Assessment of a Goat Model of Posterolateral Knee Instability

Erik J. Olson,¹ Fred A. Wentorf,² Margaret A. McNulty,¹ Josh B. Parker,¹ Cathy S. Carlson,¹ Robert F. LaPrade²

¹Department of Veterinary Population Medicine, College of Veterinary Medicine, University of Minnesota, 1988 Fitch Avenue, St. Paul, Minnesota 55108

²Department of Orthopaedic Surgery, School of Medicine, University of Minnesota, 2450 Riverside Avenue S, R200, Minneapolis, Minnesota 55454

Received 10 April 2007; accepted 21 August 2007

Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/jor.20529

ABSTRACT: The development of an in vivo animal model of posterolateral knee instability is desired for devising effective interventions for this injury. Sequential sectioning of the popliteus tendon, lateral collateral ligament, and lateral capsule was done in cadaveric goat knees to create knee joint instability, followed by in vivo studies (Studies 1 and 2) of 7 and 3 months duration, respectively. In Study 1, the popliteus tendon and lateral collateral ligament were sectioned; in Study 2, these structures as well as the lateral joint capsule were sectioned. Biomechanical testing and histological assessments were done to determine the severity of the instability and the morphological changes. Sectioning the lateral collateral ligament and popliteus tendon (Study 1) resulted in a significant increase in varus instability at 90°. Sectioning the lateral collateral ligament, popliteus tendon, and lateral capsule (Study 2) resulted in significant varus instability at 30°, 60°, and 90°, and significant internal-external rotation at 60° and 90° ; however, the lesions of osteoarthritis in the operated knees were similar to those in unoperated control knees. This study confirms that posterolateral knee instability can be created in a goat model, but we were unable to demonstrate lesions of osteoarthritis that were of sufficient severity to allow evaluation of disease reduction in future intervention procedures. Future studies will determine if further manipulation of the model results in sufficient morphological changes to allow its use in the assessment of intervention strategies. © 2007 Orthopaedic Research Society. Published by Wiley Periodicals, Inc. J Orthop Res 26:651-659, 2008 Keywords: biomechanical testing; goats; histology; osteoarthritis; posterolateral knee instability

INTRODUCTION

Posterolateral knee injuries create a complicated instability pattern^{1,2} and are usually combined with other ligamentous injuries,³ making the treatment of these patients very difficult. Although there currently are several described methods for reconstructing injuries of the posterolateral corner of the knee,⁴ there is limited information available to assist the surgeon in choosing the best treatment regimen for individuals with this injury pattern. One reason for this is the paucity of studies focusing on the natural history of untreated posterolateral injuries and on the long-term results of various methods of repair on knee joint function and articular cartilage quality. Because of the variability that is inherent in human clinical studies, a controlled set of experiments using an appropriate animal model may be the best way to approach this problem.

Animal models have been used for decades to better understand the effects of ligament injury and reconstruction on knee joint mechanics and function;^{5–7} however, most in vivo animal studies have focused on the effects of operating on either the anterior cruciate ligament^{8,9} or the medial collateral ligament.^{6,7} A posterolateral model has been developed in the rabbit^{5,10,11}; however, the size of the knee joint in this species does not allow for graft reconstruction of the posterolateral corner, and the lesions of osteoarthritis present 6 months after the induced instability are relatively mild. Thus, in order to determine if posterolateral reconstructions can affect the natural history of posterolateral knee injuries, a model is needed in which 1) posterolateral instability can reliably be produced; 2) lesions of osteoarthritis of the knee joint occur within a reasonable period of time after surgery; and 3) the knee joint is large enough to allow reproducible reconstruction of the posterolateral corner. The objective of the present

Correspondence to: Robert F. LaPrade (Telephone: 612-273-1177; Fax: 612-273-7959; E-mail: lapra001@umn.edu)

 $[\]circledast$ 2007 Orthopaedic Research Society. Published by Wiley Periodicals, Inc.

study was to evaluate the use of the goat as a model for posterolateral instability in humans.

MATERIALS AND METHODS

Cadaveric Study

Prior to performing in vivo studies, a group of nonpaired cadaveric knee joint specimens was evaluated from eight Nubian goats that had been presented to the Minnesota Veterinary Diagnostic Laboratory for necropsy examination. The skin was removed from the specimens, and the femur and tibia were cut perpendicular to their diaphyseal axes, 10 cm proximal and distal to the knee (stifle) joint, respectively. A 5-cm deep hole in the marrow cavity of each femoral and tibial diaphysis was reamed using a 12-mm drill bit. One 13-mm wide by 11-cm long bolt was then advanced into each marrow cavity (tibia and femur) to a distance of 5 cm, with the longitudinal axis of the bolt aligned with the diaphyseal axis of the bones. The intramedullary portion of the bolt was then fixed in place using polymethylmethacrylate. Specimens were wrapped in saline-soaked gauze and kept on ice in a cooler until biomechanical testing was done.

For biomechanical testing, the specimens were rigidly attached to a custom testing attachment on an Instron (Canton, MA) 5865 electromechanical testing machine. The attachment allowed the application of externally applied loads to the knee at 30° , 60° , and 90° of knee joint flexion. In the goat knee, 30° of knee flexion is essentially equal to full knee extension. The anatomic neutral position was determined for the tibia with respect to the femur at each flexion angle by manual palpation of the femoral epicondyles. This position was used as the starting point for all mechanical tests. The loads applied were 6 Newton-meters of varus and valgus moments and 0.15 Newton-meters of internal and external rotation torques. Internal and external rotation of the tibia with respect to the femur was measured by a rotatory potentiometer (Maurey Instrument Corporation, Chicago, IL). The varus and valgus rotations were quantified from the linear variable displacement transducer (LVDT) of the Instron 5865. The intact knee joints were tested first, followed by testing after sequential transection of the posterolateral structures and loading. The popliteus tendon (PLT) was transected first (total of one structure transected), followed by the lateral collateral ligament (LCL; total of two structures transected), and lastly the lateral capsule (LAT CAP; total of three structures transected). Each test was repeated five times at each flexion angle and the mean maximum and minimum excursion was evaluated at each sequential transection condition using Student's *t*-test, with p < 0.05 being considered significant.

In Vivo Studies

Two groups of Nubian goats, confirmed negative for caprine arthritis and encephalitis virus (CAE; lentivirus), were used for the in vivo studies. Approval for this study was obtained from the Institutional Animal Care and Use Committee at the University of Minnesota (Study #0401A55761).

The first group of animals included six goats (Study 1). Alternating right and left knees were operated on, with the contralateral knees used as unoperated controls. Prophylactic antibiotics, gentamicin (3 mg/kg) and ceftiofur (3 mg/kg) IV, were administered prior to surgery. After the goats were anesthetized with intravenous ketamine (10 mg/kg IV) and atropine (0.04 mg/kg IV), the operated knee was shaved and prepared with betadyne for a sterile surgical field. A lateral incision was made over the knee joint and the distal edge of the biceps femoris muscle was incised and retracted anteriorly to identify the LCL.¹² The LCL and PLT were sectioned with minimal dissection of the surrounding knee joint capsule and surrounding structures. Sectioning was performed by placing a k-wire medial to the structure, trephinating it with a #15 knife blade to weaken it, and rupturing it by lateral traction.^{5,11} The sectioned ends were left in situ. The goats were full weight bearing immediately after recovering from anesthesia. Following several days of postsurgical observation, the animals were moved to a university monitored farm and allowed free access to a pasture. The animals were euthanized and their hind limbs removed at the hip for examination 7 months following surgery. This time frame was chosen to allow sufficient time for the development of lesions of osteoarthritis of at least moderate severity.

The second group of goats (Study 2) included 10 animals that underwent a modified, more extensive, posterolateral structure sectioning procedure in order to create a more unstable posterolateral knee injury than the first group of goats (Study 1). Bilateral AP (anteroposterior; veterinary equivalent, DV = dorsoventral) and lateral knee radiographs were obtained while the goats were anesthetized. The surgical preparation and approach to the posterolateral knee were the same as for Study 1. The LCL was sectioned and 5 mm of the central aspect of the ligament was removed to simulate a retracted LCL. The PLT was transected using the same technique as described for Study 1; however, in addition, the LAT CAP was sectioned at its meniscotibial margin extending anteriorly from the extensor digitorum longus tendon to the popliteomeniscal fascicles posteriorly. The contralateral limb served as an unoperated control. The goats were full weight bearing immediately after recovering from anesthesia. Following several days of postsurgical observation, the animals were moved to a university monitored farm and allowed free access to a pasture. They were euthanized and their hind limbs removed at the hip for examination 3 months following surgery. This shortened experimental time frame was chosen because the surgical intervention used in these animals was more aggressive and we anticipated that it would result in more severe instability than had occurred in the Study 1 animals. In addition, 3 months is sufficient time to develop lesions of osteoarthritis in other surgically induced instability models.¹³⁻¹⁵ The methods for preparation and biomechanical testing of the knee joints for the animals in Studies 1 and 2 were the same as those previously described for the cadaver knee specimens.

Radiology and Histology

Following biomechanical testing, the operated and contralateral unoperated control limbs from both of the in vivo groups were evaluated radiographically and histologically. AP radiographs of each intact knee joint were taken using a cabinet radiography unit (Faxitron series, Hewlett Packard, McMinnville, OR) and highdetail film (X-Omat TL, Eastman Kodak Company, Rochester, NY). The radiographic technique included the following: exposures of 70 kvp; mAs = 3 mA continuous for 30 s; and a film-to-source distance of 61 cm. After disarticulation of each knee joint, the proximal tibial and distal femoral articular surfaces were examined grossly and the soft tissues were removed. Each proximal tibia was bisected in the coronal plane using a diamond saw (Allied High Tech Products, Inc., Rancho Dominguez, CA) and medial and lateral plateaus were placed in separate cassettes. The tissues were fixed in 10% neutral-buffered formalin and were decalcified in hydrochloric acid (HCl) solution (Decalcifier II, Surgipath Medical Industries, Inc., Richmond, IL) for approximately 10 days. Paraffin-embedded tissue blocks were serially sectioned at 5 µm and stained with hematoxylin and eosin (H&E) and toluidine blue stains.

All sections of medial and lateral tibiae were examined histologically to characterize the presence and severity of cartilage and bone lesions using a modification of a previously published semiquantitative grading scheme.^{11,16} This included the following: grading of articular cartilage structure (0–20) and loss of toluidine blue staining using a $2 \times$ objective (0–16); and notation of the number of chondrocyte clones, maximum number of tidemarks, maximum number of blood vessels crossing the most superficial tidemark line, and maximum number of chondrified blood vessels ($20 \times$ objective). Osteophyte presence and location (axial, central; abaxial, periarticular osteophytes; or both) on the lateral and medial tibial plateaus ($2 \times$ objective) also were recorded. For each tibial plateau, a grade of 2 was assigned if both an axial and abaxial osteophyte were noted, a grade of 1 was assigned if either an axial or abaxial osteophyte was present, and a grade of 0 was assigned to those specimens lacking osteophytes. Using a modification of a previously described technique,¹⁶ subchondral bone (SCB) thickness (µm), from the calcified cartilage-bone junction to the superficial aspect of the marrow space (base of the SCB plate) was measured in three equidistant locations (medial, central, and lateral aspect) of each tibial plateau using a $4 \times$ objective and Spot[®] Advanced morphometry software (Diagnostic Instruments, Sterling Heights, MI) (Fig. 1), and these measurements were averaged. For each study (In Vivo Studies 1 and 2), the nonparametric Wilcoxon signed rank test for paired data was used to evaluate the differences between the grades for each parameter in the operated and unoperated control knees; p-values < 0.05 were considered to be significant.

RESULTS

Cadaveric Study Biomechanics

In the cadaveric specimen group, transection of the PLT alone created no significant increase in varus or valgus instability at any of the knee joint flexion angles examined over that of the intact joint, but caused significant increases in internal rotation at 60° and 90° of knee joint flexion (Table 1). Transection of both the PLT and the LCL created a significant increase in varus instability at 30°, 60°, and 90° of knee flexion compared to the intact and PLT sectioned conditions and created significant increases in internal and external rotation at 60° compared to the intact joints and to joints in which only the PLT was sectioned (Table 1). Transection of both the PLT and LCL also resulted in a significant increase in external rotation at 90° of knee flexion compared to the intact joints, but there was no additional increase in internal rotation at 90° over



Figure 1. Histological section of medial tibial plateau to demonstrate subchondral bone measurement technique. Measurements (three black vertical lines) were taken from three equidistant sites and included the distance from the calcified cartilage–bone junction to the superficial aspect of the marrow space. H&E. Bar = 1000 μ m.

	Intact	PLT	PLT + LCL	PLT + LCL + LAT CAP
30°				
Varus	6.53(1.76)	6.24(1.46)	9.21** (1.63)	10.11** (2.31)
Valgus	4.86 (1.24)	4.98 (1.06)	5.10 (0.99)	5.08 (0.96)
Internal	1.90 (0.42)	2.11(0.41)	3.18(1.53)	4.78*** (1.80)
External	1.78 (0.68)	0.91 (0.71)	1.86 (0.92)	2.06 (1.10)
60°				
Varus	8.93 (1.89)	8.78 (2.26)	18.28** (3.15)	21.76** (5.25)
Valgus	4.71 (1.47)	4.68 (1.05)	4.96 (1.15)	5.38 (1.26)
Internal	6.36 (0.89)	9.68* (1.93)	12.18** (3.14)	16.18*** (2.01)
External	3.61 (0.89)	4.65 (1.34)	6.11** (1.43)	5.38^{*} (1.12)
90°				
Varus	11.24 (2.00)	11.84 (1.98)	23.39** (4.23)	27.15*** (3.51)
Valgus	9.25 (1.74)	8.54 (1.97)	9.46 (1.97)	9.64 (2.09)
Internal	9.46 (1.22)	12.68* (2.15)	12.08* (1.54)	12.28* (2.10)
External	2.91 (0.52)	4.08 (1.59)	4.26* (1.24)	4.36* (0.75)

Table 1. Biomechanical Results (Varus–Valgus and Internal–External Rotation) for Cadaveric Goat Study^a

PLT, popliteus tendon sectioned; $\rm PLT+LCL,$ popliteus tendon and lateral collateral ligament sectioned; $\rm PLT+LCL+LAT$ CAP, popliteus tendon, lateral collateral ligament, and lateral capsule sectioned.

^aValues are presented as mean degrees (standard deviation).

 $^{*}p$ < 0.05 compared to intact.

**p < 0.05 compared to intact and PLT sectioned.

***p < 0.05 compared to intact, PLT, and PLT + LCL sectioned.

joints in which only the PLT was sectioned (Table 1). Sectioning of the LAT CAP in addition to the PLT and LCL significantly increased varus instability at 30° and 60° of flexion compared to the intact and PLT sectioned joints (Table 1). Sectioning of the LAT CAP significantly increased varus instability at 90° compared to all previous sectioning conditions and significantly increased internal rotation at 30° and 60° (Table 1). Sectioning of the LAT CAP significantly increased external rotation at 60° of knee flexion compared to the intact state (Table 1). Sectioning the PLT, LCL, and LAT CAP did not produce additional significant changes in internal rotation at 90° or in external rotation at 60° or 90° of knee flexion (Table 1).

In Vivo Study 1 Biomechanics

None of the structures that were sectioned showed evidence of healing and both menisci were intact in all specimens. There was a significant increase in varus instability at 90° of knee flexion in the joints in which the PLT and LCL were sectioned compared with the unoperated control knee joints; however, there were no significant differences in varus instability at 30° or 60° of knee flexion (Table 2). There were no significant differences between the operated and unoperated control joints in valgus instability, internal rotation, or external rotation at any of the knee flexion angles examined (Table 2).

In Vivo Study 2 Biomechanics

None of the structures that were sectioned showed evidence of healing and both menisci were intact in all specimens. There was a significant increase in varus instability at 30° , 60° , and 90° of knee flexion in the animals in which the PLT, LCL, and LAT CAP were sectioned compared with the unoperated control knees (Table 2). Similarly, internal and external rotation was significantly increased in the operated knees compared to the unoperated control knees at 60° and 90° of knee flexion (Table 2).

In general, the biomechanics results of in vivo studies 1 and 2 were similar to the corresponding values in the cadaveric study (Tables 1 and 2). For example, the biomechanical values for varus instability at 30° for both in vivo studies were within 6% of the corresponding values for the cadaveric specimens (Tables 1 and 2). There was also a tendency for the in vivo values to be lower (i.e., less unstable) than the corresponding cadaveric values, with 17/24 (70.8%) comparisons (those with structures sectioned) being lower in the in vivo

	30°		60°		90°	
	Control	Operated	Control	Operated	Control	Operated
In Vivo Study 1 (PLT + LCL sectioned)						
Varus	6.17(1.85)	9.20 (3.26)	9.35 (1.29)	13.57 (4.52)	12.52(1.57)	18.13* (4.30)
Valgus	5.03 (1.18)	5.07 (1.47)	4.23 (1.16)	6.22(2.32)	8.72 (1.46)	9.63 (2.12)
Internal	2.08 (1.15)	2.55(1.14)	6.17 (1.97)	7.03(1.54)	9.62 (2.35)	10.38(2.57)
External	1.93 (1.20)	2.37(0.97)	3.75(1.30)	4.00 (1.09)	3.82(1.44)	4.30 (1.42)
In Vivo Study 2 (PLT + LCL + LAT CAP sectioned)						
Varus	6.18 (2.16)	9.52* (3.04)	9.31 (1.86)	15.19* (2.57)	12.27 (2.12)	18.17* (2.63)
Valgus	3.96 (1.30)	4.53 (1.01)	5.55(1.47)	6.18 (1.20)	7.31(1.31)	8.51 (2.50)
Internal	2.62 (1.18)	3.25(1.27)	6.22 (1.61)	9.19* (1.51)	9.30 (2.14)	13.07* (1.66)
External	1.62(0.73)	2.05 (0.61)	3.43 (1.21)	4.93* (0.97)	4.67 (1.44)	6.22* (1.09)

Table 2. Biomechanical Results (Varus–Valgus and Internal–External Rotation) for In Vivo Study 1 and Study 2^a

 $PLT+LCL, popliteus \, tendon \, and \, lateral \, collateral \, ligament \, sectioned; \\ PLT+LCL+LAT \, CAP, popliteus \, tendon, \, lateral \, collateral \, ligament, \, and \, lateral \, capsule \, sectioned.$

^aValues are presented as mean degrees (standard deviation).

p < 0.05 compared to control.

specimens. Variable degrees of healing and fibrosis in the live goats compared to the cadaveric specimens most likely explain at least some of these observed differences.

Radiology and Histology (In Vivo Studies 1 and 2)

No radiographic lesions (including periarticular osteophytes) were observed in the intact knee joints. Similarly, gross examination of disarticulated knee joints revealed no macroscopic articular cartilage lesions in any of the knee joints. Although adult goats had been requested for the study, the majority of the goats had open growth plates that were observed radiographically in the distal femur and proximal tibia and were evident in histological sections of the proximal tibia.

The histological lesions in the knee joints were more severe in the medial tibial plateau than the lateral tibial plateau in 28/32 (87.5%) of the knee joints from the two in vivo studies (Table 3). For this reason, statistical comparisons of osteoarthritis scores between the unoperated control and operated joints were done using only data from the

Table 3. Results for Histological Grades and Measurements from the Medial Tibial Plateaus in Goats from In Vivo Study 1 and Study 2, 7 and 3 Months (Respectively) after Surgical Induction of Posterolateral Instability

Parameter	Unoperated Knee Joints Median (Range)	Operated Knee Joints Median (Range)	Wilcoxon Signed Rank <i>p</i> -Value
In Vivo Study 1 (<i>n</i> =6)			
Articular cartilage structure	1.0(1-2)	1.5(0-3)	0.500
Loss of toluidine blue stain	1.5(0-1)	0 (0-2)	0.625
Chondrocyte clones	0 (0–0)	0 (0–0)	0.500
Osteophytes	0 (0–0)	0 (0–0)	0.500
Max. number of tidemarks	6.5 (5-7)	5.5(4-8)	0.570
Blood vessels crossing tidemark	4.5 (3-7)	4.0 (1-8)	0.742
Chondrified blood Vessels	0 (0-0)	0 (0–0)	1.000
Subchondral bone thickness (µm)	1120 (928-1338)	1095 (869-1356)	1.000
In Vivo Study 2 $(n = 10)$			
Articular cartilage structure	5.5(0-14)	3.5(0-14)	1.000
Loss of toluidine blue stain	6.0 (0-16)	6.5 (0-16)	1.000
Chondrocyte clones	0.5 (0-2)	1.0(0-4)	NA
Osteophytes	0.5 (0-2)	0.5(0-2)	NA
Max. number of tidemarks	7 (5–9)	6.5 (4-9)	0.438
Blood vessels crossing tidemark	9.0 (4-16)	9.0 (1-16)	0.656
Chondrified blood vessels	0 (0-0)	0 (0-1)	NA
Subchondral bone thickness (μm)	729(329 - 937)	694 (485 - 963)	0.438

NA, not applicable.



Figure 2. Histological section from medial tibial plateau demonstrating absence of articular cartilage lesions (articular cartilage structure score = 0); operated knee joint (goat #5) from In Vivo Study 2. H&E. Bar = $250 \mu m$.

medial tibial plateau in both groups of animals (In Vivo Studies 1 and 2). Furthermore, in the majority of cases, the histological lesions of osteoarthritis in these animals were minimal (Fig. 2). For example, the median score for articular cartilage structure in Study 1 was 1 (range: 0-3) in the medial tibial plateaus and 0 (range: 0-1) in the lateral tibial plateaus. The scores for other parameters in this group of animals also were low (Table 3), and no osteophytes were observed histologically. Half of the animals (n = 5) in Study 2 had similarly low scores; however, the other half of the animals in this study had higher scores (e.g., articular cartilage structure scores ranged from 2 to 14) that were present bilaterally (in both unoperated control and operated joints) (Fig. 3). Although no tibial osteophytes were observed radiographically (preoperatively or postoperatively) in any of the Study 2 animals, these same five goats had periarticular osteophytes that were evident histologically in the medial tibial plateau. There were no significant differences in severity of histological grading scores between unoperated control joints and operated knee joints for either Study 1 or Study 2 (Table 3).

The SCB of the medial tibial plateau was diffusely thick in all animals (Table 3), with a median thickness in Study 1 animals (including both operated and unoperated joints) of $1,120 \ \mu m$

(range: $869-1,356 \mu$ m) and a median thickness in Study 2 animals of 705 μ m (range: $329-963 \mu$ m). The mean ratio of articular cartilage width to SCB width was approximately 1.3.

DISCUSSION

Posterolateral knee injuries have been demonstrated to result in significant functional limitations and appear to lead to meniscal tears and osteoarthritis in humans.¹⁷ However, the natural history of untreated posterolateral knee injuries is not well understood. A rabbit model of posterolateral instability produced a significantly unstable knee joint^{5,11}; however, the rabbit knee is too small to allow surgical reconstruction for assessment of the effects of repair techniques. Thus, the present study was done to determine if the goat knee may provide a useful model of posterolateral instability.

Because we demonstrated that sectioning of the PLT and LCL in cadaveric goat knees resulted in significantly greater varus instability at all three flexion angles examined and significantly greater internal-external rotation at two of the three flexion angles examined, we hypothesized that sectioning of these structures would suffice to create significant instability in vivo. The results of In Vivo Study 1 demonstrated that this was not



Figure 3. Histological section from medial tibial plateau demonstrating fibrillation of superficial aspect of the articular cartilage (articular cartilage structure score = 14); unoperated knee joint (goat #11) from In Vivo Study 2. H&E. Bar = $250 \mu m$.

true except at 90° of flexion for varus instability, even though there was no evidence of healing of the sectioned structures at the termination of the study. In addition, and most likely due to the lack of significant instability in these knee joints, the lesions of osteoarthritis 7 months after the surgery were minimal. For this reason, and also because sectioning of the lateral joint capsule had resulted in additional varus and internal-external instability in the cadaveric study, we chose to additionally section the LAT CAP (in addition to the PLT and LCL) in In Vivo Study 2. This intervention resulted in significant varus, external, and internal rotation at 60° and 90° of flexion; however, lesions of osteoarthritis in these joints were not significantly more severe than in the contralateral unoperated joints.

As in other animal models of osteoarthritis, the histological lesions in the unstable joints were most severe in the medial joint compartment, specifically the medial tibial plateau. For unexplained reasons, half of the goats from Study 2 had high articular cartilage structure scores bilaterally. Unlike any of the other animals in this project, these animals also had periarticular tibial osteophytes that were evident histologically but not radiographically.

Skeletally mature goats had been requested for this study; however, nearly all specimens had open physes in the distal femur and proximal tibia that were evident radiographically, histologically, or both. These appeared to be actively undergoing endochondral ossification. In retrospect, all of the goats were confirmed to be at least 12 months of age at the time of the surgery. Fusion of the proximal tibial epiphysis and tibial crest in domestic goats has been reported to occur between 18 and 21 months of age in female goats and after 24 months in male castrate goats.¹⁸ Although not likely to have a major influence on this study given the severity of the instability that was induced, the fact that the goats were not mature may have made the joints somewhat less susceptible to the development of lesions of osteoarthritis.

In humans, the shapes of both the lateral femoral condyle and lateral tibial plateau are convex, creating a relatively unstable bony interface at the knee joint.¹⁹ This inherent lack of bony stability is accentuated in patients with posterolateral injuries. The interface between the convex distal femur and the more concave proximolateral tibia in the goat is more stable, and may provide sufficient bony structural support to protect against lesions induced by posterolateral injury. We speculate that the lack of a distinct fibular head in the goat and the bony anatomy of the goat knee (with the relatively proximal location of the fused fibular head) may also support the proximal tibia by acting as a buttress even in the face of a posterolateral knee injury.¹² We theorize that these differences in bony anatomy of the knee joint in humans versus goats may explain, in part, why the interventions used in this study failed to produce functionally significant changes in joint stability and instability-related lesions of osteoarthritis in the goats.

The SCB plate in all of the goat specimens was strikingly thick, being nearly three times thicker than in dogs or monkeys.^{20,21} It is possible that this is simply a reflection of body weight, since it has been demonstrated that SCB thickness increases with increasing body weight in cynomolgus monkeys.²² The ratio of articular cartilage thickness to SCB thickness in goats (approximately 1.3), however, is more similar to $rats^{23}$ (approximately 1.0) than it is to $dogs^{20}$ or cynomolgus monkeys²¹ (approximately 3.5 for both), suggesting that the increased SCB thickness observed in the goats may simply be a species difference. In support of this argument, the goats examined in this study were relatively young and did not have evidence of chronic/end stage osteoarthritis, which would be associated with an increase in SCB thickness. We also have no explanation for the differences in SCB thickness between the two operative groups.

The present study confirms that surgical transection of the PLT, LCL, and LAT CAP in goats leads to measurable posterolateral knee instability; however, the goat model does not appear to mirror the human disease in terms of osteoarthritis development in the time frames that were tested. Additional studies need to be done to determine if further manipulation of the model will result in sufficient morphological changes to allow its use in the assessment of the effectiveness of surgical stabilization procedures.

ACKNOWLEDGMENTS

This study was supported by a Career Development Grant from the Orthopaedic Research and Education Foundation (R. F. L.), and Grants RR14099 and RR018719 from the NIH (C. S. C.). No benefits were received by any author related to the subject of this manuscript. The assistance of Anne Undersander with the preparation of histological sections is acknowledged.

REFERENCES

1. Hughston JC, Andrews JR, Cross MJ, et al. 1976. Classification of knee ligament instabilities. Part II. The lateral compartment. J Bone Joint Surg [Am] 58:173-179.

- LaPrade RF, Wentorf FA. 2002. Diagnosis and treatment of posterolateral knee injuries. Clin Orthop Rel Res 402:110-121.
- 3. LaPrade RF, Terry GC. 1997. Injuries to the posterolateral aspect of the knee. Association of anatomic injury patterns with clinical instability. Am J Sports Med 25:433–438.
- 4. LaPrade RF, Johansen S, Wentorf FA, et al. 2004. An analysis of an anatomical posterolateral knee reconstruction: an *in vitro* biomechanical study and development of a surgical technique. Am J Sports Med 32:1405–1414.
- LaPrade RF, Wentorf FA, Crum J. 2004. Assessment of healing of Grade III posterolateral corner injuries: an *in vivo* model. J Orthop Res 22:970–975.
- Woo SLY, Gomez MA, Inoue M, et al. 1987. New experimental procedures to evaluate the biomechanical properties of healing canine medial collateral ligaments. J Orthop Res 5:425-432.
- Woo SLY, Inoue M, McGurk-Burleson E, et al. 1987. Treatment of the medial collateral ligament injury. II. Structure and function of canine knees in response to difficult treatment regimes. Am J Sports Med 15:22-29.
- Lundberg WR, Lewis JL, Smith JJ, et al. 1997. In vivo forces during remodeling of a two-segment anterior cruciate ligament graft in a goat model. J Orthop Res 15: 645–651.
- Smith JJ, Lewis JL, Mente PL, et al. 1996. Intraoperative force-setting did not improve the mechanical properties of an augmented bone-tendon-bone anterior cruciate ligament graft in a goat model. J Orthop Res 14:209–215.
- Crum J, LaPrade RF, Wentorf FA. 2003. The anatomy of the posterolateral aspect of the rabbit knee. J Orthop Res 21:723-729.
- LaPrade RF, Wentorf FA, Olson EJ, et al. 2006. An *in vivo* injury model of posterolateral knee instability. Am J Sports Med 34:1313-1321.
- LaPrade RF, Kimber KA, Wentorf FA, et al. 2006. The anatomy of the posterolateral aspect of the goat knee. J Orthop Res 24:141-148.
- Kamekura S, Hoshi K, Shimoaka T, et al. 2005. Osteoarthritis development in novel experimental mouse models induced by knee joint instability. Osteoarthritis Cartilage 13:632–641.
- 14. Hayami T, Pickarski M, Zhuo Y, et al. 2006. Characterization of articular cartilage and subchondral bone changes in the rat anterior cruciate ligament transection and meniscectomized models of osteoarthritis. Bone 38:234-243.
- 15. Park YS, Lim SW, Lee IH, et al. 2007. Intra-articular injection of a nutritive mixture solution protects articular cartilage from osteoarthritic progression induced by anterior cruciate ligament transection in mature rabbits: a randomized controlled trial. Arthritis Res Ther 9:R8 (doi:10.1186/ar2114).
- Ham KD, Loeser RF, Lindgren BR, et al. 2002. Long-term estrogen replacement therapy decreases osteoarthritis severity in cynomolgus monkeys. J Orthop Res 46:1956– 1964.
- Kannus P. 1989. Nonoperative treatment of grade II and III sprains of the lateral ligament compartment of the knee. Am J Sports Med 17:83–88.
- Noddle B. 1974. Ages of epiphyseal closure in feral and domestic goats and ages of dental eruption. J Archaeol Sci 1:195–204.
- 19. Jakob RP, Hassler H, Staeubli HU. 1981. Observations on rotatory instability of the lateral compartment of the knee.

Experimental studies on the functional anatomy and the pathomechanism of the true and the reversed pivot shift sign. Acta Orthop Scand Suppl 191:1–32.

- Carlson CS, Guilak F, Vail TP, et al. 2002. Synovial fluid biomarker levels predict articular cartilage damage following complete medial meniscectomy in the canine knee. J Orthop Res 20:92–100.
- 21. Ham KD, Oegema TR, Loeser RF, et al. 2004. Effects of long-term estrogen replacement therapy on articular cartilage IGFBP-2, IGFBP-3, collagen and proteoglycan

levels in ovariectomized cynomolgus monkeys. Osteoarthritis Cartilage 12:160–168.

- 22. Carlson CS, Loeser RF, Purser CB, et al. 1996. Osteoarthritis in cynomolgus macaques III: effects of age, gender, and subchondral bone thickness on the severity of disease. J Bone Miner Res 11:1209-1217.
- 23. Ekenstedt K, Sonntag WE, Loeser RF, et al. 2006. Effects of prolonged growth hormone and insulin-like growth factor 1 deficiency on osteoarthritis severity in rat knee joints. Arthritis Rheum 54:3850–3858.