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PhD Thesis

“New generation TTAT, comparison of preoperative planning methods in terms of reliability and effectiveness in vivo and ex vivo”

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“The strongest guard is placed at the gateway to nothing. Maybe because the condition of emptiness is too shameful to be divulged”

Francis Scott Fitzgerald

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List of abbreviations

AMA	tibial Anatomical-Mechanical axis Angle
BF	Bielecki Formula
CCWO	Closing Cranial Wedge Ostectomy
CrCL	Cranial Cruciate Ligament
CT	Common Tangent Method
CTT	Cranial Tibial Thrust
GRF	Ground Reaction Force
ICC	Interclass Correlation Coefficient
ICN	Intercondylar Notch
rCCL	rupture of Cranial Cruciate Ligament
ML	Mediolateral
MMP	Modified Maquet Procedure
MMT	Modified Maquet Technique
mTTA	modified Maquet Tibial Tuberosity Advancement
OA	Osteoarthritis
PRISMA	Preferred Reporting Items for Systematic reviews and Meta-Analyses
PT	Patellar Tendon
PTA	Patellar Tendon Angle
PTA_{CT}	Patellar Tendon Angle with Common Tangent method
PTA_{TP}	Patellar Tendon Angle using Tibial Plateau method
ROM	Range Of Motion
SD	Standard Deviation
SwiM	Synthesis without Meta-analysis
TAM	Tibial Anatomy-based Method
TP	Tibial Plateau method
TPA	Tibial Plateau Angle
TPL	Length of Tibial Plateau
TPLO	Tibial Plateau Leveling Osteotomy
TTA	Tibial Tuberosity Advancement
TTA-CF	Tibial Tuberosity Advancement - Cranial Fixation
TTAT	Tibial Tuberosity Advancement Techniques
TTW	relative Tibial Tuberosity Width

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Abstract

Rupture of the cranial cruciate ligament (rCCL) in dogs is a disease with a mainly degenerative etiopathogenesis; in contrast, in human medicine a predominantly traumatic aetiology is recorded. The cranial cruciate ligament (CrCL) primarily limits cranial translation of the tibia in relation to the femur (cranial drawer) and hyperextension. The CrCL and caudal cruciate ligaments twist themselves to limit internal rotation, but both ligaments play a minor role in limiting external rotation. Internal rotation and cranial translation of the tibia on the femur support functional changes and degenerative changes in the joint.

Several surgical techniques have been developed to restore joint stability and slow down secondary joint degeneration. Tibial tuberosity advancement (TTA) is one of the biomechanical corrective techniques of choice for the treatment of this pathology. New-generation tibial tuberosity advancement techniques (TTAT) use the same principles of traditional TTA but without a complete osteotomy of the tibial tuberosity (Aragosa et al., 2022; Pillard et al., 2016). For TTAT, the advancement is achieved through the use of spacers (cage or wedge). Determining the extent of advancement of the tibial tuberosity is a fundamental step of traditional TTA and of TTAT.

In **Chapter 2**, different surgical techniques for the treatment of canine rCCL were analysed in dogs, aiming to critically review the available literature, focusing on preoperative planning, surgical procedure, follow-up, and complications of rCCL treated by TTAT. Three bibliographic databases (PubMed, Google Scholar, and Scopus) were used for a board research and included studies were evaluated using five GRADE recommendations according to Grading of Recommendations Assessment, Development and Evaluation and Joanna Briggs Institute Critical Appraisal Checklists were applied to the studies included. Data regarding preoperative planning (a measure of advancement), meniscal disease (meniscectomy, meniscal release, and late meniscal tears), and postoperative patellar tendon angle were recorded. Time frame, outcome, and complications were classified according to Cook's guidelines. Of the 471 reports yielded, only 30 met the inclusion criteria. The common tangent method was the most commonly reported measurement technique for preoperative planning. The 40.21% of knee joints had a meniscal tear at surgery, while 4.28% suffered late meniscal tears. Short-, mid- and long-term follow-up showed full/acceptable function in > 90% of cases. For all new-generation techniques, minor complications were reported in 33.5% of cases and major complications in 10.67%. Compared with traditional TTA, new-generation TTAT was found to be effective in the treatment of cranial cruciate ligament failure, showing a lower rate of late meniscal injury but a higher rate of minor complications. The goal of preoperative planning is to determine the amount of advancement required to achieve a postoperative patellar tendon angle (PTA) of 90° and to select the optimal wedge size to achieve this target. In **Chapter 3**, radiographic methods for determining the advancement distance for the tibial tuberosity were investigated in terms of comparison and interobserver reliability. Among the methods developed, we decided to include the common tangent method (CT) (Dennler et al., 2006), the tibial anatomy-based method (TAM) (Ness, 2016), and the Bielecki method (BF) (Bielecki et al., 2014). As transparent overlays, conventional and correction methods have been extensively investigated and their poor reliability has already been confirmed (Cadmus et al., 2014; Etchepareborde, Mills, et al., 2011; Pillard et al., 2016), we did not analyse these methods further. For all techniques, radiographs were taken in mediolateral projection with the knee joint flexed at 135°. Three observers with different degree of experience independently evaluated and scored the degree of OA for each stifle, as previously described (Mager, 2000; Matis, 2005; Wessely et al., 2017) and performed measurements of the amount of advancement of the tibial tuberosity using CT, TAM, and BF on 33 stifles. According to the results, the overall score for OA in mediolateral view was influenced by the experience of the observers, which does not confirm a previous study (Wessely et al., 2017). However, osteophytosis does not seem to affect the identification of anatomical landmarks, as shown by several studies (Millet et al., 2013; Reif et al., 2004; Ritter et al., 2007). Regarding the measurement methods used to assess advancement, poor interobserver reliability was found for CT and BF, while only a slight moderate interobserver agreement was found for TAM. This is inconsistent with data collected by Bielecki and colleagues (Bielecki et al., 2014). Moreover, measurements from CT and TAM were overlapping, as previously confirmed (Butterworth & Kydd, 2017; Samoy et al., 2015). Conversely, BF showed no agreement with the other methods included in the present study, with a significantly higher mean rank, probably due to its correction formula (Bielecki et al., 2014). According to the results of this chapter, TAM had better interobserver reliability and was easier to perform according to the observers.

In **Chapter 4**, the efficacy of CT and TAM to calculate the amount of advancement to achieve the target PTA of 90° after MMP was examined. Twenty knee joints of adult medium-sized breeds, dead for reasons unrelated to this study, were randomly assigned to the two measurement procedures

(CT and TAM), respectively. Radiographs in mediolateral projection were used to measure the amount of advancement of the tibial tuberosity, and the size of the wedge was accordingly selected. For all stifles MMP was performed by a board-certified surgeon, and a custom-made wedge corresponding to the one commercially available was inserted into the osteotomy. A postoperative radiographic mediolateral view allowed measurement of postoperative PTA and evaluation of wedge position. This is the first report of the validity of CT for selecting the correct wedge to achieve the desired advancement, while previous evidences exist on TAM (Kapler et al., 2015). Most measurement methods have been developed and tested for traditional TTA (Dennler et al., 2006; Etchepareborde, Brunel, et al., 2011; Montavon et al., 2002), which is characterised by a different direction of advancement than TTAT. The values of advancement obtained with TAM and CT were not significantly different, confirming the results obtained in Chapter 3. The 60% of measurements obtained with CT were often lower than 5.3 mm, so we had to increase the wedge size significantly to reach the commercially available one. For this reason, a statistical difference was found between the measurements made with CT and the selected wedges. On the contrary, the selection of wedges with TAM proved to be easier. The postoperative PTA did not differ between groups, but only TAM provided the measure of the advancement of the tibial tuberosity closest to the real one to obtain a resultant mean PTA of 90°. On the other hand, 80% of the knee joints in both groups had a postoperative PTA of 90° ± 5, which is currently considered to stabilize the stifle joint. The position of the wedge in relation to the osteotomy did not differ between the studied groups, but a mean distance of 12 mm was observed between the line passing through the insertion of the distal patellar tendon (PT) and the proximal edge of the wedge. This could affect the true advancement achieved by MMP (Butterworth & Kydd, 2017) and lead to under-advancement, which has been frequently reported for TTA (Jin et al., 2019; Kapler et al., 2015; Meeson et al., 2018). In our opinion, TAM is easier to apply because it provides advancement values that are generally consistent with commercially available wedges and provides the correct measurement to achieve a postoperative PTA of 90°.

On the other hand, the measurement of the required advancement distance for the tibial tuberosity can be influenced by several factors, both preoperatively and intraoperatively: method of PTA measurement, tibial plateau angle (TPA), method of advancement measurement, limb positioning, anatomical factors, concomitant pathological conditions or spacer position (Etchepareborde, Mills, et al., 2011; Meeson et al., 2018; Millet et al., 2013; Pillard et al., 2016). This has been confirmed by several studies on discrepancies between measured values on radiographs and values obtained in vivo (Millet et al., 2013; Pillard et al., 2016; Skinner et al., 2013). For this reason, we have described in **Chapter 5** our current efforts to find an intraoperative method to measure the desired advancement until a PTA of 90° is achieved.

Aragosa, F., Caterino, C., Della Valle, G., & Fatone, G. (2022). Tibial Tuberosity Advancement Techniques (TTAT): A Systematic Review. *Animals*, *12*(16), 2114. https://doi.org/10.3390/ani12162114

Bielecki, M. J., Schwandt, C. S., & Scharvogel, S. (2014). Effect of tibial subluxation on the measurements for tibial tuberosity advancement in dogs with cranial cruciate ligament deficiency: An ex vivo study. *Veterinary and Comparative Orthopaedics and Traumatology*, *27*(6), 470–477. https://doi.org/10.3415/VCOT-14-02-0018

Butterworth, S. J., & Kydd, D. M. (2017). TTA-Rapid in the treatment of the canine cruciate deficient stifle: short-and medium-term outcome. *Journal of Small Animal Practice*, *58*(1), 35–41.

Cadmus, J., Palmer, R. H., & Duncan, C. (2014). The Effect of Preoperative Planning Method on Recommended Tibial Tuberosity Advancement Cage Size. *Veterinary Surgery*, *43*(8), 995–1000. https://doi.org/10.1111/j.1532-950X.2014.12126.x

Dennler, R., Kipfer, N. M., Tepic, S., Hassig, M., & Montavon, P. M. (2006). Inclination of the patellar ligament in relation to flexion angle in stifle joints of dogs without degenerative joint disease. *American Journal of Veterinary Research*, *67*(11), 1849–1854. https://doi.org/10.2460/ajvr.67.11.1849

Etchepareborde, S., Brunel, L., Bollen, G., & Balligand, M. (2011). Preliminary experience of a modified maquet technique for repair of cranial cruciate ligament rupture in dogs. *Veterinary and Comparative Orthopaedics and Traumatology*, *24*(3), 223–227. https://doi.org/10.3415/VCOT-10-01-0012

Etchepareborde, S., Mills, J., Busoni, V., Brunel, L., & Balligand, M. (2011). Theoretical discrepancy between cage size and efficient tibial tuberosity advancement in dogs treated for cranial cruciate ligament rupture. *Veterinary and Comparative Orthopaedics and Traumatology*, *24*(01), 27–31. https://doi.org/10.3415/VCOT-10-01-0013

Jin, D. W., Peck, J. N., Tano, C. A., & Morgan, M. J. (2019). Discrepancy between true distance of tibial tuberosity advancement and cage size: An ex vivo study. *Veterinary Surgery*, *48*(2), 186–191. https://doi.org/10.1111/vsu.13135

Kapler, M. W., Marcellin-Little, D. J., & Roe, S. C. (2015). Planned wedge size compared to achieved advancement in dogs undergoing the modified Maquet procedure. *Veterinary and Comparative Orthopaedics and Traumatology*, *28*(6), 379–384. https://doi.org/10.3415/VCOT-15-02-0026

Mager, F. W. (2000). *Zur Kniegelenkkarthrose des Hundes nach vorderer Kreuzbandruptur: ein retrospektiver Vergleich dreier Operationsmethoden*. Uitgever niet vastgesteld.

Matis, U. (2005). Radiographic evaluation of the progression of osteoarthritis after tibial plateau leveling osteotomy in 93 dogs. *Vet Comp Orthop Traumatol*, *2*, A32.

Meeson, R. L., Corah, L., Conroy, M. C., & Calvo, I. (2018). Relationship between Tibial conformation, cage size and advancement achieved in TTA procedure. *BMC Veterinary Research*, *14*(1), 1–7. https://doi.org/10.1186/s12917-018-1433-0

Millet, M., Bismuth, C., Labrunie, A., Marin, B., Filleur, A., Pillard, P., Sonet, J., Cachon, T., & Etchepareborde, S. (2013). Measurement of the patellar tendon-tibial plateau angle and tuberosity advancement in dogs with cranial cruciate ligament rupture. *Vet Comp Orthop Traumatol*, *26*(06), 469–478.

Montavon, P. M., Damur, D. M., & Tepic, S. (2002). Advancement of the tibial tuberosity for the treatment of the cranial cruciate ligament deficient stifle. *Proceedings of the 1st World Orthopaedic Veterinary Congress*, 152.

Ness, M. G. (2016). The Modified Maquet Procedure (MMP) in Dogs: Technical Development and Initial Clinical Experience. *Journal of the American Animal Hospital Association*, *52*(4), 242–250. https://doi.org/10.5326/JAAHA-MS-6304

Pillard, P., Livet, V., Cabon, Q., Bismuth, C., Sonet, J., Remy, D., Fau, D., Carozzo, C., Viguier, E., & Cachon, T. (2016). Comparison of desired radiographic advancement distance and true advancement distance required for patellar tendon–tibial plateau angle reduction to the ideal 90° in dogs by use of the modified Maquet technique. *American Journal of Veterinary Research*, *77*(12), 1401–1410.

Samoy, Y., Verhoeven, G., Bosmans, T., Van der Vekens, E., de Bakker, E., Verleyen, P., & Van Ryssen, B. (2015). TTA rapid: description of the technique and short term clinical trial results of the first 50 cases. *Veterinary Surgery*, *44*(4), 474–484.

Skinner, O. T., Kim, S. E., Lewis, D. D., & Pozzi, A. (2013). In vivo femorotibial subluxation during weight-bearing and clinical outcome following tibial tuberosity advancement for cranial cruciate ligament insufficiency in dogs. *The Veterinary Journal*, *196*(1), 86–91.

Wessely, M., Brühschwein, A., & Schnabl-Feichter, E. (2017). Evaluation of intra-and inter-observer measurement variability of a radiographic stifle osteoarthritis scoring system in dogs. *Veterinary and Comparative Orthopaedics and Traumatology*, *30*(06), 377–384.

Chapter 1

Cranial cruciate ligament rupture and biomechanical implications

Biomechanic of stifle joint and etiopathogenesis of cranial cruciate ligament deficiency

In dogs, the femoral-tibio-patellar joint plays a key role in the pelvic limb due to its strategic position between the hip and the hock. In stance, thanks to the menisci between the femoral and tibial condyles, the stifle joint absorbs and supports the body weight, while in motion it allows the transmission of the propulsive force to the hip joint and the shortening of the functional length of the pelvic limb (Spinella et al., 2021).

1.1 Anatomy of cruciate ligaments

The cruciate ligaments are located within the stifle joint, centrally in the intercondylar fossa of the tibia, and limit caudal sliding movement in respect to the femur. The cranial cruciate ligament (lig. cruciatum craniale) runs from the caudomedial aspect of the lateral femoral condyle diagonally to the cranial intercondylar region of the tibia. It is grossly divided into a larger caudolateral bundle and a smaller craniomedial band. The craniomedial fibers run outward along the course of the ligament from proximal to distal at an angle of approximately 90° (Arnoczky & Marshall, 1977). The site of attachment of the anterior cruciate ligament to the femur has an arrowhead shaped morphology. In contrast, at the tibial attachment site, the craniomedial bundle is widely attached to the cranial intercondyloid region and the caudolateral one is attached immediately caudal, with no marked change in morphology during flexion and extension. In addition, the area of the craniomedial band on the femoral and tibial attachment sites was larger than that of the caudolateral bundle (Tanegashima et al., 2019).

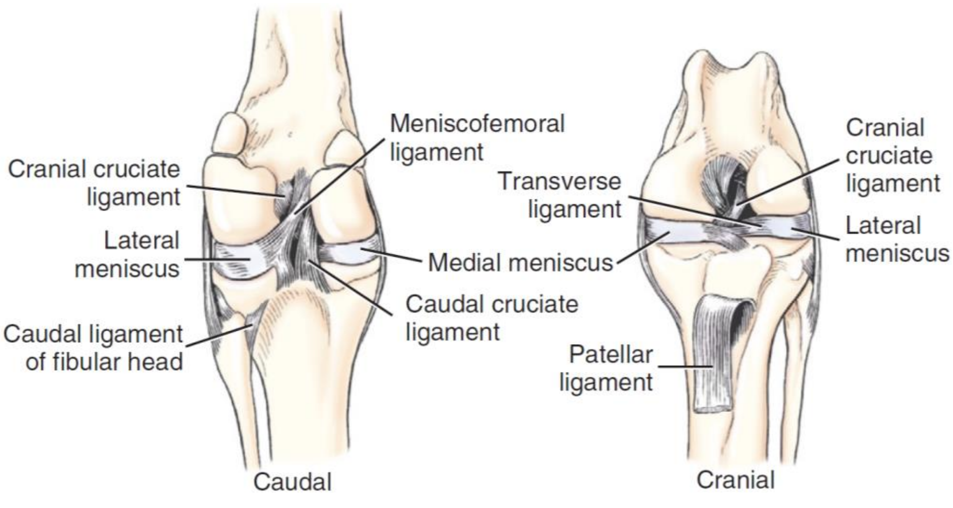

Figure 1.1 Ligaments of the stifle joint (modificated from Miller's Anatomy of the Dog, Hermanson and DeLahunta, 2020).

The caudal cruciate ligament (lig. cruciatum caudale) runs from the lateral surface of the medial femoral condyle caudodistally to the lateral edge of the popliteal notch of the tibia, medial to the caudal meniscotibial ligament of the lateral meniscus (Arnoczky & Marshall, 1977; De Rooster et al.,

2006). The caudal cruciate ligament is slightly thicker and longer than the cranial one. In addition, cruciate ligaments decussate, or cross each other at their proximal ends in the intercondylar fossa. Being intraarticular, they are covered by synovial membrane (extrasynovial) that forms an incomplete sagittal septum in the joint, allowing right and left parts to communicate (Hermanson & DeLahunta, 2020).
The vascularization of stifle joint mainly derives from branches of the middle genicular artery, which arises from the popliteal artery; it penetrates the caudal joint capsule, and passes craniodistally to the fossa intercondylaris, running cranially between the cruciate ligaments (Arnoczky & Marshall, 1977). The blood supply to both cruciate ligaments is principally of soft tissue origin and arising from infrapatellar fat pad and synovial membrane (Arnoczky, 1985; Kobayashi et al., 2006). Moreover, the existence of a blood-cruciate ligament barrier, analogous to the blood-brain barrier, is an interesting finding which could explain the mechanism that leads to incremental fiber rupture within the ligament matrix of both cruciate ligaments over time (Kobayashi et al., 2006).
Innervation of periarticular tissues of the canine stifle joint arises from branches of saphenous nerve, tibial nerve, and common peroneal nerve (O’Connor & Woodbury, 1982). The medial articular nerve, branch of the saphenous nerve, provides the major contribution to stifle joint innervation, whereas the caudal articular nerve, which derives from tibial nerve, is variably present in dogs. Finally, the lateral articular nerve arising from the common peroneal nerve, supplies the lateral aspect of the stifle joint (O’Connor & Woodbury, 1982). Nerves of differing sizes are located in the vascularized synovial tissue envelops the cruciate ligaments (Arcand et al., 2000). Yahia et al. (1992) found that canine cruciate ligaments are supplied by abundant mechanoreceptive and proprioreceptive receptors, so-called Ruffini and Pacini receptors, located within the center of the ligaments (Yahia et al., 1992).

1.2 Biomechanic of stifle joint

The stifle joint is a complex, diartrodial, synovial joint. The motion of stifle joint consists in six free degrees of motion around three planes: sagittal (flexion/extension and cranio-caudal translation), transverse (extra/intra-tibial rotation, and mid-lateral translation) and frontal (adduction/abduction and ventro-dorsal translation) (Torres, 2020). The normal range of motion (ROM) is approximately 40° in full flexion and 160° in full extension (Johnston & Tobias, 2017; Muir, 2018).

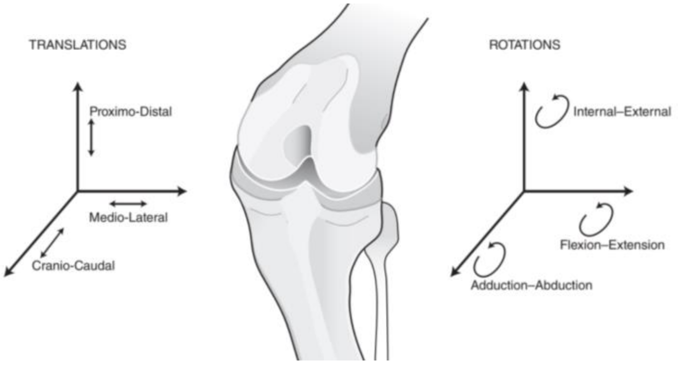

Figure 1.2 Representation of the six degrees-of-freedom of the femoro-tibial articulation (modified from Advances in the canine cranial cruciate ligament, Muir, 2018).

According to the traditional “static” biomechanical model of the femoral-tibio-patellar joint, the intrarticular and periarticular structures are responsible for stifle stability, and the only movement allowed is flexion-extension on the sagittal plane (Vezzoni et al., 2003). In the “active model”, on the other hand, the stability of knee joint is maintained by a synergism between the action of the intrarticular and periarticular structures and the forces directing on the knee: the ground reaction force (GRF) and muscle contraction. Loading of the joint results in increased stretching of the CrCL, causing simultaneous contraction of the caudal thigh muscles and relaxation of the quadriceps femoris muscle. During weight bearing, these forces result in a cranially directed shear force called the cranial tibial thrust (CTT) due to the caudal-distal inclination of the articular surface (tibial plateau) (Slocum & Devine, 1983). The CTT is progressively greater with the increase of the tibial plateau inclination, and it is passively neutralized by the CrCL (Houlton et al., 2006; Vezzoni et al., 2003).

Anatomic function of the collateral and cruciate ligaments was also investigated by Vasseur and Arnoczky (1981), measuring tension in flexion and extension. They found that the collateral and cruciate ligaments work together to limit internal rotation of the tibia on the femur. They concluded that during extension the medial and lateral collateral ligaments limit internal and external rotation of the tibia, while, during flexion the lateral collateral ligament is less taut and the cruciates are the primary restraint against internal rotation of the tibia. The laxity of the lateral collateral ligament allows the lateral femoral condyle to displace caudally on the lateral tibial condyle, allowing internal rotation of the tibia. Conversely, the lateral collateral ligament tightens during extension, allowing the lateral femoral condyle to shift cranially, resulting in external rotation of the tibia relative to the femur. Therefore, lateral rotation is mainly limited by the collateral ligaments in both flexion and extension (Vasseur & Arnoczky, 1981). In addition, during flexion-extension movement, a small amount of craniocaudal translation of the tibia with respect to the femur takes place in the sagittal plane, due to the shape of the femoral condyles (Vasseur & Arnoczky, 1981).
The major component of passive stabilization of the stifle joint is the CrCL, along with the caudal cruciate ligament, collateral ligaments, joint capsule and complex reflex arches of the hindlimb muscles. Conversely, the muscle forces provide active stabilization. Nevertheless, the CrCL provides most of the anteroposterior stabilization of the stifle (Rafael et al., 2021). This structure primary limits the cranial tibial translation in relation to the femur (cranial drawer), the hyperextension and tibial intrarotation on its axis. The CrCL and the caudal cruciate ligament twist on themselves to limit internal rotation, but both ligaments have a slight role in restrain external rotation (Muir, 2018).
As already emphasised, the cranial cruciate ligament is functionally composed of the craniomedial and caudolateral bands. The first is tense in both flexion and extension, with a primary check against cranial drawer, while the caudolateral band is taut in extension and lax in flexion, with a secondary role against cranial tibial subluxation (Johnston & Tobias, 2017). A previous relevant study demonstrated that the craniomedial and the caudolteral bundles twist and cross each other upon flexion of the stifle joint in dogs (Arnoczky & Marshall, 1977). Recent evidences suggest that each divided fibre bundle within the craniomedial and caudolateral bands is intricately twisted and the tension of each divided fibre bundle within the two bands is significantly different depending on the stifle joint angle (Ho-

Eckart et al., 2017; Tanegashima et al., 2019). Nevertheless, it is generally assumed that with the knee extended both bundles are tense, and when flexed, only the craniomedial one is tense (Arnoczky & Marshall, 1977; Comerford et al., 2005; Tanegashima et al., 2019). In addition, comparing bands tension in all joint angles, the craniomedial bundle tension tends to be always higher than caudolateral one. This suggests that the craniomedial band greatly contributes to the maintenance of tension in the CrCL in dogs (Tanegashima et al., 2019).

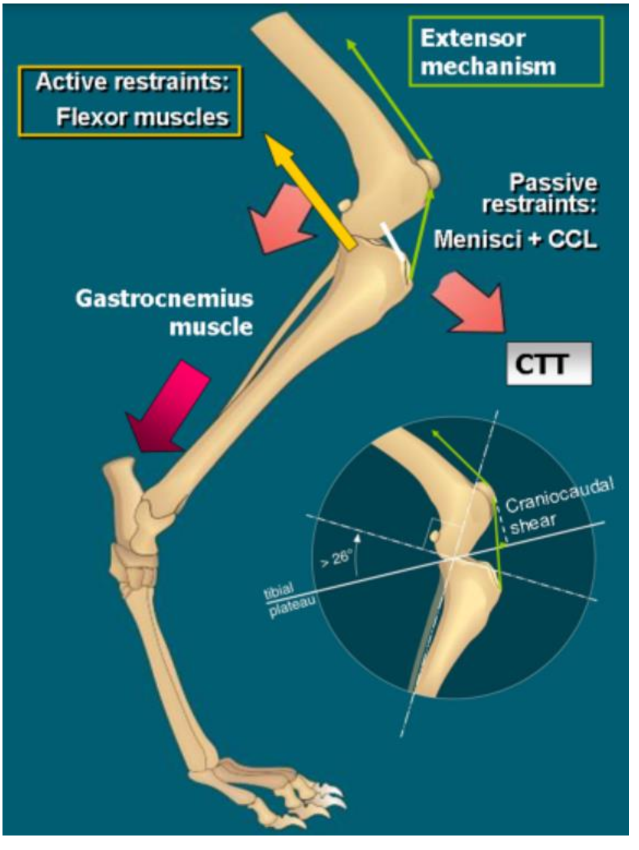

Figure 1.3 Schematic representation of forces acting on the stifle joint (modified from A Review of the Pathogenesis of Canine Cranial Cruciate Ligament Disease as a Basis for Future Preventive Strategies, Griffon, 2010).

According to the biomechanical model of Tepic (2002), the direction and entity of the CTT and consequently the greater or lesser load on the cruciate ligament change according to the angle between the patellar ligament and

the tibial plateau. The cranial tibial thrust is neutralized when this angle is equal to 90° (Tepic et al., 2002). Excessive stress on the cruciate ligament can result in further weakening and partial o total rupture. This theory explains predisposition of breeds with hyperextended pelvic limbs, such as the Boxer and Chow Chow, and with increased inclination of the tibial plateau, to cranial cruciate ligament rupture (Zink & Carr, 2018).
Supporting this theory, Dennler and colleagues (2006) measured the angles between the patellar ligament and the common tangent at the tibiofemoral contact point throughout the full ROM of the stifle joint of 16 hind limbs of dog cadavers without detectable degenerative joint disease. They observed that at approximately 90° of flexion, the shear force in the sagittal plane exerted on the proximal portion of the tibia shifts the loading from the CrCL to the caudal cruciate ligament (Dennler et al., 2006; Kim et al., 2009; Kipfer et al., 2008).
Clinically, the excessive cranial movement of the tibia in respect to the femur with the joint extended is positive evidence of a rupture of the CrCL. Rupture can be the result of trauma or excessive forces acting on the normal joint or normal forces applied to a joint ligament degeneration. Generally, the movements most likely to cause a tear of the CrCL are hyperextension or excessive medial rotation with the stifle in flexion. The failure strength reported for ex-vivo CrCL in Labrador Retrievers is 864 ± 145 N, associated with a linear stiffness of 208 ± 32 N/mm (Rafael et al., 2021).

1.2.1 Biomechanic of CrCL-deficient stifle joint

The dynamic nature of instability in the cranial cruciate ligament-deficient stifle joint was first clinically described in dogs by Henderson in 1978, along with tibial compression test. This cranially directed force was generated during weight bearing by tibial compression, of which the tarsal tendon of the biceps femoris is a major contributor, and by the slope of the tibial plateau (Henderson, 1978).
It has been demonstrated that the cranial cruciate ligament-deficient stifle joint appears more flexed throughout the gait cycle, due to joint effusion, instability and pain (Tinga et al., 2018). The decrease in the stifle extension mobilizes the hamstrings, preventing cranial traslation of the tibia. Additionally, it may also reduce the magnitude of cranial tibial subluxation, as the angle formed between the patellar tendon (PT) and the femorotibial joint line decreases.
As a compensatory effect, hip and tarsal joints respond to this increased flexion during stance phase by remaining more extended than in the normal

gait cycle. Higher stifle flexion may be associated with disruption of the balance of muscular activity of the quadriceps, gastrocnemius, or hamstrings. Persistent CrCL insufficiency may also be associated with meniscal degeneration and changes to the osseous anatomy of the joint (Tashman et al., 2004; Tinga et al., 2018).

The femorotibial kinematic changes include craniocaudal translational and axial rotational instability that is most pronounced during the stance phase of gait and therefore coinciding with maximal cranial tibial subluxation. If cranial tibial subluxation persists during the swing phase (despite this being a “CrCL-independent phase”), this is due to failure of secondary restraints such as the menisci, resulting from chronic, cyclic cranial tibial subluxation and reduction. The mid-stance phase timing of maximal cranial tibial subluxation may be due to the activity of the quadriceps, that exert a cranial force on the tibia, and gastrocnemius, which create a caudal force on the femur, promoting CTT (Spinella et al., 2021). Korvick et al. (1994) demonstrated that quadriceps muscle activation, along with body weight and inclination of the tibial plateau, promotes shear force pushing the tibia in the caudal direction during the stance phase; conversely, cranial tibial thrust is also lost during the swing phase due to low quadriceps activity and to gravitational forces (Korvick et al., 1994).

Without the containment of the cruciate ligament, the collateral ligaments become the primary restraint against cranial tibial subluxation and because the lateral collateral ligament is not as taut as medial one 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. The functional differences between the medial and lateral collateral ligaments and the medial and lateral menisci likely contribute to the tibial internal rotation that occurs when the tibia shifts cranially during stance in the absence of CrCL (Tinga et al., 2018). Surprisingly, a previous publication showed that rupture of the CrCL does not cause significant changes in external rotation of the knee, but rather reduced internal rotation (Tashman et al., 2004). This result is impressive considering that the primary function of the CrCL is to prevent excessive internal tibial rotation. However, we must consider the effects of bone geometry, muscle forces, and soft tissue constraints on rotational movements of the stifle joint in dogs (Tashman et al., 2004).

Ligament loads across stance phase were also evaluated for ligament insertion location, Tibial Plateau Angle (TPA) and femoral condyle diameter, in the intact and CrCL-deficient stifle joints (Brown et al., 2014). As displayed by results, while in intact stifle joint the cranial displacement of ligament insertion site has no effect on ligament load, in CrCL-deficient stifle ligament load is reduced and relative tibial traslation is neutralized. For this reason, the insertion site of patellar ligament is a crucial factor of stifle joint biomechanics in a CrCL-deficient stifle joint, and mainly used as a biomechanical rationale for stifle joint stabilization techniques, like tibial tuberosity advancement techniques (TTAT) and triple tibial osteotomy (Brown et al., 2014). However, outcome seems to be more sensitive to TPA and femoral condyle diameter. Tibial plateau angle, defined as the angle in the sagittal plane between the tibial plateau and a line perpendicular to the tibial functional axis, may range from 13° to 34° in dogs, with 23° to 25° being the most commonly reported (Morris & Lipowitz, 2001; Muir, 2018). However, a TPA > of 22° is more commonly associated with CrCL deficiency (Morris & Lipowitz, 2001). In both intact and CrCL-deficient stifle joints, increased TPA resulted in increased ligament loads.

In addition to the kinematic alterations previously described, kinetic analysis allows the detection of an evident decrease in the vertical peak forces and impulses during the support and propulsion phase, testifying to the patient's reluctance to load weight on the injured limb, with a frequent mild lameness during clinical examination (Evans et al., 2005; Korvick et al., 1994; Spinella et al., 2021). Stifle instability resulting from rCCL is an important pathophysiological mechanism leading to the development of progressive osteoarthritis (OA) and stifle joint deterioration (Cook, 2010; Griffon, 2010; Kim et al., 2008). Joint instability also produces an unphysiologic glinding and shearing motion, which can sequeeze the menisci between the femoral and the tibial condyles, causing degeneration (Bojrab & Monnet, 2010).

1.3 Etiopathology of cranial cruciate ligament deficiency

Deficiency of the CrCL is the leading orthopedic condition diagnosed in canine stifle joints, with a prevalence of 2.55% across all breeds (Bertocci et al., 2017). Prevalence values of 0.56% to 2.6% have been reported for CrCL disease (Taylor-Brown et al., 2015) and surprisingly, even a value of about 11% for North American hospitals between 1994 and 2003 (Witsberger et al., 2008).

Deficiency of the CrCL mainly results from a degenerative process rather than from trauma, but the pathogenesis remains unclear and has multifactorial origin. Specifically, in approximately 80% of cases of rCCL, a degenerative process occurs which leads to weakening of the ligament by deterioration of the extracellular matrix and by increased apoptotic activity, while in the remaining 20%, it results from sudden significant stress exerted on the CrCL (Rafael et al., 2021). Degenerative changes cause mechanical weakness, leading to rCCL under normal loading conditions without supraphysiological trauma. Otherwise, traumatic rCCL may occur during rotation of the stifle with the joint in 20° to 50° of flexion with excessive internal rotation of the tibia; in this position the CrCL becomes tight and more susceptible to trauma from lateral femoral condyle, as it rotates against ligament. Another mechanism of injury occurs when the animal steps into a hole while running, because when the stifle is hyperextended the CrCL is more prone to lesion. However, every direct trauma to the joint may cause damage to cruciate ligaments as well as to the other joint structures (Arnoczky & Marshall, 1977; Vasseur et al., 1985).

Risk factors for CrCL deficiency may include excessive body weight and stifle joint conformation. As body weight increases, CrCL loading increases, which leads to ligament weakness and failure. Tensile strength of the CrCL decreases with age, particularly in dogs weighing more than 15 kg, consistent with the observation cruciate disease tends to occur at a younger age in large breed dogs (Kuroki et al., 2019; Vasseur et al., 1985). In these dogs, degenerative changes are detectable microscopically as early as 5 years of age (Vasseur et al., 1985), whereas dogs weighing less than 15 kg generally show less severe changes and the onset of the degenerative process is delayed by several years (Muir, 2018).

Mechanical weakening of the CrCL in elderly dogs is associated with histologic changes of degeneration, including loss of ligament fibroblasts, chondroid metaplasia of ligamentocytes, mucoid to cartilaginous changes of the extracellular matrix, and disruption of the collagen fiber bundle arrangement (Schulze-Tanzil, 2019). As in humans, canine CrCL undergoes partial fibrocartilagenous transformation, which may represent chronic and irreversible degeneration. As rCCL progresses, more severe changes occur, such as hyalinization, mineralization, and cloning of chondrocyte-like cells. However, inflammatory or reparative responses are rarely observed. In terms of cellularity, there is a significant loss of fibroblasts in the core area in rCCL, whereas cell density is similar in rCCL and intact CrCL in the epiligamentous area (Hayashi et al., 2003).

The relationship between synovitis, spontaneous CrCL disease and OA is unclear, but evidence suggests that stifle joint degeneration is exacerbated by the presence of these conditions. Hyperplastic changes and lymphoplasmacytic inflammation are commonly observed in the synovium of knee joints with rCCL that undergo surgery and even in contralateral knee joints with intact CrCL that later develop rCCL (Kuroki et al., 2019).

A recent publication has shown that the decrease in vascularity in the CrCL core region leading to hypoxia could be a potential factor for spontaneous degeneration of the CrCL in dogs, whereas synovitis seems to play a minor role (Kuroki et al., 2019). Conversely, Hayashi and colleagues (2011) previously reported an increase in vascular density in the core region of canine rCCL (Hayashi et al., 2011), but this event may be attributed to a reparative response during progression of the disease over time. Nevertheless, the role of core region vascularity in degeneration and rCCL is not clear. However, the available literature indicates that the central region of the CrCL is most commonly affected by degeneration, with substantial loss of fibroblasts and chondroid metaplasia of surviving fibroblasts, and that the deep core region deteriorates earlier than the superficial epiligamentous region (Muir, 2018). In addition, it has been suggested that biomechanical stress produced by twisting of the two bands of the CrCL reduces blood flow to the central region, where most ruptures occur (Vasseur et al., 1985).

The predisposition of some breeds to rCCL suggests that genetic factors play a role in the pathogenesis of rCCL. Probably genetic risk factors in combination with environmental factors, such as body condition score or neuter status, influence the expression of the rCCL trait. Recent research suggests a polygenic nature of the trait and confirms moderate heritability (Lemburg et al., 2004). Analysis of global gene expression in the cranial cruciate ligaments of a high-risk breed has been compared with those of a low-risk breed, and differences have been found (Clements et al., 2008). In addition, the detection of bacterial DNA in the joints of dogs with rCCL suggests that an antigenic response to bacteria may be involved in the pathogenesis of the disease (Muir et al., 2007).

Based on evidence from the human medical literature on the role of relaxin in joint laxity and ligament tears in the knee and metacarpophalangeal joints (Galey et al., 2003), our team sought to determine relaxin and relaxin receptor expression in knees with and without rCCL. We found strong and significantly increased expression of relaxin and its receptors in ruptured cruciate ligaments and in synovial membranes (Restucci et al., 2022). Considering the property of relaxin to remodel connective tissue by collagenolysis, our results make relaxin a candidate for pathogenetic involvement and progressive ligament fiber disruption.

Canine CrCL deficiency has been associated with several conformational characteristics of the stifle, including greater TPA (Su et al., 2015), increased patellar tendon angle (PTA) (Schwandt et al., 2006), an underdeveloped tibial tuberosity and a narrow intercondylar notch (ICN). As reported by Schwandt and colleagues, comparing a group of healthy dogs and 50 partially torn cranial ligament animals, PTA in dogs with partial rupture is 5° larger and the joint flexion is 10° greater to reach the crossover point defined in healthy dogs (Schwandt et al., 2006).

Genum varum associated with femoral varus and internal rotation of the tibia has been associated with other conditions such as medial patellar luxation. The malalignment of the extensor mechanism and internal rotation of the proximal tibia place constant pressure on the CrCL, leading to degeneration and increasing the risk of rCCL (Gibbons et al., 2006).

A retrospective study conducted on 219 knee joints found that the width of the tibial tuberosity was significantly less in stifle joints with CrCL disease compared with healthy knee joints, suggesting that the shape of the tibial tuberosity in younger dogs promotes more rapid deterioration and rupture of the CrCL. The authors hypothesised that a smaller tibial tuberosity could theoretically reduce the angle of insertion of the patellar ligament, resulting in increased CTT (Inauen et al., 2009). The role of tibial plateau convexity in CrCL insufficiency in dogs has been poorly studied. A previous study revealed that dogs with CrCL insufficiency have a less convex tibial plateau (Guerrero et al., 2007).

The relationship between a greater TPA and CrCL deficiency is controversial, with inconsistencies identified among different investigations (Buote et al., 2009; Cabrera et al., 2008; Morris & Lipowitz, 2001; Slocum & Devine, 1983; Su et al., 2015). The TPA is defined as the angle created by the slope of the medial tibial condyle and the perpendicular to the functional axis of the tibia (Warzee, Dejardin et al. 2001). Morris et al. (2001) used lateral radiographs to compare the TPA of larger breed dogs such as Golden Retrievers and Rottweilers experiencing rCCL with those having healthy stifle joints. According to their results, CrCL injury is associated with higher TPA even when the normal value was set at 21.2°, but this may differ among breeds. Previously, TPA has been considered as one of the major contributing factors to abnormal stifle joint biomechanics (Morris & Lipowitz, 2001; Mostafa et al., 2009). However, the results of studies focusing on TPA in different dog breeds and its relationship to rCCL are conflicting (Venzin et al., 2004; Wilke et al., 2002). Currently, it is believed that TPA and ICN width may contribute to the process of CrCL failure, but they do not appear to be determining factors (Fauron & Perry, 2017). Although a steep tibial plateau has been associated with rCCL in some studies, no clear difference was found between dogs with CrCL insufficiency and those without (Reif & Probst, 2003; Venzin et al., 2004; Wilke et al., 2002). The discrepancy between studies highlights the difficulty in identifying the role of a single factor in the aetiology of what is likely a multifactorial disease (Fitzpatrick & Solano, 2010; Kyllar & Čížek, 2018; Taylor-Brown et al., 2015).

In addition to TPA, other tibial measurements have been described, such as the angle between the tibial mechanical axis and a line joining the most cranial aspect of the tibial tuberosity to the midpoint between the two tibial intercondylar tubercles (the Z-angle) and the relative tibial tuberosity width (rTTW) (Inauen et al., 2009; Vedrine et al., 2013). However, these measurements do not appear to have a strong association with CrCL disease (Inauen et al., 2009; Renwick et al., 2009; Vedrine et al., 2013). It has been suggested that other biomechanical parameters may be more clinically relevant than TPA with regard to the pathogenesis of rCCL (Venzin et al., 2004). Morphometric characteristics of the pelvic limbs have been studied to define any association between CrCL deficiency and proximal deformity of the tibia (Glassman et al., 2011; Mostafa et al., 2009). Premature closure of the caudal aspect of the medial tibial condyle (tibial plateau deformity) and the deformity that would result from premature closure of the caudal aspect of the proximal tibia physis (proximal shaft deformity) contribute to CrCL injuries. In other words, the underdevelopment of the tibial tuberosity and the convex shape of the tibial condyles are relevant in the pathogenesis of the cranial cruciate ligament disease (Guerrero et al., 2007), leading to a greater caudal inclination of the proximal tibial shaft relative to its distal axis and a steep TPA (Glassman et al., 2011; Griffon, 2010; Mostafa et al., 2009).

The consequence of caudal angulation of the proximal tibia is a proximal anatomic axis that is not aligned with the anatomic long axis, resulting in a misalignment between the anatomical and mechanical axes (Raske et al., 2013). The AMA-angle is defined as the angle between these two axes and is used to quantify this caudal angulation of the proximal tibia (Glassman et al., 2011; Mostafa et al., 2009). According to a recent prospective study, AMA-angle in dogs with rCCL is significantly greater than the AMA-angle in dogs at low risk for rCCL, suggesting that this may be a clinically relevant predisposing factor for the development of canine rCCL (Guénégo et al., 2017).

The biomechanics of the canine pelvis were investigated using computer simulation models of intact and CrCL-deficient knee joints during the stance phase of gait. These models predicted increased CaCL loads, cranial tibial translation, and tibial internal rotation in CrCL-deficient stifle joints, which confirmed the results of in vivo and in vitro studies (Brown et al., 2014). Computer models have predicted that stifle joint biomechanics are sensitive to ligament prestrain, TPA, and femoral condyle size, and Tibial Plateau Leveling Osteotomy (TPLO) and Tibial Tuberosity Advancement (TTA) can affect stifle joint ligament loads and kinematics (Brown et al., 2014, 2015).

Arcand, M. A., Rhalmi, S., & Rivard, C.-H. (2000). Quantification of mechanoreceptors in the canine anterior cruciate ligament. *International Orthopaedics*, *24*(5), 272–275.

Arnoczky, S. P. (1985). Blood supply to the anterior cruciate ligament and supporting structures. *Orthopedic Clinics of North America*, *16*(1), 15–28.

Arnoczky, S. P., & Marshall, J. L. (1977). The cruciate ligaments of the canine stifle: an anatomical and functional analysis. *American Journal of Veterinary Research*, *38*(11), 1807–1814.

Bertocci, G. E., Brown, N. P., & Mich, P. M. (2017). Biomechanics of an orthosis-managed cranial cruciate ligament-deficient canine stifle joint predicted by use of a computer model. *American Journal of Veterinary Research*, *78*(1), 27–35.

Bojrab, M. J., & Monnet, E. (2010). *Mechanisms of Disease in Small Animal Surgery* (p. 1761).

Brown, N. P., Bertocci, G. E., & Marcellin-Little, D. J. (2014). Evaluation of varying morphological parameters on the biomechanics of a cranial cruciate ligament–deficient or intact canine stifle joint with a computer simulation model. *American Journal of Veterinary Research*, *75*(1), 26–33.

Brown, N. P., Bertocci, G. E., & Marcellin-Little, D. J. (2015). Canine stifle biomechanics associated with tibial tuberosity advancement predicted using a computer model. *Veterinary Surgery*, *44*(7), 866–873.

Buote, N., Fusco, J., & Radasch, R. (2009). Age, tibial plateau angle, sex, and weight as risk factors for contralateral rupture of the cranial cruciate ligament in Labradors. *Veterinary Surgery*, *38*(4), 481–489.

Cabrera, S. Y., Owen, T. J., Mueller, M. G., & Kass, P. H. (2008). Comparison of tibial plateau angles in dogs with unilateral versus bilateral cranial cruciate ligament rupture: 150 cases (2000–2006). *Journal of the American Veterinary Medical Association*, *232*(6), 889–892.

Clements, D. N., Carter, S. D., Innes, J. F., Ollier, W. E. R., & Day, P. J. R. (2008). Gene expression profiling of normal and ruptured canine anterior cruciate ligaments. *Osteoarthritis and Cartilage*, *16*(2), 195–203.

Comerford, E. J., Tarlton, J. F., Innes, J. F., Johnson, K. A., Amis, A. A., & Bailey, A. J. (2005). Metabolism and composition of the canine anterior cruciate ligament relate to differences in knee joint mechanics and predisposition to ligament rupture. *Journal of Orthopaedic*

Research, *23*(1), 61–66.
Cook, J. L. (2010). Cranial cruciate ligament disease in dogs: biology versus biomechanics. *Veterinary Surgery*, *39*(3), 270–277.
De Rooster, H., De Bruin, T., & Van Bree, H. (2006). Invited review—morphologic and functional features of the canine cruciate ligaments. *Veterinary Surgery*, *35*(8), 769–780.
Dennler, R., Kipfer, N. M., Tepic, S., Hassig, M., & Montavon, P. M. (2006). Inclination of the patellar ligament in relation to flexion angle in stifle joints of dogs without degenerative joint disease. *American Journal of Veterinary Research*, *67*(11), 1849–1854. https://doi.org/10.2460/ajvr.67.11.1849
Evans, R., Horstman, C., & Conzemius, M. (2005). Accuracy and optimization of force platform gait analysis in Labradors with cranial cruciate disease evaluated at a walking gait. *Veterinary Surgery*, *34*(5), 445–449.
Fauron, A., & Perry, K. (2017). Canine cranial cruciate ligament disease part 1–pathophysiology. *Veterinary Times*, *47*(24), 26–29.
Fitzpatrick, N., & Solano, M. A. (2010). Predictive variables for complications after TPLO with stifle inspection by arthrotomy in 1000 consecutive dogs. *Veterinary Surgery*, *39*(4), 460–474.
Galey, S., Konieczko, E. M., Arnold, C. A., & Cooney, T. E. (2003). Immunohistological detection of relaxin binding to anterior cruciate ligaments. In *Orthopedics* (Vol. 26, Issue 12, pp. 1201–1204). SLACK Incorporated Thorofare, NJ.
Gibbons, S. E., Macias, C., Tonzing, M. A., Pinchbeck, G. L., & McKee, W. M. (2006). Patellar luxation in 70 large breed dogs. *Journal of Small Animal Practice*, *47*(1), 3–9.
Glassman, M., Hofmeister, E., Weh, J. M., Roach, W., Torres, B., Johnston, S., & Budsberg, S. (2011). Radiographic quantitative assessment of caudal proximal tibial angulation in 100 dogs with cranial cruciate ligament rupture. *Veterinary Surgery*, *40*(7), 830–838.
Griffon, D. J. (2010). A review of the pathogenesis of canine cranial cruciate ligament disease as a basis for future preventive strategies. *Veterinary Surgery*, *39*(4), 399–409.
Guénégo, L., Payot, M., Charru, P., & Verwaerde, P. (2017). Comparison of tibial anatomical-mechanical axis angle between predisposed dogs and dogs at low risk for cranial cruciate ligament rupture. *The Veterinary Journal*, *225*, 35–41.
Guerrero, T. G., Geyer, H., Hässig, M., & Montavon, P. M. (2007). Effect

of conformation of the distal portion of the femur and proximal portion of the tibia on the pathogenesis of cranial cruciate ligament disease in dogs. *American Journal of Veterinary Research*, *68*(12), 1332–1337.

Hayashi, K., Bhandal, J., Rodriguez Carlos O, J., Kim, S. Y., Entwistle, R., Naydan, D., Kapatkin, A., & Stover, S. M. (2011). Vascular distribution in ruptured canine cranial cruciate ligament. *Veterinary Surgery*, *40*(2), 198–203.

Hayashi, K., Frank, J. D., Dubinsky, C., Hao, Z., Markel, M. D., Manley, P. A., & Muir, P. (2003). Histologic changes in ruptured canine cranial cruciate ligament. *Veterinary Surgery*, *32*(3), 269–277.

Henderson, R. (1978). The tibial compression mechanism: a diagnostic aid in stifle injuries. *JAAHA*, *4*, 474–478.

Hermanson, J. W., & DeLahunta, A. (2020). *Miller and Evans' anatomy of the dog*. Am Vet Med Assoc.

Ho-Eckart, L. K., Seki, M., Luizza, L., Kearney, M. T., & Lopez, M. J. (2017). Joint stability after canine cranial cruciate ligament graft reconstruction varies among femoral fixation sites. *Veterinary Surgery*, *46*(2), 213–225.

Houlton, J. E. F., Cook, J. L., Innes, J. F., & Bobbs, S. J. L. (2006). Manual of canine and feline musculosletal disorders. *UK, BSAVA*, 21–26.

Inauen, R., Koch, D., Bass, M., & Haessig, M. (2009). Tibial tuberosity conformation as a risk factor for cranial cruciate ligament rupture in the dog. *Veterinary and Comparative Orthopaedics and Traumatology*, *22*(01), 16–20.

Johnston, S. A., & Tobias, K. M. (2017). *Veterinary surgery: small animal expert consult-E-book*. Elsevier Health Sciences.

Kim, S. E., Pozzi, A., Banks, S. A., Conrad, B. P., & Lewis, D. D. (2009). Effect of tibial tuberosity advancement on femorotibial contact mechanics and stifle kinematics. *Veterinary Surgery*, *38*(1), 33–39.

Kim, S. E., Pozzi, A., Kowaleski, M. P., & Lewis, D. D. (2008). Tibial osteotomies for cranial cruciate ligament insufficiency in dogs. *Veterinary Surgery*, *37*(2), 111–125.

Kipfer, N. M., Tepic, S., Damur, D. M., Guerrero, T., Hässig, M., & Montavon, P. M. (2008). Effect of tibial tuberosity advancement on femorotibial shear in cranial cruciate-deficient stifles. *Veterinary and Comparative Orthopaedics and Traumatology*, *21*(05), 385–390.

Kobayashi, S., Baba, H., Uchida, K., Negoro, K., Sato, M., Miyazaki, T., Nomura, E., Murakami, K., Shimizubata, M., & Meir, A. (2006). Microvascular system of anterior cruciate ligament in dogs. *Journal of*

Orthopaedic Research, *24*(7), 1509–1520.
Korvick, D. L., Pijanowski, G. J., & Schaeffer, D. J. (1994). Three-dimensional kinematics of the intact and cranial cruciate ligament-deficient stifle of dogs. *Journal of Biomechanics*, *27*(1), 77–87.
Kuroki, K., Williams, N., Ikeda, H., Bozynski, C. C., Leary, E., & Cook, J. L. (2019). Histologic assessment of ligament vascularity and synovitis in dogs with cranial cruciate ligament disease. *American Journal of Veterinary Research*, *80*(2), 152–158.
Kyllar, M., & Čížek, P. (2018). Cranial cruciate ligament structure in relation to the tibial plateau slope and intercondylar notch width in dogs. *Journal of Veterinary Science*, *19*(5), 699–707.
Lemburg, A. K., Meyer-Lindenberg, A., & Hewicker-Trautwein, M. (2004). Immunohistochemical characterization of inflammatory cell populations and adhesion molecule expression in synovial membranes from dogs with spontaneous cranial cruciate ligament rupture. *Veterinary Immunology and Immunopathology*, *97*(3–4), 231–240.
Morris, E., & Lipowitz, A. J. (2001). Comparison of tibial plateau angles in dogs with and without cranial cruciate ligament injuries. *Journal of the American Veterinary Medical Association*, *218*(3), 363–366.
Mostafa, A. A., Griffon, D. J., Thomas, M. W., & Constable, P. D. (2009). Morphometric characteristics of the pelvic limbs of Labrador Retrievers with and without cranial cruciate ligament deficiency. *American Journal of Veterinary Research*, *70*(4), 498–507.
Muir, P. (2018). *Advances in the canine cranial cruciate ligament*. John Wiley & Sons.
Muir, P., Oldenhoff, W. E., Hudson, A. P., Manley, P. A., Schaefer, S. L., Markel, M. D., & Hao, Z. (2007). Detection of DNA from a range of bacterial species in the knee joints of dogs with inflammatory knee arthritis and associated degenerative anterior cruciate ligament rupture. *Microbial Pathogenesis*, *42*(2–3), 47–55.
O'Connor, B. L., & Woodbury, P. (1982). The primary articular nerves to the dog knee. *Journal of Anatomy*, *134*(Pt 3), 563.
Rafael, P., Goin, B., Blanc, Q., Buttin, P., Cachon, T., & Viguier, E. (2021). Ex-vivo biomechanical analysis of cranial cruciate ligament in Labrador breed dogs. *46th Congress of the Société de Biomécanique*.
Raske, M., Hulse, D., Beale, B., Saunders, W. B., Kishi, E., & Kunze, C. (2013). Stabilization of the CORA based leveling osteotomy for treatment of cranial cruciate ligament injury using a bone plate augmented with a headless compression screw. *Veterinary Surgery*,

42(6), 759–764.

Reif, U., & Probst, C. W. (2003). Comparison of tibial plateau angles in normal and cranial cruciate deficient stifles of Labrador retrievers. *Veterinary Surgery*, *32*(4), 385–389.

Renwick, A. I. C., McKee, W. M., Emmerson, T. D., & House, A. K. (2009). Preliminary experiences of the triple tibial osteotomy procedure: tibial morphology and complications. *Journal of Small Animal Practice, 50*(5), 212–221.

Restucci, B., Sgadari, M., Fatone, G., Della Valle, G., Aragosa, F., Caterino, C., Ferrara, G., & Niebauer, G. W. (2022). Immunoexpression of Relaxin and Its Receptors in Stifle Joints of Dogs with Cranial Cruciate Ligament Disease. *Animals*, *12*(7). https://doi.org/10.3390/ani12070819

Schulze-Tanzil, G. (2019). Intraarticular Ligament Degeneration Is Interrelated with Cartilage and Bone Destruction in Osteoarthritis. *Cells*, *8*(9). https://doi.org/10.3390/CELLS8090990

Schwandt, C. S., Bohorquez-Vanelli, A., Tepic, S., Hassig, M., Dennler, R., Vezzoni, A., & Montavon, P. M. (2006). Angle between the patellar ligament and tibial plateau in dogs with partial rupture of the cranial cruciate ligament. *American Journal of Veterinary Research*, *67*(11), 1855–1860.

Slocum, B., & Devine, T. (1983). Cranial tibial thrust: a primary force in the canine stifle. *Journal of the American Veterinary Medical Association*, *183*(4), 456–459.

Spinella, G., Arcamone, G., & Valentini, S. (2021). Cranial Cruciate Ligament Rupture in Dogs: Review on Biomechanics, Etiopathogenetic Factors and Rehabilitation. *Veterinary Sciences*, *8*(9), 186.

Su, L., Townsend, K. L., Au, J., & Wittum, T. E. (2015). Comparison of tibial plateau angles in small and large breed dogs. *The Canadian Veterinary Journal*, *56*(6), 610.

Tanegashima, K., Edamura, K., Akita, Y., Yamazaki, A., Yasukawa, S., Seki, M., Asano, K., Nakayama, T., Katsura, T., & Hayashi, K. (2019). Functional anatomy of the craniomedial and caudolateral bundles of the cranial cruciate ligament in beagle dogs. *Veterinary and Comparative Orthopaedics and Traumatology*, *32*(03), 182–191.

Tashman, S., Anderst, W., Kolowich, P., Havstad, S., & Arnoczky, S. (2004). Kinematics of the ACL-deficient canine knee during gait: serial changes over two years. *Journal of Orthopaedic Research*, *22*(5), 931–

941.
Taylor-Brown, F. E., Meeson, R. L., Brodbelt, D. C., Church, D. B., McGreevy, P. D., Thomson, P. C., & O'Neill, D. G. (2015). Epidemiology of cranial cruciate ligament disease diagnosis in dogs attending primary-care veterinary practices in England. *Veterinary Surgery*, *44*(6), 777–783.
Tepic, S., Damur, D. M., & Montavon, P. M. (2002). Biomechanics of the stifle joint. *Proceedings of the 1st World Orthopaedic Veterinary Congress*, 189–190.
Tinga, S., Kim, S. E., Banks, S. A., Jones, S. C., Park, B. H., Pozzi, A., & Lewis, D. D. (2018). Femorotibial kinematics in dogs with cranial cruciate ligament insufficiency: a three-dimensional in-vivo fluoroscopic analysis during walking. *BMC Veterinary Research*, *14*(1), 1–9. https://doi.org/10.1186/S12917-018-1395-2
Torres, B. T. (2020). Objective gait analysis. *Canine Lameness*, 15–30.
Vasseur, P. B., & Arnoczky, S. P. (1981). Collateral ligaments of the canine stifle joint: anatomic and functional analysis. *American Journal of Veterinary Research*, *42*(7), 1133—1137. http://europepmc.org/abstract/MED/7271030
Vasseur, P. B., Pool, R. R., Arnoczky, S. P., & Lau, R. E. (1985). Correlative biomechanical and histologic study of the cranial cruciate ligament in dogs. *American Journal of Veterinary Research*, *46*(9), 1842–1854.
Vedrine, B., Guillemot, A., Fontaine, D., Ragetly, G. R., & Etchepareborde, S. (2013). Comparative anatomy of the proximal tibia in healthy Labrador Retrievers and Yorkshire Terriers. *Veterinary and Comparative Orthopaedics and Traumatology*, *26*(04), 266–270.
Venzin, C., Howard, J., Rytz, U., Spreng, D., Schawalder, P., Doherr, M., & Schmökel, H. (2004). Tibial plateau angles with and without cranial cruciate ligament rupture. *Veterinary and Comparative Orthopaedics and Traumatology*, *17*(04), 232–236.
Vezzoni, A., Baroni, E., Demaria, M., Olivieri, M., & Magni, G. (2003). Trattamento chirurgico della rottura del legamento crociato anteriore nel cane mediante osteotomia livellante del piatto tibiale (TPLO): presupposti teorici ed esperienza clinica in 293 casi. *Veterinaria*, *17*(3), 19–31.
Wilke, V. L., Conzemius, M. G., Besancon, M. F., Evans, R. B., & Ritter, M. (2002). Comparison of tibial plateau angle between clinically normal Greyhounds and Labrador Retrievers with and without rupture of the cranial cruciate ligament. *Journal of the American Veterinary*

Medical Association, *221*(10), 1426–1429.

Witsberger, T. H., Villamil, J. A., Schultz, L. G., Hahn, A. W., & Cook, J. L. (2008). Prevalence of and risk factors for hip dysplasia and cranial cruciate ligament deficiency in dogs. *Journal of the American Veterinary Medical Association*, *232*(12), 1818–1824. https://doi.org/10.2460/javma.232.12.1818

Yahia, L. H., Newman, N. M., & St-Georges, M. (1992). Innervation of the Canine Cruciate Ligaments: A neurohistological study. *Anatomia, Histologia, Embryologia*, *21*(1), 1–8.

Zink, C., & Carr, B. J. (2018). What is a canine athlete? *Canine Sports Medicine and Rehabilitation*, 1–22.

Chapter 2

New generation Tibial Tuberosity Advancement Techniques
A systematic review

The first step of this doctoral thesis is to systematically review the currently available literature on surgical techniques for the treatment of canine rCCL. Given the lack of evidence on new generation TTAT, the focus of our research was report data regards preoperative planning, surgical procedure, outcome, and complications, previously published only for traditional TTA. The results listed on the following pages have recently been published (Aragosa et al., 2022).

2.1 Surgical treatment of cranial cruciate ligament rupture

Management of CrCL deficiency in dogs typically requires stifle joint-stabilizing surgical intervention, also to slow the progression of OA and prevent concurrent meniscal pathology. Corrective surgical procedures include intra-articular, extra-articular, and osteotomy techniques. Intra-articular reconstruction uses a biological or synthetic tissue to replace injured CrCL. In extra-articular prosthetic surgical techniques, craniocaudal tibial instability during weight-bearing stance is limited through a prosthetic suture placing on the lateral aspect of the stifle joint, simulating CrCL function. Outcome depends on the passive restraint provided by the prosthetic suture until satisfactory periarticular fibrosis develops (Brown et al., 2015, 2017). More recently, osteotomy procedures have been developed based on kinetic and kinematic studies: they include TPLO, TTA and Closing Cranial Wedge Ostectomy (CCWO) (Boudrieau, 2009). The rationale of TPLO consists in modifying the tibial plateau slope up to be perpendicular to the long axis of the tibia causing weight-bearing forces to act along tibial axis. The technique designed by Slocum consists in the osteotomy rotated and fixated at a new plateau angle, decreasing the magnitude of CTT force and restoring stifle joint stability during stance phase (Slocum & Slocum, 1993). In 2002, an alternative biomechanical model of the knee joint was proposed, according to which the intra-articular force resulting from weight bearing is not parallel to the functional axis of the tibia, but parallel to the patellar ligament. For this reason, the principle of TTA is to move the patellar ligament at 90° to the tibial plateau at full extension of the joint, advancing the tibial tuberosity, to annihilate the cranial shear and the CTT (Hoffmann et al., 2006; Montavon et al., 2002). In the traditional TTA technique, fixation after osteotomy is performed with forks and titanium cages of different sizes, from 3 to 12 mm.

According to a recent study, both TTA and TPLO confer craniocaudal stability to the CrCL deficient stifle (Ober et al., 2019), but comparative studies have demonstrated the superiority of TPLO over TTA, achieving a higher level of functional outcome (Livet et al., 2019; Moore et al., 2020). Conversely, a systematic review established the superiority of TPLO over extracapsular sutures but found insufficient evidence concerning differences in the outcomes of TPLO and TTA (Bergh et al., 2014). Further research comparing TPLO and TTA with subjective gait analysis could not detect differences in lameness reduction between the techniques, while objective gait analysis supports the superiority of TPLO (Beer et al., 2018).

2.2 New generation Tibial Tuberosity Advancement Techniques

Numerous adaptations of TTA have been described and include the modified Maquet technique (MMT) (Etchepareborde, Brunel, et al., 2011), TTA rapid (Samoy et al., 2015), the modified Maquet procedure (MMP) (Ness, 2016), modified Maquet Tibial Tuberosity Advancement (mTTA) (Medeiros et al., 2016), tibial tuberosity advancement with cranial fixation (TTA-CF) (Zhalniarovich et al., 2018) and porous TTA (Trisciuzzi et al., 2019). These new generation TTAT involve advancing the tibial tuberosity using saw guides of different shapes and sizes, allowing an incomplete osteotomy of the tibial tuberosity (Chong, 2019).

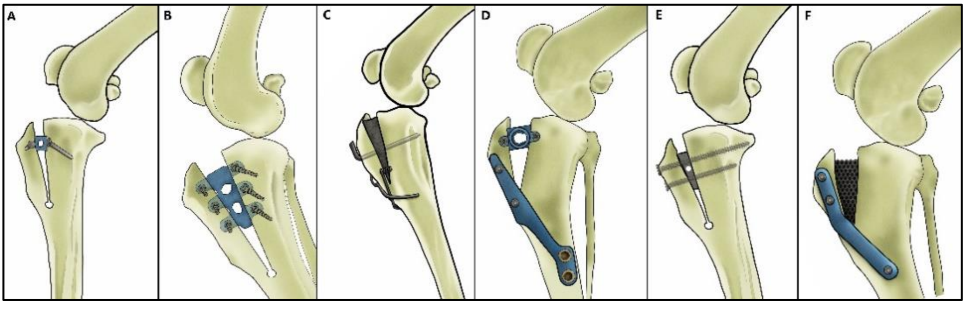

Figure 2.1 Graphic illustrations of TTAT included: (A) modified Maquet technique (MMT), (B) TTA rapid, (C) modified Maquet procedure (MMP), (D) modified Maquet tibial tuberosity advancement (mTTA), (E) tibial tuberosity advancement with cranial fixation (TTA-CF) and (F) porous TTA (designed by Claudio Palumbo).

2.2.1 Materials and Methods

The systematic review recently published by our team followed the PRISMA statement (Preferred Reporting Items for Systematic reviews and Meta-Analyses), including the published retrospective or prospective studies of dogs undergoing new generation TTAT for rCCL (Page et al., 2021). Inclusion criteria were a sound description of preoperative planning (measurement of advancement), follow-up, clinical outcome, and complications. The studies lacking descriptions of complications were excluded. Four independent reviewers (CC, GDV, FA, GF) searched the Pubmed, Google Scholar, and Scopus databases from 2011 to June 2022. without language restrictions. We examined references cited in study reports included in the systematic review and we used three known relevant studies (Della Valle et al., 2021; Kapler et al., 2015; Serrani et al., 2022) to identify records within databases. Search terms were also checked using the Pubmed

PubReMiner word frequency analysis tool. Candidate search terms were identified by looking at words in those records' titles, keywords, and abstracts. The search strategy was tested whether it could identify the three known relevant studies. The electronic search key words used were "modified Maquet technique" (canine OR dog), "TTA Rapid" (canine OR dog), "modified Maquet procedure" (canine OR dog), "mTTA" or "modified Tibial Tuberosity Advancement" (canine OR dog), "Tibial tuberosity Advancement with Cranial Fixation" or "TTA-CF" (canine OR dog), "Porous TTA" (canine OR dog) for all fields. Finally, the references list of the papers selected was critically reviewed to improve the sources. Temporal limitation was placed on 2011 for MMT for relevant publications because Etchepareborde described MMT in this year (Etchepareborde, Brunel, et al., 2011). Accordingly, for all techniques included, the data limit was chosen based on the first description in the literature: TTA Rapid, 2015 (Samoy et al., 2015); MMP, 2016 (Ness, 2016); mTTA, 2016 (Medeiros et al., 2016); TTA-CF (Zhalniarovich et al., 2018), 2018; Porous TTA, 2019 (Trisciuzzi et al., 2019).
Two review authors (FA, CC) independently screened titles and abstracts of all records and discussed inconsistencies until consensus was obtained. In case of disagreement, consensus on which articles to screen full text was reached by discussion or referred to a third researcher (GVD) to make the final decision. Next, the same researchers independently screened full texts to determine eligibility, and discrepancies were resolved between the authors or with the availability of a third-party adjudicator (GF).
Two researchers (FA, CC) independently extracted and compared data from eligible studies, and any discrepancy was resolved through discussion or consulting another researcher (GF). We extracted data regarding author's name, study year, sample size, measurement method for required advancement, presence of meniscal injuries, follow-up, and complications. Any measure of planning, outcome, and complications was eligible for inclusion. Results for preoperative planning were reported as a percentage. When recorded, we provided a percentage of dogs with meniscal injuries at presentation undergoing meniscectomy, the percentage of meniscal release performed during TTAT and the number of late meniscal tears. Postoperative PTA, expressed as a mean, was listed for each study if available. Every value regarding length of follow-up or number of measurement time points were included when interpreting study findings. We decided to summarised complications according to Cook's guidelines (Cook et al., 2010), as catastrophic, major and minor and divided in

perioperative (0–3 months), short-term (3–6 months), mid-term (6–12 months) and long-term (>12 months). If more than one assessment was performed during a time frame, the last one was considered for analysis. Clinical outcome was assessed as full function, acceptable function and unacceptable function based on restoration of performances from the preinjury period, and the results were recorded as a percentage. If the outcome was reported as lameness degree, we merged data for full/acceptable function of dogs with no lameness or sporadic lameness.
Data were grouped in tables according to the technique used, but we listed results considering every domain. When data were missing or unclear, corresponding studies were excluded from syntheses. We also assessed the quality of papers included using the Joanna Briggs Institute (JBI) Critical Appraisal Checklists and every study design was combined with the corresponding JBI checklist (Munn et al., 2019). To assess the certainty of the evidence, the five GRADE recommendations (study limitations, consistency of effect, imprecision, indirectness, and publication bias) were used by two authors (FA, CC). We assessed the certainty of evidence as high, moderate, low, or very low (Higgins et al., 2019). Meta-analyses could not be undertaken due to the heterogeneity of surgeries and study designs, so Synthesis without Meta-analysis (SwiM) checklist was applied (Campbell et al., 2020).

2.2.2 Results

We found 471 records in database searching from 2011 to June 2022. but after duplicate removal (n = 117) and exclusion of book sections, ex vivo studies, or thesis (n = 178), 176 records were elegible for screening. Among these, we reviewed 68 full-text documents and finally included 29 papers. Screening records from the reference lists of initially included studies, founding one paper that fulfilled inclusion criteria (Medeiros et al., 2016). Only 30 papers (Table 1) met the inclusion criteria, with a mean of 35 cases (range 1–174). We excluded 33 studies from this review because dealt surgical techniques different from TTAT and 6 studies about cats.
A total of 1051 stifles were reviewed: MMT (n = 415), TTA rapid (n = 292), MMP (n = 154), mTTA (n = 59), TTA-CF (n = 25) and porous TTA (n = 106). The MMT was applied in 10 studies, while TTA rapid in 8. MMP in 7. mTTA in 3. TTA-CF in 3. and porous TTA in 2. One paper included several surgical techniques (MMT, TTA rapid, MMP, and mTTA), so we listed it in tables for each domain (Serrani et al., 2022). Nine studies included have a very low level of certainty (30%), 4 papers have a low level

(13.3%), 7 moderate (23.3%), and 10 high levels (33.3%). Thirteen studies have a prospective design (43.33%).

Table 2.1 List of reviewed papers: study details, sample size, surgical planning, and meniscal injuries.

Authors	**Study design**	**GRADE**	**N. stifles**	**Surgical technique**	**Measurement technique**	**Meniscal tears at surgery**	**Meniscectomy**	**Meniscal release**	**Late Meniscal Tears**	**PTA post**	**Year**
Lorentz et al.	Case series	Very Low	1	MMP	-	1	-	-	-	-	2014
Kapler et al.	Retrospective study	Very Low	38	MMP	Orthomed & modified tibial tuberosity advancement measurement method	-	-	-	-	95.9° (86.7 - 108.2)	2015
Ness et al.	Clinical trial	Moderate	26	MMP	Orthomed	-	NO	NO	-	-	2016
Knebel et al.	Prospective, randomized, controlled study	High	35	MMP	Orthomed	22	22	NO	2	-	2020
Terreros et al.	Prospective clinical study	Moderate	15	MMP	Tibial Plateau Method	4	4	4	-	93.4 ° ± 2.1	2020
Della Valle et al.	Prospective clinical study	Moderate	35	MMP	Orthomed	27	27	6	0	89.7° ± 2.3	2021
Serrani et al.	Retrospective study	Low	4	MMP	-	-	NO	NO	NO	95.75°	2022
Etchepareborde et al.	Retrospective study	Very Low	20	MMT	Trasparency (Kyon)	8	8	NO	2	-	2011
Ramirez et al.	Retrospective study	Moderate	84	MMT	Trasparency (Kyon)	39	39	NO	3	-	2015
Marques et al.	Case report	Very Low	1	MMT	Orthomed	NO	NO	NO	NO	-	2017
Marques et al.	Case series	Very Low	2	MMT	-	NO	NO	NO	NO	-	2017
Lefbvre et al.	Retrospective study	Moderate	174	MMT	-	-	-	-	-	-	2017
Retallack et al.	Retrospective clinical cohort study	Moderate	35	MMT	-	21	21	14	NO	-	2017
De Barros et al.	Prospective clinical study	Very Low	21	MMT	sotfware?	-	-	-	-	-	2018
Valino-Cultelli et al.	Prospective randomized study	High	24	MMT	Tibial Plateau Method	-	-	-	-	-	2021
Valino-Cultelli et al.	Prospective clinical study	High	53	MMT	Tibial Plateau Method	-	-	-	-	-	2021
Serrani et al.	Case series	Low	1	MMT	Tibial Plateau Method	NO	NO	NO	1	83°	2022
Samoy et al.	Prospective clinical study	High	50	TTA Rapid	Common tangent Method	21	21	29	0	-	2015
Arican et al.	Prospective study	High	17	TTA Rapid	Template and Common tangent Method	NO	NO	NO	-	-	2017
Butterworth et al.	Retrospective study	Moderate	152	TTA Rapid	Tibial Axis Method	44	44	NO	9	-	2017
Dyall et al.	Retrospective study	Low	48	TTA Rapid	Anatomical landmark method and Common tangent Method	19	19	NO	2	90·8° ± 2·9	2017
Heremans et al.	Case report	Very Low	1	TTA Rapid	-	NO	NO	NO	NO	-	2017
Livet et al.	Prospective randomized study	High	13	TTA Rapid	Long axis method	4	4	NO	2	91·1° (89.1–92.9)	2019
Roydev et al.	Retrospective study	Low	10	TTA Rapid	Common tangent Method	5	5	5	1	-	2021
Serrani et al.	Retrospective study	Low	1	TTA Rapid	-	1	1	NO	NO	96°	2022
Trisciuzzi et al.	Retrospective study	Low	41	Porous TTA	Common Tangent Method and Tibial plateau angle inclination method	-	-	-	-	-	2019
Villavicencio et al.	Prospective study	High	65	Porous TTA	Common tangent Method	-	-	-	-	-	2020
Mendeiros et al.	Prospective clinical study	High	42	mTTA	Trasparency	-	-	-	-	-	2016
Morato et sl.	Prospective study	High	16	mTTA	-	5	5	-	-	-	2019
Serrani et al.	Retrospective study	Low	1	mTTA	-	NO	NO	-	-	94°	2022
Zhalniarovich et al.	Prospective study	High	22	TTA CF	Common tangent Method	5	5	NO	NO	-	2018
Adamiak et al.	Case report	Very Low	2	TTA CF	Common tangent Method	NO	NO	NO	NO	-	2018
Zhalniarovich et al.	Case report	Very Low	1	TTA CF	-	-	-	-	-	-	2019

The method used to measure the amount of advancement of the tibial tuberosity was reported in 24/30 studies, with the common tangent method being most represented (n = 8), followed by Orthomed (n = 5). In nine studies, no measurement technique was indicated. Only 20% of included studies reported postoperative PTA (6/30). Among these, 78.7% stifles had postoperative angles clearly defined (85/108), and postoperative PTA was in the reported range of 90° ± 5 (Kapler et al., 2015).

Meniscal tears were detected in 226 cases at surgery time and described in 15 papers, all treated by meniscectomy. In five articles no meniscal tear was detected during the surgical inspection by arthrotomy or arthroscopy. In 10 papers, no data for meniscal injuries were given. Considering 562 stifles undergoing surgery, which were described in 20 papers, 40.21% presented meniscal tears at surgery time. The meniscal release is reported in 5/30 papers (58 stifles), but it was not performed in 14/30 articles. As regards late meniscal tears, 16/30 papers reported injuries during follow-up time, with 4.28% of cases recorded (22/516).

In all papers, recovery was clinically assessed, except for two (Kapler et al., 2015; Lefebvre et al., 2018), for which only data regarding PTA or radiography were listed. Postoperative radiographic assessments were performed in 27 studies (90%), while an owners' survey was employed as an outcome assessment in 7 papers (23.3%). Other procedures assessing the follow-up, such as gait analysis (13.3%), ROM (3.3%), or baropodometric score (3.3%), were less frequently employed. According to the percentage reported in 21/30 studies (70%), the mean perioperative recovery is 64.76% of full/acceptable function. Perioperative follow-up was reported in 455/495 treated stifles, and a full/acceptable outcome was reported for 340/455 stifles (74.7%) (Table 2). Short-term follow-up was recorded in 21/30 papers (70%) with a mean of 88.9% of full/acceptable function. These studies examined 648 stifles, but follow-up was reported in 575 stifles in total, of which 93% regained full/acceptable function. Mid-term follow-up was reported in 15/30 papers (50%) with a mean of 87.8% of full/acceptable function. Follow-up evaluations revealed a full/acceptable function in 92.9% of stifles examined (313/337) during this time frame. Papers included in this review described a total of 390 surgeries, but mid-term follow-up was available in 86.4% of cases. Five papers collected data about long-term follow-up (16.7%), with a mean of 96.35% of full/acceptable outcomes. Eighty-seven stifles among these studies showed a full/acceptable function upon 92 stifles recorded (94.6%). These papers listed 208 TTATs in total, but only 92 surgeries had a long-term follow-up (44.2%).

Table 2.2 The outcome of reviewed papers is divided by surgical technique and time frame.

Authors	**N. stifles**	**Surgical technique**	**Recovery assessment**	**Peri-operative recovery**	**Recovery Short term**	**Recovery Mid term**	**Recovery Long term**	**Year**
Lorentz et al.	1	MMP	Clinical and Radiographical	0.00%	-	-	-	2014
Kapler et al.	48	MMP	PL-TPA	52.60%	-	-	-	2015
Ness et al.	26	MMP	Clinical and Radiographical	92.00%	-	84.70%	-	2016
Knebel et al.	35	MMP	Clinical, Radiographical and Gait Analysis	48.40%	77.40%	80.60%	-	2020
Terreros et al.	15	MMP	Clinical, Radiographical and Owners survey	76.92%	-	92.30%	-	2020
Della Valle et al.	35	MMP	Clinical, Radiographical and Gait Analysis	-	54.30%	-	-	2021
Serrani et al.	4	MMP	Clinical and Radiographical	0%	-	-	-	2022
Etchepareborde et al.	20	MMT	Clinical and Radiographical	80.00%	100.00%	-	-	2011
Ramirez et al.	84	MMT	Clinical, Radiographical and Owners survey	-	100.00%	-	91.00%	2015
Marques et al.	1	MMT	Clinical	100.00%	100.00%	100.00%	-	2017
Marques et al.	2	MMT	Clinical and Radiographical	-	100.00%	-	-	2017
Lefbvre et al.	174	MMT	Radiographical	-	-	-	-	2017
Retallack et al.	35	MMT	Clinical and Radiographical	-	-	-	-	2017
De Barros et al.	21	MMT	Clinical and owners survey	-	-	81.00%	-	2018
Valino-Cultelli et al.	24	MMT	Clinical and Radiographical	72.20%	100.00%	-	-	2021
Valino-Cultelli et al.	53	MMT	Clinical and Radiographical	74.30%	97.10%	-	-	2021
Serrani et al.	1	MMT	Clinical and Radiographical	0.00%	0.00%	0.00%	0.00%	2022
Samoy et al.	50	TTA Rapid	Clinical and Radiographical	-	96.00%	-	-	2015
Arican et al.	17	TTA Rapid	Clinical and Radiographical	82.35%	82.35%	-	-	2017
Butterworth et al.	152	TTA Rapid	Clinical, Radiographical and Owners survey	-	99.00%	97.00%	-	2017
Dyall et al.	48	TTA Rapid	Clinical, Radiographical and Owners survey	94.00%	-	95.30%	95.30%	2017
Heremans et al.	1	TTA Rapid	Clinical and Radiographical	0.00%	100.00%	100.00%	-	2017
Livet et al.	13	TTA Rapid	Clinical, Radiographical, Gait Analysis and Owners survey	-	100.00%	100.00%	-	2019
Roydev et al.	10	TTA Rapid	Clinical, Radiographical, Gait Analysis and ROM	70.00%	70.00%	90.00%	100.00%	2021
Serrani et al.	1	TTA Rapid	Clinical and Radiographical	0.00%	0.00%	0.00%	0.00%	2022
Trisciuzzi et al.	41	Porous TTA	Clinical, Radiographical and Baropodometric score	73.00%	-	100.00%	-	2019
Villavicencio et al.	65	Porous TTA	Clinical and Radiographical	87.69%	100.00%	-	-	2020
Mendeiros et al.	42	mTTA	Clinical and Radiographical	56.41%	95.00%	-	100.00%	2016
Morato et sl.	16	mTTA	Clinical and Radiographical	100.00%	100.00%	-	-	2019
Serrani et al.	1	mTTA	Clinical and Radiographical	0.00%	0.00%	-	-	2022
Zhalniarovich et al.	22	TTA CF	Clinical, Radiographical and Owners survey	100.00%	95.45%	95.45%	95.45%	2018
Adamiak et al.	2	TTA CF	Clinical and Radiographical	100.00%	100.00%	100.00%	-	2018
Zhalniarovich et al.	1	TTA CF	Clinical and Radiographical	0.00%	100.00%	100.00%	-	2019

Minor complications were recorded for 90% of papers included (27/30), while major complications were listed by all studies except one (Etchepareborde, Brunel, et al., 2011). No catastrophic complications were reported in any study included. The mean minor complication rate was 20.94% for 27 papers and in 28.33% of stifles tibial crest fissures and fractures were reported (274/967), representing 84.57% of minor complications collected (274/324). No one of these 70 fractures of the tibial crest and 204 fissures need further treatment. For six stifles, minor complications were not clearly defined (Arican et al., 2017; Medeiros et al., 2016). The mean major complication rate was 24.05% for 29 studies. The 10.67% of surgeries suffered major complications (110/1031). Most commonly, tibial crest fissures were reported, the 28.18% of all major complications listed. Fissures that required further treatment represented 3% of the stifles included. As regards tibial crest fractures, 25/1031 stifles were described (2.43%), followed by 14 surgical site infections (1.36%) and 13 tibial diaphysis fractures (1.26%).

2.2.3 Discussion

This systematic review aimed to summarise the available evidence of TTAT in dogs. Although TTA has become increasingly popular, limited evidence was found in the veterinary literature with a sound description of preoperative planning, outcome, and complications. Overall, according to the literature reviewed, a limited number of studies focused on new generation TTAT. The data derived mainly from retrospective studies with a limited number of cases. In addition, only 1/3 of the included papers present a high level of evidence (33.3%), so the extracted data needs critical interpretation. The debate on the surgical treatment of CrCL is still animated. Despite the high number of procedures developed to stabilise the stifle joint, few studies reported mid- to the long-term outcomes, and even fewer reported preoperative planning. As a matter of fact, the predominant form of research was observational case series, resulting in the preponderance of studies with a low level of evidence. Unfortunately, this study design is limited by confounding variables that decrease the evidentiary value. The only study design that can determine a causal interference is a randomised, controlled clinical trial, and there was only one such study included in this systematic review (Knebel et al., 2020). Beyond those included in this review, several techniques and adaptations were proposed to achieve joint stabilisation, such as TTA-2. fusion TTA, and circular TTA, but to date no evidence is available in the literature for these

techniques. Fusion TTA was only anecdotally reported in thesis or conference (Garcia Querol, 2020), while for TTA-2. only in vitro studies were published (McCartney et al., 2019; Torrington et al., 2015).
Different methods were adopted to assess the advancement required to obtain a postoperative PTA of 90° ± 5. According to the reviewed literature, 1/3 of papers selected the common tangent method. As previously reported, this method has poor reliability and the tendency to underestimate the necessary advancement, leading to undercorrection during surgical planning (Cadmus et al., 2014; Millet et al., 2013). Only 20% of studies included recorded postoperative PTA, usually as a mean. According to them, 78.7% of surgeries obtained a final PTA of 90° (±5), allowing the neutralisation of the shear forces (Burns & Boudrieau, 2008; Kapler et al., 2015). These results could influence the outcome, as a postoperative PTA outside this range could lead to instability and persistent cranial tibial subluxation (Millet et al., 2013; Skinner et al., 2013). This residual cranial tibial translation is a potentially post-operative finding after TTAT, contributing to late meniscal tears (Jin et al., 2019; Voss et al., 2008). In agreement with this consideration, we chose to analyse meniscal injuries separately from other complications, considering presentation, meniscectomy, and meniscal release. Among the studies examined, meniscal injury was found in 40.21% of stifles undergoing TTAT and consequently treated with meniscectomy. Previously published studies reported 10% of postoperative secondary meniscus damage after traditional TTA (Voss et al., 2008), these rates can be as high as 20% without meniscal release (Lafaver et al., 2007). Although the release of the medial meniscus disturbs load transmission through the meniscus, increasing instability and cartilage loading (Pozzi et al., 2008). Late meniscal tears in studies included in this review (4.28%) are lower than previously reported. As previously noted, the choice of meniscal release probably influenced the incidence of postoperative meniscal injuries. Still, it is not possible to investigate this result statistically as only five studies chose this technique (Della Valle et al., 2021; Retallack & Daye, 2018; Roydev & Goranov, 2021; Samoy et al., 2015; Terreros & Daye, 2021). Nevertheless, all late meniscal tears were recorded in 16 studies where the meniscal release was not performed, except for 1 knee (Roydev & Goranov, 2021). A possible reason for the higher number of secondary meniscal injuries after traditional TTA could be the persistent craniocaudal stifle instability (Skinner et al., 2013). However, considering that few studies evaluated longterm follow-up, probably not all meniscal injuries were identified.

Several methodologies and outcome assessments were used in the papers, including visual gait evaluation, owner perceptions, and objective force plate gait analysis. To minimise the mistakes in data interpretation, we categorised the outcome following Cook's guidelines (Cook et al., 2010). Most of the reviewed papers provided clinical and radiographic assessments during the follow-up, while other objective assessment tools such as gait analysis or baropodometric score were not routinely employed. Given all surgical techniques, 74.7% of cases regained a full/acceptable limb function in the perioperative period, 93% in short-term follow-up, 92.9% during mid-term and 94.6% up to 1 year (long-term). According to this result TTAT showed to be able to treat the stifle deficiency over time. Nevertheless, previous studies based on gait analysis concluded that despite the significant improvement after traditional TTA, normal limb function was not wholly restored (Skinner et al., 2013; Voss et al., 2008).

Numerous papers aimed to compared TTA with other techique, but all of them omitted the new generation TTAT. However, the overall comparisons of these studies are difficult due to the lack of compliance in the data among publications. To avoid mistakes, complications were classified as catastrophic, major and minor, as defined by Cook and colleagues (Cook et al., 2010). In the present study, 33.5% of surgeries suffered a minor complication, with tibial tuberosity fractures and fissures described in 84.57% of cases. These results are not conforming to the minor complication rates reported by Beer for traditional TTA, who recorded 11.6% of minor complications (Beer et al., 2018). This evidence cannot be generalised to the new TTAT since the rationale of osteotomy, the spreader and the fixation system employed in these techniques are substantially different from the original TTA, leading to a different risk of complications. Moreover, the major complications reported accounted for 10.67%, among which tibial tuberosity fractures and fissures requiring revision surgery accounting for 6%. Unlike previously published studies, late meniscal injuries requiring second surgery were not counted. Probably, if included, the major complication rate would be higher. Nevertheless, our results align with a previous systematic review of traditional TTA, where major complications accounted for 13.2% (Beer et al., 2018). This evidence highlights that the risk of requiring surgical revision is the same for traditional and new-generation TTA.

2.2.4 Conclusions

The aim of this systematic review is to summarise the currently available literature about new generation TTAT according to PRISMA guidelines. The main limitation is the lack of randomised, controlled clinical trials with a large study population and univocal data collection about preoperative planning, outcome, and complications. Our results show that the incidence of minor complications is higher than previously reported for traditional TTA. Including recently developed techniques may have conditioned this result, as experience with these techniques has not yet been accumulated over a longer period of time. Conversely, the incidence of late meniscal tears is lower for new generation TTAT than for traditional TTA, but most of the included studies only recorded data in perioperative and short-term follow-up. Further studies with prospective designs of new-generation TTAT are needed to support the hypothesis that these techniques may reduce the rate of late meniscal tears.

Aragosa, F., Caterino, C., Della Valle, G., & Fatone, G. (2022). Tibial Tuberosity Advancement Techniques (TTAT): A Systematic Review. *Animals*, *12*(16), 2114. https://doi.org/10.3390/ani12162114

Arican, M., Parlak, K., & Sahin, H. (2017). Evaluation and application of the TTA-rapid method in dogs with cranial cruciate ligament rupture. *Acta Vet Beograd*, *67*. 238–253.

Beer, P., Bockstahler, B., & Schnabl-Feichter, E. (2018). Tibial plateau leveling osteotomy and tibial tuberosity advancement - A systematic review. *Tierarztliche Praxis Ausgabe K: Kleintiere - Heimtiere*, *46*(4), 223–235. https://doi.org/10.15654/TPK-170486

Bergh, M. S., Sullivan, C., Ferrell, C. L., Troy, J., & Budsberg, S. C. (2014). Systematic review of surgical treatments for cranial cruciate ligament disease in dogs. *Journal of the American Animal Hospital Association*, *50*(5), 315–321.

Boudrieau, R. J. (2009). Tibial plateau leveling osteotomy or tibial tuberosity advancement? *Veterinary Surgery*, *38*(1), 1–22.

Brown, N. P., Bertocci, G. E., & Marcellin-Little, D. J. (2015). Canine stifle biomechanics associated with tibial tuberosity advancement predicted using a computer model. *Veterinary Surgery*, *44*(7), 866–873.

Brown, N. P., Bertocci, G. E., & Marcellin-Little, D. J. (2017). Canine cranial cruciate ligament deficient stifle biomechanics associated with extra-articular stabilization predicted using a computer model. *Veterinary Surgery*, *46*(5), 653–662.

Burns, C. G., & Boudrieau, R. J. (2008). Modified tibial tuberosity advancement procedure with tuberosity advancement in excess of 12 mm in four large breed dogs with cranial cruciate ligament-deficient joints. *Veterinary and Comparative Orthopaedics and Traumatology*, *21*(03), 250–255.

Cadmus, J., Palmer, R. H., & Duncan, C. (2014). The Effect of Preoperative Planning Method on Recommended Tibial Tuberosity Advancement Cage Size. *Veterinary Surgery*, *43*(8), 995–1000. https://doi.org/10.1111/j.1532-950X.2014.12126.x

Campbell, M., McKenzie, J. E., Sowden, A., Katikireddi, S. V., Brennan, S. E., Ellis, S., Hartmann-Boyce, J., Ryan, R., Shepperd, S., Thomas, J., Welch, V., & Thomson, H. (2020). Synthesis without meta-analysis (SWiM) in systematic reviews: reporting guideline. *BMJ*, *368*. l6890. https://doi.org/10.1136/bmj.l6890

Chong, W. L. (2019). Tibial Diaphyseal Fracture Rates Following Tibial Tuberosity Advancement Rapid (TTAR) and Traditional Tibial

Tuberosity Advancement (tTTA). *Veterinary Evidence*, *4*(1).
Cook, J. L., Evans, R., Conzemius, M. G., Lascelles, B. D. X., McIlwraith, C. W., Pozzi, A., Clegg, P., Innes, J., Schulz, K., & Houlton, J. (2010). Proposed definitions and criteria for reporting time frame, outcome, and complications for clinical orthopedic studies in veterinary medicine. *Veterinary Surgery*, *39*(8), 905–908.
Della Valle, G., Caterino, C., Aragosa, F., Micieli, F., Costanza, D., Di Palma, C., Piscitelli, A., & Fatone, G. (2021). Outcome after Modified Maquet Procedure in dogs with unilateral cranial cruciate ligament rupture: Evaluation of recovery limb function by use of force plate gait analysis. *PLoS ONE*, *16*(8), 1–11. https://doi.org/10.1371/journal.pone.0256011
Etchepareborde, S., Brunel, L., Bollen, G., & Balligand, M. (2011). Preliminary experience of a modified maquet technique for repair of cranial cruciate ligament rupture in dogs. *Veterinary and Comparative Orthopaedics and Traumatology*, *24*(3), 223–227. https://doi.org/10.3415/VCOT-10-01-0012
Garcia Querol, E. (2020). *CTWO VS. FUSION-TTA as a surgical treatment to repair the cranial cruciate ligament rupture in dogs*.
Higgins, J. P. T., Thomas, J., Chandler, J., Cumpston, M., Li, T., Page, M. J., & Welch, V. A. (2019). *Cochrane handbook for systematic reviews of interventions*. John Wiley & Sons.
Hoffmann, D. E., Miller, J. M., Ober, C. P., Lanz, O. I., Martin, R. A., & Shires, P. K. (2006). Tibial tuberosity advancement in 65 canine stifles. *Veterinary and Comparative Orthopaedics and Traumatology*, *19*(04), 219–227.
Jin, D. W., Peck, J. N., Tano, C. A., & Morgan, M. J. (2019). Discrepancy between true distance of tibial tuberosity advancement and cage size: An ex vivo study. *Veterinary Surgery*, *48*(2), 186–191. https://doi.org/10.1111/vsu.13135
Kapler, M. W., Marcellin-Little, D. J., & Roe, S. C. (2015). Planned wedge size compared to achieved advancement in dogs undergoing the modified Maquet procedure. *Veterinary and Comparative Orthopaedics and Traumatology*, *28*(6), 379–384. https://doi.org/10.3415/VCOT-15-02-0026
Knebel, J., Eberle, D., Steigmeier-Raith, S., Reese, S., & Meyer-Lindenberg, A. (2020). Outcome after Tibial Plateau Levelling Osteotomy and Modified Maquet Procedure in Dogs with Cranial Cruciate Ligament Rupture. *Veterinary and Comparative*

Orthopaedics and Traumatology, *33*(3), 189–197. https://doi.org/10.1055/s-0040-1701502

Lafaver, S., Miller, N. A., Stubbs, W. P., Taylor, R. A., & Boudrieau, R. J. (2007). Tibial tuberosity advancement for stabilization of the canine cranial cruciate ligament-deficient stifle joint: surgical technique, early results, and complications in 101 dogs. *Veterinary Surgery*, *36*(6), 573–586.

Lefebvre, M. D., Broux, O. R., Barthélémy, N. P., Hamon, M., Moyse, E. V, Bouvy, B. M., & Balligand, M. H. (2018). Risk factors for tibial damage associated with the modified Maquet technique in 174 stifles. *Veterinary Surgery*, *47*(1), 30–35.

Livet, V., Baldinger, A., Viguier, É., Taroni, M., Harel, M., Carozzo, C., & Cachon, T. (2019). Comparison of outcomes associated with tibial plateau levelling osteotomy and a modified technique for tibial tuberosity advancement for the treatment of cranial cruciate ligament disease in dogs: a randomized clinical study. *Veterinary and Comparative Orthopaedics and Traumatology*, *32*(04), 314–323.

Maquet, P. (1976). Tibial tuberosity advancement. *Clin Orthop Rel Res*, *115*. 225–230.

McCartney, W., Ober, C., Benito, M., & MacDonald, B. (2019). Comparison of tension band wiring and other tibial tuberosity advancement techniques for cranial cruciate ligament repair: an experimental study. *Acta Veterinaria Scandinavica*, *61*(1), 44. https://doi.org/10.1186/s13028-019-0481-1

Medeiros, R. M., Silva, M. A. M., Teixeira, P. P. M., Dias, L., Chung, D. G., Zani, C. C., Feliciano, M. A. R., Da Conceicao, M., Machado, M. R. F., & Rocha, A. G. (2016). Use of castor bean polymer in developing a new technique for tibial tuberosity advancement for cranial cruciate ligament rupture correction in dogs. *Veterinární Medicína*, *61*(7), 382–388.

Millet, M., Bismuth, C., Labrunie, A., Marin, B., Filleur, A., Pillard, P., Sonet, J., Cachon, T., & Etchepareborde, S. (2013). Measurement of the patellar tendon-tibial plateau angle and tuberosity advancement in dogs with cranial cruciate ligament rupture. *Vet Comp Orthop Traumatol*, *26*(06), 469–478.

Montavon, P. M., Damur, D. M., & Tepic, S. (2002). Advancement of the tibial tuberosity for the treatment of the cranial cruciate ligament deficient stifle. *Proceedings of the 1st World Orthopaedic Veterinary Congress*, 152.

Moore, E. V., Weeren, R., & Paek, M. (2020). Extended long-term radiographic and functional comparison of tibial plateau leveling osteotomy vs tibial tuberosity advancement for cranial cruciate ligament rupture in the dog. *Veterinary Surgery*, *49*(1), 146–154. https://doi.org/10.1111/vsu.13277

Munn, Z., Barker, T. H., Moola, S., Tufanaru, C., Stern, C., McArthur, A., Stephenson, M., & Aromataris, E. (2019). Methodological quality of case series studies: An introduction to the JBI critical appraisal tool. *JBI Database of Systematic Reviews and Implementation Reports*, 1–7. https://doi.org/10.11124/JBISRIR-D-19-00099

Ness, M. G. (2016). The Modified Maquet Procedure (MMP) in Dogs: Technical Development and Initial Clinical Experience. *Journal of the American Animal Hospital Association*, *52*(4), 242–250. https://doi.org/10.5326/JAAHA-MS-6304

Ober, C. A., Factor, G., Meiner, Y., Segev, G., Shipov, A., & Milgram, J. (2019). Influence of tibial plateau leveling osteotomy and tibial tuberosity advancement on passive laxity of the cranial cruciate deficient stifle in dogs. *Veterinary Surgery*, *48*(3), 401–407.

Page, M. J., Moher, D., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., Shamseer, L., Tetzlaff, J. M., Akl, E. A., Brennan, S. E., Chou, R., Glanville, J., Grimshaw, J. M., Hróbjartsson, A., Lalu, M. M., Li, T., Loder, E. W., Mayo-Wilson, E., Mcdonald, S., … Mckenzie, J. E. (2021). PRISMA 2020 explanation and elaboration: Updated guidance and exemplars for reporting systematic reviews. *The BMJ*, *372*. https://doi.org/10.1136/bmj.n160

Pozzi, A., Litsky, A. S., Field, J., Apelt, D., Meadows, C., & Johnson, K. A. (2008). Pressure distributions on the medial tibial plateau after medial meniscal surgery and tibial plateau levelling osteotomy in dogs. *Veterinary and Comparative Orthopaedics and Traumatology*, *21*(01), 8–14.

Retallack, L. M., & Daye, R. M. (2018). A modified Maquet-tibial tuberosity advancement technique for treatment of canine cranial cruciate ligament disease: Short term outcome and complications. *Veterinary Surgery*, *47*(1), 44–51. https://doi.org/10.1111/vsu.12733

Roydev, R., & Goranov, N. (2021). Long-Term Clinical and Goniometric Follow-Up of TTA Rapid Surgery in Dogs with Cranial Cruciate Ligament Rupture. *Acta Veterinaria Eurasia*, *47*(3), 154–161.

Samoy, Y., Verhoeven, G., Bosmans, T., Van der Vekens, E., de Bakker, E., Verleyen, P., & Van Ryssen, B. (2015). TTA rapid: description of the technique and short term clinical trial results of the first 50 cases. *Veterinary Surgery*, *44*(4), 474–484.

Serrani, D., Picavet, P. P., Marti, J., Bouvy, B., Balligand, M., & Witte, P. G. (2022). Tibial Plateau Leveling Following Tibial Tuberosity Advancement : A Case Series. *Veterinary Sciences*.

Skinner, O. T., Kim, S. E., Lewis, D. D., & Pozzi, A. (2013). In vivo femorotibial subluxation during weight-bearing and clinical outcome following tibial tuberosity advancement for cranial cruciate ligament insufficiency in dogs. *The Veterinary Journal*, *196*(1), 86–91.

Slocum, B., & Slocum, T. D. (1993). Tibial plateau leveling osteotomy for repair of cranial cruciate ligament rupture in the canine. *Veterinary Clinics of North America: Small Animal Practice*, *23*(4), 777–795.

Tepic, S., Damur, D. M., & Montavon, P. M. (2002). Biomechanics of the stifle joint. *Proceedings of the 1st World Orthopaedic Veterinary Congress*, 189–190.

Terreros, A., & Daye, R. M. (2021). Prospective Evaluation of a Citrate-Based Biomaterial Wedge for a Modified Maquet Procedure in the Treatment of Cranial Cruciate Ligament Rupture in Dogs. *Veterinary and Comparative Orthopaedics and Traumatology*, *34*(2), 137–143. https://doi.org/10.1055/s-0040-1719058

Torrington, A.., Hopmans, J.., & Al., E. (2015). Tibial tuberosity advancement 2: current data from multicenter clinical trial. *Kyon Symposium*, April 24-26.

Trisciuzzi, R., Fracassi, L., Martin, H. A., Monopoli Forleo, D., Amat, D., Santos-Ruiz, L., De Palma, E., & Crovace, A. M. (2019). 41 Cases of Treatment of Cranial Cruciate Ligament Rupture with Porous TTA: Three Years of Follow Up. *Veterinary Sciences*, *6*(1), 18.

Voss, K., Damur, D. M., Guerrero, T., Haessig, M., & Montavon, P. M. (2008). Force plate gait analysis to assess limb function after tibial tuberosity advancement in dogs with cranial cruciate ligament disease. *Veterinary and Comparative Orthopaedics and Traumatology: V.C.O.T*, *21*(3), 243–249.

Zhalniarovich, Y., Sobolewski, A., Waluś, G., & Adamiak, Z. (2018). Evaluation, Description of the Technique, and Clinical Outcomes After Tibial Tuberosity Advancement with Cranial Fixation (TTA CF) for Cranial Cruciate Ligament Rupture in 22 Dogs. *Topics in Companion Animal Medicine*, 33(3), 65–72.

Chapter 3

Methods to measure the amount of TTA in the preoperative planning of TTAT

Comparison and Interobserver reliability

In reviewing the literature on new-generation TTAT, we realised that there is limited evidence on surgical planning. Among the methods used to evaluate the advancement required to achieve a postoperative PTA of 90° ± 5, the common tangent method appears the most selected. However, this method is not very reliable and seems to lead to undercorrection (Cadmus et al., 2014; Millet et al., 2013). This is confirmed by our results, as only 78.7% of surgeries achieved a final PTA within the satisfactory range. For these reasons, we decided to further investigate the reliability of several preoperative measurement methods.

3.1 Reliability of methods to measure the amount of tibial tuberosity advancement in the preoperative planning of TTAT

The tibial tuberosity advancement purpose is to reduce the PTA to 90° (Montavon et al., 2002). To achieve this, different preoperative measurement methods have been proposed to assess the required advancement and have been evaluated for comparability, reliability, and clinical efficacy. All of these previous studies suggest that the measurement method may influence the value of the desired advancement and show a theoretical discrepancy between the preoperatively calculated PTA and the postoperative one (Cadmus et al., 2014; Etchepareborde, Mills, et al., 2011; Kapler et al., 2015).
As previously reported, a PTA of 90° ± 5° may be sufficient to adequately neutralize tibiofemoral shear forces, but suboptimal postoperative PTA results in instability after TTA (Skinner et al., 2013). This may explain the meniscal tear rates of 5% after TTA and up to 28% without meniscal release (Millet et al., 2013). Although this concept is widely accepted in dogs, it is largely based on a two-dimensional mathematical model of the human knee. Its validity in dogs has been undermined to some extent by the findings of Apelt et al. (2007). They developed a three-dimensional mathematical model of the canine stifle and demonstrated that the CrCL is not loaded at any point during the stance phase. These data suggest that a biomechanically relevant “crossover point” might not exist in dogs, casting some doubt upon the validity of the assumed 90° endpoint for TTA surgery (Apelt et al., 2007).
Radiological methods described for determining the advancement distance for the tibial tuberosity include the conventional method used for traditional TTA planning (Montavon et al., 2002), a correction method (Etchepareborde, Mills, et al., 2011), the Common Tangent method (CT) (Dennler et al., 2006), the Tibial Anatomy-based Method (TAM) (Ness, 2016), the modified TTA planning method (Kapler et al., 2015), the Bielecki method (BF) (Bielecki et al., 2014) and the osteotomy axis method (Pillard et al., 2017). A previous study compared the use of transparent overlays to determine the required cage size and imaging software to perform a virtual TTA (Cadmus et al., 2014). Virtual TTA was performed such that PTA was equal to 90°, and the resulting osteotomy gap is measured at the level of cage placement to determine the proper advancement cage size. Based on these results, the transparent overlay method appears to underestimate the size of the advancement cage required to achieve PTA = 90°. Furthermore,

both measurement methods for TTA planning led to different cage size recommendations in 86% of the evaluated radiographs, resulting in inconsistent functional outcomes. Therefore, there are differences between surgeons in the choice of cage size for the same dog (Cadmus et al., 2014).
As regards the **conventional method**, the required amount of advancement is measured along a line parallel to the tibial plateau slope (Montavon et al., 2002). Nevertheless, the displacement of the tibial tuberosity does not follow the same pattern for conventional TTA and new generation TTAT. Because the tibial crest is not proximally translated and is advanced in only a curvilinear fashion, the methods described for the conventional TTA might not be adapted to TTAT. For this reason, Etchepareborde et al. described an alternative planning method, the **correction method**, in which the amount of advancement needed was measured in a cranial direction perpendicular to the tibial mechanical axis (Etchepareborde, Mills, et al., 2011). Nevertheless, the results of Pillard et al. (2016) revealed that both radiographic methods of measuring advancement did not result in a reduction from PTA to near 90° in 24 canine stifle joints evaluated. Conventional method resulted in postoperative PTAs systematically higher than those achieved with use of the correction method, which were systematically higher than 90°. In addition, the degree of underestimation of the advancement distance determined by the conventional method increased with TPA; thus, surgery would fail to neutralize femorotibial shear forces at stance when either radiological method is used. Both methods of measuring advancement distance led to the same cage size recommendations as those obtained with true advancement distance in only 4% and 17% of the knee joints evaluated, respectively. The conventional and correction advancement measurements resulted in the same cage size recommendations in only 46% of stifle joints (Pillard et al., 2016).
The required TTA could also be determined by the **common tangent technique** described by Dennler et al. (2006), which is based on the evidence that the tibial thrust is neutral when the patellar tendon is perpendicular to the tibial plateau (Montavon et al., 2002) and on the assumption that this should be achieved at a stifle angle of 135°, which resemble the mid-stance phase of the gait cycle (Dennler et al., 2006). This method disregards the need of the TPA to determinate the necessary advancement. Subsequently described methods also measure the amount of advancement needed in a cranial direction (Kapler et al., 2015; Ness, 2016).
A significant difference in the **Tibial Anatomy-based Method** is the reliance on tibial landmarks exclusively (Ness, 2016). Furthermore, this

method does not require the stifle to be positioned at an angle of 135° for radiography, avoiding the inaccuracy created by tibial subluxation, as demonstrated by Bielecki et al. (Bielecki et al., 2014). This radiographic method shows a good, short-term clinical outcome in most cases, and none of the complications are attributed to over or under-advancement of the tibial tuberosity (Ness, 2016). Although TAM does not account of breed or individual differences in stifle joint angle in the mid-stance phase, this is also true for other standard methods of calculating the required amount of TTA (Butterworth & Kydd, 2017).

The **modified TTA planning method** described by Kapler et al. accounts for anticipated distal translation of the patella after MMP (Kapler et al., 2015). In this method, the line drawn perpendicular to the tibial slope is located approximately 3 mm distal to the proximal insertion of the PT along the patellar tendon axis. This method was also compared to TAM by Kapler et al. and no significant difference was found in wedge sizes recommendation. The authors suggested increasing the measured wedge size by 30% to compensate for the underestimation found. However, this correction has not been evaluated to establish its impact on radiographic or clinical outcomes (Kapler et al., 2015).

The **Bielecki method** defined the impact of femorotibial subluxation on these measurements. Using linear regression, they defined how much additional TTA would be required for each millimeter of subluxation and developed a formula to calculate the necessary addition to measured TTA for knee joints with cranial tibial subluxation (Bielecki et al., 2014). Previous studies had emphasized the importance of positioning the tibia without subluxation (Montavon et al., 2002), as this could lead to a significant decrease in measured advancement (Apelt et al., 2007). This decrease could potentially lead to persistent postoperative instability of the knee joint (Bielecki et al., 2014).

More recently, Pillard and colleagues have developed a new method that takes into account the position and length of the osteotomy, the distal translation of the patella, and the amount of advancement cage placement along the osteotomy site. The distance by which the tibial tuberosity should be advanced to achieve reduction of the PTA to 90° was measured along a line perpendicular to the planned osteotomy axis. The **osteotomy axis method** was also compared to true advancement measurements obtained with MMT in this ex vivo study (Pillard et al., 2017). The method described in this study, in which the line perpendicular to the tibial plateau was placed 5 mm distal to the proximal insertion of the patellar tendon, resulted in planning measurements that closely matched true advancement measurements after PTA reduction to 90 ± 1°, suggesting that this is an excellent method to determine the required amount of advancement (Pillard et al., 2017).

Table 3.1 Summary of techniques developed to measure required tibial tuberosity advancement for traditional TTA and TTAT. Methods included in this study are highlighted.

Technique	**Year**	**Authors**
Conventional method	2002	Montavon et al.
Common Tangent Method	**2006**	**Dennler et al.**
Correction method	2011	Etchepareborde et al.
Bielecki method	**2014**	**Bielecki et al.**
modified TTA planning method	**2015**	**Kapler et al.**
Tibial Anatomy-based Method	2016	Ness et al.
Osteotomy axis method	2017	Pillard et al.

In summary, despite advances have been made in preoperative measurement methods, a discrepancy does exist between the desired tibial tuberosity advancement measured preoperatively and the actual advancement of the tibial tuberosity surgically carried out (Bielecki et al., 2014; Pillard et al., 2017). For this reason, we decided to further investigate the reliability between preoperative measurements methods, including CT as it is the most widely used in reviewed literature (Aragosa et al., 2022), TAM because of its promising results and BF, as this formula has not been used in any previous comparative study. Conversely, transparent overlays, conventional and correction methods were excluded as their poor reliability has been previously confirmed (Cadmus et al., 2014; Etchepareborde, Mills, et al., 2011; Pillard et al., 2016). Finally, modified TTA planning method was not counted because when compared to TAM no significant difference was found (Kapler et al., 2015). To the Authors' knowledge no previous study investigated CT, TAM and BF in terms of comparison and reliability. The aim of this retrospective study was to analyse CT, TAM and BF to compare interobserver reliability and assess differences in the amount of TTA measured.

3.1.1 Materials and Methods

The medical records of adult dogs with rCCL referred to the Veterinary Teaching Hospital of University of Naples between 2013 and 2019 were retrospectively analysed. We included all preoperative mediolateral (ML) radiographic projections of dogs underwent MMP. Radiographs were included if the joint angle was close to 135° and if the superimposition of femoral condyles was < 2 mm. All radiographs were obtained under general anaesthesia, collimated with beam centred over the stifle, including distal third of the femur, intercondylar eminence above the tibial plateau, the entire tibia and talocrural joint. The observes independently evaluated and scored the OA degree for each stifle, assessing 11 points in the ML view and grading on a 4-grade scale (Mager, 2000; Matis, 2005; Wessely et al., 2017). The observers were blinded to age, weight, or breed of the dogs for the radiographs they were analysing. The overall OA score was calculated as the sum of scores for each assessment point and reported as a mean ± SD.
All measurements were performed using a digital radiographic viewing program (Horos, version 3.3.6., horosproject.org) by three observers represented by a certified surgeon (Ob1), a PhD student (Ob2) and an intern (Ob3). Observers, independently and blinded to the assessment of other observers, measured the amount of advancement of tibial tuberosity with three different methods (CT, TAM and BF). Before starting the experiment, the Ob3 was adequately trained to use the different measurement methods included. The radiographic images were submitted to the observers in three different measurement session, one for each method, at distance of one week and each time randomly archived in a file folder. Measurement methods were applied as previously described and summarized below:

- For CT, firstly observers drew two circles representing the femoral and tibial condyles, marking the centre. Next, they connected the two centres with a line and drew the line perpendicular to that, defined as the common tangent. The angle between common tangent and the line drawn from the caudal margin of patella to its insertion on the tibial tuberosity, corresponding to PTA_{CT}. To measure the amount of advancement required observers considered the distance between the tibial tuberosity and the line perpendicular to common tangent starting from the cranial margin of the patella (Dennler et al., 2006).
- For TAM the functional axis and the tibial plateau of the tibia were drawn. Secondly, from fuctional axis, a caudally directed 135° angle towards the femur was made. Next, a parallel line through the patellar insertion point on the tibial tuberosity was located. This line

intersected the tibial plateau line that was previously drawn. A perpendicular line to tibial plateau, starting from patellar insertion was placed and a parallel line through the intersection point was drawn. The distance between this line and the most cranial point of the tibial tuberosity, measured along a line perpendicular to the function axis, was the request advancement (Ness, 2016).

- For BF, the advancement measurement was performed by determining a line from the origin of the patellar ligament passing perpendicular to the tibial plateau and calculating the distance from the cranial-most point of the tibial tuberosity to that line. In order to assess the amount of tibial subluxation the center of femoral condyle, intercondylar eminence and tibial plateau were identified and marked. The length of tibial plateau (TPL) was recorded. Two line perpendicular to tibial plateau, one passed through the intercondylar eminence and the second passed through the center of femoral condyle were drawn. The subluxation was calculated as the distance (C) between these two lines. If the line through the center of femoral condyle was cranial to the line through the intercondylar eminence the subluxation amount had positive value, vice versa the value was negative (Bielecki et al., 2014). To define the necessary addition to the measured advancement taking in account the stifle subluxation, we applied this formula:

$$Addiction\ (mm) = 1.091\ x\ (TPL\ x\ 0.201) - C$$

All data were recorded using spreadsheet software (Microsoft Excel 2019. Microsoft Corporation, Redmond, WA) and imported into a software package (IBM® SPSS® Statistics, Version 26.0. IBM Corporation, Armonk, New York) used to perform the statistical analysis. Continuous variables were presented as mean, standard deviation (± SD) and range. After verifying the data were not normally distributed through Shapiro-Wilk test, Kruskal-Wallis test was used to assess the differences between OA scores, the interobserver reliability for each method and the agreement degree among techniques. Pairways multiple comparison test was used as post hoc test. The significance level for all variables was set at $p \leq 0.05$.
The interobserver reliability for TAM, CT and BF were assessed by using the interclass correlation coefficient (ICC). The ICC results were interpreted as follow: poor (ICC< 0.50), moderate (ICC 0.51 to 0.70), good (ICC 0.71 to 0.90), very good (ICC > 0.91).

3.1.2 Results

Thirty-three stifle radiographs of 24 dogs with rCCL were evaluated. The mean for age and weight were 63.7 ± 24.6 months (range 18-120) and 35.8 ± 8.1 kg (range 19.5-48.5), respectively. Breeds included were mixed breed (n = 8), Labrador Retriever (n = 4), Italian Cane Corso (n = 3), Rottweiler (n = 2), Pittbull (n = 2), Boxer (n = 1), Golden Retriever (n = 1), Bull Mastiff (n=1), Dogo Argentino (n=1), Italian Coarsehaired Pointer (n = 1).

Since data were not normally distributed, Kruskal-Wallis test and Pairways multiple comparison test were applied. Mean OA score was 18.4 ± 5.4 (range 11-35) for Ob1, 17.5 ± 4.4 (range 11-35) for Ob2, and 14.3 ± 2.9 (range 11-22) for Ob3. No statistical difference was detected between Ob1 and Ob2, while statistical differences were found between Ob1 and Ob3 ($p< 0.001$) and, Ob2 and Ob3 ($p< 0.001$).

Interobserver reliability was analysed for each method included. As regards CT, the sample average rank was 10 mm (range 0-20) for Ob1, 7.6 mm (range 1.2-17.7) for Ob2, and 6.32 mm (range 0-13.1) for Ob3 (Figure 3.1). A statistical difference was detected for CT between Ob1 and Ob3 ($p <0.001$) and between Ob1 and Ob2. No statistical differences between the observers were found for TAM, for which Ob1 obtained a mean value of 10 mm (range 3-13.5), Ob2 of 9.78 mm (range 3-15.1) and Ob3 of 9.98 mm (range 5.4-16) (Figure 3.2). When BF was applied for radiographic assessment, Ob1 got a median of 12.5 mm (range 0-19), Ob2 of 7.6 mm (range 3.4-26.6) and Ob3 of 11.92 mm (range 1.8-20.4) (Figure 3.3). For BF statistical differences were found between Ob2 and Ob3 ($p <00.5$) and between Ob1 and Ob2 ($p< 0.001$). Finally, the reliability of the three preoperative planning methods among observers was analyze by ICC, showed a slight moderate agreement for TAM (ICC= 0.491), and poor agreement for CT (ICC=0.279) and BF (ICC=0.252).

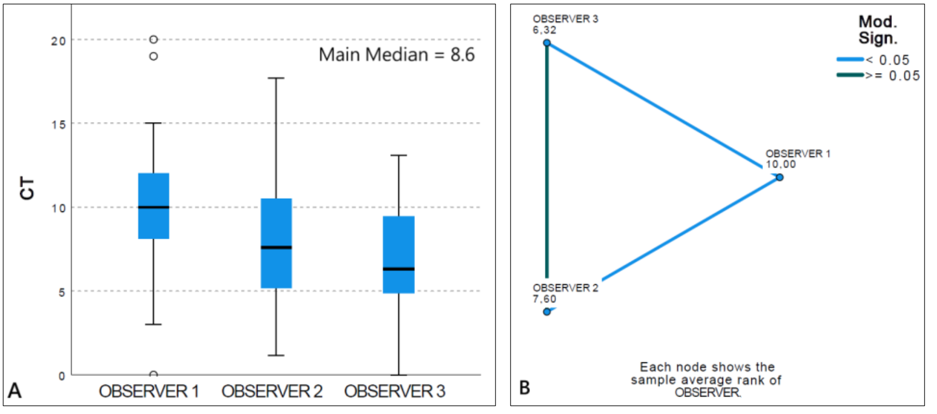

Figure 3.1 Kruskal-Wallis test (A) and Pairways multiple comparison test (B) for CT.

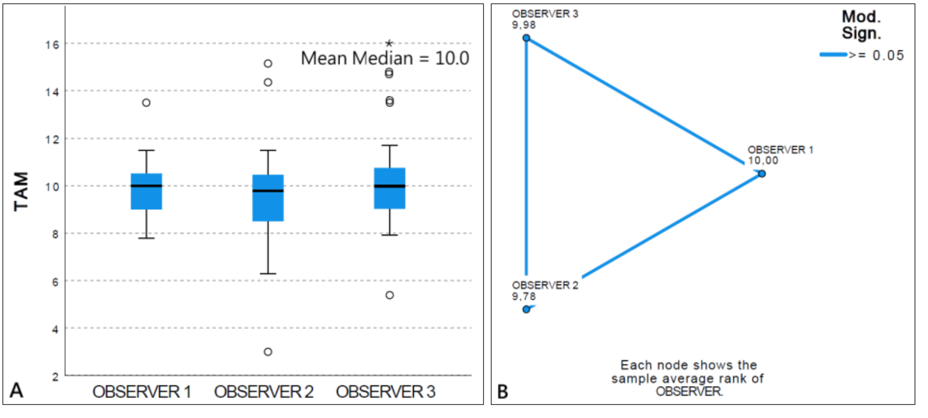

Figure 3.2 Kruskal-Wallis test (A) and Pairways multiple comparison test (B) for TAM.

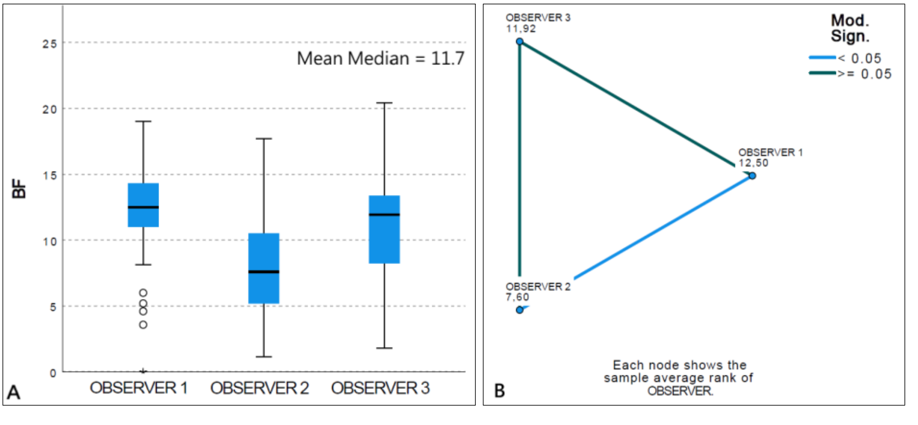

Figure 3.3 Kruskal-Wallis test (A) and Pairways multiple comparison test (B) for BF.

Mean value among observers for CT was 8.4 mm ± 4, for TAM was 9.9 mm ± 1.9 and for BF 10.2 mm ± 4.3. The agreement degree among the techniques showed differences between TAM and BF ($p< 0.01$) and, CT and BF ($p< 0.006$) with BF mean rank greater than others (Table 3.2).

Table 3.2 Pairways multiple comparison test for preoperative measurement methods to assess the amount of tibial tuberosity advancement required. Each line tests for the null hypothesis that the distributions for Samples are identical. Significance level is 0.05.

Samples	**Test statistics**	**Standard Error**	**Test statistics standard**	**Significance**	**Mod. Sign.**
CT vs TAM	-4.956	7.086	-0.699	0.484	1
TAM vs BF	-24.735	7.14	-3.464	<0.001	0.002
BF vs CT	-19.779	7.14	-2.77	0.006	0.017

3.1.3 Discussion

When applying a TTAT, the preoperative planning represents a fundamental step and affects the accuracy of the surgical procedure. The main objective of preoperative planning is to assess the amount of advancement required to obtain a postoperative PTA of 90°. Several methods have been developed for this purpose, but few studies have been published establishing reliability and degree of agreement between the different measurement methods. This study retrospectively investigated the OA score and three different TTAT preoperative planning methods, CT, TAM, and BF, in terms of comparison by three observers with different levels of experience. Moreover, for CT, TAM and BF the reliability interobserver was also assessed. In order to compare methods to assess TTA and evaluate reliability interobserver, we included CT, TAM and BF in this retrospective study. The interobserver reliability assesses the concordance degree when multiple observers use the same measurement technique in the same measurement set. By selecting observers with different levels of experience, we also aimed to determine the influence of this variable on the measurements.

The reason for CT choice lies in its extensive use among TTAT (Aragosa et al., 2022). Even if previous studies checked its poor interobserver reliability (Millet et al., 2013), this method has recently been recommended (Koch et al., 2022). We decided to include TAM because no report of its reliability exists in literature, but it was previously compared to modified TTA planning method and no difference was found in wedge selection between the two techniques (Kapler et al., 2015). According to data, both methods result in under-advancement, but we included TAM because in our opinion is the method easier to apply. As regards BF, to date the only report on its application and reliability is its first description, and its inclusion in this study is based on the excellent interobserver correlation reported (Bielecki et al., 2014).

Conversely, conventional method and the use of trasparency overlay have been more extensively explored and their lack of reliability confirmed by several reports (Cadmus et al., 2014; Etchepareborde, Mills, et al., 2011; Millet et al., 2013; Pillard et al., 2016). The correction method also results in undercorrection compared to the conventional method (Pillard et al., 2016). Therefore, these techniques were excluded.

It has been suggested that spontaneous structural failure of the CrCL is preceded by a clinically silent phase of primary OA, during which the progressive weakening of the cruciate ligament occurs (Niebauer & Restucci, 2023). Furthermore, osteoarthritic changes might hide anatomical landmarks of stifle joint (Caylor et al., 2001). Assuming that osteophyte formation could influence measurements of advancement required, we aimed to assess measurement variability among observers. The level of experience seems to affect the overall score for OA, as the less experienced observer scored significantly lower compared to Ob1 and Ob2. This result is not consistent with the study of Wessely et al. (2017), in which intraobserver and interobserver measurement variability was low. However, only a radiographic view (ML) was analysed in the present study, so our results are not fully comparable with previous data. However, several studies have found that the presence of osteophytes does not interfere with the identification of landmarks such as the tibial plateau and intercondylar eminence (Millet et al., 2013; Reif et al., 2004; Ritter et al., 2007). Although, observers reported difficulties in identifying anatomical features as the OA score increased, especially Ob3. Future studies upon the influence of OA on measurement of necessary advancement for TTAT planning are needed.

The main purpose of this phase of my research is the assessment of interobserver reliability of CT, TAM and BF, among observers with different levels of experience. Although CT is the most commonly used method for preoperative planning of TTAT (Aragosa et al., 2022), our results showed a significant influence of the observers experience, and a poor interobserver reliability consistent with the data previously reported (Millet et al., 2013). One reason for this may lie in the rationale of CT, which relies on the spatial relationship between tibia and femur, making it inherently unreliable (De Rooster & van Bree, 1999). The need to identify femoral and tibial landmarks and the use of specific graphic tools make the method poorly reproducible. In addition, the observers' different perception of the OA change, the proper position of the stifles at 135°, and the correct superimposition of the femoral condyles and of the tibial plateau, represent a critical point.

Experience did not affect the interobserver reliability for TAM, although slight moderate reliability was found. Despite its extensive use for TTAT, this method has been investigated only in terms of comparison (Aragosa et al., 2022; Kapler et al., 2015). Our results could be explained by the fact that TAM is based solely on tibial landmarks. As noted by observers of this study, this method is easier to perform compared to CT and BF, even for less experienced surgeons. Considering only tibial landmarks reduces the difficulties associated with identifying femoro-tibial relationship or positioning the limb correctly. In addition, since only two right angles need to be drawn after identifying the anatomical axis and the tibial plateau, the use of dedicated graphic tools is avoided, reducing potential errors.

In the present study, conflicting results arise from measurements made with BF, for which no influence of experience came up clearly. On the other hand, the poor interobserver reliability that came up from our results, does not confirm the excellent reliability reported in BF first description (Bielecki et al., 2014).

Furthermore, when comparing the results obtained with the different techniques, no significant difference was found between CT and TAM. This finding is supported by the study of Butterworth and colleagues, for which mean values of advancement measured using TAM corresponding closely to the ones obtained with CT by Samoy et al. in a population with similar bodyweight. However, no statistical analysis of the data of these two studies is available, so it remains only an authors' consideration (Butterworth & Kydd, 2017; Samoy et al., 2015). Conversely, BF showed no agreement with the other techniques included in the present study, with a significantly higher mean rank. This may be due to the addition to the measured advancement with the new developed formula, in order to correct femoro-tibial subluxation. As reported in the aforementioned study, there is a significant decrease in the advancement measure as the degree of subluxation increases (Bielecki et al., 2014). Among the methods considered, only TAM does not rely on the spatial femoro-tibial relationship, and the degree of subluxation should not affect measurements of TTA. Nonetheless, the measurements obtained with TAM were significantly lower than those obtained with BF.

This finding supports the study by DeRooster and VanBree (1999), which have assumed that any surgical planning method that relies upon the spatial relationship between tibia and femur could be inherently unreliable (De Rooster & van Bree, 1999).
The retrospectve design of this study represents a limit, as well as no consider intraobserver reliability. In addition, we did not account for anatomic variability in different races, so our results should be interpreted rationally.
In conclusion, when compared to CT and BF, TAM seems to be the easier preoperative planning method to perform and provides a more functionally accurate measurement of advancement required, but further studies are needed to prove this hypothesis. According to our results, none of the measurement methods investigated has good interobserver reliability, and the limitations are related to both the experience of the observer and the rationale of the different measurement methods developed. This study, anyway, paves the way to further investigations upon the effects of preoperative planning on true advancement obtained through TTAT.

Apelt, D., Kowaleski, M. P., & Boudrieau, R. J. (2007). Effect of tibial tuberosity advancement on cranial tibial subluxation in canine cranial cruciate-deficient stifle joints: an in vitro experimental study. *Veterinary Surgery*, *36*(2), 170–177.

Aragosa, F., Caterino, C., Della Valle, G., & Fatone, G. (2022). Tibial Tuberosity Advancement Techniques (TTAT): A Systematic Review. *Animals*, *12*(16), 2114. https://doi.org/10.3390/ani12162114

Bielecki, M. J., Schwandt, C. S., & Scharvogel, S. (2014). Effect of tibial subluxation on the measurements for tibial tuberosity advancement in dogs with cranial cruciate ligament deficiency: An ex vivo study. *Veterinary and Comparative Orthopaedics and Traumatology*, *27*(6), 470–477. https://doi.org/10.3415/VCOT-14-02-0018

Butterworth, S. J., & Kydd, D. M. (2017). TTA-Rapid in the treatment of the canine cruciate deficient stifle: short-and medium-term outcome. *Journal of Small Animal Practice*, *58*(1), 35–41.

Cadmus, J., Palmer, R. H., & Duncan, C. (2014). The Effect of Preoperative Planning Method on Recommended Tibial Tuberosity Advancement Cage Size. *Veterinary Surgery*, *43*(8), 995–1000. https://doi.org/10.1111/j.1532-950X.2014.12126.x

Caylor, K. B., Zumpano, C. A., Evans, L. M., & Moore, R. W. (2001). Intra- and interobserver measurement variability of tibial plateau slope from lateral radiographs in dogs. *Journal of the American Animal Hospital Association*, *37*(3), 263–268.

De Rooster, H., & van Bree, H. (1999). Radiographic measurement of craniocaudal instability in stifle joints of clinically normal dogs and dogs with injury of a cranial cruciate ligament. *American Journal of Veterinary Research*, *60*(12), 1567–1570.

Dennler, R., Kipfer, N. M., Tepic, S., Hassig, M., & Montavon, P. M. (2006). Inclination of the patellar ligament in relation to flexion angle in stifle joints of dogs without degenerative joint disease. *American Journal of Veterinary Research*, *67*(11), 1849–1854. https://doi.org/10.2460/ajvr.67.11.1849

Etchepareborde, S., Mills, J., Busoni, V., Brunel, L., & Balligand, M. (2011). Theoretical discrepancy between cage size and efficient tibial tuberosity advancement in dogs treated for cranial cruciate ligament rupture. *Veterinary and Comparative Orthopaedics and Traumatology*, *24*(01), 27–31. https://doi.org/10.3415/VCOT-10-01-0013

Kapler, M. W., Marcellin-Little, D. J., & Roe, S. C. (2015). Planned wedge size compared to achieved advancement in dogs undergoing the modified Maquet procedure. *Veterinary and Comparative Orthopaedics and Traumatology*, *28*(6), 379–384. https://doi.org/10.3415/VCOT-15-02-0026

Koch, D. A., Kiefer, O., & Richter, H. (2022). Comparison of four methods to determine cage width in tibial tuberosity advancement. *Schweizer Archiv Für Tierheilkunde*, *164*(2), 177–184.

Mager, F. W. (2000). *Zur Kniegelenkkarthrose des Hundes nach vorderer Kreuzbandruptur: ein retrospektiver Vergleich dreier Operationsmethoden*. Uitgever niet vastgesteld.

Matis, U. (2005). Radiographic evaluation of the progression of osteoarthritis after tibial plateau leveling osteotomy in 93 dogs. *Vet Comp Orthop Traumatol*, *2*. A32.

Millet, M., Bismuth, C., Labrunie, A., Marin, B., Filleur, A., Pillard, P., Sonet, J., Cachon, T., & Etchepareborde, S. (2013). Measurement of the patellar tendon-tibial plateau angle and tuberosity advancement in dogs with cranial cruciate ligament rupture. *Vet Comp Orthop Traumatol*, *26*(06), 469–478.

Montavon, P. M., Damur, D. M., & Tepic, S. (2002). Advancement of the tibial tuberosity for the treatment of the cranial cruciate ligament deficient stifle. *Proceedings of the 1st World Orthopaedic Veterinary Congress*, 152.

Ness, M. G. (2016). The Modified Maquet Procedure (MMP) in Dogs: Technical Development and Initial Clinical Experience. *Journal of the American Animal Hospital Association*, *52*(4), 242–250. https://doi.org/10.5326/JAAHA-MS-6304

Pillard, P., Livet, V., Cabon, Q., Bismuth, C., Sonet, J., Remy, D., Fau, D., Carozzo, C., Viguier, E., & Cachon, T. (2016). Comparison of desired radiographic advancement distance and true advancement distance required for patellar tendon–tibial plateau angle reduction to the ideal 90° in dogs by use of the modified Maquet technique. *American Journal of Veterinary Research*, *77*(12), 1401–1410.

Pillard, P., Livet, V., Cabon, Q., Bismuth, C., Sonet, J., Remy, D., Fau, D., Carozzo, C., Viguier, E., & Cachon, T. (2017). Evaluation of a new method to determine the tibial tuberosity advancement distance required to reduce the patellar tendon-tibial plateau angle to 90° with the modified Maquet technique in dogs. *American Journal of Veterinary Research*, *78*(4), 517–528. https://doi.org/10.2460/ajvr.78.4.517

Reif, U., Dejardin, L. M., Probst, C. W., DeCamp, C. E., Flo, G. L., &

Johnson, A. L. (2004). Influence of limb positioning and measurement method on the magnitude of the tibial plateau angle. *Veterinary Surgery*, *33*(4), 368–375.

Ritter, M. J., Perry, R. L., Olivier, N. B., Kim, S. Y., & Dejardin, L. M. (2007). Tibial plateau symmetry and the effect of osteophytosis on tibial plateau angle measurements. *Journal of the American Animal Hospital Association*, *43*(2), 93–98.

Samoy, Y., Verhoeven, G., Bosmans, T., Van der Vekens, E., de Bakker, E., Verleyen, P., & Van Ryssen, B. (2015). TTA rapid: description of the technique and short term clinical trial results of the first 50 cases. *Veterinary Surgery*, *44*(4), 474–484.

Skinner, O. T., Kim, S. E., Lewis, D. D., & Pozzi, A. (2013). In vivo femorotibial subluxation during weight-bearing and clinical outcome following tibial tuberosity advancement for cranial cruciate ligament insufficiency in dogs. *The Veterinary Journal*, *196*(1), 86–91.

Wessely, M., Brühschwein, A., & Schnabl-Feichter, E. (2017). Evaluation of intra-and inter-observer measurement variability of a radiographic stifle osteoarthritis scoring system in dogs. *Veterinary and Comparative Orthopaedics and Traumatology*, *30*(06), 377–384.

Chapter 4

Intraoperative evaluation of two measurements techniques for TTA

Ex-vivo study in dogs

To date, no definitive recommendation has been published for a preoperative planning method to achieve a PTA corresponding to 90°. Encouraged by the results of interobserver reliability, we decided to further investigate the effectiveness of TAM and CT intraoperatively to achieve the required advancement.

4.1 Comparison of two preoperative radiographic methods for TTA in dogs to achieve a postoperative PTA of 90°

Given the prevalence of CrCL disease, surgical techniques such as TTA and TPLO have gained increasing interest over the years (Vaughan, 2010). All of these techniques have been developed to restore joint stability and slow down secondary joint degeneration. In recent years, new surgical techniques have become part of TTAT. Unlike traditional TTA, the new generation techniques preserve the distal tibial hinge by an incomplete osteotomy so tibial tuberosity is advanced in a curvilinear fashion without proximal displacement (Pillard et al., 2016). Currently, the advancement required to achieve a postoperative PTA of 90° is assessed preoperatively and radiographically (Bielecki et al., 2014; Etchepareborde, Brunel, et al., 2011; Kapler et al., 2015; Ness, 2016; Pillard et al., 2017). Depending on surgical technique chosen, a cage or wedge, matching the required advancement measured, is inserted into the osteotomy to achieve the target PTA. Therefore, method to measure the intended advancement is a mandatory step for TTAT. Despite several methods have been developed to measure the tibial tuberosity advancement, the discrepancy between value obtained on radiogram and true advancement is widely confirmed in veterinary literature (Etchepareborde, Mills, et al., 2011; Jin et al., 2019; Meeson et al., 2018; Millet et al., 2013; Pillard et al., 2016; Skinner et al., 2013).
Several factors have been historically addressed to affect the measurement of the required advancement: limb positioning, TPA, anatomical factors, technique of advancement measurement and method of PTA assessment (Bush et al., 2011; Pillard et al., 2016). Tibial drawer, stifle joint extension angle, or method of stifle joint angle measurement are currently under investigation (Bush et al., 2011; Giansetto et al., 2022; Millet et al., 2013; Ševčík et al., 2021), but their effect on preoperative measurements of required advancement is still not completely clear. In a recent study, stifle angle during mid-stance phase was determined among different dog breeds, obtaining an angle close to 145°. The authors further assumed that planning the surgery on stifles in 135° extension could result in under-advancement of the tibial tuberosity (Giansetto et al., 2022). Furthermore, Bush and colleagues found that using different landmark methods to determine stifle angle resulted in different calculated advancements of the tibial tuberosity (Bush et al., 2011). Modifying stifle's angle during positioning or varying method to measure stifle angle, also alters the PTA and, accordingly, the calculated advancement. Similarly, the influence of femoro-tibial

subluxation on the measurements has been described, but as outlined in the previous chapter, the method developed to correct the measurements of TTA (BF) has a poor interobserver reliability (Bielecki et al., 2014). Nonetheless, this highlights the importance of limb positioning in assuring the accuracy of these measurements (Bielecki et al., 2014; Millet et al., 2013). As emphasised in the second phase of my research, all techniques except TAM require a radiograph in mediolateral view with the femorotibial joint flexed at 135°. Consequently, during the planning for the TTA, if the PTA is measured by a radiogram performed with a knee angle < 135°, a reduced advancement of the tibial tuberosity will be obtained, insufficient to neutralise the cranial tibial shear force. Similarly, at an angle greater than 135°, a greater advancement of the tibial tuberosity occurs, producing a caudally directed shear force (Apelt et al., 2007).

Currently, TTA is not recommended at TPA greater than 31° because of the risk of severe under-advancement (Etchepareborde, Mills, et al., 2011). As TPA increased, the measurement of advancement decreased and a greater discrepancy between preoperative measurements and postoperative outcome occurred (Etchepareborde, Mills, et al., 2011). Nevertheless, the percentage of under-advancement calculated on tibial models with a mean TPA of 24.4° ranged from 21% to 28% (Jin et al., 2019). However, it has been suggested that tibial conformation has a greater effect on the under-advancement of tibial tuberosity compared to the TPA (Meeson et al., 2018). One possible reason for the divergence between these studies is the morphological relationship between the insertion of the patellar tendon and the TPA, which was not investigated by Etchepareborde and colleagues.

With traditional TTA, several millimetres of proximal tibial tuberosity translation occur, while using MMP is not possible to shift the tibial tuberosity proximally because distal cortical hinge point is preserved. Therefore, the insertion of the patellar tendon is rotated cranially and is not allowed to move proximally, leading to patella baja. While distal displacement of the patella occurs in 15% of patients undergoing similar surgery in human medicine, no data on prevalence are available in veterinary medicine (Backstein et al., 2003). However, the degree of distal displacement of the patella increases with larger cage sizes. The clinical implications are currently unknown, but a relationship between patella baja and increased incidence of congenital lateral patellar luxation has been described in dogs (Neville-Towle et al., 2016). To date, no evidence upon the risk of postoperative lateral patellar luxation has been reported in literature (Della Valle et al., 2021). In the present study, the presence and

the effect of distal patellar displacement after MMP were not investigated, because we found no evidence of influence on advancement in literature and in a previous study made by our team (Della Valle et al., 2021).
The determination of the PTA is crucial to the resulting amount of TTA. The poor agreement between Tibial Plateau (PTA_{TP}) and common tangent (PTA_{CT}) methods to assess PTA is broadly recorded by several studies (Boudrieau, 2009; Hoffmann et al., 2011; Millet et al., 2013; Schwandt et al., 2006). To date, there is no definitive recommendation in the veterinary literature for methods to assess PTA. Nevertheless, this seems to have an impact on the measurement of required advancement. For the experiment described below, we chose to evaluate PTA using the tibial plateau method because it has good intraobserver and moderate interobserver reliability (Millet et al., 2013).
Measurement of the required advancement distance for the tibial tuberosity may also be influenced by the planning measurement method chosen. To date, all described methods for measuring the required advancement distance for the tibial tuberosity have not yielded the true advancement distance. This step of my PhD thesis aims to evaluate the validity of two preoperative radiographic planning methods (TAM and CT), to select the right wedge to achieve a final PTA of 90° in dogs using the MMP. We decided to include CT in this prospective study because of the lack of a report on its ability to achieve proper advancement. Conversely, TAM was selected based on the promising results shown in the previous chapter (Chapter 3), even if it appeared to underestimate the size of wedge needed to provide the desired advancement in a previous study (Kapler et al., 2015). Otherwise, we did not include BF in this experiment because it demonstrated the worst interobserver reliability when compared to CT and TAM.

4.1.1 Materials and Methods

Twenty knee joints from adult dogs (n=10), of mesomorphic breeds, weighing more than 20 kg, dead for reasons unrelated to this study were used. Furthermore, dogs with history or radiographical signs of trauma or skeletal disease were excluded. Samples were stored at - 20° C and then at room temperature for 6 hours before starting the experiment. The hindlimbs weren't disjointed to preserve real biomechanic. The sample was divided into 2 groups of 10 stifles, randomly assigned to the two measurement techniques (CT and TAM).
For each hindlimb a radiograph in ML prejection, centred over the stifle, was performed with the knee positioned at an angle of 135°. The position

was considered correct when the distal third of the femur, the intercondylar eminence above the tibial plateau, the entire tibia and talocrural joint were included and when the femoral and tibial condyles were superimposed (< 2 mm) in the radiolographic projection. Radiograms were used to measure the amount of advancement of the tibial tuberosity using two techniques: CT and TAM, performed as previously described. All measurements were performed using a digital radiographic viewing programme (Horos, version 3.3.6., horosproject.org) by a certified surgeon. The evaluator was unware of age, weight, or breed of the dogs for the radiographs he was assessing. The size of the wedge was selected based on the measurement of advancement of the tibial tuberosity obtained. The wedge chosen was the one closest to the measurement obtained radiographically, taking into account sizes commercially available (6, 7.5, 9, 10.5, 12 and 13.5 mm).

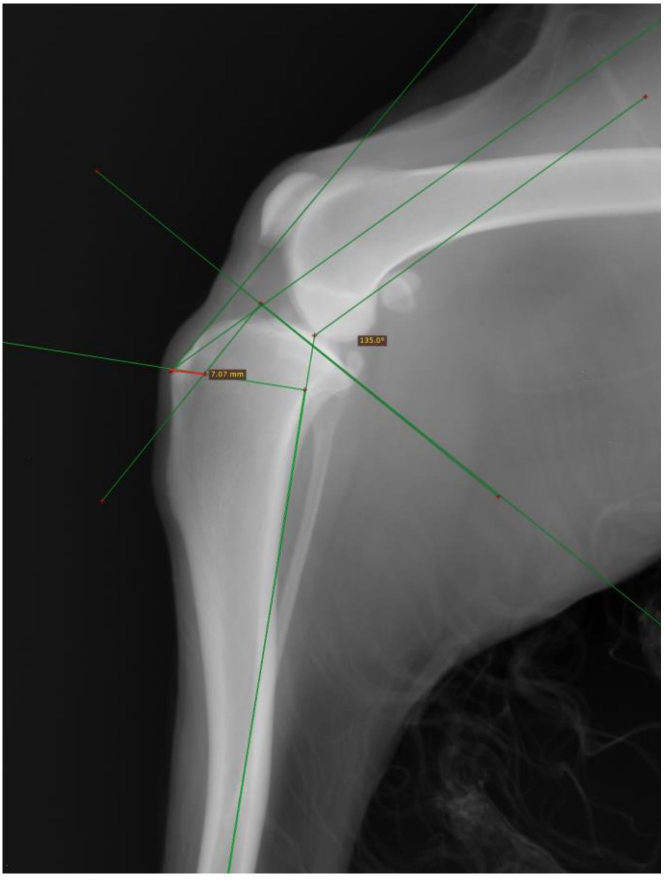

Figure 4.1 Measurement of the required advancement (in red) made by TAM.

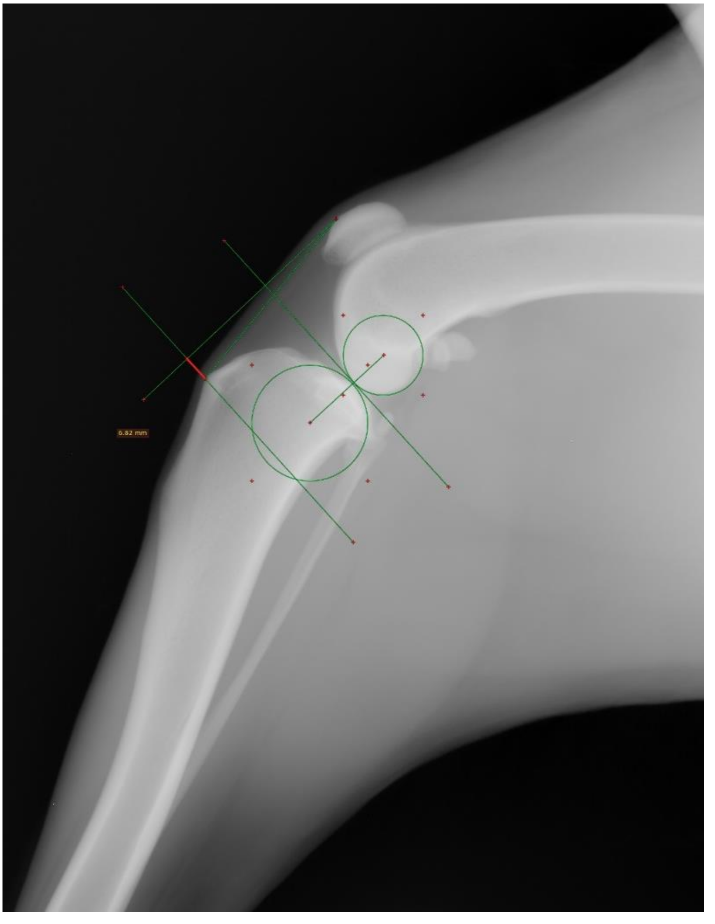

Figure 4.2 Measurement of the required advancement (in red) made by CT.

The surgical procedure, performed by an experienced surgeon, consisted of the MMP, relying on a novel implant material, Orthofoam, supplied as a preformed wedge which is used to advance and fix the tibial tuberosity (Ness, 2016). Advancement of the tibial tuberosity was obtained using a distractor, up to the size of the wedge chosen. To maintain and stabilize the advancement of the tibial tuberosity, a custom-made plastic wedge from a 3D printer (Anycubic i3 Mega, Anycubic, Tsim SHA TSUI, Kowloon) was used, which was the same shape and size as the Orthofoam MMP wedge that we would have chosen based on the measurements obtained (Figure 4.3). Performing the postoperative radiography allowed for the measurement of the PTA and the adequate position of the wedge. The measurements of preoperative and postoperative PTA were performed by using tibial plateau method (PTA_{TP}) and reported as mean ± SD (Montavon, 2002). First, we identified the tibial plateau slope and we measured the PTA_{TP} as the angle between it and the patellar tendon axis.

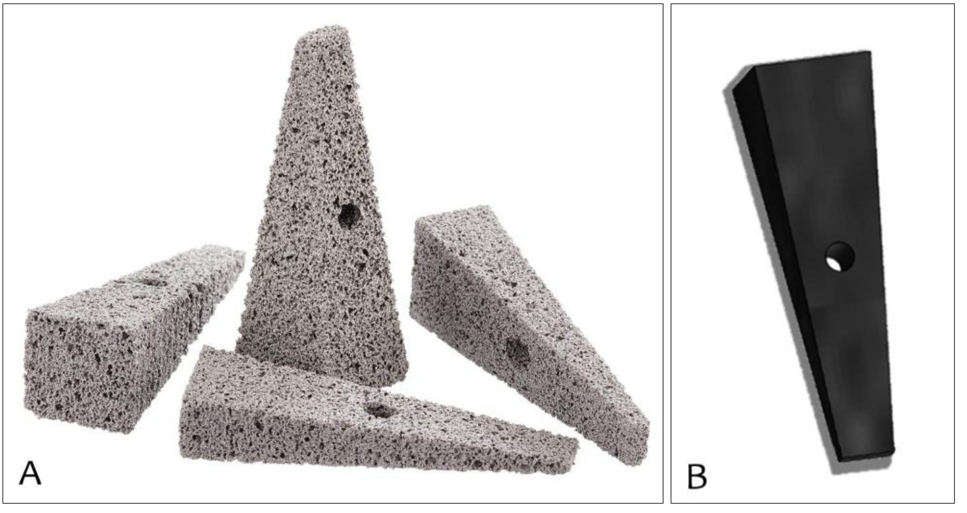

Figure 4.3 OrthoFoam™ MMP Wedge (A) (modified from www.orthomed.co.uk/product/orthofoam-mmp-wedge/) and custom made wedge (Anycubic i3 Mega) (B).

The correct location of the wedge (W) was assessed postoperatively by drawing a line corresponding to the osteotomy line, from the articular line to the Maquet hole (Mq). Then, three perpendicular lines corresponding to the proximal and distal edges of the wedge and passing through the insertion of PT on tibial tuberosity were traced. Finally, the distance between the Maquet hole and the distal edge of the wedge (Mq-W) was measured across the osteotomy line. The segment of osteotomy line between proximal edge of the wedge and patellar tendon insertion corresponded to W-PT. Both measurements were expressed in mm and reported as mean ± SD (Figure 4.4).

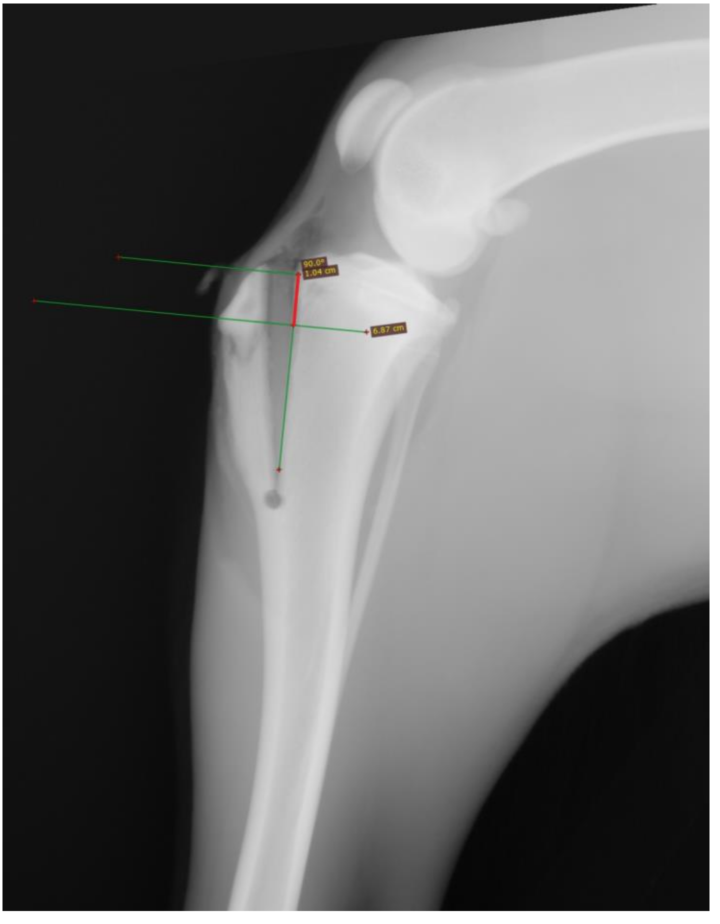

Figure 4.4 Line between proximal edge of the wedge and patellar tendon insertion corresponded to W-PT (in red).

Datas regarding preoperative and postoperative PTA, tibial tuberosity advancement measures, wedge size and position were recorded on a spreadsheet (Microsoft Excel 2019. Microsoft Corporation, Redmond, WA) and imported into a software package (IBM® SPSS® Statistics, Version 26.0. IBM Corporation, Armonk, New York) in order to perform the statistical analysis. Normal distribution was determined using the Shapiro-Wilk test. All continuous variables were expressed as mean ± SD and non-parametric as median (minimum value - maximum value). The difference between the two groups in preoperative and postoperative PTA were assessed with the Mann-Whitney test. The difference between preoperative and postoperative PTA of TAM and CT, respectively, was examined with the Wilcoxon test. The statistical significance level was set at $p<0.05$.

4.1.2 Results

Twenty stifle of adult dogs (n = 10) of mesomorphic breeds were included in this prospective ex-vivo study. The sample was randomly assigned to the two measurement techniques, 10 stifles for TAM and 10 stifles for CT, respectively. The mean weight of the subjects, expressed in kg, was 28.8 ± 5.4. All dogs included in the sample belonged to mesomorphic breeds.
The mean preoperative PTA was 95° ± 4.4 for TAM group and 97.6° ± 3.7 for CT group. No statistically significant difference was found in preoperative PTA between the two groups (p = 0.173).

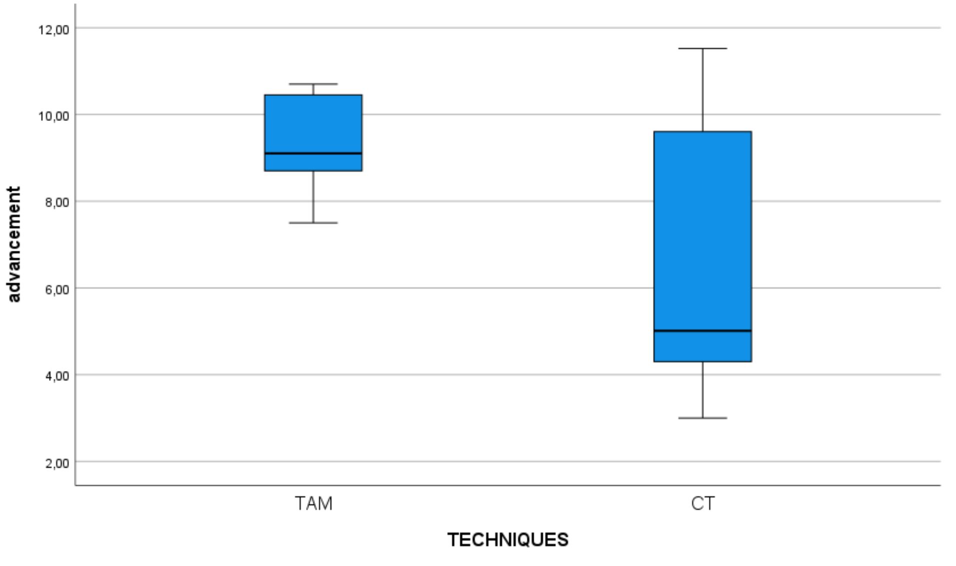

Figure 4.5 Values of advancements obtained using TAM and CT.

Measurements obtained with TAM yielded mean tibial tuberosity advancement values of 9.3 mm ± 1.2; those achieved with CT, on the other hand, gave mean advancement values of 6.5 mm ± 3.2 (Figure 4.5). Comparing advancements calculated by the two groups, no statistical difference was found (p = 0.07).
The average wedges selected by TAM and CT were 9.3 mm ± 1.2 and 8.4 mm ± 2.1, respectively. Among sizes, six 7.5 mm, six 9 mm, four 10.5 mm,

two 12 and two 6 mm wedges were used for MMP. The difference among wedges chosen was not significant (p = 0.16).
When comparing the advancement values and wedges selected for each group, a statistical difference was found only for CT (p = 0.013). The 90% of wedges chosen were larger than the advancement values assessed with CT on radiograms. For TAM group the 30% of advancement calculated totally corresponded to wedge applied and there was no overall difference between values (p = 0.499).
Postoperative PTA was 90.1° ± 3.7 for advancement measured with TAM and 88.8 mm ± 4.8 for CT, without significant statistical difference among groups (p = 0.622). In eight stifle joints in TAM group, the postoperative measured PTA was lower than preoperative one and only two stifles experienced an increase in PTA after surgery. In CT group, there was a decrease in PTA after MMP in 9 stifles and an increase in only one. In none of the included knee joints of both groups postoperative PTA was unchanged after surgery.
According to Wilcoxon test, there was no significant difference between preoperative and postoperative PTA for TAM (p = 0.059). Conversely, a statistical difference was found between preoperative and postoperative PTA for CT group (p = 0.007).
The position of wedges relative to the Maquet hole proved to be correct in both groups according to the surgical procedure proposed by Ness (Ness, 2016), with an average value of 4.7 mm ± 1.9. The distance between the proximal edge of the wedge and the insertion point of the patellar tendon averaged 12.1 mm ± 2.6. More precisely, mean Mq-W for TAM and CT were 3.9 ± 2 and 5.3 ± 1.6, respectively. The distribution for Mq-W was the same for the two groups examined (p = 0.298). Simultaneously, we found a mean W-PT of 11.2 ± 2.9 for TAM group and 12.9 ± 2.2 for CT one, and difference between groups was not significant (p = 0.245).

4.1.3 Discussion

The purpose of this cadaveric prospective study was to evaluate the efectiveness of TAM and CT in the preoperative planning of MMP to achieve a postoperative target PTA of 90°.
The TTA and its further adaptations as MMP are widely used to neutralize CTT in dogs with rCCL. The satisfactory clinical results of the MMP prompted us to further investigate its preoperative planning (Ness, 2016). The advancement of the tibial tuberosity is achieved in the MMP using a titanium foam wedge "OrthoFoam". Establishing the amount of

advancement of the tibial tuberosity is a fundamental step of the MMP as well as of TTAT in general. The goal of preoperative planning is to assess the amount of tibial tuberosity advancement required to achieve a postoperative PTA of 90° and to select the optimal wedge size to obtain this. Although the methods described are associated with reports of good clinical outcomes (Etchepareborde, Brunel, et al., 2011; Ness, 2016), other studies suggest that these methods do not determine the true advancement distance required to bring the PTA to the intended 90° (Kapler et al., 2015; Pillard et al., 2017). Historically, a PTA of 90° ± 5° has been considered adequate to neutralize tibiofemoral shear force (Etchepareborde, Mills, et al., 2011), but a suboptimal postoperative PTA and the resulting instability may explain the 4.3% of late meniscal tears after TTAT (Aragosa et al., 2022). This percentage results 28% for traditional TTA (Wolf et al., 2012), even though mesiscal release was not performed in either study. Additionally, in a recent study, the 70% of dogs with a mean PTA_{CT} of 89° after traditional TTA, showed persistent cranial tibial subluxation (Skinner et al., 2013). Probably this assumed critical point, might vary among breeds or suffer individual influences. However, it seems to not affect functional outcome, which results acceptable in most dogs after TTAT.

The aim of this study was to evaluate the validity of TAM and CT to return values of advancement to reach a target postoperative PTA of 90°, using canine knees of mesomorphic breeds without musculoskeletal diseases. To the authors' knowledge, this is the first report on the validity of CT for selecting the proper wedge to achieve the desired advancement. Although interobserver reliability was poor, we included this method to measure advancement because it is the most commonly chosen in preoperative planning of TTAT, followed by TAM (Aragosa et al., 2022). For the latter technique, a previous study reported 30% of underestimation of the size of wedge needed to provide appropriate advancement, but it was evaluated together with modified TTA planning method (Kapler et al., 2015).

Most measurement methods have been developed for traditional TTA (Dennler et al., 2006; Etchepareborde, Brunel, et al., 2011; Montavon et al., 2002), which is characterised by a different direction of advancement than TTAT. Moreover, several papers have already provided evidences on the ineffectiveness of these methods to achieve the appropriate advancement (Cadmus et al., 2014; Etchepareborde, Mills, et al., 2011; Pillard et al., 2016), for this reason we decided not to investigate these techniques any further.

We determined PTA_{TP} on preoperative radiograms because it is the method commonly used in our clinic and because it demonstrated a better intra- and interobserver reliability when compared to PTA_{CT} (Millet et al., 2013). By enrolling healthy subjects with similar morphologic characteristics, we obtained comparable preoperative PTAs between the two groups. In this way, we were able to evaluate the results of the two measurement methods on postoperative PTA minimising variability.
In our sample, the advancement amount obtained via TAM and CT did not differ significantly. This result confirms the results of the previous chapter, where no difference was found between the ranks of TAM and CT. However, in the aforementioned experiment we did not test the PTA, so an objective comparison cannot be made. Nevertheless, the data obtained from Ob3 seem to be very close to those obtained in this study.
Conversely, for CT a significant difference exists between amount of advancement calculated and wedges applied during MMP. In this group, 60% of the measurements were less than 5.3 mm, but since the wedge sizes customed for this experiment correspond to those commercially available, the smallest feasible size corresponded to 6 mm. For this reason, we used a 6 mm wedge even though the required feed was 3 mm. In fact, when analysing the data, a statistically significant difference between the advancement values and the selected wedge sizes resulted ($p = 0.013$). This limitation should be taken into account and the results interpreted critically. In contrast, the mean advancement values of the TAM group corresponded exactly to the wedge sizes selected for surgery, which greatly facilitates the application of this measurement technique in clinical practise.
It was found that the two groups did not differ in terms of postoperative PTA_{TP}. However, mean postoperative PTA obtained for TAM corresponded to the critical point of 90°, proving its ability to return proper advancement values. This did not confirm data provided by Kapler and colleagues, who reported that only the 53% of procedures resulted in a PTA within 90° ± 5°. In the present study, for both groups, the 80% of stifles had of postoperative PTA within the target range (90° ± 5) for a satisfactory clinical outcome. This is also confirmed by a study previously conducted by our team on a larger sample ($n = 35$), in which mean postoperative PTA resulted 89.7˚ after MMP (Della Valle et al., 2021).
Conversely, the average postoperative PTA for CT group was 88.8°, even though we significantly increased the average advancement value calculated to find the corresponding wedge in trade. Probably, the postoperative PTA would have been different if we had selected wedges closer to the

advancement value determined using CT. The absence of statistical difference between postoperative PTA values is also due to the selection of overlapping mean wedge sizes among the two groups. Indeed, the commercial availability of wedge sizes that differ by 1.5 mm could influence these findings, as only a significant difference between the two measurement methods will cause a change in the selected wedge size.

Another source of error is the discrepancy between the line passing through distal patellar tendon insertion, where advancement was measured, and the line corresponding to the base of the wedge. Since the wedge is trapezoidal, its size corresponds to its base. Therefore, if the proximal edge of the wedge is not located at the level of PT insertion, true advancement could differ from that determined preoperatvely. Establishing that wedge implant placement was superimposable among the two groups, we have minimised the bias caused by this variable. Even if similar, wedge position inside osteotomy may have influenced the postoperative PTA of the two groups. However, as stated previously, this shortfall is probably compensated rounding up calculated advancement to the upper wedge size (Butterworth & Kydd, 2017).

No pubblished suggestion regarding the position of the wedge for MMP can be found in literature. On the other hand, the distance from the proximal edge of the osteotomy to the cage should be between 3 and 5 mm, as currently recommended for TTA rapid (Samoy et al., 2015). However, the cage used for this surgical technique is significantly different from that designated for MMP, making this instruction not suitable. Moreover, in the present study the distance between distal insertion of the PT and proximal edge of the wedge was on average 12 mm among groups. Therefore, if the line passing through proximal edge of the wedge does not match the line on PT, advancement provided does not correspond to the wedge size. This may explain why previously studies have not consistently determined the true advancement by MMP (Kapler et al., 2015). This has recently been confirmed for traditional TTA, where implant design and cage positioning recommendation lead to an under-advancement of 15% (Meeson et al., 2018) to 21-28% (Jin et al., 2019); which is still lower than the value determined by Kapler et al. (Kapler et al., 2015).

This study presents some limitations, firstly the number of specimens included (20 stifles), due to the inclusion criteria. However, we reduced the group variability randomly assigning limbs of the same dog to the two groups. This allowed us to test the two preoperative measurement techniques on overlapping anatomic features.

4.1.4 Conclusions

In conclusion, even if postoperative PTA did not statistically differ, TAM managed to achieve the desired value of 90° when applied. In our experience, TAM was easier to apply and provided advancement values that were generally consistent with commercially available wedges. On the other hand, even if CT provided measurements of advancement that were not statistically different from TAM, it failed to yield the true advancement of the intended 90°, so it is not recommended for preoperative planning of MMP. Considering preoperative and intraoperative variables that may affect the true advancement achieved, we hope for an intraoperative method to measure the desired advancement until a PTA of 90° is achieved.

Apelt, D., Kowaleski, M. P., & Boudrieau, R. J. (2007). Effect of tibial tuberosity advancement on cranial tibial subluxation in canine cranial cruciate-deficient stifle joints: an in vitro experimental study. *Veterinary Surgery*, *36*(2), 170–177.

Aragosa, F., Caterino, C., Della Valle, G., & Fatone, G. (2022). Tibial Tuberosity Advancement Techniques (TTAT): A Systematic Review. *Animals*, *12*(16), 2114. https://doi.org/10.3390/ani12162114

Backstein, D., Meisami, B., & Gross, A. E. (2003). Patella baja after the modified Coventry-Maquet high tibial osteotomy. *The Journal of Knee Surgery*, *16*(4), 203–208.

Bielecki, M. J., Schwandt, C. S., & Scharvogel, S. (2014). Effect of tibial subluxation on the measurements for tibial tuberosity advancement in dogs with cranial cruciate ligament deficiency: An ex vivo study. *Veterinary and Comparative Orthopaedics and Traumatology*, *27*(6), 470–477. https://doi.org/10.3415/VCOT-14-02-0018

Boudrieau, R. J. (2009). Tibial plateau leveling osteotomy or tibial tuberosity advancement? *Veterinary Surgery*, *38*(1), 1–22.

Bush, M. A., Bowlt, K., Gines, J. A., & Owen, M. R. (2011). Effect of use of different landmark methods on determining stifle angle and on calculated tibial tuberosity advancement. *Veterinary and Comparative Orthopaedics and Traumatology*, *24*(03), 205–210.

Cadmus, J., Palmer, R. H., & Duncan, C. (2014). The Effect of Preoperative Planning Method on Recommended Tibial Tuberosity Advancement Cage Size. *Veterinary Surgery*, *43*(8), 995–1000. https://doi.org/10.1111/j.1532-950X.2014.12126.x

Della Valle, G., Caterino, C., Aragosa, F., Micieli, F., Costanza, D., Di Palma, C., Piscitelli, A., & Fatone, G. (2021). Outcome after Modified Maquet Procedure in dogs with unilateral cranial cruciate ligament rupture: Evaluation of recovery limb function by use of force plate gait analysis. *PLoS ONE*, *16*(8), 1–11. https://doi.org/10.1371/journal.pone.0256011

Dennler, R., Kipfer, N. M., Tepic, S., Hassig, M., & Montavon, P. M. (2006). Inclination of the patellar ligament in relation to flexion angle in stifle joints of dogs without degenerative joint disease. *American Journal of Veterinary Research*, *67*(11), 1849–1854. https://doi.org/10.2460/ajvr.67.11.1849

Etchepareborde, S., Brunel, L., Bollen, G., & Balligand, M. (2011). Preliminary experience of a modified maquet technique for repair of cranial cruciate ligament rupture in dogs. *Veterinary and Comparative*

Orthopaedics and Traumatology, *24*(3), 223–227. https://doi.org/10.3415/VCOT-10-01-0012

Etchepareborde, S., Mills, J., Busoni, V., Brunel, L., & Balligand, M. (2011). Theoretical discrepancy between cage size and efficient tibial tuberosity advancement in dogs treated for cranial cruciate ligament rupture. *Veterinary and Comparative Orthopaedics and Traumatology*, *24*(01), 27–31. https://doi.org/10.3415/VCOT-10-01-0013

Giansetto, T., Picavet, P. P., Lefebvre, M., & Balligand, M. (2022). Determination of the Stifle Angle at Standing Position in Dogs. In *Veterinary Sciences* (Vol. 9, Issue 11). https://doi.org/10.3390/vetsci9110644

Hoffmann, D. E., Kowaleski, M. P., Johnson, K. A., Evans, R. B., & Boudrieau, R. J. (2011). Ex vivo biomechanical evaluation of the canine cranial cruciate ligament-deficient stifle with varying angles of stifle joint flexion and axial loads after tibial tuberosity advancement. *Veterinary Surgery*, *40*(3), 311–320.

Jin, D. W., Peck, J. N., Tano, C. A., & Morgan, M. J. (2019). Discrepancy between true distance of tibial tuberosity advancement and cage size: An ex vivo study. *Veterinary Surgery*, *48*(2), 186–191. https://doi.org/10.1111/vsu.13135

Kapler, M. W., Marcellin-Little, D. J., & Roe, S. C. (2015). Planned wedge size compared to achieved advancement in dogs undergoing the modified Maquet procedure. *Veterinary and Comparative Orthopaedics and Traumatology*, *28*(6), 379–384. https://doi.org/10.3415/VCOT-15-02-0026

Meeson, R. L., Corah, L., Conroy, M. C., & Calvo, I. (2018). Relationship between Tibial conformation, cage size and advancement achieved in TTA procedure. *BMC Veterinary Research*, *14*(1), 1–7. https://doi.org/10.1186/s12917-018-1433-0

Millet, M., Bismuth, C., Labrunie, A., Marin, B., Filleur, A., Pillard, P., Sonet, J., Cachon, T., & Etchepareborde, S. (2013). Measurement of the patellar tendon-tibial plateau angle and tuberosity advancement in dogs with cranial cruciate ligament rupture. *Vet Comp Orthop Traumatol*, *26*(06), 469–478.

Montavon, P. M. (2002). Advancement of the tibial tuberosity for the treatment of cranial cruciate deficient canine stifle. *1st World Orth Vet Congress*, *2002*, *152*.

Montavon, P. M., Damur, D. M., & Tepic, S. (2002). Advancement of the tibial tuberosity for the treatment of the cranial cruciate ligament deficient stifle. *Proceedings of the 1st World Orthopaedic Veterinary Congress*, 152.

Ness, M. G. (2016). The Modified Maquet Procedure (MMP) in Dogs: Technical Development and Initial Clinical Experience. *Journal of the American Animal Hospital Association*, *52*(4), 242–250. https://doi.org/10.5326/JAAHA-MS-6304

Neville-Towle, J. D., Makara, M., Johnson, K. A., & Voss, K. (2016). Effect of proximal translation of the osteotomized tibial tuberosity during tibial tuberosity advancement on patellar position and patellar ligament angle. *BMC Veterinary Research*, *13*(1), 1–10. https://doi.org/10.1186/s12917-017-0942-6

Pillard, P., Livet, V., Cabon, Q., Bismuth, C., Sonet, J., Remy, D., Fau, D., Carozzo, C., Viguier, E., & Cachon, T. (2016). Comparison of desired radiographic advancement distance and true advancement distance required for patellar tendon–tibial plateau angle reduction to the ideal 90° in dogs by use of the modified Maquet technique. *American Journal of Veterinary Research*, *77*(12), 1401–1410.

Pillard, P., Livet, V., Cabon, Q., Bismuth, C., Sonet, J., Remy, D., Fau, D., Carozzo, C., Viguier, E., & Cachon, T. (2017). Evaluation of a new method to determine the tibial tuberosity advancement distance required to reduce the patellar tendon-tibial plateau angle to 90° with the modified Maquet technique in dogs. *American Journal of Veterinary Research*, *78*(4), 517–528. https://doi.org/10.2460/ajvr.78.4.517

Samoy, Y., Verhoeven, G., Bosmans, T., Van der Vekens, E., de Bakker, E., Verleyen, P., & Van Ryssen, B. (2015). TTA rapid: description of the technique and short term clinical trial results of the first 50 cases. *Veterinary Surgery*, *44*(4), 474–484.

Schwandt, C. S., Bohorquez-Vanelli, A., Tepic, S., Hassig, M., Dennler, R., Vezzoni, A., & Montavon, P. M. (2006). Angle between the patellar ligament and tibial plateau in dogs with partial rupture of the cranial cruciate ligament. *American Journal of Veterinary Research*, *67*(11), 1855–1860.

Ševčík, K., Hluchý, M., Ševčíková, M., & Ledecký, V. (2021). *Radiographic measurement of canine stifle joint angles using four different landmark methods Of all the joints in dogs , the stifle joint is most commonly affected with diseases . Most problems relate to joint instability and osteoarthritis because of deg*. 399–406.

Skinner, O. T., Kim, S. E., Lewis, D. D., & Pozzi, A. (2013). In vivo femorotibial subluxation during weight-bearing and clinical outcome following tibial tuberosity advancement for cranial cruciate ligament insufficiency in dogs. *The Veterinary Journal*, *196*(1), 86–91.

Vaughan, L. C. (2010). The history of canine cruciate ligament surgery from 1952 – 2005. *Vet Comp Orthop Traumatol*, *23*(06), 379–384.

Wolf, R. E., Scavelli, T. D., Hoelzler, M. G., Fulcher, R. P., & Bastian, R. P. (2012). Surgical and postoperative complications associated with tibial tuberosity advancement for cranial cruciate ligament rupture in dogs: 458 cases (2007–2009). *Journal of the American Veterinary Medical Association*, *240*(12), 1481–1487.

Chapter 5

Conclusions
And future perspectives

The following chapter is a summary of what has been reported so far and some hints of what our team is currently investigating.

5.1 Conclusions

In this thesis, we first examined TTAT of new generation, taking into account preoperative planning, clinical outcome and complications, through a systematic review following PRISMA statement. We found that CT is the most common preoperative technique to measure the amount of advancement. On the other hand, most of the retrospective and prospective studies did not achieve the expected postoperative PTA of 90°. However, the 94.6% of stifles regained a full/acceptable function in long-term outcomes.

A postoperative PTA of 90° ± 5° is currently considered to neutralize the tibiofemoral shear force (Etchepareborde, Mills, et al., 2011), but a suboptimal PTA could lead to instability and consequently to late meniscal tears (Skinner et al., 2013). The percentage for meniscal tears after TTAT was 4.3% without meniscal release, substantially lower than what reported for traditional TTA (28%) (Wolf et al., 2012). This could be due to the improvements accomplished with the development of new generation TTAT or to the low numer of studies recorded evaluating long-term outcomes.

After recognising that preoperative planning is poorly documented, we compared measurement methods for determining the advancement required to achieve a postoperative PTA of 90°. Of the methods described, we critically examined CT, TAM, and BF in terms of comparison and interobserver reliability. According to our results, TAM had higher interobserver reliability than CT and BF, though only with a slight moderate agreement among observers. No previous study on the reliability of TAM was found in the literature, while published data are available on CT and BF. As regards CT, it seems to cause undercorrection and its poor reliability is confirmed by previous studies (Millet et al., 2013). For BF, on the other hand, our results conflict with its first description, consistent with excellent interobserver correlation (Bielecki et al., 2014).

In addition, no difference was found between CT and TAM, which is consistent with previous studies (Butterworth & Kydd, 2017; Samoy et al., 2015). Conversely, BF showed statistically higher mean values than the other included techniques, likely due to the correction formula for tibial subluxation. Therefore, even though TAM does not account for spatial relationship between the tibia and femur, it provides lower values than BF. Anyway, none of the included measurement techniques has excellent interobserver reliability and all appear to be limited by observer experience.

In our opinion, TAM is easier to perform and provides a functionally more accurate measurement of the advancement required. Moreover, this method can be applied without placing the stifle joint at 135°, thus avoiding errors related to limb positioning. To prove this hypothesis, we further investigated TAM compared to CT, to establish its effectiveness in achieving the required advancement in Chapter 4. Both radiographic methods led to a postoperative PTA consistent with 90° ± 5 when MMP was performed, but CT failed to yield the true advancement of the intended 90°. More precisely, the 80% of stifles had a postoperative PTA of 90° ± 5, which overlaps with the percentage reported for TTAT in the systematic review of Chapter 2 (78.7%). However, the advancement values provided by TAM were close to commercially available wedges, which simplified the selection.

This thesis presents some limitations worthy of note. In our research for the systematic review upon TTAT (Chapter 2) we found few prospective studies with a large study population and univocal data collection about preoperative planning and outcome. In contrast, the analysis of interbserver reliability analysis (Chapter 3) is limited by its retrospective design, while investigation on accuracy of measurement technique (Chapter 4), was conducted on a small number of dogs. For these reasons, results must be interpreted critically.

Measurement of the required advancement distance for the tibial tuberosity may be influenced by preoperative and intraoperative variables: stifle joint extension angle, femoro-tibial subluxation, method of PTA measurement, method of advancement measurement, limb positioning, patella tendon insertion point, loss of advancement due to the saw kerf and cage position (Bielecki et al., 2014; Kapler et al., 2015; Meeson et al., 2018; Millet et al., 2013; Muir, 2018; Skinner et al., 2013). For these reasons, virtual surgery is currently recommended preoperatively, as it allows the advancement to be measured at the appropriate point of spacer position to achieve the desired PTA postoperatively (Cadmus et al., 2014).

Unlike TTA rapid (Samoy et al., 2015), there are no specific indications on wedge positioning during MMP. Although, wedge position within the osteotomy influences advancement achieved with surgery. While all methods analysed measure the advancement at the PT insertion, the mismatch between the proximal edge of the wedge, which corresponds to its size, and the insertion of the patellar tendon, is a source of improper advancement. Because the final position of the wedge depends mainly on how the osteotomy is performed, it cannot be predicted accurately preoperatively. According to these assumptions, we believe that no measurement method is able to avoid all the described preoperative variables; therefore, further studies are needed to obtain a reliable measurement method and to develop instruments that allow intraoperative assessment of PTA. Therefore, we are currently searching for an intraoperative method to measure the desired advancement until a PTA of 90° is achieved.

5.2 Future perspectives

Several studies have consistently reported the discrepancy between the value calculated in preoperative planning and the value truly obtained intraoperatively (Etchepareborde, Mills, et al., 2011; Jin et al., 2019; Meeson et al., 2018; Millet et al., 2013; Pillard et al., 2016; Skinner et al., 2013). Additionally, different rates of under-advancement were recorded, ranging from 15% for Meeson et al. (Meeson et al., 2018) to 21-28% according to Jin et al. (Jin et al., 2019) and 30% for Kapler et al. (Kapler et al., 2015), testing different planning methods.
Despite the many reports of successful surgical outcomes, there is no evidence of neutralization of tibiofemoral shear force in vivo after TTAT. Conversely, for traditional TTA cranio-caudal stifle instability following surgery was assessed using fluoroscopic kinematography. It appeared that inadequate cranialization of the tibial tuberosity and persistent cranio-caudal instability during walking, were expected after traditional TTA. Surprisingly, none of the dogs enrolled showed a postoperative PTA of 90° and the only one resulting stable after surgery had a PTA of 98.5° postoperatively (Schwede et al., 2018). Therefore, the results of the present thesis suggested that also MMP would fail to neutralize femorotibial shear forces at stance when radiographic preoperative methods of advancement measurement are used. This prompts us to reconsider the preoperative planning to determine the measure of advancement required to achieve a PTA of 90° to stabilize the stifle joint.
We are currently pursuing a prospective study aimed at determining the anatomical landmarks of the tibial plateau to identify the PTA on canine stifle specimens. There is no previous study on this topic in the veterinary literature. In 2014, an ex vivo study on validity of PTA_{CT} and PTA_{TP} was performed, comparing them to measurements of anatomical PTA (Bismuth et al., 2014). Anatomical landmarks of the tibial plateau were identified after dissection of all the soft tissue structures surrounding the tibia. The cranial and caudal extent of the medial tibial plateau were defined by inserting two Kirschner wires corresponding to cranial and caudal extent of the medial tibial plateau, as previously described (Reif et al., 2004; Warzee et al., 2001). The Kirschner wires were placed at the level of the cranial intercondylar area (by identifying the insertion of the CrCL), and at the caudal edge of the medial tibial condyle immediately medial to the caudal cruciate ligament. Tibial plateau slope so defined, together with identification of the distal PT insertion on tibial tuberosity, were used to

measure the advancement. The correct position was confirmed fluoroscopically. Anatomical PTA measurements showed very good reproducibility, according to Bismuth and colleagues (Bismuth et al., 2014). Additionally, a previous study used the same landmarks to measure anatomical TPA, which were not statistically different from radiographic ones (Reif et al., 2004).
Our following experiment aims to identify the anatomic landmarks of the tibial plateau and PT insertion intraoperatively without extensive soft tissue dissection. Identification of cranial and caudal points of the tibial plateau will be repeatedly performed by 3 observers to analyse intra- and interobserver reliability. After marking with pins, a ML projection of the stifle will be performed to check the correct identification. The discrepancy between radiographic tibial landmarks and the ones intraoperatively identified will be calculated. We expect promising results in terms of reproducibility of this intraoperative method, which could pave the way for the development of tools to support intraoperative assessment of PTA and to determine the true advancement measure without the influence of preoperative variables.

Bielecki, M. J., Schwandt, C. S., & Scharvogel, S. (2014). Effect of tibial subluxation on the measurements for tibial tuberosity advancement in dogs with cranial cruciate ligament deficiency: An ex vivo study. *Veterinary and Comparative Orthopaedics and Traumatology*, *27*(6), 470–477. https://doi.org/10.3415/VCOT-14-02-0018

Bismuth, C., Ferrand, F. X., Millet, M., Labrunie, A., Marin, B., Pillard, P., Deroy, C., Fau, D., Carozzo, C., Cachon, T., & Viguier, E. (2014). Comparison of radiographic measurements of the patellar tendon-tibial plateau angle with anatomical measurements in dogs: Validity of the common tangent and tibial plateau methods. *Veterinary and Comparative Orthopaedics and Traumatology*, *27*(3), 222–229. https://doi.org/10.3415/VCOT-13-12-0145/ID/JR0145-40

Butterworth, S. J., & Kydd, D. M. (2017). TTA-Rapid in the treatment of the canine cruciate deficient stifle: short-and medium-term outcome. *Journal of Small Animal Practice*, *58*(1), 35–41.

Cadmus, J., Palmer, R. H., & Duncan, C. (2014). The Effect of Preoperative Planning Method on Recommended Tibial Tuberosity Advancement Cage Size. *Veterinary Surgery*, *43*(8), 995–1000. https://doi.org/10.1111/j.1532-950X.2014.12126.x

Etchepareborde, S., Mills, J., Busoni, V., Brunel, L., & Balligand, M. (2011). Theoretical discrepancy between cage size and efficient tibial tuberosity advancement in dogs treated for cranial cruciate ligament rupture. *Veterinary and Comparative Orthopaedics and Traumatology*, *24*(01), 27–31. https://doi.org/10.3415/VCOT-10-01-0013

Jin, D. W., Peck, J. N., Tano, C. A., & Morgan, M. J. (2019). Discrepancy between true distance of tibial tuberosity advancement and cage size: An ex vivo study. *Veterinary Surgery*, *48*(2), 186–191. https://doi.org/10.1111/vsu.13135

Kapler, M. W., Marcellin-Little, D. J., & Roe, S. C. (2015). Planned wedge size compared to achieved advancement in dogs undergoing the modified Maquet procedure. *Veterinary and Comparative Orthopaedics and Traumatology*, *28*(6), 379–384. https://doi.org/10.3415/VCOT-15-02-0026

Meeson, R. L., Corah, L., Conroy, M. C., & Calvo, I. (2018). Relationship between Tibial conformation, cage size and advancement achieved in TTA procedure. *BMC Veterinary Research*, *14*(1), 1–7. https://doi.org/10.1186/s12917-018-1433-0

Millet, M., Bismuth, C., Labrunie, A., Marin, B., Filleur, A., Pillard, P., Sonet, J., Cachon, T., & Etchepareborde, S. (2013). Measurement of the patellar tendon-tibial plateau angle and tuberosity advancement in dogs with cranial cruciate ligament rupture. *Vet Comp Orthop Traumatol*, *26*(06), 469–478.

Muir, P. (2018). *Advances in the canine cranial cruciate ligament*. John Wiley & Sons.

Pillard, P., Livet, V., Cabon, Q., Bismuth, C., Sonet, J., Remy, D., Fau, D., Carozzo, C., Viguier, E., & Cachon, T. (2016). Comparison of desired radiographic advancement distance and true advancement distance required for patellar tendon–tibial plateau angle reduction to the ideal 90° in dogs by use of the modified Maquet technique. *American Journal of Veterinary Research*, *77*(12), 1401–1410.

Reif, U., Dejardin, L. M., Probst, C. W., DeCamp, C. E., Flo, G. L., & Johnson, A. L. (2004). Influence of limb positioning and measurement method on the magnitude of the tibial plateau angle. *Veterinary Surgery*, *33*(4), 368–375.

Samoy, Y., Verhoeven, G., Bosmans, T., Van der Vekens, E., de Bakker, E., Verleyen, P., & Van Ryssen, B. (2015). TTA rapid: description of the technique and short term clinical trial results of the first 50 cases. *Veterinary Surgery*, *44*(4), 474–484.

Schwede, M., Rey, J., & Böttcher, P. (2018). In vivo fluoroscopic kinematography of cranio-caudal stifle stability after tibial tuberosity advancement (TTA): a retrospective case series of 10 stifles. *Open Veterinary Journal*, *8*(3), 295–304.

Skinner, O. T., Kim, S. E., Lewis, D. D., & Pozzi, A. (2013). In vivo femorotibial subluxation during weight-bearing and clinical outcome following tibial tuberosity advancement for cranial cruciate ligament insufficiency in dogs. *The Veterinary Journal*, *196*(1), 86–91.

Warzee, C. C., Dejardin, L. M., Arnoczky, S. P., & Perry, R. L. (2001). Effect of tibial plateau leveling on cranial and caudal tibial thrusts in canine cranial cruciate–deficient stifles: An in vitro experimental study. *Veterinary Surgery*, *30*(3), 278–286.

Wolf, R. E., Scavelli, T. D., Hoelzler, M. G., Fulcher, R. P., & Bastian, R. P. (2012). Surgical and postoperative complications associated with tibial tuberosity advancement for cranial cruciate ligament rupture in dogs: 458 cases (2007–2009). *Journal of the American Veterinary Medical Association*, *240*(12), 1481–1487.