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Split-bolus CT urography with synchronous nephrographic and excretory phase in dogs: comparison of image quality with three-phase CT urography and optimal allocation ratio of contrast medium

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ABSTRACT

Background: Computed tomography urography (CTU), based on the excretion of contrast medium after its injection, allows visualization of the renal parenchyma and the renal collecting system.
Objectives: To determine the optimal contrast medium dose allocation ratio to apply in split-bolus CTU in dogs.
Methods: This prospective, experimental, exploratory study used 8 beagles. In 3-phase CTU, unenhanced-, nephrographic-, and excretory-phase images were obtained with a single injection of 600 mg iodine/kg iohexol. In split-bolus CTU, two different contrast medium allocation ratios (30% and 70% for split CTU 1; 50% and 50% for split CTU 2) were used. Unenhanced phase image and a synchronous nephrographic-excretory phase image were acquired.
Results: Although the attenuation of the renal parenchyma was significantly lower when using both split CTUs than the 3-phase CTU, based on qualitative evaluation, the visualization score of the renal parenchyma of split CTU 1 was as high as that of the 3-phase CTU, whereas the split CTU 2 score was significantly lower than those of the two others. Artifacts were not apparent, regardless of CTU protocol. The diameter and opacification of the ureter in both split CTUs were not significantly different from those using 3-phase CTU.
Conclusions: Split-bolus CTU with a contrast medium allocation ratio of 30% and 70% is feasible for evaluating the urinary system and allows sufficient enhancement of the renal parenchyma and appropriate distention and opacification of the ureter, with similar image quality to 3-phase CTU in healthy dogs. Split-bolus CTU has the advantages of reducing radiation exposure and the number of CT images needed for interpretation.

Keywords: contrast media; CT scan; dog; urography

INTRODUCTION

Computed tomography urography (CTU) has been applied for various genitourinary indications including congenital ureteral anomalies such as ectopic ureters, urolithiasis,

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Conflict of Interest

The authors declare no conflicts of interest.

Author Contributions

Conceptualization: Choi J; Data curation: Je H, Jung JW, Jang Y, Chhoey S; Formal analysis: Je H, Lee SK; Funding acquisition: Choi J; Investigation: Je H, Choi J; Methodology: Je H, Lee SK; Supervision: Choi J; Writing - original draft: Je H; Writing - review & editing: Je H, Choi J.

suspected urinary tract disruption in patients with trauma, and renal and urinary bladder cancers [1,2]. CTU permits visualization of contrast-enhanced renal parenchyma and the renal collecting system based on the excretion of contrast medium after its injection [3-5]. In the nephrographic phase, uniform renal enhancement without renal pelvis filling can be observed. The excretory phase provides homogeneous opacification and adequate distention of the renal pelvis and the ureter. In human study, the nephrographic- and excretory-phase images are the most commonly obtained because the nephrographic phase is optimal for detecting neoplastic or inflammatory lesions of renal parenchyma and the excretory phase is useful for detecting small masses or calculi [6-10]. Thus, a 3-phase CTU protocol, which acquires unenhanced-phase images as well as nephrographic- and excretory-phase images after a single intravenous injection of contrast medium, is widely used [4].

A split-bolus technique can be used to acquire 2 different phases in one computed tomography (CT) scan image following 2 injections of contrast medium, by splitting the total dose into 2 portions. Thus, split-bolus CTU can acquire a single CT image taken during a synchronous nephrographic-excretory-phase with 2 separate injections of the contrast medium [4]. Such a CT image contains both nephrographic- and excretory-phase information along with enhancing the renal parenchyma as well as the renal collecting system. Compared with the 3-phase technique, the split-bolus technique decreases radiation exposure to the patient by 30%–35% and reduces the number of CT images to be acquired [11,12]. In patients with a high probability of malignant diseases, 3-phase CTU is justified because it can offer dynamic information on the lesion and can assess kidney function despite the need for repetitive CT scanning and high radiation dose. On the other hand, the split-bolus CTU protocol is more beneficial for patients in whom radiation exposure is an issue especially children, young women, and patients with the possibility of benign diseases or with chronic symptomatic stone disease, urinary diversions, or in clinical settings with a low pre-test probability of malignant disease, such as the evaluation of hematuria in younger patients [4].

In split-bolus CTU, the allocation ratio of the two portions of the contrast medium dose can affect CTU image quality; however, there is no consensus on the optimal ratio of the 2 contrast medium portions, even in human medicine [13].

The purpose of this study was to investigate the feasibility of using split-bolus CTU in dogs and to determine an optimal allocation ratio for the split-bolus technique. For this, the distention and opacification of the renal collecting system and the image quality of the renal parenchyma in split-bolus CTU using 2 different contrast medium bolus allocation ratios were compared with those from a 3-phase CTU protocol. We hypothesized that the split-bolus technique is feasible in canine CTU and can provide enhancement of renal parenchyma and distention of the renal collecting system that is similar to those from 3-phase CTU.

MATERIALS AND METHODS

Animals

In this prospective, experimental, exploratory design study, eight intact male, purpose-bred beagles were enrolled. The median age of the dogs was 3 years (range, 2–4 years), and the median weight was 10 kg (range, 8.5–12 kg). All dogs were clinically healthy based on the results of physical examination, blood pressure measurement using a Doppler device, complete blood count, serum biochemistry, electrolyte analysis, urinalysis, abdominal

radiography and ultrasonography, and echocardiography. The dogs were fed commercial dry food and water *ad libitum* and housed in individual cages. The study protocol was approved by the Institutional Animal Care and Use Committee of Chonnam National University (CNU IACUC-YB-2018-65).

Preparation for CTU

After fasting for 12 h, the dogs received 250 mL of polyethylene glycol solution (Colyte, Taejoon Pharmaceutical, Korea) administered *per os* for cleansing at least 12 h before anesthesia. General anesthesia was induced by an intramuscular injection of a combination of 0.03 mg/kg medetomidine hydrochloride (Domitor®, Orion Corporation, Finland) and 0.75 mg/kg zolazepam/tiletamine (Zoletil®, Virbac, France), and maintained with 1–2% isoflurane (Terrell, Piramal Critical Care, USA) and oxygen (1 L/min).

The dogs were placed in sternal recumbency, and CT images were acquired using a 16-channel CT scanner (Siemens Emotion 16, Siemens Medical Systems, Germany) with the following settings: slice thickness = 1 mm; pitch = 0.8; rotation duration = 600 msec; tube voltage = 110 kV; and tube current = 130 mA. A breath-hold technique was performed by inducing apnea with manual hyperventilation to minimize motion artifacts.

CTU protocols

Scan delay can be affected by the amount of contrast medium, and the 3-phase and split-bolus techniques used scan delays of the nephrographic and excretory phases that were determined separately by using three different protocols (**Table 1**). The sequential CT images were acquired at the left renal pelvis level for 60 sec after injection of contrast medium: total dose in 3-phase CTU, 70% of the total dose in split CTU 1, or 50% of the total dose in split CTU 2. The time to attenuation curves were drawn from the renal cortex and the outer medulla. The scan delay of the nephrographic phase was established when the attenuation of the renal cortex and outer medulla reached the same CT value. For the scan delay of the excretory phase, CT scans of the left kidney were repeatedly performed from 8 to 22 min at 2-min intervals after injection of contrast medium: total dose in 3-phase CTU, 30% of the total dose in split CTU 1, or 50% of the total dose in split CTU 2. The excretory phase was determined when the renal pelvis had strong attenuation accompanied by markedly decreased attenuation of the renal medulla as assessed by 2 observers (J.H.C., H.J.J.).

Three CTU protocols, 3-phase CTU and 2 split CTUs using different contrast medium allocation ratios were performed in each dog in random order and with at least a 7-day interval between protocols (**Fig. 1**). In all protocols, the total contrast medium dose was 2 mL/kg (iohexol; Omnipaque 300, GE Healthcare, Norway). In 3-phase CTU, the total contrast medium dose was administered with a power injector (Optivantage DH, Mallinckrodt Pharmaceuticals, USA) at 3 mL/sec via a 22 G catheter through the cephalic vein in each dog.

Table 1. Technical factors of CTU according to the applied intravenous contrast protocol

Technical factors	Three-phase technique	Split-bolus technique 1	Split-bolus technique 2
Nephrographic phase			
Iodine dose	600 mg iodine/kg (2.0 mL/kg)	70% of the total dose (1.4 mL/kg)	50% of the total dose (1.0 mL/kg)
Excretory phase			
Iodine dose	600 mg iodine/kg (2.0 mL/kg)	30% of the total dose (0.6 mL/kg)	50% of the total dose (1.0 mL/kg)
CTU protocol			
Total iodine dose	2.0 mL/kg	2.0 mL/kg	2.0 mL/kg
Allocation ratio of contrast agent dose (%)	-	30:70	50:50

CTU, computed tomography urography.

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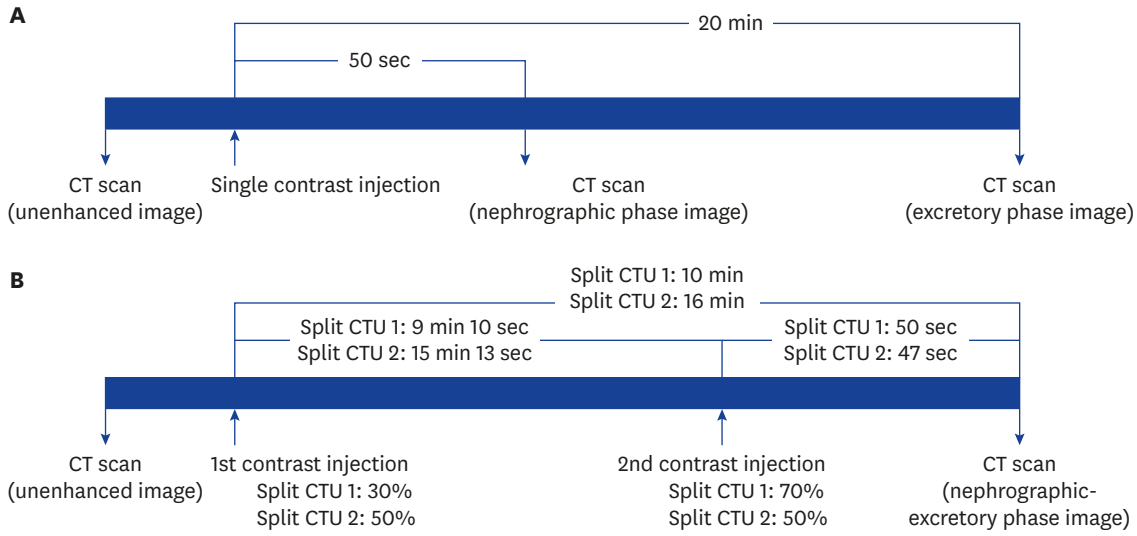

Fig. 1. Schematic view of computed tomography scanning techniques for three CTU protocols. Scan delays for nephrographic and excretory phases phase and contrast medium administration in 3-phase CTU (A) and scan delays for synchronous nephrographic-excretory phases and contrast medium bolus allocation ratios for two split-bolus CTU protocols (split CTU 1, 30% of contrast medium dose in first bolus and 70% in second bolus; split CTU, 50% of contrast medium dose in each bolus) (B) are shown.
CTU, computed tomography urography; CT, computed tomography.

Unenhanced-, nephrographic-, and excretory-phase imaging were performed. In split CTU 1, 30% of contrast medium dose was administered as the first bolus, and 70% of the contrast medium dose as the second bolus. In split CTU 2, 50% of the contrast medium dose was administered as the first and second boluses. In both split CTU protocols, an unenhanced-phase image and a synchronous nephrographic-excretory-phase image were obtained. All CT images were reconstructed with a slice thickness of 1 mm using a soft tissue kernel. CT images were reconstructed using multiplanar reformation (MPR) and curved planar reformation (CPR) by use of the installed CT software program (Syngo 3D, Siemens, Germany).

CT image evaluation

Nephrographic- and excretory-phase images in 3-phase CTU and a synchronous nephrographic-excretory-phase image in split CTU were reviewed at the workstation in random order by 2 observers (J.H.J, S.K.L.) using a window width of 400 Hounsfield units (HU) and a window level of 40 HU. In both kidneys, renal cortex, medulla, pelvis, and the ureter were assessed on all CTU images. The ureter assessment was performed after dividing the ureter into the 3 equal-length segments: proximal, middle and distal. For quantitative assessments, CT attenuations of each part of urinary tract and distention of the ureter were evaluated. CT attenuations of renal parenchyma were measured from the ventral and dorsal parts of each renal site at the mid-kidney level showing the pelvis by drawing 2 circular regions of interest (ROIs; size range, 5–15 mm^2) over the renal cortex and outer medulla in the nephrographic phase and the inner medulla in the nephrographic- and excretory-phase images. The pelvis and ureter were assessed in the excretory-phase image. The attenuation of the pelvis was measured by using an oval ROI (size range, 1–2 mm^2) in the center of the pelvis. Ureter attenuation was measured by using an oval ROI (size range, 0.5–2 mm^2) in the center of the lumen at the most enhanced point in each segment of the ureter. The distention of the ureter was assessed by measuring the maximal short-axis diameter of the ureter at each segment. All measurements were performed on the transverse plane three times, and the mean value was used for further analyses.

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Table 2. Qualitative evaluation factors and criteria for assessment of computed tomography urography protocols

Evaluation factor	Score
Opacification of each ureter segment	
No opacification of the segment	0
Less than 50% opacification	1
50%–99% opacification	2
Complete opacification	3
Visualization of the renal parenchyma	
Enhancement similar to that of the enhanced spleen	0
Slightly higher enhancement than that of the enhanced spleen	1
Notably higher enhancement than that of the enhanced spleen	2
Visualization of the renal pelvis	
Poorly distinguishable from the renal medulla because of insufficient enhancement of the renal pelvis	0
Poorly distinguishable from the renal medulla because of strong enhancement of the renal medulla	1
Easily distinguishable from the renal medulla with strong enhancement of the renal pelvis	2
Image quality regarding artifact presence	
Hard to interpret CT images due to artifacts	0
Fairly good CT images with some artifacts	1
Optimal CT images with no interference	2

CT, computed tomography.

For the qualitative assessments, the opacification of the ureter, the visualization of renal parenchyma and renal pelvis, and image quality regarding artifact were evaluated (**Table 2**). In excretory-phase imaging, the opacification of the ureter was scored using a 4-point scale based on the proportion (%) of each ureter segment that was filled with contrast medium on the dorsal plane. Visualization of the renal parenchyma and renal pelvis was evaluated by using a 3-point scale on the transverse plane in nephrographic-phase images and the dorsal plane in excretory-phase images, respectively.

During and after the CT scans, the heart rate and blood pressure of the dog were monitored. After completion of each CTU, any clinical signs, such as depression, anorexia, vomiting, diarrhea, and changes in urination, were monitored for two days.

Statistical analyses

Under the supervision of one statistician (J.K.K.), statistical analyses were performed by one observer (H.J.J) using IBM SPSS Statistics for Windows/Macintosh, Version 20.0 (IBM SPSS Statistics 21, IBM Corp., USA). Differences in attenuation of each part of the kidney and ureter, size of the renal pelvis and ureter, and qualitative assessment of the renal parenchyma and opacification of ureter according to the three CTU protocols were statistically analyzed using Kruskal-Wallis tests with multiple comparisons using Scheffe's correction. All data are presented as means and standard deviations; medians and percentiles (25th and 75th) were added to ureteral distention and opacification scores. The p value of less than 0.05 were considered significant. Interobserver agreements were analyzed using the intraclass correlation coefficient test: < 0.4, poor agreement; 0.41–0.6, moderate agreement; 0.61–0.79, good agreement; > 0.8, excellent agreement.

RESULTS

All CTU protocol applications were performed without any complications or abnormal changes in blood chemistry, urinalysis, and kidney ultrasonography. The mean numbers of total CT images per dog were 715.1 ± 39.2 images for the 3-phase technique, 512.5 ± 21.5 images for the split-bolus CTU 1 protocol, and 508.3 ± 23.0 images for the split-bolus CTU

2 protocol. The times from injection of the contrast medium to complete CTU were shorter in split-bolus CTU 1 (median, 615.5 sec) and split-bolus CTU 2 (median, 975.5 sec) than in 3-phase CTU (median, 1,219 sec). Scan delays for the nephrographic and excretory phases were set as 50 sec and 20 min for three-phasic CTU, 50 sec and 10 min for split CTU 1, and 47 sec and 16 min for split CTU 2, respectively.

The quantitative assessment of CTU images revealed that CT attenuations of the cortex, outer medulla, renal pelvis, and ureter were significantly higher in 3-phase CTU images than in images from both split-bolus CTU protocols. Split CTU 1 images had significantly higher attenuations of the cortex, outer medulla, inner medulla, and renal pelvis than those in split CTU 2 images (**Table 3**). There was no significant difference in CT attenuation of the ureter between the 2 split CTU protocols. The distention of the ureter was also not significantly different according to CTU protocol (**Table 4**).

Qualitative assessment results indicated that the opacification of the ureter was not significantly different among the CTU protocols (**Table 5**). However, opacification scores ≥ 2 of the ureteral segments were assigned to 77.1% (37/48) in 3-phase CTU, 62.5% (30/48) in split CTU 1, and 83.3% (40/48) in split CTU 2 images. Segments of the ureter opacified with contrast medium less than 25% were recorded in 10.4% (5/48) of 3-phase, 4.2% (2/48) of split CTU 1, and 8.3% (4/48) of split CTU 2 images. The entire length of the ureter was clearly visualized on CPR images regardless of CTU protocols (**Fig. 2**). The renal parenchyma was enhanced to a greater extent than the spleen in 3-phase CTU and split CTU 1 images, without a significant difference between the 2 ($p = 0.16$). However, the renal parenchyma in split CTU 2 images was enhanced only slightly higher than that of the spleen, and the intensity of the enhancement was significantly lower than that in the other 2 protocols ($p < 0.001$) (**Table 6**). The renal pelvis was visualized distinctively from the inner medulla in the synchronous nephrographic-excretory-phase images of split CTU 1 and split CTU 2 as well as in the excretory-phase images of 3-phase CTU ($p = 0.528$) (**Table 6**). In all CTU images, there was no noticeable disturbance by streak artifacts in or around renal parenchyma (**Table 6**). Interobserver agreement of all qualitative assessments was excellent (**Table 7**).

Table 3. Attenuation (Hounsfield units) of the renal parenchyma and collecting system when using the three CTU protocols

Location	Three-phase CTU		Split CTU 1	Split CTU 2
	Nephrographic phase	Excretory phase		
Cortex	277.3 ± 43.3[a]	-	218.6 ± 21.3[b]	175.9 ± 23.0[c]
Outer medulla	319.8 ± 38.8[a]	-	242.1 ± 25.6[b]	168.5 ± 27.5[c]
Inner medulla	144.6 ± 56.5[b]	246.0 ± 41.4[a]	194.0 ± 30.8[a]	167.2 ± 30.6[b]
Pelvis	-	705.3 ± 178.2[a]	473.1 ± 113.6[b]	356.4 ± 58.5[c]
Proximal ureter	-	732.5 ± 346.4[a]	307.8 ± 140.4[b]	366.9 ± 132.5[b]
Middle ureter	-	573.3 ± 299.5[a]	333.2 ± 104.8[b]	249.3 ± 99.0[b]
Distal ureter	-	634.8 ± 350.8[a]	328.6 ± 120.4[b]	296.0 ± 75.1[b]

Data expressed as mean ± SD values.
CTU, computed tomography urography.
[a-c]Within a row, values with different superscripted letters differ significantly ($p < 0.05$).

Table 4. Maximum diameter (mm) of each ureter segment according to CTU protocol

Ureter segment	Three-phase CTU	Split CTU 1	Split CTU 2
Proximal ureter	2.1 ± 0.7, 2.3 (1.3–2.6)	2.1 ± 0.4, 2.3 (1.7–2.5)	1.9 ± 0.5, 2.1 (1.4–2.4)
Middle ureter	1.8 ± 0.3, 1.7 (1.6–1.8)	1.8 ± 0.4, 1.7 (1.5–2.0)	1.6 ± 0.2, 1.6 (1.4–1.7)
Distal ureter	1.9 ± 0.3, 1.8 (1.7–2.0)	1.8 ± 0.4, 1.7 (1.6–1.9)	1.6 ± 0.4, 1.7 (1.4–1.8)

Values presented as mean ± SD and median (25th percentile, 75th percentile) values.
CTU, computed tomography urography.

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Table 5. Opacification of each ureter segment according to CTU protocol

Ureter segment	Three-phase CTU	Split CTU 1	Split CTU 2
Proximal ureter	2.1 ± 1.0, 2.3 (1.8–3.0)	2.0 ± 0.7, 2.0 (1.5–2.5)	2.1 ± 0.9, 2.0 (1.9–3.0)
Middle ureter	2.0 ± 0.6, 2.0 (2.0–2.0)	1.8 ± 0.5, 2.0 (1.5–2.0)	2.2 ± 0.4, 2.0 (2.0–2.0)
Distal ureter	2.0 ± 0.8, 2.0 (1.4–2.5)	1.8 ± 0.7, 2.0 (1.4–2.0)	2.0 ± 0.6, 2.0 (2.0–2.0)

Values presented as mean ± SD and median (25th percentile, 75th percentile) values.
Mean opacification scores (0, no opacification of segment; 1, less than 50% opacified segment; 2, 50%–99% of the segment opacified; 3, completely opacified segment).
CTU, computed tomography urography.

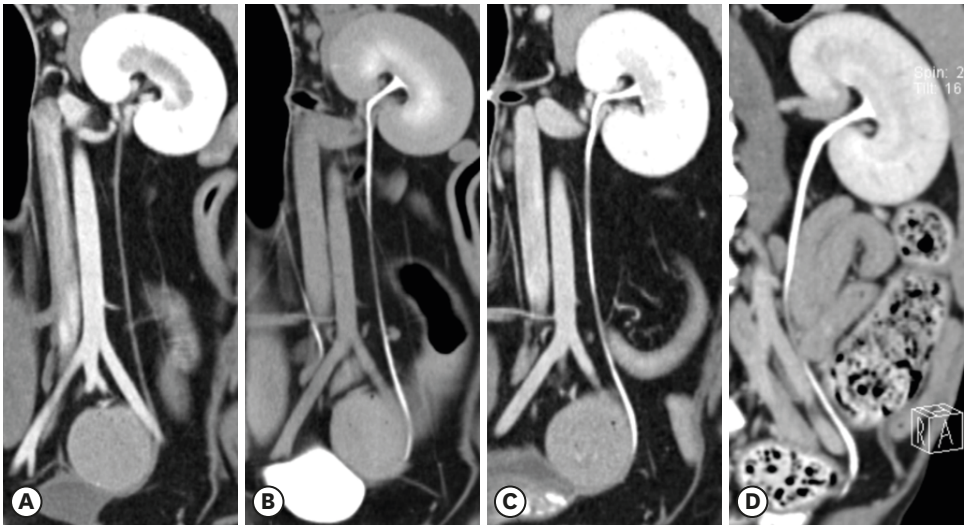

Fig. 2. CPR images (A-D) of the 3 CTU protocols along the course of the ureters in healthy beagles. (A) In the nephrographic phase of 3-phase CTU, the renal parenchyma is strongly enhanced before the contrast medium enters the renal pelvis and ureter. (B) In the excretory phase of 3-phase CTU, the renal pelvis and ureter are sufficiently filled with contrast medium and clearly visualized; however, the renal parenchyma has low enhancement. In the split-bolus CTU protocols (C, D), synchronous nephrographic-excretory-phase CPR images show the opacified and dilated renal collecting system as well as the enhanced renal parenchyma simultaneously. Split-bolus CTU using the 30% and 70% dose allocation ratio (C) shows better enhancement of renal parenchyma than that from the 50% and 50% dose allocation ratio (D).
CPR, curved planar reformation; CTU, computed tomography urography.

Table 6. Qualitative assessment of the renal parenchyma and collecting system in three CTU protocols

Evaluation factor	Three-phase CTU		Split CTU 1	Split CTU 2
	Nephrographic phase	Excretory phase		
Visualization of the renal parenchyma	2.0 ± 0.0[a]	-	1.8 ± 0.4[a]	1.2 ± 0.4[b]
Visualization of the renal pelvis	-	1.6 ± 0.5	1.7 ± 0.4	1.9 ± 0.2
Image quality regarding artifacts	2.0 ± 0.0	1.8 ± 0.3	2.0 ± 0.0	2.0 ± 0.0

CTU, computed tomography urography.
[a-b]Within a row, values with different superscripted letters differ significantly ($p < 0.05$).

Table 7. ICC values for interobserver reliability of qualitative assessments of computed tomography urography factors

Evaluation factor	Location	ICC	95% confidence interval
Opacification of the renal pelvis and ureter	Proximal ureter	0.92	0.86–0.96
	Middle ureter	0.80	0.64–0.89
	Distal ureter	0.84	0.72–0.91
Visualization of the renal parenchyma	Renal parenchyma	0.88	0.79–0.93
Visualization of the renal pelvis	Renal pelvis	0.88	0.71–0.95
Image quality regarding artifact	-	1.00	1.00–1.00

ICC, intraclass correlation coefficient.

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DISCUSSION

The split-bolus CTU technique acquires a synchronous nephrographic-excretory-phase image that shows simultaneous enhancement of the renal parenchyma and the renal collecting system based on only a single CT scanning episode. The split CTU 1 protocol provided a significantly higher visualization score than that from the split CTU 2 protocol, with similarity to that from 3-phase CTU and noticeably higher enhancement of the renal parenchyma than the spleen. Moreover, the split-bolus CTU decreased scan time, radiation exposure, and the number of CT images required for interpretation compared to those obtained via 3-phase CTU.

In synchronous nephrographic-excretory-phase images, enhancement of the renal parenchyma and distention and opacification of the renal collecting system are affected by the contrast medium bolus allocation ratio [13]. Many different protocols for split-bolus contrast medium injection have been reported; for example, a smaller first injection of 30–50 mL of contrast medium followed by a larger second injection of 80–100 mL of contrast medium, or a 75–100 mL injection followed by a 40–50 mL injection were reported in a previous review article in human medicine [4]. In a recent study into allocation ratios of split-bolus CTU, provision of a larger first injection and a smaller second injection resulted in low renal parenchyma enhancement, which was insufficient for assessment of the urinary system [13]. Thus, after modifying the human study, the allocation ratios for split-bolus CTU in this study were assessed as a 30:70 ratio in split CTU 1 and a 50:50 ratio in split CTU 2 protocols, by modifying the human study.

In the synchronous nephrographic-excretory-phase images, enhancement of the renal parenchyma is mainly affected by the second contrast medium bolus, while the enhancement, distention, and opacification of the renal collecting system are affected by the first contrast medium bolus used in the split-bolus CTU technique. The synchronous nephrographic-excretory-phase images were compared with the 3-phase CTU images to assess whether appropriate proportions of the contrast medium dose were used as first and second injections. To that end, enhancement of renal parenchyma was compared with the 3-phase CTU nephrographic phase image, and the enhancement, opacification, and distention of the renal collecting system was compared with the 3-phase CTU excretory-phase image.

In CTU, the renal pelvis and ureter must be sufficiently filled with contrast medium to determine the patency of the ureter and to delineate small lesions within the renal collecting system [2,8,14]. Ureter diameters were not significantly different among the tested CTU protocols. This result is compatible with that of a human study [13], in which the maximal diameter of the ureter did not differ significantly according to the different contrast medium allocation ratios, such as 70% and 30% of total dose as the first bolus, when the maximal diameter of the ureter was measured in each segment when using a split-bolus CTU protocol. However, in another human study, ureteral distention was significantly different when using 150 and 75 mL of contrast medium; in that study, ureteral diameters were measured at predefined locations [14]. This discrepancy in results could be related to the total volumes of contrast medium that were used. In addition, the method of measuring the ureter can be another factor related to the discrepancy between these studies. We considered the maximal size measurement in each segment more appropriate and chose that method because ureteral peristalsis randomly affects ureteral distention.

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There was no significant difference in the opacification scores of the ureter among the CTU protocols tested. However, ureteral segments opacified with contrast medium over more than 50% of the entire length were observed more often in split CTU 2 and 3-phase CTU protocols than in the split CTU 1 protocol, which applied the lowest portion of the total dose in the first bolus. In addition, ureteric segments were not filled with contrast medium simultaneously in any of the dogs, regardless of CTU protocol, and this observation was considered to be related to ureteral peristalsis. The renal pelvis filled with contrast medium was well and distinctively visualized from the inner medulla in the synchronous nephrographic-excretory-phase images of split-bolus CTU 1 and split-bolus CTU 2 as well in the excretory-phase images of 3-phase CTU.

The beam hardening artifacts associated with a dense contrast medium can produce dark streaks and deteriorate the image quality in contrast CT study [15,16]. In CTU images, the contrast medium is concentrated in the renal collecting system in the excretory phase, which can reduce the reliability of detection of small lesions in the renal pelvis or ureter in humans. In our study, artifacts did not affect the image quality in any of the CTU protocols, not only in split-bolus CTU using 2 reduced contrast boluses but also in 3-phase CTU using a single total dose bolus. This result was considered to be related to the considerably small size renal pelvis in dogs, consisting of a single main cavity without further subdivision into calyces as in the human pelvis. In the present study, the contrast medium-related dark streaks were not serious even in the excretory phase of the 3-phase CTU protocol.

The provision of a high radiation dose is an important issue in CTU in human medicine. Many efforts to reduce the radiation dose have been attempted, including reducing the number of imaging phases through the use of dual-energy CT, applying a split-bolus technique, changing the scanning parameters employed such as by lowering tube voltage or applying several iterative reconstruction algorithms [17-19]. Radiation exposure may not be as big a concern in veterinary medicine as it is in humans; however, considering the increased use of CT for assessment of the urinary tract and other organs, as well as the wide availability of multi-detector CT devices, the split CTU technique can reduce radiation exposure. Moreover, it can reduce the total number of CT images required for interpretation.

Our study has several limitations. First, only a small number of healthy dogs were enrolled, and dogs with renal or urothelial diseases were excluded. Further studies on split-bolus CTU in larger populations of dogs are required to confirm the results of this study and allow evaluation of patients with various diseases to determine if different CTU protocols can produce relevant differences in the ability to recognize pathology. Second, the allocation ratio in the split-bolus CTU was set by modifying a protocol used in a human study. Third, image assessment could not be performed in a protocol-blinded manner, because the synchronous nephrographic-excretory-phase images visualized both renal parenchymal contrast enhancement and contrast agent in the ureters. Consequently, observer bias cannot be excluded completely. Fourth, medetomidine, one of alpha 2-adrenoceptor agonist sedatives, was used as a premedication drug. Alpha 2-adrenoceptor agonist sedatives affect vasoconstriction and bradycardia, which can reduce the glomerular filtration rate. However, according to the administration route and dose, alpha 2-agonists induce diuresis via vasoconstriction on efferent arterioles and suppression of antidiuretic hormone release in dogs [20]. Moreover, the glomerular filtration rate was unchanged in dogs after intravenous injection of 750 μg/m^2 medetomidine [21]. In our study, after intramuscular injection of 0.03 mg/kg medetomidine, the systemic blood pressure remained within the range of autoregulation of glomerular filtration rate [22], that is, 65–160 mmHg, in all dogs.

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In conclusion, all CTU protocols provided subjectively acceptable image quality that was suitable for assessing the urinary system in all examined dogs. Split CTU 1 with a bolus allocation ratio of 30% and 70% of the contrast medium dose allowed enhancement of the renal parenchyma to a level similar to that of 3-phase CTU, despite the presence of less attenuation. Both split-bolus CTUs distended and filled the ureter in a manner similar to that of 3-phase CTU. Split-bolus CTU decreased scan time, radiation exposure, and the number of CT images required for interpretation compared with 3-phase CTU. The results of this study indicate that split-bolus CTU with an allocation ratio of 30% and 70% of the contrast medium dose is feasible for evaluating the renal parenchyma and ureter and can provide similar image quality to that from 3-phase CTU in healthy dogs. As well, the split-bolus technique can reduce the number of CT images required for interpretation and the radiation exposure of the animal.

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