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Review

Anterior cruciate ligament biomechanics during robotic and mechanical simulations of physiologic and clinical motion tasks: A systematic review and meta-analysis

Nathaniel A. Bates [a,b,c], Gregory D. Myer [c,d,e,f], Jason T. Shearn [a], Timothy E. Hewett [a,b,c,d,g,*]

[a] Department of Biomedical Engineering, University of Cincinnati, Cincinnati, OH, USA
[b] The Sports Health and Performance Institute, OSU Sports Medicine, The Ohio State University, Columbus, OH, USA
[c] Sports Medicine Biodynamics Center, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA
[d] Department of Pediatrics, College of Medicine, University of Cincinnati, Cincinnati, OH, USA
[e] Department Orthopaedic Surgery, College of Medicine, University of Cincinnati, OH, USA
[f] Athletic Training Division, School of Allied Medical Professions, The Ohio State University, Columbus, OH, USA
[g] Departments of Physiology and Cell Biology, Orthopaedic Surgery, Family Medicine and Biomedical Engineering, The Ohio State University, Columbus, OH, USA

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ABSTRACT

Investigators use *in vitro* joint simulations to invasively study the biomechanical behaviors of the anterior cruciate ligament. The aims of these simulations are to replicate physiologic conditions, but multiple mechanisms can be used to drive *in vitro* motions, which may influence biomechanical outcomes. The objective of this review was to examine, summarize, and compare biomechanical evidence related to anterior cruciate ligament function from *in vitro* simulations of knee motion. A systematic review was conducted (2004 to 2013) in Scopus, PubMed/Medline, and SPORTDiscus to identify peer-reviewed studies that reported kinematic and kinetic outcomes from *in vitro* simulations of physiologic or clinical tasks at the knee. Inclusion criteria for relevant studies were articles published in English that reported on whole-ligament anterior cruciate ligament mechanics during the *in vitro* simulation of physiologic or clinical motions on cadaveric knees that were unaltered outside of the anterior-cruciate-ligament-intact, -deficient, and -reconstructed conditions. A meta-analysis was performed to synthesize biomechanical differences between the anterior-cruciate-ligament-intact and reconstructed conditions. 77 studies met our inclusion/exclusion criteria and were reviewed. Combined joint rotations have the greatest impact on anterior cruciate ligament loads, but the magnitude by which individual kinematic degrees of freedom contribute to ligament loading during *in vitro* simulations is technique-dependent. Biomechanical data collected in prospective, longitudinal studies corresponds better with robotic-manipulator simulations than mechanical-impact simulations. Robotic simulation indicated that the ability to restore intact anterior cruciate ligament mechanics with anterior cruciate ligament reconstructions was dependent on loading condition and degree of freedom examined.

1. Introduction

Worldwide it is estimated that over 2 million anterior cruciate ligament (ACL) injuries occur annually (Renstrom, 2013). These injuries are devastating to athletic careers and expensive to repair and rehabilitate, as conservative estimates place the cost of an ACL reconstruction (ACLR) surgery at $17,000 plus rehabilitation (Hewett et al., 1999). These surgeries are known to exhibit short-term promise in the restoration of knee function as up to 86% of ACLR patients have a negative pivot-shift score three years post-operative (Beynnon et al., 2002). However, long-term outcomes are less desirable as up to 90% of ACLR patients continue to develop early onset osteoarthritis and knee degeneration within 20 years post-surgery (Lohmander et al., 2007).

In order to optimize preventative and reparative strategies for injured ACLs, it is essential to establish the underlying mechanics that contribute to excessive ligament loads and lead to failure. Approximately 65% of ACL ruptures occur in noncontact situations, which indicate that the injuries are likely influenced by poor neuromuscular control and mechanics, rather than an external impact force delivered directly to the knee joint (Gianotti et al., 2009). Therefore, prophylactic training protocols are effective in the enhancement of neuromuscular control and reduction of the incidence of ACL injuries (Sugimoto et al., 2012). In order to design effective training protocols, the biomechanical contributors to ACL forces and strain must be identified. An expanse of *in vivo* research has been directed at the mechanisms associated with ACL failure and has identified that factors such as excessive knee valgus,

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* Corresponding author at: 2050 Kenny Road, Suite 3100, Columbus, OH 43221, USA.
E-mail address: hewett.12@osu.edu (T.E. Hewett).

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asymmetry, and poor trunk position are associated with increased injury risk (Griffin et al., 2000, 2006; Pappas et al., 2013). Despite their contributions, *in vivo* studies are limited in that direct, invasive measurements of ACL mechanics are unethical to perform on living subjects and the presence of sensors would interrupt native function.

Unlike *in vivo* investigations, during *in vitro* studies investigators can apply invasive techniques that directly evaluate ACL mechanics relative to loads and stresses. *In vitro* studies have been used to reveal the relative contributions of anterior tibial force (ATF) force (Butler et al., 1980), resistance to internal tibial torsion (ITT) (Meyer and Haut, 2008), and muscular contributions to ACL strain (Renstrom et al., 1986). Though valuable, many of these *in vitro* investigations have been used to examine maximal, uniaxial loading, rather than complex multi-planar scenarios that are likely more physiologic. Functional tissue engineering principles indicate that the evaluation of ligament biomechanics within kinematic ranges that mimic *in vivo* activity will likely provide greater clinical relevance than information obtained from non-physiologic methodologies (Butler et al., 2000). Over the past 20 years, investigators have focused on *in vitro* approaches with methods designed to simulate *in vivo* loading conditions from daily activities or clinical settings (Boguszewski et al., 2011; Cassidy, 2013; Fujie et al., 1993, 1995; Hashemi et al., 2007; Howard et al., 2007; Lo et al., 2008; Rudy et al., 1996; Withrow et al., 2006a). Fundamental differences exist among these *in vitro* methodologies as some protocols drive motion with robotic manipulators that apply constant force and actively control limb position, while other protocols drive motion with a singular impulse force and have restraints passively regulate limb position. Though all *in vitro* methods aim to correlate with *in vivo* physiologic conditions, variation in the mechanisms used to drive motion simulations could lead to disparities in biomechanical outcomes. It is important to synthesize *in vitro* data gathered from these varied methods in order to derive optimal ACL injury prevention and treatment recommendations for the clinical environment.

In vitro investigations are particularly conducive to ACLR evaluation as investigators can injure and repair a specimen to make direct biomechanical comparisons between the native and grafted ligaments using repeated measures. ACLR is the primary method used to treat athletes intending to return to sport after ACL injury (Baer and Harner, 2007; Murray, 2009). Functionally, the ACL is the primary resistor to anterior tibial translation (ATT) and patients exhibit anterior–posterior instability at the knee following injury (Butler et al., 1980; Sernert et al., 1999). Surgeons focus on the restoration of this instability during ACLR; however, up to 25% of ACLR patients suffer secondary injuries within two years of returning to sport (Paterno et al., 2010). This rate far exceeds that of primary injury and may indicate that knee mechanics are altered following repair (Baer and Harner, 2007; Gianotti et al., 2009; Hewett et al., 1999). *In vitro* methods can be used to identify altered intra-articular mechanics between native and reconstructed ACLs in order to help explain this disparity in injury incidence.

The objective of this systematic review and meta-analysis was to synthesize the current data and compare robotic and mechanical methods of *in vitro* knee simulation. Specifically, we aimed to investigate the functional behavior of the ACL and ACLR and to analyze differences observed between methodologies. It was hypothesized that the different control mechanisms applied during robotically-driven and mechanical-impact knee simulations would elicit variation in mechanical responses during similar simulated tasks. It was further hypothesized that ACLRs will restore native ATT, but will fail to restore the additional kinetic and kinematic responses relative to the intact ligament.

2. Methods

2.1. Systematic review

A literature search related to methods of knee simulation was performed in the PubMed/MEDLINE, SPORTDiscus, and Scopus databases in May 2013. The systematic review focus was to identify research articles published within the last decade (2004–2013) that investigated *in vitro* ACL biomechanics through knee motion simulation. Search terms were limited to 'anterior cruciate ligament' OR 'ACL' and was further limited with 'robot', 'robotic', 'knee simulator', OR 'knee simulation.' Additional articles were added through cross-referencing the identified studies. As this review focused on functional biomechanics, simulations were limited to physiologic (passive flexion, gait, and jump landing) or clinical (Lachman's and pivot shift test) knee motions. Non-physiologic simulations, such as uniaxial force or torque loading to joint failure, were excluded. Knee conditions included in this review were ACL-intact, ACLD, ACLR, and ACL-only. Inclusion was also limited to whole-ligament biomechanics; thus, any studies that investigated specimens with arthroplasty or individual bundle mechanics were excluded. In order to focus the review to ACL biomechanical contributions in a normal knee, data collected after the selective alteration of additional passive restraint structures within the knee (including but not limited to tibial osteotomy, posterior cruciate ligament resection, or meniscus resection) were excluded. *In vivo* simulations, simulations on joints other than the knee, computer models, computational models, papers without kinematic or kinetic dependent variables, methodology papers, review papers, and non-English articles were also excluded. The initial search compiled 621 published papers, which were then reduced to 77 papers by as documented in Fig. 1. The included papers were divided into 3 classifications of robotic simulation (passive flexion, weight-bearing flexion, and kinematic reproduction) and one classification of mechanical-impact simulation.

2.2. Meta-analysis

Following review, the passive flexion method of robotic simulation was selected for further meta-analysis due to its prevalence and congruity between studies. To reduce confounding factors, force applications were limited to 134 N ATF in the simulated Lachman's test and 10 N m abduction torque combined with 4–5 N m internal rotation torque in the simulated pivot-shift test. Unless otherwise noted, literature that did not adhere to the prescribed loading protocols was excluded from the meta-analysis. Data and standard deviations from the literature were digitized at predetermined intervals (0°, 15°, 30°, 45°, 60°, 90°, 120° of flexion) and an average, weighted relative to the number of specimens in each qualified study, was determined. Standard deviations were used to calculate corresponding standard error of the means at each data point. This was repeated for the ACL-intact, ACLD, and ACLR conditions and the results were plotted (Figs. 2 & 3). Two-sample t-tests ($\alpha = 0.05$) determined the presence of statistical differences between each condition at each interval. ATT, internal tibial rotation (ITR), and ligament forces were tracked due to their consistently reported outcomes in passive flexion simulations during a Lachman's assessment (Fig. 1) and pivot-shift assessment (Fig. 2). This method of analysis was then adapted to assess differences in abduction loading magnitude during pivot-shift tests (Fig. 4), simulated muscle forces during Lachman's tests (Fig. 5), and ACL condition under simulated quadriceps force during Lachman's tests (Fig. 6).

3. Results

3.1. Methods of robotic simulation

In one method of robotic simulation, investigators have used a highly accurate and precise six-degree-of-freedom (6-DOF) robotic manipulator in conjunction with a universal force sensor (UFS) to articulate a specimen through passive flexion with minimal loading (Fujie et al., 1993, 1995). Specimens were resected of soft tissue outside the knee joint, cemented into rigid fixtures, and affixed to the robotic end effector (tibia) and a static frame (femur). Local coordinate frames were identified by anatomical landmarks and were digitized relative to the robot's