995; Fukubayashi et al., 1982; Gabriel et al., 2004; Hashemi et al., 2010; Kiapour et al., 2012a; Markolf et al., 2004; Mazzocca et al., 2003; Meyer and Haut, 2008; Oh et al., 2012; Renstrom et al., 1986; Romero et al., 2002; Wall et al., 2012; Wu, 2010; Yeow et al., 2009; Zantop et al., 2007). The majority of these studies simulate low-rate, sub-injurious tasks through the application of static and/or quasi-static loading conditions (Bach and Hull, 1998; Berns et al., 1992; Butler et al., 1980; Csintalan et al., 2006; Draganich and Vahey, 1990; Durselen et al., 1995; Fukubayashi et al., 1982; Gabriel et al., 2004; Kiapour et al., 2012a; Markolf et al., 2004; Mazzocca et al., 2003; Renstrom et al., 1986; Romero et al., 2002; Wu, 2010; Zantop et al., 2007). Reported findings from such studies help to understand ACL biomechanics and overall joint function. However, they are not strong representations of high-rate (dynamic) injurious conditions that occur during high-risk activities (i.e. landing and cutting maneuvers).

Experimental strategies have been developed to replicate high-risk, potentially injurious conditions and reproduce ACL injury (DeMorat et al., 2004; Hashemi et al., 2010; Meyer and Haut, 2008; Oh et al., 2012; Wall et al., 2012; Withrow et al., 2006; Yeow et al., 2009). Such experiments have focused on a variety of causative factors including muscle loading (DeMorat et al., 2004; Hashemi et al., 2010; Wall et al., 2012; Withrow et al., 2008), axial compression (Meyer and Haut, 2008; Wall et al., 2012; Yeow et al., 2009), and off-axis external loads (Meyer and Haut, 2008; Oh et al., 2012; Withrow et al., 2006) to simulate landing. Yet, such models are primarily limited by non-physiologic simulation of dynamic loading conditions (i.e. sharp impact peaks generated by a small mass, lack of muscle forces and insufficient magnitudes of off-axis external loads), unlike those experienced during actual ACL injuries.

Due to the complex, multi-factorial dynamic nature of knee injuries, validated experimental models that simulate realistic inciting events leading to consistent physiologic injuries are essential. Such models can be utilized to study the overall interaction between knee joint kinematics/kinetics with ACL tension and further investigate the relative contribution of each loading axis in the overall risk of ACL injury. Hence, this study aims to develop a novel, physiologic cadaveric model of landing (as a well-established high-risk task in non-contact ACL injury (Olsen et al., 2004; Boden et al., 2000)) in order to investigate detailed interactions between tibiofemoral joint multi-planar kinematics and ACL strain. We hypothesized that there are significant differences in temporal knee joint kinematics in different planes such that the peak knee sagittal and frontal plane motions coincide with peak ACL strain, while knee axial rotation peaks significantly later. Detailed understanding of knee joint dynamic motion during high-risk activities can lead to improved knowledge of ACL injury mechanisms and associated risk factors. This may in turn help clinicians to optimize current prevention and rehabilitation strategies in an effort to minimize the high incidence of ACL injury and early-onset post-traumatic osteoarthritis.

2. Methods

2.1. Specimen preparation

Sixteen unembalmed fresh frozen cadaveric lower limbs, mean 45(SD 7) years (*8 female and 8 male*), were acquired. Each specimen was inspected visually, and by computed tomography (CT) and magnetic resonance imaging (MRI) for signs of soft or hard tissue pathology including indications of prior surgery, mal-alignment deformities and ACL disruption. Specimens were stored at −20 °C. Specimens were slowly thawed to room temperature 24 h prior to testing. Thawed specimens were sectioned at the mid-femoral shaft (30 cm above the joint line) and all soft tissue up to 15 cm proximal to the joint line were dissected. Subsequently, the remaining segment of the proximal femur of each specimen was potted in a 3.8 cm (1.5 in.) diameter polyvinyl chloride (PVC) tube with polyester resin for rigid attachment to the testing frame.

The quadriceps (rectus femoris) and hamstring (semitendinosus, biceps femoris and semimembranosus) tendons were then isolated and clamped inside metal tendon grips to allow for the application of simulated muscle loads. The remaining musculatures along with the skin were maintained intact. The foot and ankle were also maintained intact to provide a realistic load transfer interface. The exposed tissue around the knee joint was kept moist with 0.9% buffered saline solution at all times.

2.2. Testing apparatus

A novel testing apparatus was designed to maintain specimens in an orientation that simulates lower extremity posture during ground strike while landing from a jump (Fig. 1) (Kiapour et al., 2013c; Levine et al., 2013). The unconstrained nature of this experimental setup allows for a broad range of loading conditions (i.e. anterior shear force, knee abduction and tibial axial rotation) to be applied during simulated landing (Levine et al., 2013; Quatman et al., 2013). Each specimen was rigidly fixed at the proximal femur to a fixture with an embedded custom-designed six-axis load cell (B9401, Denton, Rochester Hills, MI, USA). Specimens were positioned inverted with the tibia orientated vertically and the foot positioned above the tibia. The knee was positioned at 25° of flexion to simulate the orientation of this joint during injurious events, as reported by video analyses of ACL injuries (Koga et al., 2010). The femoral fixture was able to rotate and translate about five axes (no translation in the Z-direction) in order to orient the tibia in line with the axis of the impactor, while maintaining 25° of knee flexion.

As shown in Fig. 1, the drop stand apparatus is comprised of two independent platforms (floor and impactor). The lower platform (floor platform) acts to simulate floor contact, while the upper platform (impactor platform) imparts a simulated ground reaction force (GRF) during landing. Six vertically aligned linear bearings (three on each platform) were used to maintain platform alignment and guide the motion of each platform during the simulated landing. A second six-axis load cell (2586, Denton, Rochester Hills, MI, USA) incorporated into the floor platform captured all forces and moments applied to the specimen during simulated landing representing the GRF.

Muscle forces were simulated by multiple cable-pulley systems along with static weights that served to apply constant forces to the quadriceps and hamstring tendons. Adjustable pulley systems were used to maintain the physiologic line of action of each muscle group (Fig. 2). In order to simulate different postures during landing, an external fixation frame with an integrated pulley system was rigidly attached to the tibia. Additional cable-pulley systems along with static weights were designed to produce forces to generate anterior tibial shear, and force couples to generate pure abduction/adduction and internal/

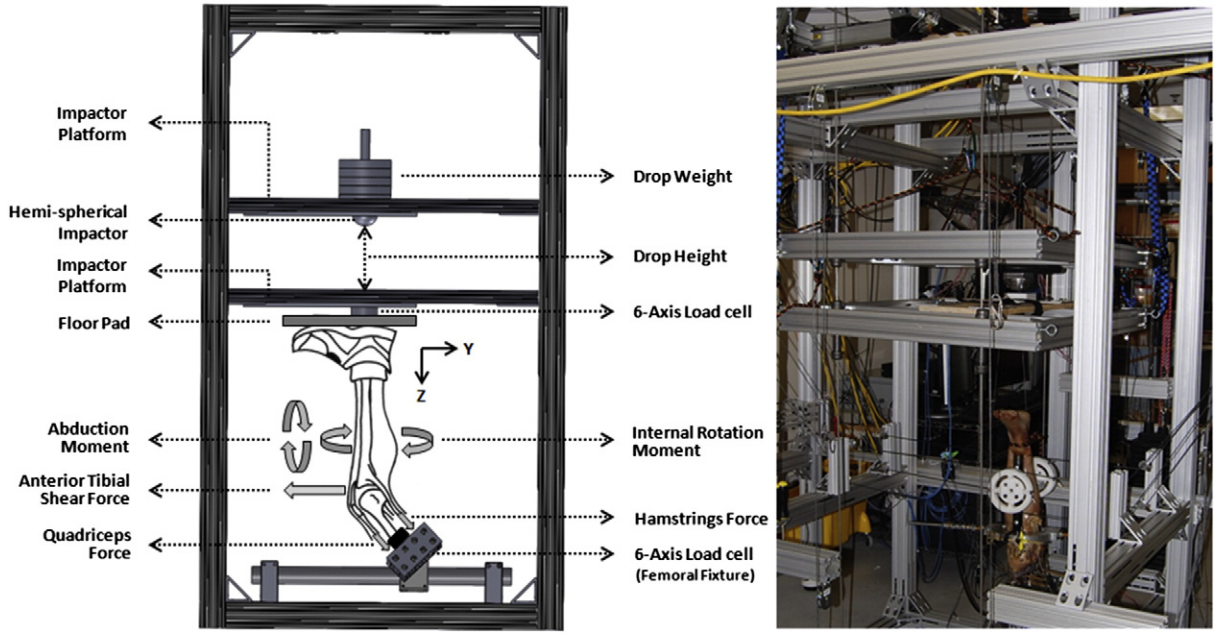

Fig. 1. Custom designed drop-stand testing apparatus.

external rotation moments about the knee without a fixed center of rotation (Fig. 2) (Levine et al., 2013; Quatman et al., 2013). To allow for the unconstrained application of external loads, the distal extremity (lower leg and foot) was free to rotate and translate during loading. Following the application of the muscle and other external loads, the specimen was repositioned through translation/rotation of the femoral fixture in order to vertically align the tibia. An athletic shoe was placed on the foot to provide a more realistic load transfer interface during initial contact. Subsequently, the floor platform was set upon the shoe to simulate a foot-planted position.

A hemi-spherical impactor combined with the weight stack was designed to drop each specified weight from each specified height onto the floor pad (embedded within the floor platform) using varying weight and drop-height magnitudes to achieve different levels of impact severity (Levine et al., 2013; Quatman et al., 2013). The drop weight exerted an impulsive axial compressive force that simulated GRF during landing from a jump. In this study, neutral bi-pedal landing was simulated by releasing half body weight (350 N) from a height of 30 cm in the presence of the pre-tensioned quadriceps (1200 N) and hamstrings (800 N; 400 to each medial and lateral groups). It is important to note that the pre-landing knee extension due to the quadriceps to hamstrings force imbalance was resisted by preventing anterior translation of the foot using a high stiffness cable connecting the foot to the back of the test frame. This fixation only constrained the anterior

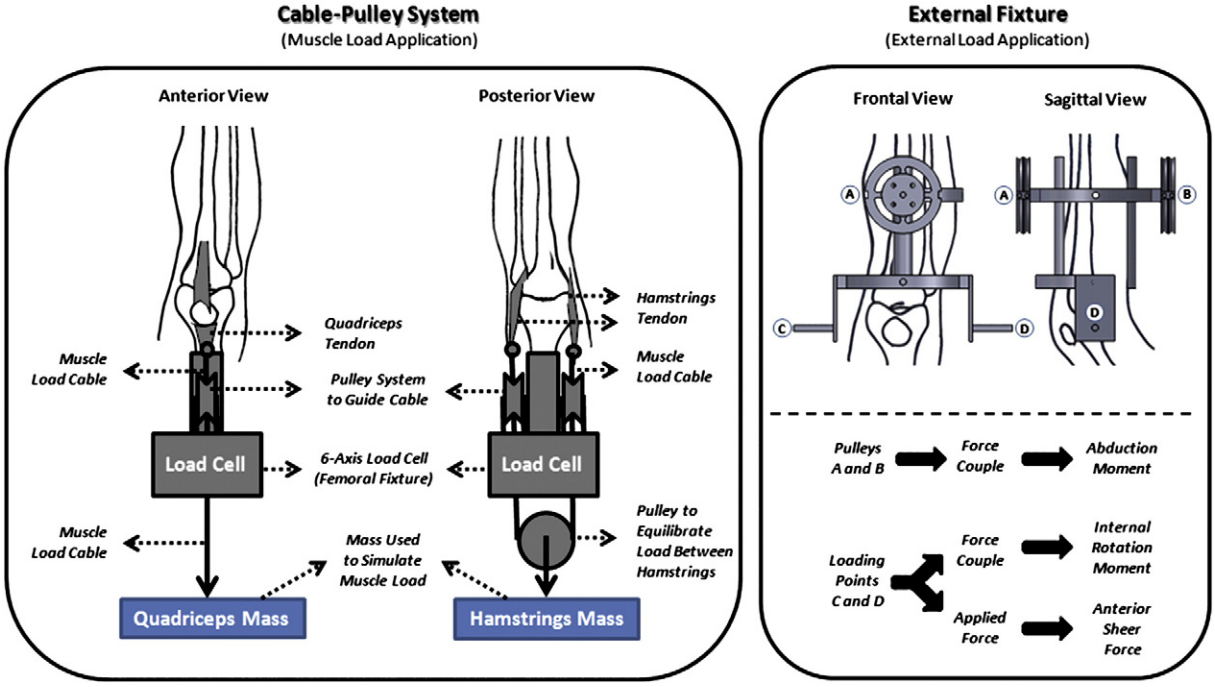

Fig. 2. Cable-pulley system used for application of the simulated muscle loads (left). External fixation frame with the embedded cable-pulley system used for application of external loads.

translation of the foot while preserving the other five-degrees of freedom (2 translations and 3 rotations) within the ankle joint.

2.3. Instrumentation

ACL strain was calculated based on the measurements of a differential variable reluctance transducer (DVRT) (MicroStrain Inc., Williston, VT, USA) that was arthroscopically placed on the distal third of the anteromedial (AM) bundle through two para-patellar incisions (Fig. 3). This system allows for quantification of displacement with an accuracy of 0.1% and the repeatability of 1 μm. In order to calculate absolute strain values, the ACL reference length was calculated based on established methods (Fleming et al., 1994; Howe et al., 1990) as the distinct inflection point in the force versus DVRT displacement curve. These data were collected by placing each specimen through four cycles of anterior–posterior (A–P) shear prior to the testing. The selected inflection point was chosen as the proper reference between ligament taut and slack conditions. Therefore the reference length is not dependent on the initial gage length of the DVRT at the time of insertion. It was assumed that the average strain across the ACL AM-bundle is equal to the change in length of the measured segment divided by the reference length obtained from DVRT measurements using the following equation:

$$\text{Strain}(\%) = \frac{L - L_0}{L_0} \times 100$$

where L is the instantaneous length measured across the DVRT, and L_0 is the length measured across the DVRT at the reference length of the ligament.

Three-dimensional (3D) rigid body motions of the femur and tibia were tracked using arrays of three infrared-LED markers rigidly attached to each bone, and an Optotrak 3020 3D motion capture system (Northern Digital, Waterloo, Ontario, Canada). This system allows for the tracking of rigid body motion with a resolution of 0.01 mm and an accuracy of 0.1 mm. Subsequent to testing, specimens were inspected arthroscopically to document any tissue damage or failure of knee joint structures.

2.4. Data acquisition and processing

Data collection from all data acquisition units was synchronized utilizing a simultaneous trigger. Analog data (load cells and the DVRT) were collected at 4 kHz, while motion data were collected at 400 Hz. A custom macro was developed in Matlab 7.1 (The MathWorks Inc., Natick, MA, USA) to process the data. Six-degree of freedom tibiofemoral joint kinematics were calculated from marker position data. Kinematics were then low-pass filtered using a 4 pole Butterworth filter with a cut-off frequency of 50 Hz (Woltring et al., 1985). Segmental angular velocity and linear acceleration were calculated from rotation and displacement data using a central difference method.

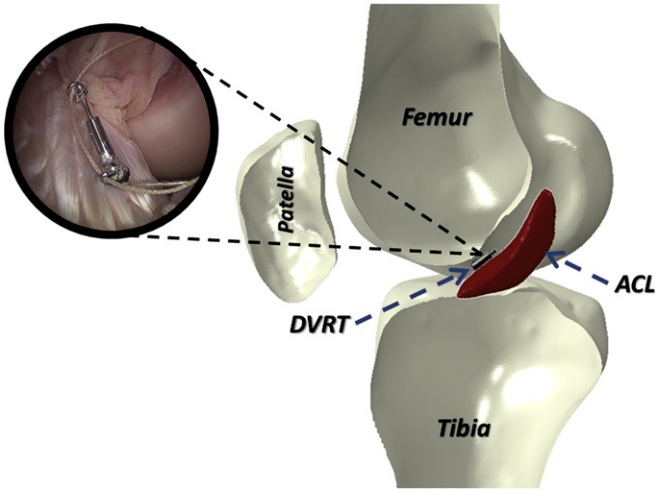

Fig. 3. DVRT insertion on the AM-bundle of the ACL.

2.5. Statistical analysis

A paired sample *t*-test was used to analyze relative changes in tibiofemoral kinematics and ACL strain due to simulated landing under axial impact. Analysis of variance (ANOVA) with a post-hoc Bonferroni Correction for multiple comparisons was used to compare the initiation time from initial contact, time to peak from initial contact, and time to peak from peak axial impact between all measured kinematics and kinetics components. Differences were considered to be statistically significant for $P < 0.05$.

3. Results

Peak axial impact force, ACL strain and tibiofemoral joint kinematic measures are presented in Table 1. Prior to impact, force imbalance between the quadriceps and hamstring muscle groups produced an anterior tibial translation of mean 3.8(SD 3.1) mm and ACL strain of mean 2.1(SD 2.1) %. Simulated pre-impact quadriceps and hamstrings force ratio did not change the initial frontal and axial plane tibiofemoral alignments, and the initial knee flexion angle was maintained at mean 25.0(SD 0.2)°.

Simulated bi-pedal landing resulted in a peak axial impact load of mean 4109(SD 691) N over a period of mean 72(SD 12) msec. A summary of average timing sequences for axial impact load, knee flexion, anterior tibial translation, knee abduction, internal tibial rotation and ACL strain are presented in Table 2. Simulated landings initiated knee flexion, anterior tibial translation, knee abduction, increased ACL strain and internal tibial rotation, sequentially. Internal tibial rotation was initiated significantly later than all other quantified parameters ($P \leq 0.01$ for all comparisons). No significant differences were observed between initiation time of knee flexion, anterior tibial translation, knee abduction and increased ACL strain following initial contact ($P > 0.35$ for all comparisons).

Load generated by axial impact significantly increased: knee flexion angle by mean 0.9(SD 0.8)° ($P < 0.0005$; mean 22.8(SD 8.9) msec after peak impact), anterior tibial translation by mean 7.3(SD 2.3) mm ($P = 0.001$; mean 23.5(SD 8.1) msec after peak impact), knee abduction by mean 2.0(SD 1.4)° ($P < 0.0005$; mean 37.6(SD 22.1) msec after peak impact) and internal tibial rotation by mean 2.8(SD 2.6)° ($P = 0.001$; mean 72.5(SD 25.6) msec after peak impact) compared to the pre-landing condition. Resultant change in tibiofemoral kinematics along with axial impact load increased ACL strain by mean 4.6(SD 2.6) % ($P < 0.0005$; mean 40.3(SD 28.1) msec following peak impact) compared to the pre-landing condition. Simulated landings resulted in a peak angular velocity of mean 68.3(SD 32.0) deg/sec (knee abduction) and mean 70.5(SD 32.3) deg/sec (internal tibial rotation), and peak anterior tibial acceleration of mean 154.7(SD 179.1) m/sec^2. No significant difference was observed between peak abduction angular velocity and peak internal rotation angular velocity ($P = 0.08$).

Peak axial impact occurred significantly earlier than peak knee flexion, anterior tibial translation, knee abduction, internal tibial rotation and ACL strain ($P \leq 0.013$ for all comparisons). While peak anterior tibial translation, knee abduction and ACL strain occurred at approximately 45 msec following initial contact, peak internal tibial rotation occurred significantly later ($P < 0.015$ for all comparisons; mean 86.5(SD 25.1) msec after initial contact). The time-history graph of normalized ACL strain, tibiofemoral kinematics and generated axial impact load for one of the specimens is shown in Fig. 4. No tissue failure was observed across the anatomical structures of the knee following testing.

Table 1
Summary of the peak axial impact load, change in tibiofemoral kinematics and ACL strain.

Specimens				Peak impact	Knee flexion		ATT[a]		Peak abduction	Peak int. rotation	ACL strain	
ID	Sex	Age	Side		Impact induced	Peak	Impact induced	Peak			Impact induced	Peak
1-C080044	F	52	L	3468 N	1.1°	25.8°	5.8 mm	10.9 mm	−0.9°	1.6°	1.4%	3.4%
2-C090105	M	38	L	3188 N	0.1°	24.8°	3.1 mm	8.0 mm	0.6°	0.8°	1.0%	6.9%
3-C080033	M	51	L	3561 N	−0.1°	24.8°	8.6 mm	14.6 mm	1.3°	2.5°	5.6%	8.5%
4-S090574	F	49	R	4050 N	0.8°	26.0°	12.0 mm	16.5 mm	1.7°	4.4°	7.6%	9.4%
5-C090155	M	46	L	4400 N	0.4	25.4°	6.6 mm	5.2 mm	0.9°	1.0°	5.7%	4.4%
6-C090105	M	38	R	4155 N	1.0°	25.9°	4.3 mm	5.3 mm	0.9°	1.9°	9.1%	13.3%
7-C090155	M	46	R	3394 N	0.7°	25.5°	5.4 mm	10.8 mm	0.9°	2.9°	1.7%	6.2%
8-C090361	M	34	R	2869 N	1.6°	26.5°	6.6 mm	7.6 mm	3.8°	5.1°	4.7%	5.1%
9-C090508	F	45	L	5076 N	−0.2°	25.1°	4.9 mm	15.2 mm	2.8°	1.3°	5.7%	9.3%
10-C090508	F	45	R	5036 N	0.7°	25.8°	8.4 mm	8.8 mm	3.6°	8.4°	8.9%	8.5%
11-C080044	F	52	R	3616 N	0.1°	25.1°	6.9 mm	8.5 mm	2.4°	2.3°	2.2%	6.0%
12-C090552	M	45	R	4751 N	0.6°	25.3°	8.9 mm	13.8 mm	3.6°	4.4°	6.4%	7.4%
13-1007889	F	29	R	4483 N	1.3°	26.6°	9.1 mm	12.1 mm	3.9°	6.8°	2.9%	6.4%
14-1008352	F	54	R	4274 N	2.3°	27.3°	9.8 mm	17.6 mm	4.0°	4.7°	2.6%	3.9%
15-C090552	M	45	L	4453 N	1.6°	26.6°	6.4 mm	11.2 mm	2.0°	−0.7°	4.4%	5.7%
16-S090706	F	50	L	4962 N	3.1°	28.2°	9.4 mm	9.9 mm	1.3°	−1.8°	3.7%	2.2%

[a] ATT: Anterior tibial translation.

4. Discussion

Challenges in accurate, *in vivo* quantification of multi-planar knee kinematics and timing sequence during injury hinder the understanding of the relative contributions of each loading axis to the overall injury mechanisms. Biomechanical testing of human cadaveric tissue, if properly designed, offers a practical means to evaluate joint biomechanics and injury mechanisms. The purpose of this study was to investigate the interaction between tibiofemoral joint kinematics and ACL strain in addition to their timing sequence using a novel, physiologic cadaveric model of landing.

A unique, custom-designed drop-stand apparatus with physiologically relevant drop weights and drop heights was employed. Simulated landings from a jump were conducted on sixteen instrumented cadaveric specimens. Event timing sequence, change in tibiofemoral kinematics and change in ACL strain during a simulated bi-pedal landing task were quantified. The proposed cadaveric model of landing demonstrated similar tibiofemoral kinematics and kinetics as reported by *in vivo* biomechanical and video analysis studies, Table 3. Comparisons (*in vivo* validation) were conducted on: landing duration (landing stance) (Chappell et al., 2002; Joseph et al., 2011), time to peak axial impact load (GRF) (Decker et al., 2003), peak knee abduction angular velocity (Joseph et al., 2011), time to peak knee abduction (as percent landing stance) (Joseph et al., 2011), peak anterior tibial acceleration (Moran and Marshall, 2006) and time to peak ACL strain (ACL rupture) (Koga et al., 2010; Krosshaug et al., 2007). These comparisons are compelling, especially in light of the lack of complete active neuromuscular control in cadaveric model, intra-specimen variability in joint geometry and tissue mechanical properties, and the limited sample size compared to *in vivo* biomechanical studies. Moreover, this cadaveric model has been reported to consistently reproduce clinically relevant injury patterns to the ACL (ACL failure in almost 90% of the specimens) and surrounding soft tissue structures (Levine et al., 2013) under injurious conditions. Finally, the resultant tibial plateau injury patterns (both articular cartilage and subchondral bone) were shown to be similar to clinically observed bone bruise patterns across the tibial plateau during actual cases of non-contact ACL injury (Kiapour et al., 2012c; Levine et al., 2013). As a result, the current cadaveric model can be considered a valid approach in simulating landing biomechanics.

Table 2
Summary of the average (SD) timing sequences.

Parameter	Initiation time from IC[a]	Time to peak	
		From IC	From peak axial impact
Axial impact load	–	13.7 (2.4) msec	–
Knee flexion	7.1 (3.5) msec	36.6 (7.8) msec	22.8 (8.9) msec
Anterior tibial translation	7.7 (1.9) msec	37.5 (7.0) msec	23.5 (8.1) msec
Knee abduction	10.8 (6.2) msec	51.5 (22.6) msec	37.6 (22.1) msec
Internal tibial rotation	21.0 (11.7) msec	86.5 (25.1) msec	72.5 (25.6) msec
ACL strain	12.4 (6.3) msec	54.2 (27.0) msec	40.3 (28.1) msec

[a] IC: Initial contact.

The results of this study demonstrate an increase in both anterior tibial translation and ACL strain due to A-P imbalance in simulated knee muscle loads prior to impact. This is in agreement with previous findings demonstrating the anterior translation of the tibia with respect to the femur and increased levels of ACL strain/force or risk of ACL injury under aggressive quadriceps force (Berns et al., 1992; Beynnon et al., 1995; DeMorat et al., 2004; Draganich and Vahey, 1990; Durselen et al., 1995; Hashemi et al., 2010; Li et al., 1999; Quatman et al., 2012; Wall et al., 2012). Simulated landings in this study sequentially resulted in increased knee flexion, anterior tibial translation, knee abduction, ACL strain and internal tibial rotation. This is in agreement with our hypothesis that temporal differences exist in multi-planar knee kinematics during dynamic landing. Previous clinical, video analysis and *in vivo* biomechanical studies indicate that knee flexion, anterior tibial translation, knee abduction and internal rotation of the tibia are associated with landing (Ford et al., 2003; Hewett et al., 2005; Koga et al., 2010; Krosshaug et al., 2007; Moran and Marshall, 2006). Additionally, these factors have been shown to contribute to non-contact ACL injuries at shallow knee flexion angles (Kiapour et al., 2013c; Levine et al., 2013; Meyer and Haut, 2008; Oh et al., 2012).

It was further noted that while knee flexion, anterior tibial translation, knee abduction and increased ACL strain were initiated and reached their maximum values almost simultaneously, internal tibial rotation was initiated ($P \leq 0.01$ for all comparisons) and peaked ($P < 0.015$ for all comparisons) significantly later (Fig. 4). This observed timing sequence highlights the primary role of the anterior tibial translation along with knee abduction in ACL loading and potential risk of injury during landing, as suggested by others (Boden et al., 2000; Ford et al., 2003; Kiapour et al., 2012d; Koga et al., 2010; Krosshaug et al., 2007; Olsen et al., 2004; Shin et al., 2009; Withrow et al., 2006). The concurrent increase in both ACL strain and internal tibial rotation during simulated landings supports internal rotation as a potential risk factor for ACL injury as previously indicated (Kiapour et al., 2012b,d; Meyer and Haut, 2008; Oh et al., 2012). Further, it was demonstrated that internal tibial rotation reached an average of mean 1.8(SD 2.5)°, almost 63% of its maximum value, by the time peak ACL strain occurs, while both anterior tibial translation and knee abduction have already reached their peaks

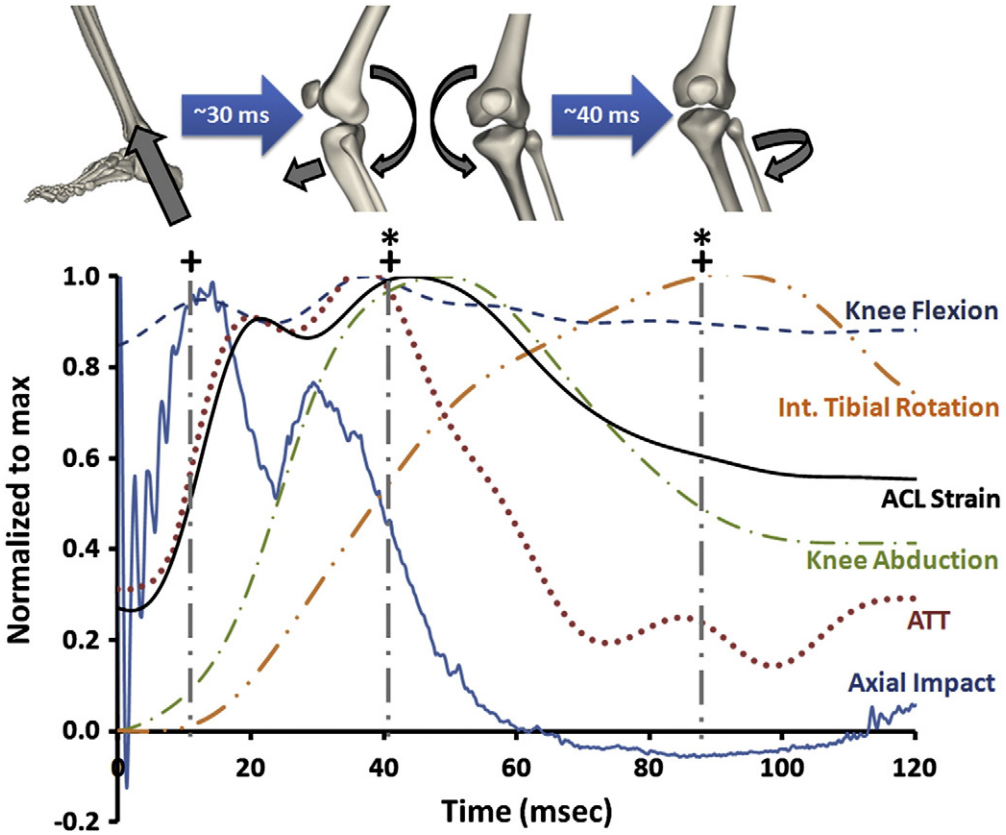

Fig. 4. Time-history graph of the normalized generated axial impact, tibiofemoral kinematics and ACL strain for a typical specimen during simulated landing. (+) Demonstrating significant delay in occurrence of the peak knee flexion, anterior tibial translation, knee abduction, ACL strain and internal tibial rotation following peak axial impact load ($P < 0.013$). (*) Shows significant delay (~40 msec) in occurrence of the peak internal tibial rotation subsequent to the concurrent peak knee flexion, anterior tibial translation, knee abduction and ACL strain ($P < 0.015$).

supporting our hypothesis. Together, these findings imply that although internal tibial rotation contributes to increased ACL strain, it is secondary to anterior tibial translation and knee abduction in affecting ACL strain and potential risk of injury, as noted by the knee joint kinematics timing sequence. This is in agreement with previous findings reporting greater peak ACL strain and higher rates of ACL injury under anterior shear force and abduction moment compared to internal tibial rotation moment (Levine et al., 2013; Quatman et al., 2013).

This is the first study, to the authors' knowledge, to demonstrate the detailed interaction and timing sequence between knee kinematics/kinetics and ACL strain during a simulated landing task using a validated physiologic cadaveric model. Current work builds upon previous cadaveric studies (DeMorat et al., 2004; Hashemi et al., 2010; Meyer and Haut, 2008; Oh et al., 2012; Wall et al., 2012; Yeow et al., 2009) by generating ACL loading via axial compression and muscle loading in an unconstrained manner. This setup was designed to replicate the range of loading observed *in vivo*. Detailed attention to real world loading/impact parameters including body mass, drop height and loading interface resulted in physiologic simulation of knee kinematics/kinetics with a timing sequence similar to *in vivo* data (Table 3).

This evolution in experimental design facilitates the use of a cadaveric model to independently evaluate extrinsic and intrinsic risk factors and underlying mechanisms associated with ACL injury. Data from this study indicates that the most critical dynamic landing scenario that leads to elevated ACL strain levels and potential injury include a combination of anterior tibial translation, knee abduction and internal tibial rotation. Further, the current findings emphasize the significant role of anterior tibial translation and knee abduction as primary contributors, and internal tibial rotation as a secondary contributor to the risk of ACL injury.

Table 3
Cadaveric model vs. *in vivo* biomechanical data (*in vivo* validation).

Parameter	*Ex vivo mean(SD)*	*In vivo mean(SD)*	References
Landing duration	72 (11) msec	75 msec	Joseph et al. (2011)
(*landing stance*)		55 (15) msec	Chappell et al. (2002)
Time to 1st and 2nd	13 (2) msec and 31 (6) msec	10 (3) msec and 40 (10) msec	Decker et al. (2003)
***peak axial impact load* (*GRF*)**			
following initial contact			
Peak abduction angular velocity	68 (32) deg/sec	57 (20) deg/sec	Joseph et al. (2011)
Time to peak knee abduction	55 (22) %	60 (10) %	Joseph et al. (2011)
(*% of landing duration*)			
Peak anterior tibial acceleration	154 (179) m/sec^2	~150 (100) m/sec^2	Moran and Marshall (2006)
***Time to peak ACL strain* (*ACL rupture*)**	54 (27) msec	39 (10) msec	Krosshaug et al. (2007)
following initial contact		~40 msec	Koga et al. (2010)

4.1. Study limitations

As with any study, inherent limitations exist in the current cadaveric study. First, ACL strain was represented by local strain measurements across the AM-bundle. However, the attachment of a second DVRT to the posterolateral bundle of the ACL would have been associated with the compromise of the posterior joint capsule and potential measurement artifacts (Bach and Hull, 1998). The choice to place a single DVRT on the ACL AM-bundle was based on a previous work that found AM-bundle strain to be a good representation of overall ACL strain (Markolf et al., 1990). Another limitation is the potential differences in tissue properties associated with cadaveric specimens compared with the *in vivo* tissue properties of young athletes, which can affect the accuracy of the absolute reported values. We have tried to minimize this artifact by testing relatively young specimens. Moreover, the effect of change in knee flexion angle was not evaluated as all the specimens were tested at 25° of knee flexion, since this flexion angle has been reported during real cases of ACL injury. Additionally, landing was simulated with the foot in a flat position with the ankle joint being semi-constrained to a limited range of dorsi flexion, which does not replicate ankle motion during landing. Finally, the primary and secondary roles of loading factors on the risk of ACL injury have been identified solely based on the temporal characteristics of knee multi-planar kinematics. Despite strong agreement with previous findings, further parametric and sensitivity analyses are required to better characterize the independent role of each loading axis in ACL injury risk.

Current findings are least likely to be affected by this limitation as this study was intended to replicate/investigate the isolated knee joint biomechanical response during the inciting event not the whole multi-joint landing phenomenon. We believe that the qualitative findings and relative comparisons presented in this work minimize such artifacts. Considering the strengths and limitations of this experimental model, the authors believe that it is well suited and able to evaluate the mechanisms of ACL injury.

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