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Citation for published version:
Schwarz, T, Bommer, N, Parys, M, Thierry, F, Bouvard, J, Perez Accino Salgado, J, Saunders, J & Longo, M 2021, 'Four dimensional CT excretory Urography as an Accurate Technique for Diagnosis of Canine Ureteral Ectopia', *Veterinary Radiology & Ultrasound*, vol. 62, pp. 190-198. https://doi.org/10.1111/vru.12934

Digital Object Identifier (DOI):
10.1111/vru.12934

Link:
Link to publication record in Edinburgh Research Explorer

Document Version:
Publisher's PDF, also known as Version of record

Published In:
Veterinary Radiology & Ultrasound

Received: 12 May 2020 | Revised: 24 August 2020 | Accepted: 1 October 2020

DOI: 10.1111/vru.12934

ORIGINAL INVESTIGATION

WILEY

Four-dimensional CT excretory urography is an accurate technique for diagnosis of canine ureteral ectopia

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Abstract

Computed tomographic (CT) excretory urography is commonly used to investigate canine ureteral ectopia (UE). Modern technology allows time-resolved CT imaging (four-dimensional CT excretory urography [4D-CTEU]) over a distance exceeding the detector collimation. Objectives of this prospective, observational, diagnostic accuracy study were to evaluate the diagnostic accuracy of CT excretory urography (CTEU) and 4D-CTEU for UE in dogs with lower urinary tract signs, assess the influence of pelvis positioning, and to determine the significance of the ureterovesical junction (UVJ) angle for UE diagnosis. Thirty-six dogs, with a total of 42 normotopic ureters, 27 intramural ectopic ureters, and three extramural ectopic ureters, underwent CTEU and 4D-CTEU with randomized pelvis positioning. Randomized CTEU and 4D-CTEU studies were scored by two observers for ureteral papilla location and murality on a grading scheme. Interobserver agreement, sensitivity, and specificity for ureter topia status and diagnosis were calculated. Computed tomographic excretory urography showed moderate interobserver agreement for the left ureter and perfect for the right ureter, whereas 4D-CTEU showed bilateral nearly perfect agreement between both observers. When comparing CTEU versus confirmed diagnosis, there was a sensitivity and specificity of 73% and 90.2%, respectively, whereas 4D-CTEU showed a sensitivity and specificity of 97% and 94.6%, respectively. An obtuse UVJ angle is significantly more commonly observed in ectopic intramural than normotopic ureters and is significantly associated with increased diagnostic confidence of UE. The use of a wedge to angle the pelvis did not increase the diagnostic confidence in determining ureteral opening position. Four-dimensional CT excretory urography is an accurate and reliable diagnostic technique to investigate UE as cause of urinary incontinence in dogs that is slightly superior to CTEU.

KEYWORDS
ectopic ureter, extramural, intramural, multiphase computed tomography, urinary incontinence

1 | INTRODUCTION

Ureteral ectopia is a common embryological disorder in dogs causing an abnormal location of the opening of the ureter into the lower urinary tract.[1] This anomaly is commonly seen as a cause of urinary

Abbreviations: 4D-CTEU, four-dimensional CT excretory urography; CTEU, CT excretory urography; UE, ureteral ectopia; UVJ, ureterovesical junction

EQUATOR network disclosure: Authors followed the Strobe-VET network guidelines.

Previous presentation disclosure: Part of the results from this paper was presented as an abstract at the ACVR Annual Scientific Meeting, Baltimore, MD, USA, October 30 to November 2, 2019.

incontinence in young dogs, more common in females; however, a number of other conditions need to be considered in the diagnostic workup. There are several studies focusing on the epidemiological distribution of the disease, technical comparison between different diagnostic modalities and therapeutic options.[1–10] Computed tomographic excretory urography in dogs was established two decades ago[11] and promoted more than a decade ago as the modality of choice for canine UE workup.[9] However, only recent investigations focused on the technical improvement of this modality in order to increase readers' confidence and diagnostic accuracy.[12–14] Most of these recent advances describe the use of postprocessing techniques such as the application of maximum intensity projection to highlight the pathways of the ureters or else they focus on the description of common features of ureteral ectopia (UE) seen in CT.[14–16] No substantial changes in the acquisition process of the CT images have been proposed other than using bolus tracking techniques or furosemide administration to increase ureteral visibility.[13,14] Four-dimensional CT is a new image acquisition technique available in the latest generation of multi-slice CT scanners, in which a patient area is scanned with a continuous series of helical scans in back and forward directions. Image data can then be reconstructed spatially and temporally for any location of the covered area and time point during the duration of the multiple helical scans.[17] This technique was developed for cardiac assessment but has potential in the study of the ureteral papilla for the peristaltic urine excretion, as already investigated in human medicine.[17]

Urine that contains iodinated contrast medium has a higher specific gravity than normal urine and will settle in the dependent portion of the urinary bladder.[18] If a dog is positioned in ventral recumbency, a urine jet can be observed from the ureteral papilla in the nondependent dorsal portion of the urinary bladder wall toward the dependent ventral pool of contrast-medium containing urine, allowing identification of the ureteral papilla in ureters entering the urinary bladder.[19] However, if the volume of contrast medium containing urine in the urinary bladder is large, the entire bladder neck area is flooded with contrast medium containing urine and the urine jet can no longer be observed. There is a potential that by positioning the dog in ventral recumbency with the pelvis elevated caudally, thereby moving the contrast medium containing urine away from the urinary bladder neck, the urine jet can be seen more consistently.[19] At the ureterovesical junction (UVJ), the ureter enters the urinary bladder at an angle and courses for a short distance intramurally toward the ureteral papilla. A recent small cohort study indicated that the UVJ angle in normotopic ureters is acute, whereas intramural ectopic ureters have an obtuse, or *reflex*, angle.[16] It would be useful to test in a larger cohort of dogs the UVJ angle and ureteral topia (normal or abnormal ureter opening location) relationship and investigate whether obtuse UVJ angles are associated with increased diagnostic confidence of UE.

More than 95% of ectopic ureters have an intramural course, which is challenging to confirm with conventional CT excretory urography (CTEU).[3–5] Knowledge of the murality (ureter location within or outside of the confines of the wall of the urinary bladder or urethra) of the ectopic ureter is critical if modern laser ablation techniques are used for treatment.[4,6,9] This is one of the reasons why fluoroscopy is still widely considered as an essential diagnostic technique for interventional radiologists lasering intramural ectopic ureters during cystoscopy.[4]

The first aim of this study was to assess interobserver agreement and diagnostic accuracy of traditional CTEU and four-dimensional CT excretory (4D-CTEU) for the determination of ureteral topia and murality of ectopic ureters. The second aim was to test the influence of a neutral versus angled positioning of the pelvis for the diagnostic confidence of determining the ureteral topia status. The third aim was to test for a correlation between UVJ angle and ureteral topia and whether the UVJ angle is associated with diagnostic confidence in ureteral topia status determination. We hypothesized that 4D-CTEU would be an accurate diagnostic test with low interobserver variability for determination of canine ureteral topia and ectopic ureter murality, exceeding results of CTEU, that a caudally elevated pelvis increases ureteral topia diagnostic confidence, and that higher UVJ angles are associated with intramural ectopic ureters and increased confidence of UE diagnosis.

2 | METHODS

This prospective, observational, diagnostic accuracy study was conducted in canine patients presenting to the Hospital for Small Animals, Royal (Dick) School of Veterinary Studies, of the University of Edinburgh for investigation of urinary incontinence between October 2017 and September 2019. The sample size was based on convenience sampling, i.e. the number of patients naturally referred during the study period. The Veterinary Ethics and Welfare Committee of the Royal (Dick) School of Veterinary Studies of the University of Edinburgh granted approval for this prospective study (Veterinary Ethics and Welfare Committee, reference 25.19). Signalment, history, clinical assessment, cystoscopy, laser ablation, surgical exploration, and necropsy data were collected from recruited patients. Criteria for dogs to be included in the study were as follows: (a) clinical signs of urinary incontinence for at least 1 week duration, (b) diagnostic quality combined with CTEU and 4D-CTEU study for ureteral topia status determination, performed within 4 weeks of initial presentation and establishment of confirmed diagnosis, (c) presence of patent ureters allowing ureter opening determination during at least one part of the CT examination, and (d) non-CT-based diagnostic confirmation of the cause of urinary incontinence. Means of confirmation acceptable included cystoscopy, celiotomy surgery, or necropsy. In case of a CTEU and 4D-CTEU diagnosis of bilateral ureteral normotopia, cessation of urinary incontinence after medical treatment or identification of other conditions, unrelated to ureteral topia, explaining urinary incontinence, was also accepted as a means of diagnostic confirmation. Data recording and inclusion criteria were defined by two authors, who are board certified in veterinary diagnostic imaging and internal medicine, respectively (TS, American College of Veterinary Radiology [ACVR] and European College of Veterinary Diagnostic Imaging [ECVDI]; NB, American College of Veterinary Internal Medicine [ACVIM]). At the time of data recording, the authors became aware of clinical history, clinical imaging, and other diagnoses of the case, but not of the scoring results of the study, which was performed later.

The CT examinations were performed with a 64-row multidetector CT scanner (Somatom Definition AS Siemens, Erlangen, Germany) using the following protocol with dogs in ventral recumbency: (a) standard precontrast-enhanced helical scan of the abdomen; (b) postintravenous contrast medium administration helical scan of the abdomen 40 s postcontrast medium injection start (parenchymal phase CT); (c) 4D-CTEU of the UVJs starting 120 s post contrast medium injection start; (d) conventional excretory helical CT urography (CTEU) starting 180 s postcontrast medium injection start. If significant hydroureter (diameter > 5 mm) was detected on the parenchymal phase CT series, a single axial scan was performed just cranial to the visible UVJ. The circular smallest ROI was manually positioned onto the widest ureteral lumen as previously described[13] and a monitoring phase was performed with an automatic peak of 100 HU triggering the 4D-CTEU series. If no ureteral jet was identified at the end of the study, a second 4D-CTEU series of the UVJs was added and the occurrence of this protocol addition was recorded.

Iodinated nonionic contrast medium (Iopamidol, Niopam 350, Bracco UK Ltd) was injected intravenously into the cephalic vein at a dose of 700 mg iodine/kg with a power injector (Empower CTA Injector System Bracco Entronque Picacho-ajusco 130, Jardines en la Montaña, 14210 Tlalpan, CDMX, Mexico), set with a maximum pressure of 325 psi.[20]

The examinations were performed by three operators (ML, FT, and TS) using a standardized protocol. Scan settings for the 4D-CTEU were the following: 100 kV, 150 mA, slice thickness = 1.5 mm, matrix = 512 × 512, scan length = 84 mm, and reconstruction with low pass filter (Siemens proprietary kernel B40f) for 20 s duration. Settings for the further series were modulated by an automatic exposure control system (Care Dose 4D, Siemens Medical Solutions, International), with a minimum scan delay of 2 s. The settings were the following: collimator pitch of 1.4, tube potential of 100-120 kVp, reference tube current of 250-320 mA, slice thickness of 2 mm, matrix of 512 × 512, image reconstruction interval of 1 mm, and reconstruction algorithms with both low (Siemens proprietary iterative kernel I40f) and high (Siemens proprietary conventional kernel B70f) pass filters. The effect of positioning the dog with the pelvis caudally elevated by use of a wedge-shaped CT positional device (extended head holder, 590 mm length × 100 mm height, 10° inclination, model number 04392700, Siemens, Erlangen, Germany) on visibility of a contrast-enhanced urine jet from the ureteral papilla was investigated, as previously reported (Figure 1).[19] The patients were randomly assigned (via flip of a coin) into wedge and nonwedge groups before the CT examination.

All images were reviewed on a computer workstation (Apple Mac Pro, Apple, USA) with a calibrated LCD flat screen monitor, using the 4D-viewer function of a dedicated DICOM viewer software (Horos, Purview, Annapolis MD, USA, version 3.3.6).

All examinations were randomized and pseudonymized in a spreadsheet file and a scoring exercise performed at least 1 month after the clinical examination of the cases and performed separately for the

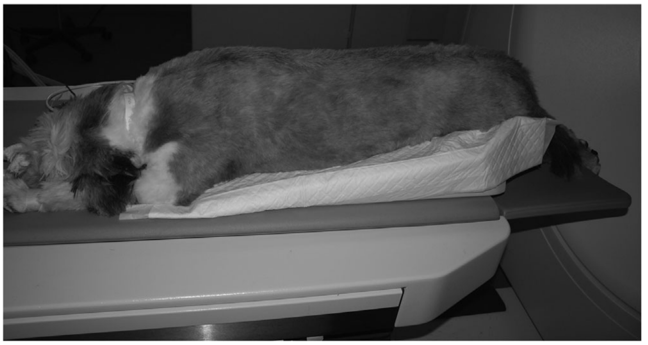

FIGURE 1 Positioning of a dog on a wedge with the pelvis caudally elevated for a CT excretory urography examination

CTEU and 4D-CTEU examinations. To score ureteral topia on both CTEU and 4D-CTEU, a modified grading system was used independently by two different observers with different levels of experience (ML, a third-year resident in veterinary diagnostic imaging, and TS, a board-certified veterinary radiologist): 0, definitely normotopic ureter; 1, probably normotopic ureter; 2, equivocal ureteral topia; 3, probably ectopic ureter; 4, definitively ectopic ureter.[14] Both observers were unaware of the confirmation of diagnosis results at the time of scoring. In a second scoring exercise performed 2 months later, both observers (ML and TS) scored in consensus the CTEU and 4D-CTEU studies with a binary scoring option of ureters being normotopic or ectopic. Moreover, murality of the ectopic ureters was scored by the same observers by consensus (ML and TS) during the second session as follows: 0, definitely extramural bridging (coursing extramurally); 1, probably extramural bridging; 2, equivocally intra/extramural; 3, probably intramural tunneling; 4, definitely intramural tunneling; 5, normal exam; 6, nondiagnostic exam for tunneling/bridging determination. If needed, multiplanar maximum intensity projections were used by the reviewers in a combined session with slab thickness of 2-5 mm as previously reported.[13,14] In all ureters, the UVJ angle was measured on the 4D-CTEU study on multiplanar reconstructed images at a temporal window displaying the ureter contrast bolus, using the angle tool of the DICOM viewer software by a single author who was experienced in the imaging anatomy and the DICOM viewer software (ML). In this context, the UVJ angle was defined as the angle of entrance of the peritoneal ureter into the next lower urinary tract structure it connected to (urinary bladder, urethra, vagina). Using the multiplanar reconstruction, the last peritoneal and the first intramural ureter segment were aligned in one image plane. The UVJ angle was measured with both segments as the sides of the angle and the UVJ as the pivot of the angle. The angle pivot point was placed in a consistent manner onto the ureteral center point at level of the UVJ, and the two sides of the angle were traced along the center lines of the adjacent straight ureter segments (Figure 2). For normotopic, all ectopic, intramural ectopic, and extramural ectopic ureter groups, the UVJ angle range was recorded and the mean and median UVJ angles were calculated. All UVJ angles were also categorized as acute (<90°) or obtuse (90-180°).

A single author, trained and experienced in biostatistics (MP), performed the statistical analysis using two commercially available

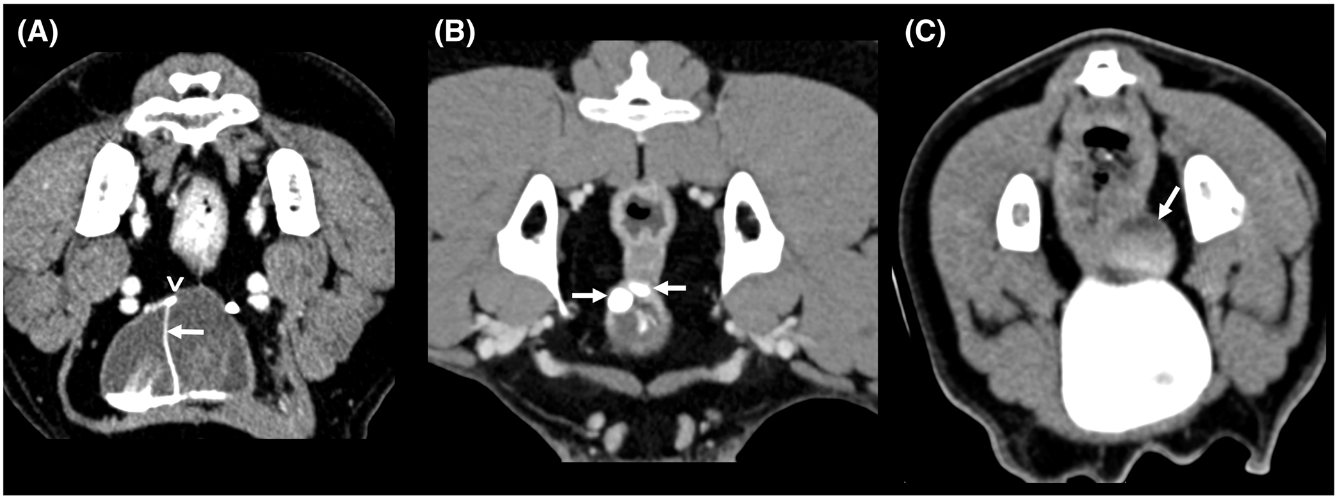

FIGURE 2 Multiplanar reconstruction images ([A] sagittal, [B] dorsal, and [C] transverse plane of the urinary bladder neck) with maximum intensity projection of the scan volume from a CTEU and 4D-CTEU exams of a male dog with a left intramural ectopic ureter, acquired with a 1-mm slice thickness and soft tissue algorithm (window level, 40; window width, 400). Arrows indicate the path of the abnormal left ureter (B and C). Arrowheads indicate the localization of the normal right ureterovesical junction (B) and the washout of contrast medium within the dependent portion of the urinary bladder lumen (C)

software (GraphPad Prism, GraphPad LLC, San Diego, CA, USA and R Studio Version 1.0.143, ren and irr libraries). A *P*-value of less than .05 was considered significant. Data were assessed for normality with the Shapiro-Wilk test. The confirmatory clinical data were used as gold standard for disease status (normotopic/ectopic ureter) and murality of ureteral ectopia (extramural bridging/intramural tunneling). Cohen's Kappa statistics were performed to investigate agreement between observers (ML and TS) in the diagnosis of ureteral topia. Agreement was deemed poor for $\kappa < 0.00$, slight for $\kappa = 0.00$-0.20, fair for $\kappa = 0.21$-0.4, moderate for $\kappa = 0.41$-0.60, substantial for $\kappa = 0.61$-0.8, and almost perfect for $\kappa = 0.81$-1.00.[21] To investigate the relationship between the UVJ angle and confirmed ureteral topia status, the Mann-Whitney test was used to compare the confirmed normotopic and ectopic ureter groups for UVJ angle magnitude differences. To investigate the influence of the UVJ angle on diagnostic confidence in ureteral ectopia, the Mann-Whitney test was performed on the numerical ureter score of the more experienced observer (TS), comparing the definitive ureteral ectopia score (4) group versus normotopia or nondefinitive ureteral ectopia score (0, 1, 2, 3) group, for differences in UVJ angle. Moreover, the Mann-Whitney test was also performed comparing the horizontal and angled pelvis groups for effect of positioning on the ureteral topia score confidence, comparing the confident score (0, 4) group with the nonconfident score (1, 2, 3) group. Sensitivity, specificity, negative and positive predictive values, and likelihood ratios of CTEU and 4D-CTEU for ureteral topia were calculated using the hybrid Wilson/Brown method.[22–24]

3 | RESULTS

Thirty-six dogs met the inclusion criteria. All dogs had one left and one right patent ureter. There were 19 dogs with bilateral normotopic ureters and 17 dogs with at least one ectopic ureter with the following breed distribution (number of dogs with bilateral normotopic/uni- or bilateral ectopic ureters): Mixed breed (6/0), Miniature Dachshund (0/1), Dalmatian (0/1), Irish Terrier (0/1), Golden Retriever (0/6), Labrador Retriever (3/1), French Bulldog (0/5), Old English Sheepdog (1/0), Cocker Spaniel (1/1), Bearded Collie (2/0), Scottish Deerhound (1/0), Cairn Terrier (0/1), Pomeranian (2/0), Shi-Tzu (1/0), Boxer (1/0) and Airedale Terrier (1/0). Thirteen dogs (five French Bulldogs, four Golden Retrievers, one Cairn terrier, one Dalmatian, one Cocker Spaniel, and one Miniature Dachshund) had bilateral ectopic ureters, making it a total of 42 normotopic and 30 ectopic ureters (Figure 3). There were 27 confirmed intramural and three confirmed extramural ectopic ureters (one Dachshund, one Irish Terrier, both left sided; one French Bulldog, right sided). The gender distribution was as follows (number of dogs with bilateral normotopic/uni- or bilateral ectopic ureters): females 25 (10/15), intact females (3/10), neutered females (7/5), males 11 (9/2), intact males (0/2), and castrated males (9/0). The age of all included dogs ranged between 2.53 and 134.2 months (median: 12.12 months, mean: 32.45 months); between 4.5 and 134.3 months (median: 26.61 months, mean: 44.92 months) for dogs with bilateral normotopic ureters; and between 2.53 and 54.9 months (median: 5.75 months, mean: 13.74 months) for dogs with uni- or bilateral UE.

Confirmation of diagnosis was achieved via cystoscopy in 16 dogs, celiotomy surgery in six dogs, necropsy in none, and successful medical treatment of urinary incontinence in nine dogs. In five dogs with a 4D-CTEU diagnosis of bilateral ureteral normotopia, a urinary incontinence-inducing condition unrelated to ureteral topia was made. These conditions included neurological urinary bladder dysfunction in two dogs, congenital rectovaginal fistula in one dog, extrahepatic portosystemic shunt with cystitis in one dog, and urinary bladder urothelial carcinoma in one dog.

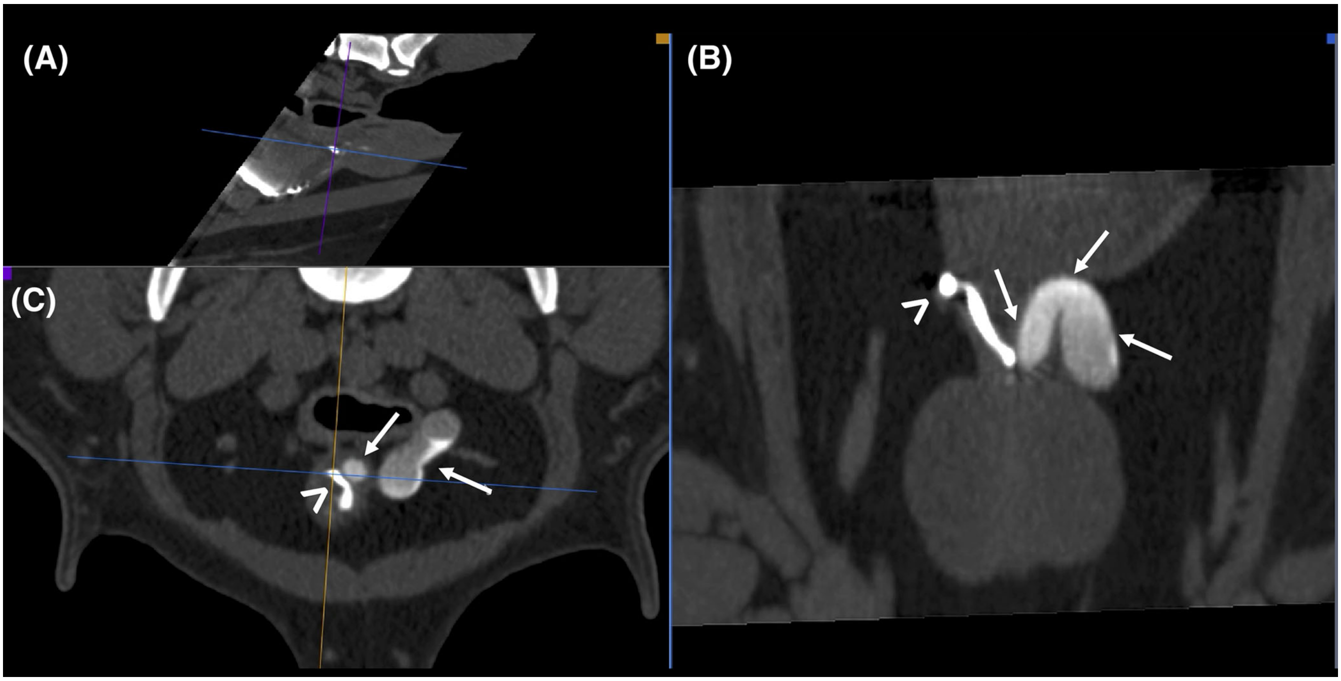

FIGURE 3 Soft tissue algorithm transverse 4D-CTEU images of three dogs showing (A) the ureteral papilla (arrowhead) of a normotopic ureter ejecting a jet of urinary contrast bolus (arrow) into the urinary bladder, (B) bilateral intramural ectopic ureters (arrows) within the wall of the very caudal urinary bladder neck, and (C) an extramural ectopic distended ureter (arrow) located in the peritoneum dorsal to the urinary bladder. (1-mm slice thickness; window level, 40; window width, 400) [Color figure can be viewed at wileyonlinelibrary.com]

Analysis of the agreement of the two observers (ML and TS) in scoring ureteral topia for the CTEU exam resulted in perfect agreement ($\kappa = 1$) for the right ureter ($P < .001$) and moderate agreement ($\kappa = 0.47$) for the left ureter ($P < .001$; confidence interval, 0.29-0.66). For the 4D-CTEU exam, the results were nearly perfect for both sides: $\kappa = 0.86$ for the right ureter ($P < .001$, confidence interval, 0.68-1.01) and $\kappa = 0.86$ for the left ureter ($P < .001$, confidence interval, 0.7-1.01).

Comparing the consensus diagnosis of the CTEU exam with the confirmed diagnosis used as gold standard, CTEU reached a sensitivity of 73% (95% confidence interval, 57-84.6%) and specificity of 90.2% (95% confidence interval, 77-96%) in determining ureteral topia (positive predictive value [PPV] 89% [75-96%] and negative predictive value [NPV] 97.4% [86-99%], likelihood ratio 9.9). Four-dimensional CT excretory urography reached a sensitivity of 97% (95% confidence interval, 85-99%) and specificity of 94.6% (95% confidence interval, 82.3-99%) for ureteral topia determination (PPV 93% [78-98.8%] and NPV 77.8% [63.7-87.5%], likelihood ratio 13.5) .

The UVJ angle could be measured in 38 normotopic, 27 intramural ectopic, and three extramural ectopic ureters (Figure 4). In the 38 normotopic ureters, the mean UVJ angle was 71.66° (median: 56.00°, range: 2° to 151°; 26 classified as acute angle and 12 classified as obtuse angle). In the 27 ectopic ureters, the mean UVJ angle was 140.4° (median: 156.5°, range: 24° to 180°; five classified as acute angle and 22 classified as obtuse angle). In the 27 intramural ectopic ureters, the mean UVJ angle was 137.9° (median: 158°, range: 24° to 180°; five classified as acute angle and 22 classified as obtuse angle). In the three extramural ectopic ureters, the mean UVJ angle was 162.3° (180°, 152°, and 155°, all classified as obtuse angle). Sufficient statistical power for the Mann-Whitney test allowed comparison of UVJ angle differences between normotopic and intramural ectopic ureter groups. Intramural ectopic ureters had a significantly higher UVJ angle than normotopic ureters ($P < .001$; Figure 5). A definitive score of ureteral ectopia made on 4D-CTEU was associated with a significantly higher UVJ angle compared to other scores for the left ureter ($P < .001$, mean normotopic: 70.12°, median: 57°, range: 22.6° to 70.12° vs mean ectopic: 137.4°, median: 150.5°, range: 24° to 180°) and right ureter ($P < .01$, mean normotopic: 74.96°, median: 56°, range: 2° to 151° vs mean ectopic: 124.1°, median: 148.5°, range: 29.9° to 180°; Figure 6).

In 17 dogs, a wedge was used to angle the pelvis, whereas 20 dogs were positioned with a horizontal pelvis position without wedge. There was no significant difference in ureteral topia scoring confidence between animals imaged with an angled pelvis or horizontal pelvis in both CTEU and 4D-CTEU examinations.

4 | DISCUSSION

The main benefit of 4D-CTEU is the combination of spatial and temporal cross-sectional image assessment of both ureters with complete freedom of multiplanar viewing to follow the ureteral anatomy (Figure 2; Video S1). Simple dynamic CT, CTEU, or other imaging modalities only offer spatial or temporal ureteral assessment, restrict multiplanar viewing, are not cross-sectional, or reduce the assessment to only one ureter. This is important, because if the anatomy of the ureter

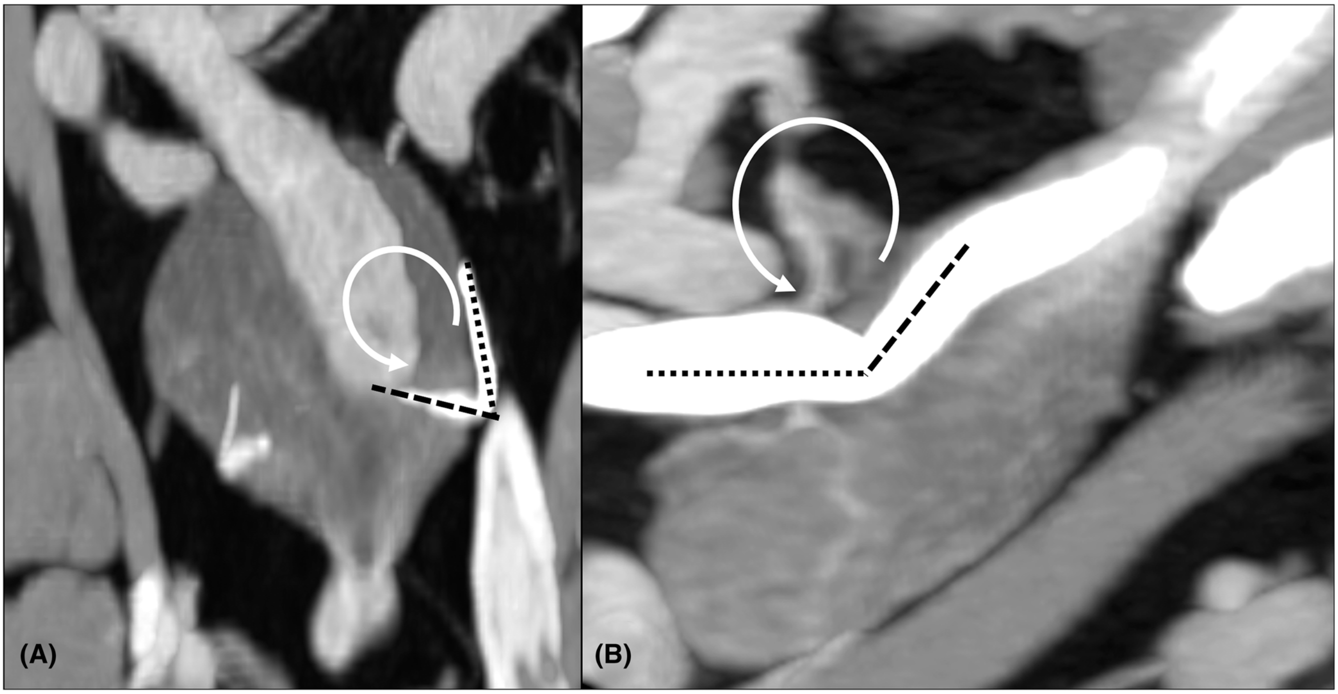

FIGURE 4 Maximum-intensity projection, CT images of the left ureterovesical junction (UVJ) in two dogs, reconstructed with a 5-mm slab thickness and soft tissue algorithm (window level, 40; window width, 400). A, Dorsal plane, normotopic ureter: The peritoneal ureter portion joins from cranial (dotted line) the UVJ, where it pivots with an acute angle (65°, curved arrow) into the intramural ureter portion (dashed line). B) Sagittal plane, intramural ectopic ureter: The peritoneal ureter portion joins from cranial (dotted line) the UVJ, where it pivots with an obtuse angle (128°, curved arrow) into the intramural ureter portion (dashed line)

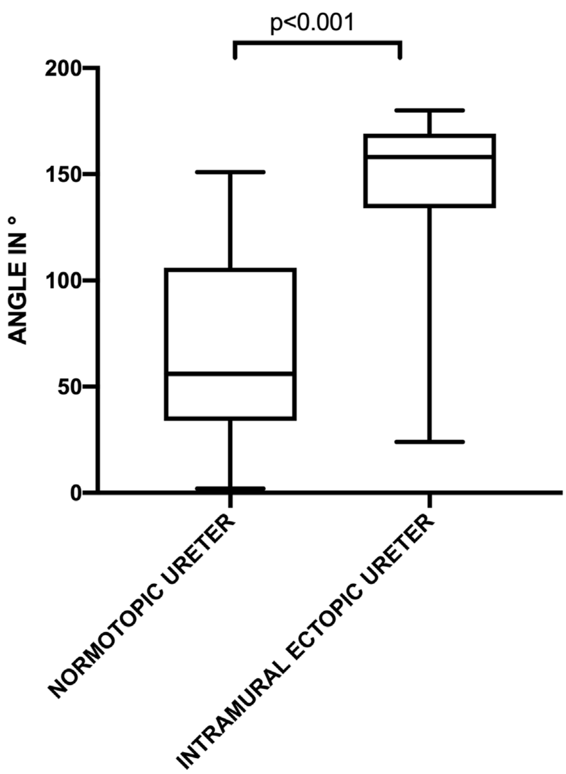

FIGURE 5 Box plot comparing the ureterovesical angle (UVJ) between normotopic and intramural ectopic ureters. The latter have significantly higher UVJ angles

is curved or tortuous, the ureteral peristalsis only permits ureteral contrast bolus phase observation within a narrow time window, which is not synchronized between both sides, and adjacent anatomic structures such as the urinary bladder, colon, and pelvis create problems of superimposition with uniplanar imaging modalities such as fluoroscopy or are insufficiently penetrable with other cross-sectional modalities such as ultrasonography.[13,14]

Traditional CTEU protocols have attempted to mitigate this by performing repeated helical CT scans,[9] but the acquisition data are not temporarily continuous and therefore the ureter contrast bolus might not be captured. If the scanning procedures are extended for too long, then pooling of contrast medium containing urine in the urinary bladder neck further decreases ureter contrast bolus jet detection. Our previous poor experience with traditional CTEU techniques led us to develop first dynamic ureter CT and then 4D-CTEU techniques to overcome these limitations. Only the latest generation of CT scanners, usually with 64- or more slice technique, has 4D-CT capacity, and only the most modern DICOM viewing software allows reviewing 4D-CT studies in a meaningful way. Some practitioners and radiologists question the need of expensive, cutting-edge CT technology, designed for human-specific cardiovascular diseases, for small animal imaging. Our study describes the value of this advanced technology for the noninvasive diagnosis of a common clinical disease in dogs, using minimal chemical restraint, and allowing improved diagnostics and, potentially, enhancing surgical planning and patient outcome.

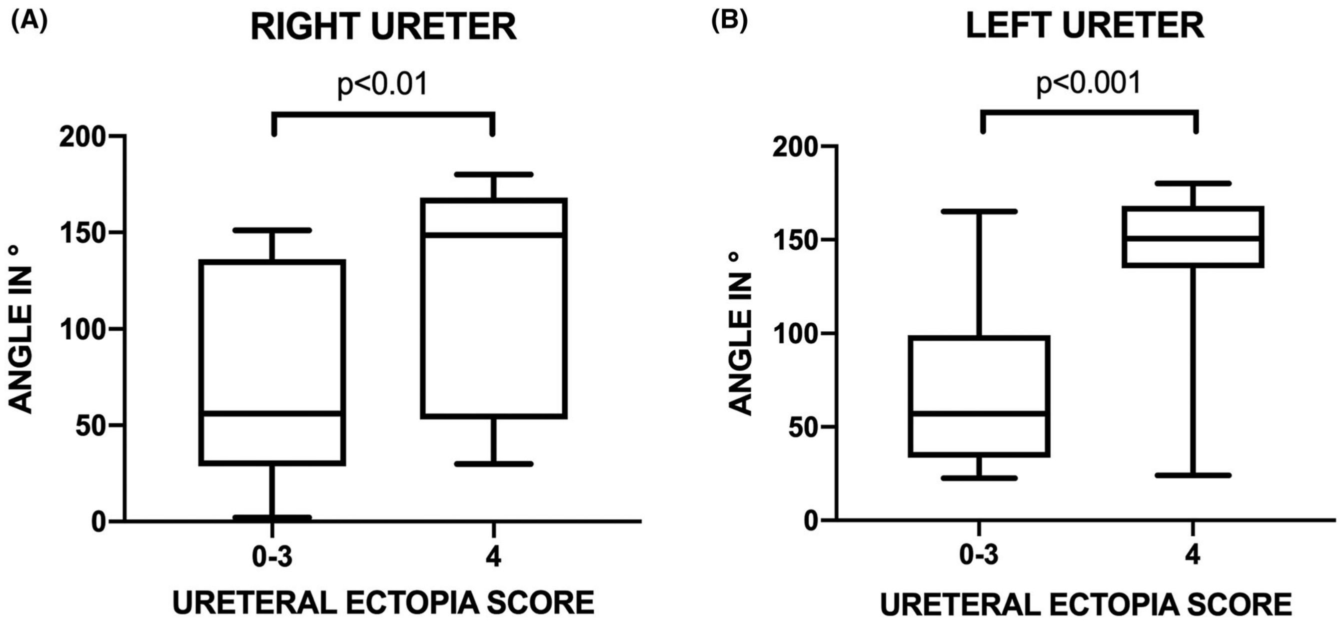

FIGURE 6 Box plot comparing the definitive ureteral ectopia scores with other score groups for differences in ureterovesical (UVJ) angle for (A) left and (B) right ureters. A definitive score of ureteral ectopia was associated with significantly higher UVJ angles bilaterally

Results of this study indicate that for determination of canine ureteral topia, 4D-CTEU is a diagnostic test with low interobserver variability and high diagnostic accuracy, confirming our first hypothesis. The 4D-CTEU proved to be an efficient technique that only rarely needed to be repeated. In all four dogs in which a repeated 4D-CTEU was performed, ureteral ectopia was bilateral, which may be a more demanding diagnostic challenge. However, none of our patients were on intravenous supportive fluids prior to the CT examination, and none received furosemide treatment. Furosemide administration has been shown to safely increase canine ureteral contrast bolus jet detectability in CTEU.[12] Further studies are needed to determine whether additional furosemide injection would increase the 4D-CTEU diagnostic value even further.

With traditional CTEU, the observer agreement for ureteral topia was a combination of moderate agreement for the left ureter and perfect for the right ureter, and this reflects the difficulty to assess both ureters at one instance in time available with this technique. The almost perfect agreement between observers for both ureters in 4D-CTEU points toward the advantage of a temporal window for individual ureter assessment. To our knowledge, this is the first application of a 4D-CT technique, designed for perfusion and cardiac imaging in humans,[25,26] for the assessment of the lower urinary tract in animals. The ureteral topia scoring confidence was only slightly lower for the less experienced observer, indicating that 4D-CTEU image interpretation is reliable in the evaluation of the lower urinary tract for radiologists with different levels of experience.

Knowledge of the topographic relationship between the intramural ectopic ureter versus the urethra and urinary bladder wall is essential for the appropriate selection of surgical corrective techniques and cystoscopic laser ablation planning.[1,4] If the shared urethral and ureteral wall is ablated beyond the intramural portion of ureter, there is risk of urethral or cystic wall perforation and uroperitoneum. If the intramural ureter portion does extend from the urethral to the urinary bladder wall, laser ablation techniques can be successfully employed, but it is crucial that the ablation procedure includes both the urethral and cystic parts, resulting in urine excretion into the urinary bladder. Four-dimensional CT excretory urography allows detailed and reliable assessment of these critical anatomic features of UE. We found that 4D-CTEU allowed us to confidently follow the ureteral course, either extramurally bridging or intramurally tunneling.

Despite the fact that the foundations for canine CTEU were already published in 1998[11] and evidence that CT is superior for the diagnosis of canine UE than other imaging modalities since 2004,[9] in many institutions fluoroscopy is still commonly used, increasing patient contrast medium dose and prolonging the patient's surgical and general anesthesia time. Fluoroscopic images can be difficult to interpret due to superimposition of structures and lack of anatomical detail. The 4D-CTEU offers an alternative, reliable, noninvasive diagnostic technique that can be performed in sedated dogs and allows surgical technique selection and detailed planning ahead of the procedure, shortening the surgery time and optimizing patient outcome. The additional radiation involved in fluoroscopy and 4D-CTEU is comparable, but only during fluoroscopy this radiation exposure includes the operator. An alternative is the use of a dynamic CTEU series, in which the urinary bladder neck is scanned over time during the urinary contrast bolus excretion.[19] Dynamic CT is widely available on most CT scanners, but it has a number of limitations, such as the limited scan length cover and the inability to reconstruct images in other planes. Current research is ongoing to investigate the potential of dynamic CTEU for ureter topia determination.

The higher frequency of UE in female dogs and breeds such as French Bulldogs, Golden Retrievers, and Labrador Retrievers seen in our study is in agreement with the prevalence previously reported.[2,9,14] In a recent study, specific features indicative of intramural UE were identified in a group of 10 dogs, including an obtuse, or *reflex*, angle of the UVJ.[16] Our study confirms our hypothesis that the presence of an obtuse UVJ angle is significantly more commonly present in intramural ectopic ureters than in normotopic ureters, and that the diagnostic confidence in ureteral ectopia diagnosis is increased with increased UVJ angles. Therefore, an obtuse or reflex UVJ angle is a useful imaging finding that radiologists can continue to use with confidence. Using 4D-CTEU technology, that confidence can be even higher, because the angle can always be observed with contrast bolus present in the UVJ area.

The urinary bladder neck is critical for assessment of ureteral topia. To keep this area free of contrast medium containing urine, we tested a published protocol using a 10° wedge for angled pelvis positioning as a standard in our institution.[19] The results of this study did not confirm our hypothesis that it is indeed beneficial employing the wedge. Because some ectopic ureters open into the urethra or vagina, bladder neck opacification may have not changed the scoring results to a level of significance. Also, in our protocol, the 4D-CTEU and CTEU examinations were performed within a 3-minute time span, which is an early stage of the opacification, but may be difficult to complete in other institutions due to technical and patient factors. Future studies are required to determine the bladder neck opacification time with horizontal and angled pelvis positions.

There are a number of limitations to this study. First, our study population is relatively small, but the fact that the number of useable ureters doubled the patient population size partially mitigated this. The extramural ectopic ureter group was particularly small, owing to the rarity of this disease subset, and this entity warrants further studies in the future, particularly for the UVJ angle assessment and comparison to intra/extramural ectopic ureters. The diagnosis of ureteral normotopia was not confirmed by direct inspection during surgical or cystoscopic procedures in all cases. In cases of UE in which the ureteral papilla is located only slightly more caudally than normally, patients may respond to medical treatment as the increasing vesicourethral sphincter tone might allow urine to go back into the urinary bladder. We argue that such cases would not require surgical or laser ablation treatment, and for the purpose of this study should remain to be regarded as true negative cases.

In conclusion, 4D-CTEU is an accurate and reliable diagnostic technique to investigate UE as cause of urinary incontinence in dogs that is slightly superior to traditional CTEU protocols. It can be used in dogs under sedation and allow better presurgical planning and decision-making. The UVJ angle can be used as a reliable imaging finding for the discrimination of normotopic and intramural ectopic ureters.

LIST OF AUTHOR CONTRIBUTIONS

Category 1

(a) Conception and Design: Schwarz, Longo
(b) Acquisition of Data: Longo, Schwarz, Thierry
(c) Analysis and Interpretation of Data: Schwarz, Bommer, Parys, Thierry, Bouvard, Pérez-Accino, Saunders, Longo

Category 2

(a) Drafting the Article: Schwarz, Longo
(b) Revising Article for Intellectual Content: Schwarz, Bommer, Parys, Thierry, Bouvard, Pérez-Accino, Saunders, Longo

Category 3

(a) Final Approval of the Completed Article: Schwarz, Bommer, Parys, Thierry, Bouvard, Pérez-Accino, Saunders, Longo

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

How to cite this article: Schwarz T, Bommer N, Parys M, et al. Four-dimensional CT excretory urography is an accurate technique for diagnosis of canine ureteral ectopia. *Vet Radiol Ultrasound*. 2020;1-9. https://doi.org/10.1111/vru.12934