Received: 23 March 2023 | Revised: 16 September 2023 | Accepted: 18 October 2023

DOI: 10.1111/vsu.14047

WILEY

CLINICAL RESEARCH

Evaluation of subchondral bone cysts in canine elbows with radiographic osteoarthritis secondary to elbow dysplasia

Gareth M. C. Jones BSc, BVetMed | **Madelaine R. Gosby BSc, BvetMed** | **Eleanore M. May BSc, BvetMed** | **Richard L. Meeson MA, VetMB, PhD, MVetMed, Diplomate ECVS, FRCVS**

Department of Clinical Science and Services, Royal Veterinary College, London, UK

Correspondence
Gareth M. C. Jones, Royal Veterinary College, Royal College Street, London, NW1 0TU, UK.
Email: gjones1@rvc.ac.uk

Abstract

Objective: To investigate whether subchondral bone cysts (SBCs) were present in dogs with radiographic elbow osteoarthritis (OA) and to investigate their relationship with radiographic OA severity.

Study design: Retrospective cross-sectional study.

Sample population: Thirty-eight Labrador retrievers (total of 76 elbows).

Methods: Elbow computed tomography (CT) images of 18 young (≤2 years old) and 20 old (>2 years old) Labrador retrievers, which presented for elbow-associated lameness, were reviewed. Radiographic elbow OA was graded into four groups based on the largest osteophyte size on CT. The presence, number, and maximum diameter of SBCs were determined.

Results: Subchondral bone cysts were only identified in elbows with osteophytic new bone formation. The number and size of SBCs were associated with radiographic OA severity ($p < .001$ and $p = .041$ respectively). Specifically, the rate at which SBCs were present increased for both moderate and severe OA in comparison with the mild OA (moderate OA RR = 2.46, 95% CI 2.08–2.92, $p < .001$; severe OA RR = 5.60, 95% CI 4.79–6.55, $p < .001$). For dogs with severe OA, there was an increased likelihood that their SBCs were larger than SBCs from dogs with mild OA (OR = 1.056, 95% CI 1.012–1.101, $p = .012$). No SBCs were observed in elbows without radiographic evidence of OA.

Conclusion: Subchondral bone cysts were identified as a feature of radiographic elbow osteoarthritis in Labrador retrievers, and their number and size were indicative of the presence and severity of radiographic elbow OA.

Abbreviations: CT, Computed tomography; DICOM, Digital Imaging and Communications in Medicine; HR-pQCT, High-resolution peripheral quantitative CT; IQR, Inter-quartile range; MPR, Multiplanar reconstruction; MRI, Magnetic resonance imaging; OA, Osteoarthritis; OARSI, Osteoarthritis Research Society International; SBCs, Subchondral bone cysts.

Madelaine R. Gosby and Eleanore M. May contributed equally to this study.

These data were presented in part as an abstract and oral presentation at the 2022 Congress of the European College of Veterinary Surgery in Porto (July 7, 2022–July 9, 2022).

Clinical significance: Subchondral bone cysts are a potential imaging biomarker for quantitative assessment for canine OA.

1 | INTRODUCTION

Osteoarthritis (OA) is the most common orthopedic condition in dogs with an estimated prevalence of 2.5%–20%,[1–5] and it has an associated negative impact on their welfare and quality of life.[3] In dogs, the commonly effected joints include the hip, stifle, elbow, and shoulder.[6,7] With the canine elbow, the development of OA is often secondary to elbow dysplasia,[8,9] a group of heritable developmental abnormalities, including medial coronoid process disease (with or without fragmentation), ununited anconeal process, osteochondritis dissecans, and elbow incongruity.[10] The prevalence of elbow dysplasia and associated OA is increased in several breeds, in particular the Labrador retriever, which has a 5.94 times increased likelihood compared with crossbred dogs (OR = 5.94, 95% CI 4.65–7.60).[11] Furthermore, the presentation of elbow disease follows a bimodal distribution, with a sharp peak at 1 year of age, and a second peak between 6 and 10 years of age.[11]

In clinical practice, the diagnosis of elbow OA is based on clinical examination and diagnostic imaging, principally radiographic examination. However, computed tomography (CT) is becoming increasingly commonplace due to its increased specificity and sensitivity in comparison with radiography.[12–14] The radiographic hallmarks of OA in the dog are osteophytosis, subchondral sclerosis, and joint effusion,[15–19] and they are assessed in several clinical and experimental scoring systems.[9,20–26] Interestingly, subchondral bone cysts (SBCs), which are an imaging hallmark of human, equine, and murine OA, are not a well established feature of OA in dogs, with their presence only sporadically reported.[15,27–29] In human OA, SBCs, also known as pseudocysts or geodes, are defined as small radiolucent defects in the subchondral bone surrounded by sclerotic margins.[30] They have a prevalence ranging from 31% to 88% in patients with end-stage knee OA,[31,32] and their importance in human OA is highlighted by their incorporation into the Osteoarthritis Research Society International (OARSI) atlas for OA diagnosis, a key OA grading system used in clinical practice.[33]

The relevance of SBCs as a diagnostic imaging feature of canine radiographic OA has not been explored previously. Although SBCs are identifiable using radiography in humans, they are typically identified in the knee joint, which does not suffer so acutely from radiographic superimposition and is a relatively large joint compared with the canine elbow.[34] The ability for CT to evaluate the structural features of the bones without superimposition could allow for detection of hitherto unidentifiable structural change such as SBCs. Human studies have demonstrated improved detection of SBCs using planar imaging.[34] The canine elbow is well suited for the investigation of the prevalence of SBCs in dogs with radiographic OA, as CT is now commonplace for the diagnosis of elbow lameness, removing the limitation of superimposition encountered with plain radiography, and providing a resolution that could potentially identify such structures in the smaller canine joint.

The aim of this study was to investigate if SBCs are present in radiographic canine elbow OA using CT and to investigate their relationship with radiographic OA severity graded with CT. To mitigate potential confounders caused by interbreed variation, only Labrador retrievers were investigated. This breed was chosen both for its high prevalence of elbow disease and its common presentation at our institution. Given the bimodal distribution of elbow disease,[11] dogs were categorized as either young (≤2 years old) or old (>2 years old). We hypothesized that SBCs would be present in elbow joints of Labrador retrievers presenting for elbow dysplasia with secondary radiographic OA, and that they would be more frequent and larger in dogs with more severe radiographic OA.

2 | MATERIALS AND METHODS

2.1 | Cases

Medical records of Labrador retrievers who presented for either unilateral or bilateral forelimb lameness clinically associated with the elbow joint were identified between June 2018 and October 2021. A sample of convenience with approximately equal number of male and female, young, and old dogs (under or over 2 years of age respectively) were included. Dogs were excluded if their medical records were incomplete. Dogs were either sedated or anesthetized at the discretion of the attending clinician and underwent imaging using a 320-slice CT scanner (Aquilion One Genesis, Canon Medical Systems, Otawara, Japan) with the following settings: 120 kVp, 150 mAs, 0.5 mm slice thickness, 25 cm field of view and 512 × 512 matrix. Elbow sequences were reconstructed using the CT scanner's associated software bone algorithm.

2.2 | Computed tomography analysis

Digital Imaging and Communications in Medicine (DICOM) files were retrieved for the cases that were included and were reconstructed using Horos v3.3.6 (Horos Project, Geneva, Switzerland). Images were repositioned using the three-dimensional (3D) multiplanar reconstruction (MPR) function to represent the mediolateral projection.

Radiographic OA severity was classified using a four-point ordinal system based on the size of the largest osteophyte (Table 1) previously validated against arthroscopic cartilage condition,[35,36] which has also been adapted into the International Elbow Working Group grading system.[37] The radiographic diagnosis of elbow dysplasia was based on the imaging findings reported by the attending board certified veterinary radiologist/orthopedic surgeon responsible for the cases.

Subchondral bone cysts were defined as hypoattenuating circular to ellipsoid structures with a hyperattenuating rim with more than half of their diameter within 6 mm of a subchondral bone margin (Figure 1). The depth of subchondral bone is defined variably in different studies. For this study, the depth of 6 mm from the cortical margin was chosen, based on other work that has examined the subchondral bone,[38] and therefore SBCs greater than 6 mm from a cortical margin or enclosed within an osteophyte were excluded. Sagittal plane reconstructions were reviewed slice by slice from medial to lateral, and SBC measurements were performed in the sagittal plane, with their frequency, size (maximum diameter), and location recorded.

2.3 | Statistical analysis

Data analysis was performed using SPSS (Version 28, IBM, New York). Categorical variables were described using frequencies. Given the repeated measures design of this study, statistical analysis was performed using generalized estimating equations. Individual dogs were set as the subject variable (repeated measure) using an exchangeable working correlation matrix. For radiographic OA grade and age, an ordinal logistic model was used, with radiographic OA grade set as the dependent variable. This was modeled with age as both a categorical and continuous variable. Results were presented as odds ratios (OR) and 95% confidence intervals (CI). The SBC number was treated as count data using a Poisson count model, with radiographic OA severity, age and sex used as factors. Results were presented as rate ratio (RR) and 95% CI. The SBC size (maximum diameter) was right skewed and was log-transformed to normalize the data prior to the analysis. A linear model of the normalized SBC size (maximum diameter) was used with radiographic OA severity, age and sex used as factors. Results were presented as OR with 95% CI. Statistical significance was set as $p \leq .05$.

TABLE 1 Osteoarthritis grading system based on the size of the largest osteophyte.[35–37]

OA Grade	Definition
0 (Normal)	No osteophytes present
1 (Mild)	Osteophyte <2 mm present
2 (Moderate)	Osteophyte 2–5 mm present
3 (Severe)	Osteophyte >5 mm present

Abbreviation: OA, osteoarthritis.

3 | RESULTS

3.1 | Study population

Thirty-eight dogs were included in the study, with 18 young dogs (mean age 1.0 years) and 20 old dogs (mean 6.7 years). The population statistics are summarized in Table 2. There were 18 female dogs and 20 male dogs.

A total of 76 elbows were examined. The most common radiographic diagnosis was medial coronoid disease (67 elbows, 88%), with 25 elbows having evidence of a fragmented coronoid process. Elbow incongruity was reported in 25 elbows (33%) and osteochondritis dissecans was reported in seven elbows (9%). No evidence of elbow dysplasia was reported in five elbows (7%)—all were contralateral normal elbows other than one dog with no evidence of disease in either elbow.

3.2 | Severity of radiographic OA

Osteophytes were not identified in five elbows; these elbows did not have evidence of elbow dysplasia. In the remaining elbows, 32 elbows were OA grade 1, 19 elbows were OA grade 2 and 20 elbows were OA grade 3 (Figure 2). There was a trend (although not statistically significant) for increasing radiographic OA severity within the older Labrador retriever group (OR = 2.969, 95% CI 0.929–7.827 $p = .068$). When age was modeled as a continuous variable, there was an increased likelihood of increased radiographic OA severity as age increased (OR = 1.198, 95% CI 1.001–1.433, $p = .048$).

FIGURE 1 Sagittal slices of three Labrador retrievers demonstrating subchondral bone cysts (SBCs). (A) Subchondral bone cysts with white arrows in a 6-year, 4-month-old female, neutered Labrador retriever. (B) Subchondral bone cysts with white arrows in a 1-year old female, neutered Labrador retriever. (C, D) Subchondral bone cysts with white arrows in a 6-year, 10-month-old male, neutered Labrador retriever.

TABLE 2 Descriptive statistics of the sample population.

Signalment	Young dog cohort	Old dog cohort
Male	10 dogs (6 ME, 4 MN)	10 dogs (4 ME, 6 MN)
Female	8 dogs (6 FE, 2 FS)	10 (1 FE, 9 FS)
Mean weight (SD)	27.4 kg (±4.4 kg)	31.9 kg (±6.2 kg)
Mean age (SD)	1.0 year (±0.4)	6.7 years (±1.8)

Abbreviations: FE, female entire; FS, female spayed; ME, male entire; MN, male neutered; SD, standard deviation.

3.3 | Subchondral bone cysts

Subchondral bone cysts were not identified in any normal (radiographic OA grade 0) elbows. These elbows were removed from further analysis. Subchondral bone cysts were identified in all elbows with radiographic OA. The median number of SBCs at OA grade 1 was three (IQR 2–4), at OA grade 2 it was nine (IQR 7–10), and at OA grade 3 it was 20 (IQR 15–22) (Figure 3A). The number of SBCs increased as the radiographic OA severity increased, with an association between the number of SBCs and radiographic OA severity ($p < .001$). Neither age nor sex was associated with SBC number ($p = .805$ and $p = .939$ respectively). The rate at which SBC number were present increased for both OA grade 2 and 3 in comparison with OA grade 1 (RR = 2.46, 95% CI 2.08–2.92, $p < .001$; RR = 5.60, 95% CI 4.79–6.55, $p < .001$).

The SBC size (maximum diameter) at each radiographic OA grade is shown in Figure 3B. Again, an association between SBC size (maximum diameter) and radiographic OA severity was observed. ($p = .041$). The SBC size was also observed to be associated with both age ($p = .013$) and sex ($p = .002$). As radiographic OA severity increased to grade 3, there was an increased likelihood that the SBCs were larger than SBCs from OA grade 1 (OR = 1.056, 95% CI 1.012–1.101, $p = .012$). A similar increased likelihood for increasing SBC size was seen for OA grade 2 in comparison with OA grade 1; however this was not significant (OR = 1.012, 95% CI 0.972–1.054, $p = .569$). Older dogs were more likely to have larger SBCs than young dogs (OR = 1.054, 95% CI 1.011–1.098, $p = .013$). Female dogs were less likely to have larger SBCs compared to male dogs (OR = 0.931, 95% CI 0.891–0.973, $p = .002$).

Most SBCs were identified in the humerus (62%), with the remainder located in the ulna (28%) and radius (10%)

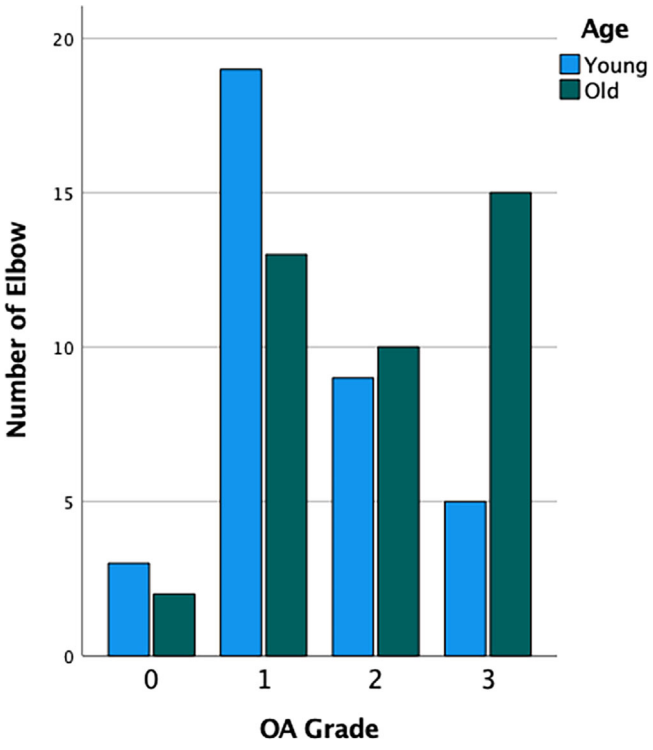

FIGURE 2 Bar chart representing the distribution of radiographic osteoarthritis (OA) severity (based on the largest osteophyte) between the young (≤2 years old, $n = 36$ elbows) and old (>2 years old, $n = 40$ elbows) Labrador retrievers.

subchondral joint bone. During the scoring process, it was observed that SBCs were predominately located in the medial compartment of the elbow.

4 | DISCUSSION

This study identified that SBCs were a diagnostic imaging feature of canine OA and that the number of SBCs present and their size were predictive of radiographic OA severity. The complete absence of SBCs in normal elbows without radiographic signs of OA further supports the view that they are a pathognomonic feature of canine OA as they are in human OA. This study also identified that the number of SBCs were proportionate to the radiographic severity of their OA and were not an independent feature of age. They also had a predilection for the humeral joint surface.

As far as the authors are aware, this is the first time that the relationship between increasing number of SBCs and radiographic OA severity has been reported in canine OA. The literature for SBCs in dogs is limited but the presence of SBCs with human OA is well established, with the number and size of SBCs also increasing with OA severity.[32,39,40] The longer established relationship between SBCs and OA in humans probably relates to

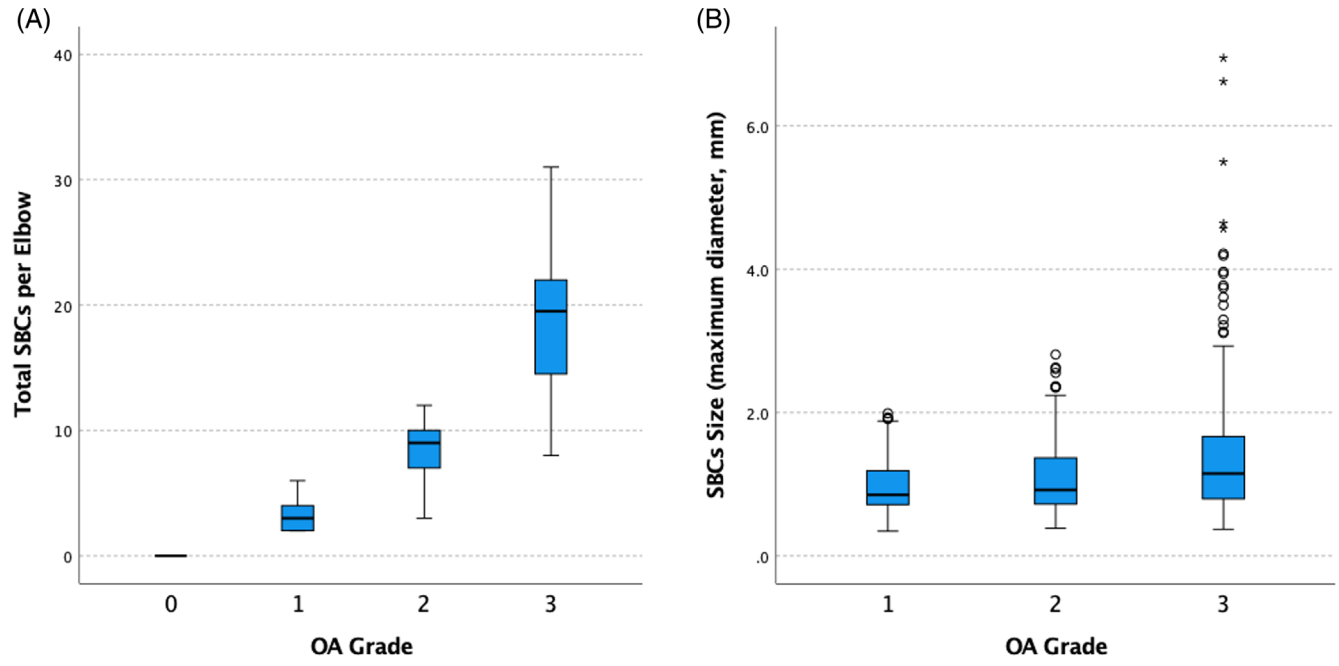

FIGURE 3 (A) Box-and-whisker plot of the total number of subchondral bone cysts (SBCs) identified per elbow ($n = 76$) separated by radiographic osteoarthritis (OA) severity (based on the largest osteophyte). (B) Box-and-whisker plot of the size (maximum diameter) of SBCs for each OA grade (total of 640 SBCs).

relative size of human joints and the different types of imaging used to evaluate them, including magnetic resonance imaging (MRI).[34,41] Subchondral bone cysts are not readily identified on plain radiographs of the canine elbow, and this is likely due in part to their size and the superimposition of the component bones of the elbow. With the introduction of CT and planar analysis at ever increasing resolution, SBCs were readily visible in the dog.

Although SBCs have been poorly described in dogs with spontaneous OA, they have been documented in experimental canine OA models using MRI,[28,42] specifically the Pond–Nuki model. These studies identified that, following transection of the cranial cruciate ligament, SBCs developed within the stifle as early as 2 weeks following destabilization, with all dogs in one study having SBCs at 12 weeks.[28,42] These studies also identified that SBCs had a predilection for the medial tibial plateau.[28,42] Direct comparison with these results is limited due to the different subtype of OA between these studies and the results reported here as well as imaging modalities used. However, these studies support our data in finding that SBCs are present in early radiographic OA, although the exact temporal relationship is unclear and requires further investigation, ideally a longitudinal study. Nevertheless, their presence in all dogs with any measurable radiographic OA in our study indicates that they may be a useful marker of radiographic elbow OA, particularly in the early stages.

The tendency for increasing SBC size in relation to OA severity has been well documented in humans, with their total, maximum, and average volumes all being positively correlated with worsening OA.[32] The relationship between increasing SBC size (as measured by their maximum diameter) and radiographic OA severity is seen in this study and highlights that SBCs are dynamic and change as radiographic OA severity worsens, principally getting larger. This dynamic nature of SBCs has been confirmed in longitudinal studies using MRI in human OA, with several reports identifying that SBCs can grow as well as regress.[40,43,44] The exact mechanism that governs SBC size is unknown; however, studies using quantitative CT identified a positive correlation with increasing bone mineral density and SBC volume.[32] Changes in the subchondral architecture have already been implicated with the development of SBCs as a close relationship between SBC number and subchondral bone sclerosis has been identified using high-resolution peripheral quantitative CT (HR-pQCT).[45] Potentially, SBC size could be intricately linked to changing environment in the subchondral bone, similar to the SBC number.

Aging is also considered to have important effects on subchondral bone remodeling in dogs with an increase in bone density with age.[46] Given the potential relationship between subchondral sclerosis and the SBC number, it is surprising, that despite a high prevalence of severe radiographic OA in the older cohort in this study, age was not found to be a significant factor with the SBC number as expected ($p = .805$), likely due to the relatively rapid onset of severe radiographic OA in elbow dysplastic dogs. This is similar to the findings in human femoral heads, for which neither SBC number nor volume was correlated with age.[47] There was, however, an observed age-dependent increase in cyst diameter with an increased likelihood of larger SBCs with older dogs. It is possible that the age-related changes in subchondral bone microarchitecture mentioned above facilitate the expansion of these cysts in OA joints. Alternatively, in these older affected dogs, these SBCs may be coalescing, creating larger cysts. These findings, nonetheless, indicate that although the formation of SBCs is not necessarily a feature of advancing age, their expansion may be age related.

An observation in this study was the tendency for SBCs to form within the medial compartment of the elbow. This medial compartment is a common site for articular cartilage degeneration with OA in the dysplastic elbow and this is commonly termed medial compartment disease.[9,48] It is thought that eccentric loading patterns caused by elbow dysplasia exacerbate these cartilage and subchondral bone changes,[48] leading to regionalized OA. This has been highlighted during an artificial loading study of canine cadaveric elbows where the proximal ulnar articular surface was shown to contribute a significant proportion of load transfer in the elbow joint.[49] It has also been demonstrated that more extensive remodeling with OA occurs in the medial aspect of the elbow, in particular around the medial coronoid process.[9] Moreover, in a case report where an SBC in a dysplastic canine elbow was identified with CT, it was localized to the medial trochlear notch.[29] This would suggest that the medial compartment is a predisposed site for more severe OA change, and hence SBC formation.

There were several limitations to this study. First, SBCs were identified purely on the basis of imaging findings and were not confirmed histologically. Moreover, some of these SBCs were at the limits of the resolution available with clinical CT imaging with a voxel size of $0.181 \times 0.181 \times 0.5$ mm, meaning that there could be a margin of error with the measurements of the smaller SBCs' diameters. Furthermore, the complex 3D shape of SBCs means that their largest diameter measurement can be challenging. Further studies could mitigate this with the use of HR-pQCT or ex vivo imaging with micro-CT by providing volumetric measurements. Micro-CT or HR-pQCT analysis would also have assisted in examining

pericystic architectural changes in subchondral bone, which could better contextualize the findings of this study; however, it is not currently possible to accommodate a canine limb within the scanning field. Moreover, it would be useful to examine these changes in a wider cohort of dogs including other breeds, as well as over a longitudinal period to establish the temporal relationship with SBC development and OA. The OA subtype included in this study is also exclusively secondary to elbow dysplasia and did not include other types of OA such as post-traumatic or primary OA. Furthermore, although there is a clear relationship between SBCs and radiographic canine OA presence and severity, we are unable to comment on whether they are predictive of clinical lameness or other clinical examination findings. It is well established that other radiographic features of OA do not always correlate with the clinical presentation;[50] however, further research would be required to determine if SBCs are also nonpredictive. In this study, OA was defined on the presence of osteophytosis, and radiographic OA severity was based on the size of the largest osteophyte. This method has been used in several other publications, and the grades of osteophytes form part of OA grading systems in humans,[33] but it is possible that this method of grading of OA severity may not capture fully the true disease status of the joint. It is also worth noting, that while osteophytosis is a cardinal radiographic hallmark of OA, they have been identified in the human vertebral column as a general indicator of aging, although it is difficult to fully isolate ageing from OA.[51]

In conclusion, this study has demonstrated that SBCs are a recognized radiographic hallmark of osteoarthritis in canine elbows. In particular, it found that SBCs were absent in elbows without any other radiographic signs of OA, and that they became more numerous in osteoarthritic elbows as radiographic OA severity increased. Furthermore, their size (maximum diameter) increased in cases of severe radiographic osteoarthritis. These findings provide a valuable basis for investigations into the clinical relevance of subchondral bone cysts in dogs, to improve current diagnostic and therapeutic frameworks for the treatment of canine osteoarthritis.

ACKNOWLEDGMENTS

Author Contributions: Jones GMC, BSc, BVetMed: Contributed to the design of the study, identified suitable cases, collected and interpreted the data, drafted, and revised the manuscript. Gosby MR, BSc, BVetMed: Identified suitable cases, collected and interpreted the data. May EM, BSc, BVetMed: identified suitable cases, collected and interpreted the data. Meeson RL, MA, VetMB, PhD, MVetMed, Diplomate ECVS, FRCVS: Contributed to concept development, the design of the study, interpreted data and revised the manuscript. All authors provided a critical review of the manuscript and endorse the final version. All authors are aware of their respective contributions and have confidence in the integrity of all contributions.

Statistical support for this work was kindly provided by Yi-Mei Ruby Chan, BSc, MSc, PhD, CSTAT, chartered statistician and associate professor in statistics.

CONFLICT OF INTEREST STATEMENT

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

DATA AVAILABILITY STATEMENT

The data collected in this trial are collated and stored at the Royal Veterinary College in London (RVC) and are available from the corresponding author upon reasonable request.

ORCID

Gareth M. C. Jones https://orcid.org/0000-0001-9519-7720

Richard L. Meeson https://orcid.org/0000-0002-8972-7067

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How to cite this article: Jones GMC, Gosby MR, May EM, Meeson RL. Evaluation of subchondral bone cysts in canine elbows with radiographic osteoarthritis secondary to elbow dysplasia. *Veterinary Surgery*. 2023;1-9. doi:10.1111/vsu.14047