IN-VIVO FEMOROTIBIAL KINEMATICS IN DOGS WITH CRANIAL CRUCIATE LIGAMENT INSUFFICIENCY BEFORE AND AFTER SURGICAL STABILIZATION

By

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Cranial cruciate ligament (CrCL) insufficiency causes stifle instability. Lateral fabellotibial suture stabilization (LFTS) and tibial plateau leveling osteotomy (TPLO) aim to address the instability, but the *in-vivo* alterations in stifle kinematics associated with CrCL insufficiency and after LFTS or TPLO have not been accurately defined. The objective of this study was to quantify the 3-dimensional (3D) kinematics of the femorotibial joint of dogs with naturally occurring CrCL insufficiency during ambulation, before and after treatment with either LFTS or TPLO. Twenty-eight client-owned dogs (15-40 kg) with naturally occurring unilateral complete CrCL insufficiency were enrolled. Lateral fluoroscopic images were obtained during treadmill walking, both pre-operatively and at 6-months post-operatively. Computed tomographic (CT) scans of the hind limbs were acquired to create subject specific digital models of the femur and tibia. Stifle flexion/extension angle, craniocaudal translation, and internal/external rotation were calculated using a previously described 3D to 2-dimensional (2D) image registration process. Results were compared between the pre-operative CrCL-deficient, 6-month post-operative, and contralateral (control) stifles.

CrCL insufficiency was associated with greater flexion throughout the gait cycle, cranial tibial translation throughout the gait cycle that was most prominent during the stance phase, and
internal tibial rotation during the stance phase. After LFTS, cranial tibial subluxation was reduced but remained present in 100% (9/9) of stifles, while axial rotation patterns were not different from control. After TPLO, craniocaudal instability was reduced in all dogs, with caudal tibial subluxation observed in 10/16 dogs and cranial tibial subluxation observed in 5/16 dogs. Craniocaudal translation patterns did not differ from control in 1 dog. After TPLO, axial rotation patterns were not different from control; however, dogs with caudal tibial subluxation had more external tibial rotation during mid to late stance phase compared to dogs with cranial tibial subluxation. Stifle flexion/extension patterns were not different from control after either LFTS or TPLO or LFTS.

Naturally occurring, complete CrCL insufficiency in dogs causes profound craniocaudal translational and axial rotational instability, which is most pronounced during the stance phase of gait. Neither LFTS nor TPLO reliably impart normal stifle kinematics. The abnormal post-operative kinematics may be a major contributing factor for meniscal damage and progressive osteoarthritis (OA). Based on our findings, the refinement of current techniques as well as the development of new techniques for CrCL insufficiency in dogs are strongly indicated.
CHAPTER 1
INTRODUCTION

Cranial Cruciate Ligament Degeneration

Cranial cruciate ligament insufficiency is a degenerative condition in dogs that is a common cause of pelvic limb lameness and OA.\textsuperscript{1-9} Importantly, CrCL degeneration is considered a bilateral disease with about 1/3 to 1/2 of dogs experiencing contralateral CrCL insufficiency, usually within 2 years.\textsuperscript{10,11} Pet owners were estimated to have spent over $1 billion treating dogs with CrCL insufficiency in 2003.\textsuperscript{12} Conservative medical management options are available and may result in improved function in some dogs, particularly dogs weighing less than 15 kg.\textsuperscript{13} Surgical management, however, is typically recommended to address joint instability, mitigate the progression of OA, and address concurrent meniscal pathology.\textsuperscript{13,14}

Experimental transection of the CrCL invariably leads to stifle joint instability, and has been used to study the development of OA.\textsuperscript{5-9,15-17} The presumed effects of CrCL insufficiency on joint motion during ambulation \textit{in-vivo} are derived from 2 studies that were performed using invasive experimental techniques in normal dogs.\textsuperscript{9,16} Both studies measured joint kinematics before and after experimental unilateral CrCL transection but used different methods: one study used surgically placed metal bone plates with removable spatial linkage, and the second study used implanted metal beads that were tracked using biplanar fluoroscopy.\textsuperscript{9,16} However, acute experimental CrCL transection may not accurately replicate the pathology and biomechanics that are present in dogs with naturally occurring CrCL insufficiency. Additionally, there are logistical and ethical issues associated with the invasive nature of implanting metallic markers when studying the effects of CrCL insufficiency in client owned animals. A recent clinical study used lateral fluoroscopy to document stifle instability in a series of client owned dogs with naturally occurring CrCL insufficiency, but unfortunately the kinematic evaluation was limited to
subjective qualitative assessments. Recently, our group validated the use of single plane fluoroscopy (without the use of metal implants) for accurate quantification of bone motion in 3 dimensions using methodology developed to study human knee kinematics. While biplanar fluoroscopy is considered the most accurate modality for determining joint kinematics, Jones, et al. demonstrated that the single plane modality was accurate to within 1.28 mm for translations and 1.58° for rotations.

**Surgical Management of CrCL Degeneration**

Extracapsular suture stabilization techniques such as lateral LFTS, and osteotomy techniques such as TPLO, are commonly performed for treatment of CRCL insufficiency. *Ex-vivo* studies have been performed to investigate the success of LFTS in providing joint stabilization after CRCL transection, but results are conflicting. Most *in-vivo* clinical outcome studies after forms of extracapsular stabilization have shown high owner satisfaction (82-90%) and subjective resolution of lameness (78-82%), but less successful resolution of stifle instability (55-76%). Additionally, 2 prospective studies using force plate gait analysis to objectively evaluate lameness have shown incomplete return of limb function after LFTS within the 1-year study period; the authors did not determine the cause of incomplete recovery. It is suspected that persistent instability is a major cause of persistent lameness after LFTS, and that persistent instability is more common than has been previously reported using subjective measures.

Similarly for TPLO, studies have shown significant clinical improvement but kinematics are not returned to normal. Tibial plateau leveling osteotomy is theorized to relieve the stifle’s mechanical dependence on the CrCL, and thereby stabilize the stifle, by decreasing the caudo-distal slope of the proximal tibia. *Ex-vivo* studies have generally shown resolution of cranial tibial subluxation following TPLO, but at the cost of inducing caudal tibial subluxation and
altered articular contact mechanics across the stifle.\textsuperscript{17,35,36} The findings from these bench-top studies, however, conflict with a clinical radiographic study that demonstrated 33\% (5/15) of stifles had persistent cranial tibial subluxation after TPLO.\textsuperscript{37} Persistent stifle instability may be a major underlying cause of deleterious outcomes such as late meniscal tears, “pivot shift,” and progressive OA.\textsuperscript{38-41}

**Knowledge Gap**

Surgical therapies developed to treat dogs with naturally occurring CrCL insufficiency aim to address the resultant instability.\textsuperscript{14} However, our knowledge of the \textit{in-vivo} kinematics of CrCL insufficiency is derived from 2 studies using normal dogs with experimental ligament transection.\textsuperscript{9,16} Additionally, the \textit{in-vivo} alterations in stifle kinematics after treatment with LFTS or TPLO have not been accurately defined. Characterization of joint kinematics of naturally diseased CrCL-deficient stifles is required because experimental CrCL transection may not accurately replicate the natural, chronically diseased state. Precise assessment of the femorotibial kinematics following LFTS and TPLO may provide further insight into suboptimal outcomes associated with these procedures, as well as guide the development of future treatment options for CrCL insufficiency in dogs.

**Aims**

Therefore, the aims of this project include:

1. To quantify the 3D femorotibial joint kinematics of dogs with naturally occurring CrCL insufficiency during ambulation

2. To quantify the 3D femorotibial joint kinematics of dogs with naturally occurring CrCL insufficiency, after treatment with LFTS, during ambulation

3. To quantify the 3D femorotibial joint kinematics of dogs with naturally occurring CrCL insufficiency, after treatment with TPLO, during ambulation
CHAPTER 2
LITERATURE REVIEW

Kinematic Gait Analysis

Kinematic gait analysis is the study and geometric and temporal quantification of motion. For example, in the case of this thesis, we are specifically interested in the rate, direction, and magnitude of motion of the femur and the tibia (in relation to each other) as the dog moves through the walking gait cycle. The motions that occur in any joint can be broken down into linear translations and rotations in 3 dimensions, meaning that we can measure and describe motion in 6 degrees of freedom.

For walking, trotting, or other gaits, the gait cycle is most simply divided into a stance phase, where the foot is planted, and a swing phase, where the foot is swinging forward. The gait cycle can be even further divided into 8 segments: initial foot contact, loading response, mid-stance, terminal stance, pre-swing, initial swing, mid-swing, and terminal swing. At each of these gait cycle segments, changes in muscular, weight bearing, and other forces cause predictable kinematics at each gait cycle segment, which have been defined in the normal human knee but not to this level of precision in the canine knee. When normal human or canine subjects are tested while performing normal gaits, the patterns of joint motion have minimal variation between subjects, although speed of gait may influence kinematic results and therefore must be controlled for or taken into account. Diseased states such as neuromuscular conditions or ligamentous instability may result in increased variation between subjects, but often a pattern is still appreciable.

Cadaveric studies provided the initial basis for understanding canine stifle kinematics. These studies generally require extensive dissection during specimen preparation for testing. With ex-\textit{vivo} studies, the relative motions of the femur and tibia can be
easily measured after the force application and/or interventions. However, cadaveric studies are generally unable to replicate the multi-faceted and complex forces acting on the stifle, and do not account for biologic responses such as the effects of stifle effusion and pain.

Multiple methods have been used to measure stifle kinematics *in-vivo*. The majority of kinematic studies in dogs have used optical motion capture, where markers are placed on the skin over bony landmarks, and specialized cameras and equipment track marker motion during ambulation. While optical motion capture has the huge benefits of being non-invasive and allowing ambulation during testing, markers cannot be placed medially due to interference from the trunk. Variability in skin marker placement and skin motion over the targeted bony landmarks imparts error of approximately 15° and 10-12mm. Ultimately, optical motion capture is limited to estimating flexion-extension motion, as this motion is visible laterally and is relatively large during various daily activities (40-57°). Changes to joint alignment *in-vivo* can also be assessed with stressed radiography: radiographic views can be obtained while the animal bears weight or when placing the limb in tibial compression position, both of which should promote cranial tibial translation. The standing radiograph method has the advantage of accounting for normal gravitational, muscular, or ligamentous forces that the live animal experiences during weight bearing, but is simply an analysis of a static joint.

A commonly used *in-vivo* kinematic measurement technique in humans is the use of fluoroscopic imaging during dynamic activity. Using this methodology, a custom-made 3D bone model is generated from CT or magnetic resonance imaging data, which is then superimposed over fluoroscopic images (taken in 1 or more planes). A 3D coordinate system is applied to the femur and tibia models independently so that the respective positions (6 degrees of freedom) of the bone models, representing the imaged bones, can be determined. This method has the
benefit of being able to study animals in motion while eliminating artifact due to skin motion, thereby greatly increasing accuracy.

There are multiple variations of this imaging technique, which affect accuracy. For example, the use of biplanar fluoroscopy provides higher accuracy than single plane fluoroscopy. Accuracy of the biplanar technique was reported to be at least 0.20 mm and 1.7°. A single plane technique has been validated for use in dogs: when a TPLO plate is present on the tibia, the accuracy is at least 1.05 mm and 1.08°, and without any metal markers, the accuracy is at least 1.28 mm and 1.64°. Elimination of the need for metal markers reduces the invasiveness of the technique, and reduction from biplanar to single planar radiography reduces the radiation exposure, increases the field of view for study, and does not require highly specialized equipment while maintaining acceptable accuracy for most applications. Unfortunately, application of this fluoroscopic technique remains limited due to high equipment expense and the time consuming nature of the data processing.

Relevant Anatomy

The canine stifle is a complex synovial joint consisting of 7 bones, with the main weight bearing bones being the tibia and femur (Figure 2-1). The femur and tibia are incongruent: the round femoral condyles sit on top of the weight bearing, sloped tibial plateau. The tibial plateau is sloped from cranioproximal to caudodistal, with a mean tibial plateau angle (TPA) of 23-28° in normal dogs. Because of the bony incongruence, the stifle joint relies on menisci, ligaments, joint capsule, and surrounding musculature to maintain stability. The cruciate ligaments, along with the collateral ligaments and menisci, provide the primary stabilizing function to the stifle joint.

There are 2 cruciate ligaments, the CrCL and the caudal cruciate ligament (CaCL), which cross in the sagittal plane to form an ‘X’. The CrCL originates from a fossa on the caudomedial
aspect of the lateral femoral condyle, courses cranially through the stifle joint passing lateral to
the CaCL, then inserts on the cranial intercondyloid area of the tibia. The CaCL originates from
a ventrally located fossa in the lateral aspect of the medial femoral condyle, courses
caudodistally through the stifle joint passing medial to the CrCL, then inserts on the medial
aspect of the popliteal notch. The ligaments are composed of collagen and are covered in a
synovial sheath. The fibers of the CrCL spiral outward by about 90° from proximal to
distal. The CrCL is generally taut in extension and lax in flexion, with the craniomedial band
being taut in both extension and flexion and the caudolateral band being taut in extension but lax
in flexion.

There are 2 theories that attempt to explain how force is transmitted across the stifle joint.
In 1993, Slocum and Slocum introduced the “active force model” of the stifle joint (Figure 2-2). It was proposed that the force of weight bearing travels parallel to the long axis of the tibia
and generates a shear force at the stifle joint because of the sloped nature of the tibial plateau.
During weight bearing, this shear force, along with contraction of the quadriceps and
gastrocnemius muscles, encourage cranial tibial translation and/or caudal and distal translation of
the femur. These forces are opposed by contraction of the hamstrings, in addition to the tether of
the CrCL and the caudal pole of the medial meniscus. Based on this “active force model”,
Slocum proposed the TPLO for treatment of CrCL insufficiency, which is expanded upon in the
section entitled Treatment of CrCL Insufficiency within this Chapter.

In 2002, Tepic, et al. introduced a different theory of force transmission across the stifle
joint, based on the work of Nisell, et al. in human subjects (Figure 2-3). In this model, it was
proposed that the force of weight bearing is parallel to the patellar tendon as it crosses the stifle
joint. In flexion/extension positions where the patellar tendon and the slope of the tibial
plateau are not perpendicular, a shear force results - similar to that described in Slocum’s active force model.\textsuperscript{70,71} This angle is not perpendicular during extension, therefore there is a cranially directed shear force during the extended weight bearing phase of gait.\textsuperscript{72} The patellar tendon does become perpendicular to the tibial plateau at approximately 110° of flexion, and with continued flexion the shear force is converted to a caudally directed force according to Tepic’s model.\textsuperscript{72} The theories of force transmission across the stifle joint are important to know because osteotomy treatments for CrCL insufficiency are aimed at neutralizing the shear force that generates cranial tibial translation in the absence of the CrCL. The correct mechanism has not been definitively identified.

**Function of the CrCL**

The CrCL is a primary stabilizer of the stifle joint and has 3 major stabilizing functions: prevention of cranial tibial translation, internal tibial rotation, and stifle hyperextension.\textsuperscript{15} One *ex-vivo* study found that transecting the CrCL resulted in 2mm cranial tibial translation in extension and 9.5mm cranial tibial translation in 90° of flexion when a cranial drawer force was applied, while other studies have found up to 15mm of cranial tibial translation in extension and negligible cranial tibial translation in deep flexion when a weight bearing force is applied.\textsuperscript{15,47,73,74} If only the craniomedial band of the CrCL is transected, cranial tibial translation can be appreciated in flexion but not in extension, whereas if only the caudolateral band is transected this is no laxity regardless of stifle position.\textsuperscript{15} Transection of the CaCL or medial or lateral collateral ligament does not result in cranial tibial laxity regardless of stifle position.\textsuperscript{15} Abnormal cranial tibial translation has also been demonstrated in *in-vivo* kinematic studies of experimental CrCL transection, most pronounced during stance phase, with a maximum of up to approximately 15mm.\textsuperscript{9,16}
Together, the cruciate ligaments limit internal tibial rotation by twisting on each other, but have no inhibitory effect on external tibial rotation. Ex-vivo, with the ligaments of the stifle intact, there is a range of 11° of axial rotational motion in extension and 27° in flexion. After transection of the CrCL, there is increased internal tibial rotation resulting in 20° of rotational motion in extension and 53° of rotational motion in flexion. The collateral ligaments contribute to prevention of external tibial rotation, but have no effect on internal tibial rotation if the cruciate ligaments are intact. Increased internal tibial rotation during ambulation has been shown in an in-vivo study of dogs with experimental CrCL transection, while this was not demonstrated in a second similar study.

The CrCL limits hyperextension due to impingement of the femur on the distal aspect of the CrCL when the stifle is in extension. Ex-vivo, with the ligaments intact the stifle can extend to 148° of extension. When the CrCL is transected, the stifle can be hyperextended to 160° of extension, while there is no increase with transection of the CaCL alone. When both the CrCL and CaCL are transected, slightly more hyperextension is allowed with a final extension angle of 166°. In contrast, in-vivo studies have shown that the CrCL-deficient stifle is actually held in approximately 5-14° less extension during the stance phase of gait. This decreased extension angle seen in-vivo may represent the decrease in weight bearing to minimize pain or joint motion, or could represent a protective neurologic feedback mechanism.

In addition to the stabilizing functions of the CrCL, the ligament also has mechanoreceptive and proprioceptive functions. The presence of receptors in the CrCL has been demonstrated using a modified gold chloride stain, with more receptors located in the proximal aspect of the CrCL. In humans, increased stress to the anterior cruciate ligament (ACL) (loaded knee extension) results in excitation of the hamstring muscles and inhibition of the
quadriceps muscles using EMG data, suspected to be via a reflex arc.\textsuperscript{80} Contraction of the quadriceps muscles increases ACL strain while contraction of the hamstring muscles decreases ACL strain, therefore this reflex arc is thought to be protective for the ACL.\textsuperscript{80} However, this study also showed that similar muscular coordination can occur in some humans after ACL tear, which the authors attributed to a theoretical alternative reflex arc implying that the maintenance of appropriate muscular function is not necessarily ACL-dependent.\textsuperscript{80}

**Etiology of CrCL Degeneration**

CrCL insufficiency is usually a degenerative condition with a multifactorial etiology, but traumatic injury can also occur (Figure 2-4).\textsuperscript{1,2} CrCL degeneration is bilateral in 35-50\% of cases.\textsuperscript{10,11} Factors that contribute to the development of CrCL insufficiency include genetic, conformational, and environmental factors, and in most cases it is unclear which factor is primary, whether the effects are cumulative, or whether some factors are simply concurrent findings.

Over the past decades, a breed predisposition to developing CrCL disease has been demonstrated. Breeds such as Newfoundlands, Labrador retrievers, Rottweilers, Staffordshire bull terriers, West Highland white terriers, and Yorkshire terriers are predisposed to developing the condition, while Greyhounds and most small breed dogs are less prone to developing CrCL degeneration.\textsuperscript{64,81-84} Specific causative genes have now been identified.\textsuperscript{81,82} Mutations in 3 different regions of the genome were significantly associated with the development of CrCL degeneration in Newfoundlands, but an important conclusion of this work was that there was incomplete penetrance and dogs required additional influences to develop CrCL degeneration.\textsuperscript{81} In a case controlled study of 749 Newfoundlands, Labrador retrievers, Rottweilers, and Staffordshire bull terriers, an association between specific single nucleotide polymorphisms and the development of CrCL disease was demonstrated.\textsuperscript{82} These mutations were associated with
genes involved in ligament strength, stability, and the formation of extracellular matrix, indicating that presence of these mutations may result in an inherent weakness in the CrCL that leads to insufficiency, rather than increased strain on the ligament.\textsuperscript{82} Importantly, the authors of these studies have acknowledged weaknesses in their methods and the need for further investigation to confirm their findings as well as potentially identify other causative genetic mutations.\textsuperscript{81,82} Despite the identification of genetic predispositions towards the development of CrCL degeneration, it is unclear whether genetic predisposition alone can cause CrCL degeneration or whether the presence of additional risk factors is required.\textsuperscript{85}

The bony conformation of the hind limb has been heavily studied as a possible causative factor for CrCL degeneration, thought to be due to mechanical overload of the ligament. An increased TPA or patellar tendon angle (PTA) are obvious considerations as risk factors for CrCL degeneration given their theorized importance in force transmission across the stifle joint. An excessively steep TPA (typically defined at \( > 35^\circ \)) has been demonstrated to induce changes to the extracellular matrix and collagen of the CrCL in an experimental model where an excessive TPA of \( 40^\circ \) was created unilaterally, while no changes were noted in the normal contralateral limb.\textsuperscript{86} A second study demonstrated that, in a population of clinical dogs with CrCL insufficiency, dogs with an excessively steep TPA developed disease at a younger age compared to dogs with a TPA < \( 35^\circ \).\textsuperscript{87} An increased but not excessive TPA (ie, < \( 35^\circ \)) has been associated with increased risk for CrCL degeneration in multiple breeds including Labrador retrievers,\textsuperscript{88-91} while other studies have failed to demonstrate this relationship in Labrador retrievers.\textsuperscript{64,92} The radius of curvature of the medial and lateral tibial plateaus may also play a role: the medial tibial plateau was found have a larger radius of curvature in CrCL insufficient stifles compared to contralateral control stifles in a clinical study; theoretically, this
conformation increases the strain on the CrCL by promoting internal tibial rotation (or external femoral rotation).\textsuperscript{93} One study has shown an increased PTA to be associated with increased risk of CrCL degeneration.\textsuperscript{94} Additional conformational qualities that may predispose to CrCL degeneration but are not routinely tested for include a narrow intercondylar region of the femur,\textsuperscript{95,96} or an increased ratio of the radius of curvature of the medial versus the lateral tibial plateau,\textsuperscript{93} however these findings may also be secondary to CrCL disease and resultant OA. Angular and torsional deformities of the femur and tibia, the presence of medially luxating patellas, and an under-developed tibial tuberosity all have the potential to increase strain on the CrCL, but these conformational abnormalities are not present in the majority of cases of CrCL degeneration.\textsuperscript{89,90,98,99}

The CrCL could also be weak primarily, rather than secondary to the mechanical stressors. As implied above, there is genetic evidence for this theory.\textsuperscript{81,82} Histopathology of naturally diseased CrCLs shows a decreased in number of ligament fibroblasts, a change in cell morphology, poor quality collagen, and poor extracellular matrix compared to young normal dogs, particularly in the core region of the ligament.\textsuperscript{2} A major limitation of this study is that it cannot differentiate whether the changes to the ligament were causative (versus being secondary to CrCL degeneration or the presence of joint disease) because only normal and grossly abnormal ligaments were examined rather than also examining predisposed ligaments. Another study attempted to provide this type of information by gathering data at the time of necropsy from Labrador retrievers and greyhounds with normal CrCLs.\textsuperscript{97} This study revealed a smaller collagen fibril diameter in the normal CrCL of Labrador retrievers compared to greyhounds, which may indicate that degeneration of the CrCL in predisposed breeds could be secondary to an inherently smaller collagen fibril diameter.\textsuperscript{97}
The environmental factors that may promote CrCL degeneration encompass a wide variety of influences including advanced age, increased body weight, obesity, exercise, inappropriate muscle tone/contraction, neuter status, and inflammation within the joint. Generally, environmental factors are suspected to promote the degeneration of the CrCL in dogs that are otherwise predisposed, rather than being primarily causative. Increased age, weight, and obesity have been correlated with the development of CrCL insufficiency in many studies, and these are interrelated. For example, in dogs over 15 kg, age related degeneration occurs earlier.\textsuperscript{83} Being obese (body weight >145\% of the ideal weight for the breed) was found to quadruple the risk of developing CrCL insufficiency.\textsuperscript{84}

The role of incomplete muscular support and unbalanced muscle activity in development of CrCL disease is not defined in dogs, though 1 study did find a difference in the distribution of power across the stifle joint between Labrador retrievers and greyhounds.\textsuperscript{100,101} The quadriceps and gastrocnemius muscles must contract to maintain the stifle in extension for weight bearing.\textsuperscript{102} However, contraction of these muscles also serves to pull the tibia cranially and the femur caudally and distally, which adds strain to the CrCL.\textsuperscript{80} Therefore, the hamstrings must also be engaged in order to balance these forces across the stifle joint by essentially pulling the tibial caudally and proximally, reducing ACL strain.\textsuperscript{80} There are numerous scenarios where aberrant muscle forces could theoretically lead to strain on the CrCL because they affect stifle stability, stifle kinematics, and joint loading. Further elucidation of the relationship between abnormal muscle function and CrCL disease is quite important because we may improve outcomes by targeting muscle function during post-operative care, or may be able to prevent or medically manage CrCL tears with focused activities for muscle strengthening, as is performed in humans.\textsuperscript{103-105}
Neutering has been shown to be a risk factor for development of CrCL disease in some studies, while other studies have failed to uphold this finding.\textsuperscript{83,84,87,91,106,107} The age at the time of neuter may be important: for example, neutering at less than 6 months of age was found to be a risk factor for having an excessively steep TPA in dogs with CrCL disease, which may be related to the fact that neutering before skeletal maturity delays growth plate closure.\textsuperscript{87,106} Another study has shown a steeper TPA in neutered dogs compared to intact dogs, though not necessarily an excessively steep TPA.\textsuperscript{91} In addition to the biomechanical implications of developing a steeper TPA predisposing to CrCL degeneration (mechanical overload), early neutering may also be associated with hormonal changes that create muscle or ligamentous weakness, but this has not been proven.

Inflammation and subclinical infection within the joint have also been proposed as causative factors in the development of CrCL degeneration, as opposed to purely secondary inflammation that is due to exposure of ligament antigens such as collagen. The CrCL ligament is normally sheathed in synovium, but collagen becomes exposed in diseased states, which is thought to initiate inflammation. Most studies have found a lymphoplasmacytic effusion with CrCL disease.\textsuperscript{108} Interleukin-8, a chemoattractant for neutrophils, can be increased in CrCL-deficient stifles, but this can be true of any arthritic joint so it is unclear whether this is a primary or secondary finding.\textsuperscript{109} Anti-collagen antibodies have also been identified in CrCL-deficient, contralateral stifles, and normal shoulder joints, making the role of anti-collagen antibodies unclear as well.\textsuperscript{110} In the most recent review article on the subject, it was concluded that the role of inflammation was unclear.\textsuperscript{111} Multiple investigators have attempted to prove a link between subclinical infection and the development of CrCL insufficiency but ultimately this etiology does not appear to be a likely cause.\textsuperscript{112-114}
The cause of CrCL degeneration in dogs has not been fully elucidated, but it is clear that a combination of genetics, signalment, and other factors are contributing. It is likely that numerous constellations of predisposing factors can combine to result in degeneration of the CrCL and that no single factor is required to be present.

**Consequences of CrCL Insufficiency**

The typical presenting complaint for a dog with CrCL degeneration is unilateral or bilateral lameness, which can range from a mild to moderate chronic intermittent lameness to an acute non-weight bearing lameness. Given the chronic nature of the disease, it is presumed that most dogs have a chronic lameness, whether recognized by the owners or not. It is likely that those dogs that present with an acute severe lameness have either converted from a partial to a complete CrCL tear or developed a displaced meniscal tear, resulting in an acute worsening. In addition to lameness, other physical examination findings that are supportive of stifle pain include an abnormal sit test, pain on stifle hyperextension, and a decreased range of stifle motion. Lameness arises from a combination of processes occurring within the joint, which are expanded upon in the following paragraphs.

From cadaveric studies, *in-vivo* studies, and clinical experience, CrCL insufficiency invariably results in abnormal joint motion.\(^5,9,15,17,36,47,75,76\) Cadaveric studies have consistently shown abnormal cranial tibial translation and internal tibial rotation after CrCL transection, which is exacerbated with simulated weight bearing in a normal weight bearing position.\(^15,17,36\) The *in-vivo* 3D kinematic effects of CrCL insufficiency during ambulation have been derived from 2 studies that were performed using invasive experimental techniques in normal dogs.\(^9,16\) These studies revealed that CrCL transection resulted in up to approximately 15 mm cranial tibial translation (worse during weight bearing) and 5-14° more stifle flexion during gait, but the studies were inconsistent with regards to axial rotational motion.\(^9,16\) While these studies provided
invaluable information, invasive methodology was required for implantation of metal markers. Furthermore, acute experimental CrCL transection may not accurately replicate the pathology and biomechanics that are present in dogs with naturally occurring CrCL insufficiency. An in vivo study of dogs naturally affected by CrCL insufficiency also showed increased cranial tibial translation during weight bearing using radiographs obtained during standing, but the methodology only examined 1 joint pose and other degrees of freedom were not studied.37 Stifle instability secondary to CrCL insufficiency can be detected on physical examination using the drawer test and the tibial thrust test.115 In addition to causing joint instability, CrCL insufficiency also causes a shift in contact mechanics on the tibial plateau to a more caudal and more concentrated position, with higher mean and peak loads compared to normal.36

Radiographic and palpable joint effusion is a hallmark of CrCL disease and may be present prior to detectable instability in dogs with early or partial CrCL tears.116 The presence of stifle effusion has been reported to be a predictor for the development of clinical CrCL insufficiency; though one could argue that these dogs already had CrCL disease and therefore this finding was actually an indicator of current CrCL disease rather than a predictor of future disease.117,118 In these studies, dogs that were diagnosed with unilateral CrCL insufficiency with contralateral stifle effusion were 13x as likely to develop contralateral clinical CrCL insufficiency within 1 year117 or had an 85% chance of developing contralateral clinical CrCL insufficiency within 3 years (compared to 25%)118 compared to dogs with unilateral CrCL insufficiency and a normal contralateral stifle. Stifle effusion associated with CrCL insufficiency is generally accepted to be lymphoplasmacytic.108

Medial meniscal injury is a common secondary finding in dogs with CrCL insufficiency, with an approximate incidence of 50% although the reported incidence ranges from 20-
The wide reported range of incidence of concurrent meniscal tears may be related to the variation in sensitivity between diagnostic techniques: sensitivity of arthroscopy is higher than arthrotomy, and either technique can be enhanced by probing of the meniscus. Reported risk factors for development of meniscal injury may be more common in dogs with complete CrCL tears, chronic CrCL tears, and overweight dogs. In most cases, the meniscal tear itself is not painful because the axial portion of the meniscus is not innervated, however displacement of the tear (ex, “bucket-handle tear”) or abaxial meniscal tears can be painful.

Multiple direct consequences of CrCL degeneration lead to the initiation of OA development and experimental transection of the CrCL is a reliable model for generating OA. Normally, variations in cartilage thickness accommodate for weight bearing such that thicker areas of cartilage are associated with areas of higher force transmission, but this association is no longer present when the joint is unstable. Joint instability and changes in magnitude or location of contact promote cartilage degeneration. Once the cartilage surface is damaged by these abnormal forces, there is increased friction which results in progression of OA. In addition to the mechanical causes of OA, the presence of inflammation may also promote progression of OA. Osteoarthritis is progressive and non-reversible, and a source of pain.

The muscle groups traversing the stifle joint, particularly the quadriceps, hamstrings, and gastrocnemius muscles, are likely to be abnormal in dogs with CrCL degeneration, but it is unclear whether this is a contributor to the development of CrCL degeneration or whether this is secondary to CrCL disease. Dogs with CrCL insufficiency have decreased quadriceps muscle mass compared to hamstring and gastrocnemius muscle mass. The muscles that traverse the stifle joint can act as secondary, active stabilizers of the joint and their function may have increased importance in the CrCL-deficient state for minimizing instability.
Treatment of CrCL Insufficiency

Given that the cause of CrCL degeneration is not fully elucidated, prevention of the condition is not often possible and we are left with treating CrCL insufficiency and the resultant joint instability and meniscal damage when it arises. CrCL insufficiency can be managed medically with weight management, pain control, and activity modification\textsuperscript{13} - potentially including targeted muscle strengthening to balance the opposing forces across the joint. However, surgical management is considered the gold standard treatment because it allows for meniscal evaluation and joint stabilization.\textsuperscript{13,14} Surgical treatments include intra-articular ligament replacement, extracapsular stabilization techniques, and osteotomy techniques. Although still under investigation, intra-articular ligament replacement appears to be challenging in dogs, usually resulting in loss of joint stability post-operatively; this is in contrast to humans where intra-articular ligament replacement is the treatment of choice. This difference may be due to the difference in femorotibial anatomy and limb alignment, as well as potential differences in pathophysiology between dogs and humans.

Extracapsular stabilization is a term that encompasses a variety of specific techniques in which some form of suture or biologic material is placed either lateral, medial, or on both sides of the joint. The material typically runs from the caudal aspect of the distal femur to the cranial aspect of the proximal tibia in an effort to replicate the restraint provided by the CrCL. Extracapsular repair therefore aims to limit cranial tibial translation and, if a suture is placed laterally, should also limit internal tibial rotation. The LFTS technique is the most common variation of extracapsular stabilization and is based on a modification of a technique originally proposed in 1970.\textsuperscript{130} To perform a LFTS, one or more lengths of heavy-gauge synthetic, non-absorbable suture is passed around the fabellofemoral ligament and through 1 or 2 bone tunnels
in the tibial tuberosity. The 2 ends are secured together near the fabella, and the entire suture loop should be superficial to the joint capsule.

In order to better understand suture failure mechanisms, multiple studies have attempted to identify isometric points for suture attachment. It has been concluded that no isometric point exists due to the cam shape of the femoral condyles and the rolling of the condyles as the stifle goes through flexion/extension motion. However, quasi-isometric points have been identified. For the LFTS, the femoral attachment site is the fabellofemoral ligament. Using this femoral attachment, most studies have identified the area just caudal to the tibial tuberosity as the most isometric tibial attachment, while one study identified the quasi-isometric tibial attachment site to be at the level of the tibial plateau just caudal to the extensor groove. Importantly, while the LFTS suture runs roughly in the same trajectory as the CrCL sagittally, it is eccentrically placed over the lateral surface of the joint. The previously identified quasi-isometric points do not account for this offset, therefore we may still under-estimate suture cycling despite using what we believe to be ideal suture attachment sites.

Major complications with LFTS occur in approximately 7-17% of cases. Complications include implant infection, swelling or irritation associated with the implant, implant failure, tearing of the fabellofemoral ligament, meniscal tear, failure to control stability, and peroneal nerve damage. Risk factors for development of post-operative complications have been reported to be male dogs, having a higher body weight, or being of younger age. Use of multifilament suture for LFTS increases the risk of fabellofemoral ligament failure and infection, especially with lower surgeon experience.

There are 3 popular tibial osteotomies (TPLO, cranial closing wedge osteotomy, tibial tuberosity advancement) used for stabilization of the CrCL-insufficient stifle. Theoretically,
these procedures work by changing the geometry of the proximal tibial so that the stifle is no longer dependent on the CrCL for stability. The TPLO procedure is the most common tibial osteotomy. The TPLO is based on Slocum’s “active force model,” which is expanded upon in the section entitled Relevant Anatomy within this Chapter. The TPLO procedure is purported to neutralize the shear force at the stifle and enhancing the effectiveness of the muscular forces of the stifle flexors by leveling the tibial plateau. TPLO is performed via a medial approach to the proximal tibia. After joint examination, a radial saw blade is used to perform a complete osteotomy of the tibial plateau segment, and the plateau is rotated by a pre-determined distance along the arc of the osteotomy, then secured with a plate once tibial thrust is confirmed to be eliminated. Originally, the recommended post-operative TPA was 0° (perpendicular to the mechanical axis of the tibia). Cadaveric studies have shown that a post-operative TPA of around 6.5° should eliminate cranial tibial translation by converting the shear force from a cranially to a caudally directed force, which is opposed by the CaCL. One in-vivo study showed no difference in ground reaction forces in dogs treated by TPLO, based on post-operative TPA (between 0-14°), leading the authors to conclude that a TPA under 14° is acceptable. At this time, the convention is to correct the slope to 5°. In some cases, TPLO may not be capable of safely obtaining a post-operative slope of 5° – for example, if the dog is too small for currently available saws and plates or if obtaining an ideal post-operative slope will require rotation beyond the level of the attachment point of the patellar tendon.

Complications associated with TPLO are not uncommon. The most notable intra-operative complication of TPLO is laceration of the cranial tibial artery, occurring in less than 1% of cases, which is treated with compression or ligation of the artery without consequence. Post-operatively, the complication rate ranges from 19% to 28%. The most commonly
reported post-operative complication is implant infection, occurring in up to 15% of cases, which is an unexplained high infection rate compared to other clean surgeries. Many theories have been proposed to explain the high infection rate after TPLO, including limited soft tissue coverage, thermal bone necrosis, and the use of stainless steel plates. Post-operative meniscal tears, seen in up to 6.3% of cases, can result in incomplete resolution of lameness or recurrence of lameness. Other major post-operative complications are less common and include tibial tuberosity fractures, patellar tendonitis, pivot shift, loss of reduction (“rockback”), catastrophic failure, and neoplasia. The introduction of locking TPLO plates appears to have decreased the risk of rockback and catastrophic failure. Minor post-operative complications include swelling, bruising, seroma, minor dehiscence, and superficial wound infection. Recently, persistence of cranial tibial subluxation with weight bearing has been reported in as high as 33% of cases, which could predispose to persistent or recurrent lameness, post-operative meniscal tears, or accelerated progression of OA.

**Evaluation of Surgical Outcome**

The mainstay of evaluation of surgical success in the clinical setting is still the physical examination. The first evaluation is in the operating room where an absence of tibial thrust should be confirmed, and if tibial thrust is detected, further action should be taken at that time. TPLO will not resolve cranial drawer, but LFTS should resolve both tibial thrust and cranial drawer. Immediate post-operative radiographs may also give some insight into the quality of the procedure – for example: the position of the bone tunnels after LFTS or the TPA after a TPLO. Additionally, the radiographic cranial tibial subluxation that is often appreciable on pre-operative stress views should be resolved.

In the weeks to months following surgery, gradual resolution of lameness and stifle range of motion is expected. Visual lameness examination is important, but objective forceplate or
pressure platform analysis is more sensitive for detection of subtle lameness. Lameness and stifle flexion angle have been shown to return to normal after either LFTS or TPLO in some studies, but lameness resolution may be delayed or incomplete after LFTS compared to TPLO. Resolution of thigh muscle atrophy, stifle swelling/effusion, and pain is also expected during recovery.

While cranial tibial subluxation is the joint instability most commonly tested for in the stifle, the CrCL also prevents internal tibial rotation. In-vitro and in-vivo studies have shown that internal tibial rotation and cranial tibial translation occur at the same time in the CrCL-deficient stifle, and anecdotally the addition of an internal rotational force on the tibia during testing for cranial tibial thrust seems to increase detection of a positive tibial thrust test. Therefore, in evaluating the success of surgical procedures used to treat CrCL insufficiency, it may be ideal to modify the tibial thrust test to include testing for thrust while applying an internal rotational force. Despite modification, the tibial thrust test remains a subjective test that cannot be relied upon to detect mild to moderate craniocaudal instability, and therefore other outcome measures should be used, especially in the research setting.

Osteoarthritis typically progresses after either LFTS or TPLO, which could be evidence of persistently abnormal contact mechanics and/or stifle kinematics, both of which promote the development and progression of OA. Resolution of lameness and other clinical abnormalities does not necessarily indicate that restoration of normal biomechanics was achieved with surgical treatment for CrCL insufficiency. An in-vitro study showed that contact mechanics remained abnormal after TPLO. Two studies have used standing radiographs to assess the relative craniocaudal positions of the femur and tibia under weight-bearing load in dogs after treatment for naturally occurring CrCL insufficiency. After TPLO, there was no difference in
the craniocaudal femorotibial alignment compared to normal in 15 dogs; however, dogs with meniscal debridement had persistent cranial tibial subluxation during standing. Recently, lateral fluoroscopy was used to visualize femorotibial motion during gait in dogs with naturally occurring CrCL insufficiency that were not recovering well after various surgical stabilizing procedures. Subjectively, 3/5 dogs treated by TPLO continued to experience cranial tibial subluxation during gait. Major limitations of the study included the small sample size and the subjective methods of data evaluation.

Multiple studies have compared the outcomes of LFTS and TPLO directly, with conflicting conclusions. Using force plate gait analysis, 3 prospective studies have shown a delayed or incomplete return to normal limb function after LFTS compared to TPLO, while 2 others found no difference between procedures. One radiographic study found that dogs with more severe OA progression after surgery were more likely to have been treated by LFTS than TPLO, whereas 2 other studies found no difference in radiographic OA up to 2 years post-operatively. In addition to the type of procedure performed, there are likely multiple confounding factors that affect post-operative outcome. For example, 1 study has found that in dogs treated with TPLO that also had meniscal debridement performed had post-operative cranial tibial subluxation while those without meniscal debridement did not. Ultimately, additional prospective research with control for confounding factors such as meniscal status and long-term follow up is necessary to determine whether LFTS or TPLO is a definitively superior stabilizing procedure.

**Knowledge Gap**

Surgical therapies developed to treat dogs with naturally occurring CrCL insufficiency aim to address the resultant instability. However, our knowledge of the *in-vivo* kinematics of naturally occurring CrCL insufficiency is limited. Most kinematic studies rely on skin markers
that have poor accuracy. Therefore, our understanding of kinematic abnormalities associated with CrCL insufficiency are derived from normal dogs with acute experimental transection, which may not appropriately represent the chronic fatigue associated the disease process. The in-vivo alterations in stifle kinematics after treatment with LFTS or TPLO have not been accurately defined. Characterizing the kinematics of naturally diseased CrCL-deficient stifles is required for comparisons against post-operative kinematics. Precise assessment of the efficacy of the LFTS and TPLO techniques in providing stifle stability may allow for greater insight into the suboptimal outcomes following these procedures, as well as guide the development of future treatment options for CrCL insufficiency in dogs.
Figure 2-1. Anatomy of the stifle joint. Used with permission from Evans H, de Lahunta A: Miller's Anatomy of the Dog (ed 4th). St. Louis, MO, Elsevier Saunders, 2013.63
Figure 2-2. Slocum’s active force model of force transmission across the stifle joint. The weight bearing force is parallel to the long axis of the tibia, and it is transmitted across the stifle joint perpendicular to the tibial plateau. Pre-operatively (A), a shear force is generated producing cranial tibial translation. With TPLO (B), the tibial plateau is rotated so that a compressive force is generated with weight bearing and consequently the instability is neutralized. Used with permission from Kim S, Pozzi A, Kowaleski M, et al.: Tibial osteotomies for cranial cruciate ligament insufficiency in dogs. Vet Surg 37:111-125, 2008.162

Figure 2-3. Tepic’s model of force transmission across the stifle joint. The weight bearing force is transmitted across the stifle joint parallel to the patellar tendon. Pre-operatively (A), a shear force is generated that results in cranial tibial translation because of the angular offset between the patellar tendon and the tibial plateau. With TTA (B), the tibial tuberosity is advanced such that the patellar tendon is approximately perpendicular to the tibial plateau, so that a compressive force is generated with weight bearing and consequently the instability is neutralized. Used with permission from Kim S, Pozzi A, Kowaleski M, et al.: Tibial osteotomies for cranial cruciate ligament insufficiency in dogs. Vet Surg 37:111-125, 2008.162
Figure 2-4. Factors implicated in the pathogenesis of CrCL disease and their potential interrelationship. Genetics may have a direct influence on the structural properties of the CrCL (dashed arrow) or influence other factors contributing to CrCL disease. Used with permission from Griffon D: A review of the pathogenesis of canine cranial cruciate ligament disease as a basis for future preventive strategies. Vet Surg 39:399-409, 2010.
CHAPTER 3
FEMOROTIBIAL KINEMATICS IN DOGS WITH CRANIAL CRUCIATE LIGAMENT INSUFFICIENCY: A THREE-DIMENSIONAL \textit{IN-VIVO} FLUOROSCOPIC ANALYSIS DURING WALKING *

Relevant Review

Cranial cruciate ligament insufficiency is a degenerative condition that is a common cause of pelvic limb lameness and OA in dogs.\textsuperscript{1,2,4-9} Pet owners were estimated to have spent over $1 billion treating dogs with CrCL insufficiency in 2003.\textsuperscript{12} Conservative medical management options are available and may result in improved function in some dogs, particularly dogs weighing less than 15 kg.\textsuperscript{13} Surgical management, however, is typically recommended to address joint instability, mitigate the progression of OA, and address concurrent meniscal pathology.\textsuperscript{13,14}

Experimental transection of the CrCL invariably leads to stifle joint instability, and has been used to study the development of OA.\textsuperscript{5-9,15-17} The presumed effects of CrCL insufficiency on joint motion during ambulation \textit{in-vivo} are derived from 2 studies that were performed using invasive experimental techniques in normal dogs.\textsuperscript{9,16} Both studies measured joint kinematics before and after experimental unilateral CrCL transection by tracking metal implants: metal bone plates with removable spatial linkage\textsuperscript{16} or implanted metal beads with biplanar fluoroscopy.\textsuperscript{9} However, acute experimental CrCL transection may not accurately replicate the pathology and biomechanics that are present in dogs with naturally occurring CrCL insufficiency. Additionally, there are logistical and ethical issues associated with the invasive nature of implanting metallic markers when studying the effects of CrCL insufficiency in client owned animals. A recent

clinical study used lateral fluoroscopy to document stifle instability in a series of client owned
dogs with naturally occurring CrCL insufficiency, but unfortunately the kinematic evaluation
was limited to subjective qualitative assessments.\textsuperscript{18} Recently, our group validated the use of
single plane fluoroscopy (without the use of metal implants) for accurate quantification of bone
motion in 3 dimensions using methodology developed to study human knee kinematics.\textsuperscript{19,21-23}
While biplanar fluoroscopy is considered the most accurate modality for determining joint
kinematics, this study demonstrated that the single plane modality was accurate to within 1.28
mm for translations and 1.58° for rotations.\textsuperscript{19}

Surgical therapies developed to treat dogs with naturally occurring CrCL insufficiency
aim to address the resultant instability,\textsuperscript{14} but the \textit{in-vivo} alterations in stifle kinematics associated
with CrCL insufficiency have not been accurately defined. Characterizing the kinematics of
naturally diseased CrCL-deficient stifles would allow for more refined assessment of the efficacy
of the currently advocated surgical stabilization techniques and guide the development of future
treatment options. The objective of the current study was to quantify the 3D femorotibial joint
kinematics of dogs with naturally occurring CrCL insufficiency during ambulation. We
hypothesized that CrCL-deficient stifles would have increased femorotibial flexion, cranial tibial
translation, and internal tibial rotation compared to each dog’s unaffected contralateral stifle
throughout the gait cycle.

\textbf{Materials and Methods}

Dogs presenting to the University of Florida Small Animal Hospital for CrCL
insufficiency between July 2012 and March 2014 were evaluated for potential inclusion into the
study. Adult non-chondrodystrophic dogs weighing between 20 to 40 kg with a history of
unilateral lameness of less than 6-months duration were considered for enrollment. Inclusion was
confirmed when (1) a unilateral complete CrCL insufficiency was diagnosed on orthopedic
examination by a board certified surgeon based on cranial drawer and tibial compression tests (positive in the affected limb, negative in the contralateral limb), (2) stifle radiographs confirmed evidence of CrCL insufficiency in the affected stifle (stifle effusion ± OA), and (3) complete CrCL insufficiency was confirmed at the time of surgery via arthroscopy or arthrotomy (surgeon preference). Dogs were excluded if concurrent clinical orthopedic disease was identified on physical examination, including palpable pain, effusion, or instability of the contralateral stifle. The study was approved by the University’s Institutional Animal Care and Use Committee and owners signed informed consent at the time of enrollment.

**Fluoroscopic Image Acquisition**

Continuous lateral view fluoroscopic images centered on the stifle joints were acquired during treadmill walking using a ceiling-mounted fluoroscopic system with a flat panel detector (Toshiba American Medical Systems, Inc., Tustin, CA). Dogs were walked at a velocity of 2.0 - 2.5 mph (0.8 – 1.1 m/s), similar to previous studies. The speed of the treadmill was set within this range at a speed that allowed a natural walking cadence. Images were acquired using a pulse rate of 30 frames/second, pulse width of 1 ms, and an image area of 410 x 300 mm, giving a 0.20 mm x 0.20 mm pixel resolution. The x-ray source was initially programmed to supply a 72 kV beam with a 50 mA beam current, with slight adjustments to parameters to optimize osseous definition for each subject. Fluoroscopic imaging was obtained for approximately 15 full gait cycles with the stifles centered in the field of view. Fluoroscopic sessions were also videotaped for later review to ensure a natural cadence was present and to aid in defining stance and swing phases of gait. Three representative gait cycles were chosen for processing. Radiation-associated risk was considered negligible.
**3D Model Creation**

Computed tomographic scans (Toshiba Aquilon 8, Toshiba American Medical Systems, Inc., Tustin, CA) were obtained extending from the hips through the tarsi. Computed tomographic scans used a 512x512 image matrix, a 0.35x0.35 pixel dim, and 0.5 mm slice thickness with 0.3 mm overlap throughout the length of the femur and tibia. Radiation-associated risk was considered negligible. Bilateral femur/fabellae and tibia/fibula digital bone models were created using an open source 3D segmentation software program (ITK-SNAP, http://www.itksnap.org) followed by a reverse engineering program (Geomagic, Inc., Research Triangle Park, NC). A 3D coordinate system based on anatomic landmarks was applied to each of the CT generated bone models similar to previous studies (Figure 3-1).\textsuperscript{19,20,44,61,62} Initially, femoral coordinates were applied such that the z-axis (mediolateral) passed through the center of the femoral condyles while remaining perpendicular to the longitudinal anatomic axis of the femur in the frontal plane. The y-axis (proximodistal) was perpendicular to the z-axis, along a plane that intersected the previously determined center of the femoral head and center of each medial and lateral femoral condyle, passing through the intercondylar notch (ICN) in the frontal plane. Initially, tibial coordinates were applied such that the z-axis passed through the most prominent medial and lateral points of the tibial condyles, perpendicular to the longitudinal axis of the tibia in the frontal plane. The y-axis was perpendicular to the z-axis, along a plane that intersected the prominent medial and lateral points on the tibial condyles as well as a point midway between the medial and lateral malleoli. For both bones, the x-axes (craniocaudal) were determined by the right hand rule, which mandates that the 3\textsuperscript{rd} axis be perpendicular to the first 2 axes. The origins of the femoral and tibial coordinate systems were then placed at the estimated center of the origin and insertion of the CrCL.\textsuperscript{44,61}
3D-to-2D Image Registration

A previously described 3D-to-2D image registration process was used to combine 3D bone model data with 2D fluoroscopic data to ascertain 3D kinematics of the femur and tibia throughout the gait cycle (Figure 3-2).\textsuperscript{19-22,44} The digital femur and tibia models were projected onto each frame of the fluoroscopic gait cycle, and models were manually rotated and translated until the anatomic contours of the models precisely matched the underlying image (JointTrack, University of Florida: http://sourceforge.net/projects/jointtrack/). The output of the software represents the individual model positions in space, and these results were converted to the relative positions of the bone models to each other using a custom computer program (MATLAB and Statistics Toolbox Release R2015a, The MathWorks, Inc., Natick, MA).

Control Kinematic Data

Contralateral limb kinematics have been shown to be affected by the presence of lameness caused by CrCL insufficiency;\textsuperscript{75} therefore, data for the contralateral limb was collected and evaluated 6-months following TPLO of the CrCL-deficient limb. A prior study has found no difference in force plate analysis between 6-month post-operative TPLO-treated naturally affected CrCL-deficient dogs and control dogs indicating that this time frame should allow return to soundness.\textsuperscript{33,34}

Kinematic Data Processing

The data were split into stance phase and swing phase and each phase was time normalized using a custom spline interpolation program (MATLAB and Statistics Toolbox Release R2015a, The MathWorks, Inc., Natick, MA) so that a data set of 101 data points was created (or 202 data points for the complete gait cycle). Every 10\textsuperscript{th} data point was chosen for statistical comparison, so that in the final data set each stance cycle had 11 data points and each swing cycle had 11 data points. This allowed averaging within and between dogs, despite
temporal differences. Kinematic data was compiled for flexion-extension angle, craniocaudal translation, and internal-external rotation for both the pre-operative CrCL-deficient and the 6-month post-operative contralateral stifle (internal control). Femorotibial kinematics after TPLO treatment will be reported in a separate study.

**Statistical Analysis**

Continuous variables are presented as mean ± standard deviation or median (range) as appropriate. For each kinematic variable, 11 stance and 11 swing data points were averaged for 3 gait cycles for each dog and results were compared between affected and control stifles using a paired T-test followed by a Bonferroni correction with significance set at P < 0.0025. Repeated measures 2-way ANOVA with post-hoc Tukey honestly significant difference was used to determine significance across the entire gait cycle for craniocaudal translation.

**Results**

**Demographic Information**

Eighteen dogs were included in the study. Nine were mixed breed dogs, 5 were Labrador Retrievers, and the remaining dogs consisted of 1 Standard Poodle, 1 German Shepherd Dog, 1 English Springer Spaniel, and 1 Husky. Eleven dogs were spayed females and 7 were castrated males. Age was 6.7 ± 2.8 years. Body weight was 30.3 ± 5.8 kg with a median body condition score of 6/9 (range 4-8). The right stifle was affected in 10 dogs and the left in 8 dogs. Duration of lameness prior to presentation was 2.4 ± 2.3 months. Tibial plateau angle was 27.9 ± 3.0° for the CrCL-deficient stifle and 28.3 ± 2.9° for the contralateral control stifle (P = 1). On pre-operative radiographs, mild (9 dogs) to moderate (9 dogs) OA of the affected stifle was noted. Ten dogs had no radiographic abnormalities noted in the contralateral stifle, while 8 dogs had mild OA and effusion of the contralateral stifle detected on radiographs, despite the lack of
abnormalities during clinical examination. At the time of surgery, Outerbridge scores\textsuperscript{164} were 1 (0-3), 1 (0-2), 0.5 (0-3), and 1 (0-2) for the medial femoral condyle, medial tibial condyle, lateral femoral condyle, and lateral tibial condyle, respectively. Meniscal pathology was not identified in 8 dogs, while 10 dogs had injury to the caudal pole of the medial meniscus that required debridement. In addition to CrCL insufficiency, 5 dogs had unilateral mild to moderate OA of the contralateral coxofemoral joint and 9 dogs had mild OA detected in one or both tarsal joints; no pain or loss of range of motion of these joints was detected on clinical examination.

**Flexion/Extension Angle**

Over the 11 data points during stance phase, the control stifle had mean flexion/extension angles between 137-147° of extension, whereas the CrCL-deficient stifle was maintained in greater flexion (P < 0.0007) with means between 124-130° of extension (Figure 3-3). Over the 11 data points during swing phase, the control stifle had means between 104-146° of extension; the CrCL-deficient stifle was maintained in greater flexion (P < 0.0001), with a means between 95-130° of extension.

**Craniocaudal Translation**

Craniocaudal translation was evaluated by measuring the distance between the femoral origin and tibial insertion of the CrCL along the craniocaudal axis at 10% increments throughout the phases of the gait cycle. *Range of craniocaudal motion*, defined as the maximum change in craniocaudal distance between the origin and insertion of the CrCL observed throughout the gait cycle, was a mean (±SD) of 1.6 ± 0.8 mm in the control stifle and 8.6 ± 2.9 mm CrCL-deficient stifle (P < 0.0001).

*Cranial tibial subluxation* was defined as a significant difference between the CrCL-deficient and control stifles, with respect to craniocaudal distance between the origin and insertion of the CrCL at an equivalent time point during the gait cycle. In CrCL-deficient stifles,
there was significant cranial tibial subluxation at all time points throughout the gait cycle (P < 0.0001) (Figure 3-4). At mid-stance, there was 9.7 ± 2.7 mm of cranial tibial subluxation (P < 0.0001) and at mid-swing there was 2.1 ± 1.7 mm of cranial tibial subluxation (P < 0.0001). The magnitude of cranial tibial subluxation was significantly greater at mid-stance phase than at mid-swing phase (P < 0.0001).

**Internal/External Rotation**

Axial rotation was determined from the flexion-abduction-axial rotation ordered angle decomposition of the transformation matrix describing the tibial pose with respect to the femur. This value can be thought of as the angular offset between the femoral and tibial x-axes. *Range of axial rotation* was defined as the difference between the maximum and minimum axial angular offsets throughout the gait cycle, within a joint. There was a mean (±SD) of 8.2 ± 4.4° of axial rotation range of motion in the control stifle and 8.0 ± 6.2° of axial rotation range of motion in the CrCL-deficient stifle throughout the gait cycle (P = 0.1085). While the range of axial rotation was similar between control and CrCL-deficient stifles, the timing of rotation differed between limbs. Both the control and CrCL-deficient stifles were maximally externally rotated in early stance phase; however, the control stifles reached maximal internal rotation at mid-swing phase and the CrCL-deficient stifles reached maximal internal rotation at mid-stance phase.

*Abnormal axial rotation* was defined as a significant difference between the CrCL-deficient and control stifles, with respect to degree of axial rotation at a given equivalent time point during the gait cycle. In the CrCL-deficient stifles, the tibia was abnormally internally rotated for the majority of stance phase (P < 0.0022 between 10-100% stance phase) (Figure 3-5). During the swing phase, there was no significant difference in axial rotational position between limbs.
Discussion

The objective of this study was to quantitatively define the 3D stifle motion in dogs with naturally occurring CrCL insufficiency. We found that flexion-extension angle and craniocaudal translation were abnormal throughout the walking gait cycle, and internal-external rotation was abnormal during the stance phase. We confirmed that naturally occurring CrCL insufficiency results in profound disturbance of stifle kinematics in dogs.

CrCL-deficient stifles were maintained in 8-20° greater flexion throughout the gait cycle when compared to control stifles. Prior in-vivo studies using optical motion capture and biplanar fluoroscopic 3D-to-2D image registration techniques have reported a similar magnitude of increased flexion in CrCL-deficient joints, ranging from 5-15°. Increased stifle flexion has been ascribed to joint effusion and pain, both of which are present in naturally occurring and experimentally induced disease states. Increased stifle flexion may also mitigate the magnitude of cranial tibial subluxation, as the angle formed between the patellar tendon and the femorotibial joint line decreases. Higher stifle flexion may be the result of a change in activity of the quadriceps, gastrocnemius, or hamstrings, or a combination of changes in activity of all 3 muscles. In humans with ACL insufficiency, a proportion of the population (“copers”) is able to stabilize the knee by altered muscular forces across the joint. However, in contrast to human copers, dogs in our study were not able to completely overcome the cranial tibial subluxation despite increased stifle flexion.

The maximal magnitude of cranial tibial subluxation observed in our study was 9.7 mm, which occurred during the mid-stance phase. The mid-stance phase timing of maximal cranial tibial subluxation may be due to quadriceps and gastrocnemius muscle activity, which are required to support weight bearing during the stance phase in addition to maintaining joint extension, these muscles also exert a cranial force on the tibia (quadriceps) and caudal force on
the femur (gastrocnemius), which may promote cranial tibial thrust. Tashman, et al. reported a similar magnitude of subluxation (10 mm) in the in-vivo study of experimental CrCL transection, but Korvick, et al. reported a larger magnitude of subluxation (17 mm) in an earlier in-vivo study of experimental CrCL transection. We suspect that numerous factors could influence the maximal magnitude of cranial tibial subluxation, such as the degree of periarticular fibrosis, differences in study methodology (such as landmark identification), and dog size, breed, and activity level (e.g. type and speed of gait). Nevertheless, our results suggest that stifles with naturally occurring complete CrCL insufficiency have a comparable degree of cranial tibial subluxation to normal stifles subjected to experimental CrCL transection.

Despite the previous thought that the stability of the dog stifle is independent of the CrCL during stifle flexion, mild cranial tibial subluxation was still present in CrCL-deficient stifles during the swing phase (when the stifle is in greater flexion). A similar phenomenon was found in the study by Tashman, et al., in which persistent cranial tibial subluxation was shown to develop over the 2 years following experimental CrCL transection. The presence of persistent cranial tibial subluxation may be a reflection of a chronically thickened stifle that is unable to return to a completely reduced position. Furthermore, maximal hock flexion has been shown to occur during mid-swing phase, which may promote cranial tibial subluxation through increased tension on the gastrocnemius muscle. Chronic CrCL insufficiency may also be associated with disruption of the balance of muscular forces (particularly quadriceps, hamstring, and gastrocnemius muscles), meniscal degeneration, and changes to the osseous anatomy of the joint. We suspect that some or all of these changes contribute to persistent cranial tibial subluxation during the swing phase, despite this being a “CrCL-independent phase”.

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Stifles with CrCL insufficiency had significantly greater internal tibial rotation when compared to control stifles, occurring maximally at the mid-stance phase and therefore coinciding with maximal cranial tibial subluxation, consistent with both in-vivo and ex-vivo studies. After CrCL loss, the collateral ligaments become the primary restraint against cranial tibial subluxation and because the lateral collateral ligament is not as taut as the medial collateral ligament in extension, the lateral aspect of the tibial plateau has more latitude to translate cranially than the medial aspect of the plateau. The medial meniscus has been demonstrated to aid in resisting cranial tibial subluxation in CrCL-deficient stifles in canine cadavers, which could provide more craniocaudal stability to the medial compartment compared to the lateral compartment. The differences in function between medial and lateral collateral ligaments and medial and lateral menisci likely contribute to the internal tibial rotation that occurs as the tibia translates cranially during stance phase in the absence of the CrCL. Surprisingly, the in-vivo study by Tashman, et al. did not report a difference in rotational alignment after CrCL transection. The authors of this study postulated that bony geometry, muscular forces, or other soft tissue constraints were able to overcome the expected rotational laxity. The cause of discrepant findings for axial rotational motion across in-vivo studies is unknown, but may be related to breed and conformational differences between study populations. Nevertheless, the prominence of rotational instability in dogs with CrCL insufficiency found in the current study supports clinical concerns that rotational instability may also need to be addressed during surgical treatment of CrCL insufficiency.

There are several limitations associated with this investigation. We had narrow selection criteria based on body weight and obvious palpable stifle laxity; therefore, our results cannot be extrapolated to other populations such as small or giant breed dogs, chondrodystrophic dogs,
dogs with excessive TPAs, dogs with partial CrCL tears, dogs with severe OA, or dogs with purely traumatic CrCL ruptures. Additionally, data were collected at a single and likely variable time point from the onset of disease and thus we are unable to provide a definitive understanding of the temporal changes associated with the course of CrCL degeneration. Fluoroscopic imaging was obtained while dogs walked on a treadmill, which has been shown to result in slight variations in joint kinematics in dogs when compared to over-ground walking.\textsuperscript{173} We did not assess activities other than walking, such as trotting or stair climbing, which may have shown different results.\textsuperscript{44} We utilized a single-plane fluoroscopic technique, which is less precise than biplanar techniques and precludes the ability to accurately quantify translation in the mediolateral plane.\textsuperscript{21} During modeling, there is subjectivity in coordinate assignation as well as determination of the stance and swing phases of the gait cycle; a single researcher (ST) performed these tasks to limit variability. We also recognize that stifle motion is a complex action and stifle stability is not controlled solely by the CrCL; additionally, in the face of CrCL insufficiency there are likely multiple concurrent (primary or secondary) neuromuscular changes that could also affect our measured kinematic results.

Limitations also include the fact that our control data was collected from the contralateral limb 6-months following surgical treatment for CrCL insufficiency of the affected limb. The 6-month time point was chosen to mitigate the effects of lameness on contralateral limb kinematics,\textsuperscript{33,34} however, the contralateral stifles may not have been normal themselves. The development of CrCL insufficiency is multifactorial with one primary contributing factor being abnormal mechanical stresses secondary to variations from normal anatomy and CrCL insufficiency is a bilateral disease in approximately 50\% of dogs affected.\textsuperscript{3,11,86,118,174-176} Despite some dogs having early (stable) contralateral CrCL disease, we considered the contralateral stifle
to be a superior kinematic control than the alternative of using a separate population of dogs with normal stifles. Given that there was no lameness, pain, loss of range of motion, or instability associated with any joint other than the studied CrCL-deficient stifle at the time of initial and follow-up orthopedic examinations, we considered the influence of very early contralateral CrCL disease or concurrent hip or hock OA would likely be minimal.

The femorotibial kinematic changes observed in dogs with naturally occurring CrCL insufficiency were largely consistent with previous experimental studies: we observed profound craniocaudal translational and axial rotational instability that was most pronounced during the stance phase of gait. Our investigation has provided an accurate, quantitative characterization of the instability that occurs with CrCL insufficiency. Based on our results, current surgical stabilization techniques should aim to address both craniocaudal translational and axial rotational instability with hopes to slow the progression of OA and mitigate the likelihood of post-operative meniscal damage.
Figure 3-1. Femoral and tibial coordinate systems. CT-generated 3D digital models of the femur (craniocaudal (1a) and lateral (1b) views) and tibia (craniocaudal (1c) and lateral (1d) views) with 3D coordinate system applied.

Figure 3-2. Image registration process. Fluoroscopic image before (2a) and after (2b) 3-D to 2-D image registration process. In Figure 2b, the bone models from Figure 1 have been projected, edge-detected, and superimposed then precisely matched to the fluoroscopic image.
Figure 3-3. Mean flexion/extension angle during a) stance and b) swing phase in CrCL-deficient and control stifles. Orange line = CrCL-deficient, Blue line = control. Error bars represent standard deviations and * represents a statistically significant difference (using paired T-test) at that time point. The CrCL-deficient stifle was more flexed throughout the gait cycle compared to the contralateral control stifle.
Figure 3-4. Mean cranial tibial translation during a) stance and b) swing phase in CrCL-deficient and control stifles. Orange line = CrCL-deficient, Blue line = control. Error bars represent standard deviations and * represents a statistically significant difference (using paired T-test) at that time point. The CrCL-deficient stifle had more cranial tibial translation throughout the gait cycle compared to the contralateral control stifle.
Figure 3-5. Mean internal/external rotation during a) stance and b) swing phase in CrCL-deficient and control stifles. Orange line = CrCL-deficient, Blue line = control. Error bars represent standard deviations and * represents a statistically significant difference (using paired t-test) at that time point. The CrCL-deficient stifle had more internal tibial rotation throughout stance phase compared to the contralateral control stifle and there was no difference during swing phase.
CHAPTER 4
FEMOROTIBIAL KINEMATICS IN DOGS TREATED WITH LATERAL FABELLOTIBIAL SUTURE STABILIZATION FOR CRANIAL CRUCIATE LIGAMENT INSUFFICIENCY: AN IN-VIVO FLUOROSCOPIC ANALYSIS DURING WALKING

Relevant Review

Cranial cruciate ligament insufficiency is a degenerative condition that is a common cause of pelvic limb lameness and osteoarthritis in dogs.\(^1,2,4-9\) As reported in Chapter 3, naturally occurring CrCL insufficiency results in greater stifle flexion and cranial tibial subluxation throughout the gait cycle, as well as excessive internal tibial rotation during the stance phase.\(^177\) Abnormal joint motion is thought to be the major cause of lameness, meniscal injury, and development of OA in dogs with CrCL insufficiency.\(^5-9\) While conservative medical management options are available, surgical management is recommended to address joint instability, mitigate the progression of OA, and manage concurrent meniscal pathology.\(^13,14\)

Extracapsular suture stabilization techniques such as LFTS are commonly performed for treatment of CrCL insufficiency.\(^24\) With the LFTS procedure, a heavy gauge nylon suture is passed around the fabellofemoral ligament and through a bone tunnel in the cranioproximal tibia, then secured to itself.\(^14\) Most in-vivo clinical outcome studies after forms of extracapsular stabilization have shown high owner satisfaction (82-90%) and subjective resolution of lameness (78-82%), but less successful resolution of stifle instability based on stifle palpation at follow-up (55-76%).\(^30-32\) Additionally, 2 prospective studies using force plate gait analysis to objectively evaluate lameness have shown incomplete resolution of lameness after LFTS within the 1-year study period; the authors did not determine the cause of incomplete recovery.\(^33,34\)

It is suspected that persistent instability is a major cause of persistent lameness after LFTS, and that persistent instability is more common than has been previously reported using
subjective measures (palpation). *Ex-vivo* studies have been performed to investigate the success of LFTS in providing joint stabilization after CrCL transection, but results are conflicting.\textsuperscript{25-29} Using methodology developed to study human knee kinematics, our group has validated the use of single plane fluoroscopy for accurate quantification of bone motion in 3D with an accuracy of \( \leq 1.28 \) mm for translations and \( \leq 1.58^\circ \) for rotations.\textsuperscript{19,21-23}

A more complete understanding of joint biomechanics can be obtained by ascertaining *in-vivo* kinematics during ambulation, which have not been obtained after LFTS for CrCL insufficiency. This information could provide a basis for improvements to the current LFTS technique or could serve to eliminate the recommendation of the procedure. The objective of the current study was to quantify the 3D femorotibial joint kinematics during ambulation in dogs treated with LFTS for naturally occurring CrCL insufficiency. Based on clinical experience and prior literature, we hypothesized that LFTS would not reliably restore stifle kinematics to normal.

**Materials and Methods**

Adult dogs weighing 15-35 kg with a history of unilateral lameness of less than 6-months duration ascribed to CrCL insufficiency were evaluated for inclusion in the study between January 2013 and April 2015. Only dogs with a unilateral, complete CrCL insufficiency were enrolled in the study, based on (1) positive cranial drawer sign and positive tibial compression test during examination by a board certified surgeon, (2) stifle radiographs demonstrating stifle effusion with or without OA, and (3) visual confirmation at the time of surgery via arthroscopy or arthrotomy. Dogs were excluded if concurrent clinical orthopedic disease was identified on physical examination, including palpable pain, effusion, or instability of the contralateral stifle at any point during the study period. The study was approved by the University’s Institutional Animal Care and Use Committee and owners signed informed consent at the time of enrollment.
Lateral fabellotibial suture stabilization was performed by 1 of 2 board certified small animal surgeons (SEK, DDL). Two strands of 18, 27, or 36 kg test nylon leader line were passed around the lateral fabella/fabellofemoral ligament, from lateral to medial under the patellar tendon and from medial to lateral through 1 or 2 bone tunnels in the tibial tuberosity such that the suture created a figure-8 pattern, then secured with square knots at the level of the lateral fabella. Post-operatively, modified Robert-Jones bandages were applied for 2-4 weeks. A total of 3 months of activity restriction was recommended.

Dogs were evaluated with an orthopedic examination by a board-certified surgeon and fluoroscopic imaging at 6-months post-operatively. Lameness was graded using an ordinal scale (0 = no lameness and weight bearing on all strides observed, 1 = mild subtle lameness with partial weight bearing, 2 = obvious lameness with partial weight bearing). Additionally, owners quantified the degree of lameness using a visual analog scale (VAS) (0 = always lame to 10 = never lame). The following raw data collection and kinematic data processing methodology has been consistent throughout the prior studies performed in our laboratory and previously described in detail elsewhere.

**Fluoroscopic Image Acquisition**

Pre-operatively and at 6-months after LFTS, continuous lateral view fluoroscopic images centered on the stifle joints were acquired during treadmill walking using a ceiling-mounted fluoroscopic system with a flat panel detector (Toshiba American Medical Systems, Inc., Tustin, CA), both pre-operatively and at 6-months post-operatively. The treadmill speed was set at a walking velocity of 2.0 - 2.5 mph (0.8 – 1.1 m/s), adjusted for each dog to allow a natural walking cadence. The x-ray source was initially programmed to supply a 72 kV beam with a 50 mA beam current, with slight adjustments to parameters to optimize osseous definition for each subject. Images were acquired using a pulse width of 1 ms, pulse rate of 30 frames/second, and
an image area of 410 x 300 mm, giving a 0.20 mm x 0.20 mm pixel resolution. Fluoroscopic imaging was obtained for at least 15 full gait cycles with the stifles centered in the field of view, and 3 representative gait cycles were identified for processing. Fluoroscopic sessions were videotaped and reviewed to ensure a natural cadence was present and to aid in defining stance and swing phases of gait. Radiation-associated risk was considered negligible.\textsuperscript{179}

3D Model Creation

Computed tomographic scans (Toshiba Aquilon 8, Toshiba American Medical Systems, Inc., Tustin, CA) were obtained pre-operatively extending from the hips through the tarsi bilaterally. Computed tomographic scans used a 0.35x0.35 pixel dim, a 512x512 image matrix, and 0.5 mm slice thickness with 0.3 mm overlap. Digital bone models of the femur/fabellae and tibia/fibula were created using an open source 3D segmentation software and a reverse engineering program (ITK-SNAP, http://www.itksnap.org; Geomagic, Inc., Research Triangle Park, NC).

A 3D coordinate system based on anatomic landmarks was applied to each of the CT generated bone models (Figure 3-1).\textsuperscript{9,19,20,44,62,177} Initially, femoral coordinates were applied such that the z-axis (mediolateral) passed through the center of the femoral condyles while remaining perpendicular to the longitudinal anatomic axis of the femur in the frontal plane. The y-axis (proximodistal) was perpendicular to the z-axis, along a plane that intersected the previously determined center of the femoral head and center of each medial and lateral femoral condyle, passing through the ICN in the frontal plane. Initially, tibial coordinates were applied such that the z-axis passed through the most prominent medial and lateral points of the tibial condyles, perpendicular to the longitudinal axis of the tibia in the frontal plane. The y-axis was perpendicular to the z-axis, along a plane that intersected the prominent medial and lateral points on the tibial condyles as well as a point mid-way between the medial and lateral malleoli. For
both bones, the x-axes (craniocaudal) were determined by the right hand rule, which mandates that the 3rd axis be perpendicular to the 1st 2 axes. The origins of the femoral and tibial coordinate systems were then placed at the estimated center of the origin and insertion of the CRCL.

3D-to-2D Image Registration

A previously described 3D-to-2D image registration process was used to ascertain 3D kinematics of the femur and tibia throughout the gait cycles (Figure 3-2) by combining 3D digital bone models with the 2D fluoroscopic images.19-22,44 The digital femoral and tibial models were projected onto each fluoroscopic image, and models were manually rotated and translated until the anatomic contours of the models precisely matched those of the underlying image (JointTrack, University of Florida: http://sourceforge.net/projects/jointtrack/). This process was repeated for each frame of the selected gait cycles. From the JointTrack output (individual model positions in space), the relative positions of the femoral and tibial bone models were obtained using a custom computer program (MATLAB and Statistics Toolbox Release R2015a, The MathWorks, Inc., Natick, MA).

Control Kinematic Data

Because contralateral limb kinematics are altered in unilaterally lame dogs,75,76 contralateral limb data was evaluated 6-months following LFTS when lameness was no longer apparent. By 6-months post-operatively, the lameness was mitigated to the point that we felt that contralateral kinematics would be minimally affected, if at all. Dogs were excluded from the study if clinical evidence (lameness, stifle instability, pain) of a contralateral CrCL insufficiency was identified within the 6-month study period following LFTS.
Kinematic Data Processing

The data were split into stance and swing phases. Each phase was time normalized using a custom spline interpolation program (MATLAB and Statistics Toolbox Release R2015a, The MathWorks, Inc.) resulting in a data set of 101 data points for each phase (or 202 data points for the complete gait cycle). Interpolation allowed for averaging within and between dogs, despite temporal stride differences between dogs.

Kinematic data was compiled for the pre-operative CrCL-deficient, 6-month post-operative LFTS-treated, and control stifles for craniocaudal translation, internal/external rotation, and flexion/extension angle. Craniocaudal translation was evaluated by measuring the distance between the femoral and tibial attachment sites of the CrCL (origins of the coordinate systems) along the craniocaudal axis (x-axis). Range of craniocaudal motion was defined as the maximum change in craniocaudal distance between the origin and insertion of the CrCL within a period of the gait cycle (stance vs swing) or the entire gait cycle. Cranial tibial subluxation was defined as the tibia being positioned > 2mm more cranial (relative to the femur) when compared to the control stifles. Axial rotation was the angular offset between the femoral and tibial mediolateral axes (z-axes). Range of axial rotation was defined as the maximum change in axial rotational position observed within a period of the gait cycle (stance or swing phases) or the entire gait cycle. Abnormal axial rotation (internal or external rotation) was defined as a significant difference between affected and control stifles with respect to degree of axial rotation at an equivalent time point during the gait cycle. Flexion/extension angle was the angular offset between the femoral and tibial y-axes. Abnormal flexion/extension was defined as a significant difference between affected and control stifles with respect to degree of flexion/extension at an equivalent time point during the gait cycle.
**Statistical Analysis**

Continuous variables are presented as mean ± standard deviation or median (range) as appropriate. For each kinematic variable, every 10th data point was utilized from the interpolated data set, leaving 11 stance (0-100%) and 11 swing (0-100%) data points. These were averaged for 3 gait cycles for each stifle and results were compared between the pre-operative CrCL-deficient, LFTS-treated, and control stifles using a repeated measures ANOVA with post-hoc Tukey honestly significant difference at each time point (0, 10%, 20%…100%) of the stance and swing phases. Range of motion (craniocaudal translation, axial rotation) was compared between the CrCL-deficient, LFTS-treated, and control stifles using paired t-tests.

**Results**

**Demographic Information**

Ten dogs were initially enrolled but 1 dog was excluded during the study period due to development of contralateral CrCL insufficiency; consequently, results are reported for 9 dogs. Breeds consisted of: 6 mixed breed dogs, 1 Labrador Retriever, 1 Pitbull, and 1 Beagle. Five dogs were spayed females and 4 were castrated males. Age was 7.1 ± 2.6 years. Body weight was 26.3 ± 5.8 kg with a body condition score of 5/9 (4-7). The left stifle was affected in 8 dogs and the right in 1 dog. Duration of lameness prior to presentation was 2.1 ± 1.3 months. Tibial plateau angle was 28.8 ± 2.6° in the CrCL-deficient stifle and 28.1 ± 2.4° in the control stifle (P = 0.20).

On pre-operative radiographs, mild (8 dogs) to moderate (1 dog) OA of the affected stifle was noted. Five dogs had no radiographic abnormalities noted in the contralateral stifle, while 4 dogs had mild effusion of the contralateral stifle detected on radiographs, despite the lack of abnormalities during clinical examination. In addition to CrCL insufficiency, 3 dogs had mild to
moderate OA of one or both coxofemoral joints and 1 dog had mild OA detected in the ipsilateral tarsal joint; no pain or loss of range of motion of these joints was detected on clinical examination.

All affected stifles had positive cranial tibial drawer and tibial thrust tests pre-operatively. The menisci were considered normal upon inspection at the time of surgery in 3 dogs and no meniscal treatment was performed, while 6 dogs had injury to the caudal pole of the medial meniscus that required debridement [hemimeniscectomy (n=4) or partial meniscectomy (n=2)]. The tibial bone tunnel was positioned at 10.3 ± 2.1 mm caudal to the tibial tuberosity and 12.7 ± 2.6 mm distal to the cranial aspect of the tibial plateau. Suture (nylon leader line) sizes included 18 kg, 27 kg, and 36 kg test (Table 4-1).

At 6-month follow-up after LFTS, lameness was improved in all dogs based on orthopedic examinations and owner surveys (Table 4-2). Cranial tibial drawer and tibial thrust tests were negative in 1/9 affected stifles and both tests remained positive in 8/9 affected stifles. Surgeons reported a post-operative lameness grade of 0 (0-2) at the walk and 0 (0-1) at the trot. Owners reported mild post-operative lameness on a VAS scale with a value of 8.9 ± 1.9.

**Craniocaudal Translation**

Cranial cruciate ligament insufficiency resulted in cranial tibial subluxation that is more prominent during the stance phase: there was 8.0 ± 1.6 mm cranial tibial subluxation during stance phase and 4.1 ± 1.7 mm cranial tibial subluxation during swing phase (Figure 4-1). After LFTS there was 6.5 ± 0.5 mm cranial tibial subluxation during stance phase and 4.0 ± 1.1 mm during swing phase; cranial tibial subluxation was reduced during stance phase and unchanged during swing phase compared to CrCL-deficient stifles. The data from each dog was examined individually and no dog had resolution of cranial tibial subluxation after LFTS. The range of
craniocaudal motion in the pre-operative CrCL-deficient stifles was $7.5 \pm 2.4$ mm during stance phase; the range of craniocaudal motion during stance phase decreased to $3.8 \pm 1.1$ mm in LFTS-treated stifles, which remained higher than the control value ($2.2 \pm 0.8$ mm). The range of craniocaudal motion was not different between LFTS-treated stifles and other groups during swing phase (Table 4-3).

**Internal/External Rotation**

Cranial cruciate ligament insufficiency resulted in $8.3 \pm 0.8^\circ$ internal tibial rotation compared to control stifles during mid-stance phase (Figure 4-1). After LFTS, there was no difference in axial rotational position compared to control stifles and there was a $7.3^\circ$ decrease in internal tibial rotation at mid-early stance and $7.8 \pm 0.4^\circ$ in late swing phase compared to CrCL-deficient stifles. After LFTS, there was no difference in axial rotational range of motion compared to pre-operative CrCL-deficient or control stifles over the gait cycle (Table 4-4).

**Flexion/Extension Angle**

Cranial cruciate ligament insufficiency resulted in $10.2 \pm 3.9^\circ$ increased stifle flexion throughout the gait cycle when compared to control stifles (Figure 4-1). LFTS resulted in resolution of increased stifle flexion throughout the gait cycle.

**Discussion**

The objective of this study was to quantitatively define 3D stifle motion during ambulation in dogs with naturally occurring CrCL insufficiency after treatment with LFTS. We found that substantial cranial tibial subluxation persisted after LFTS, whereas axial rotation and flexion angles were not different from control. Our hypothesis was accepted as it was found that LFTS does not restore normal stifle kinematics in dogs with naturally occurring CrCL insufficiency.
Cranial tibial subluxation was not resolved after LFTS in any dog. Although LFTS resulted in a decrease in the magnitude of abnormal cranial tibial translation during stance phase, cranial tibial translation remained greater than the control stifle throughout the entire gait cycle. Contrary to previous studies reporting palpable stifle instability in fewer cases (24-45%) after LFTS, we found 8/9 stifles had persistent cranial drawer and cranial tibial thrust during examination at 6 months following surgery.\textsuperscript{30-32} It is possible that dogs in those previous studies had greater stifle stability because of differences in surgical technique and/or dog related factors, including the degree of disease chronicity; however, the discrepancy between our results and those of previous studies could also be explained by study methodology issues, such as how persistent palpable instability is defined, completeness of follow-up, and duration of follow-up.

We were not able to identify the cause of persistent craniocaudal instability in this study. It is unlikely that poor suture tension at the time of surgery was an issue because resolution of cranial drawer and tibial thrust was confirmed by the surgeon intra-operatively. Therefore, LFTS loosening must have occurred during the 6-month post-operative period. Suture cycling can cause LFTS loosening at the suture, knot, or tissue level. For instance, knot slippage, failure of the fabellofemoral ligament, remodeling of soft tissues, or widening of the tibial bone tunnel have all been reported.\textsuperscript{31,41,136-139} Quasi-isometric suture attachment sites proposed to minimize cycling fatigue have been identified, and the attachment sites used in the current study are in agreement with most studies.\textsuperscript{131-135} Mechanical overload of the native CrCL is one proposed mechanism for CrCL degeneration,\textsuperscript{86-91} and even with optimal surgical technique the LFTS suture does not appear to be able to sufficiently counter-act to this excessive thrust force.

Interestingly, the abnormal internal tibial rotation that is seen with CrCL insufficiency appears to return to normal after LFTS, despite the presence of persistent cranial tibial
subluxation. This may be a reflection of the eccentric lateral position of the suture, which could preferentially limit internal tibial rotation over craniocaudal translation, similar to the anterolateral ligament (ALL) which is found in 50-100% of humans.\textsuperscript{180,181} The ALL passes in a similar orientation to a LFTS suture.\textsuperscript{180,181} Most \textit{ex-vivo} and \textit{in-vivo} studies have shown the ALL to provide resistance to internal tibial rotation,\textsuperscript{182-186} although other cadaveric studies have not supported a consistent stabilizing function of the ALL.\textsuperscript{187-189} Alternatively, the resolution of internal tibial rotation may actually represent a loosening of the construct, as the tibia is likely placed in external rotation acutely.\textsuperscript{190} It is also possible that a type II statistical error is present and we were unable to detect a difference in axial rotational position due to low power and high variability of the axial rotational measurement between dogs.

The increased stifle flexion seen with CrCL insufficiency appeared to be resolved after LFTS; there was no difference between LFTS-treated flexion/extension data and control flexion/extension data. Normalization of the flexion/extension curve is likely representative of an increase in comfort level and weight bearing. Improvement in owner evaluation of comfort and surgeon visual gait examination is likely a reflection improved stifle flexion patterns because this motion is the most visibly apparent kinematic parameter. Despite resolution of abnormal stifle flexion, objective measures of lameness such as force plate gait analysis may have identified subtle abnormalities in these dogs, as has been previously shown 6-months after LFTS.\textsuperscript{33,34}

There are multiple potential explanations for the observed improvement in comfort level in the absence of complete resolution of abnormal kinematics. It is theorized that stifle joint instability results in a pain response due to shear stress to free nerve endings within the joint capsule.\textsuperscript{191} It is possible that, with the reduced instability seen after LFTS, this shear stress is not generated beyond a threshold level that is required to result in pain sensation. Injection of benign
fluid into the stifle joint in anesthetized dogs has been shown to cause peri-articular nerve stimulation.\textsuperscript{192} While the degree of post-operative stifle effusion was not specifically reported in this study, stifle effusion seems to be reduced after LFTS anecdotally and reduced effusion may be a reason for improved comfort post-operatively. Lastly, in the 6/9 dogs that received meniscal debridement, meniscal treatment alone may have provided improved comfort as has been previously proposed.\textsuperscript{193}

The post-operative abnormalities in kinematic parameters identified in this study may be associated with a number of detrimental effects. Though lessened, the persistent joint instability likely potentiates the progression of OA.\textsuperscript{40,126,127,194} Additionally, persistent joint instability will put the medial meniscus at risk for medial meniscal injury following surgery, which can cause lameness that necessitates further surgical intervention. Therefore, it is important to acknowledge that evaluation of post-operative comfort level alone, as assessed by the owner and veterinarian at only several months after surgery, may over-estimate the success of procedures such as LFTS.

This investigation has many limitations. We had narrow initial selection criteria based on body weight and obvious palpable stifle laxity; therefore, our results cannot be extrapolated to other demographics or stages of disease. We only tested one version of the LFTS, and therefore these results may not apply to other extracapsular repair techniques such as bone anchor procedures or use different bone tunnel positions and suture types, or the use of crimps. Additionally, we did not include a control group of dogs without surgical stabilization; thus we were not able to definitively discern whether changes to kinematics and clinical outcomes were attributable to the LFTS. Fluoroscopic imaging was obtained while dogs walked on a treadmill, which has been shown to result in slight variations in joint kinematics compared to over-ground walking.\textsuperscript{173} We also did not assess activities other than walking, such as trotting or stair
climbing, which may have shown different results. The single-plane fluoroscopic technique is less precise than biplanar techniques and precludes the ability to accurately quantify translation in the mediolateral plane. During modeling, there is subjectivity in coordinate assignment as well as determination of the stance and swing phases of the gait cycle; a single researcher (ST) performed these tasks to limit variability. Stifle motion is complex, and in the face of CrCL insufficiency there are likely multiple concurrent (primary or secondary) neuromuscular changes that could also affect our measured kinematic results; these were not accounted for. The 6-month time point for control data collection was chosen to mitigate the effects of lameness on contralateral limb kinematics, however, the contralateral stifles may not have been a perfect representation of normal.

Summarily, persistent cranial tibial subluxation was observed in all dogs following LFTS. Stifle flexion-extension and axial rotational motions were not different from control. Because LFTS does not restore normal kinematics, there is concern for late meniscal tears and the progression of OA. Further research is needed to investigate the relationship between persistent instability after LFTS and OA, as well as improve methods for providing optimal stifle stability for CrCL insufficiency.

Table 4-1. Suture (nylon leader line) size selection was based on body weight

<table>
<thead>
<tr>
<th>Suture size (test)</th>
<th>n</th>
<th>Median body weight (range) (kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>18 kg</td>
<td>3</td>
<td>21.3 kg (17.7-21.8)</td>
</tr>
<tr>
<td>27 kg</td>
<td>2</td>
<td>24.2 kg (24.1-24.2)</td>
</tr>
<tr>
<td>36 kg</td>
<td>4</td>
<td>32.4 kg (29.0-34.0)</td>
</tr>
</tbody>
</table>

* All dogs received 2 strands of nylon leader line.
Table 4-2. Clinical outcome after LFTS in 9 dogs.

<table>
<thead>
<tr>
<th></th>
<th>Pre-operative</th>
<th>LFTS-treated</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-month orthopedic examination (walk)</td>
<td>2 (1-3)</td>
<td>0 (0-2)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>6-month orthopedic examination (trot)</td>
<td>3 (2-3)</td>
<td>0 (0-1)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>6-month owner survey</td>
<td>2.3 ± 2.9</td>
<td>8.9 ± 1.9</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

*p-values were calculated using a Wilcoxon rank sum test or unpaired t-test, as appropriate.

Table 4-3. Range of craniocaudal motion (mean ± SD) after LFTS.

<table>
<thead>
<tr>
<th></th>
<th>1. CrCL-Deficient</th>
<th>2. LFTS-Treated</th>
<th>3. Control</th>
<th>p-value (1 vs 2)</th>
<th>p-value (2 vs 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Entire gait cycle</td>
<td>8.1 ± 2.1 mm</td>
<td>4.8 ± 1.0 mm</td>
<td>2.4 ± 0.8 mm</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Stance phase</td>
<td>7.5 ± 2.4 mm</td>
<td>3.8 ± 1.1 mm</td>
<td>2.2 ± 0.8 mm</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Swing phase</td>
<td>4.9 ± 2.8 mm</td>
<td>2.8 ± 0.8 mm</td>
<td>2.1 ± 0.8 mm</td>
<td>0.06</td>
<td>0.17</td>
</tr>
<tr>
<td>p-value (stance vs swing)</td>
<td><strong>0.02</strong></td>
<td><strong>0.02</strong></td>
<td>0.76</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*p-values were calculated using paired t-tests.

Table 4-4. Range of axial rotational motion (mean ± SD) after LFTS.

<table>
<thead>
<tr>
<th></th>
<th>1. CrCL-Deficient</th>
<th>2. LFTS-Treated</th>
<th>3. Control</th>
<th>p-value (1 vs 2)</th>
<th>p-value (2 vs 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Entire gait cycle</td>
<td>9.9 ± 3.2°</td>
<td>9.5 ± 2.2°</td>
<td>9.9 ± 4.0°</td>
<td>0.57</td>
<td>0.69</td>
</tr>
<tr>
<td>Stance phase</td>
<td>6.4 ± 3.9°</td>
<td>6.2 ± 3.6°</td>
<td>6.2 ± 2.5°</td>
<td>0.93</td>
<td>1.00</td>
</tr>
<tr>
<td>Swing phase</td>
<td>8.7 ± 2.6°</td>
<td>9.1 ± 2.1°</td>
<td>8.6 ± 3.7°</td>
<td>0.62</td>
<td>0.59</td>
</tr>
<tr>
<td>p-value (stance vs swing)</td>
<td>0.14</td>
<td>&lt;0.01</td>
<td>0.07</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*p-values were calculated using paired t-tests.
Figure 4-1. Kinematic outcomes of LFTS in 9 dogs. Orange line = CrCL-deficient; Blue line = LFTS-treated; Black line = Control. Increased y-value indicates cranial tibial translation, internal tibial rotation, or stifle extension. X-values indicate % progression through stance (left graphs) or swing (right graphs) phases. Error bars represent standard deviations. (a) represents a significant difference between LFTS-treated and CrCL-deficient data, and (b) represents a significant difference between LFTS-treated and control data at that time point. LFTS resulted in resolution of abnormal internal tibial rotation and stifle flexion, but not cranial tibial translation.
CHAPTER 5
FEMOROTIBIAL KINEMATICS IN DOGS TREATED WITH TIBIAL PLATEAU LEVELING OSTEOTOMY FOR CRANIAL CRUCIATE LIGAMENT INSUFFICIENCY: AN IN-VIVO FLUOROSCOPIC ANALYSIS DURING WALKING

Relevant Review

Cranial cruciate ligament insufficiency is a common cause of pelvic limb lameness and OA in dogs.\textsuperscript{4-9} The CrCL is a critical stabilizer of the stifle joint.\textsuperscript{15} Pre-operative CrCL-deficient data was previously published from the same population of dogs reported here, showing that naturally occurring CrCL insufficiency results in greater stifle flexion and cranial tibial subluxation throughout the gait cycle, as well as excessive internal tibial rotation during the stance phase.\textsuperscript{177} Abnormal joint motion is thought to be the major cause of lameness, meniscal injury, and development of OA in dogs with CrCL insufficiency.\textsuperscript{5-9}

Surgical intervention is typically recommended to address joint instability.\textsuperscript{13,14} One of the most commonly utilized stabilizing procedures is the TPLO.\textsuperscript{24} Tibial plateau leveling osteotomy is theorized to relieve the stifle’s mechanical dependence on the CrCL by decreasing the caudo-distal slope of the proximal tibia.\textsuperscript{67} Ex-vivo studies have generally shown resolution of cranial tibial subluxation following TPLO, but at the cost of inducing caudal tibial subluxation and altered articular contact mechanics across the stifle.\textsuperscript{17,35,36} The findings from these bench-top studies, however, conflict with a clinical radiographic study that demonstrated 33\% (5/15) of stifles had cranial tibial subluxation after TPLO.\textsuperscript{37} Persistent stifle instability may be a major underlying cause of deleterious outcomes such as post-operative meniscal tears, “pivot shift”, and progressive OA.\textsuperscript{38-41}

A more complete understanding of joint biomechanics can be obtained by ascertaining in-vivo kinematics during ambulation. Femorotibial joint kinematics after TPLO have not been
accurately and objectively quantified during dynamic activity *in-vivo*. The objective of the current study was to quantify the 3D femorotibial joint kinematics during walking in dogs treated with TPLO for naturally occurring CrCL insufficiency. We hypothesized that TPLO would not reliably restore stifle kinematics to normal.

**Materials and Methods**

Non-chondrodystrophic adult dogs weighing 20-40 kg with a history of unilateral lameness of less than 6-months duration ascribed to CrCL insufficiency were evaluated for inclusion in the study between July 2012 and March 2014. Only dogs with a unilateral, complete CrCL insufficiency were enrolled in the study, based on (1) positive cranial drawer sign and positive tibial compression test during examination by a board certified surgeon, (2) stifle radiographs demonstrating stifle effusion with or without OA, and (3) visual confirmation at the time of surgery via arthroscopy or arthrotomy. Dogs were excluded if concurrent clinical orthopedic disease was identified on physical examination, including palpable pain, effusion, or instability of the contralateral stifle at any point during the study period. The study was approved by the University’s Institutional Animal Care and Use Committee and owners signed informed consent at the time of enrollment. Pre-operative CrCL-deficient femorotibial and patellofemoral kinematics and TPLO-treated patellofemoral kinematics have been previously reported from this population of dogs. The data in this chapter is from a subset of the dogs reported in Chapter 3.

Tibial plateau leveling osteotomy was performed by 1 of 3 board certified small animal surgeons (SEK, DDL, AP) with the goal of obtaining a post-operative TPA of 5°. The osteotomy was stabilized using a TPLO plate and screws (DePuySynthes VET, West Chester, PA) of appropriate size based on pre-operative planning and intra-operative assessment. Locking
screws were used in the proximal segment, and cortical ± locking screws were used in the distal segment.

Dogs were evaluated with an orthopedic examination by a board-certified surgeon and fluoroscopic imaging at 6-months post-operatively. Lameness was graded using an ordinal scale (0 = no lameness and weight bearing on all strides observed, 1 = mild subtle lameness with partial weight bearing, 2 = obvious lameness with partial weight bearing). Additionally, owners quantified the degree of lameness using a visual analog scale (VAS) (0 = always lame to 10 = never lame). The following raw data collection and kinematic data processing methodology has been consistent throughout the prior studies performed in our laboratory, including the pre-operative data collection and processing of the dogs included in this report.19,20,44,177

Fluoroscopic Image Acquisition

Six months after TPLO, continuous lateral view fluoroscopic images centered on the stifle joints were acquired during treadmill walking using a ceiling-mounted fluoroscopic system with a flat panel detector (Toshiba American Medical Systems, Inc., Tustin, CA). The treadmill speed was set at a walking velocity of 2.0 - 2.5 mph (0.8 – 1.1 m/s),163 adjusted for each dog to allow a natural walking cadence. The x-ray source was initially programmed to supply a 72 kV beam with a 50 mA beam current, with slight adjustments to parameters to optimize osseous definition for each subject. Images were acquired using a pulse width of 1 ms, pulse rate of 30 frames/second, and an image area of 410 x 300 mm, giving a 0.20 mm x 0.20 mm pixel resolution. Fluoroscopic imaging was obtained for at least 15 full gait cycles with the stifles centered in the field of view, and 3 representative gait cycles were identified for processing. Fluoroscopic sessions were videotaped and reviewed to ensure a natural cadence was present and
to aid in defining stance and swing phases of gait. Radiation-associated risk was considered negligible. 179

3D Model Creation

Computed tomographic scans (Toshiba Aquilon 8, Toshiba American Medical Systems, Inc., Tustin, CA) were obtained pre-operatively and post-operatively extending from the hips through the tarsi bilaterally. Computed tomographic scans used a 0.35x0.35 pixel dim, a 512x512 image matrix, and 0.5 mm slice thickness with 0.3 mm overlap. Digital bone models were created of the femur/fabellae and tibia/fibula (and TPLO plate in TPLO-treated stifles) using an open source 3D segmentation software and a reverse engineering program (ITK-SNAP, http://www.itksnap.org; Geomagic, Inc., Research Triangle Park, NC). For post-operative tibia models, a portion of the proximal tibia was excluded due to metal artifact from the TPLO plate, however the weight bearing surface was preserved and the bone model was combined with a model of the TPLO plate. 20

A 3D coordinate system based on anatomic landmarks was applied to each of the CT generated bone models (Figure 3-1). 9,19,20,44,62,177 Initially, femoral coordinates were applied such that the z-axis (mediolateral) passed through the center of the femoral condyles while remaining perpendicular to the longitudinal anatomic axis of the femur in the frontal plane. The y-axis (proximodistal) was perpendicular to the z-axis, along a plane that intersected the previously determined center of the femoral head and center of each medial and lateral femoral condyle, passing through the ICN in the frontal plane. Initially, tibial coordinates were applied such that the z-axis passed through the most prominent medial and lateral points of the tibial condyles, perpendicular to the longitudinal axis of the tibia in the frontal plane. The y-axis was perpendicular to the z-axis, along a plane that intersected the prominent medial and lateral points on the tibial condyles as well as a point mid-way between the medial and lateral malleoli. For
both bones, the x-axes (craniocaudal) were determined by the right hand rule, which mandates that the 3rd axis be perpendicular to the 1st 2 axes. The origins of the femoral and tibial coordinate systems were then placed at the estimated center of the origin and insertion of the CrCL. Coordinates were applied to the post-operative model by precisely matching the distal tibia to the previously generated pre-operative bone model.

**3D-to-2D Image Registration**

A previously described 3D-to-2D image registration process was used to ascertain 3D kinematics of the femur and tibia throughout the gait cycles (Figure 3-2) by combining 3D digital bone models with the 2D fluoroscopic images.\(^{19-22,44,177}\) The digital femoral and tibial models were projected onto each fluoroscopic image, and models were manually rotated and translated until the anatomic contours of the models precisely matched those of the underlying image (JointTrack, University of Florida: http://sourceforge.net/projects/jointtrack/). This process was repeated for each frame of the selected gait cycles. From the JointTrack output (individual model positions in space), the relative positions of the femoral and tibial bone models were obtained using a custom computer program (MATLAB and Statistics Toolbox Release R2015a, The MathWorks, Inc., Natick, MA).

**Control Kinematic Data**

Contralateral limb data was collected and evaluated 6-months following TPLO for use as a paired control. While contralateral limb kinematics are affected by the presence of lameness caused by CrCL insufficiency, a prior study reported no difference in force plate analysis between 6-month post-operative TPLO-treated CrCL-deficient dogs and that of control dogs.\(^{33,34,75,76}\) Consequently, it was concluded that the kinematics of the contralateral limb at 6-months following surgery sufficiently represented normal conditions. If clinical evidence
(lameness, stifle instability) of a contralateral CrCL insufficiency was identified within the 6-month study period following TPLO, the dog was excluded from the study entirely.

**Kinematic Data Processing**

The data were split into stance and swing phases. Each phase was time normalized using a custom spline interpolation program (MATLAB and Statistics Toolbox Release R2015a, The MathWorks, Inc.) resulting in a data set of 101 data points for each phase (or 202 data points for the complete gait cycle). Interpolation allowed for averaging within and between dogs, despite temporal stride differences between dogs.

Kinematic data was compiled for the 6-month post-operative TPLO-treated and control stifles for craniocaudal translation, internal/external rotation, and flexion/extension angle. Craniocaudal translation was evaluated by measuring the distance between the femoral and tibial attachment sites of the CrCL (origins of the coordinate systems) along the craniocaudal axis (x-axis). Range of craniocaudal motion was defined as the maximum change in craniocaudal distance between the origin and insertion of the CrCL within a period of the gait cycle (stance vs swing) or the entire gait cycle. Cranial tibial subluxation or caudal tibial subluxation was defined as the tibia being positioned > 2mm more cranial or caudal (relative to the femur) when compared to the control stifle. Axial rotation was the angular offset between the femoral and tibial mediolateral axes (z-axes). Range of axial rotation was defined as the maximum change in axial rotational position observed within a period of the gait cycle (stance or swing phases) or the entire gait cycle. Abnormal axial rotational position (internal or external rotation) was defined as a significant difference between affected and control stifles with respect to degree of axial rotation at a given time point during the gait cycle. Flexion/extension angle was the angular offset between the femoral and tibial y-axes. Abnormal flexion/extension was defined as a
significant difference between affected and control stifles with respect to degree of flexion/extension at a given time point during the gait cycle.

**Statistical Analysis**

Continuous variables are presented as mean ± standard deviation or median (range) as appropriate. For each kinematic variable, every 10th data point was utilized from the interpolated data set, leaving 11 stance (0-100%) and 11 swing (0-100%) data points. These were averaged for 3 gait cycles for each stifle and results were compared between the TPLO-treated, control, and previously reported CrCL-deficient stifles using a repeated measures ANOVA with post-hoc Tukey honestly significant difference at each time point (0, 10%, 20%…100%) of the stance and swing phases. Range of motion (craniocaudal translation, axial rotation) was compared between the TPLO-treated, control, and CrCL-deficient stifles using a paired t-test. Tibial plateau angle, duration of pre-operative lameness, body weight, and owner VAS survey results were compared between kinematic outcome groups (caudal or cranial tibial subluxation) using unpaired t-tests. Meniscal status was compared between kinematic outcome groups (caudal or cranial tibial subluxation) using a Fisher’s exact test. Surgeon lameness examination scores were compared between kinematic outcome groups (caudal or cranial tibial subluxation) using a Wilcoxon rank sum test.

**Results**

**Demographic Information**

Eighteen dogs were initially enrolled but 2 dogs were excluded during the study period due to development of contralateral CrCL insufficiency; consequently the pre-operative data reported here will differ slightly that reported in Chapter 3 because only 16/18 dogs are included. Breeds consisted of: 7 mixed breed dogs, 5 Labrador Retrievers, 1 Standard Poodle, 1 German Shepherd Dog, 1 English Springer Spaniel, and 1 Siberian Husky. Ten dogs were spayed females
and 6 were castrated males. Age was 6.6 ± 2.8 years. Body weight was 30.7 ± 6.1 kg with a body condition score of 6/9 (4-8). The right stifle was affected in 9 dogs and the left in 7 dogs. Duration of lameness prior to presentation was 2.3 ± 2.3 months. Pre-operative TPA was 28.1 ± 3.1°, post-operative TPA was 4.1 ± 3.3°, and control stifle TPA was 28.2 ± 3.1°.

All affected stifles had positive cranial tibial drawer and tibial thrust tests pre-operatively. On pre-operative radiographs, mild (9 dogs) to moderate (7 dogs) OA of the affected stifle was noted. Ten dogs had no radiographic abnormalities noted in the contralateral stifle, while 6 dogs had mild effusion of the contralateral stifle detected on radiographs despite the lack of abnormalities during clinical examination throughout the duration of the study. In addition to CrCL insufficiency, 4 dogs had unilateral mild to moderate OA of the contralateral coxofemoral joint and 7 dogs had mild OA detected in one or both tarsal joints; no pain or loss of range of motion of these joints was detected on clinical examination. The menisci were considered normal upon inspection at the time of surgery in 6 stifles and no meniscal treatment was performed, while 10 stifles had injury to the caudal pole of the medial meniscus that required hemimeniscectomy.

Fifteen dogs had complete orthopedic examinations recorded at 6-months post-operatively. At the 6-month post-operative examination, cranial tibial drawer was no longer identified in 4/15 affected stifles and remained present in 11/15 affected stifles. The tibial compression test was negative in 14/15 stifles and remained positive in 1 stifle. Lameness was improved in all dogs based on orthopedic examinations and owner surveys (Table 5-1). Surgeons reported a post-operative lameness grade of 0 (0-1) at the walk and 0 (0-2) at the trot. Owners reported mild post-operative lameness on a VAS scale with a value of 8.9 ± 1.5.
**Craniocaudal Translation**

Cranial cruciate ligament insufficiency resulted in cranial tibial subluxation that is more prominent during the stance phase: there was $8.4 \pm 1.9$ mm cranial tibial subluxation during stance phase and $2.7 \pm 1.2$ mm cranial tibial subluxation during swing phase (Figure 5-3). After TPLO, there was $2.8 \pm 0.5$ mm caudal tibial subluxation during early stance phase and throughout swing phase; tibial subluxation was converted from cranial to caudal over the entire gait cycle.

Upon assessing each dog individually, 3 craniocaudal translational patterns were noted after TPLO: 10/16 dogs had caudal tibial subluxation (> 2 mm more caudal than paired control), 5/16 dogs had cranial tibial subluxation (> 2 mm more cranial than paired control), and only 1 dog had a craniocaudal tibial position within 2 mm of the paired control (Figure 5-4). In stifles with caudal tibial subluxation, the caudal tibial subluxation was $-4.3 \pm 0.4$ mm throughout the entire gait cycle, and in stifles with cranial tibial subluxation the cranial tibial subluxation was $4.1 \pm 0.3$ mm at mid to late stance phase. Dogs with cranial tibial subluxation had a higher post-operative TPA and longer duration of pre-operative lameness than dogs with caudal tibial subluxation (Table 5-2).

Tibial plateau leveling osteotomy shifts relationship between the long axis of the tibia and the tibial plateau, therefore the positions of the tibial attachment site of the CrCL (i.e. the origin of the 3D coordinate system) was compared between TPLO-treated and pre-operative CrCL-deficient tibial models. Plateau rotation was determined to account for a maximum of 10% of the measured caudal tibial displacement.

The craniocaudal range of motion in the pre-operative CrCL-deficient stifles was $9.6 \pm 2.9$ mm; the range of craniocaudal motion decreased to $4.5 \pm 2.5$ mm after TPLO, but this
remained higher than the control value (2.3 ± 0.7 mm). (Table 5-3). When the range of craniocaudal motion was compared between stifles with caudal versus cranial tibial subluxation, stifles with cranial tibial subluxation had a higher range of craniocaudal motion during stance phase (2.3 ± 1.5 mm vs 6.1 ± 2.0 mm, respectively) (Table 5-4).

**Internal/External Rotation**

Cranial cruciate ligament insufficiency resulted in 9.0 ± 1.7° internal tibial rotation during stance phase, compared to control stifles (Figure 5-3). After TPLO, there was no difference in axial rotational position compared to control stifles at any point during the gait cycle, and there was a 8.4 ± 2.0° decrease in internal tibial rotation during stance and early swing phases compared to CrCL-deficient stifles. However, TPLO-treated stifles with cranial tibial subluxation had more internal tibial rotation and TPLO-treated stifles with caudal tibial subluxation had more external tibial rotation during mid-late stance phase, with a difference between groups of 11.0 ± 1.1° (Figure 5-4).

The axial rotational range of motion in the pre-operative CrCL-deficient stifles was 13.1 ± 3.5°; the range of axial rotational motion was unchanged after TPLO (13.3 ± 3.8°) and was also not different between TPLO-treated and control stifles (12.1 ± 3.6°) (Table 5-4). However, dogs with post-operative caudal tibial subluxation had an axial rotational range of motion of 6.0 ± 1.9° during stance phase, which was lower than (1) pre-operative CrCL-deficient stifles, (2) control stifles, and (3) TPLO-treated stifles with cranial tibial subluxation (Table 5-5). Additionally, dogs with post-operative caudal tibial subluxation had less axial rotational range of motion during stance phase compared to swing phase.
**Flexion/Extension Angle**

Cranial cruciate ligament insufficiency resulted in $13.0 \pm 3.8^\circ$ increased stifle flexion throughout the gait cycle when compared to control stifles (Figure 5-3). TPLO resulted in resolution of abnormal stifle flexion throughout the gait cycle, regardless of whether the animal developed caudal or cranial tibial subluxation post-operatively (Figure 5-4).

**Discussion**

The objective of this study was to quantitate 3D stifle kinematics during ambulation in dogs with naturally occurring CrCL insufficiency after treatment with TPLO. We found that craniocaudal translation and axial rotation remained abnormal after TPLO, while the flexion/extension angle patterns were not different from control. Therefore, our hypothesis was accepted and we confirmed that TPLO does not restore normal stifle kinematics in dogs with naturally occurring CrCL insufficiency.

When assessing the entire population of 16 dogs, an abnormal magnitude of caudal tibial subluxation was evident following TPLO. Additionally, the majority (10/16) of TPLO-treated stifles had caudal tibial subluxation throughout the gait cycle (-4.3 ± 0.4 mm). Caudal tibial subluxation after TPLO has been previously noted in *ex-vivo* studies of TPLO treated limbs during simulated weight bearing, which has been ascribed to shifting of the cranially directed shear force to a caudally directed shear force after plateau rotation. Additionally, the magnitude of caudal tibial subluxation reported in our study is in agreement with previous *ex-vivo* investigations, which have also shown that the magnitude of caudal tibial subluxation increases with greater tibial plateau rotation and with increasing loads. It is therefore possible that a larger magnitude of caudal tibial subluxation occurs during activities with higher demands than treadmill walking.
Cranial tibial subluxation during the stance phase of gait was identified in 5/16 TPLO-treated stifles, although the magnitude of cranial tibial subluxation was reduced to approximately 40% of that observed before surgery. A similar finding was reported in a prior in-vivo study using standing radiography in which 5/15 stifles had cranial tibial subluxation after TPLO.\textsuperscript{37} In that study, stifles with a medial caudal pole hemimeniscectomy had significantly more cranial tibial subluxation than those with an intact meniscus, which appeared to corroborate the importance of the meniscus in stabilizing the stifle.\textsuperscript{170} Meniscal status, however, did not influence joint alignment in the current study. Factors that were associated with post-operative cranial tibial subluxation included a higher post-operative TPA and a longer pre-operative duration of lameness. Whereas having a higher post-operative TPA might easily explain persistent cranial tibial subluxation, all dogs with post-operative cranial tibial subluxation had post-operative TPA of $\leq 10^\circ$, which was previously considered acceptable.\textsuperscript{140} In dogs with a longer duration of lameness pre-operatively, there may have been an imbalance of muscle forces across the stifle joint contributing to persistent joint instability, there could be periarticular fibrosis fixing the joint in a subluxated position, or this finding may be coincidental. Several human studies have shown the importance of muscle function in maintaining joint stability and coping after ACL rupture.\textsuperscript{166} A drift towards permanent cranial tibial subluxation with increasing chronicity was found in a study of dogs with experimental CrCL transection without surgical stabilization; a similar phenomenon may have been present in the dogs with cranial tibial subluxation in our study.\textsuperscript{9} Additional factors that could lead to either caudal or cranial tibial subluxation after TPLO include differences in axial and/or coronal alignment of the tibia, or inherent differences in condylar geometry; these factors were not assessed by our study.
The abnormal post-operative kinematic patterns identified in our study population (cranial or caudal tibial subluxation) could have varying detrimental effects on the stifle.\textsuperscript{126,127} Stifles with caudal tibial subluxation had less craniocaudal shear motion throughout the gait cycle than stifles with persistent cranial tibial subluxation. In this respect, stifles with persistent cranial tibial subluxation may degenerate more rapidly because shear insults are thought to accelerate cartilage degradation.\textsuperscript{198} Furthermore, residual cranial tibial subluxation is likely to increase the risk of post-operative meniscal injury. In contrast, stifles with caudal tibial subluxation are likely to have higher stresses on the CaCL,\textsuperscript{17} which is already pathologic in the majority of dogs with CrCL insufficiency.\textsuperscript{199} While both abnormal kinematic patterns are likely to promote progressive degenerative joint disease by altering articular cartilage contact mechanics,\textsuperscript{126,127} the kinematic abnormalities that are more detrimental to long-term joint health is unknown. We were not able to demonstrate a difference in short-term clinical outcomes between dogs with caudal versus cranial tibial subluxation.

When assessing all 16 dogs, axial rotation did not differ between TPLO-treated stifles and control stifles at any point during the gait cycle. However, TPLO-treated stifles with cranial tibial subluxation had more internal tibial rotation compared to both control stifles and stifles with caudal tibial subluxation during mid-late stance phase. In the CrCL-deficient stifle, internal tibial rotation becomes coupled with cranial tibial subluxation.\textsuperscript{177} However, in our results, dogs with cranial tibial subluxation had more internal tibial rotation and dogs with caudal tibial subluxation had more external tibial rotation. This implies that the coupling between cranial tibial subluxation and internal tibial rotation (and caudal tibial subluxation and external tibial rotation) persists after TPLO, such that craniocaudal tibial position dictates axial rotational position. We suspect that the minimal evidence of significant difference in axial rotational
position between TPLO-treated stifles and control stifles according to subgroup (caudal versus cranial tibial subluxation) was due to a type II statistical error, and a correlation between axial rotation and craniocaudal subluxation does exist after TPLO for CrCL insufficiency.

Stifle flexion was restored to normal following TPLO. This finding is consistent with the results of a kinematic study using video-camera analysis, in which stifle flexion angle was not different from normal during trotting following TPLO. Lameness associated with CrCL insufficiency is generally characterized by decreased weight-bearing, which can occur by increasing joint flexion. Hence, restoration of flexion-extension patterns likely reflects improved comfort and weight bearing, as was identified on both owner and veterinarian evaluations. There is ample evidence showing TPLO improves limb use and weight-bearing in dogs with CrCL insufficiency, and our findings suggest that the resolution of lameness is due to reduced instability. Additionally, meniscal debridement in 10/16 dogs may have contributed to improvement in lameness.

There are several limitations associated with this investigation. We had narrow initial selection criteria based on body weight and palpable stifle laxity; therefore, our results may not be directly applicable to other populations. Fluoroscopic imaging was obtained while dogs walked on a treadmill, which has been shown to result in slight variations in joint kinematics in dogs when compared to over-ground walking. Walking is a low-demand activity; more demanding activities such as trotting or stair-climbing may induce different patterns of kinematic abnormalities. We utilized a single-plane fluoroscopic technique, which is less precise than biplanar techniques and precludes the ability to accurately quantify translation in the mediolateral plane. Owner assessment may have been affected by bias, but the VAS scale used has been validated. Stifle motion is complex and there are likely multiple concurrent primary
or secondary neuromuscular and musculoskeletal alterations with CrCL insufficiency; these were not accounted for in this study. The contralateral limb was used as a control, but may not have been an ideal representation of normal. Due to anatomic variability between dogs, we considered the contralateral stifle to be a superior control when compared to the alternative of using a separate population of normal dogs. We also considered the influence of concurrent subclinical hip or hock osteoarthritis to be minimal.

Our results demonstrated that TPLO failed to restore normal femorotibial kinematics in 94% of dogs with naturally occurring CrCL insufficiency. Both caudal and cranial tibial subluxation were common, but the magnitude of subluxation was reduced in all cases. Stifles with post-operative cranial tibial subluxation had a kinematic pattern that was similar in shape to the patterns observed prior to surgery (see Chapter 3), although the magnitude of abnormalities were lower. The coupling of cranial tibial translation and internal tibial rotation (and caudal tibial translation and external tibial rotation) that is present with CrCL insufficiency was also present after TPLO. Therefore, it may be important to consider addressing axial rotational instability as well as craniocaudal translational instability. The abnormal kinematics associated with TPLO may be responsible for post-operative complications such as meniscal tears, pivot shift, and progressive OA. While the TPLO is an acceptable procedure, our results have highlighted the potential for improvements to the techniques for treating CrCL insufficiency.

Table 5-1. Clinical outcome after TPLO in 15 dogs.

<table>
<thead>
<tr>
<th></th>
<th>Pre-operative</th>
<th>LFTS-treated</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-month orthopedic</td>
<td>2 (1-4)</td>
<td>0 (0-1)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>examination (walk)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6-month orthopedic</td>
<td>2 (1-4)</td>
<td>0 (0-2)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>examination (trot)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6-month owner survey</td>
<td>2.1 ± 2.4</td>
<td>8.6 ± 1.7</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

* p-values were calculated using a Wilcoxon rank sum test or unpaired t-test, as appropriate.
Table 5-2. Comparison of clinical factors between TPLO-treated dogs with post-operative caudal tibial subluxation and cranial tibial subluxation.

<table>
<thead>
<tr>
<th></th>
<th>Caudal tibial subluxation (n=10)</th>
<th>Cranial tibial subluxation (n=5)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-operative TPA (degrees)</td>
<td>27.6 ± 2.8</td>
<td>29.6 ± 3.8</td>
<td>0.26</td>
</tr>
<tr>
<td>Post-operative TPA (degrees)</td>
<td>2.9 ± 2.7</td>
<td>7.2 ± 2.6</td>
<td><strong>0.01</strong></td>
</tr>
<tr>
<td>Difference in TPA (degrees)</td>
<td>24.7 ± 3.2</td>
<td>22.4 ± 3.0</td>
<td>0.21</td>
</tr>
<tr>
<td>Meniscal status</td>
<td>6 debrided</td>
<td>4 debrided</td>
<td>0.60</td>
</tr>
<tr>
<td></td>
<td>4 intact</td>
<td>1 intact</td>
<td></td>
</tr>
<tr>
<td>Duration of lameness (months)</td>
<td>0.9 ± 0.6</td>
<td>4.2 ± 2.5</td>
<td><strong>&lt;0.01</strong></td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>30.3 ± 5.8</td>
<td>33.6 ± 5.1</td>
<td>0.30</td>
</tr>
<tr>
<td>6-month orthopedic examination (walk)</td>
<td>0 (0-1)</td>
<td>0 (0-0)</td>
<td>0.32</td>
</tr>
<tr>
<td>6-month orthopedic examination (trot)</td>
<td>0 (0-2)</td>
<td>0 (0-0)</td>
<td>0.33</td>
</tr>
<tr>
<td>6-month owner survey</td>
<td>8.8 ± 1.1</td>
<td>9.6 ± 0.5</td>
<td>0.15</td>
</tr>
</tbody>
</table>

* Continuous variables are represented as a mean ± SD, binomial variables are reported as raw data, and categorical variables are represented as a median (range). An unpaired t-test or Wilcoxon rank sum test was used for statistical analysis, as appropriate.

Table 5-3. Range of craniocaudal motion (mean ± SD) in all 16 dogs and in dogs with post-operative caudal tibial subluxation, cranial tibial subluxation, or no difference from control.

<table>
<thead>
<tr>
<th></th>
<th>1. CrCL-Deficient</th>
<th>2. TPLO-Treated</th>
<th>3. Control</th>
<th>p-value (1 vs 2)</th>
<th>p-value (2 vs 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Entire population (n=16)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Entire gait cycle</td>
<td>9.6 ± 2.9 mm</td>
<td>4.5 ± 2.5 mm</td>
<td>2.3 ± 0.7 mm</td>
<td><strong>&lt;0.01</strong></td>
<td><strong>&lt;0.01</strong></td>
</tr>
<tr>
<td>Stance phase</td>
<td>8.2 ± 3.3 mm</td>
<td>3.4 ± 2.5 mm</td>
<td>1.9 ± 0.7 mm</td>
<td><strong>&lt;0.01</strong></td>
<td><strong>0.05</strong></td>
</tr>
<tr>
<td>Swing phase</td>
<td>6.6 ± 2.6 mm</td>
<td>2.8 ± 1.4 mm</td>
<td>2.0 ± 0.8 mm</td>
<td><strong>&lt;0.01</strong></td>
<td><strong>0.02</strong></td>
</tr>
<tr>
<td>Caudal tibial subluxation (n=10)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Entire gait cycle</td>
<td>9.6 ± 3.5 mm</td>
<td>3.3 ± 1.6 mm</td>
<td>2.5 ± 0.7 mm</td>
<td><strong>&lt;0.01</strong></td>
<td>0.11</td>
</tr>
<tr>
<td>Stance phase</td>
<td>7.9 ± 3.9 mm</td>
<td>2.3 ± 1.5 mm</td>
<td>2.0 ± 0.8 mm</td>
<td><strong>&lt;0.01</strong></td>
<td>0.60</td>
</tr>
<tr>
<td>Swing phase</td>
<td>6.9 ± 2.6 mm</td>
<td>2.7 ± 1.5 mm</td>
<td>2.2 ± 0.6 mm</td>
<td><strong>&lt;0.01</strong></td>
<td>0.21</td>
</tr>
<tr>
<td>Cranial tibial subluxation (n=5)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Entire gait cycle</td>
<td>9.8 ± 1.6 mm</td>
<td>7.3 ± 1.9 mm</td>
<td>2.0 ± 0.9 mm</td>
<td><strong>0.03</strong></td>
<td><strong>&lt;0.01</strong></td>
</tr>
<tr>
<td>Stance phase</td>
<td>9.2 ± 1.7 mm</td>
<td>6.1 ± 2.0 mm</td>
<td>1.7 ± 0.7 mm</td>
<td><strong>0.05</strong></td>
<td><strong>0.01</strong></td>
</tr>
<tr>
<td>Swing phase</td>
<td>6.2 ± 3.2 mm</td>
<td>3.1 ± 1.3 mm</td>
<td>1.7 ± 1.1 mm</td>
<td>0.09</td>
<td>0.07</td>
</tr>
<tr>
<td>No difference from control (n=1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Entire gait cycle</td>
<td>8.4 mm</td>
<td>2.4 mm</td>
<td>2.2 mm</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>Stance phase</td>
<td>5.6 mm</td>
<td>0.8 mm</td>
<td>2.2 mm</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>Swing phase</td>
<td>6.3 mm</td>
<td>2.4 mm</td>
<td>1.4 mm</td>
<td>n/a</td>
<td>n/a</td>
</tr>
</tbody>
</table>

* p-values were calculated using paired t-tests.
Table 5-4. Range of craniocaudal motion (mean ± SD) after TPLO, compared between dogs with caudal versus cranial tibial subluxation and between stance and swing cycles.

<table>
<thead>
<tr>
<th></th>
<th>Caudal tibial subluxation (n=10)</th>
<th>Cranial tibial subluxation (n=5)</th>
<th>p-value (caudal vs cranial)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Entire Gait Cycle</td>
<td>3.3 ± 1.6 mm</td>
<td>7.3 ± 1.9 mm</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Stance Phase</td>
<td>2.3 ± 1.5 mm</td>
<td>6.1 ± 2.0 mm</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Swing Phase</td>
<td>2.7 ± 1.5 mm</td>
<td>3.1 ± 1.3 mm</td>
<td>0.56</td>
</tr>
<tr>
<td>p-value (stance vs swing)</td>
<td>0.32</td>
<td>0.09</td>
<td></td>
</tr>
</tbody>
</table>

* p-values were calculated using paired or unpaired t-tests as appropriate.

Table 5-5. Range of axial rotational motion (mean ± SD) in all 16 dogs and in dogs with post-operative caudal tibial subluxation, cranial tibial subluxation, or no difference from control.

<table>
<thead>
<tr>
<th></th>
<th>1. CrCL-Deficient</th>
<th>2. TPLO-Treated</th>
<th>3. Control</th>
<th>p-value (1 vs 2)</th>
<th>p-value (2 vs 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Entire population (n=16)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Entire gait cycle</td>
<td>13.1 ± 3.5°</td>
<td>13.3 ± 3.8°</td>
<td>12.1 ± 3.6°</td>
<td>0.88</td>
<td>0.26</td>
</tr>
<tr>
<td>Stance phase</td>
<td>10.1 ± 5.0°</td>
<td>7.8 ± 3.8°</td>
<td>8.0 ± 3.5°</td>
<td>0.16</td>
<td>0.86</td>
</tr>
<tr>
<td>Swing phase</td>
<td>11.0 ± 2.9°</td>
<td>11.4 ± 3.3°</td>
<td>10.2 ± 4.5°</td>
<td>0.64</td>
<td>0.32</td>
</tr>
<tr>
<td>Caudal tibial subluxation (n=10)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Entire gait cycle</td>
<td>13.5 ± 2.6°</td>
<td>12.9 ± 3.8°</td>
<td>12.3 ± 3.0°</td>
<td>0.66</td>
<td>0.63</td>
</tr>
<tr>
<td>Stance phase</td>
<td>10.2 ± 4.2°</td>
<td>6.0 ± 1.9°</td>
<td>9.0 ± 3.4°</td>
<td>&lt;0.01</td>
<td>0.02</td>
</tr>
<tr>
<td>Swing phase</td>
<td>11.3 ± 3.0°</td>
<td>11.7 ± 3.8°</td>
<td>9.9 ± 4.7°</td>
<td>0.76</td>
<td>0.29</td>
</tr>
<tr>
<td>Cranial tibial subluxation (n=5)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Entire gait cycle</td>
<td>12.5 ± 5.5°</td>
<td>14.1 ± 4.5°</td>
<td>12.8 ± 4.0°</td>
<td>0.64</td>
<td>0.58</td>
</tr>
<tr>
<td>Stance phase</td>
<td>10.5 ± 7.1°</td>
<td>11.6 ± 4.3°</td>
<td>6.8 ± 3.0°</td>
<td>0.81</td>
<td>0.12</td>
</tr>
<tr>
<td>Swing phase</td>
<td>10.6 ± 3.2°</td>
<td>10.8 ± 2.6°</td>
<td>11.7 ± 4.1°</td>
<td>0.91</td>
<td>0.63</td>
</tr>
<tr>
<td>No difference from control (n=1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Entire gait cycle</td>
<td>11.2°</td>
<td>12.6°</td>
<td>5.6°</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>Stance phase</td>
<td>7.0°</td>
<td>6.3°</td>
<td>3.6°</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>Swing phase</td>
<td>9.7°</td>
<td>11.9°</td>
<td>5.6°</td>
<td>n/a</td>
<td>n/a</td>
</tr>
</tbody>
</table>

* p-values were calculated using paired t-tests.

Table 5-6. Range of axial rotational motion (mean ± SD) after TPLO, compared between dogs with caudal versus cranial tibial subluxation and between stance and swing cycles.

<table>
<thead>
<tr>
<th></th>
<th>Caudal tibial subluxation (n=10)</th>
<th>Cranial tibial subluxation (n=5)</th>
<th>p-value (caudal vs cranial)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Entire gait cycle</td>
<td>12.9 ± 3.8°</td>
<td>14.1 ± 4.5°</td>
<td>0.64</td>
</tr>
<tr>
<td>Stance phase</td>
<td>6.0 ± 1.9°</td>
<td>11.6 ± 4.3°</td>
<td>0.04</td>
</tr>
<tr>
<td>Swing phase</td>
<td>11.7 ± 3.8°</td>
<td>10.8 ± 2.6°</td>
<td>0.61</td>
</tr>
<tr>
<td>p-value (stance vs swing)</td>
<td>&lt;0.01</td>
<td>0.48</td>
<td></td>
</tr>
</tbody>
</table>

* p-values were calculated using paired or unpaired t-tests as appropriate.
Figure 5-1. Femoral and tibial coordinate systems using TPLO-treated bone models. CT-generated 3D digital models of the femur (craniocaudal (1a) and lateral (1b) views) and tibia (craniocaudal (1c) and lateral (1d) views) with 3D coordinate system applied.

Figure 5-2. Image registration process. Fluoroscopic image before (2a) and after (2b) 3-D to 2-D image registration process. In Figure 2b, the bone models from Figure 1 have been projected, edge-detected, and superimposed then precisely matched to the fluoroscopic image.
Figure 5-3. Kinematic outcomes of TPLO in 16 dogs. Orange line = CrCL-deficient; Blue line = TPLO-treated; Black line = Control. Increased y-value indicates cranial tibial translation, internal tibial rotation, or stifle extension. X-values indicate % progression through stance (left graphs) or swing (right graphs) phases. Error bars represent standard deviations. (a) represents a significant difference between TPLO-treated and CrCL-deficient data, and (b) represents a significant difference between TPLO-treated and control data at that time point. TPLO converted the pre-operative cranial tibial subluxation to a less severe caudal tibial subluxation and resulted in resolution of abnormal internal tibial rotation during stance phase and resolution of abnormal stifle flexion throughout the gait cycle.
Figure 5-4. Kinematic outcomes of TPLO in 10 dogs with caudal tibial subluxation and 5 dogs with cranial tibial subluxation. Orange line = CfCL-deficient; Green line = TPLO-treated with caudal tibial subluxation; Purple line = TPLO-treated with cranial tibial subluxation; Black line = Control. Increased y-value indicates cranial tibial translation, internal tibial rotation, or stifle extension. X-values indicate % progression through stance (left graphs) or swing (right graphs) phases. (c) represents a significant difference between TPLO-treated with caudal tibial subluxation and TPLO-treated with cranial tibial subluxation, (d) represents a significant difference between TPLO-treated with caudal tibial subluxation and control data, and (e) represents a significant difference between TPLO-treated with cranial tibial subluxation and control data at that time point. After TPLO, dogs with cranial tibial subluxation had a more internally rotated tibia compared to dogs with caudal tibial subluxation during the 2nd half of stance phase. Abnormal stifle flexion was resolved regardless of whether the dogs developed caudal or cranial tibial subluxation.
CHAPTER 6  
CONCLUSIONS  

Aim 1  

The femorotibial kinematic changes observed in dogs with naturally occurring CrCL insufficiency were largely consistent with previous experimental studies: we observed profound craniocaudal translational and axial rotational instability that was most pronounced during the stance phase of gait, as well as 8-20° greater stifle flexion. Cranial tibial subluxation results when the tether of the CrCL is lost because the CrCL is the main restraint against cranial tibial subluxation. Cranial tibial subluxation is maximal, at 9.7 mm, at mid-stance phase because of the contraction of the muscles required for weight bearing (quadriceps, gastrocnemius) that promote cranial tibial subluxation / caudal femoral subluxation, as well as the transmission of weight bearing force across the stifle joint that is converted to a shear force per Slocum’s “active force model.” Contrary to the belief that the swing phase is CrCL-independent, cranial tibial subluxation is also present during swing phase. This may be a reflection of chronic fibrous tissue partially stabilizing the joint in an abnormal position, muscular imbalance, bony changes, or other causes. Abnormal internal tibial rotation is also maximal at mid-stance phase. The cranial tibial subluxation and internal tibial rotation motions are coupled in the CrCL-deficient state. This is suspected to be because the collateral ligaments become the major ligamentous stabilizers against cranial tibial subluxation in the absence of the CrCL, and the lateral collateral ligament is looser than the medial collateral ligament. Consequently, internal tibial rotation occurs with cranial tibial subluxation. Additionally, the medial meniscus provides some stabilizing function so the medial compartment may be more stable than the lateral compartment, creating a medially based pivot point. Despite lack of rotational instability in 1 prior in-vivo kinematic study, our finding of prominent internal tibial rotation supports
clinical concerns that rotational instability may also be of primary concern in CrCL insufficiency. Increased stifle flexion is likely an effort to bear less weight on the limb as a result of pain, which is caused by the previously noted instability as well as abnormal contact mechanics, stifle effusion, and meniscal tears in some cases. These prominent kinematic derangements in dogs with CrCL insufficiency lead us to believe that stabilization techniques should address both craniocaudal instability and axial rotational instability with hopes to slow the progression of OA and mitigate the likelihood of post-operative meniscal damage.

**Aim 2**

After LFTS treatment for naturally occurring CrCL insufficiency, we observed persistent cranial tibial subluxation in 100% of dogs while stifle axial rotational motions and flexion/extension positions were not different from the contralateral control. Previous studies have reported fewer cases with post-operative instability (25-45%), but these studies used palpation rather than a more objective methodology like fluoroscopy to make this determination. The average maximal magnitude of cranial tibial subluxation after LFTS was 7.5 ± 1.5 mm, which occurred during stance phase and was significantly reduced compared to CrCL-deficient stifles. Interestingly, despite minimal reduction in cranial tibial subluxation, abnormal axial rotation was resolved after LFTS. Given the low case number and high variability of this measurement of axial rotation between dogs, it is possible that this represents a type II statistical error. However, it is also possible that the discrepant finding of incomplete resolution of cranial tibial subluxation with resolution of internal tibial rotation is true, in which case it could be due to the eccentric position of the suture which may limit axial rotational motion better than cranial tibial translational motion similar to the ALL in humans. The normal flexion angle observed after LFTS is likely a representation of improved comfort level, as was supported by
orthopedic examination and owner surveys. However, if we had utilized more objective measures of lameness such as force plate gait analysis, we may have detected persistent, though mitigated, lameness. Regardless, comfort was improved in all dogs after LFTS in the absence of normal kinematics in any dog, which is perplexing because joint instability causes pain\textsuperscript{191} – why is comfort improved in the presence of what should be a painful stimulus? There are multiple potential explanations, including that the post-operative instability may be below the threshold level needed to trigger pain receptors, that joint effusion was decreased below the threshold level needed to trigger pain receptors, or meniscal debridement could have played a major role in the 6/9 dogs that had meniscal treatments during surgery.\textsuperscript{192,193}

**Aim 3**

TPLO also failed to restore normal femorotibial kinematics in 94% of dogs with naturally occurring CrCL insufficiency. All dogs had resolution of abnormal flexion, but both caudal and cranial tibial subluxation was common and associated with different axial rotational patterns. In stifles with caudal tibial subluxation after TPLO (10/16 dogs), the average maximal magnitude of caudal tibial subluxation was $-5.9 \pm 2.2$ mm. Stifles with persistent cranial tibial subluxation (5/16) after TPLO had a craniocaudal kinematic pattern that was similar, but dampened, compared to that of CrCL insufficiency, with average maximal magnitude of $5.6 \pm 1.7$ mm. One dog (1/16) had a kinematic pattern that was not distinguishable from control after TPLO. The resolution of abnormal flexion is, again, likely a reflection of improved comfort level.

Interestingly, cranial tibial subluxation and internal tibial rotation appeared to remain coupled after TPLO treatment: dogs with cranial tibial subluxation had a more internally rotated tibia and dogs with caudal tibial subluxation had a more externally rotated tibia during stance phase. It is not clear which kinematic outcome (cranial tibial subluxation or caudal tibial
subluxation, with associated axial rotational patterns) is more detrimental to joint health because both instability and abnormal contact mechanics contribute to the development and progression of OA. Dogs with cranial tibial subluxation had both abnormal relative positions of the femur and tibia and more instability than normal (evidenced by having a larger range of motion during the stance phase), but dogs with caudal tibial subluxation still had abnormal relative positions of the femur and tibia despite having a stable joint, therefore both abnormal kinematic outcomes are detrimental to joint health. However, dogs with more instability (ie, dogs with post-operative cranial tibial subluxation) may have more stimulus for OA development and may be at higher risk for post-operative meniscal tears compared to dogs with less instability after TPLO, but this was not investigated here. Possible risk factors for cranial tibial subluxation after TPLO included a higher post-operative TPA or a longer pre-operative duration of lameness. However, all dogs had a TPA of $<10^\circ$, which has been previously thought to be acceptable for stifle stabilization. A longer term study with a larger population of dogs would be necessary to attempt to differentiate clinical outcomes between these groups and define risk factors for poor kinematic outcome.

**Comparison of LFTS and TPLO**

We have concluded that LFTS does not normalize kinematics in any case and TPLO does not normalize kinematics in 94% of stifles, giving concern that OA will continue to progress in most or all cases despite apparent resolution of lameness during the 6-month follow-up period. While not the direct aim of this study, comparison between LFTS and TPLO is of great interest in order to attempt to determine which of these common procedures is truly more successful. In previous literature, mainly looking at clinical outcomes such as force plate gait analysis or progression of OA, reports show either an equivalent outcome between procedures or TPLO having a better outcome than LFTS. Kinematics should relate to clinical outcome
because instability causes pain primarily, as well as contributing to the development of OA and causing abnormal contact mechanics, stifle effusion, and meniscal damage.

If the 3 kinematic outcome groups are compared – LFTS-treated, TPLO-treated with caudal tibial subluxation, and TPLO-treated with cranial tibial subluxation, the groups are significantly different from each other at almost all time points with regards to craniocaudal position. More specifically, LFTS-treated stifles have more cranial tibial subluxation (7.5 ± 1.5 mm) than TPLO-treated stifles with cranial tibial subluxation (5.6 ± 1.7 mm), and both of these groups have more cranial tibial subluxation than TPLO-treated stifles with caudal tibial subluxation (-5.9 ± 2.2 mm). Additionally, the range of craniocaudal stifle motion after LFTS and after TPLO with cranial tibial subluxation is higher than after TPLO with caudal tibial subluxation. These differences are statistically significant and may also be clinically significant, because it may be that the magnitude of abnormal position and the magnitude of instability is important – rather than just determining whether the results are normal or not. In other words, this comparison may support the conclusion of multiple prior studies that have concluded that the clinical outcome of TPLO is superior to the outcome of LFTS.

**Future Studies**

Further research is needed to determine whether the abnormal kinematic outcomes of LFTS or TPLO found in this project are clinically relevant, or beyond that, whether we can distinguish clinical outcomes based on different kinematic outcomes (LFTS-treated, TPLO-treated with caudal tibial subluxation, and TPLO-treated with cranial tibial subluxation). We encourage continued research into advancing the techniques for treating CrCL insufficiency with hopes of normalizing post-operative kinematics to maximize the potential for good long term clinical outcome, decreasing the incidence of persistent instability, pivot shift, post-operative
meniscal tears, and OA. Given the apparent persistent coupling between cranial tibial subluxation and internal tibial rotation after TPLO, it may be wise to consider also addressing axial rotational instability primarily, in addition to addressing craniocaudal translational instability. Additionally, there are many other stabilizing procedures for CrCL insufficiency - different forms of extracapsular stabilization or tibial osteotomy procedures may provide a more ideal kinematic outcome but this has yet to be investigated.

Despite implying multiple times that the goal of stabilizing procedures for CrCL insufficiency should be normal post-operative kinematics, we must acknowledge that creating normal kinematics with any surgical procedure is likely to be significantly challenging. The stifle joint is complex and the CrCL and CaCL work together by providing balanced and opposing forces to maintain joint stability in the face of bony incongruity. Our stabilizing procedures attempt to either replace the function of the CrCL (ex, LFTS) or eliminate the need for the CrCL by creating a joint that is independent of the CrCL (+/- dependent on the CaCL) (ex, TPLO). We categorized only 1 dog (6%) treated with TPLO and 0 dogs treated with LFTS as having normal post-operative kinematics despite planning and executing the procedures as recommended. Obtaining a higher success rate of returning stifle kinematics to normal will require further advanced knowledge of the forces acting across the joint and how these can be manipulated as well as perfect execution of pre-operative planning and surgery.

In addition to continuing to study stifle kinematics before and after various stabilizing procedures and link kinematic findings to clinical outcome, a sampling of other questions that have arisen during this project include: (1) Is Tepic’s model of force transmission more accurate than Slocum’s, and therefore is the TPLO procedure based on incorrect forces? (2) Would we obtain a more reliable outcome if we used different measurements for planning, such as
measuring the TPA in relation to the ground instead of the long axis of the tibia? (3) How accurate is the TPLO osteotomy and rotation with regards to TPA, varus/valgus angulation, and axial rotation of the plateau segment? (4) Can we design a rehabilitation plan to improve post-operative stifle stability as has been promoted in humans?
LIST OF REFERENCES


BIOGRAPHICAL SKETCH

Selena attended the University of Hawaii and Cornell University to obtain a Bachelor of Science degree in Animal Science, graduating cum laude in 2005. She attended Cornell University College of Veterinary Medicine to obtain a Doctorate of Veterinary Medicine, graduating in 2012. She completed an internship in small animal medicine and surgery at Texas A&M University in 2012-2013, then completed a combined small animal surgery residency and PhD program at the University of Florida from 2013-2018. Selena became a Diplomate of the American College of Veterinary Surgeons (small animal) in February 2018 and defended her dissertation June 2018 and graduated with her PhD in August 2018.