**Factors influencing enhancement timing in a triple-phase abdominal CT angiography protocol in dogs**

Aditya C. Davé, DVM, DACVR*; Christopher P. Ober, DVM, PhD, DACVR2; Aaron Rendahl, PhD3

1Idexx Telemedicine, Clackamas, OR
2Department of Veterinary Clinical Sciences, College of Veterinary Medicine, University of Minnesota, St. Paul, MN
3College of Veterinary Medicine, University of Minnesota, St. Paul, MN

*Corresponding author: Dr. Davé (acdave87@gmail.com)

https://doi.org/10.2460/ajvr.21.03.0031

**OBJECTIVE**
To evaluate the enhancement accuracy of a triple-phase abdominal CT angiography (CTA) protocol in dogs and explore the patient, scan, and contrast parameters associated with accuracy of enhancement.

**ANIMALS**
233 client-owned dogs that underwent routine abdominal CTA.

**PROCEDURES**
During each CTA study, the subjective timing accuracy (early, ideal, late) of the 3 obtained vascular phases (arterial, venous, delayed) was scored by consensus (2 reviewers) at 4 target organs (liver, pancreas, left kidney, and spleen). These scores were evaluated for statistical associations with 21 study variables (patient, scan, and contrast medium). The objective enhancement (HU) for each target organ was also compared statistically with subjective timing accuracy scores and the study variables.

**RESULTS**
The study protocol performed best for the pancreas, moderately for the liver, and worse for the spleen and left kidney. Measurements of scan length and time were associated positively with phase lateness for most target organs and phases. Increased heart rate was the most significant patient factor associated positively with phase lateness within the liver (all phases), pancreas (arterial and venous phases), and kidney (arterial phase). Contrast medium variables were less associated with timing accuracy in this protocol. Objective enhancement (HU) correlated poorly with subjective phase timing accuracy and study variables.

**CLINICAL RELEVANCE**
Scan time, scan length, and heart rate were the predominant variables contributing to lateness in this canine abdominal CTA protocol. The findings of this exploratory study may aid in protocol adjustment and choice of included anatomy for dogs undergoing routine abdominal CTA.

Computed tomography angiography (CTA) has gained widespread acceptance as a powerful diagnostic tool in evaluating abdominal disease in veterinary patients. Multidetector helical technology permits rapid scanning of multiple vascular phases within a single study, and this has facilitated the application of CTA for assessment of lesions associated with vasculature,1-7 discrimination of benign from neoplastic parenchymal lesions,8-12 as well as evaluation of numerous other clinical scenarios.13-21

3-D reconstructions based on CTA also serve as a clinical tool for characterization of vasculature and associated lesions, and requires adequate and precise vascular enhancement.1,2,22

The introduction of CTA into veterinary medicine has also led to challenges in developing scanning and contrast administration protocols that result in adequate synchronization between desired vascular phases and CT data acquisition.14,23-26 This challenge arises because the timing and degree of vascular enhancement in CTA is dependent on dynamic interactions between patient, contrast medium administration, and CT scan–associated factors.23-26 The rapid acquisition times associated with advancements in multidetector CT have also shortened the temporal window for capturing a desired vascular phase, further compounding this challenge.23-26 As a result, discrepancies between the desired and acquired vascular phases are common and have been encountered with many described veterinary CTA protocols.8,10,13,15,27 If precise synchronization between enhancement of the vascular phase of interest and acquisition of CT data is not achieved, this may negate the benefits of CTA relative to conventional contrast CT.23-26
At our institution, triple-phasic (arterial, venous, and delayed) CTA is performed for most routine abdominal CT scans. This protocol relies on a bolus tracking technique for arterial scans and fixed-time delays for the venous and delayed (parenchymal) phases. Although this approach is less technically challenging and requires less contrast medium than test bolus techniques, it has the disadvantages of less defined vascular phases, limited tailoring to organ of interest, and greater influence of patient variability. Because the accurate enhancement of vascular phases is vital to the diagnostic utility of CTA, a characterization of the parameters that contribute to inadequate enhancement would be useful if a fixed-time approach is applied routinely to highly variable veterinary patients.

The primary objectives of this study were to evaluate in dogs the overall accuracy of a standardized triple-phase CTA protocol with fixed-time venous and delayed phases, and to explore which patient, contrast medium, and scan parameters most contributed to the accuracy of vascular phase achieved. A secondary exploratory objective of this study was to assess whether an objective criterion (HU) was correlated with subjective timing accuracy and study variables. We hypothesized that patient body weight, heart rate (HR), and study type (ie, inclusion of additional anatomic regions) would be the most significant factors associated with enhancement timing accuracy.

Materials and Methods

Animals

For this retrospective exploratory study, the University of Minnesota College of Veterinary Medicine picture archiving and communication system was searched for client-owned canine patients undergoing standard protocol triple-phase abdominal CTA at the University of Minnesota Veterinary Medical Center between October 2012 and August 2016. All studies were initially evaluated for quality and pathology by a single reviewer (ACD). A pathology rank was recorded for each patient: 0, normal scan; 1, only incidental lesions present; 2, only thoracic disease present; 3, abdominal disease present but not affecting the organs of interest (liver, spleen, left kidney, or pancreas); 4, any vascular abnormalities present; or 5, any pathology within the organs of interest. Patients with a pathology rank of 4 or 5 were excluded from the study.

CTA procedures

All dogs were sedated or anesthetized for CT under direct supervision by the University of Minnesota anesthesia service. CTA scans were performed with a 64-slice CT scanner (Toshiba Aquilion 64 CFX CT). The protocol for all CTA scans consisted of precontrast images and postcontrast images in the arterial, venous, and delayed phases. Patients were placed in either dorsal or ventral recumbency, and transverse images of the abdomen were obtained at a 1.0-mm slice thickness and a 0.8-mm slice interval, and reconstructed into a 2-mm slice thickness by a 2-mm slice interval. Additional standard scanning parameters included a rotation time of 0.5 second, standard pitch (pitch factor = 0.828), 120 kVp, and a variable mAs (20 to 200 mAs) autocalculated by dose reduction software. Ioversol (770 mg iodine/kg) followed by a 5-mL saline (0.9% sodium chloride) solution flush was administered intravenously (IV) using a dual-head power injector without bolus shaping at a standardized rate based on the patient’s body weight (< 11.3 kg = 1.5 mL/s, 11.4 to 22.6 kg = 2.5 mL/s, 22.7 to 45.3 kg = 3.0 mL/s, 45.4 to 90.7 kg = 3.5 mL/s, and > 90.8 kg = 4.0 mL/s). Pressure was adjusted based on flow rate up to a maximum of 2,240 kPa. Bolus tracking of an aortic region of interest (placed at the level of the diaphragm) with a threshold at 180 HU was used to trigger the arterial scan. Venous and delayed phase images were subsequently acquired at 35 and 90 seconds after the start of arterial scan, respectively.

The following parameters were recorded from the anesthesia record immediately after the CT scan: body weight (kilograms) as assessed by the anesthesiology service prior to induction; HR (beats per minute) as measured immediately prior to precontrast scan; systolic, diastolic, and mean arterial blood pressure (millimeters of mercury) as measured immediately prior to precontrast scan; catheter size (gauge); catheter site (saphenous or cephalic); recumbency (dorsal or ventral); and degree of anesthesia (sedated or general). Sedated patients were defined as those who received only injectable anesthetic agents (including total IV anesthesia); anesthetized patients were defined as those maintained under inhalant anesthesia. Additional contrast and scan parameters including total contrast medium volume (milliliters), contrast medium administration time (seconds), contrast medium flow rate (milliliters per second), scan length (centimeters), study type (abdomen, thorax/abdomen, or thorax/pelvis), total scan time (seconds), included thorax length (centimeters), included thorax time (seconds), included abdomen length (centimeters), included abdomen time (seconds), included pelvis length (centimeters), and included pelvis time (seconds) were recorded after the scan from the CT workstation.

Subjective image evaluation

Two reviewers, a board-certified radiologist (CPO) and a resident in the 3rd year of a veterinary radiology training program (ACD), reviewed each CT scan using DICOM image analysis software. Images were reviewed in a soft tissue window (width, 500 HU; level, 70 HU) in transverse and reconstructed sagittal and dorsal planes. Reviewers were blinded to other patient and scan data. For the CTA studies, the accuracy of vascular phase timing (early, ideal, late) for the 3 vascular phases (arterial, venous, delayed) was assigned by consensus for 4 target organs (liver, spleen, left kidney, pancreas). A standardized rubric (Supplementary Appendix S1 and S2) was used for all patients based on clinical judgment and published
The presence or absence of streamlining\textsuperscript{18} within the caudal vena cava was also recorded after initial image review.

**Objective image evaluation**
Quantitative measurements were performed by a single reviewer (ACD). For each scan, mean attenuation (HU) was recorded once using a circular region of interest (ROI) with electronic calipers at all phases (precontrast, arterial, venous, delayed) at the following locations: liver (aorta, hepatic artery, hepatic vein, intrahepatic portal vein, portal vein, caudal vena cava, hepatic parenchyma at the periphery of the right lateral lobe), spleen (splenic artery, splenic vein, splenic parenchyma), left kidney (renal artery, renal vein, cortex, medulla, pelvis), and pancreas (pancreaticoduodenal artery, pancreaticoduodenal vein, pancreatic parenchyma). ROI size was not standardized among patients, but an attempt was made to place ROIs within a uniform location and to avoid overlapping with other structures.

**Statistical analysis**
Statistical analyses were selected and performed by a statistician (AR) using commercially available software (R Core Team 2017; R Foundation for Statistical Computing). A statistical power analysis was performed for sample size estimation. For a binary predictor variable, an estimated sample size of \( n = 200 \) was determined to be adequate to detect a Cohen's \( \text{d} \) effect size of 0.22 with 80% power at the .05 significance level. As an example, this corresponds to an increase in the proportion early from 25% to 43%, and a corresponding decrease for the proportion late.

For univariate analysis, to evaluate each vascular phase at each organ of interest, ordered logistic regressions were performed with the 3 levels of subjective accuracy of vascular phase timing as the response and each study variable in turn as the explanatory variable. Variables with a \( P \) value \( \leq .05 \) were considered statistically significant. Additional analyses were performed to assess for potentially correlated study variable predictors that may introduce bias. The Welch 2-sample \( t \) test was performed to assess for a significant difference in HR between sedated and anesthetized patients. Pearson product-moment correlation and Spearman rank correlation tests were performed to assess for linear and nonparametric associations, respectively, between body weight and HR. A \( P \) value \( \leq .05 \) was considered statistically significant.

A multivariate model was built using the Bayesian information criterion (BIC). Study variables were added or removed from the model predicting vascular accuracy for each organ and phase until changing the model by one variable did not reduce the BIC. Order was determined in a stepwise manner based on the degree of improvement in the BIC. The significance of each variable in each final model after accounting for all other included variables was assessed with a likelihood ratio test, and \( P \) values were reported. Only scans with a complete study variable data set \( (n = 202) \) were evaluated in this model. To avoid correlated predictors, the measures of thorax time, abdomen time, and pelvis time were removed from the model (based on the direct linear relationship between these and corresponding length variables). Variables were considered significant with a \( P \) value \( \leq .05 \).

Objective HU data for each organ and phase were compared with subjective vascular phase timing using univariate ANOVA for each objective variable separately, with the subjective score as the explanatory variable. To assess whether these objective HU data were associated with the study variables, univariate regression with a quadratic fit (for continuous study variables) and ANOVA models (for categorical study variables) were performed. Adjusted \( R^2 \) values were reported.

**Results**
Of the 894 dogs that underwent abdominal CT during the period evaluated for this retrospective study, 233 met criteria for inclusion and were enrolled. Basic data recorded for enrolled patients included body weight (range, 1.4 to 69.4 kg; mean, 26.3 kg), HR (range, 29 to 180 beats/min; mean, 88.4 beats/min), systolic arterial blood pressure (range, 55 to 180 mm Hg; mean, 108.3 mm Hg), diastolic arterial blood pressure (range, 24 to 105; mean, 57.3 mm Hg), and mean arterial pressure (range, 32 to 130 mm Hg; mean, 75.3 mm Hg).

Contrast medium variables recorded for enrolled patients included contrast medium flow rate (range, 1 to 3.5 mL/s; mean, 2.5 mL/s), contrast medium administration time (range, 3 to 43 seconds; mean, 20 seconds), and total volume of contrast medium (range, 3 to 153 mL; mean, 57 mL). Enrolled dogs had study types that included abdomen only (29 patients), thorax and abdomen (137 patients), abdomen and pelvis (20 patients), and thorax, abdomen, and pelvis (47 patients). A total of 206 patients were anesthetized for CT scan and 27 patients were sedated. Overall, 142 scans were performed with the patient in dorsal recumbency; 91 scans were performed with the patient in ventral recumbency. A total of 200 patients had a cephalic catheter placed and 33 patients had a saphenous catheter placed. Enrolled dogs had a pathology rank of 0 (31 patients), 1 (29 patients), 2 (106 patients), or 3 (67 patients). Enrolled dogs had catheter sizes of 18 gauge (51 patients), 20 gauge (144 patients), and 22 gauge (18 patients). Thirty-one dogs had missing variable data points that included systolic blood pressure (5 patients), diastolic blood pressure (10 patients), mean arterial pressure (13 patients), and catheter size (20 patients).

A plot of the distribution of the subjective timing accuracy score for each organ and phase was created (**Figure 1**). On univariate analysis, ordered logistic regression detected variables contributing significantly to subjective vascular timing accuracy for each organ and phase (**Supplementary Table S1**). The significant variables in order of prevalence for all
organs and phases (No. of organ phases for which this variable was significant/Total number of study organ phases) were HR (75%, 9/12); scan time (67%, 8/12); study and thorax time (both 58%, 7/12); included thorax length scanned (50%, 6/12); field of view (33%, 4/12); abdomen time, mean arterial pressure, pathology rank, and systolic blood pressure (each 25%, 3/12); contrast time, contrast flow rate, volume contrast, degree of anesthesia, and ventral recumbency (each 17%, 2/12); and body weight, streamlining, and diastolic blood pressure (each 8%, 1/12). Catheter size, catheter site, pelvis length, and pelvis time were not significant for any organ or phase. All significant variables correlated positively with scan lateness except for the presence of streamlining (spleen delayed) and contrast time (liver delayed), which correlated negatively with scan lateness. In other words, an increase in any of the positively correlated variables was associated with the subjective scan timing being assessed as later than ideal for various vascular phases in the assessed organs. As an example, Figure 2 displays proportions of subjective phase timing evaluated in univariate analysis for one study variable (HR) during the venous phase at the 4 target organs and the organ-specific relationship of timing accuracy to study parameters. The Welch 2-sample t test did not demonstrate a significant (P = .98) difference in the HR of sedated patients (mean HR, 88.7 beats/min) and anesthetized patients (mean HR, 88.4 beats/min). The Pearson produce moment-correlation (P = .64) and Spearman rank correlation (P = .78) did not indicate a significant relationship between body weight and HR in our study cases.

For multivariate analysis of subjective vascular timing, BIC models were created for each organ and phase. Significant variables for each organ phase and their step in the BIC model were tabulated (Supplementary Table S2). Due to model restrictions, the 31 patients with missing variable data points were excluded from multivariate analysis. Significant variables were incorporated into models for all organs and phases apart from the splenic venous and splenic delayed phases for which the model did not detect significant variables contributing to timing accuracy. Significant variables detected in multivariate analysis in order of model prevalence included HR (58%, 7/12), thorax length (42%, 5/12), body weight (16%, 2/12), and study, field of view, recumbency, and contrast flow rate (each 8%, 1/12).

ANOVA comparing objective measurements (HU) with subjective vascular timing score as the predictor revealed the highest adjusted R² values for hepatic vein venous phase (0.54), portal branch arterial phase (0.46), portal vein arterial phase (0.46), portal branch venous phase (0.36), left renal vein arterial phase (0.35), pancreaticoduodenal vein venous phase (0.32), portal vein venous phase (0.32), and pancreaticoduodenal vein arterial phase (0.32). The remaining adjusted R² values were < 0.3. Models comparing HU with study data (quadratic fit for continuous variables and ANOVA for categorical variables) resulted in the highest adjusted R² values for left renal vein delayed phase with abdomen length (0.33) and volume contrast (0.30). The remaining R² values for correlation of study variables and HU were < 0.3.
Discussion

This study detected variables influencing the accuracy of vascular phase timing within the triple-phase CTA study protocol, as hypothesized. HR was the most frequent patient variable influencing accuracy in both univariate (83% of vascular phases) and in multivariate (70% of vascular phases) analysis. Although not specifically assessed, cardiac output is related linearly to HR and is described as the most important patient factor affecting the timing of contrast enhancement, as a reduction in cardiac output results in a linear delay in time of contrast bolus arrival and peak enhancement.\textsuperscript{23,24,26,29} The increased probability of CT scan lateness associated with increased HR detected in this study may therefore reflect imaging after peak enhancement in patients with higher HRs and associated higher cardiac outputs. The remaining patient variables were incorporated less frequently into the multivariate model, with the next most common variable, body weight, associated positively with lateness only in the venous phases of the liver and left kidney. The absence of a more significant role of body weight may be in agreement with a recent study\textsuperscript{28} comparing abdominal CTA protocols wherein body weight had no effect on image quality. This finding may also be unsurprising as, although body weight is the most important patient factor affecting the magnitude of vascular enhancement, the timing of contrast enhancement is unaffected by body weight, and the study protocol reported herein may have accounted sufficiently for the impact of body weight by adjusting contrast volume and contrast flow rate proportionally to body weight.\textsuperscript{14,23,24,26} The relationship of body weight to renal and hepatic venous phase latency is less clear because body weight has an inverse relationship to the magnitude of peak contrast enhancement,\textsuperscript{24,26} and increases would be expected to result in earlier rather than later subjective scoring of timing accuracy if they were a result of this relationship, as supported by a recent veterinary study.\textsuperscript{30} This may suggest that the increased lateness of CT scans associated with heavier body weights may be the result of other factors, such as the relationship between body weight and patient size (influencing length of scan).

Ventral recumbency was associated with increased lateness compared with dorsal recumbency, and this was significant for both univariate and multivariate models for the pancreas delayed phase and in the univariate model for the pancreas (venous phase) and left kidney (arterial phase). The nature of this relationship is unclear, although one consideration is that scans performed in ventral recumbency were performed more frequently in unstable patients and related hemodynamic factors could affect the timing of enhancement (such as tachycardia or decreased blood volume). A similar relationship could explain the univariate significance of increased phase lateness with higher pathology rank for the left kidney (arterial phase), liver (venous phase), and pancreas (delayed phase).

Figure 2—Proportions of subjective phase-timing accuracy scores (1 = early, 2 = ideal, and = 3 late) for the explanatory study variable heart rate (HR) during the venous phase for the 4 target organs. \(P\) values from univariate ordered logistic regression are reported.
The remaining patient variables (systolic blood pressure, diastolic blood pressure, mean arterial pressure, degree of anesthesia) were not significant in the multivariate models and may play a lesser role in explaining phase lateness when accounting for other related variables.

Among scan variables, longer scan times and larger lengths were associated frequently and significantly with an increased probability of phase lateness on univariate analysis. This relationship is likely explained by protocol design with fixed timings, a standard bolus trigger centered at the aorta, and a craniocaudal direction of scan. Scanning in the same directional flow of contrast medium in this manner results in improved contrast enhancement efficiency but necessitates moving downstream at an adequate rate without falling behind the peak enhancement.24 In scans with a larger scan length, the increased time delay before reaching the abdominal organ of interest would unsurprisingly result in phase-lateness from falling-behind the contrast bolus. With the fixed CT speed in the study protocol, the linear relationship of scan time with scan length likely accounts for the significance of both these variables in univariate analysis. Among scan variables, thorax length (42%) and, less frequently, study (8%) and field of view (8%) were incorporated into the multivariate BIC model, suggesting that, when accounting for related variables, thorax length was the more important scan variable contributing to lateness compared with other scan variables.

Contrast medium variables were less predictive of phase timing in this study protocol, with the variables contrast medium time, contrast medium flow rate, contrast medium volume, and streamlining reaching significance in 17% of phases in the univariate analysis. The only contrast medium variable incorporated into the multivariate model was contrast medium flow rate for the pancreas delayed phase. This finding is consistent physiologically because faster injection times result in earlier enhancement and a shortened temporal window of enhancement.24 The overall scarcity of significant contrast medium parameters in the multivariate analysis could reflect protocol design because all contrast medium variables except streamlining were all related directly or indirectly to body weight. In the stringent BIC model, inherent collinearity of contrast medium variables with body weight may have dampened the relative impact of contrast medium variables. The lesser impact of contrast medium variables may alternatively mirror the overall less significant impact of body weight to enhancement timing, particularly as both body weight and contrast medium variables were less commonly significant in the univariate model, without the potential impacts of collinearity.

When evaluating the overall accuracy of the study protocol, the pancreas had the greatest phase timing accuracy comparatively: arterial, 82% ideal; venous, 84% ideal; and delayed, 87% ideal. The greater accuracy of the pancreatic phases could be explained by the nonconvoluted and relatively short vascular supply of the pancreas for which the temporal pattern of enhancement follows that of the abdominal aorta,15,24 which was used for triggering bolus tracking. This could suggest that the current protocol may be adequate for most cases of pancreatic imaging without the need for large adjustments. Although timing accuracy for all liver phases was most commonly ideal, there were large proportions of lateness for all phases: arterial phase, 74% ideal and 20% late; venous phase, 51% ideal and 43% late; and delayed phase, 54% ideal and 42% late. The relatively greater timing accuracy of the arterial phase of the liver may be a result of a similar cause as the pancreatic phases, given the close relationship of hepatic arterial enhancement to that of the abdominal aorta, whereas enhancement in the portal and delayed phases of the liver is more variable and dependent on contrast medium in venous return (forming 80% of hepatic blood flow) from splanchnic, pancreatic, and splenic sources.1,3,24,31 Even more dramatically than the liver, left renal phase timing was often late in our protocol: arterial phase, 29% ideal and 70% late; venous phase, 21% ideal and 79% late; and delayed phase, 14% ideal and 86% late. This degree and consistency of lateness may suggest that the time delays used in this standardized protocol are inherently excessive for this organ. In one study in Beagles,17 optimal time delays for phases equivalent to the current venous and delayed phases were 10 seconds and 44 seconds, respectively. As the time delays in our study were 15 and 90 seconds (with the potential for even greater effective delays in some patients imaged with a larger scan length or addition of the thorax), this may be an unsurprising consequence of the use of a one-size-fits-all abdominal protocol. Adjustment of scan delays depending on primary organ of interest and imaging question may be a method to address this if a standardized abdominal protocol is used. Timing accuracy was high for the spleen arterial phase (93% ideal); but, in contrast to the other study organs, the splenic venous and delayed phases were most frequently early: venous, 31% ideal and 67% early; and delayed, 44% ideal and 55% early. This finding may also have been a predictable consequence of the less optimized time delays in the study protocol. For example, compared with time delays in a recently published splenic CTA report21 (20 seconds for the venous phase and 3 to 5 minutes for the delayed phase), the relatively shorter time delays in our study protocol would likely account for this earliness. The univariate model found contrast streamlining to be a predictor for excessive earliness during the splenic delayed phase, which is presumably associated with secondary inadequate enhancement from poor admixture.18 However, the multivariate model failed to find variables associated with the relative earliness of the splenic venous and delayed phases. The absence of significant findings could reflect an inadequate case number and/or that splenic enhancement may be more related to other unmeasured or standardized variables (such as the programmed time delays). Adjusting time delays (i.e., scanning later or performing additional delayed
scans if the spleen is the organ of interest) and/or performing a more optimized scan could be necessary if enhancement accuracy of later splenic phases is of vital diagnostic importance.

Based on multivariate analysis, a measure of scan length (thorax length and study) contributed frequently to lateness for the liver and left kidney. One method to address this impact could be the adjustment of scan length to the smallest necessary for evaluation of the organs of interest, as described in most dedicated published veterinary protocols for CTA of the liver\textsuperscript{1,3,4} and kidney,\textsuperscript{17} but this would not be applicable to CTA performed for routine evaluation of the entire abdomen. The specific incorporation of thoracic length and study into the model for scan accuracy in the liver and left kidney could also suggest that adjustment of study choice (ie, a conscious decision to exclude the thorax or pelvis from abdominal scans) may also be a consideration for improving scan timing accuracy. At our institution, the thorax is added frequently for staging or other purposes by the requesting clinician (as in 78% of the current study cases) and is performed contiguously with the abdomen. However, the current findings could suggest that incorporation of the thorax in abdominal CTA studies may affect the accuracy of phase timing adversely, and it may be advisable to only include the thorax if this is necessary for the diagnostic purpose of the scan.

HR was the other significant multivariate variable contributing to liver (all phases) and left renal (arterial phase) lateness. The intrapatient and temporal variability of this parameter could be more challenging to address when designing abdominal CT protocols, especially as the most common method to adjust the timing of phase timing adversely, and it may be advisable to only include the thorax if this is necessary for the diagnostic purpose of the scan.

HR was the other significant multivariate variable contributing to liver (all phases) and left renal (arterial phase) lateness. The intrapatient and temporal variability of this parameter could be more challenging to address when designing abdominal CT protocols, especially as the most common method to minimize patient variation from cardiac output is to use a test bolus or bolus tracking technique,\textsuperscript{14,27} the latter of which had already been incorporated into the study protocol. The fixed use of the diaphragmatic aorta as the site of trigger for bolus tracking, rather than vasculature closer to the organ of interest, could potentially account for this discrepancy and, accordingly, choosing a bolus-tracking trigger location closer to the organ of interest could be a potential recourse. Although anesthetic depth and protocol (other than the use of sedation or general anesthesia) were not assessed in our study, these could also play a role in influencing HR at the time of scan. In one study\textsuperscript{12} of coronary CTA in dogs, anesthetic protocols were designed to stabilize a physiologic HR (80 to 120 beats/min) and resulted in diagnostic quality studies. A similar study could be warranted for abdominal CTA. For example, as depicted in Figure 2, patients with a HR < 100 beats/min tended to have a greater proportion of ideal enhancement for the liver venous phase. However, as also demonstrated in Figure 2, the relationship between timing accuracy and HR varied considerably between target organs, and an optimal range that maximizes timing accuracy for one organ may not exist and/or does not always remain true for the other organs. This further suggests that an organ-optimized protocol would be ideal if timing accuracy is critical to the diagnosis. However, based on the trends identified in this study, maintaining a physiologic HR as low as reasonably and safely achievable could serve as a starting point if a CTA protocol similar to the study protocol is used.

The subjective timing accuracy score overall correlated poorly with HU value, with most of the phases scoring < 0.3. The highest adjusted $R^2$ value was for the hepatic vein venous phase (0.54), for which the increased HU value corresponded with lateness of scan, as expected. However, as depicted in Figure 3, plotting the distribution of HU for each subjective timing accuracy score for this phase in the hepatic vein, there was a very wide degree of latitude and overlap in objective values for each subjective accuracy category (including a range of 39 to 278 HU for those ranked as ideal). These findings may mirror similar descriptions in human medicine in which one study described a 3-fold individual variation in aortic enhancement following similar injection conditions in patients with normal cardiac output.\textsuperscript{35} It is suspected that this wide degree of overlap in HU values is contributing to poor correlation in this model. Low $R^2$ values for some sites and phases may also be the result of the more convoluted relationship between HU and vascular phase accuracy, for which an increasing HU does not always correspond with lateness (such as for the arteries on venous and delayed phases). Correlation of HU with study variables was also relatively low, with all adjusted $R^2$ values < 0.33. The objective findings in our study may suggest that subjective assessment overall is more important than absolute HU value when interpreting the timing accuracy for CTA. This corresponds with human literature,\textsuperscript{23} in which it has been suggested that a clear quantitative definition of adequate enhancement has not yet been defined, and human perception along with clinical context remains the standard.

**Figure 3**—Plot of the distribution of HU values and subjective vascular timing score for the hepatic vein venous phase.
There were several limitations to our study. The BIC was used in developing our multivariate model given the large number of interrelated variables analyzed and the exploratory nature of the study. Use of other models and a larger sample size may detect other significant variables and relationships. Another limitation was the inclusion of abdominal CT studies including a continuous scan of the thorax and/or pelvis. These were included in this study with the intent to reflect the variety of multiarea angiographic scans performed at our institution and to assess whether (and the degree to which) inclusion of these regions affected timing accuracy adversely for the abdominal organs of interest. However, the addition of these regions could potentially introduce additional bias or mask more subtle relationships among study variables that a study of similar sample size excluding extraneous anatomy may demonstrate. The results reported herein may also be specific to the described study protocol. Given the numerous parameters involved in protocol design and implementation, these findings may not always apply to other protocols, as demonstrated in a recent study.

Similarly, although an attempt was made to design the subjective scoring rubric in reference to published human and veterinary literature, this evaluation was ultimately subjective, and the perceived enhancement factors constituting an ideal scan may vary among viewers and across institutions. Given the exploratory nature, a stringent methodology for ROI measurements was not adopted for the objective portion of this study. A narrower study of objective enhancement with more rigorous ROI placement methodology (multiple data points, standardized ROI size, standard deviation thresholds) may show relationships not detected herein. The diagnostic utility of each CT scan was also not assessed in our study, and cases for which the timing accuracy could be less than ideal could very well be adequate for the purposes of obtaining a diagnosis. To our knowledge, few veterinary papers evaluate a standardized abdominal CTA protocol; but, those that do demonstrate diagnostic utility despite some limitations in scan quality. Further study into the diagnostic utility for each organ of interest could be beneficial in evaluating a standardized protocol in addition to evaluating timing accuracy.

For the protocol used in our study, the CTA vascular timing accuracy was greatest for the pancreas, moderate for the liver, and least for the left kidney and spleen. Increased HR and scan length variables (particularly thorax length) were the most significant variables contributing to scan lateness, whereas contrast medium variables were less significant in this analysis. The HU values correlated poorly with timing accuracy and study variables. These findings may be beneficial in baseline protocol adjustment and choice of included anatomy for undergoing abdominal CTA with a standardized fixed time delay multiphase protocol. In situations when achieving a diagnosis is highly dependent on accurate vascular timing, use of a specifically optimized protocol to the organ of interest would be advantageous over a one-size-fits-all approach.

Acknowledgments

Funded by a Small Companion Animal Grant from the College of Veterinary Medicine at the University of Minnesota. The authors declare that there were no conflicts of interest.

References

14. Makara M, Dennler M, Kühn K, Kalchofen K, Kircher P. Effect of contrast medium injection duration on peak enhancement and time to peak enhancement of canine pulmonary arteries: effect of injection duration on

Supplementary Materials

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