UNIVERSITÀ DEGLI STUDI DI NAPOLI
"FEDERICO II"

Tesi di dottorato

An innovative approach to humeral intracondylar fissure disease in Spaniel breed dogs

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Al mio papà

1 UNDERSTANDING THE DISEASE: HUMERAL INTRACONDYLAR FISSURE

1.1 Anatomy of the elbow joint

The humeral condyle of the dog represents the distal end of the humerus exclusive of the epicondyles. It can be divided into a lateral articular surface, the capitulum (for articulation with the head of the radius), and a medial articular surface, the trochlea, that articulates extensively with the trochlear notch of the ulna in forming one of the most stable hinge joints in the body. Laterally it also articulates with a portion of the fovea of the radius.

The olecranon fossa is a deep excavation of the caudal part of the humeral condyle. It receives the anconeal process of the ulna when the elbow joint is extended. The olecranon fossa, in life, is covered by the muscle anconeus, which arises from its margin. Proximal to the olecranon fossa is situated the supratrochlear foramen. No structures pass through this foramen. The lateral epicondyle is a lateral prominence on the humeral condyle that lies caudoproximal to the lateral articular margin of the capitulum. It gives origin to the muscles extensor digitorum communis, extensor digitorum lateralis, and the ulnaris lateralis. The proximal end of the lateral ligament of the elbow joint attaches to the articular margin and adjacent surface of the lateral epicondyle. The lateral supracondylar crest extends proximally from the lateral epicondyle. It is a thick, rounded crest that ends by blending with the caudal border at the beginning of the distal fourth of the humeral body. The muscle brachioradialis arises from the proximal part of the crest, and the muscle extensor carpi radialis arises from the remaining part.

The medial epicondyle is a prominence on the medial side of the condyle just proximal to the medial border of the articular surface of the trochlea. Larger than the lateral epicondyle, it gives origin to the muscle flexor carpi radialis, the flexor digitorum superficialis, and the humeral

heads of the muscles flexor digitorum profundus and flexor carpi ulnaris. The proximal end of the medial ligament of the elbow joint attaches to the articular margin and adjacent surface of the medial epicondyle.

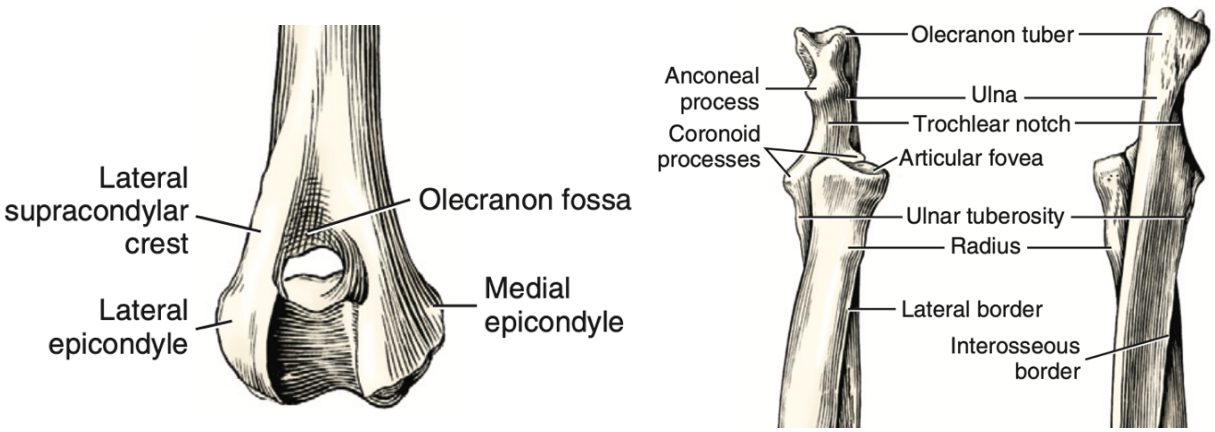

Fig. 1: Anatomy of distal humerus and of proximal radius and ulna. (from Evans HE, de Lahunta A, Miller's Anatomy of the Dog, 4th ed. Elsevier, 2013)

The elbow joint is a composite joint formed by the humeral condyle with the head of the radius, the humeroradial joint, and with the trochlear notch of the ulna, the humeroulnar joint. The proximal radioulnar joint freely communicates with the humeroradial and humeroulnar joints. Although the proximal radius initially was believed to provide most of the weight-bearing surface of the combined radial and ulnar joint surfaces, it later was found to carry about 51% to 52% of the forces applied to the elbow joint (Mason et al, 2005). Therefore, the proximal articular surface of the ulna appears to contribute substantially to load transfer through the canine elbow joint. In specific, the ulna articulates with the humerus, at level of the trochlear notch, the anconeal process and the medial portion of the coronoid process (Evans, 1993). The humeroulnar part stabilizes and restricts the movement of the joint to a sagittal plane, and the proximal radioulnar joint allows rotation of the antebrachium. Lateral movements of the elbow

joint are minimal because of the thick collateral ligaments and the cranial extension of the anconeal process of the ulna into the deep olecranon fossa of the humerus. When the elbow is fully extended, the anconeal process articulates with the olecranon fossa to act as the only primary stabilizer in pronation. Enough rotational movement occurs at the radioulnar and carpal joints so that the forepaws can be supinated approximately 90 degrees (De Ryeke et al 2002). The normal range of motion of the elbow joint is approximately 130 degrees, with normal limits being around 36 degrees in flexion and 165 degrees in extension (Jaegger et al, 2002). Extension of the elbow joint is achieved by contraction of the triceps brachii muscles that attaches to the olecranon whilst flexion of the elbow joint relies on biceps brachii and brachialis muscles.

1.2 Signalment

Dogs most commonly predisposed to humeral intracondylar fissure (HIF) include the spaniel breeds (English Springer Spaniels in particular) but it has also been reported in several other breeds such as Shetland sheepdog, Labrador retriever, German Shepherd dog, Rottweiler, Yorkshire Terries, Siberian Husky and English Pointer. Male dogs seemed to be more commonly affected than female (Karydas et al, 2023, Moores, 2021, Gnudi et al, 2005).

Dogs usually present with a weight-bearing lameness of one of the thoracic limbs and moderate to severe discomfort can be elicited in extension of the diseased elbow. Flexion of the elbow joint is usually not cause of discomfort in dogs affected by HIF unless fragmentation of the medial coronoid process or cartilage disease is concomitantly present.

1.3 DIAGNOSTIC IMAGING

Radiography

A radiolucent line extending from the articular surface to, or toward, the supratrochlear foramen can be seen on cranio-caudal images in the midsagittal plane of the humeral condyle. Partial fissures extend partway across the condyle from the caudal articular surface, while complete fissures traverse the entire condyle. High-quality craniocaudal radiographs of the elbow may reveal the radiolucent fissure, but its visibility depends on the x-ray beam alignment and on the positioning of the elbow. A craniomedial-caudolateral oblique projection at a 15-degree angle has been reported to be the most effective for visualizing the fissure, with deviations greater than 5 degrees decreasing detectability (Rovesti et al, 1998). When compared to CT, radiography has a sensitivity of 83% and specificity of 100% whilst, when compared to magnetic resonance, it has a sensitivity of 68% and specificity of 100% (Martin et al, 2010; Piola et al, 2012).

Computed Tomography (CT)

CT allows excellent observation of the elbow joint without superimposition of bony structures and is the preferred diagnostic modality for HIF. The fissure can be observed either as complete hypoattenuation through the entirety of the humeral condyle, or as a partial fissure (Figure 2). Notably, all partial fissures seem to originate from the caudal articular surface of the humeral condyle and an area of sclerosis surrounding the condylar defect is also usually present (Danielski et al, 2022). New bone formation is frequently seen on the lateral humeral epicondyle (80%) and this is considered to be new bone remodelling due to abnormal stresses placed on the lateral condyle (Carrera et al, 2008). One additional advantage of employing CT as a diagnostic tool is its capability to investigate additional bone structures, including the

medial coronoid process. It's noteworthy that up to 25% of spaniels diagnosed with HIF may also have concurrent medial coronoid disease (Carrera et al, 2008).

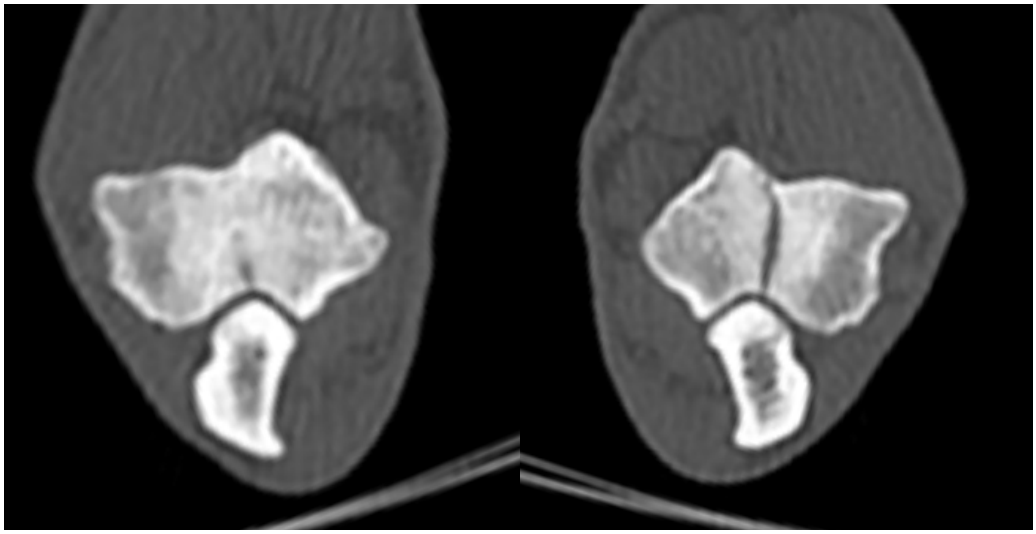

Fig 2: Coronal CT images of a 4-year-old ESS. A partial HIF is present on the left elbow (left image) whilst a complete HIF is present on the right elbow (right image). Note the intense bone sclerosis surrounding the fissure.

Magnetic Resonance Imaging (MRI)

MRI is also a valuable tool for identifying HIF and demonstrates superior sensitivity compared to radiography. On STIR sequences, the HIF area appears hyperintense to the radial head and hypo- or isotense to the humeral articular cartilage (Piola et al, 2012). MR also seems to be able to detect even subtle changes in the humeral condyle before the fissure occurs (evident as a heterogeneous humeral condyle in STIR images with a central area of hyperintensity) (Piola et al, 2012).

1.4 Historical perspective

The predisposition for Spaniel breed dogs to develop humeral condylar fractures was firstly reported by Denny in 1983 and by Vannini et al 1988. In the first study, encompassing 133 instances of humeral condylar fractures from the United Kingdom, Denny reported that approximately 35% of these cases occurred in spaniel breeds, with the majority being English Springer Spaniels, accounting for 23% of all humeral condylar fractures. Furthermore, it was acknowledged that these fractures frequently manifested during routine physical activity. In the second study, encompassing 20 dogs in the United States that sustained humeral condyle fractures during normal activities, Vannini and colleagues reported that 55% of these cases were observed in Cocker Spaniels. Notably, some of the American Cocker Spaniels identified by Vannini and colleagues had displayed lameness prior to the fracture, and some exhibited radiographic evidence of remodelling of the lateral epicondylar crest.

In both these studies a precise aetiology behind the heightened susceptibility of these breeds to humeral condylar fractures could not be individuated. Nonetheless, they hypothesized that this susceptibility may be attributed to conformational factors, structural weaknesses in the distal humerus or strenuous activities over rough terrain.

The initial description of humeral incomplete ossification was provided in four dogs displaying chronic intermittent forelimb lameness. All four dogs exhibited a discernible fracture line or fissure between the two segments of the humeral condyle, which was exclusively visible on oblique craniocaudal radiographs. Subsequently, one of these dogs experienced a humeral condyle fracture shortly after diagnosis, and all four showed favourable progress following lag screw fixation (Meutstege, 1989).

The fact that humeral condylar fractures and radiolucent lines have an identical location to the cartilaginous remnant present between the lateral and medial centres of ossification in immature dogs, led Marcellin-Little in 1994 to coin the term Incomplete Ossification of the Humeral Condyle (IOHC).

1.5Aetiopathogensis

The process of mineralization in the cartilaginous anlage of the humeral condyle commences at two distinct centres of ossification around 14 ± 8 days after birth (Figure 3). One of these centres ultimately forms the capitulum and the lateral aspect of the humeral condyle, while the other gives rise to the trochlea and the medial portion of the humeral condyle. As mineralization progresses, the two centres of ossification become separated by a thin cartilaginous plate, eventually fusing between 8 to 12 weeks of age (Thrall at el 2023).

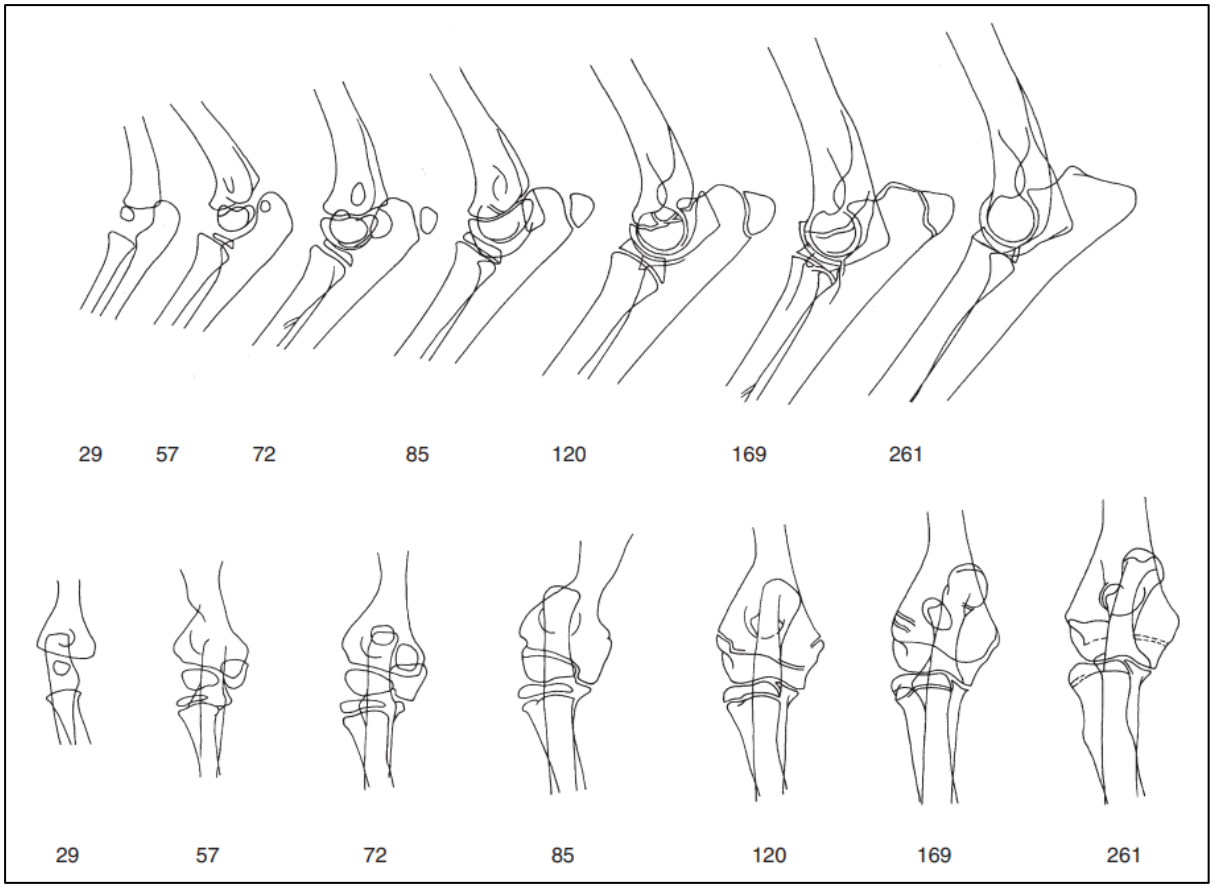

Fig 3: Development of the physes of the canine elbow, lateral and craniocaudal views. Age in days. (From Thrall D, Robertson I. Atlas of normal radiographic anatomy and anatomic variants in the dog and cat. 3rd ed. Elsevier; 2023)

As mentioned above, the location of the fissure observed in dogs with HIF corresponds to the position of the cartilaginous plate that separates these two centres of ossification. Consequently, in early reports of this condition, it was proposed to result from the failure of these two centres to unite, hence the initial designation as IOHC.

However, in many cases, fissures visible in clinically affected dogs extend proximal to the physis and this cannot be accounted for by incomplete ossification of the epiphysis (Moores et al, 2006). Moreover, this theory was recently challenged by a study that reported the development of a fissure in the humeral condyle of a 5-year-old Cocker Spaniel that 2 years previously had a completely normal elbow on computed tomography (Farrell et al, 2011). A similar case report documented propagation of a partial fissure of the humeral condyle in an American Cocker Spaniel, most likely due to abnormal joint biomechanics (Witte et al, 2010). The findings of these two cases seemed to support a previously made hypothesis that stress fracturing may be involved in formation of humeral intracondylar fissures or incomplete fractures.

An electron microscopy study on failure mode of transcondylar screws further supported the role of intracondylar instability due to abnormal biomechanical forces across the humeral condyle that might be associated with HIF (Charles et al, 2009).

HUMERO-ANCONEAL INCONGRUITY

The first part of this project study was to report a previously undocumented cartilaginous lesion, henceforth referred to as a humero-anconeal lesion (HA lesion) throughout the text, present on the caudal aspect of the medial humeral condyle of dogs with HIF, which the authors believe to represent a form of incongruity between anconeal process and humeral condyle that may support the stress fracture theory.

2.1 Material and methods

Dogs presenting for assessment of unilateral or bilateral thoracic limb lameness and signs of pain on elbow manipulation were included in the first part of this clinical research project. Dogs not undergoing both CT assessment and elbow arthroscopy were excluded. Elbows were subsequently divided into two groups depending on the presence or absence of HIF on CT imaging. The groups were termed “HIF positive” and “HIF negative”. Computed tomography of both thoracic limbs from the carpi to the shoulders was performed preoperatively with the dog under deep sedation (3-8 mcg/kg dexmedetomidine and 0.2 mg/kg butorphanol, IV). Dogs were positioned in sternal recumbency, with the elbow joints parallel and extended cranially at approximately 130-140° of extension. If CT revealed changes of the humeral condyle compatible with development or presence of HIF (as previously described by Carrera et al, 2008), the affected elbow was included in the HIF positive group. All remaining cases that showed no evidence of HIF on preoperative CT examination but where there were other bone changes suggestive of joint pathology (such as fragmented coronoid process, kissing lesions, and medial compartment disease) were included in the HIF negative group.

2.1.2 Arthroscopic technique

Elbow arthroscopy, using a 2.4 mm, 30° oblique arthroscope (Arthrex®, Munich, Germany), was performed with the dog under general anaesthesia in dorsal recumbency. A sand bag was positioned adjacent to the affected elbow, to be used as a fulcrum for initial joint distraction. The skin was aseptically prepared and the limb draped according to standard surgical technique. A surgical assistant held the distal limb such that the humerus was parallel to the floor with the sandbag positioned under the distal humerus to help as a fulcrum. The distal extremity was concomitantly externally rotated (pronated) to allow additional opening of the medial aspect of the joint space (Figure 4).

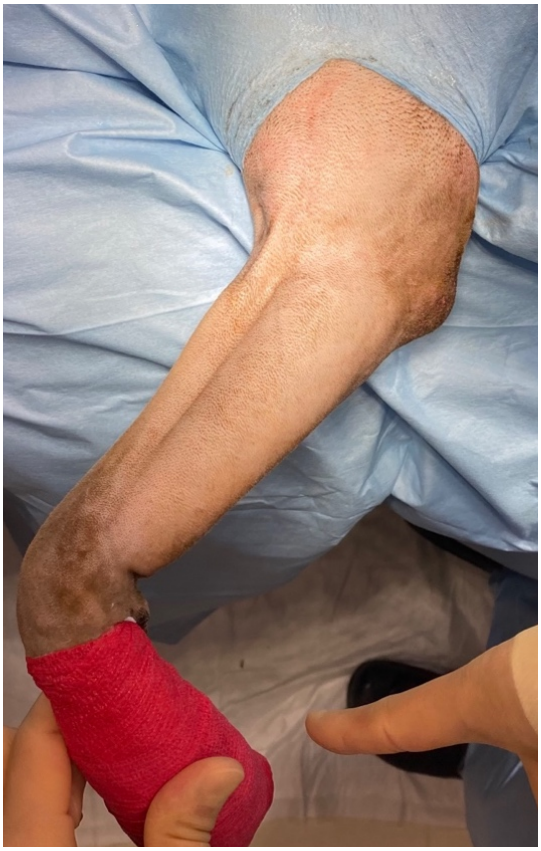

Fig. 4: Positioning of the limb during arthroscopy to allow distraction of the medial compartment

The egress portal (Figure 5A) was established first by inserting an 18-gauge needle, connected to a 10 mL syringe filled with sterile lactated Ringer's solution, cranio-medially to the elbow joint, aiming just caudal to the medial collateral ligament and to the median nerve in a caudo-lateral direction. Once synovial fluid was aspirated to confirm intra-articular placement, the sterile Ringer's solution was instilled to distend the joint. The arthroscope portal was established next by making a small skin incision with a no. 11 blade and inserting the arthroscope cannula with the attached blunt obturator caudal to the medial epicondyle and the ulnar nerve, in a cranio-lateral direction, parallel to the medial surface of the anconeal process of the ulna (Figure 5B, label “C”). The arthroscope portal was located midway between the most prominent part of the medial epicondyle of the humerus and the olecranon tuber of the ulna, being more caudally located than that previously reported (Figure 5B, label “B”) (Beale et al 2003). Typically, the skin incision would be made along the palpable and visible line of indentation between the cranial border of the triceps muscle and the caudal aspect of the medial humeral epicondyle, taking care to avoid the ulnar nerve in this region.

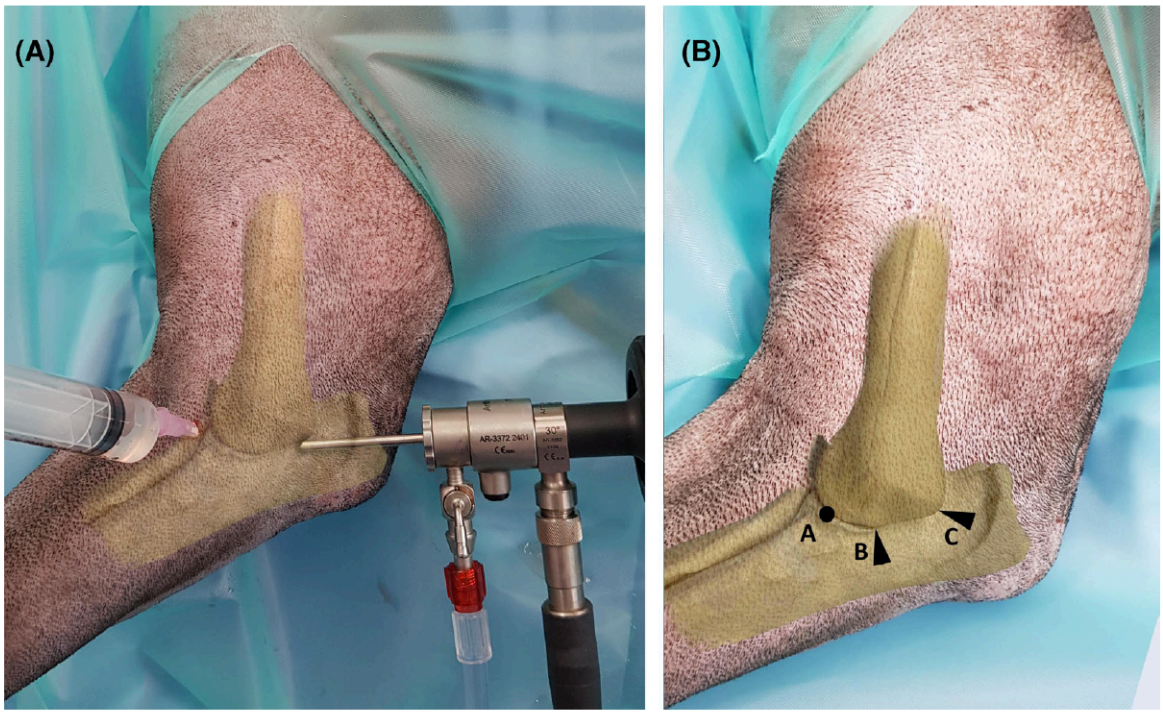

Figure 5: A: Medial view of right elbow with bone model overlay showing the positioning of the egress and arthroscope portals. B: Medial view of right elbow showing annotated positioning of the instruments for joint arthroscopy ("A": egress portal; "B": traditional medial location and entry orientation of the arthroscope portal as described by Beale et al; "C": "novel" caudo-medial location and entry orientation of the arthroscope portal used in this study)

The following structures were arthroscopically inspected: medial aspect of the coronoid process of the ulna, radial head, medial collateral ligament, insertion of the biceps brachii muscle adjacent to the medial aspect of the coronoid process of the ulna, lateral aspect of the coronoid process of the ulna, medial humeral condyle, medial aspect of the ulnar notch up dorsally to include the anconeal process, medial humeral condyle up to the olecranon fossa, and approximately the medial third of the lateral humeral condyle. Particular attention was given to the area where the anconeal process was engaging the humeral condyle at the caudal aspect of the humero-ulnar articulation (Figure 6).

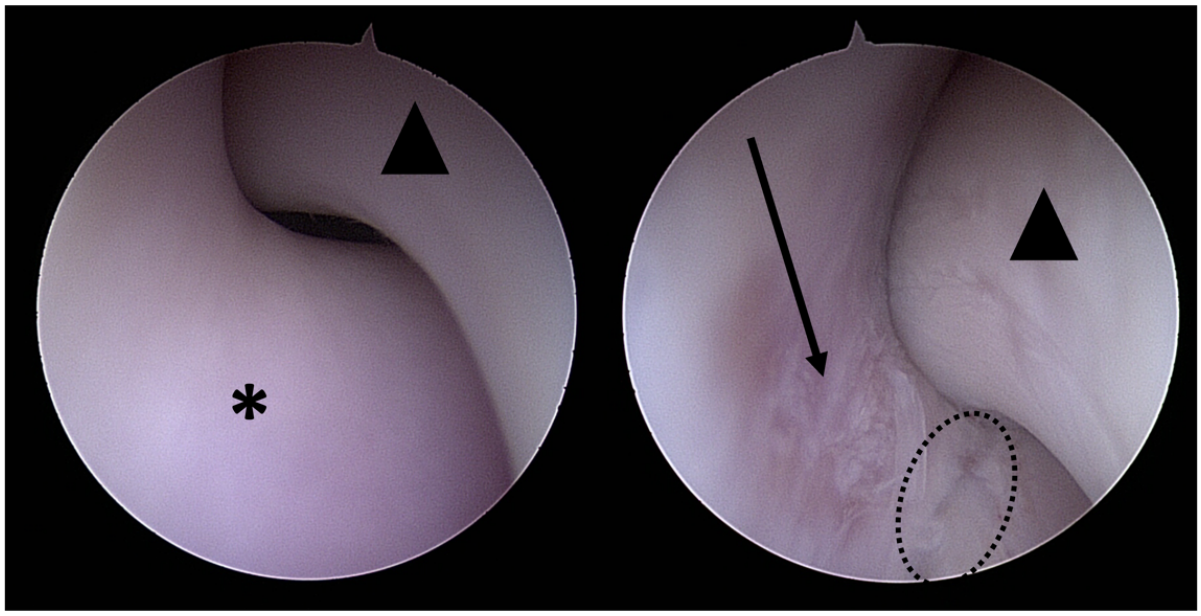

Fig. 6: Intra-articular structures of the caudal aspect of the right elbow as seen through the caudo-medial arthroscopic portal. The figure on the left represents a normal elbow whilst the figure on the right represents an elbow with HIF. Black triangle: anconeal process; black asterisk: humeral condyle; black arrow: HA cartilaginous lesion; dotted circle line: intracondylar fissure

During arthroscopy, the limb was manipulated throughout a range of motion from maximal extension to approximately 120-140° of flexion to assess if the anconeal process was impinging the humeral condyle and if there were signs of dynamic incongruency, such as if a steplike clunk could be felt and to evaluate for variations in humero-ulnar joint space width, particularly in the area of the tip of the anconeal process and olecranon fossa. During limb manipulation, no pronation or supination force was applied to the distal limb, with the exception of gentle pronation with the elbow held in approximately 120-140° of flexion to allow subjective evaluation of joint congruity during this manipulation. Presence of fragmentation or fissure formation of the medial aspect of the coronoid process of the ulna was recorded, as was the severity and location of any cartilage damage present, including use of the previously described modified Outerbridge classification system (Farrell et al, 2014).

2.1.2 Statistical analysis

Fisher's exact test was used to test the incidence of presence or absence of the HA lesion in the HIF positive and HIF negative groups. The test was repeated including only spaniel breed dogs in the HIF negative group to explore the possibility of breed as a confounding variable. P-values <.05 were considered to be statistically significant.

2.2 Results

The HIF positive group consisted of 21 elbows (14 dogs). These dogs (9 English Springer Spaniels and5 Cocker Spaniels) had a median age of 6 years 1 month (range 9-101 months); 11 were males (5 neutered) and 3 were neutered females. All dogs presented with signs of lameness of at least one thoracic limb, and all had pain on elbow joint manipulation, particularly in elbow extension. Computed tomography of these elbows revealed presence of complete hypoattenuating (n=11) or incomplete hypoattenuating (n=10) lines between the medial and lateral condyle and presence of sclerosis adjacent to the hypoattenuating lines consistent with the previous description of HIF by Carrera et al (2008). All elbows in the HIF positive group showed an arthroscopically visible focal cartilage lesion (4-10 mm in diameter) on the caudal aspect of the humeral condyle, immediately distal to the supratrochlear foramen, at its closest point, which was approximately 0.5-3 mm medial to the “isthmus” of the humeral condyle (or, when visible, medial to the HIF line, which was evident in19/21 elbows). This HA lesion was, variously, an indentation into the humeral cartilage but with cartilage appearance being grossly normal (n=3; Figure 7A and B), a lesion with cartilage fibrillation (modified Outerbridge grade II, n=4; Figure 7C), a partial thickness focal lesion (grade III, n=13; Figure 7D–H), or a full thick-ness focal cartilage loss (modified Outerbridge grade IV, n=1; Figure 7I).

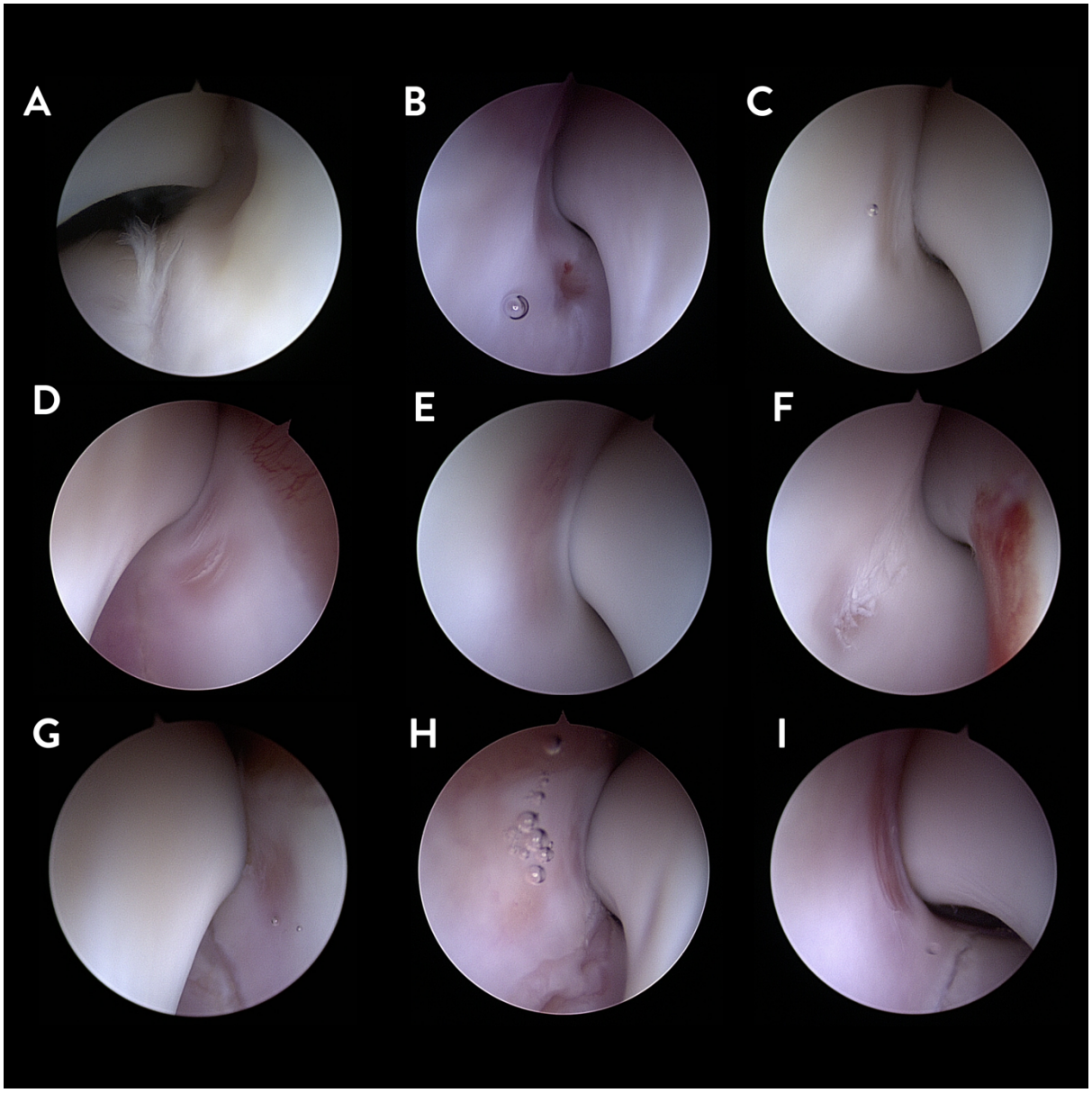

Fig. 7: Different examples of HA lesions. A-B: indentation into the humeral cartilage but with cartilage appearance being grossly normal; C: lesion with superficial cartilage fibrillation (modified Outerbridge grade II); D-E-F-G-H: partial thickness cartilage abrasion (modified Outerbridge grade III); I: full thickness cartilage abrasion with exposure of subchondral bone (modified Outerbridge grade IV). Images A, D and G are of left elbows. Images B, C, E, F, H and I are of right elbows.

In most elbows the HA lesion appeared to be circular or elliptical in shape, but in 6/21 elbows the main focal lesion was accompanied by 1-2 smaller lesions present in the immediate vicinity,

typically immediately dorsal to the main lesion, presenting the same degree of cartilage damage of the main lesion.

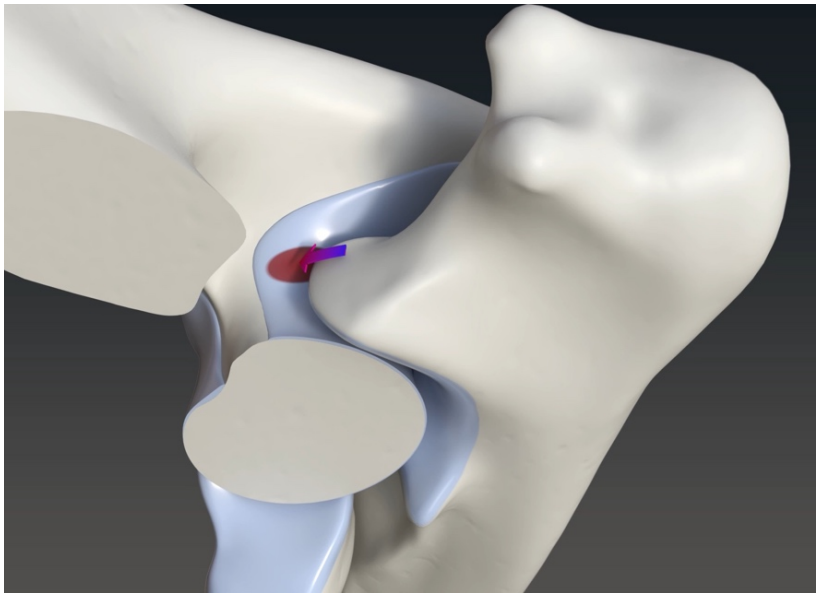

Fig 8: 3D schematic representation of the conflict between the tip of the anconeal process of the ulna and the caudal aspect of the humeral condyle, leading to formation of the focal cartilaginous lesion (red dot) and representing humero-anconeal incongruity.

In all cases, when the elbow was extended to 120-140°, the tip of the anconeal process perfectly matched the HA lesion and in 16/21 elbows it was possible to feel a clunk-like sensation when the extension-flexion movement was repeated or when pronation was performed at this joint angle; this reproducibly coincided with the anconeal process visibly "dropping" into the indented lesion and "re-emerging" from it. Precise additional data regarding incidence of this phenomenon were not recorded as consistent reproduction of this, even in a single elbow, was felt to be slightly variable and subjective in nature. In this circumstance, the humero-ulnar joint space was always absent at the level of the tip of the anconeal process, and it was noticeably wider further distally along the ulnar notch. Subjectively, when the anconeal process was engaging the lesion and concomitant pronation and supination were applied, there appeared to be an opening of the HIF line by approximately 0.5 mm in 5/21 elbows, all of which were

confirmed as having a complete hypoattenuating line on CT. Fragmentation of the medial aspect of the coronoid process of the ulna was concomitantly identified in 6/21 elbows but no elbow had any evidence of significant cartilage pathology (modified Outerbridge grade ≥ I) associated directly with this lesion or at any part of the cranial portion of the elbow joint. The HIF negative group consisted of 31 elbows (20 dogs). Median age was 5 years 8 month (range 9-141 months); 12 were male (7 neutered) and 8 female (7 neutered). Breed included Labrador Retrievers (8), cocker and English Springer Spaniels (4), cross breed (3) and 1 each of boxer, Staffordshire bull terrier, German shepherd, labradoodle and basset hound. Eleven elbows were diagnosed with fragmentation of the medial coronoid process, 4 had focal medial humeral condyle "kissing lesions" (representing areas of cartilage pathology of modified Outerbridge grade II or higher) and 5 with advanced medial compartment disease (representing areas of diffuse cartilage pathology of modified Outerbridge grade IV or V affecting both the cranial portion of the medial humeral condyle and the coronoid process of the ulna). Areas of cartilage pathology in all elbows were limited to the cranial portion of the elbow joint and did not extend into the caudal portion of the humero-ulnar articulation. No dog in the HIF negative group had any arthroscopic evidence of the HA lesion on the caudal aspect of the medial humeral condyle, with cartilage of normal visual appearance in the area of the HA lesion in the HIF positive group. When the joint was arthroscopically assessed and the elbow extended and flexed, the joint space between humerus and ulnar notch always appeared uniform, and maintained a consistent joint space width at the level of the tip of the anconeal process. The incidence of the HA lesions was different between the HIF positive group and the HIF negative group (P-value <.0001), and between the HIF positive group and HIF negative spaniel breed dogs (P-value <.0001). In all elbows, examination of all joint structures listed above was possible through the arthroscope portal location described.

2.3 Discussion

A previously unreported cartilage lesion on the caudal aspect of the medial humeral condyle was identified in dogs with HIF and it was not present in a control group of unaffected dogs. The incomplete ossification hypothesis does not fit with the cohort of dogs of this study because of the delay in onset of clinical signs. In fact, in the veterinary literature, most case series documented a median age at presentation of approximately 3-4 years (whereas age of onset for true incomplete ossification might be expected to be somewhat younger), and, in our study, this was supported by a median age at presentation of more than 6 years (Moores et al, 2012; Moores et al, 2017; Marcelling-Little et al 1994). Furthermore, the histopathology findings published by Marcellin-Little in 1994 (presence of fibrous tissue, increased osteoclastic activity and increased plasma cells, surrounded by a border of osteosclerosis) might in fact be considered suggestive of, or at least consistent with, an adaptive response to persistent mechanical forces rather than being related to failed endochondral ossification (Marcellin-Little et al, 1994; Farrell et al, 2011). Similarly, the histological features of a bone biopsy harvested from the fissure line of a pointer dog with HIF seemed to support the effect of an adaptive response to excessive and recurrent mechanical forces (Gnudi et al, 2005). Analysis of broken transcondylar screws published by Charles et al. in 2009 suggested that chronic multiplanar intracondylar instability might result in subsequent fatigue failure of transcondylar implants at the level of the intracondylar fissure. It was postulated that there could be the potential for the condyles to be "driven apart" by the wedge-shaped proximal ulna resulting in fatigue failure of the screw. Our arthroscopic findings suggest that mechanical impingement of the anconeal process within the olecranon fossa, as evidenced both by presence of the cartilage lesion and the apparent humero-anconeal joint space narrowing on arthroscopy in our HIF-positive group might better account for this predicted intracondylar instability. By comparison, we would postulate that the "wedge theory" might be expected to produce a more diffuse

pattern or cartilage pathology along the ulnar trochlear notch and/or the opposing portion of the humeral condyle. In 5 HIF-positive elbows, widening of the HIF line was identified arthroscopically when the tip of the anconeal process was engaged into the HA lesion and pronation/supination was applied, supporting an association between these lesions. The presence of the HA lesion only at the medial aspect of the HIF line, with no abnormalities of the lateral humeral condyle seen, along with the palpable “clunk” or a visual “flick” of the image when the tip of the anconeal process was engaged into and out of the HA lesion in 16/21 elbows, suggests that these lesions are likely to be associated with a focal incongruity, making the broad “humero-ulnar incongruency” terminology being considered a much less probable explanation. We therefore proposed that a terminology of “humero-anconeal incongruity” might be considered to describe these findings. In 10 of 21 HIF-positive elbows, preoperative CT imaging revealed that an incomplete HIF line was present. In these cases, the fissure was subjectively considered to be most evident at the most caudo-dorsal aspect of the humeral condyle but not at the most cranial aspect. This finding, that the HIF line appears to start caudally and may then progress further cranially, could perhaps also be consistent with our theory that HIF may be a consequence of “humero-anconeal incongruity” affecting the caudal portion of the joint. However, this cannot be confirmed in the absence of sequential CT studies of the same cases or further biomechanical data, which may be subjects for further study. A similar pattern of fissure propagation was demonstrated whilst investigating the etiopathogenesis of fragmentation of the medial aspect of the coronoid process of the ulna (Danielson et al, 2006). Radio-ulnar incongruency caused the greatest amount of fatigue microdamage to the subchondral bone in the proximity of the area where the radial head and coronoid process were in conflict but also, to a lesser extent, to the adjacent areas. A similar fatigue fracture theory could potentially be applied to the development of HIF with humero-anconeal incongruency instigating a fissure at the caudal aspect of the humeral condyle and

subsequently progressing cranially. Our observation of the HA lesion in elbows with an incomplete HIF line on CT further supports the theory that humero-anconeal incongruity may precede HIF development, although the precise sequence and etiopathogenesis of development of these features cannot be definitively confirmed from our study. It is worth noting that no elbow in our HIF-negative group had any evidence of the HA lesion, and that this group included four spaniel breed dogs (seven elbows), therefore suggesting that the HA lesion is directly associated with HIF development and is not likely to be a coincidental breed-related variant or incidental finding. Our statistical analysis supports the view that the HA lesion appears to be associated with HIF and does not appear to be a breed-dependent finding. Further study is warranted to establish whether early identification of humero-anconeal incongruity or the HA lesion might be viable as a potential screening modality in spaniel breed dogs to help predict future HIF development, or whether it might reliably facilitate diagnosis of HIF as an isolated diagnostic test where CT is not available. Two major limitations of the first part of this project are the small case number and the overrepresentation of spaniel breed dogs, although the statistical findings of Fisher's exact testing suggest that these were relatively minor limitations. Other limitations include the lack of elbows free of any form of pathology as a control group and the fact that the study was not blinded, which could have introduced further bias to the results.

OBLIQUE PROXIMAL ULNAR OSTEOTOMY AS A TREATMENT OF HIF: PROSPECTIVE CLINICAL STUDY

If we consider the hypothesis that abnormal cyclical loading on the humeral condyle results from humero-anconeal incongruity leading to fissure formation as a stress fracture outcome, it becomes theoretically possible to achieve healing of the HIF by addressing or improving this incongruity. This could be achieved by performing an oblique proximal ulnar osteotomy (PUO) to allow proximal translation and tilting of the proximal ulnar segment as a result of the upward pull of the triceps muscle (Turner et al, 1998; Fitzpatrick et al, 2009).

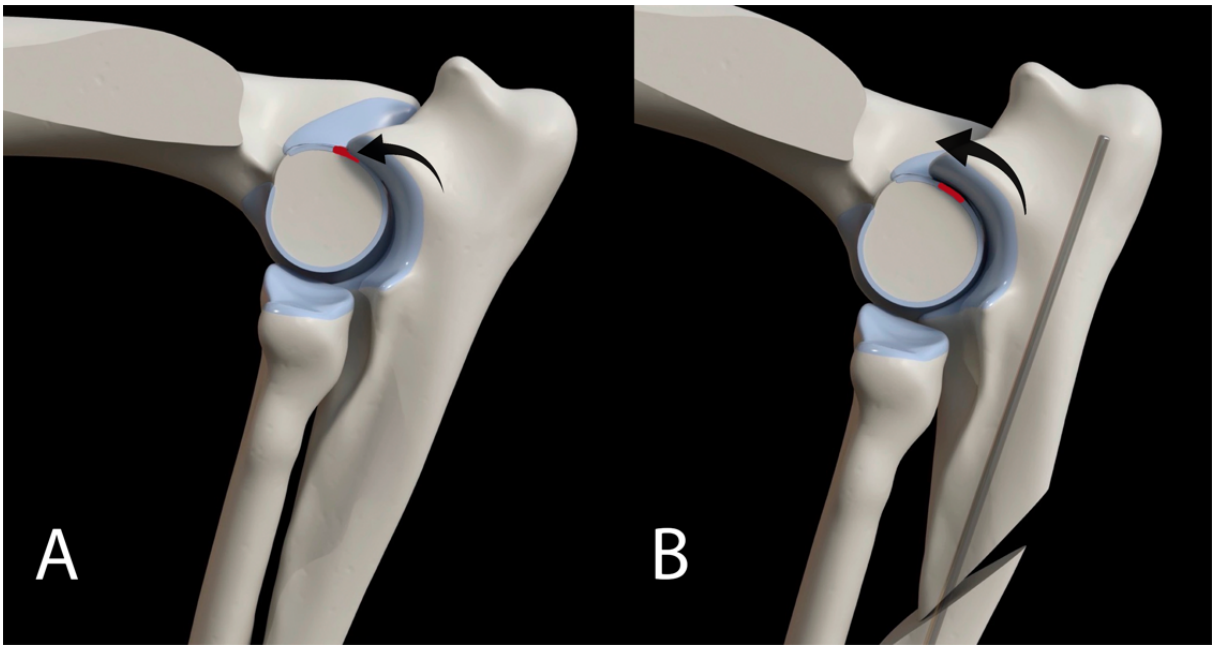

Fig. 9: Schematic representations of the motion of the ulna relative to the humeral condyle and the focal cartilaginous lesion. A: 3D representation of the conflict between tip of the anconeal process and the caudal aspect of the humeral condyle, leading to the formation of a focal cartilaginous lesion (red dot) (humero-anconeal incongruity). B: 3D representation of the humero-ulnar relationship after performing an oblique PUO, illustrating proximo-cranial displacement of the tip of the anconeal process in direction of the supratrochlear foramen and hypothetical amelioration of humero-anconeal incongruity.

In specific, the hypothesis to be tested on the second part of this thesis is that, following a PUO, the tip of the anconeal process will move in a cranio-proximal direction, towards the supracondylar foramen, disrupting the abnormal cyclical load applied to the humeral condyle, thereby allowing some degree of healing of the humeral intracondylar fissure.

3.1 Material and methods

Dogs presenting for unilateral/bilateral thoracic limb lameness and had HIF diagnosed by CT scan were included in the study. Dogs that did not undergo 6-week follow-up radiographs or later follow-up CT scans at a later stage were excluded from the study. Information retrieved included age, sex, breed, uni/bilateral lameness, subjective degree of discomfort on elbow extension (classified as *mild*, *moderate* and *severe*) pre-operatively and at the 6-week follow-up appointment, partial/complete fissure, arthroscopic findings, post-operative complications, time between initial surgery and follow-up CT scan, and time between initial surgery and the last telephonic/written follow-up. Ethical approval for this long-term prospective study was obtained by the RCVS Ethics review panel (2021-47).

3.1.1 Pre-operative imaging and surgical management

Computed tomography of both thoracic limbs from the carpi to the shoulders was performed with the dog under deep sedation (3-8 mcg/kg dexmedetomidine and 0.2 mg/kg butorphanol, IV). Dogs were positioned in sternal recumbency, with the elbow joints parallel and extended cranially at approximately 130°-140° of extension. If CT revealed changes compatible with presence of HIF (as previously described by Carrera et al, 2008), elbow arthroscopy, using a 2.4mm, 30° oblique arthroscopy (Arthrex®, Munich, Germany) was subsequently performed using our novel caudal portal previously described. The presence or absence of medial coronoid disease, a visible humeral intracondylar fissure, the recently described focal cartilaginous

lesion on the caudo-proximal aspect of the humeral condyle, and cartilage damage affecting the medial compartment were recorded. If fragmentation of the medial coronoid process was present, arthroscopic subtotal coronoid ostectomy was performed. An oblique proximal ulnar osteotomy was subsequently performed as previously described (Caron et al, 2016) with the aim to ameliorate humero-anconeal incongruity. The interosseous ligament was always released by placing a Freer periosteal elevator in the space between the proximal radius and ulna, and by application of a force in a distal direction until the portion of the interosseous ligament of the proximal ulnar segment was completely transected. An intramedullary K-wire (1.25mm-1.4mm) was then placed into the ulna in a retrograde fashion to prevent excessive caudal displacement of the proximal ulnar segment. A 0.5mls (equivalent to 0.75mg of dibotermin alfa) of reconstituted recombinant human bone morphogenetic protein-2 (rhBMP-2) was uniformly distributed on a collagen haemostatic matrix and it was applied at the osteotomy site with the aim to stimulate early bone healing. If previous metallic implants such as transcondylar screws or laterally applied plates were present, these were subsequently removed. A compressive bandage was applied for 3 days to limit post-operative swelling.

3.1.2 Postoperative management

Postoperative analgesia was provided by the administration of methadone (0.2 mg/ kg intramuscular, every 4 hours) whilst in the hospital and oral *nsaids* for 3 weeks whilst at home. Trazodone hydrochloride (5-10mg/kg) was also dispensed for 6 weeks to reduce anxiety and distress in those active dogs unaccustomed to crate confinement and lead-only activity. Cage rest for 6 weeks and lead-only walk for 12 weeks were instructed at discharge. Dogs were radiographically re-assessed at 6 weeks to assess the degree of healing of the ulnar osteotomy and to screen for possible complications. Complications were classified as described by Cook

and colleagues in 2010. A follow-up CT scan was then performed at a later date to assess the degree of healing of the HIF.

3.1.3 Radiographic and CT assessment of the effect of PUO on the ulna

Given that the ulna would not only displace proximally but would also tilt, we took two measurements (one more cranial and one more caudal) to better assess the magnitude of proximal ulnar displacement. On the preoperative medio-lateral radiograph, two lines (L1, more cranial and L2, more caudal) were measured to assess the length of the ulna (in millimeters). To normalize these two measurements, the length of both these lines was divided by the width of the radius measured at its exact half (L3) (Figure 10). The same measurements were repeated on the 6-week follow-up radiographs taking particular care in selecting the exact same landmark points that were used on the pre-operative images. An increase in ratio of these two measurements was interpreted as proximal displacement of the proximal ulnar segment with subsequent elongation of the ulna as a result of the PUO.

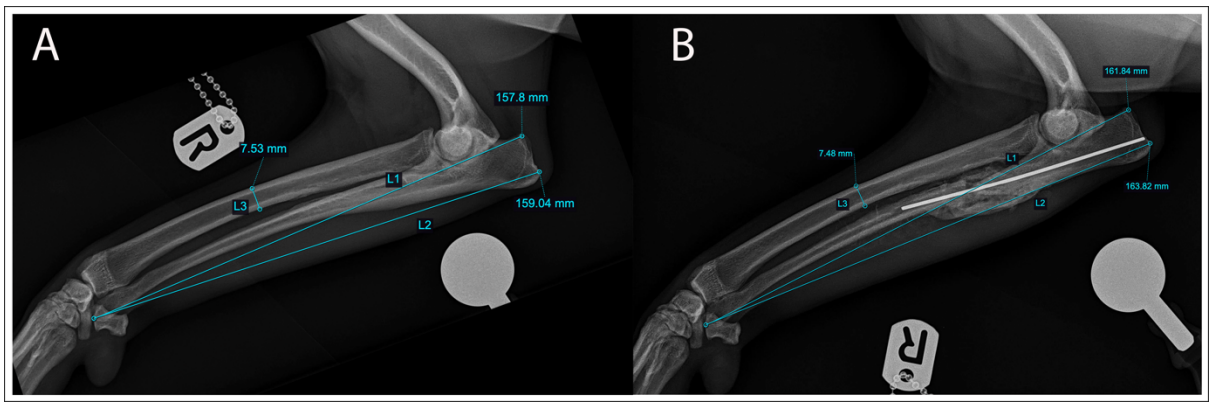

Fig.10: Radiographic measurements performed on the medio-lateral view of the affected antebrachium, prior to surgery and at the time of 6-week follow-up radiographs. The first line (L1) was drawn and measured from a point at the most cranial aspect of the dorsal cortex of the olecranon to an easily recognizable point at the distal end of the styloid process of the ulna. A second line (L2) was then drawn and measured from an easily recognizable point (such as where the k-wire was engaging the cortex for example) at the caudal aspect of the dorsal cortex of the olecranon to exactly the same point at the distal end of the styloid process of the ulna where the first line ended

Furthermore, to assess if ulnar elongation also corresponded to cranial displacement of the tip of the anconeal process in direction of the supratrochlear foramen, additional measurements were performed on pre-operative and follow-up CT images. On sagittal images, the width of the proximal radius was measured in two points and a line intersecting the exact midpoint of these two lines was drawn. A second perpendicular line was drawn from the tip of the anconeal process to the point where the first line intersected the anconeal process. The distance between the tip of the anconeal process and the first line was then measured (Figure 11). A positive change in measurement was interpreted as cranial displacement of the anconeal process as a result of the tilting movement achieved by the PUO. All measurements were performed by the same investigator.

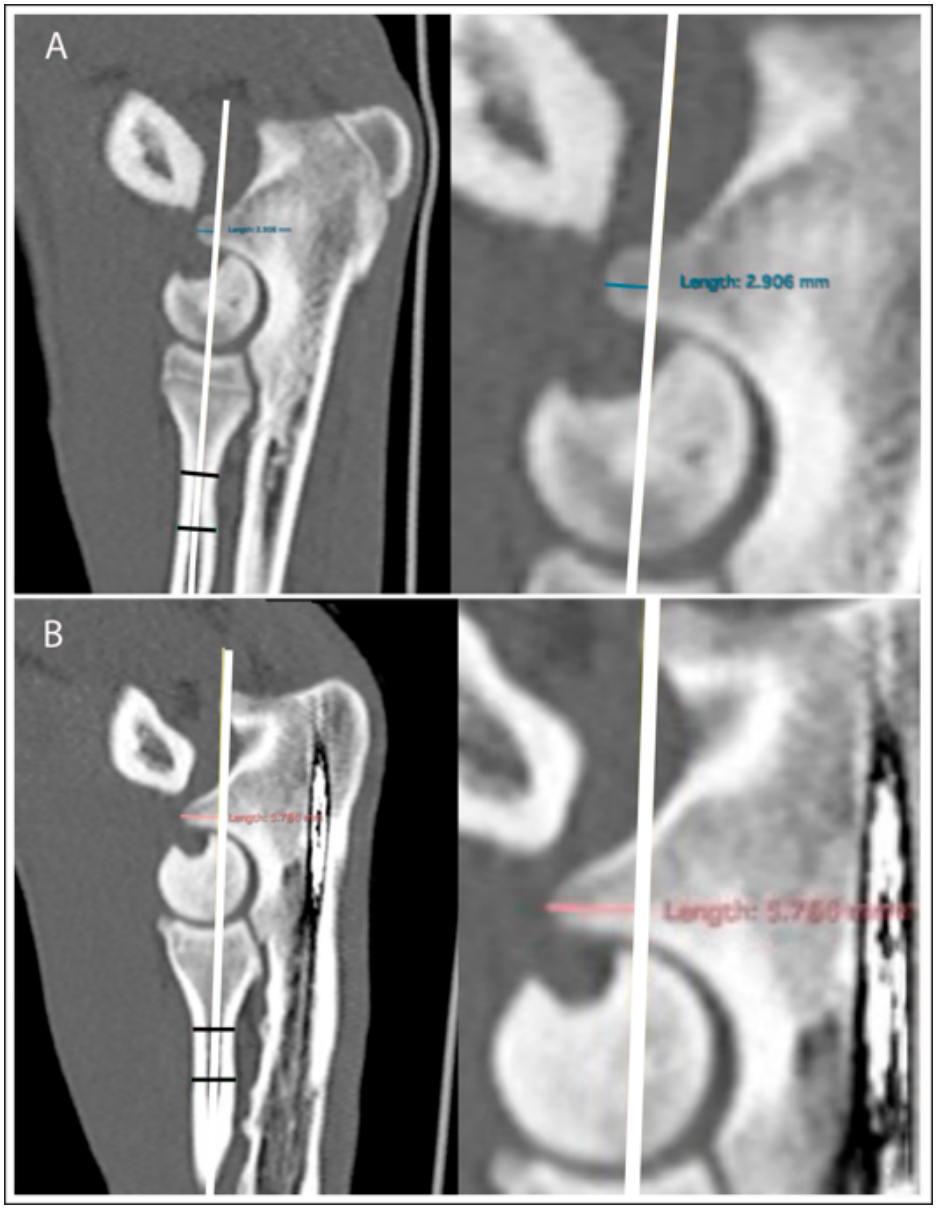

Fig. 11: The measurement of the cranial displacement of the tip of the anconeal process in direction of the supratrochlear foramen on pre-operative (A) and follow-up (B) CT scans. On sagittal images, the width of the proximal radius was measured in two points and a line intersecting the exact midpoint of these two lines was drawn. A second perpendicular line was drawn from the tip of the anconeal process to the point where the first line intersected the anconeal process (A1 and B1). The distance between the tip of the anconeal process and the first line was then measured (A2 and B2).

3.1.4 Objective assessment of HIF healing on CT images

The bone density of the medial and lateral humeral condyle was assessed on coronal planes and recorded in Hounsfield units (HU) on the pre-operative and last follow-up CT images. A medical image viewer (Horos, New York, USA) and its built-in tools were used to perform the measurements. On the pre-operative images, a rectangular region of interest (ROI) (with the area calculated in mm^2) was drawn on the midline of the humeral condyle to include the entirety of the hypo-attenuated humeral fissure. In dogs with a complete fissure, this rectangle was extended from the caudal to the cranial aspect of the humeral condyle whilst, in dogs with partial fissures, the rectangle was extended from the caudal aspect of the humeral condyle to a cranial direction until where the hypo-attenuated line of the fissure ended.

A free-hand ROI was then drawn to measure separately the bone density of the medial humeral condyle and of the lateral humeral condyle next to the ROI of the fissure (Figure 12).

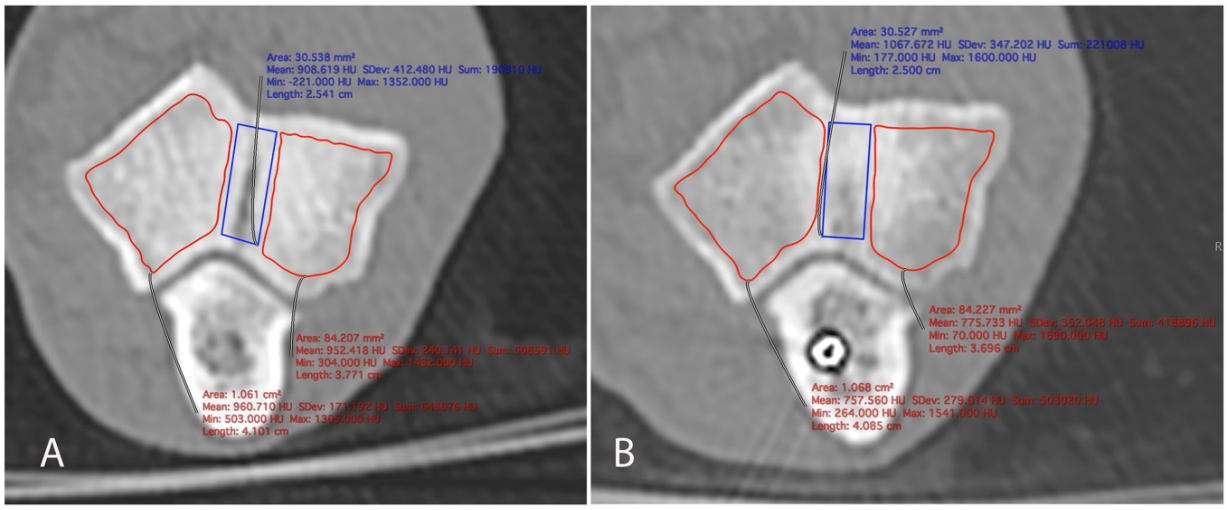

Fig.12: The measurement of the region of interest (ROI) of the humeral condyle on coronal CT images. A rectangular ROI (mm^2) was drawn on the midline of the humeral condyle to include the entirety of the hypo-attenuated humeral fissure. In dogs with a complete fissure, this rectangle was extended from the caudal to the cranial aspect of the humeral condyle (A) whilst, in dogs with partial fissures, the rectangle was extended from the caudal aspect of the humeral condyle to a cranial direction until where the hypo-attenuated line of the fissure ended (B). A free-hand ROI was then drawn to measure separately the bone density of the medial humeral condyle and of the lateral humeral condyle next to the ROI of the fissure.

The selected ROIs were standardized to avoid cortical bone inside the areas of density measurements. In order to standardize the density values as much as possible, and to reduce the dependence of the results of the spatial orientation of ROIs, three difference coronal planes were chosen. The density measurements of these three planes were then summed and divided by three to obtain an average sample bone density value for each elbow. Extreme care was taken to select matching coronal images and the same ROI area's size on pre-operative and follow-up CT images to ensure consistency of measurements between time points. All measurements were performed by the same investigator. For those dogs where metallic implants were already present at the time of surgery, a CT scan was repeated following surgery once the metallic implants were removed to avoid metallic artifacts and the hypo-attenuated area corresponding to the bone tunnel was not included in the measured ROIs. A decreasing mineral density of the ROIs of the medial and lateral condyle was interpreted as reduction of the sclerosis of the bone whilst, an increased mineral density of the rectangular ROI of the HIF was interpreted as healing of the fissure.

The bone density of both the medial and lateral condyle was measured in the same way on CT images of spaniel dogs with no signs of HIF or elbow disease. A standard rectangular area on the midline was excluded from the measurements to account for the possible presence of a hypothetical fissure. This data was used to create a baseline for normal humeral condyle bone density.

The extent of fissure healing at the latest follow-up CT scan was also evaluated subjectively, and it was categorized into three groups based on the condition of the HIF observed in the pre-operative images: *healed*, *healing*, and *not-healing*.

3.1.5 Statistics

All statistical analyses were performed using software (SPSS v19, August 2010, IBM). Results were expressed as mean ± SD for normally distributed variables. Continuous variables in the study were normally distributed (Kolmogorov-Smirnov test $P>0.05$). Univariate statistical analyses were performed to evaluate association/correlation between postoperative complications and categorical/continuous variables. Fisher's exact test was used for discrete variables (i.e., partial/complete humeral intracondylar fissure and complications). A paired t-Test was used to evaluate the difference between means before and after surgery or at the last follow-up. Independent t-Test test was used to evaluate the relationship between continuous variables and categorical variables (i.e., body weight and post-operative complications). A Kruskal Wallis test was used to compare 3 or more independent samples and a continuous variable (i.e., degree of healing of the HIF after surgery with variables none/partial/complete fissure and weight). Pearson's correlation was performed to assess linear correlation between continuous variables. Statistical significance was set to $P < 0.05$ (type 1 error). For statistical purposes, dogs were divided into three age groups: immature dogs (0-14 months), adult dogs (15-95 months), and old dogs (>96 months).

3.2 Results

Fifty-one elbows (35 dogs) were included in the study and 2 dogs were excluded because of the lack of follow-up CT images. The breeds most commonly represented were English springer spaniel (24), followed by Cocker spaniels (8) and Sprockers (3). Twenty-nine dogs were male and 6 were female. Six of these dogs were active working dogs at the time of first consultation. At the time of surgery, the mean weight was 18.08 ±3.8kg (range 7-23.6kgs) and the mean age was 47.6 ±27.9 months (range 5-101 months). Twenty percent of dogs were younger than 14 months (n=10) and 4% were older than 96 months. On pre-operative clinical examination, 13 elbows (25.4%) had mild discomfort, 23 (45%) had moderate discomfort, 4 (7.8%) had severe discomfort, and 11 (21.5%) had no discomfort on elbow extension. Upon the 6-week follow-up assessment, extension of the elbows resulted in the absence of discomfort in 48 elbows (94%), accompanied by mild discomfort in 2 elbows, and moderate discomfort in another elbow (notably, these 3 latter cases coincided with observed cartilage damage determined through arthroscopy). The follow-up CT scan assessment was performed at a median 18.5 months (range 10-49 months).

Surgery to treat HIF had already been performed in 9 elbows (4 elbows had a transcondylar screw only and 4 elbows had a transcondylar screw and a plate applied). In 4 of these elbows an infection was present, in 2 elbows the implants were poorly placed, in 2 dogs (2 elbows) significant lameness was still present and in 1 elbow the implant had become loose and it was backing out (Figure 13).

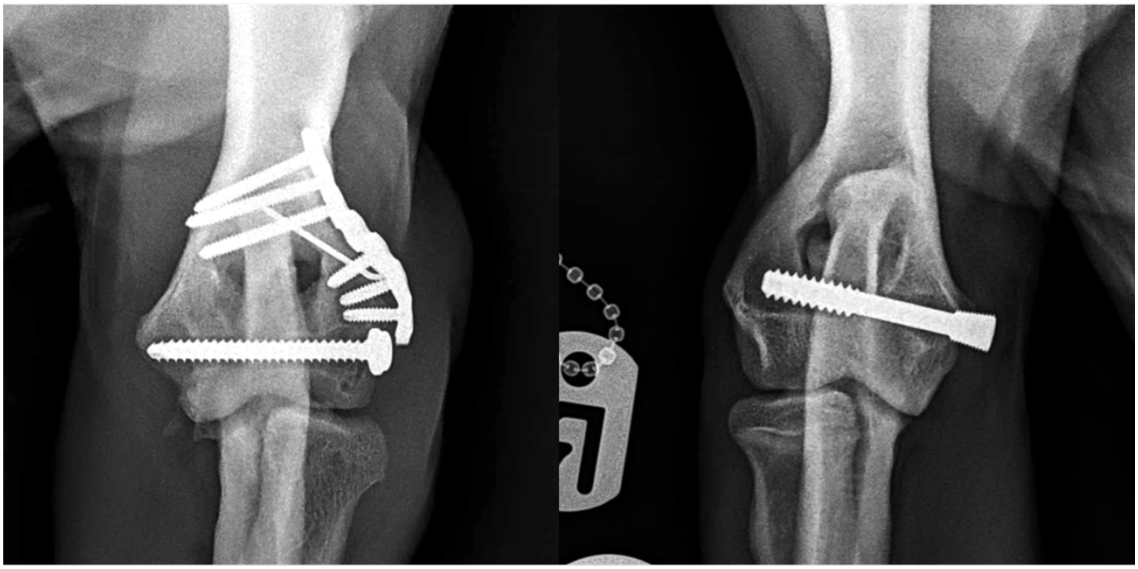

Fig 13: Left: cranio-caudal radiograph of the elbow of a 1year 8month old ESS with signs of chronic infection at level of the implants. Note the radiolucency around the transcondylar screw and around the three most distal screws of the lateral plate to suggest implant loosening. Right: cranio-caudal radiograph of an 8-month-old ESS with implant loosening and backing out of the screw.

3.2.1 Arthroscopic findings

Arthroscopy confirmed presence of concomitant medial coronoid disease in 12 elbows (23.5%). Radial incisure fragmentation of the medial coronoid process was present in 7 elbows, tip fragmentation in 2 elbows and a combination of tip-radial incisure fragmentation in 4 elbows. Concomitant cartilage damage of the medial compartment was present in 10 elbows (ranging from modified Outerbridge grade I to grade IV). The humeral intracondylar fissure was visible in all but one elbow (98%). Similarly, the focal cartilaginous lesion recently described on the caudal aspect of the humeral condyle of spaniels with HIF was seen in all but two elbows (96%).

3.2.2 Objective assessment outcomes

On presentation, CT examination revealed the HIF to be partial in 24 elbows (47.1%) and a complete in 27 elbows (52.9%). Objective assessment confirmed that a significant difference was found between the mean HU of the HIF's ROI on pre-operative CT images and last-follow-up images (p=0.001). The same was true for the mean HU of the lateral humeral condyle (p=0.001), the mean HU of the medial humeral condyle (p=0.001), and the total mean HU of the humeral condyle (sum of the medial and lateral condyle HUs) (p=0.001). The average HU of the humeral condyle before surgery was 1703.7 ±294, at the last follow-up CT scan was 1520.7 ±206, and in normal elbows (n =64) was 689.5 ±105. Data also confirmed that young dogs have a wider fissure (HU 481 ± 221 vs HU 675 ± 177; p = 0.03) and less sclerosis of the humeral condyle (HU 1386 ± 193 vs. HU 1869 ± 271; p= 0.001) than older dogs.

A significant difference was also found between anconeal tip displacement on pre-operative CT images *vs* last follow up images (p=0.001), and between L1 and L2 ratios on pre-operative *vs* 6-week follow-up radiographs (p=0.001). (Table 1)

Table 1: Summary of imaging assessment.

Radiographic assessment			
	Pre-Surgical	Follow-up	Paired t-test (*p*-value)
Ratio Radio ulnar length Cranial (L1)	17.60	18.14	0.01
Ratio Radio ulnar length caudal (L2)	17.68	18.31	0.01
CT scan assessment			
HU medial aspect humeral condyle	834.80	735.12	0.01
HU lateral aspect humeral condyle	852.01	785.60	0.01
HU total condylar region	1686.89	1520.73	0.01
HU fissure	640.87	835.20	0.01
Anconeal tip displacement (mm)	2.36	3.24	0.01

Objective assessment confirmed that the age of the dog was predictor of healing of the humeral intracondylar fissure (Kruskal-Wallis p= 0.03). Dogs in the youngest group (0-14 months) had the highest mean increase in HU at the level of the fissure (384.54 units). Dogs in the middle group (15-96 months) had a mean increase of 156 HU, and dogs in the oldest group (>96 months) had a mean decrease of 22.9 HU.

No relationship was found between the objective healing assessment of the fissure on CT scan and the difference in L1 length ratio between pre- and post-treatment (p=0.278, or the difference in L2 length ratio (p=0.233) or anconeal tip displacement (p-value = 0.894).

3.2.3 Subjective assessment outcomes

Subjective assessment revealed the HIF to be *healed* in 28 elbows (54.9%), to be *healing* in 13 dogs (25.4%) and to be *not-healing* in 7 elbows (13.7%) (the two broken elbows were not counted) (Figures 14-16). A non-parametric Kruskal-Wallis test confirmed a positive association between subjective and the objective assessment in terms of fissure healing (p=0.001).

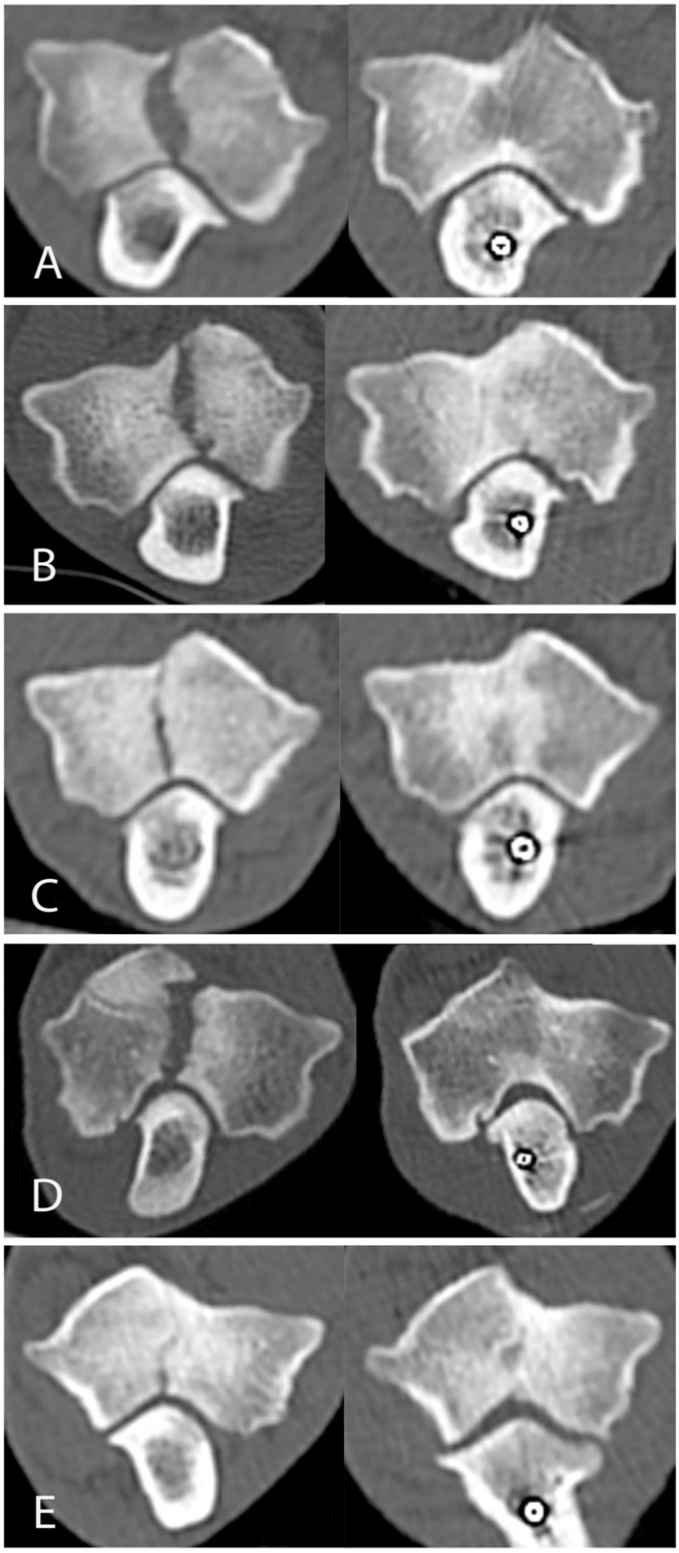

Fig. 14: Examples of good healing of the fissure achieved by performing an oblique PUO (left column: pre-operative CT images; right column: latest follow-up CT images). A: a 6-month-old ESS (A2: 10-month follow-up). B: a 7-month-old ESS (B2: 10-month follow-up). C: a 2-year-old ESS (C2: 18-month follow-up). D: an 8-month-old Sprocker (D2: 6-month follow-up). E: a 3-year and 8-month-old ESS (E2: 16-month follow-up).

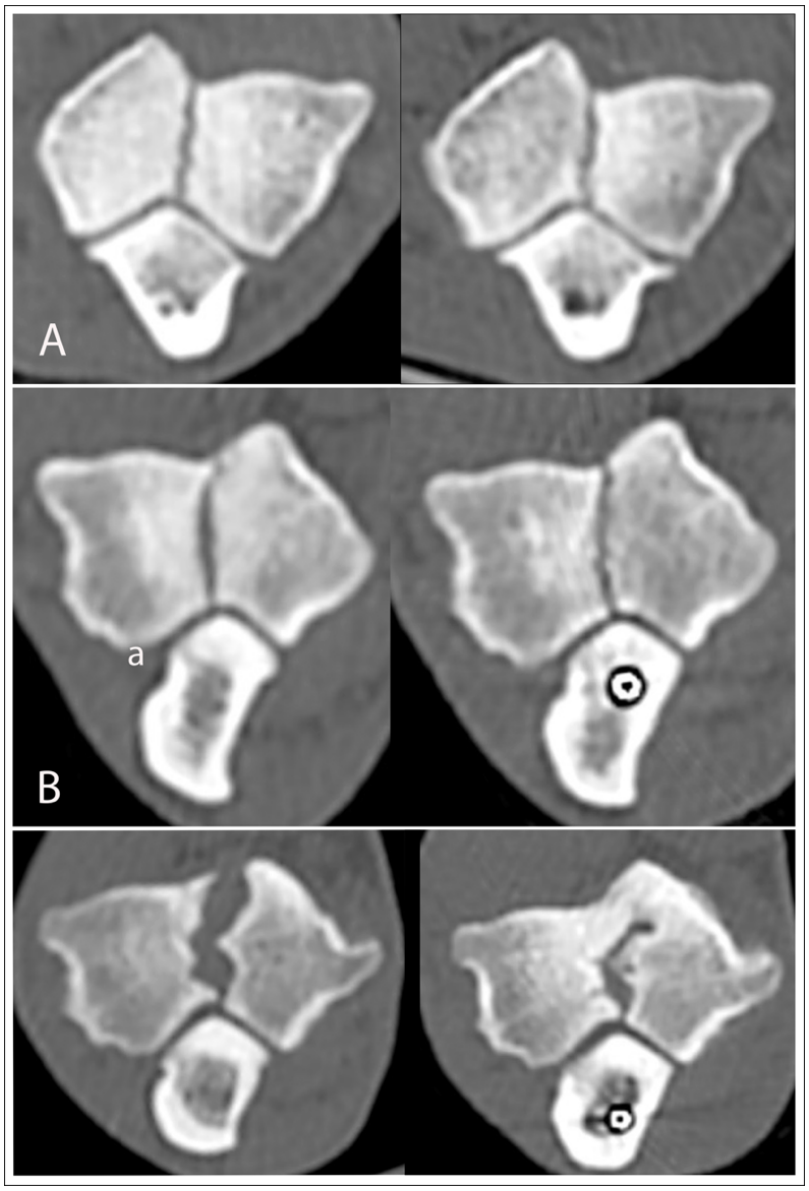

Fig. 15: Examples of progressive healing of the fissure achieved after performing an oblique PUO (left column: pre-operative CT images; right column: latest follow-up CT images). A: a 2-year-old cocker spaniel (A2: 24-month follow-up). B: a 4-year-old ESS (B2: 10-month follow-up). C: an 8-month-old ESS (C2: 18-month follow-up).

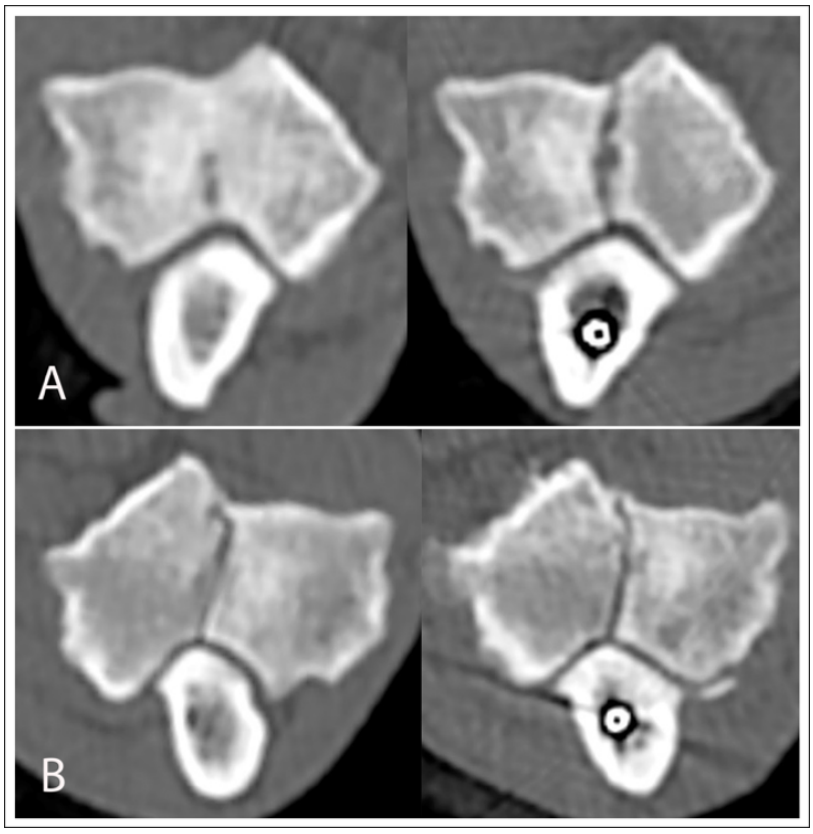

Fig.16: Example of poor/lack of healing of the fissure after performing an oblique PUO (left column: pre-operative CT images; right column: latest follow-up CT images). A: a 3-year-old cocker spaniel (A2: 23-month follow-up). B: a 6-year 5-month-old ESS (B2: 24-month follow-up).

Subjective assessment confirmed that there was not association between the healing of the HIF and weight or age of the dogs, regardless of whether the degree of healing was categorized as *healed*, *healing* or *non-healing*. This was determined using t-tests (p=0.786 and 0.284) and Kruskal-Wallis tests (p=0.475 and 0.183), respectively.

3.2.4 Complications

Minor complications (n=3, 5.8%) were experienced in 3 limbs and they were due to the intramedullary pin that migrated proximally and needed to be removed under sedation through a stab incision of the skin. A broken intramedullary pin was noted at the level of the osteotomy at the 6-week follow-up radiographs (n=4). However, due to the fact the bone healing progression at the level of the osteotomy was already considered satisfactory at that stage and that the outcome and the post-operative care were not changed following this discovery, these cases were not classified as having minor complications. Major complications were encountered in 5 dogs (6 limbs); 4 of these major complications were related to healing of the fissure (7.8%) whilst 2 were related to healing of the proximal ulnar osteotomy (3.9%) (Table 2).

Table 2: List of sustained major complications and relative surgical treatment

	Type of major complication	**Surgical treatment**
Dog 1	Lateral condylar fracture	4.5mm transcondylar plate and 2.7mm SOP applied laterally
Dog 2 *Left elbow*	Bicondylar "Y" fracture	4.5mm transcondylar screw, 2.7mm SOP applied laterally and 2.7mm LCP applied
Right elbow	Persistent intense sclerosis of the humeral condyle and widening of the HIF on 2nd	4.5mm transcondylar screw and 2.7mm LCP applied medially

Dog 3	Lack of healing of the HIF, increased bone production on lateral epicondylar crest, discomfort on manipulation	3.5mm transcondylar screw and 2.7mm SOP applied laterally
Dog 4	Broken IM pin and excessive displacement of the proximal ulnar segment	Pin removal, debridement of bone ends, realignment of ulnar segments, placement of larger size IM pin, BMP application
Dog 5	Non-union PUO	Debridement, removal of the IM pin, application of a 2.7mm locking plate, bone

Dog 1 experienced a lateral condylar fracture when he slipped on a wet surface 3 months after the initial surgery. Dog 2 had a follow-up CT scan performed 1 year and 4 months after surgery which revealed almost complete healing of the partial fissure previously present, bilaterally. However, the owner contacted us again 2 months later reporting a certain degree of stiffness (bilaterally) that was previously not present. One month later the dog suddenly screamed in pain and a Y-fracture was diagnosed on radiographs. CT scan of the contra-lateral elbow was concomitantly performed, and it revealed no improvement of the degree of sclerosis of the humeral condyle and also that, at the most caudo-proximal aspect of the humeral condyle, the fissure was mildly visible again. We therefore decided to prophylactically stabilize the humeral condyle with a transcondylar screw and a medially applied plate to prevent a fracture at the same time of performing the repair of the Y-fracture. The owner of dog 3 reported persistent lameness despite a transcondylar screw had been placed elsewhere several months earlier. The

screw was removed and an oblique proximal ulnar osteotomy was performed. A follow-up CT scan was performed 1 year 9 months later, and it revealed that the bone tunnel left by the screw was still present and that new bone had formed in the centre of the condyle at level of the humeral intracondylar fissure but that the latter was surprisingly still visible. The dog did not appear lame or stiff at this stage. Six months later, the owner started reporting occasional lameness and a repeated CT scan confirmed the lateral epicondylar crest to be visibly thicker and more sclerotic than what it previously was, suggesting presence of persistent instability. A transcondylar screw and a locking plate were applied to prevent fracture development.

No significant association could be found between the variables we assessed in this study (age: $p=0.420$ and weight: $p=0.984$) and the development of complications or the need for revision surgery.

At the time of writing this manuscript (median time of 30 months from when surgery was performed), all owners were contacted again either by email or by telephone for an update and no additional complications or problems were reported.

3.3 Discussion

This second part of the thesis objectively demonstrated that performing an oblique PUO in dogs with HIF resulted in healing of the humeral intracondylar fissure and concomitant reduction of the sclerosis of the humeral condyle in the majority of dogs.

HIF has been reported in both adult and young spaniel breed dogs and its aetiopathogenesis is still under debate (Meyer-Lindenberg et al, 2002; Moores et al, 2017, Moores et al, 2021, Witte et al, 2010, Farrell et al, 2011). In the authors' opinion, the different manifestations of humero-anconeal incongruity in young and old dogs (wider fissure and less sclerosis in young dogs, increased sclerosis and stress fracture formation in older dogs) are likely caused by the same underlying conformational issue. The combined axial and rotational loading of the tip of the anconeal process against the caudo-proximal aspect of the medial humeral condyle during weight bearing may in fact prevent the fusion of the humeral condylar ossification centres in young dogs, and lead to stress fracture formation in older dogs. This seems to be supported by our statistical analysis, which confirmed that young dogs have a wider fissure and less sclerosis of the humeral condyle than older dogs.

Fatigue fractures (also commonly called “stress fractures”) are the result of abnormal cyclical loading on normal bone (Fredericson et al, 2006). As stress on bone is increased, it begins to deform through the bone’s elastic range but can ultimately return to its original configuration. Stress beyond the elastic range creates microfractures and persistent plastic deformity. Eventually these microfractures coalesce into a discontinuity within the cortical bone taking the name of stress fracture. Histologic studies of stress fractures show that repetitive response to stress leads to osteoclastic activity that surpasses the rate of osteoblastic new bone formation, resulting in temporary weaking of the bone. If the osteoclastic activity continues to exceed the rate of osteoblastic new bone formation, a full cortical break occurs (Li et al, 1985; Stanitski et

al, 1978). In humans, it is still under debate whether stress fractures occur owing to the increased load after fatigue of supporting structures or to contractile muscular forces acting across and on the bone but, in principle, both factors are thought to contribute to it (Stanitski et al, 1978; Markey, 1987; Daffner et al, 1992). In baseball players, the tip of the olecranon is forced into the olecranon fossa during rapid elbow extension which leads to compensatory compression on the medial aspect of the olecranon–olecranon fossa articulation. This compression is believed to be caused by repetitive abutment of the olecranon against the olecranon fossa, triceps traction on the olecranon during the deceleration phase of throwing, and medial olecranon impaction onto the olecranon fossa due to valgus stress (Mauro et al, 2011; Smith et al, 2018; Greif et al, 2020). Whilst the human olecranon has a similar but more open semilunar notch, it lacks a prominent anconeal process such as dogs have. When humero-anconeal incongruity is present, such a prominent process may apply a supra-physiologic cyclic force to the caudo-proximal aspect of the humeral condyle (at level of where the focal cartilaginous lesion is) which will result in cumulative bone strain leading to bone damage and fracture if net bone damage exceeds bone repair.

Our study found that PUO causes the tip of the anconeal process to move in a cranio-proximal direction. This suggests that the tip of the anconeal process will no longer apply an anormal load on the caudal aspect of the humeral condyle at the level of the cartilaginous lesion during weight bearing.

The effect we achieve is similar to the reparative action in humans diagnosed with a stress fracture, where the first step is to discontinue the offending activity (such as running or throwing). Halting this repetitive mechanical overload of the humeral condyle should lead to rebalance of the osteoblastic/osteoclastic activity and lead to healing of the skeletal lesion, which in our study was achieved in 80% of elbows.

In this study, release of the interosseous ligament was considered an essential part of the surgery aimed at achieving significant proximal displacement and tilting of the proximal ulnar segment. The osteotomy cut was started 1-2 cm distal to the radial head at level of where the periosteal elevator can physically be inserted in the space between radius and ulna. The interosseous ligament was then disrupted all the way distally until the proximal ulnar segment was completely released. In most cases, a small osteotome was necessary to release the most distal part of the proximal ulnar segment due to mineralized-like adhesions that were present at that specific level and that could not be broken with the periosteal elevator alone. Placement of an intramedullary pin is considered important after the interosseous ligament is released, as the risk of excessive caudal displacement is high. In our dogs, we always tried to place the smallest possible IM pin, which was inserted by only 2–3 cm into the distal ulnar segment. This allowed us to achieve the desired caudal displacement of the proximal ulnar segment up to the point where the pin contacted the caudal cortex of the distal segment and the cranial cortex of the proximal ulnar segment. Human recombinant bone morphogenetic protein-2 (a human protein with osteoinductive activity that leads to accelerated bone healing) (Schaefer et al, 2009; Schmiedt et al, 2007) was routinely used in all dogs older than 8 months to promote bone union of the two ulnar segments, as we were concerned about the risk of delayed or non-union, which is reported to be as high as 31.1% in a recent manuscript analyzing the complication rate following oblique PUO in dogs (Danielski et al, 2023). In our study, this type of complication was drastically reduced to 1.9% (1/51 case of delayed union). Although it is difficult to make a direct comparison to this other study, we suspect that our significantly lower complication rate associated to early healing of the osteotomy, which is anecdotally difficult to achieve in adult and old dogs, is attributable to the use of rhBMP-2. However, it is important to consider additional factors that may explain the reduced incidence of delayed- or non-unions observed in our cases. These may include the use of an ulnar intramedullary pin, the use of a new sagittal

blade in all surgeries and the meticulous attention given to thorough irrigation of the bone and of the blade with a cold sterile solution during the cutting procedure (to minimize damage to the cellular environment) and the advanced experience of the surgeon in performing this technique.

Traditional surgical treatment of this condition involves placement of a transcondylar screw to bridge the fissure, stabilize the condyle and reduce the risk of fracturing (Moores aet al, 2014; Moores, 2006; Hattersley et al, 2011, Chase et al, 2019). Healing of fissures following this type of surgical treatment has been inconsistently reported in the veterinary literature. Although data from a few studies suggest that up to 77% of fissures can heal or reduce in size (Meyer-Lindenberg et al, 2002; Butterworth et al, 2001; Moores et al, 2014; Chase et al, 2019; Walton et al, 2020; Fitzpatrick et al, 2009), it is important to note that the data presented may be influenced by the significant limitations of radiographs as a sensitive method for objectively assessing the degree of fissure healing. In certain cases, even diagnosing the presence of HIF itself can be exceptionally challenging, further questioning the accuracy of these results. Additionally, it is important to acknowledge that the use of post-operative advanced imaging such as CT as a method to reliably assess the degree of healing of the fissure is significantly limited by the presence of the transcondylar screw and the metallic artifacts it generates. Use of allograft or autograft in combination with a strong implant fixation have also been described to manage these challenging non-healing stress fractures but lack of adequate sequential imaging, of objective assessment of the degree of healing and presence of metallic implants precludes again the reliable assessment of the degree of healing achieved (Walton et al, 2020; Fitzpatrick et al, 2009). In our study, absence of metallic implants allowed us to reliably and objectively assess the degree of HIF healing in all elbows.

This study confirmed our clinical impression that the degree of healing of HIF in dogs younger than 14-month-old is far superior than in older dogs. Histological samples harvested from the fissure line of adult dogs revealed presence of amorphous and necrotic material and of significant amount of intermediate fibro-connective and cartilaginous tissue surrounded by two borders of osteosclerosis (Marcellin-Little et al, 1994; Gnudi et al, 2005). It is intuitive to think that the amount of fibrous and necrotic tissues present in the HIF of an older dog would somehow impede or at least slow down the healing of the fissure. In young dogs, instead, this does not seem to be the case as we suspect that the superior healing activity and bone metabolism of a young dog can relatively easily overcome the presence of a smaller amount of fibrotic and/or necrotic tissue present within the fissure and lead to complete healing of the bone defect. Additionally, young dogs are favored by an increased vascular capacity or angiogenesis at the site of skeletal repair that also contributes to accelerate the healing process (Tomlinson et al, 2013). On the contrary, angiogenesis has been shown to be impaired as a function of age in two different animal models and Cocker Spaniels aged between 2- and 3-year-old have been shown to have a decrease in the number and density of vessels within the humeral condyle when compared to a non-Cocker spaniel control group (Rivard et al, 1999; Larsen et al, 1999). Lastly, it has to be noted that the sclerosis present on either side of the fissure of older dogs can further act as an important barrier to angiogenesis across the fissure.

A histological characteristic of sclerotic bone is a significant reduction in vascular supply of the affected area. Due to its significant impact on the vascular supply of the humeral condyle, the authors suspect that the sclerosis of the humeral condyle plays a crucial role in influencing the degree of healing of the fissure. In certain cases where severe sclerosis of the condyle was observed on pre-operative CT images, the fissure width and length initially increased before subsequently reducing. These instances indicated the persistent presence of severe sclerosis of the humeral condyle during the first follow-up CT assessment, coinciding with the period when

the fissure appeared enlarged. However, the sclerosis notably decreased by the time of the last follow-up CT scan when the fissure exhibited a reduction in size. A Pearson test was therefore used to assess the linear relationship between the difference in total sclerosis of the humeral condyle (at the first and last CT scan) and the objective degree of healing of the fissure. Although statistical significance was not achieved ($p = 0.120$), indications of a potential association between subchondral sclerosis and fissure healing have arisen. It is plausible that the limited case number in our study has contributed to this outcome, potentially leading to a type II error.

Sclerotic bone has been shown to have reduced creep responses in cortical and trabecular bone (Chen et al, 2013). This may bear implications in terms of increased microcrack propagation and altered mechanical load distribution thereby implying reduced bone toughness and increased stiffening during cyclic loading (Chen et al, 2013). Stiffer materials are generally more brittle and this means that they are more likely to suddenly break without warning. This would explain the authors' conjecture that the severely sclerotic humeral condyle of an adult dog is more susceptible to sudden catastrophic failure than the humeral condyle of a young dog with a large HIF. Dog 2 suddenly experienced a Y fracture of the left elbow without any warning except for stiffness at the time of getting up from lying down for a while. His 1 year 4-month follow-up CT scan confirmed that the partial fissure had healed but that intense sclerosis of the humeral condyle was still present. Arthroscopy of the fractured elbow was repeated immediately prior to fracture repair. Whilst the original focal cartilaginous lesion appeared to have some degree of fibrocartilage coverage, the lesion was more proximally elongated in the direction of the supratrochlear foramen (along the sagittal plane) (Figure 17).

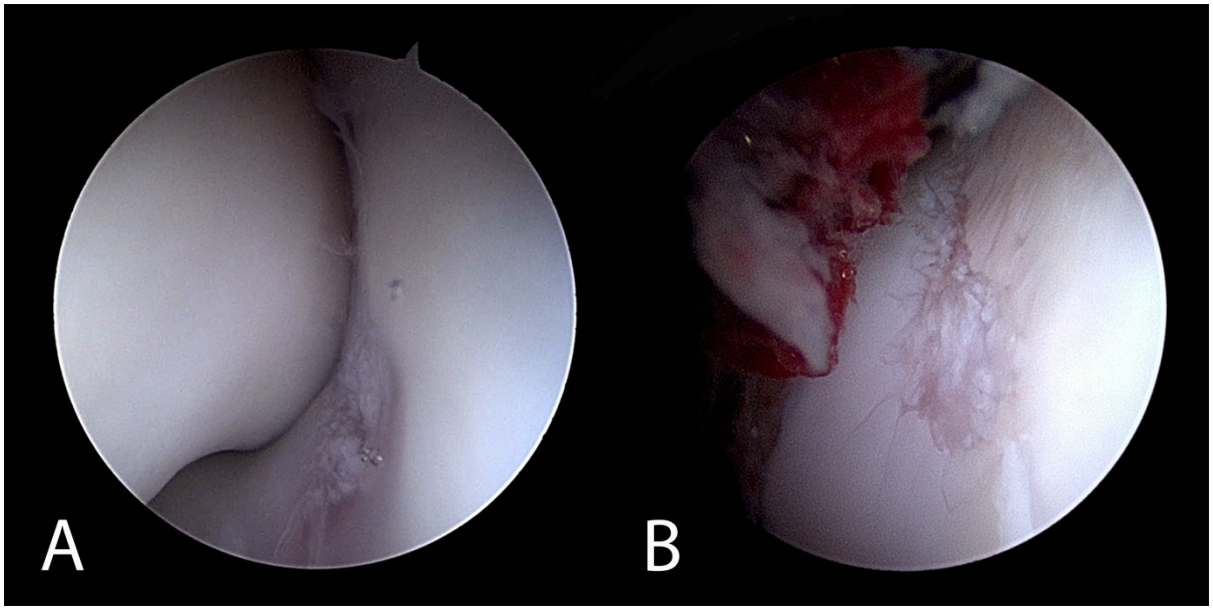

Fig. 17: Arthroscopic view of the left elbow of dog 2 using the caudal portal. A: pre-operative view of the focal cartilaginous lesion caused by humero-anconeal incongruity. B: Arthroscopic view of the cartilaginous lesion performed at the time of bicondylar fracture repair 19 months after the initial surgery. The initial focal lesion seems to be covered by a thin layer of fibrocartilage and the cartilage damage seems to be extending more proximally, along the sagittal plane, in direction of the supratrochlear foramen.

This would suggest that the cranio-proximal displacement achieved by the anconeal process was insufficient to completely resolve humero-anconeal incongruity and that some degree of cyclical overload was still applied to the humeral condyle by the anconeal process. These findings are contrasting with the result of the second-look arthroscopy of the contra-lateral elbow which confirmed that, despite the fact that the anconeal process was more proximally displaced into the supratrochlear foramen and the partial thickness focal cartilaginous lesion had healed, the intracondylar fissure was wider than what it initially was. Whilst the fissure was not so visible on last follow-up CT images, the humeral condyle appeared to be still severely sclerotic (mean HU of the humeral condyle before surgery: 1085, at the first follow-up: 782, at the last follow-up: 941). It is not clear if the widening of the fissure and the increased

sclerosis are due to the anconeal process not displacing proximo-cranially enough or to impaired vascularization of the humeral condyle.

Traditional surgical management of HIF involves the placement of a large transcondylar screw in a lag or positional fashion (Butterworth et al, 2001; Moores et al, 2014; Hattersley et al, 2011; Chase et al, 2019; McCarthy et al, 2020; Jenkins et al, 2022; Carwardine et al, 2021; Carwardine et al, 2023). The overall complication rate following a transcondylar screw placement is notably high and varies from 15% to 69.2%. Seroma appears to be the most common minor complication and ranges from 7.1% to 44%. Surgical site infection (SSI) is instead the most reported major complication following the use of a transcondylar screw and it has an incidence of up to 42.3%. This incidence of SSI vastly exceeds the average reported SSI rate for clean, elective orthopaedic surgeries and it has been linked in several studies with a poor long-term outcome. Other commonly reported major complications include implant failure (with an incidence of broken screws ranging from 2.5% to 9%), implant loosening (1.2%-9%) and medial epicondylar fissure fracture (16.5%) (Butterworth et al, 2001; Moores et al, 2006; Hattersley et al, 2011, Chase et al, 2019; McCarthy et al, 2020; Jenkins et al, 2022; Carwardine et al, 2021; Carwardine et al, 2023; Potamopoulou et al, 2023). By avoiding placing a transcondylar screw, all the aforementioned complications were avoided in our study. The minor complication related to migration of the IM pin that we experienced was attributed to the creation of a larger hole and the use of a smaller diameter IM pin, intended to facilitate breaking of the pin below the dorsal cortex of the anconeus to avoid impingement of the insertion of the triceps brachii tendon. Once we realized that creating a larger hole at the level of the cortex contributed to pin migration, we returned to using the same size pin and we broke it at the level of the cortex of the anconeus. We acknowledge that some surgeons may be reluctant to consider using an IM pin in the ulna due to the potential risks of infection and difficulty of retrieval of the metalwork. However, in our study, no infections were experienced,

and the IM pins were easily retrieved in those dogs where they migrated or when ulnar osteotomy revision surgery was needed. Performing a proximal ulnar osteotomy is certainly not a procedure free of complications and these can include excessive proximal segment caudal migration, delayed osteotomy union, infection, seroma formation, haemorrhage and radial head subluxation (Caron et al, 2016; Danielski et al, 2023; Gilson, 1989; Williams et al, 2019). In our study, two major complications were experienced at level of the osteotomy site: one hypertrophic non-union of the osteotomy (which required debridement, grafting with autologous cancellous bone and stabilization with a locking plate) and excessive caudal displacement of the proximal ulnar segment (which required debridement, retrieval of the broken pin, reduction of the ulnar segments back into position and replacement of the IM pin with a larger one). Despite these two complications, a large callus osseous formation was documented in all dogs at the 6-week follow-up appointment most likely as a result of the use of rhBMP-2. Our overall complication rate related to oblique PUO was 9.8%, consisting of 2 major and 3 minor complications. This rate was significantly lower than the complication rates reported in the literature, which range from 13% to 54% (Caron et al, 2016; Danielski et al, 2023; Gilson et al, 1989; Williams et al, 2019). While this complication range is similar to the reported complication rate associated to the use of a transcondylar screw as a treatment for HIF (15-69%), we believe that the complications associated with PUO are generally more benign and easily addressed. Moreover, these complications do not seem to impact the long-term outcome to the same extent as the complications associated with the use of a transcondylar screw. Lastly, while it is generally accepted that dogs undergoing PUO experience more pain in the post-operative period than dogs undergoing screw placement, our study found that the majority of our dogs was pain-free at the 6-week follow-up appointment. We suspect that this is due to the high degree of bone healing achieved at the osteotomy site (by the combined use of rh-BMP-2 and of the IM pin) and to the amelioration of humero-anconeal incongruity.

In a study where 34 dogs with HIF were managed conservatively, 18% of these subsequently experienced a fracture at a mean of 14 months and 2 dogs needed placement of a screw at a later stage to treat persistent lameness, increasing to 23.5% the rate of dogs needing surgery (Moores et al, 2017). The same study reported that the mean follow-up for dogs not requiring surgery was 56 months, concluding that a low number of non-symptomatic HIFs will fracture and that if this happens, it is most likely to happen within 2 years from when the diagnosis is performed (Moores et al, 2017). In our study, the rate of dogs needing revision surgery to address a fracture (3.9%) or to stabilize un unstable humeral condyle (3.9%) was significantly lower (7.8%) with a median follow-up for all dogs of 30 months. Four major HIF-related complications were experienced in three dogs. Dog 2, as previously discussed, suffered a Y-fracture of the left elbow and had a transcondylar screw and a medial plate applied to the right elbow to prevent a fracture. Dog 3 sequential CT scans revealed that the fissure was still present 16 months after surgery and that a large amount of new sclerotic bone formation was present at level of the lateral epicondylar crest. The medial compartment of the elbow appeared to be collapsed medially more than what it was at the time of the initial surgery, potentially increasing the force applied to the lateral condyle by the radial head therefore causing excessive instability. The humeral condyle was stabilized with a 3.5mm medio-lateral transcondylar screw and one 2.7mm locking plate applied laterally. Dog 1 (which previously had suboptimal placement of a 4.5mm transcondylar screws) slipped on a wet sea slipway and suffered a lateral condylar fracture of the right humerus 5 months after having PUO and screw removal performed. Six weeks after the first surgery was performed on the right antebrachium, this dog underwent surgery on the left side to remove a sub-optimally placed transcondylar screw and to perform an oblique PUO to treat a partial HIF. The follow-up CT scan of the left elbow performed one year later demonstrated complete infilling of the hole left by the screw and complete healing of the partial HIF initially diagnosed.

In humans, nonsurgical management is generally recommended for sclerotic stress fractures. The resolution of such fractures can take up to 6 months as they tend to heal at a slower pace compared to complete fractures (Ahmad et al, 2004; Greif et al, 2020). Being aware of this, we typically discharge our dogs with instructions of lead-only walk for 3 months but we also recommend that clients keep their dogs on the lead for the majority of walks for up to 6 months, and only return to normal off-lead exercise after that time. We suspect that dog 1 engaged in vigorous exercise too soon and the trauma happened when the stress fracture was still in an early healing phase. The long recovery phase is a potential significant drawback of performing a PUO compared to stabilization with a transcondylar screw, which allows for a faster return to normal activity. However, we believe that the long-term benefits of achieving healing of the fissure and avoidance of post-operative complications such as screw breakage/loosening and infection, vastly outweigh this negative factor. Some exceptions are to be made. Since this study was concluded, the authors routinely perform a PUO and place a transcondylar screw in dogs older than 8 years (due to the documented poor healing of the fissure in older dogs), in adult dogs that present severe sclerosis of the humeral condyle (due to the high risk of sudden fracture) and in the adult dogs of clients that are not willing to strictly follow the post-operative instructions.

This study has also demonstrated that performing a PUO can be considered as a revision strategy for dogs experiencing major complications after the placement of a transcondylar screw. In four dogs, chronic infection and signs of implant loosening were observed, leaving amputation the only option considered by the referring veterinarians. In all these dogs, the implants were removed and an oblique PUO was performed. Follow-up CT scans confirmed complete healing of the HIF in all these dogs, even though the bone tunnels left by the previous implants were still visible. Notably, a severely sclerotic border was observed along these bone tunnels, which is suspected to have impeded neovascularization of this area, subsequently

hindering the process of bone formation. The authors now commonly perform a debridement of the sclerotic borders of the bone tunnels by over-drilling the hole with a larger drill bit followed by packing of autologous cancellous bone graft into the tunnel.

A number of limitations need to be acknowledged in this study. The most important limitation is the absence of second-look arthroscopy to confirm the resolution of humero-ulnar incongruity (and healing of the cartilaginous lesion). With the data currently available, the study can only conclude that the condition was ameliorated. However, from an ethical point of view, it was not justifiable to perform such a procedure in dogs that were clinically well and sound on the operated limbs. Other limitations include the lack of a control group, a relatively small sample size, lack of objective measurement of clinical outcomes and errors related to the measurement of ROIs on CT images.

CONCLUSION

The advantages of the new findings of our research lie in their potential to enhance our understanding of HIF, improve treatment outcomes, reduce intra- and post-operative complications, and offer veterinarians a more tailored and effective approach to managing this challenging orthopaedic condition in dogs. These findings contribute to advancing the field of veterinary orthopaedics and ultimately benefit the well-being of canine patients.

Etiopathogenesis: Our first study explored the aetiology of HIF, shedding light on its underlying mechanisms. We identified a previously unreported cartilage lesion on the caudal aspect of the medial humeral condyle, a critical finding that challenges the prevailing notion of incomplete ossification as the primary cause. Instead, our research suggests that this cartilage lesion may be indicative of an adaptive response to persistent abnormal mechanical forces rather than failed endochondral ossification. This novel perspective introduces the concept of "humero-anconeal incongruity" as a more appropriate terminology to describe these findings. The presence of the HA lesion at the medial aspect of the HIF line, along with arthroscopic evidence of mechanical impingement, further supports this theory. Importantly, our statistical analysis establishes a direct association between the HA lesion and HIF, irrespective of breed, emphasizing its clinical relevance.

Surgical Management: The second part of our research focused on the surgical management of HIF, with a particular emphasis on oblique PUO as an alternative surgical treatment. Our findings showcase the effectiveness of PUO as a promising surgical intervention. Notably, PUO resulted in healing of the humeral intracondylar fissure and concomitant reduction of sclerosis in the majority of cases. Age-related differences were also evident, with younger dogs exhibiting a wider fissure and less sclerosis than their older counterparts. PUO has proven extremely valuable as a revision strategy technique in cases of HIF experiencing post-operative

complications such as chronic infection and implant loosening. Its effectiveness in resolving complications (and therefore avoiding the need for amputations) and promoting bone healing underscores its significance in clinical practice. PUO therefore offers a valuable alternative for veterinarians faced with challenging cases of HIF, ultimately improving patient outcomes and enhancing the arsenal of treatment options available in veterinary orthopaedics.

List of abbreviations

HIF: Humeral intracondylar fissure

IOHC: Incomplete Ossification of the Humeral Condyle

CT: Computed Tomography

MRI: Magnetic Resonance Imaging

STIR: Short Tau Inversion Recovery

HA: Humero Anconeal

IV: intravenous

mg: milligrams

kg: kilograms

mm: millimeters

PUO: Proximal Ulnar Osteotomy

RCVS: Royal College of Veterinary Surgeons

HU: Hounsfield Units

ROI: Region Of Interest

nsaids: non-steroidal anti-inflammatory drugs

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