Growth dynamics of the canine proximal tibial physis

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Abstract

Objective- To determine growth of the proximal tibial physis in the Labrador Retriever, a breed of dog at risk for rupture of the cranial cruciate ligament (RCCL).

Animals- 6 male Labrador Retriever dogs

Methods- 0.5 mm tantalum markers were implanted in the right proximal tibial epiphysis and metaphysis of each dog at sixteen weeks of age. Lateral and cranio-caudal radiographs of the tibia were made monthly and longitudinal growth was assessed from the radiographs. A growth curve was generated from the data. Data from previous patients that had undergone proximal tibial epiphysiodesis (PTE) was compared to the growth curve to demonstrate if the growth curve accurately predicted changes in growth associated with this procedure.

Results- Growth rate decreased slowly and non-linearly over the first year of age. Growth from the proximal tibial physis is described.

Conclusions- The growth curve generated here follows the model of saltation and stasis. The growth curve generated here predicted the change in tibial plateau angle (TPA) for two Labrador Retrievers that underwent PTE (+/- 1°).

Clinical relevance- The growth curve generated in the present study may be considered for use for the surgical planning of PTE in Labrador Retrievers.

Key Words- Proximal tibial epiphysiodesis, growth, saltation and stasis, Labrador Retriever

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Introduction

Rupture of the cranial cruciate ligament (RCCL) in the dog is a common and economically important problem faced by veterinarians.[1] To date, the authors know of no diagnostic test or prophylactic intervention to decrease the incidence of this disease. While most CCL injuries occur in adult dogs, they have also been reported to occur in juvenile dogs [2,3,3-5] and often as an avulsion of the CCL insertion. [2,4]These cases present a therapeutic dilemma, as many current stabilization techniques (those involving osteotomies) may be inappropriate for the growing animal. Reattachment of the avulsed fragment has been recommended in conjunction with another stabilization technique, particularly if the ligament is stretched or the avulsed fragment comminuted.[2]

Proximal tibial epiphysiodesis has recently been described as a therapy for juvenile dogs with cranial cruciate ligament deficient stifles. [5,6]In a prospective case series of 14 juvenile dogs (aged 4.5 to 8 months) with a total of 22 affected joints, patients had a cancellous screw placed in the cranio-medial center of the proximal tibial plateau to cause proximal tibial epiphysiodesis (PTE) with an end result of decreasing the tibial plateau angle (TPA) as the dog continued to grow. The principle of PTE is that fusion of the central portion of the proximal tibial epiphysis (cranial aspect of the tibial plateau) halts growth centrally while allowing the caudal aspect of the plateau to continue to grow resulting in a decreased TPA at maturity. Greater than one year follow up was available for all cases and subjectively the gait in all dogs returned to normal. Although this technique shows some promise, it is important to note that four cases required additional surgery and the resultant TPA at the time of the dog’s maturity varied. Patient age at the time of intervention has an obvious effect on the final TPA. Serendipitous estimates could lead to unwanted results and complications such as excessive change in the TPA, which may place excess strain on the caudal cruciate ligament [7] or inadequate reduction in the TPA (TPA greater than 14°) with failure to achieve the clinical results associated with the ostensible biomechanical advantage the procedure provides.[8] Canine musculoskeletal growth and development have been investigated [9] and the three separate centers of ossification of the proximal tibial physis and their time of closure have been described (lateral condyle, medial condyle and tibial tuberosity)[10]The center of ossification of the proximal tibial epiphysis is reported to appear between three and four months of age and growth plate fusion is reported to occur between six and eleven months of age.[11] To our knowledge, however, the growth dynamics of the proximal tibial physis of the juvenile dog have not been reported. The objectives of the present study were to document the growth dynamics from the proximal tibial epiphysis in a breed of dog that is commonly affected with CCL insufficiency and to generate a growth curve of the proximal tibial physis. We hypothesized that the mean growth rate of the proximal tibial epiphysis would decrease over the first year of life. Additionally, we hypothesized that the growth curve generated in the study would allow estimation of the final TPA of a patient after PTE surgery.

Materials and Methods

The study design and protocol was approved by the University Of Minnesota Institutional Animal Care and Use Committee.

Dogs- Six male Labrador Retrievers were enrolled in the study at sixteen weeks +/- five days of their reported age. Dogs were preanesthetized with hydromorphone (0.1 mg/kg) and acepromazine (0.02 mg/kg) given intramuscularly and were induced with propofol given to effect (2-4 mg/kg intravenously). Endotracheal tubes were placed and anesthesia was maintained with isoflurane. Post-operative discomfort was addressed with a three day course of tramadol (2 mg/kg PO q 12h *PRN)* administered as needed. All dogs were part of a local hearing and service program and have subsequently resumed hearing and service training or were adopted as healthy pets.

Surgical Procedure- Dogs were positioned in right dorso-lateral recumbency. After standard aseptic preparation of the right medial stifle and pre-scrotal areas, a 3-cm approach over the cranio-medial proximal stifle using sharp and blunt dissection was made to expose the proximal tibia. With a goal of implanting a minimum of two markers above and below the proximal tibial epiphysis to account for attrition a 22-gauge needle was used to create two or three small, incomplete holes in the epiphysis and metaphysis of the proximal tibia. 0.5 mm spherical tantalum markers were implanted into each hole under direct visualization. Closure of the surgical site was performed in routine manner. Routine closed castration was performed during the same anesthetic episode following marker implantation. Medio-lateral and caudo-cranial radiographic views of each tibia were used to confirm implant placement (Figure 1).

Radiographs- Standard table top medio-lateral and caudo-cranial images of the tibia including tarsus and stifle were made every four weeks (±3 days) beginning at 16 weeks of age until the proximal tibial physis was radiographically closed and longitudinal growth of the tibia had ceased (56 weeks of age). Radiographs were similarly positioned each time by trained personnel with the center of the beam focused on the stifle. The beam was collimated to include only the stifle, tibia and hock.

Data Analysis- Analogue radiographs were evaluated and the distance between each marker was measured on both projections using a ruler. Each marker above and below the proximal tibial physis was assigned a letter (e.g. 'a', 'b' for two markers in the proximal epiphysis and 'c', 'd' for the two markers in the proximal metaphysis). Distances were measured between markers in the epiphysis and metaphysis (e.g. a-c, a-d, b-c, b-d). These measurements were performed each month and the distance between markers compared, the difference was considered to represent longitudinal growth (e.g. Month 5 a-c distance minus Month 4 a-c distance equals the growth of that dog's proximal tibia between months 4 and 5). Thus, the longitudinal growth measured here encompassed thickening of the epiphysis, thickening of the growth plate as well as longitudinal lengthening of the metaphysis and diaphysis. Measurements were always made in duplicate by the same individual (CSM). After all data collection, measurements were compared. If a difference >1mm was found between two measurements, a third measurement was taken and the two closest measurements were entered as data points. For the purposes of determining distance between tantalum markers in the epiphysis and metaphysis, only data from the medio-lateral projection was used. The caudo-cranial view was used to assess implant stability, i.e. migration. To assess for magnification in any radiograph, a plexiglass template containing metal markers a known size and distance (Biomedtrix ®, Boonton, NJ) was taped to the cranial or medial portion of the tibia of each dog for the medio-lateral and caudo-cranial radiographs, respectively. Accuracy was also assured by measurement of the distance between the markers in the metaphysis and between the markers in the epiphysis as a change in distance between those points was expected to be near zero. If migration of a marker was found at any time during the study, all measurements from that marker were excluded. Data points consisting of the distance between markers from each dog were entered into a spreadsheet. A growth curve was generated by graphing the data documenting mean growth from 4-13 months of age. Linearity was assessed based on the profile of these graphs (Figures 2,3). Once the growth curve was generated, a secondary y-axis was added to allow growth to be measured as a percent of growth from four to 13 months of life (Figure 4). Finally, data from a previous study[5] of fourteen dogs that underwent PTE (for a total of 22 joints) was evaluated. Reported values included beginning TPA, dog age at time of PTE and end TPA at follow up. This data was plotted along the mean cumulative growth curve with the secondary y-axis (Figure 4).

Results

No implant associated complications were noted. However, two markers in the epiphysis migrated in one dog and one marker in the epiphysis migrated in another dog. At the end of the study, dogs had a minimum of one marker in the proximal epiphysis and two markers in the metaphysis; all remaining dogs had at least two markers in both the epiphysis and metaphysis. All data points (including those collected before migration) from migrated markers were eliminated from analysis. For markers used in data collection, no duplicate measurement was more than one millimeter different from its initial measurement.

The maximum longitudinal growth that occurred in an individual dog was 11.4-mm, and this occurred between months 4 and 5 of age. During that same interval, another dog grew only 6.5 mm while the mean growth of all dogs was 8.15 mm (Figure 2). One dog experienced virtually no growth (< 0.5 mm) between months 10 and 11 while growing 1.2 mm the following month.

Average monthly growth rate decreased steadily as time progressed (solid thick black line, Figure 2). Average monthly growth rate was greatest between months four and five and decreased steadily and non-linearly for individual dogs until 13 months with the exception of the interval between months 11 and 12 in which average growth rate increased. Mean cumulative growth (longitudinal growth of all 6 dogs averaged) was 8.1 mm between 4 and 5 months of age and increased steadily and non-linearly until 13 months of age (Figure 3).

Finally, data from a previous study[5] of fourteen dogs of various breeds and ages that underwent PTE (for a total of 22 joints) was plotted along the mean cumulative growth curve with the secondary y-axis (Figure 4). For Labradors (a total of two dogs and two joints), the model predicted the end TPA to within +/- 1°. For non-Labradors, the model predicted end TPA within 3.6° with a range of 0° (exact) to 8° (difference between actual and predicted). Thus for non-Labradors, our reported Labrador data predicted end TPA only 45% of the time within the reported inter-observer variability of 3.4°. [12]

Discussion

The idea of studying growth of the proximal tibial physis arose from a desire to provide an opportunity to surgeons for more deliberate planning of PTE in juvenile dogs with RCCL. These data provide insight into the outcome in the Labrador Retriever dog after proximal tibial epiphysiodesis. When comparing previous data from Labrador Retrievers that underwent PTE the growth curve reasonably predicted (± 1°) the actual change in TPA. While these two cases are promising in their conformity to the curve generated, the result must be considered preliminary given the small number of dogs studied and the fact that individual growth rates can vary greatly from the mean. For example, when considering the effect of PTE in an individual dog the clinician does not know if that dog has just completed a growth spurt or will have one immediately after the surgery; these scenarios may lead to different outcomes. However, given that TPA is reported to remain unchanged from the age of four months [13], these data may be considered for use in Labrador Retrievers from that age. Even though growth, and the effect of PTE, on a month to month basis is somewhat unpredictable because growth of individual dogs follows a model of saltation and stasis, the end effect was relatively consistent in the two Labradors we studied. The data was less accurate for non-Labrador Retriever breeds. Simply, the data presented is arguably better than guessing what the effect of PTE might be.

We would suggest that the steps in calculating *the age at which* to perform PTE when presented with a clinical patient are: 1. Measure current TPA. 2. Calculate desired end TPA as a percentage of current TPA. 3. From the graph, plot from the secondary y-axis (percent) to the growth curve. Alternatively, *one may predict the end TPA* if PTE were performed at any age by plotting from the x-axis (age) to the growth curve and matching that point to the secondary y-axis (percentage), determining what end TPA will be as a percentage of the current TPA.

For example, a 16- week-old puppy is presented with a traumatic cranial cruciate ligament rupture. 1. The TPA at the time of injury is 25°. 2. Desired end TPA (5°) as a percentage of current TPA is 5/25 = 0.2 or 20%. 3. Plotting from the secondary y-axis (20%) to the growth curve, the age on the x-axis (corresponding point along the growth curve to 20% on the secondary y-axis) is mid-way between 4 and 5 months. Thus, PTE performed at 18 weeks should effect the desired change in TPA. Alternatively, a 7-month-old puppy is presented for traumatic cranial cruciate ligament injury. If PTE was performed at 7 months, one might expect the resultant TPA to be 62.5% of the original (plotting age from the x-axis to the corresponding point along the curve on the secondary y-axis). Thus a 7-month-old dog with a TPA of 25° would be expected to have a resultant TPA of >14° (25 * 0.625 = 15.625) if PTE were performed, therefore an alternative therapeutic modality should be considered.

We caution against using these findings for the employment of PTE as a prophylactic surgery for dogs without RCCL as it is unknown whether changing the TPA has any merit for prophylaxis or even if prophylaxis is epidemiologically justifiable. Additionally, it is critical this be carefully studied before PTE be considered for prophylaxis as it has been reported that in the human cadaveric knee, strain on the anterior cruciate ligament *increased* with *decreased* tibial plateau slope[14]. That is to say that while tibial osteotomy techniques have a record of clinically improving patients with known RCCL, tibial plateau angles that are not excessive have been shown not to be associated with the etiopathogenesis of RCCL[15].

It is not surprising that our hypothesis of non-linear growth with a rate that decreased over time was confirmed, as this is a widely accepted model of normal mammalian growth termed saltation and stasis. Saltation and stasis is a model derived from studies in children and proposes that growth occurs as an intermittent process of long pauses and sudden bursts.[16-18]This pattern of growth has also been documented in the canine radius[19] and ulna. [20] The model of saltation and stasis has a direct clinical bearing because even with the use of a cumulative curve to predict results of PTE, one must acknowledge the possibility of anomalous results. While one dog in this study showed a relatively constant rate of growth, wide variability is noted when comparing the growth rates among all dogs (Figure 2). It is also likely that more frequent imaging of each dog (daily or weekly) would have captured the bursts and pauses of saltation and stasis, however this was outside the scope of this study.

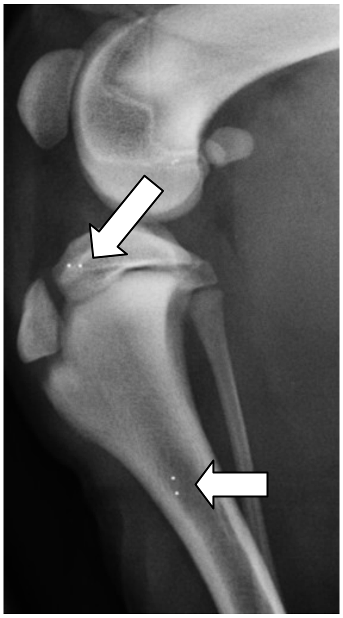
In the present study we did not separate the cranial and caudal aspects of the proximal tibial epiphysis. Thus, we cannot suggest that differential growth between the two aspects of the epiphysis contributes to the development of a normal TPA. However, from the previous report of PTE[5] and the findings reported here, it seems reasonable to suggest that a change in the rate of growth of either the cranial or caudal portion of the proximal tibial epiphysis can alter the TPA.

We may have improved the precision of the data by using simultaneous biplanar radiography as has been done in previous studies [19,20]However, it is our belief that we satisfactorily addressed the question that we sought to answer with acceptable precision. A further potential limitation is the number of dogs that was used. Power analysis was not performed to determine the ideal number of dogs to enroll. However, previous similar studies in other species [21] have used this number of subjects. One must also consider that there is variability in size within as well as among breeds and that the population of Labradors that were studied here may not represent all Labradors. Despite these limitations, it is our belief that using this curve to estimate the outcome of PTE is superior to not using it. Furthermore, assessing growth of the entire tibia may have been possible by adding markers to the distal epiphysis. Total tibial length was not reported in the previous study of proximal tibial epiphysiodesis [5], so it is unknown whether total tibial length was affected. It is ultimately unknown if PTE causes significant tibial shortening. While it would have been interesting, we elected to focus on the proximal tibia and center the primary beam of the radiograph over the region of interest so error from radiographic technique could be minimized.

Finally, a recent paper suggested a relationship between early neutering and RCCL as well as early neutering and excessive TPA[22]. We may have strengthened this work by including intact subjects to establish comparative data.

This study documented growth of the proximal tibial physis in the Labrador Retriever, a breed known to be at risk for rupture of the CCL. These data may serve as a starting point for the further study of PTE as a therapy for RCCL in the juvenile dog and could be used in the surgical planning of juvenile Labrador Retrievers with RCCL for PTE. Broadening our understanding of the growth of the proximal tibial physis in dogs is an important step in optimizing management strategies for RCCL.

Figures



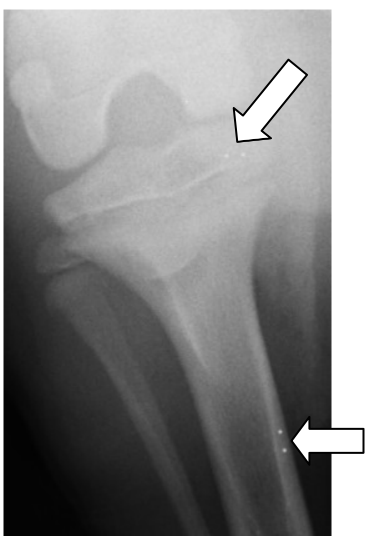


Figure 1. Lateral and cranio-caudal radiographs of the right stifle after tanatalum marker implantation. The arrows indicate the position of the 0.5 mm diameter markers.

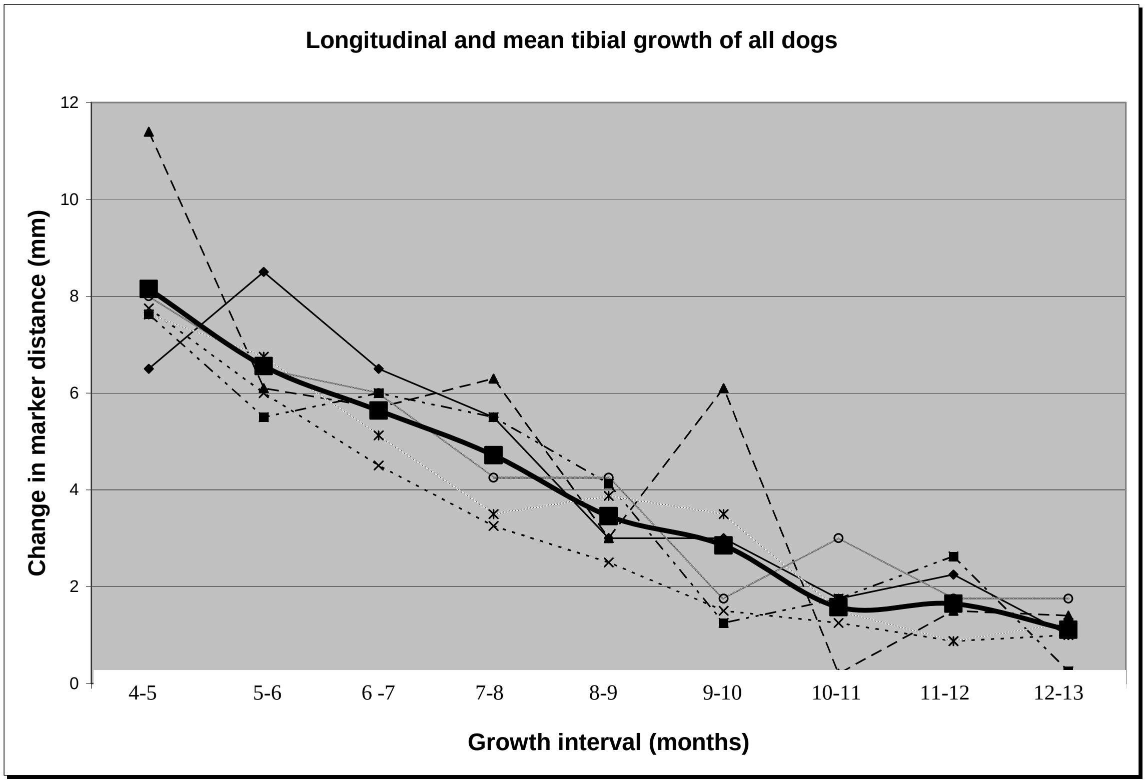


Figure 2. The longitudinal bone growth from the proximal tibial physis of all six dogs is represented as the change in marker distance (y-axis) plotted against time (x-axis). The thick solid line represents the mean change in marker distance of all six dogs (proximal tibial physeal growth rate).

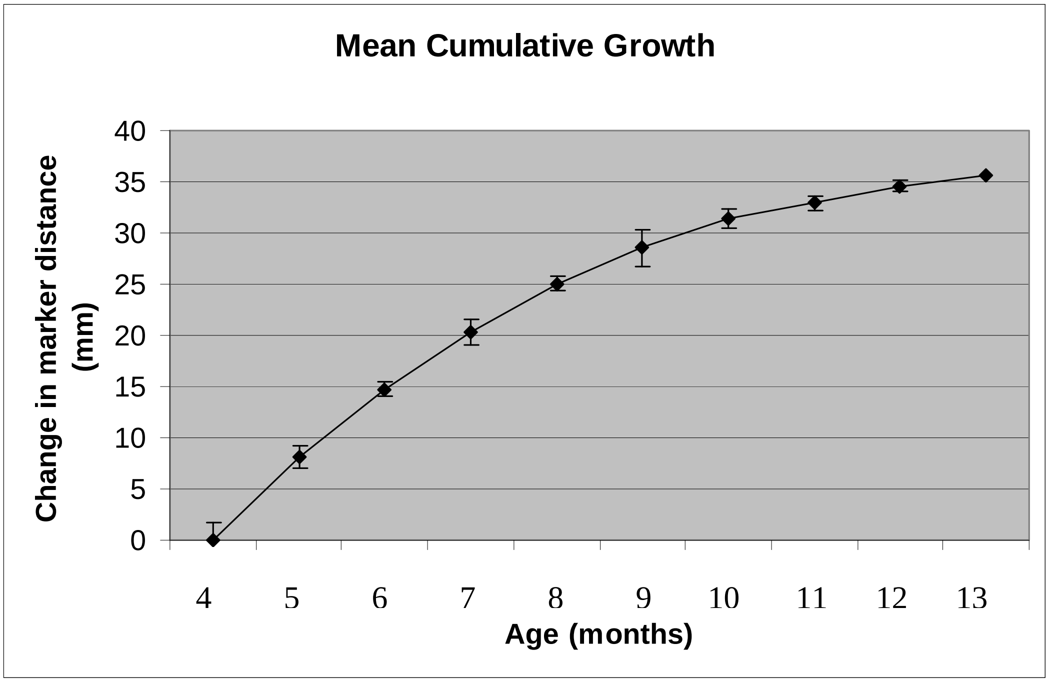


Figure 3. Mean Cumulative Growth. Longitudinal bone growth from the proximal tibial physis ("growth curve") including standard deviation.

Figure 4. A secondary y-axis indicating percentage growth is added to the growth curve. Data from a previous study [5] of 14 patients with a total of 22 treated joints that underwent PTE is plotted along the growth curve. Labrador Retrievers (two) are represented by open circles while the joints that received surgery (20) from non-Labrador dogs are represented by closed squares. Five stifles had nearly identical outcomes indicated by a 2 next to the closed square. The closer to the growth curve, the more accurately the model predicted the outcome (change in TPA). Refer to discussion for using this graph as a clinical tool.

Bibliography

1. Wilke VL, Robinson DA, Evans RB, Rothschild MF, Conzemius MG. Estimate of the annual economic impact of treatment of cranial cruciate ligament injury in dogs in the united states. J Am Vet Med Assoc. 2005 Nov 15;227(10):1604-7.

2. Fossum TW, Hedlund CS, Johnson AL, Schulz KS, Seim HB, Willard MD, Bahr A, Carroll GL, editors. Small Animal Surgery. Third ed. St. louis, MO: Mosby Elsevier; 2007 .

3. Duval JM, Budsberg SC, Flo GL, Sammarco JL. Breed, sex, and body weight as risk factors for rupture of the cranial cruciate ligament in young dogs. J Am Vet Med Assoc. 1999 Sep 15;215(6):811-4.

4. Piermattei DL, Flo GL, DeCamp CE, editors. Brinker, Piermattei and Flo's Handbook of Small Animal Orthopedics and Fracture Repair. 4th ed. St. Louis, Missouri: Saunders Elsevier; 2006.

5. Vezzoni A, Bohorquez Vanelli A, Modenato M, Dziezyc J, Devine Slocum T. Proximal tibial epiphysiodesis to reduce tibial plateau slope in young dogs with cranial cruciate ligament deficient stifle. Vet Comp Orthop Traumatol. 2008;21(4):343-8.

6. Slocum B, Slocum TD. [Internet].

7. Warzee CC, Dejardin LM, Arnoczky SP, Perry RL. Effect of tibial plateau leveling on cranial and caudal tibial thrusts in canine cranial cruciate-deficient stifles: An in vitro experimental study. Vet Surg. 2001 May-Jun;30(3):278-86.

8. Robinson DA, Mason DR, Evans R, Conzemius MG. The effect of tibial plateau angle on ground reaction forces 4-17 months after tibial plateau leveling osteotomy in labrador retrievers. Vet Surg. 2006 Apr;35(3):294-9

9. Evans HE, editor. Miller's Anatomy of the Dog. 3rd ed. Philadelphia, Pennsylvania: W.B. Saunders Company; 1993

10. Adams, DR. Canine Anatomy A Systemic Study. 4th ed. Ames, Iowa: Iowa State Press; 2004.

11. Sumner-Smith G, Fackelman GE, editors. Bone in Clinical Orthopedics. second, enhanced ed. Stuttgart, Germany and Thieme, New York: AO Publishing; 2002.

12. Caylor KB, Zumpano CA, Evans LM, Moore RW. Intra- and interobserver measurement variability of tibial plateau slope from lateral radiographs in dogs. J Am Anim Hosp Assoc. 2001 May-Jun;37(3):263-8.

13. Odders JW, Jessen CR, Lipowitz AJ. Sequential measurements of the tibial plateau angle in large-breed, growing dogs. Am J Vet Res. 2004 Apr;65(4):513-8.

14. Fening SD, Kovacic J, Kambic H, McLean S, Scott J, Miniaci A. The effects of modified posterior tibial slope on anterior cruciate ligament strain and knee kinematics: A human cadaveric study. J Knee Surg. 2008 Jul;21(3):205-11

15. Wilke VL, Conzemius MG, Besancon MF, Evans RB, Ritter M. Comparison of tibial plateau angle between clinically normal greyhounds and labrador retrievers with and without rupture of the cranial cruciate ligament. J Am Vet Med Assoc. 2002 Nov 15;221(10):1426-9.

16. Lampl M, Veldhuis JD, Johnson ML. Saltation and stasis: A model of human growth. Science. 1992 Oct 30;258(5083):801-3.

17. Lampl M, Ashizawa K, Kawabata M, Johnson ML. An example of variation and pattern in saltation and stasis growth dynamics. Ann Hum Biol. 1998 May-Jun;25(3):203-19.

18. Lampl M, Johnson ML, Frongillo EA,Jr. Mixed distribution analysis identifies saltation and stasis growth. Ann Hum Biol. 2001 Jul-Aug;28(4):403-11.

19. Conzemius MG, Smith GK, Brighton CT, Marion MJ, Gregor TP. Analysis of physeal growth in dogs, using biplanar radiography. Am J Vet Res. 1994 Jan;55(1):22-7.

20. Conzemius MG, Brown DC, Brabec M, Smith GK, Washabau R, LaFond E, Chakraborty PK. Correlation between longitudinal bone growth, growth hormone, and insulin-like growth factor-I in prepubertal dogs. Am J Vet Res. 1998 Dec;59(12):1608-12.

21. Smith BL, Auer JA, Taylor TS, Hulse DS, Longnecker MT. Use of orthopedic markers for quantitative determination of proximal radial and ulnar growth in foals. Am J Vet Res. 1991 Sep;52(9):1456-60.

22. Duerr FM, Duncan CG, Savicky RS, Park RD, Egger EL, Palmer RH. Risk factors for excessive tibial plateau angle in large-breed dogs with cranial cruciate ligament disease. J Am Vet Med Assoc. 2007 Dec 1;231(11):1688-91.

23. Abel SB, Hammer DL, Shott S. Use of the proximal portion of the tibia for measurement of the tibial plateau angle in dogs. Am J Vet Res. 2003 Sep;64(9):1117-23.

24. Bullough PG, Yawitz PS, Tafra L, Boskey AL. Topographical variations in the morphology and biochemistry of adult canine tibial plateau articular cartilage. J Orthop Res. 1985;3(1):1-16.

25. Chauvet AE, Johnson AL, Pijanowski GJ, Homco L, Smith RD. Evaluation of fibular head transposition, lateral fabellar suture, and conservative treatment of cranial cruciate ligament rupture in large dogs: A retrospective study. J Am Anim Hosp Assoc. 1996 May-Jun;32(3):247-55.

26. Conzemius MG, Evans RB, Besancon MF, Gordon WJ, Horstman CL, Hoefle WD, Nieves MA, Wagner SD. Effect of surgical technique on limb function after surgery for rupture of the cranial cruciate ligament in dogs. J Am Vet Med Assoc. 2005 Jan 15;226(2):232-6.

27. Fettig AA, Rand WM, Sato AF, Solano M, McCarthy RJ, Boudrieau RJ. Observer variability of tibial plateau slope measurement in 40 dogs with cranial cruciate ligament-deficient stifle joints. Vet Surg. 2003 Sep-Oct;32(5):471-8.

28. Jurvelin JS, Arokoski JP, Hunziker EB, Helminen HJ. Topographical variation of the elastic properties of articular cartilage in the canine knee. J Biomech. 2000 Jun;33(6):669-75.

29. Kaweblum M, Aguilar MC, Blancas E, Kaweblum J, Lehman WB, Grant AD, Strongwater AM. Histological and radiographic determination of the age of physeal closure of the distal femur, proximal tibia, and proximal fibula of the new zealand white rabbit. J Orthop Res. 1994 Sep;12(5):747-9.

30. Khoury JG, Tavares JO, McConnell S, Zeiders G, Sanders JO. Results of screw epiphysiodesis for the treatment of limb length discrepancy and angular deformity. J Pediatr Orthop. 2007 Sep;27(6):623-8.

31. Kowaleski MP, Apelt D, Mattoon JS, Litsky AS. The effect of tibial plateau leveling osteotomy position on cranial tibial subluxation: An in vitro study. Vet Surg. 2005 Jul-Aug;34(4):332-6.

32. Lazar TP, Berry CR, deHaan JJ, Peck JN, Correa M. Long-term radiographic comparison of tibial plateau leveling osteotomy versus extracapsular stabilization for cranial cruciate ligament rupture in the dog. Vet Surg. 2005 Mar-Apr;34(2):133-41.

33. Markel MD, Wikenheiser MA, Chao EY. Formation of bone in tibial defects in a canine model. histomorphometric and biomechanical studies. J Bone Joint Surg Am. 1991 Jul;73(6):914-23.

34. Morris E, Lipowitz AJ. Comparison of tibial plateau angles in dogs with and without cranial cruciate ligament injuries. J Am Vet Med Assoc. 2001 Feb 1;218(3):363-6.

35. Reif U, Dejardin LM, Probst CW, DeCamp CE, Flo GL, Johnson AL. Influence of limb positioning and measurement method on the magnitude of the tibial plateau angle. Vet Surg. 2004 Jul-Aug;33(4):368-75.

36. Reif U, Hulse DA, Hauptman JG. Effect of tibial plateau leveling on stability of the canine cranial cruciate-deficient stifle joint: An in vitro study. Vet Surg. 2002 Mar-Apr;31(2):147-54.

37. Reif U, Probst CW. Comparison of tibial plateau angles in normal and cranial cruciate deficient stifles of labrador retrievers. Vet Surg. 2003 Jul-Aug;32(4):385-9.

38. Shahar R, Milgram J. Biomechanics of tibial plateau leveling of the canine cruciate-deficient stifle joint: A theoretical model. Vet Surg. 2006 Feb;35(2):144-9.

39. Slocum B, Devine T. Cranial tibial thrust: A primary force in the canine stifle. J Am Vet Med Assoc. 1983 Aug 15;183(4):456-9.

40. Slocum B, Slocum TD. Tibial plateau leveling osteotomy for repair of cranial cruciate ligament rupture in the canine. Vet Clin North Am Small Anim Pract. 1993 Jul;23(4):777-95.

41. Swainson SW, Conzemius MG, Riedesel EA, Smith GK, Riley CB. Effect of public symphysiodesis on pelvic development in the skeletally immature greyhound. Vet Surg. 2000 Mar-Apr;29(2):178-90.

42. Whitehair JG, Vasseur PB, Willits NH. Epidemiology of cranial cruciate ligament rupture in dogs. J Am Vet Med Assoc. 1993 Oct 1;203(7):1016-9.

43. Wilke VL, Conzemius MC, Rothschild MF. SNP detection and association analyses of candidate genes for rupture of the cranial cruciate ligament in the dog. Anim Genet. 2005 Dec;36(6):519-21.

44. Wilke VL, Conzemius MG, Kinghorn BP, Macrossan PE, Cai W, Rothschild MF. Inheritance of rupture of the cranial cruciate ligament in newfoundlands. J Am Vet Med Assoc. 2006 Jan 1;228(1):61-4.

45. Zeltzman PA, Pare B, Johnson GM, Zeltzman V, Robbins MA, Gendreau CL. Relationship between age and tibial plateau angle in dogs with cranial cruciate rupture. J Am Anim Hosp Assoc. 2005 Mar-Apr;41(2):117-20.