Journal of Biomechanics 88 (2019) 78–87

Contents lists available at ScienceDirect

Journal of Biomechanics

journal homepage: www.elsevier.com/locate/jbiomech
www.JBiomech.com

Three-dimensional *in vivo* kinematics and finite helical axis variables of the ovine stifle joint following partial anterior cruciate ligament transection

Kristen I. Barton [a], Mehdi Shekarforoush [a,b], Bryan J. Heard [a], Johnathan L. Sevick [a,b], C. Ryan Martin [a,c], Cyril B. Frank [1], David A. Hart [a,c,d,e], Nigel G. Shrive [a,b,*]

[a] McCaig Institute for Bone & Joint Health, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada
[b] Schulich School of Engineering, University of Calgary, Calgary, AB, Canada
[c] Section of Orthopaedics, Department of Surgery, Foothills Hospital, Calgary, Alberta, Canada
[d] Faculty of Kinesiology, University of Calgary, Calgary, AB, Canada
[e] Bone & Joint Strategic Clinical Network, Alberta Health Services, AB, Canada

ARTICLE INFO

Article history:
Accepted 13 March 2019

Keywords:
Kinematics
Anterior cruciate ligament
Post-traumatic osteoarthritis
Knee joint
Knee injury

ABSTRACT

Partial anterior cruciate ligament (p-ACL) rupture is a common injury, but the impact of a p-ACL injury on *in vivo* joint kinematics has yet to be determined in an animal model. The *in vivo* kinematics of the ovine stifle joint were assessed during 'normal' gait, and at 20 and 40 weeks after p-ACL transection (Tx). Gross morphological scoring of the knee was conducted. p-ACL Tx creates significant progressive post-traumatic osteoarthritis (PTOA)-like damage by 40 weeks. Statistically significant increases for flexion angles at hoof-strike (HS) and mid-stance (MST) were seen at 20 weeks post p-ACL Tx and the HS and hoof-off (HO) points at 40 weeks post p-ACL-Tx, therefore increased flexion angles occurred during stance phase. Statistically significant increases in posterior tibial shift at the mid-flexion (MF) and mid-extension (ME) points were seen during the swing phase of the gait cycle at 40 weeks post p-ACL Tx. Correlation analysis showed a strong and significant correlation between kinematic changes (instabilities) and gross morphological score in the inferior-superior direction at 40 weeks post p-ACL Tx at MST, HO, and MF. Further, there was a significant correlation between change in gross morphological combined score (ΔGCS) and the change in location of the helical axis in the anterior direction (ΔsAP) after p-ACL Tx for all points analyzed through the gait cycle. This study quantified *in vivo* joint kinematics before and after p-ACL Tx knee injury during gait, and demonstrated that a p-ACL knee injury leads to both PTOA-like damage and kinematic changes.

1. Introduction

Anterior cruciate ligament (ACL) ruptures are common knee injuries, with an estimated 250,000 ruptures a year in the United States alone (Griffin et al., 2006). Concomitant injuries and sequelae including damage to the meniscus, medial collateral ligament, and articular cartilage are also common (Lohmander et al., 2007; Murrell et al., 2001; Noyes et al., 1980). ACL rupture leads to relative joint instability and, if left untreated, can result in tissue damage and lead to the development of post-traumatic osteoarthritis (PTOA) (Lohmander et al., 2007). However, although most patients opt for ACL reconstruction in attempt to restore the biomechanical function of the knee joint, this does not reliably prevent PTOA despite the restoration of relative joint stability (Barenius et al., 2014; Leiter et al., 2014).

The ACL is comprised of two distinct functional bundles: the anterior medial (AM) bundle and posterior lateral (PL) bundle. Acting together, the bands of the ACL are the primary restraints to anterior displacement of the tibia relative to the femur, and as a secondary stabilizer to tibial rotation. Partial ACL (p-ACL) ruptures are commonly seen clinically, making up between 10–28% of all ACL tears (Sonnery-Cottet and Colombet, 2016; Temponi et al., 2015). Currently, there is no consensus on what defines a p-ACL rupture. While complete ACL rupture can be diagnosed through clinical examination (Amis and Dawkins, 1991), p-ACL rupture is

* Corresponding author at: Department of Civil Engineering, Schulich School of Engineering, McCaig Institute for Bone and Joint Health, Cumming School of Medicine, Health Sciences Centre, University of Calgary, 3330 Hospital Drive NW, Calgary, Alberta T2N 4N1, Canada.

E-mail address: ngshrive@ucalgary.ca (N.G. Shrive).

[1] Deceased.

https://doi.org/10.1016/j.jbiomech.2019.03.021
0021-9290/

usually more difficult to diagnose. Typically, imaging examination (plain radiographs and magnetic resonance imaging) and arthroscopic investigation (when indicated) are required to diagnose a p-ACL (Temponi et al., 2015). Further, ACL tears involving 50–75% of the ligament have been shown to have a significant probability of progressing to a complete tear and can be associated with further meniscal, ligamentous, and osteochondral injuries (Noyes et al., 1989). Thus, surgical reconstruction of a p-ACL rupture is often performed, but is challenging as the surgery requires both precise positioning of the bone tunnel and conservation of the remaining torn bundle (Temponi et al., 2015).

Multiple studies have assessed motion of the knee joint during normal gait and following ACL injury in human (Andriacchi and Dyrby, 2005; Beynnon et al., 2002; Wu et al., 2010; Zhang et al., 2003) and laboratory animal studies (Atarod et al., 2014b; Tapper et al., 2008; Tapper et al., 2006; Tashman et al., 2004). These studies have demonstrated that after ACL rupture there is increased anterior translation and increased internal rotation of the tibia relative to the femur. Increased tibial medial translations and valgus rotations (Li et al., 2009) and articular cartilage contact kinematics in the medial-lateral direction have also been reported (Yin et al., 2017). More recently, a few studies have analyzed finite helical axes in human knees, specifically in relation to ACL injury (Dhaher and Francis, 2006; Grip et al., 2015; Mannel et al., 2004). Although p-ACL ruptures are common and clinically relevant (Sonnery-Cottet and Colombet, 2016; Temponi et al., 2015), only a few studies have used p-ACL transection (Tx) in animal models to study partial knee injury (Bozynski et al., 2015; Mifune et al., 2013; Tochigi et al., 2011). *In vivo* kinematics has been studied to analyze effects from ACL and medial collateral ligament transection (Shekarforoush et al., 2018), none that we are aware of have studied the impact of p-ACL Tx on *in vivo* joint kinematics, and attempted to quantify detailed information on the resultant biomechanical alterations. Furthermore, none have studied the combination of gross PTOA-like changes after p-ACL Tx and changes to knee kinematic integrity over time. The rationale for using a p-ACL Tx model was to simulate a human p-ACL rupture, and study the effects of AM band Tx and the biomechanical functioning of the PL band after such injuries (Atarod Pilambaraei et al., 2012). In our model, p-ACL Tx was defined as transecting the AM band completely through its mid-substance, and leaving the PL band completely intact. Thus, we considered the p-ACL injury to be '50%' ruptured.

The objective of the present study was to (1) examine ovine *in vivo* knee kinematics pre- and post- p-ACL Tx during gait and to (2) investigate the alterations in the finite helical axes (FHA) variables and the absolute translational change of the bones in the tibiofemoral joint after p-ACL Tx. We hypothesized that (1) AM band deficiency would alter the *in vivo* kinematics during gait in both translational and rotational degrees of freedom (DOF) and (2) there would be a correlation between change in kinematic variables and PTOA-like damage, irrespective of the large inter-animal variability.

2. Methods

2.1. Animal model and surgical intervention

All animal surgeries and procedures were approved by the University of Calgary Animal Care Committee and comply with the guidelines of the Canadian Council on Animal Care. Skeletally mature, 3 to 5-year-old female Suffolk-cross sheep (n = 5) were trained to walk on a treadmill at 2.0 mph. Surgeries were performed on the right stifle joint, with the left joint serving as an internal control. Two stainless steel modified bone fracture plates (Zimmer, Warsaw, IN, USA) were surgically implanted on the lateral side of the femur and the medial side of the tibia, and fixed as close to the stifle joint as possible. Animals were given at least four weeks to recover before undergoing assessment of intact kinematics.

Four weeks after intact kinematic collection (explained subsequently), under arthroscopic guidance, an orthopedic surgeon made two small incisions on the anterior aspect of the knee joint. The AM band of the ACL was then transected sharply, through the full thickness. The PL band was left intact and was visualized the entire time to ensure the p-ACL Tx.

2.2. Recording 3-Dimensional in vivo kinematics

The 3D motion of the femur relative to the tibia (the stifle joint motion) during normal and pathological gait was recorded accurately using an instrumented spatial linkage (ISL) (0.3 ± 0.1 mm, 0.3 ± 0.1 deg). As described previously (Atarod et al., 2014b; Rosvold et al., 2015), the ISL was attached rigidly to the implanted plates on the bones for motion capture. The kinematics of the stifle joint motion was defined while the sheep walked on a standard treadmill (2.0 mph) and the data was collected for a minimum of 250 strides. Kinematics was measured before p-ACL Tx, and at 20 and 40 weeks after p-ACL Tx.

2.3. Gross morphological grading

All animals were sacrificed at 40 weeks post p-ACL Tx. The animals' hind limbs were disarticulated and then the tissue was harvested. Gross morphological grading of the patella, femoral groove, femoral condyles, and tibial plateau was conducted by two expert observers for gross defects (Drez et al., 1991), osteophyte formation (Cummings et al., 2002), and meniscal damage (Hellio Le Graverand et al., 2001).

2.4. Kinematic data processing

As described previously (Atarod et al., 2014b), the joints were digitized using a portable coordinate measuring machine (FaroArm Platinum, Faro Technologies, Lake Mary, FL, USA; accuracy 0.025 mm) and anatomically relevant coordinate systems were defined on the femur and tibia (Grood and Suntay, 1983). The anatomical degrees of freedom, i.e. flexion–extension (FE), abduction–adduction (AA), and internal-external (IE) rotations and the medial–lateral (ML), posterior-anterior (PA) and inferior-superior (IS) translations were defined by defining the joint coordinate system (Grood and Suntay, 1983). The periods between successive hoof-strikes were calculated and used for normalization (0–100% gait cycle).

In addition, the finite helical axis (FHA) was defined from four variables n, s, ϕ and t as previously described by Spoor and Veldpaus (Spoor and Veldpaus, 1980). The orientation of the FHA is defined by n ($[\theta_1,\theta_2,\theta_3] = [\theta_{ML},\theta_{ML},\theta_{IS}]$), the unit vectors along the FHA, while the location of the FHA is defined by s ($[s_1,s_2,s_3] = [s_{ML},s_{ML},s_{IS}]$), the vector of the line from the location of the closest point on the FHA to the origin of the TCS. ϕ and t are the angle of rotation about and the translation along the FHA, the details provided by Shekarforoush et al. (2018). Finally, the magnitude of the change of the translation vector from intact after injury was defined as the tibiofemoral absolute translational change (Shekarforoush et al., 2018).

2.5. Statistics

Mann-Whitney tests were used to investigate the changes in gross morphological damage between the 40 weeks post p-ACL

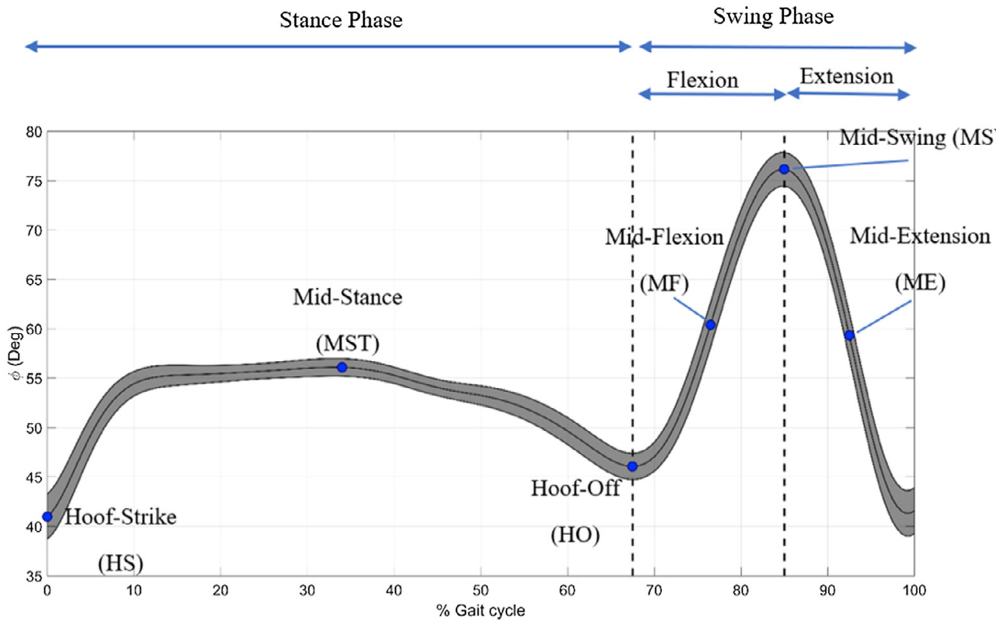


Fig. 1. The kinematic variables are defined at six points in the gait cycle: Hoof strike (HS), mid-stance (MST) and hoof-off (HO) during the stance phase of the gait cycle, and mid-flexion (MF), mid-swing (MSW), and mid-extension (ME) during the swing phase.

Tx group and non-operative control group. Paired Wilcoxon signed ranked tests were used to investigate the alterations in kinematics between groups at the six distinct gait points (hoof strike (HS), mid-stance (MST), hoof off (HO), mid-flexion (MF), mid-swing (MSW) and mid-extension (ME); Fig. 1). Spearman rank correlations were used to investigate correlations between kinematic changes at these gait points and adjusted gross morphological combined score (ΔGCS). Statistics were conducted using SPSS (IBM Software, Armonk, NY, USA) and significance for the statistical test was accepted at $p \leq 0.05$.

3. Results

3.1. Gross morphological grading

p-ACL Tx resulted in significant gross joint damage compared to the non-operative control group (Fig. 2). There was considerable meniscal damage and osteophyte formation in the 40 weeks post p-ACL Tx group (Barton et al., 2018a), whereas the control group rarely exhibited osteophyte formation and sustained no meniscal damage (Fig. 2C and G).

3.2. Joint angles and joint translations during gait

All animals, with the exception of animal 2, shifted to a more flexed position particularly in the stance phase of the gait cycle after 20 and 40 weeks post p-ACL Tx and the patterns continued to change over time (Fig. 3). The increases in flexion angles were statistically significant at HS and MST at 20 weeks post p-ACL Tx (both $p = 0.043$) and HO and MF at 40 weeks post p-ACL-Tx (both $p = 0.043$). In the AA component, animals 1–4 shifted to a more abducted position overall post injury, with statistically significant changes at HS both 20 and 40 weeks after injury (both $p = 0.043$). For the IE rotation, there was a shift from intact to 20 weeks and another shift from 20 weeks to 40 weeks but there was a variation between the subjects and the changes were not statistically significant (Fig. 3).

In the ML degree, there was a considerable shift from intact to 20 weeks to 40 weeks in all sheep; however, the changes were not statistically significant as there was large individual variability in the direction and magnitude of change from pre-injury (Fig. 4). Further, there was a statistically significant increase in the posterior direction at MF and ME points during swing phase of the gait cycle at 40 weeks post p-ACL Tx (both $p = 0.043$).

3.3. Knee finite helical axes during gait

For the p-ACL Tx group, the orientation of the FHA significantly changed during the stance phase of the gait cycle. There was a consistent significant decrease in $\Delta\theta_{ML}$ and $\Delta\theta_{AP}$ at the HS and MST points 40 weeks after p-ACL Tx. The inter-subject variation in the inferior-superior direction ($\Delta\theta_{IS}$) was higher than in the other two directions (Fig. 5), but no significant alterations were detected between groups for the points analyzed during the gait cycle. Moreover, the locations of the helical axes were changed 20 and 40 weeks after p-ACL Tx with high inter-subject variation. Variation in the IS direction was higher than the other two directions (Fig. 5). Rotation about the FHA (ϕ) was increased in early part of the stance phase at HS and also at the MST point of the gait cycle after p-ACL Tx; the increase was significant at 20 weeks (Fig. 5). No significant alterations were detected for translation along the FHA (Δt) (Fig. 5). Variations of the finite helical axis variables throughout the gait cycle for one representative subject from the p-ACL Tx group is represented in Fig. 6.

3.4. Correlation between gross combined morphological score and in vivo kinematics variables

There was no correlation between rotational degrees of freedom and change in ΔGCS at the selected gait points analyzed. However, there was a significant correlation between an increase in the tibial superior direction and gross morphological combined score (ΔGCS) at 40 weeks post p-ACL Tx (MST, HO, and MF; Fig. 7). Besides, there were correlations between ΔGCS and the absolute translational change ($|\Delta d|$) at 4/6 points analyzed through the gait cycle (significant at the ME point and trends for the HS, MF and MSW points) (Fig. 7). Considering FHA variables, there was a significant correlation between ΔGCS and change in the location of the helical

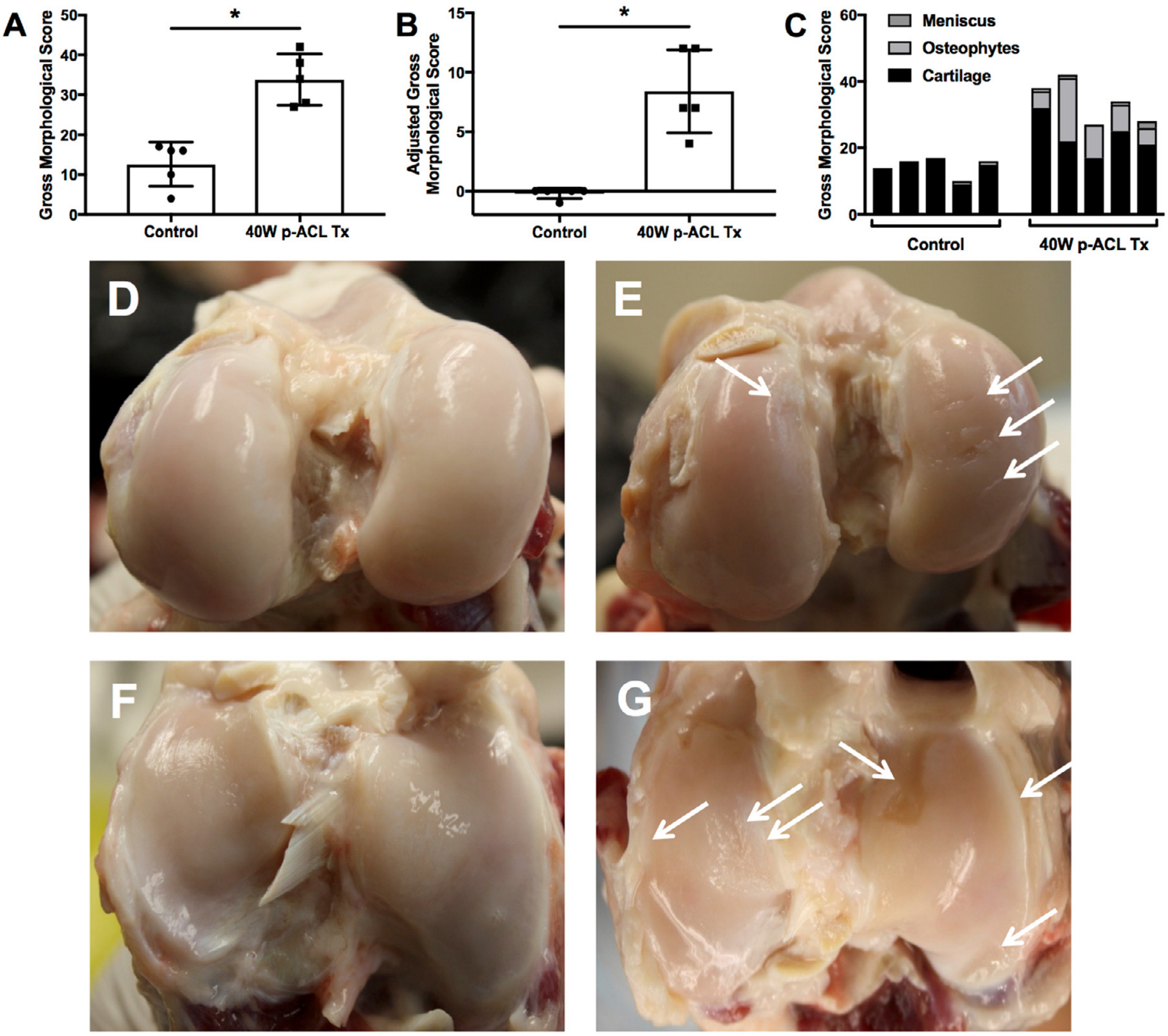


Fig. 2. Gross morphological combined score of the ovine stifle joint for the 40 weeks post p-ACL Tx group and the non-operative control group (A). Adjusted combined gross morphological score (Δ GCS) of the ovine stifle joint for the 40 weeks post p-ACL Tx group and the non-operative control group (B). ΔGCS breakdown of the ovine stifle joint for meniscal damage, osteophytes, and articular cartilage damage for the 40 weeks post p-ACL Tx group and the non-operative control group (C). Data are reported as mean ± SD. * = significantly different. Images of the femoral condyles and tibial plateaus during gross morphological scoring for osteophytes and articular cartilage damage for the non-operative control group (D, F) and 40 weeks post p-ACL Tx group (E, G). White arrows indicate irregularities, osteophytes, and cartilage damage.

axis in the anterior direction (Δs_{AP}) for all six points analyzed through the gait cycle (Fig. 8). Although, increase of Δs_{AP} was only significant at 1/6 gait point analyzed, closer inspection of animals' data for Δs_{AP} at the other 5 gait points showed that there was an increase at the same 4/5 animals.

4. Discussion

In the present study, we examined the change in ovine *in vivo* joint 6 DOF kinematics and FHA variables before and after p-ACL Tx. Similar to previous ovine ligament studies (Atarod et al., 2014a; Tapper et al., 2009) and human studies (Chaudhari et al., 2008; Decker et al., 2011; Georgoulis et al., 2010), there was considerable inter-subject variability in both damage and kinematics following a knee joint injury. Also, there appeared to be 'copers' and 'non-copers' after knee injury in the ovine model (Barrance et al., 2007); with some of the animals demonstrating significant kinematic changes after the p-ACL Tx knee injury, whereas others with the same knee joint injury either progressed more slowly over time or did not progress much at all. This could be due to several contributing factors: bone and meniscal shapes, musculature and neuromuscular control mechanisms, or biological changes to specific tissues after p-ACL Tx (Smith et al., 2012a, b). Thus, multiple aspects contribute to the knee joint acting as an organ system (Frank et al., 2004; Loeser et al., 2012).

Clinically, this study demonstrates that even partial damage to the ACL can lead to PTOA-like changes. Of interest, considerable osteophyte formation and minor meniscal damage was present in the surgical limbs. This is consistent with previous ovine (Atarod Pilambaraei, 2013) and lapine (Tochigi et al., 2011) models of full ACL injury and p-ACL injury, respectively, where it was shown that damage develops progressively over time with knee instability.

The most significant kinematic change across all p-ACL Tx sheep was the increase in joint flexion, particularly during the stance phase of the gait cycle. The increased flexion might be due to quadriceps weakness, during the early phase of stance; as quadriceps function to avoid shock to the knee, its weakness can result in increased flexion angles. Also, the weight, and therefore torque, of the ISL may be a factor as well. Relevant to this point, previous

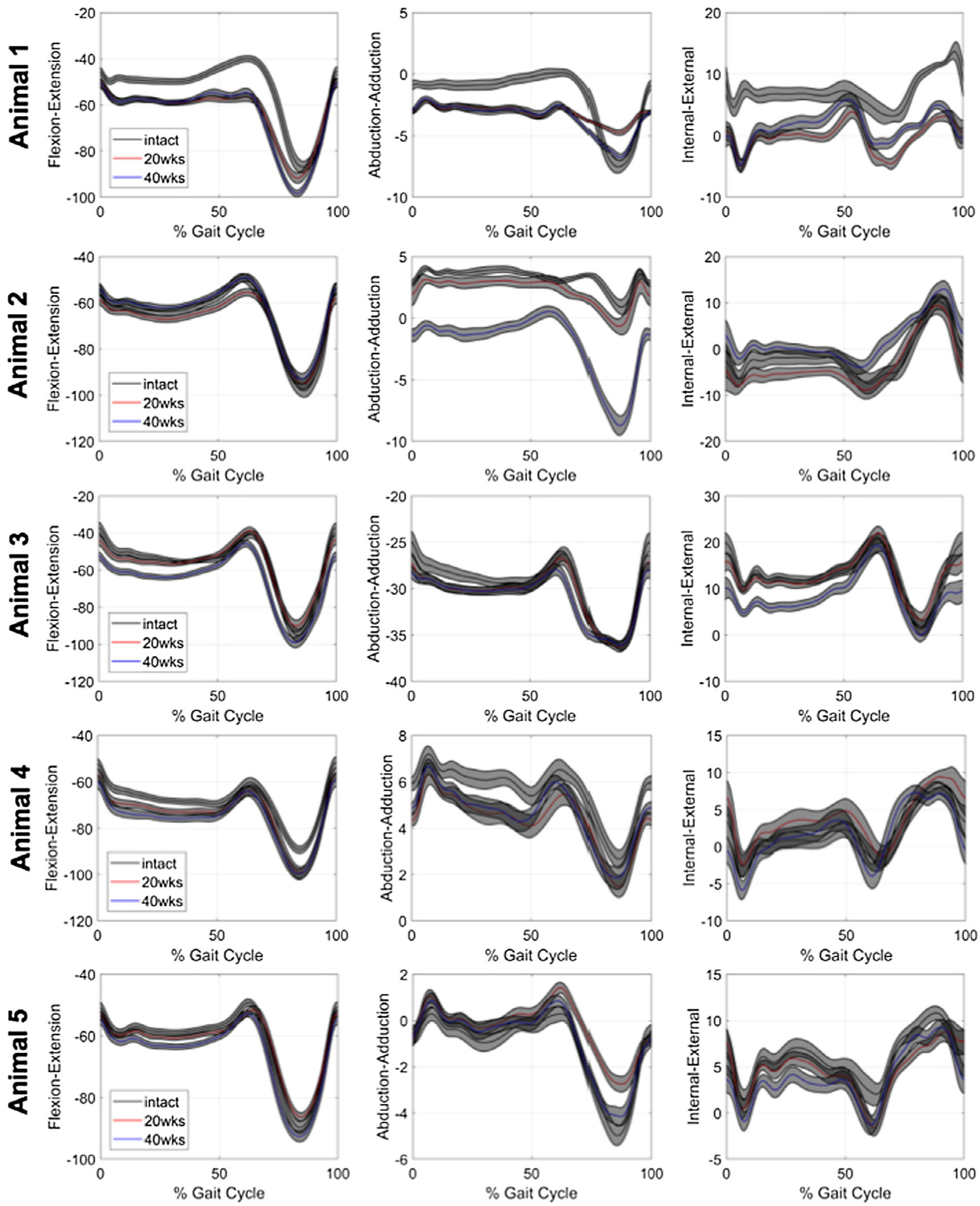


Fig. 3. The three rotational degrees of freedom *in vivo* kinematics (in degrees) of the ovine stifle joint of all animals (1–5) during gait, before (black hashed line), at 20 weeks post p-ACL Tx (red line), and 40 weeks post p-ACL Tx (blue line). Data are reported as median stride ± standard deviation. Positive Y values indicate increased joint flexion, adduction, internal tibial rotation. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

literature has reported quadriceps weakness after ACL injury (Hart et al., 2010; Kim et al., 2016; Konishi et al., 2011; Thomas et al., 2013). Contrary to our expectation, none of these significant changes in these degrees of freedom were correlated to the development of PTOA-like changes in the subjects. This suggests that kinematic variables were not the critical factor for initiation of PTOA in these subjects.

Interestingly, the changes in the IS degree of freedom, in MST, HO, and MF points, were significantly correlated to the PTOA-like change and increased posterior tibial translation was significantly correlated with ΔGCS. The main reason was probably an increase in the pressure distribution on the cartilage surfaces as a result of increased tibial posterior translation (equivalent to joint narrowing). Consequently, normal stress on the cartilage increases. Future studies are needed to evaluate other potential mechanical pathways including altered pressure distribution and shear stresses, altered contact locations, and altered surface interactions (such as increased frictional force and cartilage wearing).

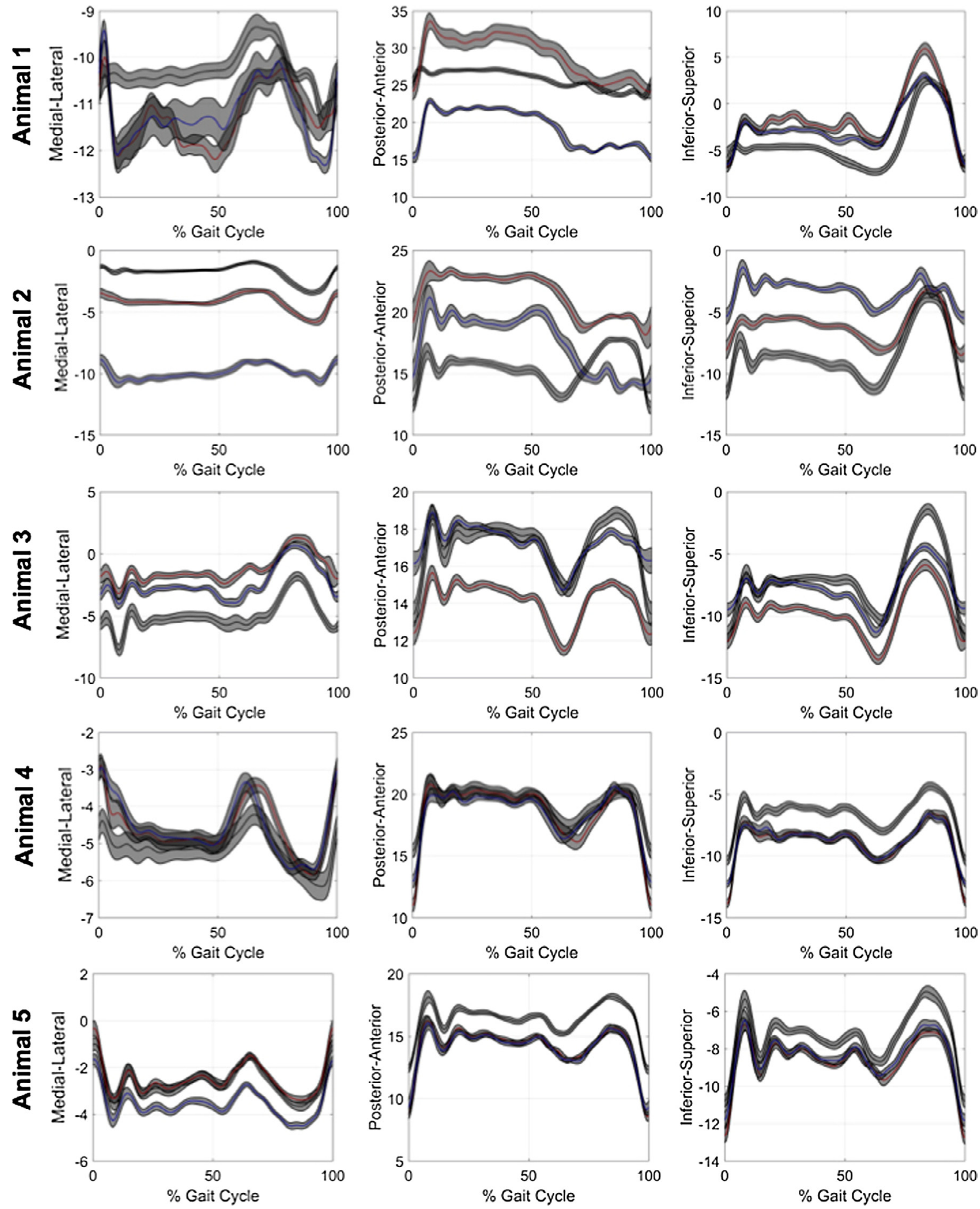


Fig. 4. The three translational degrees of freedom *in vivo* kinematics (in millimetres) of the ovine stifle joint of all animals (1–5) during gait, before (black hashed line), at 20 weeks post p-ACL Tx (red line), and 40 weeks post p-ACL Tx (blue line). Data are reported as median stride ± standard deviation. Positive Y values indicate increased lateral tibial translation, anterior tibial translation, and superior tibial translation. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Addressing the above mechanical factors could provide insight into other mechanical contributors to PTOA development.

Another interesting finding was the significant correlation between ΔGCS and the change in location of the helical axis in the anterior direction (ΔsAP) after p-ACL Tx for all points analyzed through the gait cycle (Figs. 7 and 8). Although, increases in ΔsAP was only significant at 1/6 gait point analyzed, closer inspection of the animal data for ΔsAP at the other 5 gait points showed that there was an increase at the same 4/5 animals. In a recent longitudinal study on ACL-reconstructed patients, the abnormality in the PA shift of the knee's centre of rotation, which is equivalent to a two-dimensional axis of rotation, was correlated with clinical outcomes up to 8 years after surgery (Titchenal et al., 2017). Besides, there were correlations between ΔGCS and the absolute translational change (|Δd|) at 4/6 points analyzed through the gait cycle (significant at the ME point and trends for the HS, MF and MS

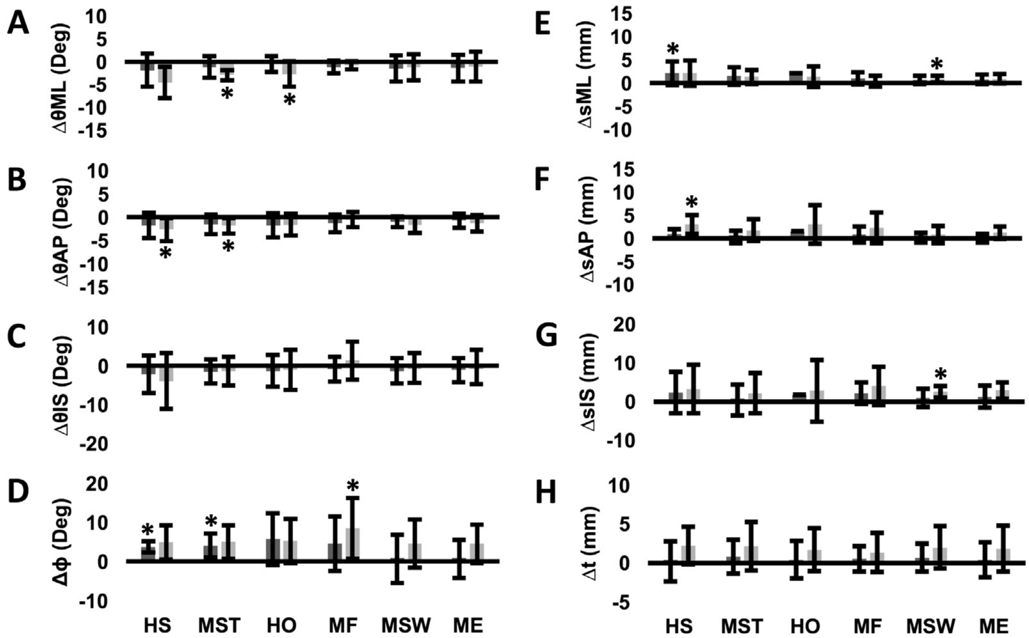


Fig. 5. The mean values ± standard deviation of the alterations in the finite helical axis (FHA) parameters (A-H) from the intact after 20 weeks post p-ACL Tx (dark grey) and 40 weeks post p-ACL Tx (light grey). Data presented are for six points during the gait cycle, i.e. hoof-strike (HS), mid-stance (MST), hoof-off (HO), mid-flexion (MF), mid-swing (MSW) and mid-extension (ME). * = significantly different.

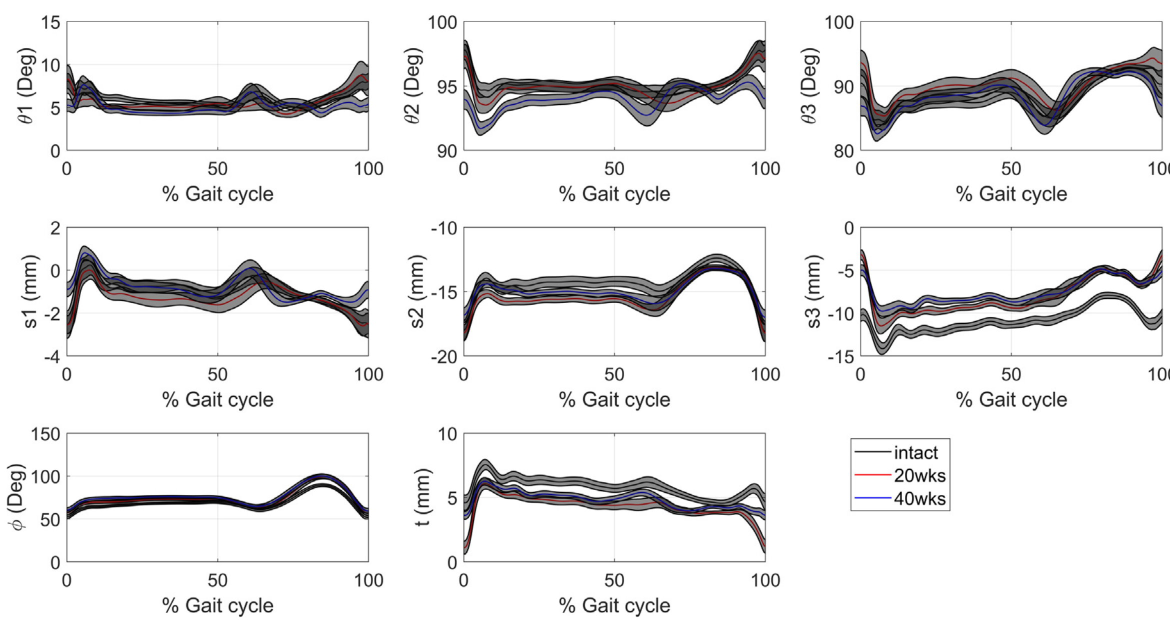
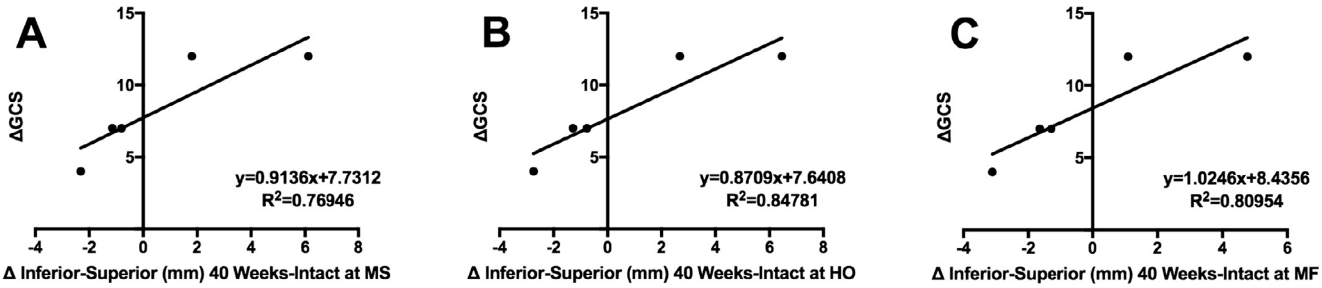


Fig. 6. Variations of the finite helical axis variables throughout the gait cycle for one representative subject from the p-ACL Tx group, before (black line), at 20 weeks post p-ACL Tx (red line), and 40 weeks post p-ACL Tx (blue line). The orientation of the FHA is defined by the $[\theta_1,\theta_2,\theta_3] = [\theta_{ML},\theta_{ML},\theta_{IS}]$ and the location of the FHA is defined by $s = [s_1,s_2,s_3] = [s_{ML},s_{ML},s_{IS}]$, which is the vector from the location of the closest point on the FHA to the origin of the tibial coordinate system (TCS). ϕ and t are the angle of rotation about and the translation along the FHA. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

points) (Fig. 7). Moreover, Shekarforoush *et al.* reported that PTOA-like morphological damage after complete ACL and MCL transection was more critically correlated to the absolute tibiofemoral translational change than each translational degrees of freedom (Shekarforoush et al., 2018). Overall these results suggest that shift of the location of the FHA in the PA direction and the tibiofemoral absolute translational change might be more important kinematic risk factor than each translational DOF, such as PA instability, for PTOA development after the ACL injury.

This study is not without limitations. First, as described previously (Atarod et al., 2014b; Beveridge et al., 2011; Frank et al., 2012; Tapper et al., 2008, 2006, 2004), the kinematic surgery and testing is, to some extent, invasive. Although other techniques offer less invasive approaches for kinematic collection, the method we utilized is extremely precise. It should be noted that, unlike our previous studies using arthrotomy, we used arthroscopy for the current model, and thus, the intervention aimed to mimic real ligament injuries during sport activities. Second, during kinematic col-



D **Correlation (ΔGCS, 6 DOF Kinematics and the Absolute Translation Vector)**

	ΔFE	ΔAA	ΔIE	ΔML	ΔPA	ΔIS	|Δd|
HS							r=0.821 p=0.089
MST						**r=0.950* p=0.014**	
HO						**r=0.950* p=0.014**	
MF						**r=0.950* p=0.014**	r=0.821 p=0.089
MSW							r=0.821 p=0.089
ME							**r=0.975* p=0.005**

E **Correlation (ΔGCS, Finite Helical Axis Variables)**

	Δs_{ML}	Δs_{AP}	Δs_{IS}	$\Delta\theta_{ML}$	$\Delta\theta_{AP}$	$\Delta\theta_{IS}$	Δϕ	Δt
HS		**r=0.975* p=0.005**						r=0.872 p=0.054
MST		**r=0.975* p=0.005**			r=-0.821 p=0.089			r=0.872 p=0.054
HO		**r=0.975* p=0.005**		r=-0.872 p=0.054				r=0.872 p=0.054
MF		**r=0.975* p=0.005**			r=-0.821 p=0.089			
MSW		**r=0.975* p=0.005**						
ME		**r=0.975* p=0.005**						

Fig. 7. Correlation of gross morphological score and *in vivo* kinematics in the inferior-superior (IS) direction at mid-stance (MST) (A), hoof-off (HO) (B), and mid-flexion (MF) (C). Kinematic variables are 6 degrees of freedom kinematics (i.e. flexion-extension (FE), abduction-adduction (AA), internal-external (IE), medial-lateral (ML), posterior-anterior (PA), IS), finite helical axis variables (i.e. the orientation of the FHA n ($[\theta_1,\theta_2,\theta_3] = [\theta_{ML},\theta_{ML},\theta_{IS}]$), the location of the FHA s ($[s_1,s_2,s_3] = [s_{ML},s_{ML},s_{IS}]$), ϕ and t) and the absolute tibio-femoral translational change (|Δd|) (D). The Spearman correlation analyses between the change of finite helical axis variables after injury and adjusted Δ gross morphological combined score (ΔGCS) at hoof-strike (HS), MST, HO, MF, mid-swing (MSW) and mid-extension (ME) during the gait cycle (E). * = significantly different.

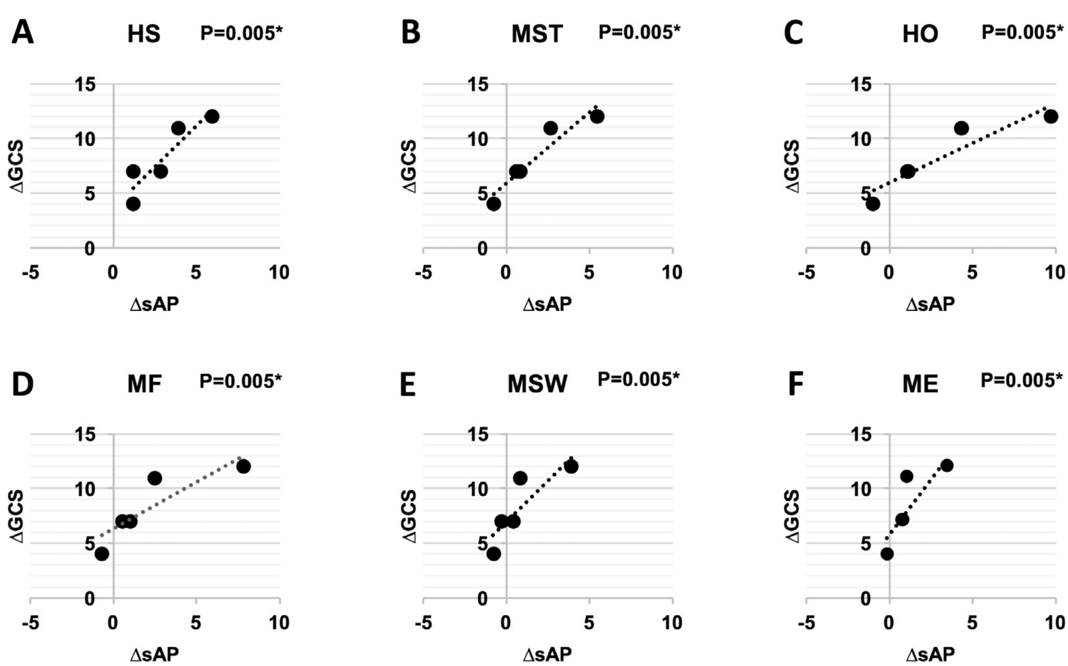


Fig. 8. Scatter plots of Δs_{AP} (the location of helical axis in the anterior-posterior direction) versus Δgross combined score (ΔGCS) at all points of the gait cycle, hoof-strike (HS), mid-stance (MST), hoof-off (HO), mid-flexion (MF), mid-swing (MSW), and mid-extension (ME), analyzed 40 weeks post p-ACL Tx (A). * = significant correlation.

lection, the animal has the ISL (1 kg) attached directly to the previously implanted then pooled the data to determine trends. Third, drawing human applications by extension from the ovine stifle joint model is a limitation; however, the ovine model has been shown to be a suitable biomechanical model (Allen et al., 1998; Osterhoff et al., 2011; Tapper et al., 2008, 2009). Fourth, there was large inter-animal variability and a low sample size (n = 5). However, this is also commonly seen and observed in humans as there can be 'copers' and 'non-copers' after knee injury (Barrance et al., 2007). To overcome this limitation, we evaluated each animal individually utilizing a single-subject design initially. We also then pooled the data to determine trends. Lastly, we acknowledge that sham groups are commonly used to investigate the effects of walking patterns on the stifle joint, however we decided not to include this group in this present study based on results from previous studies that have shown shams do not to differ from the controls (Beveridge et al., 2011; Tapper et al., 2008, 2009).

This study quantified *in vivo* kinematics in a p-ACL rupture model. Two strengths of this study are that it quantified gait longitudinally over time and that it allows animals to be compared to themselves, so that trajectories of kinematic change and gross damage could be studied over bone plate and could alter their 'normal' gait patterns. This research lays the foundation for future studies, highlighting the necessity of addressing individual responses and adaptations to identical knee ligament injuries, as there is substantial individual variation. We demonstrated that in this p-ACL Tx model, PTOA develops and is progressive over time (Barton et al., 2018b), and there is correlation between change in the location of the FHA axis in the AP direction and PTOA damage. Correlation analysis showed a strong and significant correlation between kinematic changes (instabilities) and gross morphological score in the IS direction at 40 weeks post p-ACL Tx at MST, HO, and MF. In addition to the mechanical factors, the biological factors especially acute joint inflammation should be assessed; studies investigating glucocorticoid intervention, with the aim of mitigating acute injury-induced inflammation, need to be conducted in the p-ACL Tx model. The results indicate that a p-ACL knee injury can lead to PTOA-like damage and kinematic changes over time. In summary, this study has provided further understanding for the function of the knee joint following p-ACL Tx in an ovine model.

Acknowledgments

The authors would like to gratefully acknowledge Leslie Jacques and Yamini Achari for their technical expertise.

Conflicts of interest

This work was funded by the Canadian Institutes of Health Research, The Arthritis Society, Alberta Innovates Health Solutions, Vanier Canada Graduate Scholarships, and the Cumming School of Medicine at the University of Calgary. The authors have received no financial support that may be perceived as a conflict of interest.

References

Allen, M.J., Houlton, J.E., Adams, S.B., Rushton, N., 1998. The surgical anatomy of the stifle joint in sheep. Veterinary Surgery: VS 27, 596–605.

Amis, A.A., Dawkins, G.P., 1991. Functional anatomy of the anterior cruciate ligament. Fibre bundle actions related to ligament replacements and injuries. J. Bone Joint Surgery British 73, 260–267.

Andriacchi, T.P., Dyrby, C.O., 2005. Interactions between kinematics and loading during walking for the normal and ACL deficient knee. J. Biomech. 38, 293–298.

Atarod, M., Frank, C.B., Shrive, N.G., 2014a. Decreased posterior cruciate and altered collateral ligament loading following ACL transection: a longitudinal study in the ovine model. J. Orthopaedic Res.: Off. Publ. Orthopaedic Res. Soc. 32, 431–438.

Atarod, M., Frank, C.B., Shrive, N.G., 2014b. Kinematic and kinetic interactions during normal and ACL-deficient gait: a longitudinal in vivo study. Ann. Biomed. Eng. 42, 566–578.

Atarod Pilambaraei, M., 2013. Possible Mechanical and Biological Drivers of Osteoarthritis following ACL Injury. University of Calgary.

Atarod Pilambaraei, M., O'Brien, E.J., Frank, C.B., Shrive, N.G., 2012. There is significant load sharing and physical interaction between the anteromedial and posterolateral bundles of the ovine ACL under anterior tibial loads. The Knee 19, 797–803.

Barenius, B., Ponzer, S., Shalabi, A., Bujak, R., Norlen, L., Eriksson, K., 2014. Increased risk of osteoarthritis after anterior cruciate ligament reconstruction: a 14-year follow-up study of a randomized controlled trial. Am. J. Sports Med. 42, 1049–1057.

Barrance, P.J., Williams, G.N., Snyder-Mackler, L., Buchanan, T.S., 2007. Do ACL-injured copers exhibit differences in knee kinematics?: an MRI study. Clin. Orthopaedics Related Res. 454, 74–80.

Barton, K.I., Heard, B.J., Sevick, J.L., Martin, C.R., Shekarforoush, M., Chung, M., Achari, Y., Frank, C.B., Shrive, N.G., Hart, D.A., 2018a. Post-traumatic osteoarthritis development and progression in an ovine model of partial anterior cruciate ligament transection and effect of repeated intra-articular methylprednisolone acetate injections on early disease. Am. J. Sports Med.

Barton, K.I., Heard, B.J., Sevick, J.L., Martin, C.R., Shekarforoush, S.M.M., Chung, M., Achari, Y., Frank, C.B., Shrive, N.G., Hart, D.A., 2018b. Posttraumatic osteoarthritis development and progression in an ovine model of partial anterior cruciate ligament transection and effect of repeated intra-articular methylprednisolone acetate injections on early disease. Am. J. Sports Med. 363546518765098.

Beveridge, J.E., Shrive, N.G., Frank, C.B., 2011. Meniscectomy causes significant in vivo kinematic changes and mechanically induced focal chondral lesions in a sheep model. J. Orthopaedic Res.: Off. Publ. Orthopaedic Res. Soc. 29, 1397–1405.

Beynnon, B.D., Fleming, B.C., Labovitch, R., Parsons, B., 2002. Chronic anterior cruciate ligament deficiency is associated with increased anterior translation of the tibia during the transition from non-weightbearing to weightbearing. J. Orthopaedic Res.: Off. Publ. Orthopaedic Res. Soc. 20, 332–337.

Bozynski, C.C., Kuroki, K., Stannard, J.P., Smith, P.A., Stoker, A.M., Cook, C.R., Cook, J. L., 2015. Evaluation of partial transection versus synovial debridement of the ACL as novel canine models for management of ACL injuries. J. Knee Surgery 28, 404–410.

Chaudhari, A.M., Briant, P.L., Bevill, S.L., Koo, S., Andriacchi, T.P., 2008. Knee kinematics, cartilage morphology, and osteoarthritis after ACL injury. Med. Sci. Sports exercise 40, 215–222.

Cummings, J.F., Grood, E.S., Levy, M.S., Korvick, D.L., Wyatt, R., Noyes, F.R., 2002. The effects of graft width and graft laxity on the outcome of caprine anterior cruciate ligament reconstruction. J. Orthopaedic Res.: Off. Publ. Orthopaedic Res. Soc. 20, 338–345.

Decker, L.M., Moraiti, C., Stergiou, N., Georgoulis, A.D., 2011. New insights into anterior cruciate ligament deficiency and reconstruction through the assessment of knee kinematic variability in terms of nonlinear dynamics. Knee Surgery Sports Traumatol. Arthrosc.: Off. J. ESSKA 19, 1620–1633.

Dhaher, Y.Y., Francis, M.J., 2006. Determination of the abduction-adduction axis of rotation at the human knee: helical axis representation. J. Orthopaedic Res.: Off. Publ. Orthopaedic Res. Soc. 24, 2187–2200.

Drez Jr., D.J., DeLee, J., Holden, J.P., Arnoczky, S., Noyes, F.R., Roberts, T.S., 1991. Anterior cruciate ligament reconstruction using bone-patellar tendon-bone allografts. A biological and biomechanical evaluation in goats. Am. J. Sports Med. 19, 256–263.

Frank, C.B., Beveridge, J.E., Huebner, K.D., Heard, B.J., Tapper, J.E., O'Brien, E.J., Shrive, N.G., 2012. Complete ACL/MCL deficiency induces variable degrees of instability in sheep with specific kinematic abnormalities correlating with degrees of early osteoarthritis. J. Orthopaedic Res.: Off. Publ. Orthopaedic Res. Soc. 30, 384–392.

Frank, C.B., Shrive, N.G., Boorman, R.S., Lo, I.K., Hart, D.A., 2004. New perspectives on bioengineering of joint tissues: joint adaptation creates a moving target for engineering replacement tissues. Ann. Biomed. Eng. 32, 458–465.

Georgoulis, A.D., Ristanis, S., Moraiti, C.O., Paschos, N., Zampeli, F., Xergia, S., Georgiou, S., Patras, K., Vasiliadis, H.S., Mitsionis, G., 2010. ACL injury and reconstruction: clinical related in vivo biomechanics. Orthopaedics Traumatol. Surgery Res.: OTSR 96, S119–S128.

Griffin, L.Y., Albohm, M.J., Arendt, E.A., Bahr, R., Beynnon, B.D., Demaio, M., Dick, R.W., Engebretsen, L., Garrett Jr., W.E., Hannafin, J.A., Hewett, T.E., Huston, L.J., Ireland, M.L., Johnson, R.J., Lephart, S., Mandelbaum, B.R., Mann, B.J., Marks, P.H., Marshall, S.W., Myklebust, G., Noyes, F.R., Powers, C., Shields Jr., C., Shultz, S.J., Silvers, H., Slauterbeck, J., Taylor, D.C., Teitz, C.C., Wojtys, E.M., Yu, B., 2006. Understanding and preventing noncontact anterior cruciate ligament injuries: a review of the Hunt Valley II meeting, January 2005. Am. J. Sports Med. 34, 1512–1532.

Grip, H., Tengman, E., Hager, C.K., 2015. Dynamic knee stability estimated by finite helical axis methods during functional performance approximately twenty years after anterior cruciate ligament injury. J. Biomech. 48, 1906–1914.

Grood, E.S., Suntay, W.J., 1983. A joint coordinate system for the clinical description of three-dimensional motions: application to the knee. J. Biomech. Eng. 105, 136–144.

Hart, J.M., Pietrosimone, B., Hertel, J., Ingersoll, C.D., 2010. Quadriceps activation following knee injuries: a systematic review. J. Athletic Train. 45, 87–97.

Hellio Le Graverand, M.P., Vignon, E., Otterness, I.G., Hart, D.A., 2001. Early changes in lapine menisci during osteoarthritis development: Part I: cellular and matrix alterations. Osteoarthritis Cartilage/OARS, Osteoarthritis Res. Soc. 9, 56–64.

Kim, H.J., Lee, J.H., Ahn, S.E., Park, M.J., Lee, D.H., 2016. Influence of anterior cruciate ligament tear on thigh muscle strength and hamstring-to-quadriceps ratio: a meta-analysis. PloS One 11, e0146234.

Konishi, Y., Oda, T., Tsukazaki, S., Kinugasa, R., Hirose, N., Fukubayashi, T., 2011. Relationship between quadriceps femoris muscle volume and muscle torque after anterior cruciate ligament rupture. Knee Surgery Sports Traumatol. Arthrosc.: Off. J. ESSKA 19, 641–645.

Leiter, J.R., Gourlay, R., McRae, S., de Korompay, N., MacDonald, P.B., 2014. Long-term follow-up of ACL reconstruction with hamstring autograft. Knee Surgery Sports Traumatol. Arthrosc.: Off. J. ESSKA 22, 1061–1069.

Li, K., Li, P., Luo, L., Li, Y., Xu, Y., Zhao, Y., 2009. [Effect of anterior cruciate ligament rupture on biomechanics of lateral collateral ligament]. Zhongguo xiu fu chong jian wai ke za zhi = Zhongguo xiufu chongjian waike zazhi. Chinese J. Reparative Reconstruct. Surgery 23, 287–289.

Loeser, R.F., Goldring, S.R., Scanzello, C.R., Goldring, M.B., 2012. Osteoarthritis: a disease of the joint as an organ. Arthritis Rheum. 64, 1697–1707.

Lohmander, L.S., Englund, P.M., Dahl, L.L., Roos, E.M., 2007. The long-term consequence of anterior cruciate ligament and meniscus injuries: osteoarthritis. Am. J. Sports Med. 35, 1756–1769.

Mannel, H., Marin, F., Claes, L., Durselen, L., 2004. Anterior cruciate ligament rupture translates the axes of motion within the knee. Clin. Biomech. (Bristol, Avon) 19, 130–135.

Mifune, Y., Ota, S., Takayama, K., Hoshino, Y., Matsumoto, T., Kuroda, R., Kurosaka, M., Fu, F.H., Huard, J., 2013. Therapeutic advantage in selective ligament augmentation for partial tears of the anterior cruciate ligament: results in an animal model. Am. J. Sports Med. 41, 365–373.

Murrell, G.A., Maddali, S., Horovitz, L., Oakley, S.P., Warren, R.F., 2001. The effects of time course after anterior cruciate ligament injury in correlation with meniscal and cartilage loss. Am. J. Sports Med. 29, 9–14.

Noyes, F.R., Bassett, R.W., Grood, E.S., Butler, D.L., 1980. Arthroscopy in acute traumatic hemarthrosis of the knee. Incidence of anterior cruciate tears and other injuries. J. Bone Joint Surgery 62, 687–695. 757.

Noyes, F.R., Mooar, L.A., Moorman 3rd, C.T., McGinniss, G.H., 1989. Partial tears of the anterior cruciate ligament. Progression to complete ligament deficiency. J. Bone Joint Surgery British 71, 825–833.

Osterhoff, G., Loffler, S., Steinke, H., Feja, C., Josten, C., Hepp, P., 2011. Comparative anatomical measurements of osseous structures in the ovine and human knee. The Knee 18, 98–103.

Rosvold, J.M., Atarod, M., Frank, C.B., Shrive, N.G., 2015. An instrumented spatial linkage for measuring knee joint kinematics. The Knee.

Shekarforoush, M., Beveridge, J.E., Hart, D.A., Frank, C.B., Shrive, N.G., 2018. Correlation between translational and rotational kinematic abnormalities and osteoarthritis-like damage in two in vivo sheep injury models. J. Biomech. 75, 67–76.

Smith, H.C., Vacek, P., Johnson, R.J., Slauterbeck, J.R., Hashemi, J., Shultz, S., Beynnon, B.D., 2012a. Risk factors for anterior cruciate ligament injury: a review of the literature - part 1: neuromuscular and anatomic risk. Sports Health 4, 69–78.

Smith, H.C., Vacek, P., Johnson, R.J., Slauterbeck, J.R., Hashemi, J., Shultz, S., Beynnon, B.D., 2012b. Risk factors for anterior cruciate ligament injury: a review of the literature-part 2: hormonal, genetic, cognitive function, previous injury, and extrinsic risk factors. Sports Health 4, 155–161.

Sonnery-Cottet, B., Colombet, P., 2016. Partial tears of the anterior cruciate ligament. Orthopaedics Traumatol. Surgery Res.: OTSR.

Spoor, C.W., Veldpaus, F.E., 1980. Rigid body motion calculated from spatial co-ordinates of markers. J. Biomech. 13, 391–393.

Tapper, J.E., Fukushima, S., Azuma, H., Sutherland, C., Marchuk, L., Thornton, G.M., Ronsky, J.L., Zernicke, R., Shrive, N.G., Frank, C.B., 2008. Dynamic in vivo three-dimensional (3D) kinematics of the anterior cruciate ligament/medial collateral ligament transected ovine stifle joint. J. Orthopaedic Res.: Off. Publ. Orthopaedic Res. Soc. 26, 660–672.

Tapper, J.E., Fukushima, S., Azuma, H., Thornton, G.M., Ronsky, J.L., Shrive, N.G., Frank, C.B., 2006. Dynamic in vivo kinematics of the intact ovine stifle joint. J. Orthopaedic Res.: Off. Publ. Orthopaedic Res. Soc. 24, 782–792.

Tapper, J.E., Funakoshi, Y., Hariu, M., Marchuk, L., Thornton, G.M., Ronsky, J.L., Zernicke, R., Shrive, N.G., Frank, C.B., 2009. ACL/MCL transection affects knee ligament insertion distance of healing and intact ligaments during gait in the Ovine model. J. Biomech. 42, 1825–1833.

Tapper, J.E., Ronsky, J.L., Powers, M.J., Sutherland, C., Majima, T., Frank, C.B., Shrive, N.G., 2004. In vivo measurement of the dynamic 3-D kinematics of the ovine stifle joint. J. Biomech. Eng. 126, 301–305.

Tashman, S., Anderst, W., Kolowich, P., Havstad, S., Arnoczky, S., 2004. Kinematics of the ACL-deficient canine knee during gait: serial changes over two years. J. Orthopaedic Res.: Off. Publ. Orthopaedic Res. Soc. 22, 931–941.

Temponi, E.F., de Carvalho Júnior, L.H., Sonnery-Cottet, B., Chambat, P., 2015. Partial tearing of the anterior cruciate ligament: diagnosis and treatment. Revista Brasileira de Ortopedia 50, 9–15.

Thomas, A.C., Villwock, M., Wojtys, E.M., Palmieri-Smith, R.M., 2013. Lower extremity muscle strength after anterior cruciate ligament injury and reconstruction. J. Athletic Train. 48, 610–620.

Titchenal, M.R., Chu, C.R., Erhart-Hledik, J.C., Andriacchi, T.P., 2017. Early changes in knee center of rotation during walking after anterior cruciate ligament reconstruction correlate with later changes in patient-reported outcomes. Am. J. Sports Med. 45, 915–921.

Tochigi, Y., Vaseenon, T., Heiner, A.D., Fredericks, D.C., Martin, J.A., Rudert, M.J., Hillis, S.L., Brown, T.D., McKinley, T.O., 2011. Instability dependency of osteoarthritis development in a rabbit model of graded anterior cruciate ligament transection. J. Bone Joint Surgery 93, 640–647.

Wu, J.L., Hosseini, A., Kozanek, M., Gadikota, H.R., Gill, T.J., Li, G., 2010. Kinematics of the anterior cruciate ligament during gait. Am. J. Sports Med. 38, 1475–1482.

Yin, P., Li, J.S., Kernkamp, W.A., Tsai, T.Y., Baek, S.H., Hosseini, A., Lin, L., Tang, P., Li, G., 2017. Analysis of in-vivo articular cartilage contact surface of the knee during a step-up motion. Clin. Biomech. (Bristol, Avon) 49, 101–106.

Zhang, L.Q., Shiavi, R.G., Limbird, T.J., Minorik, J.M., 2003. Six degrees-of-freedom kinematics of ACL deficient knees during locomotion-compensatory mechanism. Gait Posture 17, 34–42.