

Feasibility of computed tomography for differentiating calcium oxalate and struvite calculi using mean Hounsfield unit and Hounsfield density

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Abstract

Accurate preoperative prediction of cystic calculi composition is essential for effective treatment planning in dogs. This prospective study aims to investigate the utility of non-contrast multi-detector computed tomography (MDCT) in differentiating calcium oxalate (CaOx) and struvite calculi based on mean Hounsfield unit (HU) and HU density values. Nineteen client-owned dogs with confirmed cystic calculi underwent non-contrast MDCT imaging at 80 and 120 kilovoltage peak (kVp) settings prior to surgical removal. Calculi composition was determined via laboratory analysis. Mean HU and HU density were measured and compared between calculi types. The results showed CaOx calculi demonstrated significantly higher mean HU (1317.53 ± 84.38) and HU density (191.89 ± 18.11) compared to struvite calculi (959.38 ± 202.92 and 101.27 ± 22.17 , respectively) at 120 kVp. The optimal cut-off value for HU density at 120 kVp is greater than 137.295 HU/mm, indicating CaOx (84.6% of sensitivity and 83.3% of specificity). No significant differences were observed between groups at 80 kVp. These findings suggest that both mean HU and HU density at 120 kVp may be used as parameters for distinguishing between CaOx and struvite calculi. In conclusion, this study supports the clinical application of non-contrast MDCT, particularly using mean HU and HU density at higher kVp settings, as a non-invasive modality for predicting calculi composition in dogs.

Keywords: canine, calcium oxalate, computed tomography, Hounsfield unit, struvite

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Introduction

Urolithiasis, the formation of calculi in the urinary tract, is a common disease in veterinary medicine, particularly in dogs and cats (Picavet *et al.*, 2007; Das *et al.*, 2017; Burggraaf *et al.*, 2021). Calculi formation is influenced by various factors, including urinary supersaturation with minerals, metabolic disorders, and infections that alter urine pH (Das *et al.*, 2017; O'Kell *et al.*, 2017). Clinical signs range from incidental findings or mild to severe presentations such as pain, dysuria, and other indicators of urinary obstruction (Gerber *et al.*, 2005; Syme, 2012). Furthermore, calculi can result in significant morbidity and, if untreated, may lead to mortality due to complications such as urethral obstruction, renal failure, or systemic infections (Lulich *et al.*, 2011; Defarges *et al.*, 2020).

Accurate and early diagnosis, along with determining the composition of calculi, are essential for selecting the most effective treatment and management strategies for this disease. (Lulich *et al.*, 2016). Conventional diagnostic imaging techniques, including radiography and ultrasonography (US), play crucial roles in diagnosing this disease. However, these modalities also have several limitations (Langston *et al.*, 2008). Radiographs may be insufficient in detecting certain radiolucent calculi, such as urate and cystine (Ray *et al.*, 2010). While US is a highly sensitive technique for detection, it offers limited information regarding the characteristics of calculi (Lulich *et al.*, 2011).

Computed tomography (CT), particularly multi-detector computed tomography (MDCT), has proven to be a highly effective tool for diagnosing and characterizing calculi (Niemann *et al.*, 2008; Atici *et al.*, 2012; Gücük and Uyetürk, 2014; Andrabi *et al.*, 2015). In addition to detecting calculi, CT can differentiate calculi types by their attenuation values measured in Hounsfield Units (HU), with calcium oxalate (CaOx) calculi demonstrating higher attenuation compared to struvite or urate calculi (Grosjean *et al.*, 2008; Atici *et al.*, 2012; Gücük and Uyetürk, 2014). This capability is essential for determining the appropriate therapeutic strategy, whether medical management or surgical intervention is required (Lulich *et al.*, 2016). In human medicine, CT is regarded as the gold standard for calculi detection and characterization, facilitating individualized treatment plans. (Niemann *et al.*, 2008; Andrabi *et al.*, 2015; Al-Shawi *et al.*, 2022). This modality is increasingly utilized in veterinary medicine, offering a higher detection rate, precise localization, improved detection of small calculi, and reduced reliance on operator skill, thereby enhancing preoperative planning and treatment outcomes (Testault *et al.*, 2021; Bruwier *et al.*, 2022). Although CT attenuation values can aid in predicting calculus composition, overlapping values among different calculus types can make accurate differentiation challenging (Pressler *et al.*, 2004; Bruwier *et al.*, 2022). HU density provides advantages over mean HU alone as it normalizes for calculi size, improving accuracy and highlighting density distribution. (Pressler *et al.*, 2004; Shahnani *et al.*, 2014). Information on using HU density to predict calculus composition remains limited. Therefore, this study aims to evaluate the

feasibility of using MDCT to assess calculi in the urinary tracts of dogs by correlating mean HU and HU, based on density from CT imaging with laboratory compositional analysis. The hypothesis is that the mean HU and HU density differ among urinary calculi, and can be utilized to predict the composition of calculi.

Materials and Methods

Study design and ethical approval: This prospective study involved dogs diagnosed with calculi requiring surgical intervention for calculi removal. Approval was obtained from the Institutional Animal Care and Use Committee, and the study was conducted from March 2018 to March 2019. Informed consent was obtained from all dog owners prior to enrollment.

Study population: A total of 30 dogs with cystic calculi were included in this study. Each dog underwent a physical examination, including body weight measurement, body condition scoring, heart rate, respiratory rate, mucous membrane assessment, and evaluation of hydration status. Blood samples were collected for complete blood count and serum biochemistry analysis to determine their suitability for surgery.

Inclusion Criteria: Dogs were included in the study if they had a confirmed diagnosis of cystic calculi based on radiographic and/or US findings and underwent non-contrast MDCT imaging. The diagnosis was further validated through post-operative calculi analysis to determine calculi composition.

Exclusion Criteria: Dogs were excluded from the study if they met any of the following criteria: i) incomplete diagnostic imaging, ii) absence of post-operative calculi composition analysis, and iii) presence of underlying conditions that could interfere with the surgical procedure or post-operative recovery, such as severe systemic disease or coagulopathies.

Computed tomographic protocol: On the day of surgery, each dog was premedicated and induced with appropriate anesthetic agents based on individual patient needs. An endotracheal tube was inserted, and anesthesia was maintained using isoflurane (1.5–2.0%) in oxygen. Dogs were positioned in sternal recumbency. Non-contrast MDCT scans were performed under general anesthesia prior to surgery for calculus removal. Dogs were positioned in sternal recumbency, and images of the abdomen were acquired using a single-energy 64-slice CT scanner (Optima CT660, GE Healthcare, Tokyo, Japan). The scans were conducted with helical acquisition, using a slice thickness of 1.25 mm, a pitch of 0.8, and a reconstruction interval of 0.625 mm. Imaging was performed using a fixed tube current of 200 milliamperere (mA) at both 80 kilovoltage peak (kVp) and 120 kVp settings, following a previous study (Pressler *et al.*, 2004), with the field of view covering the entire lower urinary tract.

Measurement mean HU values and HU densities: All CT images were retrieved from the Picture Archiving and Communication System (PACS) in Digital Imaging and Communications in Medicine (DICOM) format and re-analysed using DICOM viewer software (OsiriX, Geneva, Switzerland) to measure the HU of calculi. Multiplanar reconstruction (MPR) images in the transverse, sagittal, and dorsal planes were obtained and reviewed by a radiologist with 20 years of experience (N.C.). The image window was adjusted with a window width of 1,500 HU and a window level of 450 HU. All measurements were conducted by the same radiologist on transverse images at the level of the maximal diameter of each calculus (Figs 1A and C). A manual region of interest (ROI) was delineated for each calculus, ensuring that the ROI encompassed the largest area of the calculus while excluding adjacent anatomical structures (Figs 1B and 1D). Three measurements were performed for each calculus at both 80 and 120 kVp. The average of the mean HU values was then calculated and recorded. HU density was calculated as the mean HU of the largest calculus divided by its maximal transverse diameter in millimeters (mm) (Motley *et al.*, 2001).

Surgical procedure and calculi analysis: Following the CT scan, all dogs underwent surgical intervention under sterile conditions. Calculi were extracted using

standard cystotomy or urethrotomy techniques, depending on the size and location of the calculi. Post-operatively, the calculi were submitted to a specialized laboratory for compositional analysis using standardized analytical methods. All analysis records were reviewed at the Minnesota Urolith Center, University of Minnesota, USA. Only calculi classified as pure CaOx or pure struvite were included in the study; all other compositions, including mixed calculi, were excluded.

Data were presented as mean $\pm$ standard deviation (SD) for normally distributed variables and as median with range for non-normally distributed variables. The Shapiro-Wilk test was used to assess data distribution. Quantitative variables with normal distribution, including HU values and HU densities, were presented as the mean $\pm$ SD and were compared between groups using the Student's t-test. Non-normally distributed quantitative variables, such as calculus size, were presented as the median and range and compared between groups using the Mann-Whitney U test. Receiver operating characteristics (ROC) curve and area under the curve (AUC) were used to determine the optimal cut-off values for mean HU and HU density at both 80 and 120 kVp for the two groups. Statistical significance was set at $P < 0.05$.

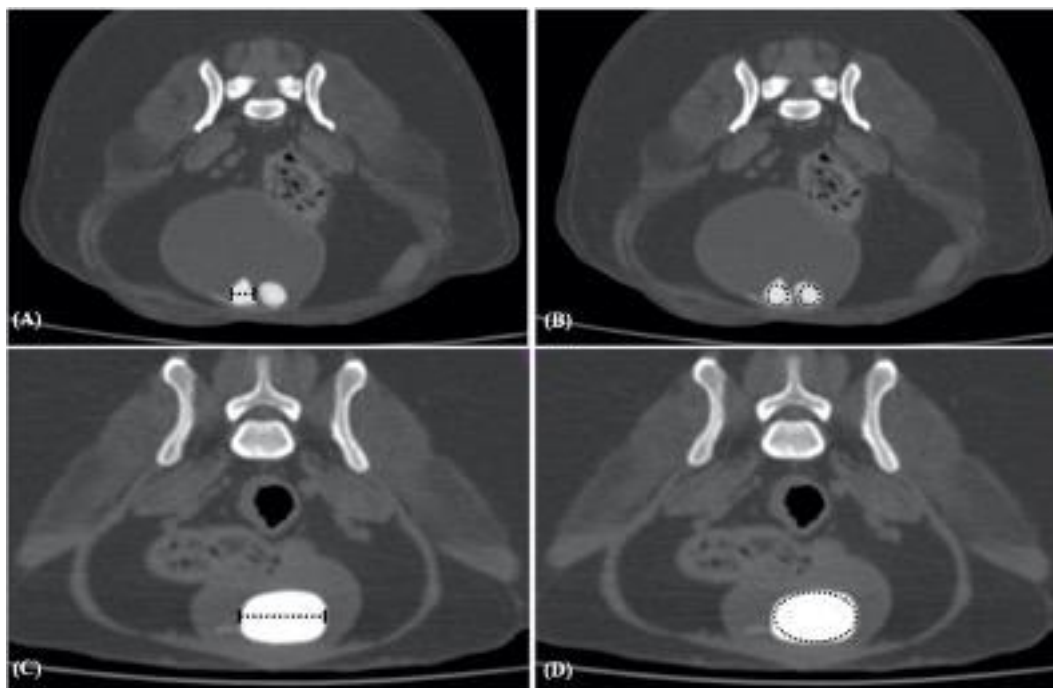


Figure 1 Computed tomographic images of calculi analyzed as struvite (A-B) and calcium oxalate (C-D). The maximal diameter of calculus was measured on transverse images (dotted lines; A, C). Manual region of interest was delineated for each calculus, excluding adjacent anatomical structures (dotted circles; B, D). Hounsfield unit density was calculated as the mean HU of the largest calculus divided by its maximal transverse diameter in millimeters.

Result

Clinical demographic data: Nineteen dogs met the inclusion criteria, including 13 (68.4%) with CaOx calculi and 6 (31.57%) with struvite calculi. The CaOx group comprised 4 Pomeranians, 3 Pugs, 2 mixed-breed dogs, and one each of Chihuahua, Miniature Schnauzer, Yorkshire Terrier, and Shih Tzu. The

struvite group included 2 Pomeranians and one each of Chihuahua, French Bulldog, Miniature Pinscher, Shih Tzu, and All clinical demographic data are presented in Table 1.

Characteristic of calculi: Both CaOx and struvite calculi were observed as single or multiple calculi, with a similar tendency toward multiple calculi in each

group. The median number of calculi in the CaOx group was slightly higher than in the struvite group. In terms of surface characteristics, no significant differences were observed between the two groups, with calculi exhibiting either smooth or irregular contours. Similarly, both CaOx and struvite calculi displayed round, oval, or irregular shapes, with no significant differences between the groups. The median maximum diameter of struvite calculi is significantly larger than that of CaOx, at 9.35 (4.40 – 21.30) and 7.100 (4.10 – 9.40) mm, respectively ($P = 0.024$). Data on the number, characteristics, and mean maximum diameter of CaOx and struvite calculi are presented in Table 2.

Mean HU and HU density values: At 120 kVp, CaOx calculi exhibited a significantly higher mean HU value compared to struvite calculi ($P = 0.034$). Similarly, the HU density of CaOx calculi was also significantly

greater than that of struvite calculi at this energy level ($P = 0.004$). In contrast, no statistically significant differences were observed between CaOx and struvite calculi in either mean HU value ($P = 0.137$) or HU density value ($P = 0.084$) at 80 kVp. The small sample size in the struvite group, however, may have limited the statistical power to detect differences at the 80 kVp setting. The mean HU and HU density values for both types of calculi are summarized in Table 3.

Determining optimal cutoff values of mean HU and HU density for differentiating CaOx and struvite calculi: The ROC curve and AUC analysis at 120 kVp demonstrated the significance of HU density for differentiating CaOx from struvite. The optimal cut-off value was greater than 137.295 HU/mm, with an AUC of 0.885, a sensitivity of 84.6%, and a specificity of 83.3% (Fig. 2).

Table 1 Clinical demographic data of dogs between calcium oxalate (CaOx) and struvite groups.

	CaOx	Struvite
Number	13	6
Sex		
Male	11	4
Intact	6	3
Neuter	5	1
Female	2	2
Intact	1	1
Neuter	1	1
Age (years)	8.57 ± 3.54 (3–15)	8.83 ± 4.53 (3–16)
BW (kg)	6.88 ± 3.37 (3.30–12.80)	2.90 ± 2.88 (2.90–11.20)

Table 2 Number, characteristics, and mean maximum diameter of cystic calculi in dogs with calcium oxalate (CaOx) and struvite group.

	CaOx	Struvite
Number	7 (1–20)	6 (2–14)
Characteristics		
Contour		
Smooth	6/13	3/6
Irregular	7/13	3/6
Shape		
Round	3/13	2/6
Oval	1/13	0/6
Irregular	9/13	4/6
Maximum diameter (mm)		
Median (range)	7.100 (4.10 – 9.40)	9.35 (4.40 – 21.30)

* Significant difference between CaOx and struvite at $P = 0.024$

Table 3 Mean Hounsfield unit (HU) and HU density values between calcium oxalate (CaOx) and struvite.

	80 kVp, 200 mAs		P-value
	CaOx	Struvite	
Mean HU	1,699.98 ± 110.81	1,289.92 ± 311.13	0.069
HU density/mm	247.28 ± 25.57	175.55 ± 55.71	0.084
	120 kVp, 200 mAs		P-value
	CaOx	Struvite	
Mean HU	1317.53 ± 84.38	959.38 ± 202.92	0.034
HU density/mm	191.89 ± 18.11	101.27 ± 22.17	0.004

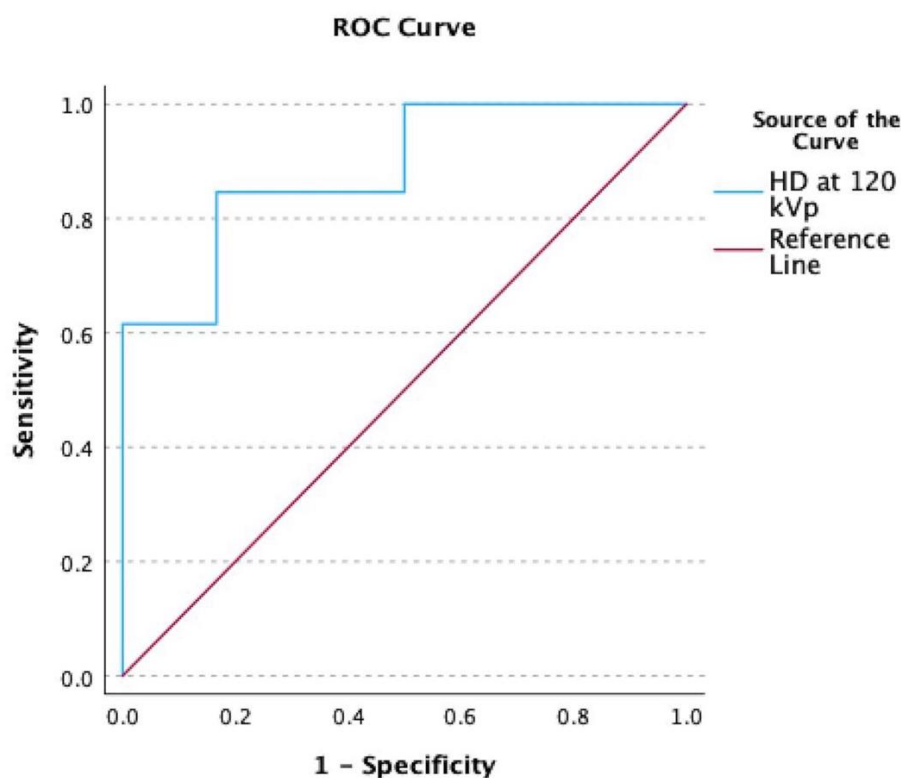


Figure 2 Receiver Operating Characteristic (ROC) Curve for Hounsfield units (HU) density at 120 kVp distinguishing calcium oxalate from struvite. The optimal cutoff value of HU density was greater than 137.295 HU/mm, with an AUC of 0.885, a sensitivity of 84.6 %, and a specificity of 83.3 %

Discussion

In this study, the mean HU and HU density values were significantly different between CaOx and struvite calculi at 120 kVp. In contrast, no significant differences in these values were observed between the two groups at 80 kVp. Although struvite calculi were significantly larger than CaOx calculi, other characteristics did not differ significantly. These findings suggest that mean HU and HU density at 120 kVp may serve as useful parameters for differentiating between CaOx and struvite calculi.

Calculi are composed of various minerals, with each type characterized by distinct mineral compositions, resulting in differences in their densities. (Ibrahim *et al.*, 2014; Dvorska and Saganuwan, 2015; Gomes *et al.*, 2022). Although radiography is commonly used to detect cystic calculi due to the presence of radiopaque materials, not all cystic calculi are radiopaque, such as those composed of urate or cystine (Nell *et al.*, 2021; Elkewahy *et al.*, 2023; Marolf, 2024). The absence of radiopaque structures within the urinary bladder does not rule out this disease (Marolf, 2024; Yaygingül, 2024). Furthermore, radiography cannot differentiate between different types of calculi (Yaygingül, 2024). In the US, both radiopaque and non-radiopaque calculi are typically visualized as hyperechoic, curvilinear structures with distal acoustic shadowing. This advantage addresses the limitation of radiography in detecting non-radiopaque calculi (Langston *et al.*, 2008; Elkewahy *et al.*, 2023). The US has high sensitivity and specificity to detect calculi, not only radiopaque calculi, but also radiolucent or small-sized calculi (Bruwier *et al.*, 2022). Unlike radiography, US has high sensitivity and specificity for detecting

both radiopaque and radiolucent calculi, including small-sized calculi (Bruwier *et al.*, 2022). However, the US exhibited notable artifacts, including streaks and false echoes, which contributed to its tendency to overestimate the calculi size by a few millimeters compared to other imaging methods (Byl *et al.*, 2010). Moreover, very small calculi, less than 2 mm, may not generate a detectable acoustic shadow, making them difficult to differentiate from normal bladder debris or sediment (Lisciandro, 2013).

Currently, CT plays a crucial role in diagnosing various diseases in veterinary medicine. This imaging modality provides superior detection of cystic calculi compared to radiography and US (Testault *et al.*, 2021; Bruwier *et al.*, 2022). Moreover, CT provides detailed anatomical information, aiding in the identification of calculi as well as associated pathologies that may not be visible with other imaging techniques (Testault *et al.*, 2021; Bruwier *et al.*, 2022). HU measurements on CT images provide valuable insight into differentiating calculi types, including CaOx, struvite, and uric acid calculi (Pressler *et al.*, 2004; Yoon and Lee, 2015; Bruwier *et al.*, 2022). Mean HU can be used to predict calculi composition, where a mean HU greater than 1,000 HU tends to indicate calcium oxalate calculi (Bruwier *et al.*, 2022). In vitro studies have established HU reference ranges for pure calculi, demonstrating an accuracy of 86% to 93% in distinguishing between mineral compositions such as struvite and calcium oxalate (Pressler *et al.*, 2004). Mean HU values in non-contrast CT images have been utilized in human medicine to predict the chemical composition of urinary calculi. These values provide a non-invasive method for assessing calculi composition, which is crucial for selecting appropriate treatment strategies

(Deveci *et al.*, 2004; Chua *et al.*, 2012; Ibrahim *et al.*, 2014). Studies have shown that CaOx calculi exhibit the highest mean attenuation values, while urate calculi have the lowest (Chua *et al.*, 2012; Ibrahim *et al.*, 2014). Similar to findings in veterinary medicine, CaOx calculi demonstrated the highest mean attenuation values (Chua *et al.*, 2012; Bruwier *et al.*, 2022). A cutoff value greater than 1,000 HU can be used as a predictor for this type of calculus. (Bellin *et al.*, 2004; Bruwier *et al.*, 2022). In contrast, uric acid calculi exhibit the lowest CT attenuation values (Bellin *et al.*, 2004). Similar to our study, the results demonstrated that CaOx calculi exhibited a mean HU greater than 1,000 HU at both 80 and 120 kVp. However, a significant difference in mean HU between CaOx and struvite calculi was observed only at 120 kVp. This finding may be attributed to variability in stone composition, CT acquisition parameters, and the partial volume effect (Saw *et al.*, 2000; Motley *et al.*, 2001).

Although mean HU values alone are insufficient to reliably distinguish between different calculus compositions due to overlapping ranges, this may be attributable to the influence of calculus size, where a larger calculus is associated with a higher mean HU (Motley *et al.*, 2001). Previous studies have shown that HU density serves as a more reliable predictor of stone composition (Motley *et al.*, 2001; Gücük and Uyetürk, 2014; Shahnani *et al.*, 2014). This method normalizes HU by accounting for the largest transverse diameter of the calculi, thereby reducing bias related to calculi size (Motley *et al.*, 2001). Previous studies have reported that CaOx calculi exhibit HU densities greater than 50 HU/mm (Nakada *et al.*, 2000; Motley *et al.*, 2001; Shahnani *et al.*, 2014). In contrast, our findings demonstrated that CaOx calculi had HU densities exceeding 247 HU/mm and 192 HU/mm at 80 and 120 kVp, respectively. This discrepancy may be attributed to variations in CT acquisition parameters, particularly collimation width. A wider collimation maximizes partial volume averaging (PVA), where the high HU of the small, dense object is averaged with the large volume of surrounding low-density tissue, thereby making the measured HU less accurate (Saw *et al.*, 2000; Schwarz and O'Brien, 2011).

Variations in kVp settings have been shown to influence the accuracy of predicting calculi composition based on HU measurements (Pressler *et al.*, 2004; Stolzmann *et al.*, 2010). Although lower kVp settings (80 kVp) are associated with higher mean HU values for calculi—particularly calcium oxalate—and enhance the differentiation between calculi types (Pressler *et al.*, 2004), higher kVp settings (120 kVp) also provided high accuracy in detecting CaOx (Nakada *et al.*, 2000; Pressler *et al.*, 2004; Shahnani *et al.*, 2014). In the current study, two voltage settings—80 kVp and 120 kVp—were utilized to evaluate the effect of kVp on mean HU and HU density values for determining calculi composition. Significant differences in both mean HU and HU density between CaOx and struvite calculi were observed at 120 kVp. Moreover, this study established the optimal cut-off value for HU density at 120 kVp to differentiate CaOx from struvite: a value greater than 137.295 HU/mm, which provided a sensitivity of 84.6% and a specificity of 83.3%. Conversely, no significant differences were detected

between these calculi types at 80 kVp. These results diverge from the previous *in vitro* study, which reported enhanced differentiation of calculi at 80 kVp settings (Pressler *et al.*, 2004). This phenomenon probably results from the inherent differences between *in vitro* and *in vivo* studies, where image-degrading factors—including beam hardening, scatter radiation, and tissue attenuation—significantly alter the measured HU values during the *in vivo* acquisition (Schwarz, 2011). Moreover, a higher kVp may improve the accuracy of calculus diagnosis by increased beam attenuation, reducing image noise caused by beam hardening artifacts (Rozeau and Tidwell, 2003; Pressler *et al.*, 2004; Bruwier *et al.*, 2022).

Several limitations should be acknowledged in this study. First, the sample size was relatively small, particularly in the struvite group, which may have limited the statistical power. Second, the study included only two types of calculi—CaOx and struvite—excluding other common types such as urate, cystine, and mixed-composition calculi. This limits the broader applicability of CT-based attenuation and density values for differentiation of calculi types. Future studies should incorporate a wider range of calculus compositions to enhance diagnostic accuracy. Third, the study employed single-energy, non-contrast MDCT, which may not provide optimal contrast resolution. Future studies should include contrast-enhanced techniques or dual-energy CT techniques.

In conclusion, this study demonstrated that mean HU and HU density values obtained from non-contrast MDCT provide a promising non-invasive method for differentiating CaOx from struvite calculi in dogs. Although HU and HU density values at 80 kVp showed variability and overlap between the two calculi types, both parameters at 120 kVp revealed statistically significant differences. The optimal cut-off value for HU density at 120 kVp was determined to be greater than 137.295 HU/mm, indicating CaOx, which provided a sensitivity of 84.6% and a specificity of 83.3%. These findings highlight the potential of mean HU and HU density, particularly at higher voltage settings, as reliable indicators for distinguishing CaOx from struvite calculi. These results support that non-contrast MDCT is feasible for the preoperative assessment of canine cystic calculi, guiding the decision between surgical removal for non-dissolution calculi and medical dissolution for dissolution calculi.

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