Published in final edited form as:

Ann Biomed Eng. 2012 July ; 40(7): 1545–1553. doi:10.1007/s10439-011-0500-5.

Applying Simulated *In Vivo* Motions to Measure Human Knee and ACL Kinetics

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Abstract

Patients frequently experience anterior cruciate ligament (ACL) injuries but current ACL reconstruction strategies do not restore the native biomechanics of the knee, which can contribute to the early onset of osteoarthritis in the long term. To design more effective treatments, investigators must first understand normal *in vivo* knee function for multiple activities of daily living (ADLs). While the 3D kinematics of the human knee have been measured for various ADLs, the 3D kinetics cannot be directly measured *in vivo*. Alternatively, the 3D kinetics of the knee and its structures can be measured in an animal model by simulating and applying subject-specific *in vivo* joint motions to a joint using robotics. However, a suitable biomechanical surrogate should first be established. This study was designed to apply a simulated human *in vivo* motion to human knees to measure the kinetics of the human knee and ACL. In pursuit of establishing a viable biomechanical surrogate, a simulated *in vivo* ovine motion was also applied to human knees to compare the loads produced by the human and ovine motions. The motions from the two species produced similar kinetics in the human knee and ACL. The only significant difference was the intact knee compression force produced by the two input motions.

Keywords

Anterior cruciate ligament; Biomechanics; Activities of daily living; Ovine; Surrogate

INTRODUCTION

Osteoarthritis is a prevalent clinical problem following anterior cruciate ligament (ACL) injury, even after ACL reconstruction.^{18,23,40} Among other factors, the chronic degeneration of the knee joint has been attributed to the failure of current ACL reconstructions to restore the native joint biomechanics.⁴ The ACL serves as the primary restraint to anterior tibial translation and also exhibits 3D forces and moments during daily activities.^{6,9,12,19,25,30,33,34} Following ACL reconstruction, surgeons currently use clinical laxity tests such as the Lachman test to determine the reconstruction efficacy. While this clinical test can at best quantify the relative restoration of anterior tibial translation, the test does not address the other degrees of freedom (DOF) of knee laxity. Additionally, ACL reconstructions have been shown to inadequately restore rotational stability in the knee joint.^{2,11} These abnormal knee motions shift joint contact regions and cause wear to thinner regions of articular cartilage which are not accustomed to higher or frequent loading.⁴ Therefore, the abnormal

knee biomechanics resulting from ACL injury and uncorrected by ACL reconstruction may contribute to an the early onset of osteoarthritis.

To design more effective ACL reconstructions, investigators require design parameters based on normal *in vivo* knee biomechanics for multiple activities of daily living (ADLs). However, the 3D *in vivo* forces and moments of the normal intact knee, as well as those for just the ACL have not yet been determined for any ADL. Walking is the most common dynamic ADL in the general population. While knee kinematics have been measured in humans during walking,^{3,16,22} the joint and tissue forces are impossible to directly measure *in vivo*. Investigators have attempted to measure tissue forces in the human knee during passive flexion/extension motions using implanted force sensors.³² However, ACLs from human subjects cannot be isolated to calibrate the sensors using physiologic loading conditions. Investigators have also estimated knee joint kinetics from inverse dynamics calculations using kinematic and ground reaction force measurements,^{26,38,39} as well as knee models which include muscle contributions.^{21,37,38} Unfortunately, these methods require many assumptions and produce highly variable estimates. Another group has directly measured *in vivo* joint contact forces in knee arthroplasty patients using an instrumented total knee replacement.¹⁰ However, these results may not reflect normal joint loading in a healthy population. While the *in vivo* 3D forces and moments of the knee joint cannot be directly measured in humans, an animal model can be used to simulate the subject-specific 3D kinematics and measure the corresponding 3D knee and ACL kinetics using robotics. Investigators can also use an animal model to investigate the effects of injury and healing, as well as to evaluate the functional efficacy of ACL reconstructions.

The ovine stifle joint has been widely used in orthopaedic research. Investigators have used the ovine model to study the biological, structural, and mechanical effects of injury (including the progression of osteoarthritis), as well as to evaluate surgical treatments.^{5,17,24,27,28,35} The ovine stifle joint consists of the same major soft tissue structures found in the human knee and is a valid surgical model for the human cruciate ligaments.^{1,31} In addition, the ovine stifle joint allows for sensors or marker systems to be rigidly fixed to the tibia and femur to accurately measure the 6 deg of freedom (DOF) kinematics of the tibiofemoral joint.^{15,36} However, there are biomechanical differences between the ovine stifle joint and human knee. The range of flexion exhibited by the ovine stifle joint during gait is approximately half that of the human knee.^{22,36} The human knee is at or near full extension at heel-strike and flexes to about 60° during swing whereas the ovine stifle joint never achieves the straight-leg orientation that the human knee exhibits at heel-strike.^{22,36} Instead, the ovine stifle joint is flexed near 43° at hoof strike and reaches near 77° of flexion during swing.^{22,36} Also, the magnitudes and directions of ACL force significantly differ between human and ovine when subjected to the same anterior tibial loads.⁴³

Knee biomechanics investigations using the ovine stifle joint could provide valuable insight for better understanding the normal function of the human knee, as well as the effects of injury and repair. The long term goal of this research is to minimize joint degeneration after ACL injury by designing more effective ACL reconstructions. To achieve this goal, we plan to use an animal surrogate to establish design criteria and evaluation benchmarks for traditional and tissue-engineered ACL reconstructions based on normal ACL function during ADLs.⁸ To gain a better understanding of human knee and ACL function during an ADL, we first apply a simulated human *in vivo* motion to human knees to measure the 3D kinetics of the human knee and ACL. In pursuit of establishing a viable biomechanical surrogate, we also apply a simulated ovine *in vivo* motion to human knees to compare the knee and ACL loads produced by the human and ovine motions, focusing on the direction of effect. If the simulated motions from the two different species challenge the human knee/

ACL similarly, we would proceed to use the ovine model to establish design criteria for ACL reconstructions and to evaluate ACL reconstructions *in vivo*. The ability to measure knee kinematics for the normal, injured, and surgically-repaired ovine surrogate and to apply these motions to both ovine and human knees would allow investigators to predict the biomechanical effects of various injuries and surgical treatments for the human knee.

MATERIALS AND METHODS

Experimental Design

Six human knees (no pairs) were tested using a 6° of freedom (DOF) robot. A Kuka robot (KR210; Kuka Robotics Corp., Clinton Township, MI) equipped with a 6-axis load cell (Theta Model; ATI Industrial Automation, Apex, NC) was used to reproduce a 6 DOF ovine *in vivo* walking motion measured by Tapper *et al.*³⁶ and a 6 DOF human *in vivo* walking motion measured by Lafortune *et al.*²² Each human knee was subjected to 10 cycles of the ovine gait path and 10 cycles of the human gait path while recording the 3D joint forces and moments. Next, the bony interaction and all soft tissue except the ACL were removed from each joint, leaving the ACL as the only structure transmitting force and moments across the joint. The testing procedures were then repeated for the ACL condition to acquire 3D ACL forces and moments. The intact joint and ACL kinetics were analyzed to determine the differences in joint kinetics produced by the human and ovine motions.

Joint Preparation

Human cadaveric lower limbs (4 female, 2 male, age: 83 ± 4 (SEM) years) were stored at -20°C until the day prior to testing. All human knees were screened for soft tissue injuries and joint degeneration. Each knee was dissected free of all muscles and tendons, leaving the knee joint capsule, the collateral and cruciate ligaments, and both menisci intact. The tibia was then potted in a custom tibial fixture. The detailed joint preparation, including the use of the custom tibial fixture to establish the tibial joint coordinate system¹³ has been reported previously.⁷

Robot Setup

The tibial fixture was attached to the robot and aligned to the robot axes, and the tibial joint center point (JCP) was digitized using a 3D coordinate measurement machine (CMM; Faro Digitizer Model #F04L2; FARO Technologies Inc., Lake Mary, FL). We first attached the tibial fixture to the load cell (attached to the robot end effector) and adjusted the fixture to align the tibial joint coordinate system with the robot and load cell axes. A point on the tibial ACL insertion site (between the tibial spines) was digitized as our tibial JCP. We input the 3D tibial JCP coordinates into our robot software and load cell software so that all rotations and translations were imposed about this point and all forces and moments were recorded about this point. Note that the remaining portion of the setup procedure depended on the motion which was being simulated, due to the different starting positions for the human and ovine motions.

For the *human* motion, we attached the femur to the base fixture and adjusted the joint position to the starting position for the human motion. The robot arm was adjusted to guide the hanging femur onto the femoral base fixture. The forces and moments were zeroed in the load cell software prior to securing the femur to the base fixture. The flexion angle was measured with the CMM and adjusted to 45° , where small translations were used to minimize the forces and moments to $<5\text{ N}$ and $<1\text{ Nm}$, respectively. This flexion angle corresponds to a point during swing where we assume joint loads to be minimal. A portion of the human gait path was applied to move the joint to 20° of flexion, which corresponds to the maximum flexion angle during stance of the human gait path. At this flexion angle, the

anatomical points required to establish the tibial and femoral joint coordinate systems¹³ were marked. These points were then digitized and the 3D coordinates were input into a custom MATLAB program which output the 6 DOF position of the tibial JCP with respect to the femoral JCP and calculated the 3 rotations required to match the rotational positions reported by Lafortune *et al.*²² at mid-stance. The robot was adjusted to achieve these rotations. This process was repeated until each rotational position was validated to within $\pm 0.5^\circ$. The robot was then adjusted to achieve the anterior-posterior and medial-lateral displacements reported by Lafortune *et al.*²² at mid-stance. Subsequently, 500 N of force in compression was applied to the joint. This magnitude was determined from average knee compression forces from unpublished data acquired by Hewett *et al.* We then applied 10 cycles of the human gait path, which reduced the force in compression. The process of applying 500 N was repeated until the joint maintained a compression force of 500 ± 10 N after 10 cycles.

For the *ovine* motion, we attached the femur to the base fixture and adjusted the joint position to the starting position for the ovine motion. The robot arm was adjusted to guide the hanging femur onto the femoral base fixture. The forces and moments were zeroed in the load cell software prior to securing the femur to the base fixture. The flexion angle was measured with the CMM and adjusted to 60.5° , where small translations were used to minimize the forces and moments to <5 N and <1 Nm, respectively. This flexion angle was selected as our ovine starting point because we hypothesized that the joint is minimally loaded at the midpoint of joint flexion during swing since there is an absence of ground reaction forces.

Robot Testing

All tests were performed at room temperature. The intact human knee was subjected to two different simulated motions, each with a different starting position. At the ovine starting position, we applied the first set of 10 cycles of the ovine gait path to precondition the joint, followed by another 10 cycles to record the forces and moments for the intact knee. We then adjusted the robot position to the starting position of the human motion, where we applied 10 cycles of the simulated human gait path to precondition the joint, followed by another 10 cycles to measure the forces and moments for the intact knee. All soft tissue and the distal portions of the femoral condyles were removed to attain the ACL condition. Another 10 cycles of the human gait path were again applied to record the ACL forces and moments. We then adjusted the robot position to the ovine starting position and applied 10 cycles of the ovine gait path to record the human ACL forces and moments for the ovine motion. Finally, the ACL was removed and the forces and moments were recorded for the bone-only conditions of both the ovine and human motions.

Data Analysis

The forces and moments recorded for the bone-only condition were subtracted from the joint and ACL kinetic measurements to eliminate the effect of tibial weight and robot inertia. The 8th and 9th cycles of each 10 cycle test were averaged, normalized to consecutive heel strikes, and used for analysis to eliminate initial cycle effects. For each intact joint and ACL, forces and moments were analyzed in the tibial reference frame based on the knee joint coordinate system.¹³ All forces and moments were analyzed for the stance and swing phases of gait.

Statistical Analysis

All force and moment data was normal and heteroscedastic. For both the intact and ACL conditions, a repeated measures analysis of variance (ANOVA) was performed for the stance and swing phases across all directions of force and moment with the motion as a

fixed factor. *Post hoc* comparisons were performed using a Tamhane correction. The significance level for all comparisons was set at $p < 0.05$.

RESULTS

Intact Joint

The intact knee force and moment measurements (average and peak) for both the applied human and ovine motions are listed in Table 1. The anterior–posterior (A-P), medial–lateral (M-L), compression–distraction (C-D) forces and corresponding flexion angle are plotted for the entire gait cycle in Figs. 1, 2, and 3, respectively.

During both stance and swing phases, only C-D forces (Fig. 3) significantly differed between the human and ovine applied motions. The A-P (Fig. 1) and M-L (Fig. 2) forces, and all directions of moments did not significantly differ between the two motions during stance or swing. During stance, the only significant difference was the larger compression force produced by the human motion ($p < 0.016$); Fig. 3. During swing, the human motion produced a significantly larger compression force than the ovine motion ($p < 0.017$); Fig. 3.

ACL

The ACL force and moment measurements (average and peak) for both the applied human and ovine motions are listed in Table 2. The A-P, M-L, C-D forces and corresponding flexion angle are plotted for the entire gait cycle in Figs. 4, 5, and 6, respectively. During both stance and swing phases, the human and ovine motions did not produce significant force or moment differences.

DISCUSSION

This study investigated the 3D kinetics of the human intact knee and ACL using simulated *in vivo* motions. To our knowledge, this is the first study to measure the 3D intact knee and ACL forces and moments using this methodology. The intact knee and ACL loads reported in this study coincide with findings from previous studies which implemented different methods to estimate these loads. Since we are unable to conduct controlled *in vivo* investigations of injuries and healing in human subjects, a biomechanical surrogate is needed. By applying both human and ovine simulated *in vivo* motions to the human knee, we began to explore the ovine stifle joint as a biomechanical surrogate for the human knee. While the compression–distraction (C-D) force significantly differed between motions for the intact knee, there were no other significant differences between the intact knee or ACL kinetics produced by the human and ovine motions. The method used to apply the human motion may have contributed to the significantly higher compression force produced by the human motion. Since the simulated ovine and human kinematics produced similar intact knee and ACL kinetics, we will proceed to use the ovine surrogate to investigate the biomechanical effects of various knee injuries and repair strategies (e.g. ACL reconstructions).

The human joint compression forces for the simulated human motion are comparable to some previous findings. The peak compression forces reported in this study are comparable to some previous estimates of human tibiofemoral contact forces. Several studies applied inverse dynamics approaches to estimate joint compression forces of 2.0–3.0 BW, with some estimates as high as 6.0 BW, for the normal human knee joint during level walking.^{14,26,41} Alternatively, D'Lima *et al.*¹⁰ used instrumented total knee replacements to measure compression forces of 1.8–2.5 BW for treadmill walking. Our average human knee compression forces (Human–Human condition) peaked at 1232 ± 112 (SEM) N which would correspond to ≈ 2.0 BW in a 63 kg individual. Unfortunately, we had no knowledge of

the actual body weights. Thus, we applied 500 N of compression force to each human knee prior to applying the human motion, based on average knee compression forces from unpublished data acquired by Hewett *et al.* In comparison to a previous study in which Thambyah *et al.*³⁹ used inverse dynamics techniques to calculate an average compression force of 779 N at mid-stance and a peak compression magnitude of 2075 N, we applied only 500 N of compression force at mid-stance and reached a peak compression magnitude of only 1232 N. For future studies, we will investigate using a higher compression force at the mid-stance starting position for the human motion.

The restraining roles of the human ACL reported in this study are similar to those previous findings^{6,9,12,19,25,30,33,34} but the ACL loads reported in this study are lower than those previously reported for human gait using computational modeling. For both input motions, the ACL restrained anterior, medial, and distraction displacements, as well as adduction, external, and flexion rotations. It is not possible to directly compare our results to previous ACL biomechanics studies which were conducted using simulations of clinical tests rather than actual *in vivo* motions. However, the directions of anatomical displacements and rotations restrained by the ACL in this study coincide with previous findings that the human ACL serves as a major restraint to anterior tibial translation^{9,25,33} and a secondary restraint to medial tibial translation, joint abduction/adduction, and joint flexion.^{6,12,19,30,34} Shelburne *et al.*³³ used knee computational models to estimate ACL kinetics during walking in young healthy subjects. They reported an estimated peak ACL load of 303 N which is much higher than the peak resultant ACL load of 52 N (averaged across subjects) which we measured during stance by applying the human motion to the human ACL. A limitation of this study which could have contributed to lower forces in the intact human knees and ACLs was the use of cadaveric knees from elderly subjects. The *in vivo* human motion which was simulated in this study was an average of motions acquired from young healthy subjects.²² However, the simulated motion was applied to older knees which exhibit reduced biomechanical properties compared to the knees of young healthy subjects.^{20,42} Although all joints were screened for soft tissue damage and signs of osteoarthritis, some cadaveric ACLs were minimally loaded when subjected to the human motion and thereby increased the deviation among samples.

This study had other limitations. The methods used to apply the ovine and human motions differed. The best method for each motion was selected based on the *in vivo* data that was available. The ovine motion was initiated during swing, where joint forces and moments were assumed minimal. Alternatively, the human motion was initiated at mid-stance, where 500 N was applied to the joint. Another limitation was that we applied average *in vivo* motions in this study. Ideally, the subject-specific kinematics for each joint should be recorded *in vivo* and applied to the same joint since the joint morphology and biomechanics will vary among subjects. Using an animal model, this methodology would allow for the measurement of 3D kinetics that would be more indicative of *in vivo* forces and moments. Finally, the limitations of our robot methodology including testing at room temperature have been reported previously.⁷

The results of this study suggest that although there are biomechanical and morphological differences between the human knee and ovine model, the walking kinematics of the two species produce similar loads in the human knee. There are differences between the knee kinematics of the two species during gait, notably the considerably smaller range of flexion in the ovine joint.³⁶ Although the ovine stifle joint contains all of the major soft tissue structures of the human knee, there are differences in joint size and morphology between the ovine stifle and human knee joints.^{1,29} However, the 3D kinetic measurements suggest that there are similarities in the knee kinetics produced by the motions of the different species.

With the exception of compression-distraction forces, the ovine and human motions did not produce significantly different forces and moments in the human intact knee.

These findings have important implications for designing future studies. Since the normal ovine and human motions produced similar human knee kinetics, applying ovine *in vivo* motions recorded for injury and repaired conditions to human knees may provide helpful parameters for the development of treatments for the human knee. We have also begun to measure and simulate the subject-specific 3D kinematics of normal and injured ovine knees to measure the corresponding 3D joint and ACL kinetics. Applying subject-specific kinematics should provide more accurate estimates of *in vivo* joint and ACL forces. Using ovine stifle joint kinematics for normal, injury, and repaired conditions, we plan to establish design criteria and evaluation benchmarks for traditional and tissue-engineered ACL reconstructions with the long term goal of minimizing joint degeneration after ACL injury.

Acknowledgments

This work was partially supported by NIH grants EB004859 and AR056660. The authors do not have any conflicts of interest.

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FIGURE 1. Anterior/posterior force of the intact knee for the human motion (left) and ovine motion (right); $N=6$.

FIGURE 2. Medial/lateral force of the intact knee for the human motion (left) and ovine motion (right); $N=6$.

FIGURE 3.

Compression force of the intact knee for the human motion (left) and ovine motion (right); $N=6$.

FIGURE 4. Anterior ACL force for the human motion (left) and ovine motion (right); $N=6$.

FIGURE 5. Medial ACL force for the human motion (left) and ovine motion (right); $N=6$.

FIGURE 6. Distraction ACL force for the human motion (left) and ovine motion (right); $N=6$.

TABLE 1

Intact knee forces and moments produced by the human and ovine motions.

	Human motion			Ovine motion		
	Avg. $\pm$ SEM	Direction	Peak	Avg. $\pm$ SEM	Direction	Peak
Stance phase						
Forces (N)	12.6 $\pm$ 31.2	Posterior	135	49.0 $\pm$ 10.3	Posterior	74.8
	33.6 $\pm$ 23.5	Medial	47.8	34.6 $\pm$ 15.3	Medial	38.1
Moments (N-m)	609 $\pm$ 45.8	Compression	1.23 $\times 10^3$	202 $\pm$ 91.7	Compression	238
	10.7 $\pm$ 6.95	Adduction	18.1	9.29 $\pm$ 3.26	Adduction	10.2
	2.22 $\pm$ 2.26	Extension	12.4	3.59 $\pm$ 0.866	Extension	4.35
	2.09 $\pm$ 1.89	Internal	5.24	1.56 $\pm$ 0.654	Internal	2.34
Swing phase						
Forces (N)	23.2 $\pm$ 29.7	Posterior	135	0.711 $\pm$ 8.03	Posterior	71.3
	27.8 $\pm$ 30.6	Medial	42.6	13.4 $\pm$ 8.66	Medial	34.6
Moments (N-m)	522 $\pm$ 115	Compression	1.23 $\times 10^3$	98.1 $\pm$ 60.2	Compression	215
	6.72 $\pm$ 5.06	Adduction	17.6	2.85 $\pm$ 2.20	Adduction	9.94
	6.52 $\pm$ 2.90	Extension	21.4	1.45 $\pm$ 1.24	Extension	4.35
	0.584 $\pm$ 0.852	Internal	2.33	0.0392 $\pm$ 0.297	Internal	2.29

TABLE 2

ACL forces and moments produced by the human and ovine motions.

	Human motion			Ovine motion		
	Avg. $\pm$ SEM	Direction	Peak	Avg. $\pm$ SEM	Direction	Peak
Stance phase						
Forces (N)	24.0 $\pm$ 8.45	Anterior	41.4	0.0480 $\pm$ 0.0964	Anterior	0.256
	8.78 $\pm$ 2.95	Medial	16.3	0.0327 $\pm$ 0.0636	Medial	0.224
	17.5 $\pm$ 6.28	Distraction	26.8	0.175 $\pm$ 0.0657	Distraction	0.345
Moments (N-m)	0.445 $\pm$ 0.154	Adduction	0.868	0.0136 $\pm$ 0.0191	Adduction	0.071
	1.56 $\pm$ 0.593	Flexion	2.82	Negligible load (<0.01 N-m)		
	0.104 $\pm$ 0.0405	External	0.176	Negligible load (<0.01 N-m)		
Swing phase						
Forces (N)	15.1 $\pm$ 5.94	Anterior	28.9	12.6 $\pm$ 6.58	Anterior	35.0
	7.95 $\pm$ 3.31	Medial	14.3	4.25 $\pm$ 2.52	Medial	12.6
	9.38 $\pm$ 3.49	Distraction	21.37	5.30 $\pm$ 2.65	Distraction	13.0
Moments (N-m)	0.420 $\pm$ 0.199	Adduction	0.857	0.197 $\pm$ 0.217	Adduction	0.662
	1.02 $\pm$ 0.410	Flexion	1.94	0.877 $\pm$ 0.475	Flexion	2.38
	0.0805 $\pm$ 0.0456	External	0.143	0.0778 $\pm$ 0.0598	External	0.216