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Injection rate, scanning position, and values of parameters on pulmonary computed tomography perfusion in normal Beagles

Hyunju Hwang, DVM, MS[1]; Changhyeon Cho, DVM[1]; Myounghun Kim, DVM[1]; Wonbeom Jung, PhD[2]; Hackjoon Shim, PhD[2]; Jaehwan Kim, DVM, PhD[1]†*; Kidong Eom, DVM, PhD[1]†

[1]Department of Veterinary Medical Imaging, College of Veterinary Medicine, Konkuk University, Gwangjin-gu, Seoul, Republic of Korea
[2]Medial Imaging AI Research Center (MiAiRC), Canon Medical Systems Korea, Seoul, Republic of Korea

†Contributed equally to this work.

*Corresponding authors: Dr. Jaehwan Kim (jaehwan@konkuk.ac.kr) and Dr. Eom (eomkd@konkuk.ac.kr)

OBJECTIVE
This study evaluated the effects of scanning position and contrast medium injection rate on pulmonary CT perfusion (CTP) images in healthy dogs.

ANIMALS
7 healthy Beagles.

METHODS
Experiments involved 4 conditions: dorsal and sternal recumbency at 2.5 mL/s (first) and sternal recumbency with additional rates of 1.5 and 3.5 mL/s (second). Various parameters, including the initial time of venous enhancement (T_v), peak time of arterial enhancement (PT_a), and peak enhancement values of the artery, were measured. The PT_a to T_v interval was calculated. Perfusion mapping parameters (pulmonary blood flow, pulmonary blood volume, mean transit time, time to maximum, and time to peak) were determined in different lung regions (left and right dorsal, middle, and ventral).

RESULTS
There are significant variations in most perfusion mapping parameters based on the pulmonary parenchymal location. Dorsal recumbency had a lower peak value of arterial enhancement than sternal recumbency. Pulmonary blood flow in the dorsal region and mean transit time and time to maximum in all regions showed no significant differences based on position. Pulmonary blood volume and time to peak varied with scanning position. The PT_a to T_v interval did not differ based on the injection rate, but the injection time at 1.5 mL/s was longer than at other rates. All perfusion mapping parameters of the ventral region increased with higher injection rates.

CLINICAL RELEVANCE
The recommended CTP imaging approach in dogs is a low injection rate of 1.5 mL/s in the sternal recumbency. This study provides reference ranges for perfusion parameters based on the pulmonary parenchymal location, contributing to the acquisition and application of pulmonary CTP images for differential diagnosis in small-breed dogs.

Keywords: pulmonary CT perfusion; perfusion map; scanning position; injection rate; canine

Some pulmonary diseases related to hemodynamics, such as tumors, emphysema, and thromboembolism, develop in dogs. In veterinary medicine, the diagnosis of pulmonary diseases relies mainly on anatomical evaluations using radiography, CT, and other imaging modalities, which have limitations. However, various modalities, including CT, MRI, dual-energy CT, nuclear medicine scintigraphy, single-photon emission CT, PET, perfusion MRI, and CT perfusion (CTP), have been studied and used for the diagnosis of various pulmonary diseases in human medicine.[1,2]

In particular, CTP is an imaging technique that serially images changes in the density of the pulmonary parenchyma over time after the administration of contrast agents. This allows for the derivation of time-density curves (TDCs) that reflect the degree of contrast density change as the contrast agent moves

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through the pulmonary artery, parenchyma, and pulmonary veins. With the use of these TDCs, various perfusion maps of the pulmonary parenchyma can be generated for quantitative evaluation.[3]

CTP is a useful technique for the quantitative evaluation of hemodynamic abnormalities and has been used in human medicine for the diagnosis and prognostic assessment of various diseases related to vasculature and blood flow.[2,4] Furthermore, several studies[5–9] have been conducted in veterinary medicine on the CTP of the brain, kidney, pancreas, and liver.

Additionally, several studies[1,10–13] have been conducted on the quantification of pulmonary CTP in human medicine, and it is being used for various purposes, such as assessing pulmonary thromboembolism and emphysema, where decreased perfusion (evaluated by decreasing pulmonary blood flow [PBF] and pulmonary blood volume [PBV] and increasing mean transit time [MTT], time to maximum of residual function [TMAX], and time to peak of tissue [TTP]) is often observed. It is also used for quantifying pulmonary tumor volume, assessing malignancy, and classifying tumor types and stages.[1,10–13]

However, in veterinary medicine, there is a lack of research on the quantitative assessment of appropriate protocols and perfusion parameters for pulmonary CTP in dogs, mainly owing to the absence of high-performance CT equipment and analysis software in most veterinary hospitals.

Therefore, the primary aim of the study was focused on characterizing the effects of scanning positioning and contrast medium injection rate on pulmonary CTP findings to determine the appropriate conditions. Additionally, as a secondary aspect of this study seeks to establish reference ranges for normal perfusion parameters based on the location of the pulmonary parenchyma, thereby providing a foundation for the application of CTP in veterinary patients.

Methods

Animal preparation

Seven intact male Beagles were included in this study. The mean age of the dogs was 9.4 months, and their mean body weight was 11.2 ± 2.1 kg. None of the dogs showed evidence of pulmonary disease and were clinically healthy, as confirmed by physical examination, CBC, serum biochemistry, digital radiography, abdominal ultrasonography, and echocardiography. This study was approved by the Institutional Animal Care and Use Committee of Konkuk University (approval No. KU23054).

Scanning of pulmonary CTP

Anesthesia—All dogs were fasted for at least 12 hours before the experiment. Heart rate (STAR8000E-V; Shenzhen Comen Medical Instruments Co, Ltd) and blood pressure (OPUS V3; KPI Healthcare) were monitored before, during, and after anesthesia and were specially measured every 5 minutes during anesthesia. The anesthesia was induced 0.3 mL/kg body weight of alfaxalone (Alfaxan; 10 mg/mL; Jurox Pty Ltd) via an IV catheter and maintained with 2.0% isoflurane (IsoVet; Piramal Pharma Ltd) to conduct the experiments. Maintenance and monitoring of respiratory anesthesia and controlling respiratory rate were performed using a mechanical ventilator (Gaia α; Gigamedical), and the anesthetic depth was controlled in the state of no spontaneous respiration to maintain a certain range of heart rates. All dogs were hydrated with normal saline (2.5 mL/kg/h, IV) before, during, and after anesthesia for a certain period but not during CTP scanning.

Designs of the experiment condition—This was a crossover study, and all dogs were scanned 4 times under the following conditions between February 7, 2023, and April 20, 2023: (1) 2 different scanning positions (sternal and dorsal recumbencies) at 2.5 mL/s **(Supplementary Figure S1)**, and (2) additional 2 injection rates of contrast medium (1.5 and 3.5 mL/s) in sternal recumbency.

In the first experiment, 2 scanning positions were used, and each position was injected at a rate of 2.5 mL/s to compare the effect of the scanning position. In the second experiment, 2 additional injection rates (1.5 and 3.5 mL/s) were applied in the sternal recumbency to compare the effect of 3 total injection rates. The order of scanning was as follows **(Supplementary Figure S2)**: (1) dorsal recumbency with 2.5 mL/s, (2) sternal recumbency with 2.5 mL/s, (3) sternal recumbency with 1.5 mL/s, and (4) sternal recumbency with 3.5 mL/s.

All dogs were scanned using 160-multislice CT (Aquilion Lightening 160; Canon Medical Systems), and precontrast CT (tube voltage, 100 kV; slice thickness, 0.5 cm; and tube current, 100 mA) was performed to set the scan range of the pulmonary CTP. Pulmonary CTP was initiated by simultaneously administering 1 mL/kg of the nonionic contrast medium iohexol (Omnipaque; 300 mg iohexol/mL; GE Healthcare) with a power injector (ADV CT 9000 injector; Liebel-Flarsheim) via an IV catheter.[6] CTP was performed on the lung parenchyma, with a scan range of 4 cm covering the distance from the aorta to the left atrium of the heart at 0.5-mm collimation, continuously for 50 seconds with 2-second intervals between each scan (tube voltage, 100 kV; tube current, 100 mA; and 0.5 × 80 row; **Supplementary Figure S3**). Inspiratory pressure was maintained at 10 mm Hg without spontaneous respiration during the scanning period in all experiments to minimize the effects of respiration. The scans were performed 4 times for each dog, and the interval between each scan was set to 10 minutes to wash out the contrast medium from the pulmonary artery. CTP images were reconstructed at 1-mm intervals.

Analysis of pulmonary CTP images

Analysis of TDC—The main pulmonary artery was set as the arterial input flow and the left atrium as the venous output flow for pulmonary CTP images.[14] The TDC for each experiment was derived from the pulmonary CTP images using analysis software (OLEA Sphere, version 3.0.32; Canon Medical Systems). The initiation time of venous enhancement (T_v; seconds),

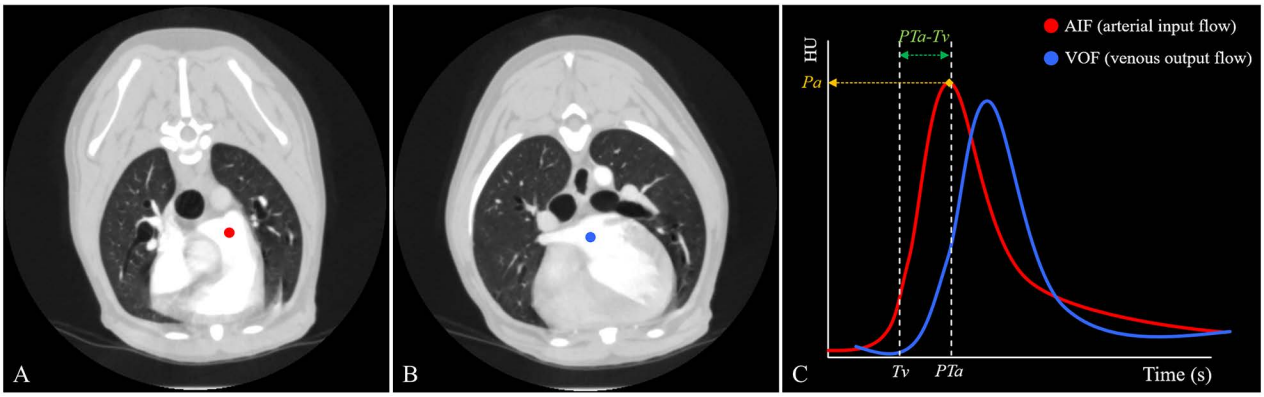

Figure 1—Pulmonary computed tomographic perfusion (CTP) images at the level of main pulmonary artery as the arterial input flow (AIF) and the level of left atrium as the venous output flow (VOF) of 1 of the Beagles after administration of the nonionic contrast medium iohexol (Omnipaque; 300 mg iohexol/mL, GE Healthcare) via IV catheter. A and B—The images were reconstructed with a 0.5-mm slice thickness in the lung window (window width, 1,500 HU; window level, −400 HU). A—On the image of the most strongly enhanced pulmonary artery CTP, the main pulmonary artery (solid red circle) is localized to the region of interest of AIF. B—On the image of the most strongly enhanced left atrium CTP, the left atrium (solid blue circle) is localized to the region of interest of VOF. C—The relative changes of arterial and venous flow over time are presented as time-density curves. The parameters of the time-density curve, including the initiation time of venous enhancement (T_v, seconds [s]), the peak time of arterial enhancement (PT_a; s), and the peak value of arterial enhancement (P_a; HU), are measured on the curves, and the interval between PT_a and T_v (PT_a-T_v; s) can be calculated.

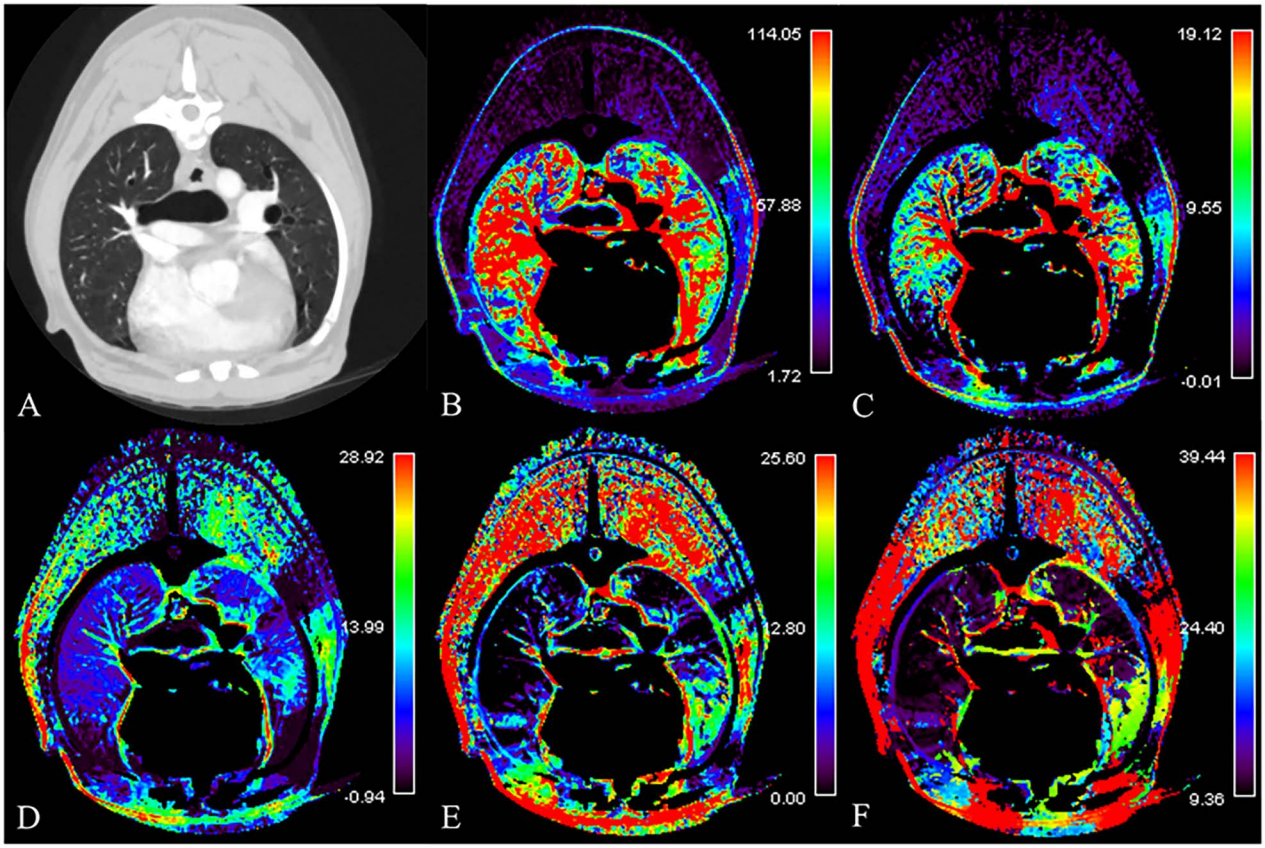

Figure 2—Representative transverse thoracic postcontrast CT (A) and CT perfusion mapping images of pulmonary blood flow (mL/100 mg/min; B), pulmonary blood volume (mL/100 mg; C), mean transit time (s; D), time to maximum of residual function (s; E), and time to peak of tissue (s; F) of the dog described (Figure 1), positioned in sternal recumbency and given iohexol (Omnipaque; GE Healthcare; 300 mg iohexol/mL; 1 mL/kg, IV; 1.5 mL/s). The images were obtained at the level of bronchus bifurcation, with the dog in sternal recumbency. The dog's right is toward the left in all images. A—window width, 1,500 HU; window level, −400 HU; 0.5-mm slice thickness. B–F—The color scale toward the right in each image represents the respective perfusion parameter from low (black) to high (red).

peak time of arterial enhancement (PT_a; seconds), and peak value of arterial enhancement (P_a; HU) were individually measured for each experiment. The interval between PT_a and T_V (PT_a-T_V; seconds) was also calculated **(Figure 1)** and considered as a parameter to evaluate the compatibility of TDC.

The TDC parameters were evaluated under the following conditions: (1) comparison according to the scanning position of sternal and dorsal recumbencies, and (2) comparison according to injection rates of 1.5, 2.5, and 3.5 mL/s.

Measurement and quantitative analysis of perfusion mapping parameters—The perfusion maps were derived from the TDC of each experiment using the Bayesian estimation algorithm based on deconvolution method in the OLEA Sphere software, and each of the following perfusion mapping parameters was measured **(Figure 2)**: relative PBF (mL/100 mg/min), which means the rate of blood flow per unit of tissue; relative PBV (mL/100 mg), which is the volume of blood in the pulmonary circulation relative to tissue mass; MTT (in seconds), which means the average time it takes for blood to pass through the lung tissue; TMAX (in seconds), which is the duration to reach its peak contrast concentration within the tissue; and TTP (in seconds), which means the time for the tissue to reach its maximum contrast enhancement.[7,15]

The regions of each perfusion mapping parameter estimated were selected in the dorsal, middle, and ventral regions of both the right and left lung parenchyma of cranial, middle, and caudal slices and were estimated at each of the conditions according to the scanning position and injection rates. The dorsal region was defined as the area from the carina of the bronchus toward the spine, whereas the middle and ventral regions were located above and below the midpoint of the heart, respectively. All regions of interest were estimated at 3 points of each region to fill each region tightly and avoid overlapping large blood vessels and bronchi, and mean values and SDs of each region were obtained **(Figure 3)**.

The values of each parameter were evaluated under the following conditions: (1) comparison according to bilateral pulmonary parenchyma of the right and left sides; (2) comparison according to the gravitational direction of dorsal, middle, and ventral regions in sternal and dorsal recumbency; (3) comparison according to the scanning position in sternal and dorsal recumbency; and (4) comparison according to the injection rates of 1.5, 2.5, and 3.5 mL/s.

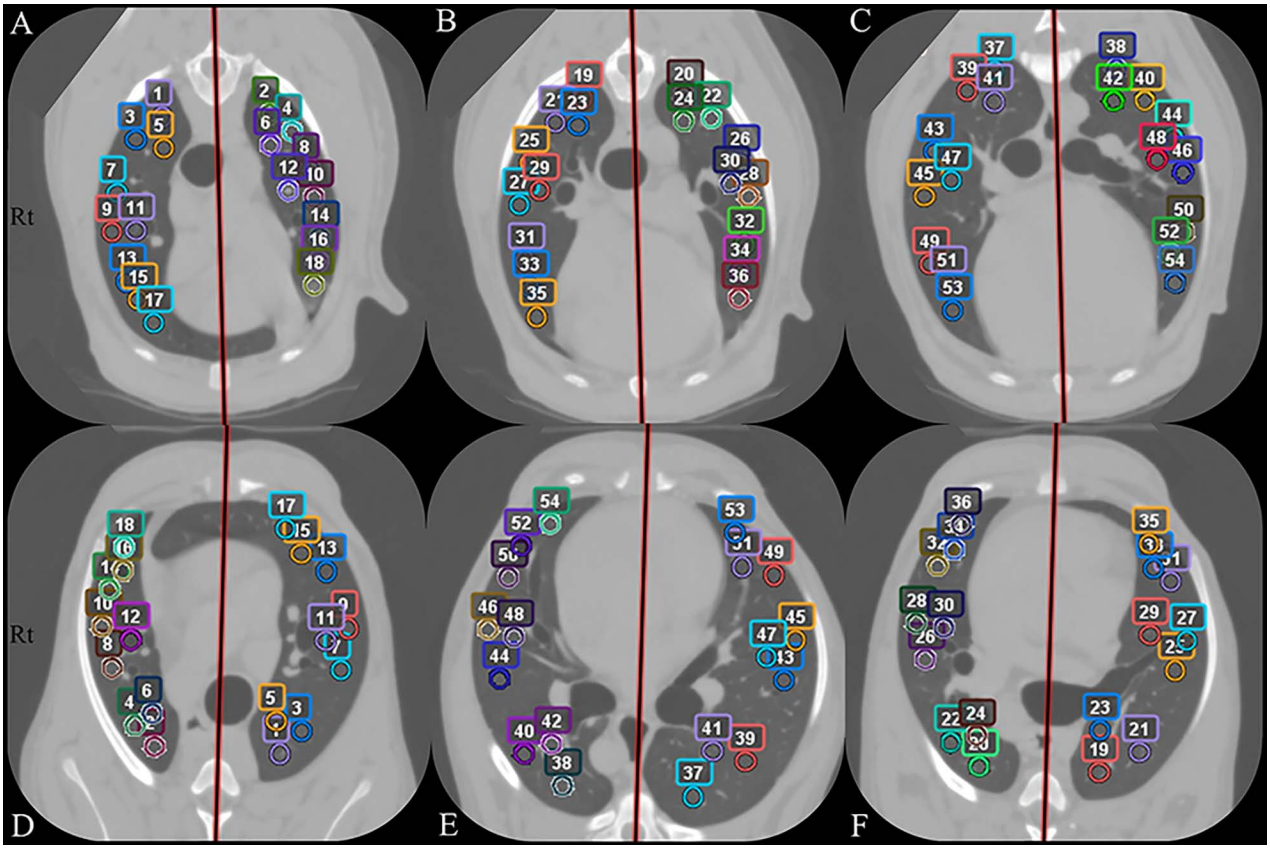

Figure 3—Regions of interest for pulmonary perfusion mapping parameters. All the regions of interest in sternal (A–C) and dorsal recumbency (D–F). The dog's dorsal region is toward the top (A–C) and bottom (D–F) and the dog's right is toward the left in all images. The regions of interest were selected in the dorsal, middle, and ventral regions of both the right and left sides of cranial, middle, and caudal slices.

Statistical analysis

Data are presented as mean values and SD. The Kolmogorov-Smirnov test was individually conducted for all data as a normality test, based on the conditions and the measured variables. To assess TDC parameters based on scanning position, pairwise comparisons between sternal and dorsal recumbency were conducted using the Wilcoxon signed-rank test. Additionally, for the evaluation based on injection rates, the Friedman test and repeated-measures ANOVA were employed, with consideration of normality. Subsequently, the tests were followed by the Wilcoxon signed-rank test and Bonferroni post hoc test for each. The Wilcoxon signed-rank was conducted to evaluate perfusion mapping parameters according to the right and left sides or scanning positions. The Friedman test, followed by the Wilcoxon signed-rank test, was performed to evaluate perfusion mapping parameters based on the gravitational direction of the pulmonary parenchyma in the dorsal, middle, and ventral regions during sternal and dorsal recumbencies or different injection rates.

A *P* value of < .05 was considered statistically significant in Wilcoxon signed-rank tests and repeated-measures ANOVA followed by Bonferroni post hoc tests and Friedman tests. However, the Wilcoxon test, as the post hoc of the Friedman test, was used to compare TDC parameters or perfusion mapping parameters according to the injection rate and to compare perfusion mapping parameters according to gravitational direction, in which a *P* value of < .017 was considered statistically significant. All analyses were performed using Statistical Package for the Social Sciences Statistics, version 29 software (IBM Corp).

Table 1—Comparison of time-density curve (TDC) according to scanning positions.

	Scanning position		
TDC parameters	**Sternal recumbency**	**Dorsal recumbency**	***P* value**
T_v (s)	5.71 ± 0.756	7.14 ± 1.069	.025*
PT_a (s)	6.00 ± 0.000	7.43 ± 2.225	.102
PT_a-T_v (s)	0.29 ± 0.756	0.29 ± 1.799	1.000
P_a (HU)	474.69 ± 78.732	316.48 ± 109.021	.018*

Data are presented as mean ± SD.

P_a = Value of arterial peak enhancement. PT_a = Peak time of arterial enhancement. PT_a-T_v = Difference of PT_a and T_v. T_v = Initiation time of venous outflow.

*P < .05, statistically significant using the Wilcoxon signed-rank test.

Results

Physiological evaluation of animals

All pulmonary CTP experiments were performed without technical errors or adverse effects in any Beagles during or after the experiments. Heart rates remained within the range of 85 to 130 beats/min during CTP scanning. No abnormal regions of the pulmonary parenchyma were observed in any Beagle.

Evaluation of TDC

Comparison according to 2 different scanning positions—The values of the TDC parameters according to the scanning position are listed **(Table 1)**. P_a was significantly lower (P < .05) in dorsal recumbency. The mean values of P_a of dorsal recumbency were close to 300 HU, and the P_a of dorsal recumbency was below 300 HU in 3 of the 7 dogs. T_v was found to be significantly lower (P < .05) in sternal recumbency, but there were no significant differences in PT_a and PT_a-T_v according to the scanning position.

Comparison according to 3 different injection rates in sternal recumbency—The values of the TDC parameters according to the injection rate in sternal recumbency are listed **(Table 2)**. The injection times were significantly decreased (P < .017) while increasing the injection rates, and the highest mean value and SD of injection time were 7.429 ± 1.24 seconds in injection rate at 1.5 mL/s. The PT_a (P < .017) and P_a (P < .05) were significantly lower at an injection rate of 1.5 mL/s than that at 2.5 or 3.5 mL/s. However, there were no significant differences in PT_a and P_a between injection rates of 2.5 and 3.5 mL/s. There were no significant differences in T_v and PT_a-T_v according to the injection rate.

Table 2—Comparison of time-density curve (TDC) according to injection rates in sternal recumbency.

	Injection rate (mL/s)			*P* value			
TDC parameters	**1.5**	**2.5**	**3.5**	**1.5 vs 2.5 vs 3.5**	**1.5 vs 2.5**	**1.5 vs 3.5**	**2.5 vs 3.5**
Injection time (s)	7.43 ± 1.24	4.46 ± 0.75	3.18 ± 0.53	< .001*	< .001‡	< .001‡	< .001‡
T_v (s)	6.86 ± 1.07	5.71 ± 0.76	4.86 ± 1.07	.018†	.102	.038	.083
PT_a (s)	7.71 ± 0.76	6.0 ± 0.00	4.86 ± 1.07	.002†	.014§	.015§	.046
PT_a-T_v (s)	0.86 ± 1.07	0.29 ± 0.76	0.00 ± 1.16	.247			
P_a (HU)	348.03 ± 52.66	484.69 ± 78.73	491.49 ± 112.45	.021*	.048‡	.015‡	1.000

Data are presented as mean ± SD.

P_a = Value of arterial peak enhancement. PT_a = Peak time of arterial enhancement. PT_a-T_v = Difference of PT_a and T_v. T_v = Initiation time of venous outflow.

*P < .05, statistically significant using the repeated measures ANOVA. †P < .05, statistically significant using the Friedman test. ‡P < .05, statistically significant using the repeated measures ANOVA followed by Bonferroni post hoc test. §P < .017, statistically significant using the Friedman post hoc Wilcoxon test.

Evaluation of perfusion mapping parameters

Comparison between the left and right lungs—The PBF, PBV, MTT, TMAX, and TTP values for each scanning position, injection flow rate, and region of the pulmonary parenchyma are presented **(Table 3)**.

In the comparison of the right and left sides of each gravitational region, the PBF of the right side was found to be greater ($P < .05$) than the left side of the dorsal region in sternal recumbency with a flow rate of 3.5 mL/s and less ($P < .05$) than the left side of the ventral region in dorsal recumbency with a flow rate of 2.5 mL/s (Table 3).

The PBV of the right side was greater ($P < .05$) than the left side of the ventral region in sternal recumbency with a flow rate of 1.5 mL/s and less ($P < .05$) than the left side of the middle region with a flow rate of 3.5 mL/s and of the ventral region in dorsal recumbency with a flow rate of 2.5 mL/s (Table 3).

The MTT of the right side was greater ($P < .05$) than the left side of the ventral region in sternal recumbency with a flow rate of 1.5 mL/s (Table 3).

The TMAX of the right side was greater ($P < .05$) than the left side of ventral region in sternal recumbency with a flow rate of 1.5 mL/s but less ($P < .05$) than the left side of the middle region in sternal recumbency with a flow rate of 1.5 mL/s and of both dorsal and middle regions with a flow rate of 3.5 mL/s (Table 3).

The TTP of the right side was less ($P < .05$) than the left side of the middle region in sternal recumbency with a flow rate of 3.5 mL/s and the dorsal region in dorsal recumbency with a flow rate of 2.5 mL/s (Table 3).

Comparison according to the gravitational direction—In the comparison of the dorsal, middle, and ventral regions on the right and left sides, the PBF of the right middle region was less ($P < .017$) than ventral, and the left dorsal region was less ($P < .05$) than middle or ventral in sternal recumbency with a flow rate of 3.5 mL/s. In addition, The PBF of the right dorsal region was greater ($P < .017$) than ventral in dorsal recumbency at a flow rate of 2.5 mL/s (Table 3).

The PBV of the left middle region was greater ($P < .017$) than ventral in sternal recumbency with a flow rate of 1.5 mL/s and the left ventral region was greater ($P < .017$) than dorsal and middle with a flow rate of 3.5 mL/s. Additionally, the PBV of the right side was greater ($P < .017$) in the order of middle, dorsal, and ventral regions with a flow rate of 3.5 mL/s (Table 3).

The MTT of the left ventral region was greater ($P < .017$) than dorsal and middle in sternal recumbency

Table 3—Values and comparison of pulmonary perfusion mapping parameters according to different conditions.

Perfusion mapping parameters	Scanning position	Flow rate (mL/s)	Regions of pulmonary parenchyma					
			Right side			Left side		
			Dorsal	Middle	Ventral	Dorsal	Middle	Ventral
PBF	Sternal recumbency	1.5	74.6 ± 24.6	91.3 ± 36.0§§	81.3 ± 31.2	79.0 ± 39.9	87.5 ± 34.4	69.9 ± 22.1‖
		2.5	70.0 ± 25.5**	77.8 ± 30.1#	83.2 ± 19.6#	64.3 ± 17.9**	82.4 ± 43.1	82.5 ± 25.4
		3.5	68.0 ± 19.1*	61.9 ± 18.4¶	89.6 ± 26.9	54.4 ± 16.6§¶	72.8 ± 27.2	99.6 ± 34.6
	Dorsal recumbency	2.5	84.7 ± 26.6‖	72.5 ± 25.1	63.7 ± 21.6†	83.7 ± 20.7	76.0 ± 28.2	82.2 ± 31.4
PBV	Sternal recumbency	1.5	7.30 ± 2.65	7.12 ± 3.06	9.21 ± 7.21*‖	7.43 ± 3.79	8.66 ± 4.56‖	4.41 ± 4.21‖
		2.5	6.87 ± 3.62	8.13 ± 6.00	12.92 ± 8.81#	6.10 ± 2.50	7.55 ± 4.23	10.28 ± 8.32‖
		3.5	7.67 ± 3.14‡¶	5.09 ± 2.31†¶	16.82 ± 11.10	6.46 ± 2.22¶	9.22 ± 5.97¶	22.46 ± 14.41
	Dorsal recumbency	2.5	7.10 ± 3.69	7.06 ± 3.02	7.61 ± 3.98†	7.64 ± 3.58	6.28 ± 3.35	11.13 ± 5.72
MTT	Sternal recumbency	1.5	5.82 ± 1.81	5.01 ± 1.77	4.99 ± 3.28*‖	5.73 ± 1.89‖	5.90 ± 2.50‖	2.77 ± 2.69‡‡‖
		2.5	5.47 ± 1.84	5.54 ± 2.58	7.14 ± 4.41	4.98 ± 2.10	4.83 ± 2.14	6.42 ± 4.16
		3.5	6.34 ± 2.08‡	4.51 ± 1.79¶	8.52 ± 5.35	5.76 ± 1.76¶	6.33 ± 3.42¶	10.46 ± 5.21
	Dorsal recumbency	2.5	4.70 ± 2.19	5.53 ± 1.72	5.84 ± 2.85	5.14 ± 2.24	4.62 ± 2.16	6.54 ± 2.48
TMAX	Sternal recumbency	1.5	3.90 ± 0.74¶	3.89 ± 1.09†¶	6.38 ± 1.15*	4.35 ± 0.90¶	4.88 ± 0.98	5.54 ± 1.23‡‡‖
		2.5	3.74 ± 0.67¶	4.00 ± 1.25¶**	6.60 ± 1.49	3.76 ± 0.78¶‖	4.45 ± 1.24¶	6.69 ± 1.33
		3.5	4.26 ± 0.90†¶	4.52 ± 0.92†¶	7.05 ± 1.67	4.76 ± 1.04¶	5.09 ± 1.24¶	7.01 ± 1.38
	Dorsal recumbency	2.5	3.97 ± 1.18§¶	4.91 ± 1.18¶	6.52 ± 1.63	4.25 ± 1.08¶	4.73 ± 1.35¶	6.38 ± 1.60
TTP	Sternal recumbency	1.5	14.07 ± 2.85§§	13.48 ± 1.50¶§§	15.94 ± 3.26	17.77 ± 2.68††§§	13.93 ± 1.56	15.46 ± 4.46
		2.5	12.54 ± 3.55¶	12.15 ± 2.83¶#§§	17.10 ± 3.13**	11.68 ± 3.10¶**	12.54 ± 3.20¶**	18.49 ± 6.50
		3.5	10.95 ± 2.13‡¶	9.89 ± 1.83†¶	16.61 ± 7.98	11.63 ± 3.05¶	12.66 ± 5.84¶	17.81 ± 8.21
	Dorsal recumbency	2.5	14.63 ± 3.97†¶	16.01 ± 3.43¶	22.58 ± 6.44	16.53 ± 6.11	15.98 ± 4.09¶	20.76 ± 6.07

Data are presented as mean ± SD. $P < .05$ is considered statistically significant using the Wilcoxon test. $P < .017$ is considered statistically significant using the Friedman post hoc Wilcoxon test.

MTT = Mean transit time (s). PBF = Relative pulmonary blood flow (mL/100 mg/min). PBV = Relative pulmonary blood volume (mL/100 mg). TMAX = Time to maximum (s). TTP = Time to peak (s).

*Significantly higher versus left side ($P < .05$) at same flow rate and position with same region. †Significantly lower versus left side ($P < .05$) at same flow rate and position with same region. ‡Significantly higher versus middle region ($P < .017$) at same flow rate and position with same side. §Significantly lower versus middle region ($P < .017$) at same flow rate and position with same side. ‖Significantly higher versus ventral region ($P < .017$) at same flow rate and position with same side. ¶Significantly lower versus ventral region ($P < .017$) at same flow rate and position with same side. #Significantly higher versus dorsal recumbency ($P < .05$) at same flow rate, side, and region. **Significantly lower versus dorsal recumbency ($P < .05$) at same flow rate, side, and region. ††Significantly higher versus flow rate 2.5 ml/s ($P < .017$) at same position, side, and region. ‡‡Significantly lower versus flow rate 2.5 ml/s ($P < .017$) at same position, side, and region. §§Significantly higher versus flow rate 3.5 ml/s ($P < .017$) at same position, side, and region. ‖‖Significantly lower versus flow rate 3.5 ml/s ($P < .017$) at same position, side, and region.

at a flow rate of 1.5 mL/s. Moreover, at a flow rate of 3.5 mL/s in sternal recumbency, the right middle region was less (P < .017) than dorsal and ventral regions, and the left ventral region was greater (P < .017) than dorsal and middle regions (Table 3).

The TMAX of the ventral regions on both sides was greater (P < .017) than dorsal and middle regions on each side at flow rates of 1.5, 2.5, and 3.5 mL/s in sternal recumbency except the middle region on the left side at a flow rate of 1.5 mL/s. Additionally, TMAX of the right side was greater (P < .017) in the order of dorsal, middle, and ventral regions and of the left ventral region was greater (P < .017) than dorsal and middle regions in dorsal recumbency with a flow rate of 2.5 mL/s (Table 3).

The TTP of the ventral region in sternal recumbency was greater (P < .017) than the middle region on the right side with a flow rate of 1.5 mL/s and greater than the middle and ventral regions on both sides with flow rates of 2.5 and 3.5 mL/s. The TTP of the right middle region was also greater (P < .017) than the dorsal region at a flow rate of 3.5 mL/s. Moreover, in dorsal recumbency at a flow rate of 2.5 mL/s, the TTP of the right ventral region was greater (P < .017) than dorsal and middle regions, and the left ventral region was greater (P < .017) than the middle region (Table 3).

Comparison according to 2 different scanning positions—According to the scanning position for each region of the perfusion mapping parameters (Table 3), PBF in sternal recumbency was greater (P < .05) than dorsal recumbency in the dorsal regions on both sides and less (P < .05) than in the right middle and ventral region. The PBV of the right ventral region in sternal recumbency was greater, and TMAX of the right middle region was less than (P < .05) in dorsal recumbency. TTP in sternal recumbency was less (P < .05) than dorsal recumbency in the right middle, right ventral, left dorsal, and left middle regions. No significant differences were observed in the MTT.

Comparison according to 3 different injection rates—In comparison, according to the injection rate for each region of the perfusion mapping parameters in sternal recumbency, the PBF at a flow rate of 1.5 mL/s in the right middle region was greater (P < .017) than at a flow rate of 3.5 mL/s and at a flow rate of 1.5 mL/s in left ventral regions was less (P < .017) than at a flow rate of 3.5 mL/s (Table 3).

The PBV at a flow rate of 3.5 mL/s was greater (P < .017) than at a flow rate of 1.5 mL/s in each right and left ventral region and at a flow rate of 2.5 mL/s in the left ventral region (Table 3).

The MTT at a flow rate of 1.5 mL/s was less than (P < .017) at a flow rate of 3.5 mL/s in the right and left ventral regions. Additionally, MTT at a flow rate of 1.5 mL/s was also less (P < .017) than at a flow rate of 2.5 mL/s in the left ventral region (Table 3).

The TMAX at a flow rate of 2.5 mL/s in the left dorsal region was less (P < .017) than at a flow rate of 3.5 mL/s. In addition, the TMAX at a flow rate of 1.5 mL/s in the left ventral region was less (P < .017) than at the flow rates of 2.5 and 3.5 mL/s (Table 3).

The TTP at a flow rate of 1.5 mL/s was greater (P < .017) than at a flow rate of 3.5 mL/s in the right dorsal, right middle, and left dorsal regions and at a flow rate of 2.5 mL/s in the left dorsal region. Moreover, the TTP at a flow rate of 2.5 mL/s in the right middle region was greater (P < .017) than at a flow rate of 3.5 mL/s (Table 3).

Discussion

This study aimed to measure the values of perfusion parameters in different regions of the lung parenchyma in dogs, evaluate the effects of the scanning position and contrast medium injection rate on pulmonary perfusion, and present reference ranges of normal perfusion parameters for each condition. For this purpose, lung parenchymal perfusion parameters were measured at different injection rates and scanning positions. No technical errors or adverse effects were observed in any of the dogs. Therefore, the pulmonary perfusion technique can be performed stably, even in small animals.

In the results of the comparison between the left and right sides, the perfusion parameter values of the right side were generally lower than those of the left side in TMAX and TTP. The greater number of lobes and the larger size of the right lung compared to the left suggest that the blood vessels on the right side are likely to be more developed, leading to better perfusion on the right side.[16]

In this study, the PBF of the dorsal region was generally lower than that of the middle and ventral regions in sternal recumbency, and the PBF of the dorsal region was generally higher in dorsal recumbency. Similarly, in previous human studies,[2,17] the PBF in the dorsal region, which is poorly ventilated, was higher than that in the middle and ventral regions in dorsal recumbency. This can prove that ventilation in the dorsal region is poorer than in the middle or ventral regions, even in dogs, and that the PBF in the dorsal region is influenced by changes in position due to gravity direction. However, it is believed that other perfusion parameters are not significantly affected by changes in position. However, another study[18] using dynamic first-pass perfusion CT to measure PBF in Landrace pigs reported that PBF in the dorsal region was the highest in all positions, followed by the middle and ventral regions. This finding is different from the results of this study, where the PBF in the dorsal region was the lowest in sternal recumbency, suggesting that the PBF is influenced by gravity in different positions.

It has been reported that optimal CTP imaging requires strong contrast enhancement of the pulmonary artery, with proper visualization typically achieved at 300 HU or higher in CT angiography in human studies.[19] Based on this consideration, the comparison of P_a values between the 2 positions in this study confirmed that sternal recumbency, considered an appropriate position for scanning, yielded more ideal results. Furthermore, a comparison of perfusion parameters like PBF, PBV, and TTP between the 2 positions revealed higher perfusion,

especially in the middle and ventral regions, in sternal recumbency than in dorsal recumbency. Previous studies[17,20] have reported that in dorsal recumbency, a significant portion of the body weight, including that of the heart, is transferred to the lungs. Consequently, in patients with respiratory failure, sternal recumbency reduces the degree of dependence on mechanical ventilation more effectively than dorsal recumbency.[17,20] Considering these reports, it can be inferred that increased perfusion of the lungs in sternal recumbency contributes to improved ventilation.

To achieve an ideal TDC graph, characterized by the venous phase starting after the arterial peak with complete tissue perfusion and without contrast agent washout, a rapid injection rate is required to ensure that the contrast agent reaches the arterial peak as quickly as possible after injection.[7,21–23] In this study, the mean values of PT_a-T_v for all 3 injection rates were close to 0 second, and no significant differences were observed between the injection rates. Therefore, all 3 injection rates can be evaluated as having TDC graphs close to the ideal form. However, the appropriate contrast agent injection time for evaluating the pulmonary arteries in humans has been reported to be 7 to 10 seconds,[21] and the ideal results were observed at a rate of 1.5 mL/s in this study. When examining the values of the perfusion parameters in this study, the ventral region showed an increase in PBF with increasing injection rate, which is consistent with the results of a previous human study[22] demonstrating an increase in PBF with increasing injection rate. However, the PBF in the dorsal and middle regions decreased with increasing injection rates. While this contradicts findings in human brain CTP studies, where blood flow increases with faster injection rates, there is a report[24] suggesting that excessively rapid injection rates can lead to the underestimation of blood flow. Taking this into consideration, the injection rates of 2.5 and 3.5 mL/s used in this study may be considered too fast and potentially lead to the underestimation of pulmonary perfusion in dogs.

There have been reports that the deconvolution method can provide accurate results even at low-contrast injection rates in brain perfusion CT.[5,25] In this study, the deconvolution method was applied to demonstrate the effect of low-contrast injection rates on pulmonary CTP in healthy Beagles. To the best of our knowledge, this study is the first to provide reference ranges for 5 perfusion mapping parameters of normal pulmonary parenchyma in dogs, considering the location of the pulmonary parenchyma, scanning positions, and contrast injection rates using 160-slice multidetector CT. The findings of this study are expected to serve as a foundation for future studies aimed at evaluating pulmonary parenchymal diseases.

This study had several limitations. First, the evaluation was conducted by a single observer, and the differences between evaluations by different observers were not assessed. However, several studies[26,27] involving multiple observers have reported high interobserver reliability for CTP among skilled radiologists. Second, perfusion mapping parameters were measured as estimated values using TDC analysis, which may differ from the actual pulmonary perfusion values. However, the method used in this study was consistent with previous CTP studies,[5,25] and the analysis was conducted assuming that the estimated values were similar to the actual perfusion values. Third, this study used single-syringe injectors for contrast medium injections. The result is a diluted, delayed peak enhancement compared with the result obtained using dual-syringe injectors that inject contrast medium followed by a saline chase.[28] However, several CTP studies[5] have used single-syringe injectors in veterinary medicine, and this study acquired sufficient results for the peak enhancement time using single-syringe injectors. Finally, although the weight ranges of the participants used in this study were narrow, they had different weights. Therefore, the amount of contrast agent used varied among the patients, and the impact of this difference on contrast agent injection time was not considered. Since contrast agent injection timing can influence proper visualization of the pulmonary artery,[21] further research is needed to investigate the quantity and injection time of the contrast agent over a wider range of weights.

This study demonstrated that a low contrast agent injection rate of 1.5 mL/s and sternal recumbency position are appropriate for CTP imaging of the lungs in dogs. Additionally, this study provides reference ranges for perfusion parameters that vary depending on the location of the pulmonary parenchyma and variable conditions in veterinary medicine. Based on these results, we believe that this study could be useful for the acquisition and application of pulmonary CTP images for the differential diagnosis of various lung diseases in small-breed dogs.

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References

1. Arimbrakkunnan M, Garg PK, Khera PS, et al. Computed tomography perfusion (CTP) in primary lung cancer: results from a tertiary care centre. *Lung India.* 2022;39(3): 220–229. doi:10.4103/lungindia.lungindia_365_21
2. Sun H, Gao F, Li N, Liu C. An evaluation of the feasibility of assessment of volume perfusion for the whole lung by 128-slice spiral CT. *Acta Radiol.* 2013;54(8):921–927. doi:10.1177/0284185113490151
3. Kurz KD, Ringstad G, Odland A, Advani R, Farbu E, Kurz MW. Radiological imaging in acute ischaemic stroke. *Eur J Neurol.* 2016;23(suppl 1):8–17. doi:10.1111/ene.12849

4. Kambadakone AR, Sahani DV. Body perfusion CT: technique, clinical applications, and advances. *Radiol Clin North Am.* 2009;47(1):161–178. doi:10.1016/j.rcl.2008.11.003
5. Choi W, Ko J, Kim J, Cho CH, Kim J, Eom K. Optimal injection rate and catheter size for brain perfusion computed tomography using non-ionic contrast medium in clinically normal Beagles. *Am J Vet Res.* 2023;84(5):ajvr.22.12.0211. doi:10.2460/ajvr.22.12.0211
6. Lee SK, Kim C, Yoon S, Choi J. Effect of contrast medium injection rate on computed tomography-derived renal perfusion estimates obtained with the maximum slope method in healthy. *Am J Vet Res.* 2019;80(2):168–173. doi:10.2460/ajvr.80.2.168
7. Kishimoto M, Tsuji Y, Katabami N, et al. Measurement of canine pancreatic perfusion using dynamic computed tomography: influence of input-output vessels on deconvolution and maximum slope methods. *Eur J Radiol.* 2011;77(1):175–181. doi:10.1016/j.ejrad.2009.06.016
8. Kloer TB, Rao S, Twedt DC, Marolf AJ. Computed tomographic evaluation of pancreatic perfusion in healthy dogs. *Am J Vet Res.* 2020;81(2):131–138. doi:10.2460/ajvr.81.2.131
9. Amaha T, Ishigaki K, Ishikawa C, et al. Effect of different contrast medium injection protocols for analysis of hepatic computed tomography perfusion in healthy dogs. *Am J Vet Res.* 2022;83(6):ajvr.21.08.0125. doi:10.2460/ajvr.21.08.0125
10. Li Y, Yang ZG, Chen TW, Deng YP, Yu JQ, Li ZL. Whole tumour perfusion of peripheral lung carcinoma: evaluation with first-pass CT perfusion imaging at 64-detector row CT. *Clin Radiol.* 2008;63(6):629–635. doi:10.1016/j.crad.2007.12.012
11. Ng CS, Chandler AG, Wei W, et al. Reproducibility of perfusion parameters obtained from perfusion CT in lung tumors. *AJR Am J Roentgenol.* 2011;197(1):113–121. doi:10.2214/AJR.10.5404
12. Warwick H, Guillem J, Batchelor D, et al. Imaging findings in 14 dogs and 3 cats with lobar emphysema. *J Vet Intern Med.* 2021;35(4):1935–1942. doi:10.1111/jvim.16183
13. Zhu B, Zheng S, Jiang T, Hu B. Evaluation of dual-energy and perfusion CT parameters for diagnosing solitary pulmonary nodules. *Thorac Cancer.* 2021;12(20):2691–2697. doi:10.1111/1759-7714.14105
14. Jimenez-Juan L, Mehrez H, Dey C, et al. Arterial input function placement effect on computed tomography lung perfusion maps. *Quant Imaging Med Surg.* 2016;6(1):25–34. doi:10.3978/j.issn.2223-4292.2016.01.05
15. Boutelier T, Kudo K, Pautot F, Sasaki M. Bayesian hemodynamic parameter estimation by bolus tracking perfusion weighted imaging. *IEEE Trans Med Imaging.* 2012;31(7):1381–1395. doi:10.1109/TMI.2012.2189890
16. Dyce KM, Sack WO, Wensing CJ. The lungs, the respiratory apparatus, general anatomy. In: *Textbook of Veterinary Anatomy.* 4th ed. WB Saunders Co; 2009:160–162.
17. Rampon GL, Simpson SQ, Agrawal R. Prone positioning for acute hypoxemic respiratory failure and ARDS: a review. *Chest.* 2023;163(2):332–340. doi:10.1016/j.chest.2022.09.020
18. Kay FU, Beraldo MA, Nakamura MAM, et al. Quantitative dual-energy computed tomography predicts regional perfusion heterogeneity in a model of acute lung injury. *J Comput Assist Tomogr.* 2018;42(6):866–872. doi:10.1097/RCT.0000000000000815
19. Prokop M. Multislice CT angiography. *Eur J Radiol.* 2000;36(2):86–96. doi:10.1016/s0720-048x(00)00271-0
20. Liu S, Margulies SS, Wilson TA. Deformation of the dog lung in the chest wall. *J Appl Physiol (1985).* 1990;68(5):1979–1987. doi:10.1152/jappl.1990.68.5.1979
21. Bae KT. Intravenous contrast medium administration and scan timing at CT: considerations and approaches. *Radiology.* 2010;256(1):32–61. doi:10.1148/radiol.10090908
22. Hu CH, Wu QD, Hu XY, Fang XM, Zhang TH, Ding Y. Hemodynamic studies on brain CT perfusion imaging with varied injection rates. *Clin Imaging.* 2007;31(3):151–154. doi:10.1016/j.clinimag.2007.01.008
23. Leiva-Salinas C, Provenzale JM, Wintermark M. Responses to the 10 most frequently asked questions about perfusion CT. *AJR Am J Roentgenol.* 2011;196(1):53–60. doi:10.2214/AJR.10.5705
24. Wintermark M, Maeder P, Thiran JP, Schnyder P, Meuli R. Quantitative assessment of regional cerebral blood flows by perfusion CT studies at low injection rates: a critical review of the underlying theoretical models. *Eur Radiol.* 2001;11(7):1220–1230. doi:10.1007/s003300000707
25. Eastwood JD, Provenzale JM, Hurwitz LM, Lee TY. Practical injection-rate CT perfusion imaging: deconvolution-derived hemodynamics in a case of stroke. *Neuroradiology.* 2001;43(3):223–226. doi:10.1007/s002340000528
26. Popiela T, Pera J, Chrzan R, Włoch D, Urbanik A, Słowik A. Interobserver agreement in perfusion computed tomography evaluation in acute ischaemic stroke. *Neurol Neurochir Pol.* 2008;42(5):391–395.
27. Abul-Kasim K, Strömbeck A, Maly P, Overgaard A, Persson E, Sundgren PC. Interobserver and intraobserver agreement in the evaluation of CT perfusion in ischemic stroke. *Funct Neurol.* 2009;24(3):139–145.
28. Auler MA, Heagy T, Aganovic L, Brothers R, Costello P, Schoepf UJ. Saline chasing technique with dual-syringe injector systems for multi-detector row computed tomographic angiography: rationale, indications, and protocols. *Curr Probl Diagn Radiol.* 2006;35(1):1–11. doi:10.1067/j.cpradiol.2005.10.001

Supplementary Materials

Supplementary materials are posted online at the journal website: avmajournals.avma.org