Proximal Femoral Morphology and Bone Quality Assessment in Dogs

THESIS

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Abstract

Assessment of the proximal femoral anatomy in dogs is important for determining suitability for total hip replacement (THR) surgery, surgical planning for THR, and assessment for the risk for potential complications. Femoral anatomy has particular significance for evaluating the suitability of a patient for cementless implants that rely on a press-fit for stability in the immediate post-operative period. Breed variations in proximal femoral anatomy have been posited in the veterinary literature. In humans, variations in femoral anatomy have been identified as normal, stovepipe, and champagne-fluted; these varying morphologies have different associated bone qualities and suitability for THR. A stovepipe femur in humans is characterized by a straight, cylindrical, wide proximal femur with relatively weak trabecular bone. However, the significance of a stovepipe femoral morphology in dogs has not been determined. We hypothesize that dogs with stovepipe femora will have larger proximal femoral volumes and weaker trabecular bone than a dog with a normal, conical shaped proximal femur. Femoral morphology will be determined via three-dimensional reconstructions of computed tomography scans performed on client owned dogs presented for evaluation for THR. Trabecular bone quality will be assessed via a micro-computed tomographic scan and direct mechanical testing on cylindrical bone cores obtained at THR surgery. The results of this study will have profound implications for surgical planning for
THR and will enable us to provide robust and scientifically sound recommendations for implant selection, implant design, and the assessment of potential complications following THR in dogs.
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Chapter 1: Background and Introduction

1.1. Normal development of the canine proximal femur

The femur and pelvis form embryologically from a cartilage precursor and mineralize over time through endochondral ossification. The femur begins with a centrally placed nutrient foramen that becomes radiographically visible at 6 weeks of age. [1, 2] The length of the femur is approximately 95% of its total adult length by 30 weeks of age in a large breed dog (Greyhound). [1] The bone begins with an hour-glass shape, with a slightly larger distal end than proximal end. [2] By 12 days of age, ossification of the head and distal condylar epiphysis is radiographically visible. [2]

The femur has growth plates at the femoral condyles, greater trochanter, and femoral head, with the latter two starting as a common epiphysis that under the forces of the divergent muscles becomes separated into two physes. [2] The greater trochanter becomes visible under the pull of the gluteals between the 8th and 9th week of life with the lesser trochanter visible between 10-12 weeks of age. [2] The proximal physis close between 11 and 14 months of age. [2]

The acetabulum is formed from four anlages of the ilium, ischium, pubis, and acetabular bones: the ilium and ischium each contribute 40% of the acetabulum with the remaining 20% coming from the acetabular bone and pubis. [2] At birth, all of the components of the coxofemoral joint are present. The majority of the increase in growth
for the ilium and ischium is between 10 and 30 weeks of life. [2] The last area to ossify within the acetabulum is the Y shaped endochondral cartilage seam joining the anlages. [2]

The first radiographically visible evidence of the femoral head is seen within the acetabulum at 12 days of age. In normal dogs, approximately 2/3 of the femoral head will be covered within the acetabulum throughout development and does not change during ossification of these structures. [2] Full congruity will allow for continued normal development of the coxofemoral joint. This is reflected in the histology that shows the trabeculae in the femoral head, neck, and acetabulum align in a linear fashion following the tensile and compressive stresses applied. The cortical bone is thin along the neck and acetabular rim with the medial cortex in the proximal femur comprised of thin, dense bone. [2] The development of the hip is a result of the biomechanical forces applied to it and will form normally as long as full congruency is maintained between the femoral head and acetabulum. [2]

1.2. Alterations in femoral development in canine hip dysplasia (CHD)

Ossification of the femoral chondroepiphyseal region occurs later in dysplastic hips when compared with normal dogs. [3, 4] There are also differences in the volume of the secondary center of ossification with dysplastic dogs when compared with non-dysplastic dogs as evaluated by computed tomography. [5] For the hip joint to form properly, normal joint contact mechanisms must be present to influence the shaping of
the femoral head and acetabulum; this congruent contact is absent in dysplastic dogs. It is unclear which comes first, laxity or subluxation and non-conformity.

Early evaluation performed by Paatsama and Rissenen recognized histopathologic changes characterized by disruption of the columnar architecture within the growth plates of dogs predisposed to CHD. [6] CHD has been noted in dogs as early as 14 days of age by Henricson. More notably, Henricson noted the relationship between early joint laxity and later development of CHD. [7] Evaluation of the normal and abnormal development of the canine hip was performed by Riser who noted that while the joints of genetically predisposed German Shepherd Dogs (GSD) were grossly normal at birth, changes within the round ligament were evident as early as 30 days of life. [1, 2] Riser also noted that the radiographic changes lagged behind the histopathologic abnormalities, with the first detectable radiographic change being a delay in the ossification of the craniodorsal acetabular rim. [2] Delayed onset of femoral capital ossification has been correlated with the development of CHD in both GSD and Labrador Retrievers (LR). [3]

Proposed theories of the etiopathogenesis of CHD include a disparity or asynchronous development between the musculature and chondroepiphyseal growth. [1, 8, 9] Reduced pelvic muscle volume or strength may lead to joint instability in young dogs, as was shown when GSD were compared with Greyhounds. [10] One finding of this abnormal soft tissue component contributing to CHD is pectineal hypotrophy which was noted in the GSD study population at 8 weeks of age. [11] Additionally, changes have been noted in the volume of the ligament of the head of the femur. [12-14] The
joint capsule and ligament of the head of the femur provide early stability for the underlying bony structures. During the first 30 days, the ligament of the head of the femur is the primary stabilizer of the coxofemoral joint. [2, 15] The ligament of the head of the femur begins to lengthen after the initial two weeks of life and may become excessively lengthened resulting in coxofemoral laxity. [2, 15]

Changes in the joint capsule architecture and structural composition have also been noted. Dysplastic hip joint capsules have a higher ratio of type III to type I collagen than capsules from normal hips. [16, 17] In one dysplastic Labrador, the joint capsule had a heterogeneous group of collagen fibrils when evaluated with transmission electron microscopy compared with the homogeneous collagen fibrils in normal joint capsule composition. [18] This alteration in collagen composition represents a resulting difference in function. [18]

Increases in synovial fluid also contribute to increased joint laxity, but the underlying mechanism for regulation of synovial volume is not understood. [10] Increased synovial volume may also be an effect rather than a cause of CHD. [10] The relationship between joint capsule laxity and concurrent synovitis is unclear, especially with regards whether it is causal or simply associative. [19, 20]

The onset of clinical signs of CHD typically begins during development and is often noticed between 3 to 12 months of age. [18] Initially, laxity of the coxofemoral joint and subluxation occur, leading to clinical signs that include reluctance to play, bunny hopping gait, hesitation to jump, reluctance to rise, sitting suddenly when running,
and hind limb lameness. As the femoral head abnormally rides along the dorsal acetabular labrum, wear of the cartilage surface just dorsal to the fovea occurs and initiates the cartilage destruction and development of osteoarthritis (OA) as a larger joint reaction force is spread over a smaller surface area of cartilage surface. [10] Pain most likely arises from microtearing of the ligament of the head of the femur, the joint capsule, and microfracture of the dorsal acetabular rim. [10] Other clinical diseases may manifest as hind limb lameness in the young dog so osteochondrosis dissecans, hypertrophic osteodystrophy, panosteitis, physeal fractures, and cranial cruciate ligament rupture/avulsion should be ruled out prior to diagnosing CHD.

Over time, changes in the joint capsule secondary to laxity lead to periarticular fibrosis. This can create increased stability within the joint and lead to a resolution of clinical signs for a period of time. As the osteoarthritis progresses, stiffness and reluctance to extend the hip become more prominent and lead to signs of lameness, difficulty rising, reluctance or refusal to jump, and decreased ability to exercise. The clinical consequences of secondary OA are typically seen from 2 to 12 years of age. [18] Osteoarthritic changes may be noted incidentally on radiographs, leading to a diagnosis without recognition of any clinical signs of lameness. [10, 18] As the dog ages, other orthopedic and neurologic diseases should be considered as potential differential diagnoses, including lumbosacral disease, discospondylitis, neoplasia, cranial cruciate ligament rupture, polyarthropathies, or neurologic diseases such as degenerative myelopathy.
1.3. Surgical management of canine hip dysplasia

Treatment of CHD for the skeletally mature dog involves a limited number of options, including medical management of OA and surgical management through either femoral head and neck ostectomy (FHO) or total hip replacement (THR). In the immature, growing dog with residual plasticity in the development of its hip, a number of preventative surgical procedures may be considered, including juvenile pubic symphysiodesis (JPS), triple pelvic osteotomy (TPO), double pelvic osteotomy (DPO), intertrochanteric ostectomy, and pectineus muscle release. The challenge with the preventative procedures is that their overall effectiveness is difficult to predict or assess. Due to the limitations of FHO, total hip replacement (THR) provides the most predictably successful outcome in both larger dogs and in toy breeds. [21-29]

Canine total hip replacement was developed clinically at the Ohio State University College of Veterinary Medicine in 1974. [30, 31] Prior to this, case reports and techniques were reported but none garnered favor or wide clinical application. [30-34] The first system developed was the Richard’s Canine II Total Hip Prosthesis as a modular, fixed-head, cemented THR implant system. This established a surgical technique and commercially available implant system with a reported outcome of 92.5% satisfactory results. [31]

Improvement in the available implants for cemented THR came with the completely modular BioMedtrix system in 1990. Additional systems such as the
cementless PCA Canine Total Hip System and the Kyon Zurich Cementless systems followed. [35] Introduction of the BioMedtrix Universal Total Hip system followed the modification of the PCA cementless system in 2003. The two most prevalent cementless systems are the Kyon Zurich implant system and the BioMedtrix Universal implant system. New resurfacing techniques have also been developed. Additionally, implant systems that preserve the femoral neck such as the Helica hip and the BioMedtrix Centerline hip have been developed more recently.

1.4. Factors controlling implant survival in canine total hip replacement

The goals of femoral implant design include faithful replication of proximal femoral geometry, restoration of normal joint kinematics, and selection of appropriate materials to ensure effective load transfer and (for cementless implants) osseointegration. [36, 37] The implant should also be easy to implant in an accurate and reproducible manner. The implant should be aligned parallel with the femoral long axis, have a sufficient rim of cancellous bone (or a cement mantle), with no distal contact with the femoral diaphysis. [37, 38] Contact of the distal stem with the cortex results in a thin or absent cement mantle at this level. The length of the femoral stem affects contact with the femoral cortex that may contribute to aseptic loosening in cemented implants. [35, 39]

Implant design impacts implant positioning in dogs, and mismatches between the anatomy and the geometry of the implant can lead to malpositioning. [36] For example,
changes in the cervicodiaphyseal angle may contribute to subsidence. [36, 37, 40] The presence or absence of a collar also impacts the stem integration and fit; initially this was only available in the cemented stem but this has now been expanded to cementless fixation with the introduction of a collared titanium femoral stem manufactured through electron beam melting (EBM).[41] The calcar region may be protected from strain-adaptive bone remodeling but this demands that the implant collar be firmly in contact with the calcar in order to maximize its benefit and minimize any implant migration. [36, 42] Use of a collar may reduce cortical remodeling in the femoral cortex in cementless systems.[42]

Development of implant stability within the femur is a critical component of THR. The fixation must help to transfer load and maximize stability between the implant, cement if present, and the bone. [36] The modulus of acrylic bone cement is similar to that of native bone but very different from that of the metallic femoral implant. Femoral implant failure may occur due to debonding of the cement-implant interface, although it more commonly occurs at the cement-bone interface. Long-term integrity of the cement mantle is critical to successful cemented application of THR. The quality of the PMMA regarding its heat generation and phase of solidification in which it is applied, the technique in which the cement is applied, the size of the cement mantle, the temperature of the femoral stem, and the presence of additives to the PMMA all effect the quality of the fixation and the durability of the construct. [35, 36] Understanding and application of these factors contribute to development of a successful cement mantle. Failure to adhere to these
principles can lead to failure of the fixation, typically through aseptic loosening. The generation of cement wear particles and cracks from increased cement stress leads to failure of the implant system. [36, 43-45] To reduce this, texturizing the implant surface can improve the cement-implant bond although it has also been shown to have some downside risk due to the potential for abrasive damage to the cement mantle. [36, 46]

Concerns with the long-term survivability and durability of cemented fixation systems prompted the development of a cementless system of implants. The Zurich Cementless Total Hip System uses locking screw technology to attach the femoral implant to the medial, weight-bearing surface of the proximal femur. This mechanical interlock provided by the locking screws allows for short-term stability while bony ingrowth occurs for long-term stability. [35, 47] The Zurich THR system uses three stem sizes, small, medium, and large, that can fit a wide array of femoral sizes.[48]

The BioMedtrix cementless, or BFx, system relies on a press fit that is developed by slightly undersizing the femoral preparation in relation to the actual implant size. Long-term stability occurs through bony ingrowth into the implant. Initial reports evaluated had a successful outcome 98% of the time. [24] The aim of biologic fixation to achieve a long-term implant system is ideal for younger, active patients. [35] However, not every femur can support a press fit implant and patients with questionable bone quality or a stovepipe conformation may predispose to a high rate of complications if a cementless system is used. [35, 40]
In humans, as the cancellous (trabecular) bone within the proximal femur increases in strength and rigidity within 2-5mm of the cortical wall, it is key for the femoral component to be supported by this segment of the endosteal surface. [49] This requires that implants and instruments to prepare the femoral canal be available that create a preparation of the endosteal surface that closely matches the geometry of the bone and the implant to be inserted. [49] This required close fit has been noted in several studies for both cementless and cemented implants. [49] Achievement of a stable and geometrically accurate fit allows for improved clinical outcome and avoidance of micromotion. [49] Micromotions of around 10-20 µm are expected for press-fit implants under active loading, but motion in excess of 200 µm can occur if the implant is undersized or mismatched with respect to the geometry of the endosteum. [49] Bone ingrowth into porous implants is critically dependent on controlled micromotion, with excessive micromotion decreasing bone ingrowth and increasing the risk of a fibrous interface. [49] Reductions in the incidence of intraoperative fractures may also be achieved if the geometry of the implant is a close match for the femur into which is it being implanted. [49]

1.5. The influence of proximal femoral anatomy on total hip replacement

Knowledge and understanding of proximal femoral morphology is of prime importance for successful THR. [49] Numerous studies have identified that the femoral
stem must match the femoral shape to allow for both short- and long-term durable implant fixation. [49] In addition to matching the endosteal geometry, femoral implants should also mimic the overall natural femoral anatomy to restore normal hip biomechanics. [49] Consequently, modular system of implants can allow for the variability to accommodate various overall hip morphologies that may vary based upon age, race, sex, and life-style in people. [49]

Variations in proximal femoral anatomy have been noted in humans and these variations need to be considered when planning THR surgery. Noble and then Dorr determined femoral anatomical variables and methods of measuring them to assess whether or not a stovepipe femur existed. [49, 50] In the study by Noble, two hundred cadaveric femora were evaluated to assess the endosteal and cortical measurements throughout the proximal femoral region. [49] This work developed the concept of a canal flare index, or CFI, that could be used to classify femora into one of three morphologic groups: normal, stovepipe, and champagne-fluted. [49] (Noble 1988) Canal flare index was defined as the measured intracortical width of the femur at a point 20 millimeters proximal to the lesser trochanter and the measured intracortical distance at the canal isthmus to form a ratio (Figure 1). (Noble 1988) The CFI had a skewed normal distribution and the femoral shapes each fell within a different range of values of CFI. [49] Femora with CFI less than 3.0 were considered stovepipe, CFI between 3.0 and 4.7 were normal, and 4.7 to 6.5 where considered champagne-fluted in appearance. [49] This study also noted that with an
increase in age, there is a decrease in CFI with a tendency towards a more stovepipe conformation in older patients.

Based upon human measurement studies, a measurement system has been developed to use in dogs.[40, 51-55] Validation of the ability to perform these measurements has previously been used to evaluate the dog as a model for total hip replacement research for humans. Dogs were determined to be adequate representations anatomically of the human hip for research purposes. These studies identified specific measurements used to compare the femora of various species. This study will use these previously described measurements to compare GSD to Golden and Labrador Retrievers (LR) as controls.[53, 56]

1.6. Moving beyond simple geometry: the importance of bone quantity and bone quality

Bone quantity, previously referred to as bone mass, is a critical determinant of overall bone strength but is also important to the short- and long-term survival of THR implants. Bone quality, a term that has proved to be much harder to define, is of similar importance. Bone quality can be recognized by the surgeon, but not easily articulated. To define it is much harder, and the source of tremendous ongoing controversy, particularly in the human literature. [57] What is clear is that both quantity (total amount) and quality (distribution, microstructure, mineral density, microfracture density, collagen quality etc.) (Lester, 2005) can both influence the mechanical performance of bone and, as a consequence, both initial and long-term stability of an implant.
In human THR, an association has been identified between bone geometry and bone quantity/distribution. Dorr et al assessed bone quality in reference to CFI based canal morphology. Based upon radiographic, serum biochemistry, and histomorphometry, three distinct patterns of femoral bone shape and bone structure were identified. To determine the relationship between radiographic appearance and bone quality, Dorr et al studied the radiographic appearance to determine variations in bone morphology and associated “bone quality”. “Type A” bone was noted in heavier, younger males and is characterized by thick, dense cortices and a narrow diaphyseal medullary canal with a funnel shape. “Type B” bone was seen more commonly in men than women and had thinner cortices than Type A. Patients with type B bone also showed evidence of cortical bone loss in the medial and posterior regions, with a wider intramedullary canal proximally, along with a wider proximal diameter and thinner cortices proximally. “Type C” bone was seen predominantly in women and was characterized by wider bones with straight cortices that were relatively thin and osteoporotic. Type C bone had significant loss of the cortical margin characterized by a thin appearance on radiographs with a wide intramedullary canal diameter and was often found in older patients that had structural and cellular compromise. Although the methods used to describe bone “quality” in this paper were not quantitative, the subjective observations led the author to suggest that differences in bone shape, with their associated changes in bone quality, could have important implications for implant selection and prediction of outcome in human patients undergoing THR.
Much less has been reported on either femoral geometry or bone quality in the proximal femur of dogs, despite the fact that dogs have been studied extensively as models for human THR. The popularity of the canine model stems from a general familiarity with the species, the relatively low cost and easy availability of research hounds, and the availability of clinical implants and instrumentation. Dogs also have similar loading conditions, external and internal anatomical features and patterns of cortical microstructure and cortical blood supply. [53] Over the years, preclinical canine THR studies have been used to evaluate implant materials, surgical technique, implant design, the use of biologically active coatings to enhance bone ingrowth, and the pathophysiology of aseptic implant loosening. [53, 58]

In assessing the suitability of the dog as a model for human THR, several authors have undertaken comparative studied on the anatomy of dogs versus humans. Many of these studies evaluated femoral shape in dogs use Greyhounds [51, 53], a breed that does not commonly experience CHD and that, as a consequence, is rarely seen for clinical THR. Other studies have looked at inbred mongrel dogs, which is more representative of the type of animal that is typically used in research. Sumner et al noted that the external angles in the proximal femur of the dog varied from humans suggesting the prosthesis shape should also vary. [53, 59, 60] Dogs undergo different weight distribution to their limbs, femoral strain magnitudes, and patterns of locomotion than humans [53] The cervico-diaphyseal angle and the anteversion angle in dogs is also significantly difference than in humans. [53]
The canine medullary canal is wider with a thinner cortical bone mantle relative to the external dimensions when compared with humans. [60]

Although these studies provide useful information regarding normal bone geometry and can help inform implant design, they are not representative of the clinical population presenting for CHD. More recently, Palierne et al evaluated different dog breeds to assess their suitability for a model for human THR studies. [52] This was the first study that looked at a diverse sample of dogs’ femoral morphology. This study was undertaken to develop a database of dog breeds representative of the diversity that Noble achieved in his human study evaluating femoral morphology. This study defined 18 parameters that were measured on 41 pairs of cadaveric bones harvested from dogs ranging from 2 to 65kg of 19 different breeds of dog. Four dogs were small poodles ranging in weight from 4 to 10 kg and 14 of the 41 dogs weighted less than 15 kg. This population of dogs was diverse and represented significant variability in size and morphology. [52] The authors noted that breed differences would have significant consequences when dogs are used as THR models due to the variability of the medullary canal. The aim of this study was to provide morphology information for implant design and not to be usable clinically. [52]

In the Palierne et al study, the range of CFI noted was narrow suggesting that most dogs fall within a tight range of canal flare indices. This study used the same criteria for CFI size ranges as Noble and found most dogs were within the stovepipe group when the human measurement ranges were used. It used Noble’s CFI measurements and placed the majority of dogs in the stovepipe group and showed little variability in the endosteal
surface between dogs. [52] A correlation between increasing age and decreased CFI was noted. The cortico-medullary index was variable which may influence the design of canal-fill within the femoral stem component. [52]

As part of a larger study evaluating canal fill in clinical dogs undergoing cementless THR, Rashmir-Raven et al. evaluated canal flare index in 36 femora. The femora tested all fell within a narrow range for CFI of 1.8-2.6.[40] The authors extrapolated the shapes described by Noble and assigned values for CFI relative to each of the three described morphologies with stovepipe femora have a CFI less than or equal to 1.8, normal CFI from 1.8 to 2.5, and a champagne-fluted shape CFI greater than or equal to 2.5. [40] With this in mind, the Palierne et al average CFI of 2.4 represents a normal shape proximal canal morphology and not a stovepipe configuration.

Taken as a whole, these previous studies have helped to identify measurement parameters and outline important anatomic considerations in load, structure, and biomechanics within the canine femur. [51, 53] Using these measurements, differences between dogs and humans have been identified, while relatively less attention has been paid to comparing dogs breeds.

1.7. Imaging approaches to assessing proximal femoral bone geometry and bone quality

The most common imaging approaches for assessing bone geometry are plain film radiography and computed tomography. The utility of radiographs in quantifying femoral measurements has been assessed in both humans and in dogs, and in both cases the results
indicate acceptable measurement errors. [49, 52, 61, 62] For example, Palierne et al. reported coefficients of variation of around 3% for measuring femoral dimensions in dogs. However, other studies have concluded that radiographs provide poor accuracy for morphometric analysis. [56, 62]

Given the increasing dependence on three-dimensional assessment of tissue structures, CT has also been widely studied in the context of modeling and measuring bone geometry. The CT scan is the most commonly used imaging modality to develop three-dimensional (3-D) reconstruction of the musculoskeletal system. [63] It offers the advantage of providing excellent contrast between soft and hard tissues, good spatial resolution, and is widely available. [63] The major limiting factors in using CT include more limited availability of the equipment, scanning costs and the increased radiation exposure to the patient.

With appropriate calibration, the grayscale values of individual voxels can be converted into quantitative bone density data, and discrete regions of interest (ROI) can be identified. [63] Post-scanning, software can be used to reformat images to explore geometry in orthogonal planes, to build digital models that can be manipulated for computational modeling, or that can be output as digital files to 3-D printers in order to create free-form models of the bone.

Inaccuracies in CT measurements can occur with variation between the bone varying from 10% to 40% as a result of beam hardening and partial volume effects. [64, 65] With these considerations, the reported mean index of accuracy within the femur is
0.8mm ± 0.7mm in one study. Consequently, CT is a precise technique for experimental conditions.

The accuracy of radiography versus computed tomography (CT) was evaluated in a cadaveric study in humans. Radiographs accurately portray the distal portions of the femur but are less accurate in the proximal area or cross-sectional measurements. In another study, identification of the isthmus was found to be the least accurate measurements. Radiographic measurements are not accurate enough for implant design; CT scans were shown to have better accuracy and are considered the gold standard for non-invasive imaging and measurement in anatomic studies.

Previous studies have evaluated the utility of different imaging modalities in assessing bone quality. Townsend et al showed that micro-computed tomography (µCT) predicted bone strength and quality better than dual energy X-ray absorptiometry (DEXA) and quantitative CT. Micro-CT provided a method to assess the architecture that creates the structure that contributes to the bone strength. However, this ex-vivo study evaluated normal femora in dogs without any evidence of orthopedic disease. One of the goals of the current study was to expand this approach to use imaging to assess the distribution, microarchitecture and mechanical properties of trabecular bone in the proximal femur of clinically affected dogs presenting for THR. This will help to understand the distribution of trabecular bone in the proximal femur that is important for initial implant stability as well as evaluate if there are variations in the quality of bone present.
1.8. Clinical significance of variations in bone morphology and CFI

THR is a reliable surgical solution for reducing pain and restoring mobility in dogs with OA secondary to CHD. Despite the proven benefits, THR remains a procedure with potentially serious or even catastrophic intra- or post-operative complications. The most serious intra-operative surgical complication is femoral fissure fracture, which can occur during femoral broaching but more usually occurs during stem insertion. Early post-operative complications of THR (occurring within the first 6 weeks) include fractures, coxofemoral luxations, patellar luxations, acetabular cup displacement, sciatic neuropraxia, pulmonary embolism and femoral implant subsidence. Potential late complications include implant-associated infection and septic loosening, aseptic loosening, and implant failure may occur later. All of these complications may require a revision surgery or explantation of the implant and conversion to an excision arthroplasty.

In an evaluation of risk factors after cementless THR in dogs, increased age and decreased canal flare index (CFI) were positively associated with femoral fracture. [67] The development of femoral fracture was noted to occur within the first 30 days post-operatively and was not associated with fissure fracture development and correction intraoperatively.[67] A CFI of 1.8 was statistically significantly different than the CFI for the nonfracture group of 1.98.[67] In this study, GSD, LR, and GR were the most commonly represented breeds.
The results of the evaluation of risk factors for subsidence include that implants with a higher percentage of canal fill are less likely to subside as well and that stovepipe femora had a significantly greater risk for developing subsidence. Rashmir-Raven et al found a similar correlation between shape and age as was initially reported by Palierne et al and in human studies by Dorr et al and Noble et al.[49, 50, 52] Rashmir-Raven et al noted that breed was also an important factor influencing stovepipe femoral conformation, noting that GSD and Rottweilers were more likely to have a stovepipe femoral configuration.[40] The risk of subsidence was related to the percentage of canal fill with a canal fill by the implant of less than 85% in the distal or middle region having a 6- or 10-fold increased risk of subsidence. [40] If the canal shape does not taper towards a narrow isthmus but an implant that is conically shaped is used, the mismatch in the canal fill will predispose to subsidence and failure of the implant. Consequently, femora with a stovepipe CFI were 6 times more likely to subside than normal morphology and 72 times more likely than a champagne fluted morphology. [40]

1.9. Gaps in current knowledge and the goals of this project

Accumulated evidence from humans as well as dogs shows that proximal femoral bone geometry impacts the clinical outcomes of THR. Anecdotal evidence from experienced veterinary surgeons also supports the hypothesis that the bone within the proximal femur of an older German Shepherd Dog with a relatively stovepipe morphology
behaves very differently from that within the proximal femur of a Retriever with a more defined femoral isthmus. The work described in this thesis therefore has **three key specific goals.**

The first aim of this study was to assess proximal femoral morphology of clinical cases of CHD presented for THR through computer modeling using CT reconstructions of the femur. We hypothesized that there will be a significant difference in proximal femoral geometry and morphometry between the stovepipe CFI and normal CFI groups. This would be seen as differences in the volume of the proximal femur with the stovepipe volume being larger and based upon a cylindrical shape compared with the smaller volume of a conical proximal femur in the normal dogs. Additionally, the cortical wall thickness would be thinner in the stovepipe group of dogs when compared with the normal group.

The second aim of this study is to assess the trabecular bone quality. This will be performed through morphometry based upon micro-CT scans of a bone core sample of trabecular bone obtained at surgery. We hypothesized that the stovepipe group will have fewer trabeculae per volume (a lower BV/TV) than normal femora. Additionally, the trabeculae will be thinner in the stovepipe group.

The third aim of this study was to use destructive mechanical testing to mechanically assess the trabecular bone within the proximal region of the proximal femur, in a region that corresponds to the trabecular bone that is in direct contact with the osseointegration surface on a cementless femoral implant. We hypothesized that the dogs
with stovepipe femora would have significantly weaker bone microarchitecture that would fail at a lesser load than dogs with a normal morphology.

In the short-term these results will lay a foundation for future studies that will explore the role of age-related and disease-related changes in bone quality. In the longer term, the identification of significant differences in bone microstructure and/or mechanical properties will open up new opportunities for developing better predictive tests that can be used to identify dogs that are the best candidates for cementless rather than cemented THR. Additionally, considerations for implant design or selection may be made.
Chapter 2: Materials and Methods

2.1 Pilot Study

A THR database of 550 dogs was used to identify cases of German Shepherd dog (GSD), Golden Retriever (GR) and Labrador Retriever (LR) with complete sets of THR radiographs. 32 dogs of each breed were identified and data collected included body weight, age at time of surgery, gender and femoral implant selection (BioMedtrix cementless BFX femoral stem versus cemented CFX stem). CFI measurements were made by a single observer (the author), using pre-operative craniocaudal radiographs of the operated femur. CFI was calculated by dividing the intra-cortical width at the level of the lesser trochanter by the intra-cortical width at the isthmus of the mid-diaphysis. (Figure 1) Between-group comparisons of CFI, age at the time of surgery, and weight were made using one-way ANOVA with a post-hoc Tukey test. The relationship between CFI and age was investigated using regression analysis. Femoral implant use (cemented CFX versus cementless BFX) was compared in the three groups using a Chi-squared test. CFI values in dogs receiving BFX or CFX implants were compared with an independent Student’s t-test. A significance level of p<0.05 was used throughout.
Figure 1. Canal flare index. Radiograph showing proper femoral alignment with the fabellae bisected by the cortices of the femur and the patella located centrally within the trochlea. The level of measurement is noted in yellow. B. Radiograph showing a CFI of 1.3. Note the cylindrical, “stovepipe” conformation of the proximal femur. C. Radiograph showing CFI 2.2, a normal proximal femoral morphology that is conical in shape.
Clinical cases presented for evaluation of THR were radiographed under sedation. With informed consent and under a clinical protocol that was reviewed and approved by the local IACUC, client-owned dogs underwent CT of the femoral region prior to THR. The CT images were reconstructed using computer modeling software (Mimics; Materialise, Inc.) into 3D models that encompassed the proximal femur between the lesser trochanter and the isthmus. Global thresholding was then used to differentiate cortical versus trabecular bone. Bone volumes and surface areas were determined for cortical and cancellous (intramedullary) bone envelopes. Statistical analyses, including descriptive statistics and independent t-tests, were performed using statistical software (SPSS for Windows, version 21) with a significance level of p<0.05.

2.2 Definitive clinical research study

Clinical canine patients presented to the OSU Orthopedic Surgery Service for evaluation for total hip replacement were considered for inclusion in this study, the protocol for which was reviewed and approved by the Institutional Animal Care and Use Committee (IACUC) and the Veterinary Medical Center Clinical Research & Teaching Advisory Committee (CRAC). Dogs were eligible if they had canine hip dysplasia and did not have any other reason for coxofemoral pain or hind limb lameness on examination by a board certified surgeon. Informed consent was sought from each owner prior to entry into the study (see Appendix D). The study covered the cost of the CT scan and the additional
anesthesia time necessary for the CT scan to be performed but did not cover any of the surgery or examination costs.

Each dog had physical and orthopedic examinations performed by a board certified veterinary surgeon. Radiographs under sedation were performed for each dog. Sedation included dexmedetomidine (4 mcg/kg IV) and butorphanol (0.2mg/kg IV) with atipamazole reversal available at an equal volume to the dexmedetomidine to be given IM. Dogs were monitored during their sedation to prevent complications.

2.3 Diagnostic imaging

Radiographic projections including an OFA style ventro-dorsal (VD) pelvis, a lateral pelvis, a medial-lateral femur, and a craniocaudal (CrCa) femur view. Each radiograph contained a 10 cm magnification correction marker (BioMedtrix, Boonton, NJ) that was positioned at the same distance from the x-ray table as the acetabulum of the femur. Radiographic technique followed the established parameters per the technique charts developed by the Diagnostic Imaging Service at the OSU Veterinary Medical Center. Patients were monitored and supervised for the duration of their sedation until they were able to stand on their own and a heart rate was maintained above 40 beats per minute. A pre-operative CBC and biochemical profile was completed. A small area of hair was gently clipped over the ilial wing on the surgery side to assess for evidence of pyoderma prior to scheduling surgery.
Radiographic measurements were made on scaled radiographs. Each image was corrected for calibration using the eFilm system (Sound Eklin, Carlsbad, CA) and a known length measure marker of 10cm (BioMedtrix, Boonton, NJ). Canal flare index was measured as previously described (Figure 1).

Dogs underwent a CT scan under general anesthesia prior to surgery for total hip replacement. The anesthesia protocol was developed for each patient by the OSU anesthesia service. All dogs received pre-operative prophylactic antibiotic coverage with cefazolin (22mg/kg IV). An 8-slice CT scanner (GE Lightspeed; GE Healthcare, Milwaukee, WI) was used to make or 0.625mm helical slices through both femora from just cranial to the acetabulum, through the entire femoral head and neck, to extend distally through the femoral condyles through the proximal portion of the tibia. Both femora were included in this scan. A CT phantom was used under the hind limbs (CT Calibration Phantom- Head, Mindways, Austin, TX) Additionally, axial slices at 0.625mm were obtained from the trochanteric fossa to the level of the isthmus of the surgical side femur for 80 slices. The CT scans were performed using a lumbar spine algorithm with a kV of 120 and mA of 250. Images were viewed using imaging software (eFilm; Sound Eklin Carlsbad, CA) and stored on a local server.

2.4 Computed tomography image reconstruction and volume measurements

CT images were transferred from the VMC PACS server to Mimics and the entire femur was reconstructed to create a 3-D model of the femur (Figure 2, Figure 3, Figure 4)
(see Appendix for Standard Operating Procedure). The affected femur was segmented into two separate regions of interest (ROI), one 60mm in length extending from the distal extent of the intertrochanteric fossa at the level of the osteotomy to 60mm distal (Figure 5) and one 20mm in length centered around the lesser trochanter region extending from distal to the distal extent of the intertrochanteric fossa at the level of the osteotomy to 20mm distal. (Figure 6) The 20-mm scan length was selected on the basis that it represents the volume of trabecular bone that is adjacent to the porous ingrowth collar on a cementless femoral stem. Grayscale thresholding was performed to identify all of the bone (standard bone window on Mimics, with grayscale values of >226), manually thresholded for cortical bone alone (grayscale >450), thresholded for the trabecular bone (227 to 445), and a soft tissue region was identified to define the medullary space (threshold -700 to 225).

Measurements were made within Mimics to evaluate bone surface area (mm²), bone volume (mm³), cortical thickness (mm), proximal and distal cortical widths, and proximal and distal segment end diameters in both the mediolateral and craniocaudal direction (mm) and recorded in a data spreadsheet. The medullary canal was defined as the space that did not consist of bone within the endosteal surface. The trabecular bone was defined as the bone within the endosteal canal. The endosteal canal was defined as the medullary space and the trabecular bone together to represent all of the contents within the endosteal canal.
Figure 2. Three-dimensional CT reconstruction of the cortical bone (A) and the medullary canal containing trabecular bone (B) for a normal femur.
Figure 3. Three-dimensional CT models of the cortical bone (A) and the medullary canal containing trabecular bone (B) for a stovepipe femur.
Figure 4. Three-dimensional CT reconstructions of the endosteal compartments of normal (A) and stovepipe (B) femora. Note the tapered geometry of the normal femur as compared with the relatively parallel-sided geometry of the stovepipe femur.
Figure 5. Segmentation of the 60-mm and 20-mm segments of normal femora into cortical and trabecular bone compartments.
Figure 6. Segmentation of the 60-mm and 20-mm segments of stovepipe femora into cortical and trabecular bone compartments.
Evaluation of the proximal geometry aimed to describe the endosteal shape to known geometric shapes. The Mimics volume was compared to the volume of a cylinder and a frustum (Figure 7).

Measurements were made on the endosteal surface (trabecular bone and medullary space combined) on the 60mm segment to determine the diameter of the proximal surface and the distal surface. This was performed on the craniocaudal bone endosteal canal and the mediolateral bone endosteal surface. Measurements were made in Mimics using the measurement tool. To ensure the bone was orientated similarly between cases, the toggle reference planes tool was used to orient the core end surface in 3D (Figure 8). (See SOP in Appendix A)

These measurements were used to calculate the radii of the mediolateral and craniocaudal surfaces of the 60mm segment. The area of the ellipse was calculated using the equation \( A=\pi a b \) where \( A \) is the area, \( a \) is the craniocaudal radius, and \( b \) is the mediolateral radius. From this, the taper index was calculated. The taper index was calculated using the equation \( TI=100 \times \frac{(A1-A2)}{A1} \) where \( A1 \) is the proximal area and \( A2 \) is the distal area (Figure 9).
Comparisons and Pearson’s correlations were made between the ML radii, CrCa radii, and the Mimics calculated volumes. Regression analysis was performed between the stovepipe group and the normal group to assess closeness of fit to the geometric model.

The aspect ratio of the ML radius to the CrCa radius was calculated. This was calculated for the proximal and distal end of the endosteal canal to assess contributions of each dimension to the change in volume.

**Figure 7.** Diagram of the frustum and volume equation

(http://jwilson.coe.uga.edu/emt725/Frustum/Frustum.cone.html)
**Figure 8.** Diagram depicting the measurements for the diameters from the endosteal surface. The cortical bone is gray, the medullary space red, and the trabecular bone is salmon.
Figure 9. Diagram depicting the taper index (TI) and the equation used to calculate the index from CT measures of proximal and distal medullary areas (A1 and A2, respectively).
2.5 Sampling of the proximal femur for obtaining the bone core

Dogs were prepared for routine aseptic surgery. A total hip replacement was performed as described in the Universal Total Hip guide[68] with implant selection at the discretion of the surgeon. Prior to femoral preparation after femoral head and neck excision using the resection guide, a 5.25mm diameter by 10mm long trephine head coring device was used to remove a core of cancellous bone from the proximal femur (5.25mm Two Piece Trephine Head; Ace Surgical Supply, Brockton, MA). (Figure 10) This was obtained on an extension apparatus (Contra angle shank with depth stop for two piece trephine head; Ace Surgical Supply, Brockton, MA) that attached to a drill (Stryker System 5, Stryker, Kalamazoo, MI).
Figure 10. Illustration of alignment of the coring tool for bone core sampling.
2.6 Handling and storage of the bone cores

The bone core sample and the femoral head were saved. The bone core sample was wrapped in a saline moistened gauze sponge within the coring device and frozen at -20°C. The femoral head was placed in saline and frozen at -20°C.

The bone cores were removed from the coring device using either a small extraction pin (Extraction pin; Ace Surgical Supply, Brockton, MA) provided with the coring device set (5 cores). This resulted in breakage of a 2 cores so a modified technique was developed. This modification involved removal of the closed end of the coring device using a bandsaw. This allowed for a larger pin to be used to gently push the core with the flat ended Steinmann pin with a diameter of (4.75mm) that matched the inner diameter of the coring device. The core was pushed into a hollow, thin walled, polypropylene semi-rigid protective sleeve for further storage and imaging. The polypropylene sleeve could be cut to length for each core using a razor blade so that the storage tube was 0.75cm longer than the bone core so the ends of the core were protected. The cores were then wrapped again in saline moistened gauze and kept frozen until micro-CT could be performed.

2.7 Microcomputed tomography

Microcomputed tomography (micro-CT, or µCT) was performed using a bench top micro-CT scanner (SkyScan Model 1172; SkyScan Bruker, Kontich, Belgium). The images were obtained at a nominal resolution of 13.3 µm. Images (Figure 11) were reconstructed using commercial software (NRecon; SkyScan Bruker, Kontich, Belgium)
and the following 3D micro architectural parameters calculated using proprietary software (CTAn; Skyscan Bruker, Kontich, Belgium): degree of anisotropy, trabecular volume as a fraction of total tissue volume (BV/TV, %), trabecular thickness (mm), trabecular spacing (mm), trabecular number (mm⁻¹), and polar moment of inertia (PMI, mm⁴) to assess the structure’s ability to resist torsion. This was assessed for a standardized central segment of 5mm of the bone core. Adjustments were made to exclude cortical bone if it was attached to the core if possible. For 4 cores, the software would not create 3D measures so trabecular thickness, trabecular spacing, and trabecular number were averaged over 10 slices of 2D data.

Micro-CT scans of the cores were reconstructed using 3-D image visualization and modeling software (Mimics version 15.1; Materialise Inc., Ann Arbor, MI) and a standard operating procedure (see Appendix B). The entire core was reconstructed and an image of the 3D model recorded. The image was bisected along the long axis to visualize the internal structure of the core. The same segment that was imaged in CTAn was imported into Mimics and an entire core and a longitudinally sliced hemi core were created with the images saved.
Figure 11. Micro-CT image. The images from left to right are 3-D micro-CT reconstructions of the entire core visualized in Mimics, the 5-mm central ROI viewed in Mimics, a longitudinal 2-D slice through the entire bone core visualized in Data Viewer, and an axial view of the core visualized in Data Viewer.
2.8 Bone core preparation and mechanical testing

Bone cores were defrosted to room temperature and gently removed from the polyethylene tube casing. The bone core was rinsed with saline using a commercially available lavage system (WaterPik Inc., Fort Collins, CO) to remove marrow and blood. (Figure 12) Custom designed end-caps of polyethylene were made by cutting the material bar into 1cm pieces and then custom drilling an indenting center dimple using a 5.5mm drill bit on a drill press. Bone cores were inserted into the dimple and secured in place using cynanoacrylate adhesive (Super Glue; Staples, Inc., Framingham, MA). (Figure 13) They were allowed to set for 24 hours and stored at 4°C.
Figure 12. Gross photograph of a bone core that has been lavaged in preparation for mechanical testing.
Figure 13. Bone core in end cap. Image courtesy of Dr. Katy Townsend and produced by Mr. Tim Vojt.
The cores were axially tested in a screw driven MTS machine under displacement control at 1mm per minute to the failure point. This was defined as greater than 5mm of axial displacement, a maximum of 250N of applied load, or a strain difference of 50%. Evaluated parameters included peak load (N) and initial stiffness (N/mm). (Figure 14)
Figure 14. Bone core in end caps being mechanically tested. *Figure courtesy of Dr. K Townsend and created by Mr. T. Vojt.*
2.9 Statistical analysis

Descriptive statistics were performed using statistical software (SPSS version 21, IBM, Armonk, NY). Comparisons between parametric data collected from normal and stovepipe femora were made using an independent (unpaired) Student’s t test, and correlations between parameters were reported as Pearson correlation coefficients. Regression analysis was performed to assess exactness of fit for the geometric model to measured CT volume. A significance level of p<0.05 was used throughout.
3.1 Pilot data on CFI and femoral geometry in German Shepherd Dogs and Retrievers

In the retrospective clinical series, the mean CFI values were 1.57 (SD ± 0.22, range 1.11-2) for GSD, 1.78 (SD ± 0.29, range 1.06-2.33,) for GR and 1.84 (SD ± 0.30, range 1.29-2.89 ) for LR. CFI values were significantly lower in GSD than in GR (p=0.007) or LR (p=0.001) but similar in GR and LR. p=0.711). The body weights were significantly different between the GSD and GR (p=0.007) but not between the GR and LR (p=0.166) or LR and GSD (p=0.404). The ages were similar for all groups (p=0.208). There was no relationship between age and CFI for any breed evaluated (GSD p=0.303; GR 0.693; LR p=0.916; overall p=0.137). There was also no significant relationship between weight and CFI (p=0.137). Implant use differed across the three groups (p=0.00014). CFI values were higher in dogs that went on to receive BFX stems than in dogs that were implanted with CFX stems (p=0.003).

Six dogs were included in a pilot series of CT scans prior to the main study, with three dogs assigned to the SP group and three to the normal group, as determined from radiographic evaluation of CFI. There were similar body weights between the groups (p=0.07) and the CFI were statistically significantly different between the groups (stovepipe CFI mean 1.6, normal mean 2.1, p=0.01). Evaluation of the medullary cavity revealed no statistically significant difference for medullary surface area between groups. However, medullary volume, medullary bone surface area to volume ratio, and trabecular
bone volume fraction were all statistically significantly different between the groups. The stovepipe femora group had a larger volume and a smaller bone volume fraction than the normal group. These results are summarized in Table 1. Evaluation of the cortical bone revealed no statistically significant differences between the stovepipe femora group and the normal group when mean cortical bone volume, mean cortical bone surface area, cortical bone volume fraction, and cortical thickness at half the overall distance were assessed. These results are summarized in Table 2.
Table 1. Preliminary data of 6 cases evaluating medullary volume and surface area.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Stovepipe</th>
<th>Normal</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medullary surface area (mm$^2$)</td>
<td>4396.6 (± 1353.8)</td>
<td>2663.9 (± 379.6)</td>
<td>P= 0.1</td>
</tr>
<tr>
<td>Medullary volume (mm$^3$)</td>
<td>13612.5 (± 4639.2)</td>
<td>5362.7 (± 496.2)</td>
<td>P= 0.038*</td>
</tr>
<tr>
<td>Medullary bone surface area to volume ratio</td>
<td>0.33 ± 0.01</td>
<td>0.5 ± 0.09</td>
<td>P= 0.034*</td>
</tr>
<tr>
<td>Trabecular bone volume fraction (%)</td>
<td>25.3 ± 4.77</td>
<td>49.6 ± 10.9</td>
<td>P=0.024*</td>
</tr>
</tbody>
</table>
Table 2. Preliminary cortical bone data from 6 dogs.

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Stovepipe (SD)</th>
<th>Normal (SD)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean cortical volume (mm$^3$)</td>
<td>11341.3 (± 2653.1)</td>
<td>13550.3 (± 5629.6)</td>
<td>P=0.572</td>
</tr>
<tr>
<td>Mean cortical bone surface area (mm$^2$)</td>
<td>9050.5 (± 3090.8)</td>
<td>6775.3 (± 1001.6)</td>
<td>P= 0.292</td>
</tr>
<tr>
<td>Cortical bone volume fraction (%)</td>
<td>59.5 (± 2.9)</td>
<td>62.3 (± 2.2)</td>
<td>P= 0.252</td>
</tr>
<tr>
<td>Cortical thickness at 50% distance</td>
<td>2.43 (± 0.79)</td>
<td>2.74 (± 0.69)</td>
<td>P= 0.643</td>
</tr>
</tbody>
</table>
3.2 Definitive clinical study

A total of 26 dogs were enrolled in the main study. One dog was excluded as the primary reason for coxofemoral pain was due to a femoral capital physeal fracture. Six dogs were excluded due to technical issues with the CT images due to a variation of the study protocol being used that provided insufficient trabecular bone detail for analysis.

Nineteen dogs had data that was sufficient for evaluation that were included in this study, with 9 dogs in the stovepipe group and 10 dogs in the normal group based upon CFI measurements. There were 10 male castrated dogs and 9 female spayed dogs. All dogs were bilaterally affected, with the predominantly lame limb being 11 right hips and 8 left hips. There were 5 German Shepherd Dogs (GSD), 4 Labrador Retrievers (LR), 4 Golden Retrievers including one Golden Doodle, 2 Bernese Mountain Dogs, and 1 each of Great Dane, Bloodhound, St. Bernard, and Newfoundland. The mean age for the stovepipe group was 33.67 months (SD ± 29.8 months, range 12-96 months) and the normal group was 34.6 months (SD ± 32.4 months, range 11-84 months), which were not statistically significantly different (p=0.949). The body weight in the stovepipe group was 44.0kg (SD ± 12.3 kg, range 31.6-73kg) and the normal group 33.8 kg (SD ± 6.3kg, range 23.8-43.8kg), which were statistically significantly different between the groups (p=0.03). The mean CFI for the stovepipe group was 1.69 (SD ± 0.07) and the normal group was 2.15 (SD ± 0.16), which were statistically significantly different (p<0.0001).
3.3 CT assessment of bone morphometry

*Morphometry of the 60-mm bone segment:* There were statistically significant differences between the stovepipe and the normal femora for the total endosteal volume, the total medullary space, and the fractional trabecular bone volume. (Table 3) There was a positive and statistically significant correlation between the total tissue volume and body weight. There were negative and statistically significant correlations between CFI and body weight, as well as between age and fractional trabecular bone volume. (Table 4) The correlations between CT-based morphometric variables within the 60-mm bone segment are summarized in Table 5.
Table 3. CT morphometry of the proximal canine femur. Data represent mean ± SD for 19 measurements collected from a 60-mm length of the proximal femur, as described in the Methods section and reported p-values are derived from independent sample (unpaired) Student’s t-test.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>unit</th>
<th>Stovepipe</th>
<th>Normal</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total tissue volume (TV)</td>
<td>mm³</td>
<td>25238.9 ± 7765.33</td>
<td>22106.38 ± 6032.24</td>
<td>0.337</td>
</tr>
<tr>
<td>Total cortical bone volume (CortV)</td>
<td>mm³</td>
<td>10178.94 ± 1898.55</td>
<td>8346.88 ± 1990.14</td>
<td>0.056</td>
</tr>
<tr>
<td>Total endosteal volume (EndV)</td>
<td>mm</td>
<td>14432.63 ± 4833.66</td>
<td>9190.92 ± 3247.42</td>
<td>0.012</td>
</tr>
<tr>
<td>Total medullary space volume (MedV)</td>
<td>mm³</td>
<td>12379.0 ± 4713.12</td>
<td>7049.04 ± 2683.17</td>
<td>0.007</td>
</tr>
<tr>
<td>Total trabecular bone volume (TbV)</td>
<td>mm³</td>
<td>2053.64 ± 429.8</td>
<td>2141.88 ± 899.95</td>
<td>0.792</td>
</tr>
<tr>
<td>Fractional trabecular bone volume (TbV/EndV)</td>
<td>%</td>
<td>15.49 ± 5.4</td>
<td>23.48 ± 7.3</td>
<td>0.016</td>
</tr>
<tr>
<td>Proximal cortical width 60mm slice</td>
<td>mm</td>
<td>5.9 ± 2.0</td>
<td>6.1 ± 2.7</td>
<td>0.866</td>
</tr>
<tr>
<td>Distal cortical width 60 mm slice</td>
<td>mm</td>
<td>3.7 ± 0.9</td>
<td>3.3 ± 0.8</td>
<td>0.347</td>
</tr>
</tbody>
</table>
Table 4. Pearson correlation coefficient (r) for comparisons between morphometric and
demographic variables (60 mm segment pooled data, both groups). Statistically
significant relationships are identified in bold.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Body weight</th>
<th>p-value</th>
<th>Age</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total tissue volume</td>
<td>0.749</td>
<td>0.0001</td>
<td>0.167</td>
<td>0.495</td>
</tr>
<tr>
<td>Cortical bone volume</td>
<td>0.152</td>
<td>0.533</td>
<td>-0.322</td>
<td>0.179</td>
</tr>
<tr>
<td>Medullary space volume</td>
<td>-0.300</td>
<td>0.212</td>
<td>0.282</td>
<td>0.242</td>
</tr>
<tr>
<td>Endosteal space</td>
<td>-0.310</td>
<td>0.197</td>
<td>0.285</td>
<td>0.237</td>
</tr>
<tr>
<td>Total trabecular bone volume</td>
<td>-0.155</td>
<td>0.526</td>
<td>0.101</td>
<td>0.682</td>
</tr>
<tr>
<td>Fractional trabecular bone volume</td>
<td>-0.032</td>
<td>0.897</td>
<td>-0.536</td>
<td>0.018</td>
</tr>
<tr>
<td>Cortical width, proximal</td>
<td>-0.289</td>
<td>0.230</td>
<td>0.351</td>
<td>0.141</td>
</tr>
<tr>
<td>Cortical width, distal</td>
<td>-0.126</td>
<td>0.607</td>
<td>0.218</td>
<td>0.371</td>
</tr>
<tr>
<td>Age</td>
<td>-0.065</td>
<td>0.790</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CFI</td>
<td>-0.521</td>
<td>0.022</td>
<td>0.045</td>
<td>0.845</td>
</tr>
</tbody>
</table>
Table 5. Pearson correlation coefficient (r) for comparisons within morphometric variables (60 mm segment, pooled data, both groups). Statistically significant relationships are identified in bold.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>TV</th>
<th>CortV</th>
<th>MSV</th>
<th>EndV</th>
<th>TbV</th>
<th>TbV/V</th>
<th>CortWP</th>
<th>CortWD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tissue volume (TV)</td>
<td>0.142</td>
<td>0.201</td>
<td>0.191</td>
<td>-0.005</td>
<td>-0.549</td>
<td></td>
<td>0.045</td>
<td>-0.016</td>
</tr>
<tr>
<td>Cortical bone volume (CortV)</td>
<td>0.142</td>
<td>0.829</td>
<td>0.831</td>
<td>0.263</td>
<td>-0.002</td>
<td>-0.109</td>
<td>-0.006</td>
<td></td>
</tr>
<tr>
<td>Medullary space volume (MSV)</td>
<td>0.201</td>
<td>0.829</td>
<td>0.990</td>
<td>0.226</td>
<td>-0.197</td>
<td>-0.035</td>
<td>-0.105</td>
<td></td>
</tr>
<tr>
<td>Endosteal volume (EndV)</td>
<td>0.191</td>
<td>0.831</td>
<td>0.990</td>
<td>0.363</td>
<td>-0.194</td>
<td>0.001</td>
<td>-0.060</td>
<td></td>
</tr>
<tr>
<td>Trabecular bone volume (TbV)</td>
<td>-0.005</td>
<td>0.263</td>
<td>0.226</td>
<td>0.363</td>
<td>-0.041</td>
<td>0.240</td>
<td>0.276</td>
<td></td>
</tr>
<tr>
<td>Fractional trabecular bone volume (TbV/TV)</td>
<td>-0.549</td>
<td>-0.002</td>
<td>-0.197</td>
<td>-0.194</td>
<td>-0.041</td>
<td>-0.325</td>
<td>-0.372</td>
<td></td>
</tr>
<tr>
<td>Cortical width, proximal (CortWP)</td>
<td>0.045</td>
<td>-0.109</td>
<td>-0.035</td>
<td>0.001</td>
<td>0.240</td>
<td>-0.325</td>
<td>0.694</td>
<td></td>
</tr>
<tr>
<td>Cortical width, distal (CortWD)</td>
<td>-0.016</td>
<td>-0.006</td>
<td>-0.105</td>
<td>-0.060</td>
<td>0.276</td>
<td>-0.372</td>
<td>0.694</td>
<td></td>
</tr>
</tbody>
</table>
The proximal craniocaudal (CrCa) radius, distal mediolateral (ML) radius, distal craniocaudal radius, proximal area (A1), and distal areas (A2) were all statistically significantly different. The proximal mediolateral radius and the TI were not statistically significantly different. (Table 6) Correlations are denoted in Table 7.
Table 6. Endosteal canal surface area, radii, and taper index (TI). Data represent mean (± SD) and comparisons were made using independent sample Student’s t-test. Significant differences are highlighted in bold.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Unit</th>
<th>Stovepipe</th>
<th>Normal</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proximal ML radius</td>
<td>Mm</td>
<td>15.04 ± 2.46</td>
<td>13.16 ± 2.04</td>
<td>0.087</td>
</tr>
<tr>
<td>Proximal CrCa radius</td>
<td>Mm</td>
<td>4.82 ± 1.30</td>
<td>3.28 ± 1.04</td>
<td><strong>0.011</strong></td>
</tr>
<tr>
<td>Distal ML radius</td>
<td>Mm</td>
<td>6.68 ± 1.34</td>
<td>4.86 ± 0.78</td>
<td><strong>0.002</strong></td>
</tr>
<tr>
<td>Distal CrCa radius</td>
<td>Mm</td>
<td>6.84 ± 1.31</td>
<td>4.99 ± 0.79</td>
<td><strong>0.001</strong></td>
</tr>
<tr>
<td>Proximal area (A1)</td>
<td>mm²</td>
<td>234.25 ± 99.7</td>
<td>137.8 ± 56.23</td>
<td><strong>0.017</strong></td>
</tr>
<tr>
<td>Distal area (A2)</td>
<td>mm²</td>
<td>148.04 ± 54.79</td>
<td>77.71 ± 25.30</td>
<td><strong>0.002</strong></td>
</tr>
<tr>
<td>Proximal aspect ratio</td>
<td></td>
<td>3.22 ± 0.54</td>
<td>4.31 ± 1.22</td>
<td><strong>0.039</strong></td>
</tr>
<tr>
<td>Distal aspect ratio</td>
<td></td>
<td>0.9772 ± 0.07</td>
<td>0.9739 ± 0.07</td>
<td>0.602</td>
</tr>
<tr>
<td>Taper index (TI)</td>
<td>%</td>
<td>33.99 ± 21.24</td>
<td>39.36 ± 17.47</td>
<td>0.554</td>
</tr>
</tbody>
</table>
Table 7. Pearson correlation coefficients for the surface areas, radii, and taper index relative to demographic information (60mm segment, all data pooled). Statistically significant associations are highlighted in bold.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Proximal ML radius</th>
<th>Proximal CrCa radius</th>
<th>Distal ML radius</th>
<th>Distal CrCa radius</th>
<th>Proximal area</th>
<th>Distal area</th>
<th>Taper ratio</th>
<th>Age</th>
<th>Weight</th>
<th>CFI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proximal ML Radius</td>
<td>1</td>
<td><strong>.666</strong></td>
<td><strong>.795</strong></td>
<td><strong>.722</strong></td>
<td><strong>.837</strong></td>
<td><strong>.764</strong></td>
<td>.112</td>
<td>.152</td>
<td>.606*</td>
<td>-.455</td>
</tr>
<tr>
<td>Prox CrCa radius</td>
<td><strong>.666</strong></td>
<td>1</td>
<td><strong>.679</strong></td>
<td><strong>.739</strong></td>
<td><strong>.953</strong></td>
<td><strong>.717</strong></td>
<td>.374</td>
<td>.318</td>
<td>.475*</td>
<td>-.557*</td>
</tr>
<tr>
<td>Distal ML radius</td>
<td><strong>.795</strong></td>
<td><strong>.679</strong></td>
<td>1</td>
<td><strong>.954</strong></td>
<td><strong>.762</strong></td>
<td><strong>.985</strong></td>
<td>-.297</td>
<td>.026</td>
<td>.765**</td>
<td>-.723**</td>
</tr>
<tr>
<td>Distal CrCa radius</td>
<td><strong>.722</strong></td>
<td><strong>.739</strong></td>
<td><strong>.954</strong></td>
<td>1</td>
<td><strong>.785</strong></td>
<td><strong>.981</strong></td>
<td>-.302</td>
<td>.145</td>
<td>.687**</td>
<td>-.758**</td>
</tr>
<tr>
<td>Proximal Area</td>
<td><strong>.837</strong></td>
<td><strong>.953</strong></td>
<td><strong>.762</strong></td>
<td><strong>.785</strong></td>
<td>1</td>
<td><strong>.787</strong></td>
<td>.297</td>
<td>.245</td>
<td>.552*</td>
<td>-.530*</td>
</tr>
<tr>
<td>Distal Area</td>
<td><strong>.764</strong></td>
<td><strong>.717</strong></td>
<td><strong>.985</strong></td>
<td><strong>.981</strong></td>
<td><strong>.787</strong></td>
<td>1</td>
<td>-.302</td>
<td>.097</td>
<td>.759**</td>
<td>-.718**</td>
</tr>
<tr>
<td>Taper ratio</td>
<td>.112</td>
<td>.374</td>
<td>-.297</td>
<td>-.302</td>
<td>.297</td>
<td>-.302</td>
<td>1</td>
<td>.344</td>
<td>-.222</td>
<td>.196</td>
</tr>
<tr>
<td>Age</td>
<td>.152</td>
<td>.318</td>
<td>.026</td>
<td>.145</td>
<td>.245</td>
<td>.097</td>
<td>1</td>
<td>-.065</td>
<td>.045</td>
<td></td>
</tr>
<tr>
<td>Weight</td>
<td><strong>.606</strong></td>
<td><strong>.475</strong></td>
<td><strong>.765</strong></td>
<td><strong>.687</strong></td>
<td><strong>.552</strong></td>
<td><strong>.759</strong></td>
<td>-.222</td>
<td>-.065</td>
<td>1</td>
<td>-.521*</td>
</tr>
<tr>
<td>CFI</td>
<td>-.455</td>
<td>-.557*</td>
<td><strong>.723</strong></td>
<td><strong>.758</strong></td>
<td><strong>.530</strong></td>
<td><strong>.718</strong></td>
<td>.196</td>
<td>.045</td>
<td>-.521*</td>
<td>1</td>
</tr>
</tbody>
</table>
**Figure 15:** Graph of the aspect ratio comparing the radii from ML to CrCa for the proximal aspect of the 60mm segment showing the differences between the groups. The p-value was 0.039.
The correlation between the volume of a frustrum in both planes and the Mimics endosteal volume was statistically significant and strongly correlated. (Table 8) The aspect ratio of the ML to CrCa diameters in the proximal segment was statistically significantly different between the groups (p= 0.039). (Figure 15)

**Figure 16.** Regression analysis showing the relationship between frustum volume and CT derived volumes. The equation of the line of best fit is shown ($r^2 = 0.85$, p<0.001). When broken down by group, the corresponding $r^2$ values are 0.94 for the normal group (p<0.0001) and 0.77 for the normal group (p<0.01).
**Table 8.** Pearson’s correlation between the calculated frustrum volumes based on radii in both planes compared with the endosteal volume from the 60mm segment CT derived measurements.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>ML frustum volume</th>
<th>CrCa frustum volume</th>
<th>CT derived volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>ML frustum volume</td>
<td></td>
<td><strong>0.828</strong></td>
<td><strong>0.920</strong></td>
</tr>
<tr>
<td>CrCa frustum volume</td>
<td><strong>0.828</strong></td>
<td></td>
<td><strong>0.899</strong></td>
</tr>
<tr>
<td>CT derived volume</td>
<td><strong>0.920</strong></td>
<td>0.899</td>
<td></td>
</tr>
</tbody>
</table>

The regression analysis showed that the ML frustum volume strongly and significantly described the geometrical shape of the normal femur ($r^2 = 0.94$, $p<0.0001$) and was less strongly correlated with the geometrical shape of the stovepipe femur ($r^2 = 0.733$, $p = 0.003$).
Morphometry of the 20-mm bone segment: There were statistically significant differences for the total tissue volume, the total medullary space volume, the total endosteal volume, and fractional trabecular bone volume for the 20mm segment. (Table 9) There were positive and statistically significant correlations between body weight and tissue volume, cortical bone volume, medullary space volume, and endosteal volume. (Table 10) The correlations between CT-based morphometric variables within the 20-mm bone segment are summarized in Table 11.

The relationship between fractional bone volume (BV/TV) data from the two bone segments (20- and 60-mm) and the micro-CT assessment of the bone core is provided in Table 12.
Table 9. CT morphometry of the 20-mm “osseointegration zone” from the proximal canine femur. Data represent mean ± SD for 19 measurements, as outlined in Results section and reported p-values are derived from independent sample (unpaired) Student’s t-test.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>unit</th>
<th>Stovepipe</th>
<th>Normal</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total tissue volume</td>
<td>mm³</td>
<td>11521.89 ± 2721.78</td>
<td>8961.2 ± 2400.03</td>
<td>0.044</td>
</tr>
<tr>
<td>Total cortical bone volume</td>
<td>mm³</td>
<td>3331.16 ± 672.49</td>
<td>2672.23 ± 884.51</td>
<td>0.088</td>
</tr>
<tr>
<td>Medullary space volume</td>
<td>mm³</td>
<td>5083.14 ± 2073.11</td>
<td>2945.28 ± 1199.41</td>
<td>0.013</td>
</tr>
<tr>
<td>Total endosteal volume</td>
<td>mm³</td>
<td>6846.83 ± 2164.19</td>
<td>4833.22 ± 1281.75</td>
<td>0.023</td>
</tr>
<tr>
<td>Total trabecular bone volume</td>
<td>mm³</td>
<td>1763.7 ± 681.09</td>
<td>1887.95 ± 798.61</td>
<td>0.721</td>
</tr>
<tr>
<td>Fractional trabecular bone volume</td>
<td>%</td>
<td>27.32 ± 11</td>
<td>39.49 ± 14</td>
<td>0.050</td>
</tr>
<tr>
<td>Cortical width, proximal</td>
<td>mm</td>
<td>4.7 ± 0.76</td>
<td>5.4 ± 1.2</td>
<td>0.159</td>
</tr>
<tr>
<td>Cortical width, distal</td>
<td>mm</td>
<td>3.7 ± 1.1</td>
<td>3.4 ± 0.9</td>
<td>0.591</td>
</tr>
</tbody>
</table>
Table 10. Pearson correlation coefficient (r) for comparisons between morphometric and demographic variables (20 mm segment pooled data, both groups). Statistically significant relationships are identified in bold.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Body weight</th>
<th>p-value</th>
<th>Age</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tissue volume</td>
<td>0.713</td>
<td>0.001</td>
<td>0.191</td>
<td>0.433</td>
</tr>
<tr>
<td>Cortical bone volume</td>
<td>0.604</td>
<td>0.006</td>
<td>0.253</td>
<td>0.296</td>
</tr>
<tr>
<td>Medullary space volume</td>
<td>0.625</td>
<td>0.004</td>
<td>0.194</td>
<td>0.427</td>
</tr>
<tr>
<td>Endosteal space volume</td>
<td>0.704</td>
<td>0.001</td>
<td>0.140</td>
<td>0.569</td>
</tr>
<tr>
<td>Total trabecular bone volume</td>
<td>0.245</td>
<td>0.311</td>
<td>-0.139</td>
<td>0.570</td>
</tr>
<tr>
<td>Fractional trabecular bone volume</td>
<td>-0.304</td>
<td>0.206</td>
<td>-0.237</td>
<td>0.329</td>
</tr>
<tr>
<td>Age</td>
<td>-0.065</td>
<td>0.790</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 11. Pearson correlation coefficient (r) for comparisons within morphometric variables (20mm segment pooled data, both groups). Statistically significant relationships are identified in bold.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>TV</th>
<th>CortV</th>
<th>MSV</th>
<th>EndV</th>
<th>TbV</th>
<th>TbV/V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tissue volume (TV)</td>
<td>0.832</td>
<td>0.891</td>
<td>0.969</td>
<td>0.258</td>
<td>-0.456</td>
<td></td>
</tr>
<tr>
<td>Cortical bone volume (CortV)</td>
<td></td>
<td></td>
<td>0.716</td>
<td>0.745</td>
<td>0.115</td>
<td>-0.415</td>
</tr>
<tr>
<td>Medullary space volume (MSV)</td>
<td>0.891</td>
<td></td>
<td></td>
<td>0.932</td>
<td>-0.137</td>
<td>-0.751</td>
</tr>
<tr>
<td>Endosteal space volume (EndV)</td>
<td>0.969</td>
<td>0.745</td>
<td>0.932</td>
<td></td>
<td>0.230</td>
<td>-0.475</td>
</tr>
<tr>
<td>Trabecular bone volume (TbV)</td>
<td>0.258</td>
<td>0.115</td>
<td>-0.137</td>
<td>0.230</td>
<td></td>
<td>0.722</td>
</tr>
<tr>
<td>Fractional trabecular bone volume (TbV/TV)</td>
<td>-0.456</td>
<td>-0.415</td>
<td>-0.751</td>
<td>-0.475</td>
<td>0.722</td>
<td></td>
</tr>
</tbody>
</table>
**Table 12.** Pearson correlation coefficient (r) for comparisons between fractional trabecular bone volume (BV/TV) in the 60-mm segment, the 20-mm segment and from the micro-CT data (pooled data, both groups). Statistically significant relationships are identified in bold.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>60mm BV/TV</th>
<th>20mm BV/TV</th>
<th>Micro-CT BV/TV</th>
<th>PMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>60mm BV/TV</td>
<td></td>
<td>0.875</td>
<td>-0.031</td>
<td>0.113</td>
</tr>
<tr>
<td>20mm BV/TV</td>
<td></td>
<td></td>
<td>0.213</td>
<td>0.333</td>
</tr>
<tr>
<td>Micro-CT BV/TV</td>
<td>-0.031</td>
<td>0.213</td>
<td></td>
<td>0.849</td>
</tr>
<tr>
<td>Polar moment of inertia (PMI)</td>
<td>0.113</td>
<td>0.333</td>
<td></td>
<td>0.849</td>
</tr>
</tbody>
</table>
3.4 Micro-CT morphometry of the bone cores

Bone cores were obtained from 18 of the 19 cases. One bone core was lost during processing due to breakage and one patient did not undergo THR. Micro-CT data were available for 17 cases, with 7 stovepipe and 10 normal dogs comprising the cases. Four cases could not be reconstructed for 3D measurements and only had 2D data collected (3 normal, 1 stovepipe).

There was no evidence of a statistically significant difference in any of the micro-CT parameters recorded from the two groups. The results are summarized in Table 13. Twelve of the micro-CT scans were reconstructed for visual analysis and these images are available in the Appendix.
Table 13. Morphometric and mechanical test data collected from micro-computed tomography of 17 bone cores from normal (N=10) and stovepipe (N=7) femora. Data represent mean ± SD and reported p-values are derived from independent sample (unpaired) Student’s t-test.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>unit</th>
<th>Stovepipe</th>
<th>Normal</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total tissue volume</td>
<td>mm³</td>
<td>385225972.3 ± 131707171.6</td>
<td>505422827.2 ± 199847911.3</td>
<td>0.186</td>
</tr>
<tr>
<td>Total bone volume</td>
<td>mm³</td>
<td>21250945.9 ± 12515246.5</td>
<td>29531842.3 ± 17182326.9</td>
<td>0.295</td>
</tr>
<tr>
<td>Trabecular number</td>
<td>/mm</td>
<td>0.00008853 ± 0.00003</td>
<td>0.00011 ± 0.00009</td>
<td>0.582</td>
</tr>
<tr>
<td>Trabecular thickness</td>
<td>µm</td>
<td>0.1258 ± 0.05</td>
<td>0.1274 ± 0.03</td>
<td>0.939</td>
</tr>
<tr>
<td>BV/TV</td>
<td>%</td>
<td>6.6 ± 3.95</td>
<td>7.5 ± 5.44</td>
<td>0.689</td>
</tr>
<tr>
<td>Polar moment of inertia</td>
<td></td>
<td>490189879.2 ± 207387947.6</td>
<td>566951204.6 ± 348216257.4</td>
<td>0.611</td>
</tr>
</tbody>
</table>
3.5 Mechanical testing

The peak load and initial stiffness were similar between the stovepipe group and the normal group (Table 14). The correlation between the peak load, the stiffness, and the BV/TV were strong, positive, and significant. (Table 15)

Table 14. Mechanical testing data, including ranges, of bone cores compared using a Student’s t-test.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Unit</th>
<th>Stovepipe mean</th>
<th>Range</th>
<th>Normal mean</th>
<th>Range</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak load</td>
<td>N</td>
<td>9.00 ± 9.06</td>
<td>3.41 - 27.08</td>
<td>24.8 ± 46.45</td>
<td>5.22 - 130.04</td>
<td>0.432</td>
</tr>
<tr>
<td>Initial stiffness</td>
<td>N/mm</td>
<td>33.8 ± 54.1</td>
<td>4.47 - 143.68</td>
<td>39.0 ± 69.7</td>
<td>2.18 - 195.32</td>
<td>0.884</td>
</tr>
<tr>
<td>Peak load (Townsend study)</td>
<td>N</td>
<td>N/A</td>
<td>N/A</td>
<td>27.98 ± 27.13</td>
<td>3.99 - 93.75</td>
<td></td>
</tr>
<tr>
<td>Stiffness (Townsend study)</td>
<td>N/mm</td>
<td>N/A</td>
<td>N/A</td>
<td>85.30 ± 75.28</td>
<td>1.3 - 221.6</td>
<td></td>
</tr>
</tbody>
</table>
Table 15. Pearson correlation coefficient (r) for comparisons between trabecular bone volume fraction by micro-CT (BV/TV), peak load and stiffness for the 13 bone cores (pooled data from both groups). Statistically significant relationships are identified in bold.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Peak Load</th>
<th>Stiffness</th>
<th>BV/TV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak load</td>
<td></td>
<td>0.879</td>
<td>0.748</td>
</tr>
<tr>
<td>Stiffness</td>
<td>0.879</td>
<td></td>
<td>0.850</td>
</tr>
<tr>
<td>BV/TV</td>
<td>0.748</td>
<td>0.850</td>
<td></td>
</tr>
</tbody>
</table>
Chapter 4: Discussion

4.1 CT assessment of bone geometry

Proximal femoral morphology has been identified as an important factor in the development of femoral complications, including stem subsidence and femoral fracture.[40, 67, 69] However, clinical differences in proximal femoral morphology have been incompletely studied in the dog. The dogmatic notion of a stovepipe femur has been present within the veterinary literature and veterinary orthopedic surgery field, and assumptions have been made through clinical experience that this morphology has an associated poorer bone quality, similar to human elderly females with stovepipe femora and osteoporosis. To our knowledge this is the first study systematically assess the geometry, microstructure and mechanical properties of bone from the proximal femur of clinically affected dysplastic dogs.

The results support the suggestion that GSD have a lower CFI and a more stovepipe femoral geometry than Golden or Labrador Retrievers. In the assessment of overall geometry, differentiating between a conical proximal femur, which is normal, and the cylindrical stovepipe femur, evaluation of 3D structures is key. In order to compare volumes, a fixed height of femur was evaluated. This allowed for variations in the radius of the proximal femur as well as changes in the structure over its height to be assessed. Additionally, comparison of the volumes can be performed to identify if the underlying geometry is different.
This research supports the hypothesis that there is morphologic variation and the existence of a stovepipe femur. These femora have larger medullary canals but similar amounts of cortical bone present. This was reflected both in the medullary space that is not filled by bone and the endosteal space containing both the trabecular bone and medullary space. The total tissue volume which included all of the bone, cortical and trabecular, as well as the medullary space was also statistically significantly different between the groups when the 20 mm proximal segment was considered.

Canal flare index (CFI) is a 2D measure that helps to identify the three dimensional geometry of the proximal femur. By recognizing the similarity in the bone diameter at the lesser trochanter and the femoral isthmus, a more straight-sided, cylindrical femur can be identified. Due to the smaller distribution of trabecular bone relative to the larger endosteal diameter associated with this conformation, implant selection should aim to provide a stable implant that can fill the canal or be supported through cement or a collared stem.

CFI and the fractional trabecular bone volume had a moderate to strong positive correlation suggesting that CFI does have utility in predicting bone microstructure, with a lower CFI reflecting a smaller volume fraction of trabecular bone within the endosteal cavity than a bone with a higher CFI. This helps to explain the previous clinical experience and dogmatic notion that a stovepipe femur may be less able to support a cementless implant, be more likely to undergo subsidence of the implant, and may be more prone to femoral fracture.
4.2 CT assessment of bone size and composition

Although there was a strong and statistically significant correlation between body weight and overall bone size (as determined via measurement of total tissue volume), there was no difference in overall bone size between the two groups, despite differences in breed and body weight. Significant differences were identified for the total endosteal volume and marrow space volume, but not in the volumes of cortical or trabecular bone. The combination of a larger medullary volume and preserved cortical volume would naturally suggest that the overall bone must be larger, so we suspect that the failure to identify changes in total tissue volume reflect a type II error due to sample size limitations.

4.3 Geometric descriptions of the endosteal canal

Evaluation of the proximal and distal surface areas of the 60mm segment showed significant differences. This was primarily reflected in the craniocaudal measurement of the bone which would translate to the canal diameter as seen on the lateral radiograph of the femur. Previous studies have evaluated femoral fill by the implant and radiographic evaluation of the implant fill of the endosteal canal. [37, 40, 70, 71] Evaluation of the canal geometry revealed that there are differences between the stovepipe femora and the normal femora in both the mediolateral and caudocranial plane. This suggests that the implant fill for an implant is dependent on both planes having appropriate implant to trabecular bone contact.

As the bone radii were different, the surface area of the endosteal canal was also different at the proximal and distal level of the 60mm segment. Previous work, as well as
the distribution of the trabecular bone in the proximal 20mm segment of bone noted in this study, suggest that the distal fit of the stem is less important for establishment of the initial press fit and has greater affects on long term stability of the implant. [36, 72, 73] Conversely, the proximal fit is of paramount importance in developing the interference fit of a press fit, cementless implant.

By evaluating the 2D measurements of the proximal and distal ellipse, we were able to determine in which plane the size variability occurred within to contribute to a larger endosteal canal. The proximal mediolateral distance, or the diameter spanning from the medial to lateral endosteal surface, was similar in the groups. However, the craniocaudal diameter was different suggesting that the proximal femur in the stovepipe group is more circular and less ovoid than the normal femur. There was a strong and significant correlation between these diameters.

The distal radii were also statistically significantly different between groups. This was found in both the craniocaudal and mediolateral direction suggesting the canal overall becomes more circular at the level of the isthmus. The stovepipe group remains a larger circumference than the normal group.

To predict the 3D structure from two known areas and the amount of change in the endosteal diameter throughout the height of the proximal segment, the taper index was developed. This did not have the effect of being able to predict geometry or detect a difference between the groups. Determining a system of evaluation involving both planes on radiographs could help to better predict implant fit and fill of the endosteal canal.
The stovepipe femur is expected to be more cylindrical in shape while the normal femur is more conical. This was supported by the change in the radii from proximal to distal. The ratio of the proximal ML radius to the distal ML radius was 2.2 for the stovepipe group and 2.7 for the normal group. While both groups have a narrowing as the endosteal cavity proceeds from proximal to distal, the degree of change is greater in the normal group, more consistent with a conical shape. The change in the CrCa plane is similar with 0.71 in the stovepipe femur and 0.65 in the normal femur. However, the overall surface area for an elliptical 2D region, as a product of these radii, is significantly different.

A cone that has two different radii at the ends is termed a frustum. Evaluation of this geometric shape showed that it very well described the shape of a normal femur. However, while it was still statistically significant, the fit of the frustum to the stovepipe femur was not as strong. The best geometric shape to describe a femur is not the frustum. This supports the previous descriptive evaluation that a stovepipe femur is more cylindrical. However, the normal femur is most closely matched by a frustum, or a truncated cylinder. Further evaluation of the champagne-fluted femur may reveal that it is more closely geometrically related to the cone.

4.3 CT assessment of bone mass and distribution

The contents of the endosteal space (the space that is bounded by the endosteum of the femoral cortex) include bone marrow, fat and medullary trabecular bone. The total volume of trabecular bone within the endosteal space was similar between the two groups,
but when corrected for total endosteal space, the fractional trabecular bone volume was significantly smaller in the stovepipe femur. The same observation was made in both the 60mm segment and the 20mm segment. The fractional volume reflects the relationship between the trabecular bone and the entire endosteal volume, suggesting that the same amount of trabecular bone is spread over a larger area in the stovepipe femur. This may explain why differences are experienced intra-operatively as the bone is dispersed along the cortical margin and does not extend to the center of the endosteum in a stovepipe femur. Consequently, penetration with the broach and preparation with the reamer during THR is met with less resistance in the center region despite there being the same amount of trabecular bone lining the walls.

The area examined included the proximal femur from approximately the level of the femoral head and neck ostectomy to both the isthmus and through the implant interface region of a press-fit implant; this was represented by the 60-mm and 20-mm slices, respectively. As the trabecular bone has a focal extent primarily through the calcar region, both areas were evaluated. Despite there being a smaller medullary space with more trabecular bone visible on the computer reconstructions, the amount of fraction of trabecular bone was similar between the two segment lengths. This supports that the trabecular bone is primarily confined to the proximal aspect of the femur in the region of the lesser trochanter.

The differences in trabecular bone density within the proximal femur are likely to have significant implications for both initial and long-term stability of a cementless
implant. It was unfortunately impossible in this study to re-image the femur after implantation of the femoral component to study the periprosthetic bone in greater detail. Finite element modeling studies may be useful for better assessing canal fill and the interaction with surrounding trabecular bone. It is also unknown what affect preparation of the femoral canal has on the trabecular microarchitecture. Broaching, reaming, and finishing with files should collapse the trabecular spacing, remove cancellous bone, and break the trabecular framework. While this creates a slightly undersized cavity to fill with a cementless implant, removal of trabecular bone in an already large medullary canal may explain the increased risk of complications seen with press fit implants in stovepipe femora. The microarchitecture of the trabeculae that are present may be so disrupted that there is secondary collapse or a significant depletion of the biomechanical strength of the tissue that it is consequently unable to support a press fit implant.

Subjectively, the cortical bone appears thinner on radiographs in stovepipe femora but the data from this study do not support this hypothesis. The cortical bone volume was similar although trended towards statistically significant differences. Measures of the cortical thickness at the proximal and distal ends of the investigated segments were not different between groups either. When the cortical volume was assessed relative to the total tissue volume, it was not different between the groups nor was the total cortical bone volume. This was also found over the 20mm segment as well.
4.4. Micro-CT assessment of bone quality

Micro-CT provides an increased level of 3D detail given the greater resolution that is attainable with this imaging modality. This allowed for the more detailed assessment of trabecular bone, building on an earlier study that had used micro-CT to characterize trabecular bone harvested from healthy cadavers with no evidence of orthopedic disease.[66] The results from the current study showed that there were no significant differences in trabecular bone density, trabecular thickness or trabecular spacing.

This lack of statistically significant difference does not match with the subjective or clinical impression of this bone. The micro-CT images of the bone cores provided in Appendix C help to visualize the noted differences in trabecular density, trabecular width, and trabecular spacing that were appreciated during the testing of the bone cores. Additionally, the cores from the stovepipe dogs were often so fragile as to not tolerate handling for processing into end caps including being washed with water to remove soft tissue debris. While the data suggests there is no difference, this is suspected to be a false negative result from a type II error due to lack of power for this measurement.

The microstructure of trabecular bone taken from this location appears to be similar in healthy dogs and in dysplastic dogs. Interestingly, though, the correlations between microstructural properties and mechanical properties were not as strong in this series of bone cores as they were in the Townsend study.[66] While it is hard to make direct comparisons, in part because the cores came from slightly different trajectories within the femur, these observations open up the intriguing possibility that the underlying disease
process (CHD) or perhaps chronic lameness and unloading may alter the material properties of the bone, without any measurable effect on bone microstructure. Additional samples will be needed to evaluate this further, and a more complete examination of bone material properties will likely require the use of more advanced analytic techniques such as scanning electron microscopy to assess porosity and microfracture density and perhaps chemical analysis to probe for the levels of advanced glycation end-products that have been implicated as a potential marker of bone degradation and fragility.[74]

4.5 Clinical ramifications of this work

Evaluation of cemented stems to assess the effect of surgical technique on implant positioning showed reliable reconstruction of the femoral head offset position when the stem was slightly undersized relative to the canal. [37] Removal of additional bone from the subtrochanteric region allowed for optimal stem alignment with a centralized distal stem tip. [37] Translation of this cemented technique may not be applicable in the cementless stem as this would deplete the trabecular bone necessary to support the implant. Although the overall trabecular bone volume was similar between groups, the relative amount of trabecular bone within the volume of endosteal space was different. As the trabecular size, number, and spacing were similar, the clinical observation of less robust bone within the canal of a stovepipe femur is likely the result of differences in the distribution of trabecular bone and/or the material properties of the trabecular bone. Both
seem likely, although additional samples and methodologies will be needed to explore this issue in greater detail.

Previous reports have suggested that a stovepipe configuration may lead to a higher complication rate, particularly for subsidence or femoral fracture after THR.[67] This may be due to either failure of the trabecular bone to provide mechanical support for the implant or a failure to ensure optimal implant fill within a SP canal. The tapered cone of the press fit implant may lack support within a cylindrical proximal femoral morphology, particularly if there is less trabecular bone present to fill the space between the implant and the cortical bone.

The data from this study suggest that optimal stem fixation in dogs with stovepipe femora may be more dependent on cortical than cancellous bone. These results now need to be confirmed in a larger series of clinical cases, but they provide a rationale for the use of bone-conserving procedures such as surface replacement or alternative stem designs for more adequate canal fill. This may include the use of custom implants with geometries that mirror those of the endosteum into which they are to be seated.

In contrast with prior reports, we did not find any association between CFI and the age of the animal. The decision as to whether to use cemented or cementless femora implants was made by the attending surgeon without any input from the research team and without knowledge of the CT or micro-CT data, but it was interesting to note that dogs with a lower CFI were more likely to receive a cemented rather than cementless femoral implant. There was some variability in CFI within all three breeds and it is likely that other
factors may also play an important role in determining the success of femoral stem fixation. Future studies will focus on trying to identify whether the combination of CFI with objective measures of bone quality (e.g. bone mineral density) or quantity (e.g. fractional bone volume, determined from computed tomography) will provide a more robust prediction of femoral implant performance.

As Dorr et al has established in humans, different femoral conformations have differences in bone quality. In Noble’s initial work detailing each of the morphologic types of the proximal femur, he saw an age-related correlation between increasing age and decreasing CFI, or a trend towards becoming stovepipe as the patient ages. Studies in dogs have shown a similar association but have also found that there is no correlation between age and conformation.

In dogs, the correlation between morphology and bone quality has not been thoroughly investigated. It is known that the mechanical properties of the bone change with age, regardless of species. [67] The change in the overall shape as defined by CFI, cervico-diaphyseal angle, and femoral neck anteversion is less consistent. Reports supporting a correlation between increasing age and decreasing CFI in dogs have been noted previously.[75] Studies that do not support this change suggest [51, 53, 76] dogs do not have age-related remodeling changes that alter the proximal femoral morphology. In these studies, older human females have changes in the proximal femur that is suspected to exert a protective effect on the decreased mechanical strength of the bone within the region. [51]
The relationship between femoral anatomical variations and implant fit and biomechanics is complex. Variations in the morphology may affect the longevity of the implant, cemented or cementless. [37] Femoral medullary canal width variations are suspected to affect the implant fit and function of cemented implants. [37] Implants need to reconstruct the proximal segment of the femur in order to allow for normal loading and range of motion. [37]

Since implant geometry should closely match proximal femoral morphology, and proximal femoral morphology can be variable, implant design should follow this different endosteal conformation in order to maximize implant stability. As precise anatomic symmetry between implant and femur allows for normal loading, normal range of motion, and a long-term, stable implant-bone interface, it is important that the proper stem be placed within the stovepipe femur.

Cemented stems negate the need for a precise implant-endosteal interface match as the cement mantle can be custom fit to the endosteal surface while simultaneously bonding to the implant. This provides immediate implant stability and has been the implant system of choice for the stovepipe femur traditionally. Concerns over cement failure, aseptic loosening, and the lack of long-term cement durability make this a less desirable implant system in the young dog as the implant may not survive the lifespan of the patient.

The collared cementless stem developed by BioMedtrix aimed to provide support at the level of the calcar to prevent subsidence while allowing for bony ingrowth. The implant applies some of the cemented stem design with a flange protrusion over the calcar.
region that should rest intimately on the bone surface. The porous coating on the underside of this area allows for bone ingrowth in this region as well. Long-term durability and assessment of this implant is not currently available but previous studies evaluating a cementless collared stem have noted stress shielding in this region of the implant. [42]

The Kyon THR system uses a smaller intramedullary implant and supports it with locking screws along the medial cortex. This allows for implant stability without a cement mantle. While this implant system should not be able to undergo subsidence, femoral fracture remains a risk. [47] Femoral fractures would perpetuate during both medullary preparation and post-operatively propagating from the screw holes. [47] Reports on the outcome of the Kyon hip system suggest that the medial cortical fixation allows for better biologic remodeling and cortical thickening in this region due to reduced stress shielding. [47] This implant system may also be a consideration for dogs with stovepipe femora.

The Helica hip abandons the intramedullary femoral stem design of the previous THR systems. It is based on a screw prosthesis methodology involving a modular system that inserts along the femoral neck. This avoids the proximal femoral morphologic variations and aims to provide a firm anchorage for the femoral head component. As it also aligns along the femoral neck, head offset and anteversion can be matched. [77] Biomechanical evaluation of this system revealed that there were differences in the strain distribution of the proximal femur, vertical displacement of the implant during cyclic loading, and alterations in the femoral geometry after implantation. [78]
From this work, recommendation on implant selection can be made. For a stovepipe femora with suspected poor bone quality, use of a cementless system should be avoided. Preference would be for a cemented femoral stem in dogs with a CFI <1.8 and with poor bone quality, usually older GSD dogs or similar giant breeds. A collared cementless stem may not have adequate stability to avoid rotation within the proximal stovepipe canal but could be used in a dog of increased age with increased risk of subsidence without a stovepipe conformation.

4.6 Limitations of this work

Canal flare index has been used since defined by Noble in 1988 to determine morphologic groups. Grouping in this research was based upon breeds of dogs that are commonly suspected to have a stovepipe configuration. However, the preliminary data for this when evaluated GSD showed that within the CHD affected dogs presenting for THR, the range of CFI represented within these dogs was 1.11 to 2 with a mean of 1.57.

Since this was a clinical study in client-owned animals, computer modeling based upon CT scans was employed as an alternative to direct measurement of bone size and geometry, as would have been possible in a cadaveric study. There may be some loss of accuracy with this indirect technique to measure the bones. As all of the dogs were scanned using the same imaging protocol, the degree of error should be the same for all cases. As the modeling was based upon these scans and was used for descriptive quantification of morphology, not specific implant design parameters, the technique is satisfactory to
provide accurate, reproducible images and measurements to compare the morphologic variables.

As with many clinical studies, the primary limitation with this work lies in the accrual of clinical cases and tissue specimens. Some interesting (but not statistically significant) trends were noted in our data, and we suspect that the variability in the data was such that a type II error resulted. The clinical protocol for collecting CT scans and bone cores is still active, so further sample accrual should be possible as a means of increasing statistical power and decreasing the risk of false-negative statistical tests. Initial power calculations based upon the pilot data on CFI indicated that 9 to 11 dogs were needed for each group to determine a difference. However, this was established based upon one measurement variable from cadaveric studies on normal femora. A preliminary evaluation of the six cases from a pilot study with CT reconstruction revealed statistically significant differences among two of the variables studied, so the power calculation did seem appropriate to determine a real difference. Nevertheless, more cases would certainly help to clarify this issue.

A related and important limitation relates to the protocol for collecting the bone core. In contrast with the specimens that were collected from cadavers in the earlier study[66], the cores for this study came from dogs that were undergoing THR surgery. As a result, we were limited to collecting cores in a manner that was consistent with the THR procedure and that would not be anticipated to negatively impact clinical outcomes. For this reason, the cores were taken from a region that is very close to the cortical wall that
borders the intertrochanteric fossa. In some specimens, part of this cortical wall was visible, complicating the interpretation of micro-CT and especially mechanical test data. There is no easy solution to this issue, but in future it would be good to modify the entry point of the coring instrument slightly to ensure collection of only trabecular bone.

Additionally, as to not impair the quality of the THR implantation, direction of coring was not controlled. This assumes bone anisotropy was even in all directions. The direction of load applied to the cores may not reflect the biologic direction of the stresses applied to the bone.

An unforeseen complication was the incredibly delicate nature of some of the bone cores, particularly from the stovepipe group. Initial practice and evaluation of a coring device in normal cadaveric bones did not suggest that removing the bone core from the coring device would pose any difficulty. The first 5 cores in this study were removed in a similar manner as the cadaveric pre-test samples using the company supplied pin removal device. This device inserted through the hole at the connecting end of the coring device and focally pushed the bone core out the open cutting end of the coring device. The focal pressure may have locally crushed the core as it applied a small surface area for the force to be distributed. In addition, some of these cores were so fragile that once removed from the coring device, did not have enough connections between trabeculae to remain structurally intact. This precluded them from mechanical testing but simultaneously attested to the weakness and poor quality of this trabecular bone. Due to this, a modification removal technique was developed that allowed the cores to be deposited into
a supportive structure to maintain their moisture, structure, and protect them during the wrapping and freezing process. By placing the cores into a polypropylene tube, they could maintain their structural integrity through the initial phases of storage and imaging. To help reduce the focal force of pushing the core out with the pin removal device, the closed end of the coring device was removed using a band saw and then the core was pushed out of the corer using a pin that matched the inner diameter of the coring device, dispersing the force over the surface area of the core. Using this technique, no core was broken or damaged during the initial testing and storage phase.

A number of cores could not be mechanically tested due to unanticipated loss during handling. The cores are very fragile, and this is exacerbated if the volume fraction of bone is low. While inadvertent breakage clearly falls far short of a quantitative method for determining mechanical strength, it subjectively provides a qualitative measure of the delicate nature of the trabecular bone in the proximal femoral region. If the section of bone could not undergo gentle removal of soft tissue using a water stream, or removal from the coring device with gentle pressure, it would also follow that it would easily compact against the cortical bone and not provide a rigid biomaterial with which to support a stem/implant. The study that we performed was stimulated by the clinical observation that the bone from stovepipe femora tends to be less robust than that from normal femora; it therefore came as no surprise that it is easier to collect intact cores from femora with more robust bone. The data that we have collected from stovepipe femora may not therefore accurately reflect the poor quality bone that is sometimes present in these clinical cases.
This study did not aim to evaluate the entire femoral head and neck region as well as the proximal metaphyseal and diaphyseal region. As only the metaphyseal/diaphyseal region was evaluated, no comment can be made about cervicodiaphyseal angle or anteversion, which have been shown in previous studies to be highly variable in dogs. Consequently, overall implant stem design cannot be modified based upon these results. However, consideration for further study into the exact measurement parameters of a stovepipe femur could be undertaken in order to modify the implant stem design to better interface with the proximal femur in stovepipe morphology dogs.

We did not identify a difference in the cortical bone volume. However, subjective interpretation of the radiographs suggests a thinner cortical bone mantle throughout the proximal femur. It is unknown whether this bone is denser or has different mechanical properties. CT modeling has inherent limitations that reflect image creation and storage of data. With the entire femur modeling, there were occasional voxel deficits that created holes in the reconstructed image that had to be edited. This may have been due to an artifact while scanning or in the computer rendering of the data. It may also have been due to the thresholding values of the bone. Threshold levels are set by the computer to match a certain Hounsfield unit and identifies any other voxels of similar density. More work will be needed to explore this in greater detail, perhaps through direct comparisons of CT data and direct measurement from cadaveric femora.
4.7 Conclusions

At the whole-bone level, there are significant differences in femoral geometry, endosteal canal sizing and the relative amount of trabecular bone in normal versus stovepipe femora. On 3D analysis, significant differences were found for femoral taper, supporting the concept that the geometry of the stovepipe femur differs from that of the normal femur. Care should be taken in preparing the endosteal surface of femora with a low CFI to ensure that the marginal trabecular bone is left in place to provide both initial support (for the mechanical interlock) and long-term support through effective osseointegration. The mechanical properties of trabecular bone were similar in cores taken from the two groups, but there was a suggestion that the material properties of the bone from these clinically affected dogs may differ from that of bone collected from healthy young dogs. Much more work needs to be performed to expand and confirm these observations, and the clinical research protocol that has been established should provide an efficient vehicle for collecting these specimens.
References


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61. <morphology of hip noble.pdf>.


Appendix A. Standard operating procedures (SOP)

Appendix A.1. SOP for Macro CT reconstructions

1. Open DICOM images, select all in the series, save as Dicom images.
2. Open Mimics and import the Dicom images
3. Confirm the orientation of the patient with the directions provided
4. File – Crop image for the affected femur
   a. Adjust the boxes in each plane to include the entire femur and as little of
      the pelvis as possible
   b. Save as “patient side femur”
5. With the affected femur, threshold for bone (Segmentation – threshold- Bone
   (CT) >226)
6. Volume render the image to create a 3D model
   a. Segmentation- edit mask in 3D- edit out any pelvis
   b. Save file
7. For entire femora measurements
   a. Develop a bone threshold (green)
   b. Duplicate the mask and window for soft tissue (Soft Tissue (CT) <225)
      (yellow)
   c. Segmentation region grow and click the medullar canal of the bone (cyan)
   d. Duplicate the green mask (bone) to develop the cortical bone mask
      i. Manually threshold this to highlight the cortical bone but not the
         trabecular bone in the proximal region while trying to maintain a
         continuous cortical bone margin.
      ii. The bone margin was inconsistent throughout the region of the
         lesser trochanter when an appropriate level of trabecular bone was
         thresholded out
   e. Build the masks in 3D
f. Select i button to collect volume, surface area, and Y value for height for each mask
g. Record data

8. For fixed height segment of femur
   a. With the isolated affected femur as a 3D model, orient the image in a Craniocaudal view
   b. File – reslice project
      i. Draw a line that is the anatomic axis for the femur on the Craniocaudal view
      ii. Adjust the line on the Mediolateral view to be along the center of the proximal femoral diaphysis along the line of insertion of the femoral stem (aiming towards the proximal aspect of the femoral condyles/ patella region)
      iii. Save project as reslice
   c. Crop the image for a 60mm segment
      i. Proximal end is just distal to the distal extent of the intertrochanteric fossa and 2-4 slices proximal to the lesser trochanter
      ii. Distal extent is 60mm distal in the region of the isthmus
   d. A fixed height, 60 mm segment of proximal femur is isolated
      i. Segmentation- threshold for bone (CT)
      ii. Duplicate mask and threshold for soft tissue (CT)
      iii. Segmentation – region grow- medullary space
      iv. Duplicate bone mask and manually threshold for cortical bone
      v. Build the masks in 3D
      vi. Edit the bone and cortical bone masks for any pelvis
         1. Segmentation- edit mask in 3D- lasso and remove any non-femur bone
2. Delete and build 3D model again of the edited mask
   (should be the edited femur only now)

vii. Confirm that the segment is 60mm in height with the measurement tool

viii. Collect the data on segment volume, surface area, and height and record

ix. Rotate segment to an end on axial view of the proximal aspect of the segment
   1. Measure the cortical thickness using the measurement tool at the medial cortex above the lesser trochanter
   2. Record measurement

x. Rotate segment to an end on axial view of the distal aspect of the segment
   1. Measure the cortical thickness of the medial cortex and the level of the lesser trochanter
   2. Record measurement

e. Save segment

f. This can be repeated for the 20mm segment

9. Thresholding for the bone shells
   a. Segmentation to thresholding bone (green) (bone (CT) >226)
   b. Segmentation to thresholding soft tissue (yellow) (soft tissue (CT) <225)
   c. Segmentation to thresholding. Manually adjust to globally threshold >450 for cortical bone
   d. Segmentation thresholding 227 to 445 for trabecular bone

10. Measuring the cortical width endosteal diameter
    a. The segment was rotated to be end on proximally and then distally
    b. To ensure the segment was end on, the grid Toggle Reference tool was used
c. Measurements were made from the widest points from medial to lateral
d. Measurements were made at the mid level of the cranial to caudal surface within endosteal cavity
e. The distal segment was measured from the widest points ML and CrCa.
f. Before final recording of the measurement, the reconstructed image was rotated to ensure the measurement points were fixated on the edge of the endosteal margin.
Appendix B. SOP for micro-CT studies and obtaining histomorphometric data

Appendix B.1 Nrecon

1. Open Nrecon local by clicking on desktop icon
2. Program will display a message that it is looking for other computers. Let this finish.
3. A screen will open up that is titled “Open data set”
4. Click on any one of the .tif files for the case with the exception of the file with “arc” in the name
5. Under “Settings” make sure that “smoothing” is clicked off, and that “misalign comp” and “show” are both checked.
6. “Ring artifacts” should be set to 5 and “beam hardening” should be set to 20
7. Click “start”.
8. On the shadow image, drag the red line so only have trabecular bone and no plastic caps are inside of the boundaries. Aim for: “top” = 810 and “bottom” = 410 but select a portion that is not broken in the middle and avoid sections with high amounts of soft tissue or cortical bone.
9. Place the green line in the middle of the two red lines.
10. Click on “Fine tuning”, “post alignment”, then 5 trials with a parameter step of 1.
11. Select the image with the fewest artifacts and clearest image from the 5 trials.
12. Click on “Fine tuning”, then on “beam hardening”, then 3 trials with a parameter step of 5.
13. Select the image with the fewest artifacts and clearest image from the 3 trials
14. Click on “Fine tuning”, then on “ring artifacts”, then 5 trials with a parameter step of 1.
15. Select the image with the fewest artifacts and clearest image from the 5 trials.
16. Most likely your post alignment will be 1, beam hardening, 20 and ring artifacts, 5. Try to stay consistent with this unless there are extreme artifacts showing up.
17. Click on the “Start” tab, then click on “Preview”
18. Click on the “Output” tab, then click on the “Auto” tab
19. Record numbers for min and max
20. Save the file in the same directory that you started off in.
21. Double check the “Settings” tab to make sure that your settings are: “post alignment: 1, beam hardening: 20 and ring artifacts: 5.
22. Click on “Start” and then “Add to Batch”
23. Click “Start” under the “Batch” box to run a batch.

Appendix B.2 Mimics
1. Open Mimics by clicking on desktop icon
2. Click on “File” then on “New Project Wizard”
3. Select all of the numbered files for your case with “rec” in the file name.
4. Click next, next, next to convert the study
5. Select any orientation as the anatomical directions are not pertinent for this
6. Click on “Thresholding” and start at min = -945 and max = -771 and then adjust from there to capture all of the trabecular bone
7. Create a mask by clicking on “Region Growing” and make sure all trabecular bone is selected
8. Then click on “3D model”
9. Click on “Export”, then “Capture Movie” then in the “Options” box make sure “rotate” is selected. For “View to Capture” click on “bottom right view”. Within this box, make sure you select the correct folder to save this to (Pugliese drive) and save this as “casename.avi”.
10. Then hit the record button and you should see the video of the image spinning when it is done creating it.
11. Click “Save project as” and save it to the same drive as “casename.recon”

Appendix B.3 CTAN
1. Click on the desktop logo for CTAN
2. Click on “File” and pick one of the numbered recon files somewhere in the middle
3. Click on “View Selection” and count the number of files you have in total and find the midpoint. Then take 50 files on either side of this midpoint. Then click “okay”.
4. Click on “Define Region” (icon looks like a globe)
5. Draw a line around the image using your mouse and make sure you aren’t missing any of the bone by scrolling up and down through the files. Leave some room around the bone.
6. Then click on the next screen for binary images. Adjust the gray scales so all pores and spicules are visible and similar to those seen in the first image.
7. Then click on the button for histomorphometry. (icon looks like a red branch)
8. Click on 3D analysis and make sure you have the “trabecular thickness” and “trabecular separation” boxes selected. Then click “Okay”. Processing after this step can take 30-40 minutes.
9. After it has finished, click on save and save the file to the same directory you have been using with the name “casename_rec”

For the 5mm segment
1. Identify the center of the core. If the core contains cortical bone, alter the center point to avoid this
2. Select 375 slices for 13.4 micrometer slices is 5mm
3. Evaluate this in 2D and 3D for morphologic parameters as described above.
Appendix C. Owner consent form for enrollment in the study.

Owner consent form

The Ohio State University Veterinary Medical Center

Name of study: Proximal Femoral Morphology and Bone Quality Assessment in Dogs

Undergoing Total Hip Replacement

Name of Investigators: Drs. J. Dyce, L. Pugliese and M. Allen

This is a prospective study to assess the shape and quality of the bone in the upper part of the thighbone (femur) in dogs undergoing total hip replacement (THR). It is suspected that difference in the amount, distribution and overall quality of the bone in the upper femur significantly impact the long-term performance of THR implants. In particular, we want to know whether we can identify dogs that are at increased risk of implant complications. Knowing more about the bone shape and quality of individual dogs can help us make better medical decisions and design better implants for our canine patients.

For this study, we ask that we can obtain a CT scan of your dog’s femurs. A CT scan is a non-invasive imaging technique that can then be used to re-create models of your dog’s femur. These images will be used to make measurements to assess the shape and size of the proximal femur. The imaging will occur at no cost to you and will either occur under the same sedation as for the radiographs obtained before total hip replacement surgery. If any additional sedation or anesthesia time is required for the CT scan, this will be covered by the study. A CT scan generally costs $400 but this will be covered by the study. The radiographs and initial sedation,
as part of the total hip surgery, will be your responsibility.

In addition, assuming that your dog undergoes THR at OSU, we would also like to use a sample of bone obtained at surgery to perform mechanical testing to assess bone strength. Bone sample collection will occur at the time of total hip replacement and is a routine part of the surgery. Generally, this bone is removed and discarded as unnecessary when the femoral stem is implanted. Instead of this valuable bone not having any additional benefit to your dog and becoming surgical waste, we ask that we can save it to use in our study. There is no cost to you for this.

If your dog does not have THR performed at OSU, we would still like to obtain CT scan data in order to develop a database on information on femur morphology across different breeds.

By comparing the mechanical properties of this bone with the CT measurements, we will be able to determine whether differences in bone shape and/or bone quality are associated with differences in the mechanical performance of bone in the upper femur from dogs undergoing THR. The results from this study will allow us to develop improved screening procedures to identify dogs that are at increased risk for implant-related complications. Ultimately, this information will enable us to make better choices with implant selection and to reduce the risk of complications after THR.

1. I, the undersigned, am the owner, or authorized agent for the owner, and agree to enter my animal into the above clinical study. The design and objectives of this study have been clearly explained to me.
2. I have been informed of the costs covered by the study and those that are my responsibility. The additional imaging of a CT scan and the mechanical testing of the bone samples will be covered by the study. All other costs typically associated with total hip replacement, will be the client’s responsibility.
3. I agree to allow the use of data collected as a result of my animal’s inclusion in the study for publication in scientific journals and presentation at scientific meetings with the goal of benefitting other dogs.

4. I have been given an opportunity to ask any questions of the investigators relating to this study and my animal’s condition. I certify that I have read and fully understand this authorization and consent to have my animal participate in this study.

____________________________________  __________________
Signature of Owner/Agent                Date

____________________________________  __________________
Witness                                 Date
Appendix D.

Micro-CT reconstructed images for reference and visual appreciation. The patients are identified by name and group is indicated. These images have been provided for reference.
Aussie entire core and hemicore of 5mm segment (stovepipe group)
Belde entire core (normal group)
Daisy 5mm core, hemi. (Normal group)
Dakota entire core and 5mm core hemi (stovepipe group)
Finn entire micro-CT core and 5mm segment hemicore (normal group)
Gatsby entire core and 5mm core micro-CT images (stovepipe group)
Hans micro-CT entire course and 5mm segment (normal group)
Hope entire core micro-CT. (normal group)
Lucia micro-CT entire core and 5mm segment hemi-core (normal group)
Riley micro-CT entire core (normal group)
Shadow micro-CT entire core and 5mm hemi-segment (stovepipe group)
Storm micro-CT entire core and 5mm segment (stovepipe group)
Theodore micro-CT entire core and 5mm segment hemi-core (stovepipe group)