The comparison of bolus tracking and test bolus techniques for computed tomography thoracic angiography in healthy beagles

by

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DECLARATION

I hereby declare that this dissertation, submitted for the MMedVet (Diagnostic Imaging) degree, to the University of Pretoria, is my own work and has not been submitted to another university for a degree, and that the data included in this dissertation are the results of my investigations.

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Table of Contents

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List of Tables

List of Figures

List of Abbreviations

Ao = aorta

Ao_{art} = aorta in the arterial phase

Ao_{ven} = aorta in the venous phase

BSA = body surface area

BT = bolus tracking

CIN = contrast induced nephrotoxicity

CT = computed tomography

CTA = computed tomography angiography

CTDI = computed tomography dose index

CTDI(vol) = volume computed tomography dose index

CVC = caudal vena cava

CVC_{art} = caudal vena cava in the arterial phase

CVC_{ven} = caudal vena cava in the venous phase

DLP = dose length product

DYNAEVA = dynamic evaluation software program (SIEMENS)

ED = effective dose

FBC = full blood count

GFR =glomerular filtration rate

GGT =gamma glutamyltranspeptidase

HU = Hounsfield units

i/v = intravenous

mA = milliampere

mg/dl = milligrams per decilitre

mg/ml = milligrams per millilitre

mgI/ml = milligrams of Iodine per millilitre

ml/kg = millilitres per kilogram

ml/sec = millilitres per second

MPR = multiplanar reformatting

OTAU = Onderstepoort Teaching Animal Unit

PME = point of maximum enhancement

Psi = pounds per square inch (1 psi = 6894.75 N/m^2 = 6894.75 Pa)

rCPA = right caudal pulmonary artery

$rCPA_{art}$ = right caudal pulmonary artery in the arterial phase

$rCPA_{ven}$ = right caudal pulmonary artery in the venous phase

ROI = region of interest

ROIAo = region of interest in the aorta

ROICVC = region of interest in the caudal vena cava

ROIrCPA = region of interest in the right caudal pulmonary artery

TB = test bolus

tPME = time to point of maximum enhancement

UPBRC = University of Pretoria Biomedical Research Centre

WL = window level

WW = window width

μBT= theoretical mean for bolus tracking

μTB= theoretical mean for test bolus

Summary

The comparison of bolus tracking and test bolus techniques for computed tomography thoracic angiography in healthy beagles

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Computed tomography (CT) is gaining popularity as a minimally invasive diagnostic modality in veterinary science. The use of contrast agents is well described and used with increasing frequency, having marked benefits over the invasive angiographic procedures used previously. Methods to perform CT angiographic (CTA) studies include bolus tracking, test bolus and empirical scan delay techniques. In human medicine, empirical scan delays have been extensively investigated but due to the marked patient variability encountered in veterinary medicine, this technique cannot, at this stage, be confidently used. This then poses the question that if both techniques can be used, is one significantly better than the other one when performing, in particular thoracic CTA?

CTA studies were performed on 6 adult beagles, using the bolus tracking (BT) technique and the test bolus (TB) technique on two separate occasions, at least 2 weeks apart. Each beagle acted as its own control. The patients were placed under general anaesthesia. Two ml/kg of 300mgI/ml iodinated contrast agent was injected through a 20 gauge catheter place in the cephalic vein for the BT technique. Scans were initiated when the contrast in the aorta reached 150 Hounsfield units (HU). For the TB technique, the dogs received a test dose of 15% of 2ml/kg of 300mgI/ml iodinated contrast agent injected manually into the cephalic catheter, followed by a series of low dose sequential scans. Time attenuation curves were generated using dynamic evaluation software programs (DYNAEVA®). The full dose of 2ml/kg of the 300mgI/ml iodinated contrast agent was then administered and the scans were conducted at optimal times as identified from the time attenuation curves. The full dose of contrast administration was administered using a pressure injector operated at 3ml/sec and was followed by a manual saline flush for all studies. Mean attenuation in HU was taken at three consecutive levels in the aorta (Ao), caudal vena cava (CVC) and right caudal pulmonary artery (rCPA) by placing a region of interest (ROI) in the vessel of interest. These observations were done for both arterial and venous phases using the BT and TB studies in five of the six dogs. Additional observations included the visualisation of the smaller

thoracic vessels, in particular the arteries, the study duration, milliampere (mA), computed tomography dose index volume (CTDI(vol)), dose length product (DLP) and the pressure and the duration of the contrast injection. These observations were done in all six dogs. Statistical analysis included the comparison of the attenuation achieved in the major vessels (Ao, CVC and rCPA) for the two techniques. The test bolus technique was deemed to be the gold standard, as this is adapted for each individual patient.

In one beagle the study was considered non diagnostic with a later time to peak enhancement noted in the Ao than the CVC. No statistical analysis was done on the dynamic and attenuation data obtained in this dog. In all the other studies, the attenuation achieved in the vessels evaluated was deemed to be of diagnostic quality except for the attenuation achieved in the CVC during the arterial phase. The attenuation in the Ao during the arterial phase for the BT technique was not significantly different (660.52 HU ± 138.49) than the TB technique (469.82 HU ± 199.52)($p = 0.13$). The attenuation in the Ao during the venous phase for the BT and TB techniques was also not significantly different (BT = 190.6 HU ± 28.29 and TB = 188.8 HU ± 21.9, $p = 0.92$). The attenuation in the CVC during the arterial phase and venous phases for the BT techniques were not significantly different (arterial phase BT = 37.84 HU ± 20.8, arterial phase TB = 91.48 HU ± 66.54, $p = 0.069$; venous phase BT = 171.3 HU ± 32.36, venous phase TB = 191.08 HU ± 19.59, $p = 0.087$). The attenuation in the rCPA during the arterial phase was not statistically different between the two techniques (BT= 606.34 HU ± 143.37 and TB = 413.72 HU ± 174.99, $p = 0.28$), nor was the attenuation in the rCPA during the venous phase (BT = 174.34 HU ± 27.25 and TB = 164.46 HU ± 18.51, $p = 0.51$).

The mean mA for the BT technique (3538.5 ± 171.27) was significantly lower than the TB technique (3929.6 ± 312.3) with $p = 0.024$. The mean CTDI(vol) for the BT technique (24.42 ± 11.89) was significantly lower than the TB CTDI(vol) (45.32 ± 0.94) with a p-value of 0.013. The mean DLP did not differ significantly between the two techniques (BT = 139.1 ± 7.65, TB = 162.8 ± 33.1) ($p = 0.12$). The BT technique resulted in a significantly shorter procedural duration and utilised less contrast material than the TB technique. The injection duration and injection pressures did not differ significantly between the two techniques ($p = 0.23$ and $p = 0.62$ respectively).

This study identifies that there is no preference for either technique when evaluating the Ao, CVC or rCPA, however, the BT technique is shown to be shorter in procedural duration, utilises less contrast material and results in less radiation dose to the patient when compared to the TB technique.

Chapter 1: Introduction

1.1 Background

It is well accepted that Computed tomography (CT) has gained popularity as a diagnostic modality in veterinary science, due to the increasing accessibility, enhanced application and minimal invasiveness. Computed tomography is deemed superior to conventional radiography, largely because it eliminates the superimposition that is encountered with radiography. Additional benefits of CT include the ability to stage neoplasia, perform biopsies accurately and provide visual reconstructions for surgical planning and prognostication. Thoracic CT in veterinary medicine is largely in the explorative stage with many of the human applications being investigated for use in veterinary patients.

As computed tomography utilises the attenuation of x-ray beams, the use of iodinated contrast agents is successfully and commonly employed in CT. The indications to use contrast agents in CT studies include investigating tumour and organ perfusion as well as vascular anatomy and angiographic studies[1-4]. The techniques used to perform these studies and protocols for using the contrast agents successfully have been well documented in the literature[2, 4-24]. Although the research into the use of CT for human medicine pioneers the way, the demand for quick, convenient and minimally invasive diagnostic modalities in veterinary medicine also necessitates research in this field.

The methods that can be used to perform computed tomography angiography (CTA) include bolus tracking (BT), test bolus (TB) and empirical scan delays. In human medicine, empirical scan delays (which employ the use of standard time delays) have been researched for various organ perfusion studies[25, 26]. However, this method is still the topic of ongoing investigation in veterinary medicine[60] and proves challenging, as veterinary patients provide not only intra-species, but also inter-species variability, which is not encountered to such a degree in human medicine. Bolus tracking monitors the level of contrast agent in a vessel of interest following intravenous administration. The machine will automatically trigger the scan to begin when the desired level of

attenuation (in Hounsfield units)(HU) of the contrast agent is reached in the vessel of interest. Time delay studies involve administering a test bolus of contrast agent, generally equating to approximately 15% of the total contrast dose, to the patient. Following administration of contrast, low dose sequential scans of the region of interest are done. Time attenuation curves are then generated using inherent software programs. From these time delay curves, the empirical scan delays, adapted for the patient being studied, can be acquired and applied to the clinical scan whilst using the full dose of contrast agent. These two techniques currently used in veterinary medicine (BT and TB) prompt one to question whether one technique is significantly better than the other.

As CT utilises ionising radiation, one of the concerns regarding the use of CT is the radiation dose received by patients, and handlers who may be required to be in the room at the time of the scan. Computed tomography dosimetry makes use of two radiation parameters: dose length product (DLP) and computed tomography dose index (CTDI). Computed tomography dose index quantifies the intensity of radiation used to perform the CT examination whereas the DLP quantifies the amount of radiation used[2, 5, 6, 10, 21, 25, 27-30]. During CT imaging the factors that influence the CTDI and DLP include the x-ray tube voltage, the scan length, the scan region as well as the patient size[31, 32].

1.2 Problem statement

When faced with the choice of doing CTA of the thorax of a dog using either the BT technique or the TB technique, one should be able to choose the technique that provides adequate, reliable information in a time and cost efficient manner with minimal radiation dose. No literature has been found comparing these techniques in dogs based on the attenuation of the vessels of interest, the time taken to complete the study, the dose of radiation to the patient or the amount of contrast agent used. This knowledge will help the operator make an informed and confident decision when faced with the choice, as well as provide ancillary information for future CTA thoracic studies in veterinary medicine.

1.3 Research questions

1. What is the mean attenuation, measured in HU, in the descending thoracic aorta (Ao), caudal vena cava (CVC) and the right caudal pulmonary artery (rCPA), respectively at the level of the 8th thoracic vertebra when using the BT technique?
2. What is the mean attenuation, measured in HU, in the descending thoracic Ao, CVC and rCPA, respectively at the level of the 8th thoracic vertebra when using the TB technique?
3. Is there a significant difference between the mean attenuation in the descending thoracic Ao, CVC and rCPA at the level of the 8th thoracic vertebra between the BT technique and the TB technique?
4. Can the attenuation of the smaller thoracic arteries (the brachiocephalic trunk, the left and right subclavian arteries, the left and right internal carotid arteries, the internal thoracic arteries and the vertebral arteries) be subjectively and (if possible) objectively assessed?
5. Is there a significant difference in the attenuation of the smaller thoracic arteries (the brachiocephalic trunk, the left and right subclavian arteries, the common carotid artery, the costocervical trunk, the internal thoracic arteries and the vertebral arteries) between the BT and the TB?
6. What is the mean mA, CTDI(vol) and DLP for the BT technique?
7. What is the mean mA, CTDI(vol) and DLP for the TB technique?
8. Is there a significant difference in the mA, CTDI(vol) and DLP between the BT and the TB techniques?
9. What is the mean duration for the BT technique?
10. What is the mean duration for the TB technique?
11. Is there a significant difference in the duration of the studies between the BT technique and the TB techniques?
12. What is the mean duration of the arterial and venous phase scans for the BT technique?
13. What is the mean duration of the arterial and venous phase CT scans for the TB technique?
14. What is the mean duration of the delays experiences prior to the CT scans for the BT technique?

15. What is the mean duration of the delays experiences prior to the CT scans for the TB technique?
16. What is the mean volume of contrast agent used for the BT technique?
17. What is the mean volume of contrast agent used for the TB technique?
18. Is there a significant difference in the volume of contrast agent used between the BT and TB techniques?
19. What is the average pressure of injection (in pound force per square inch (PSI)) when performing the BT technique?
20. What is the average pressure of injection (PSI) when performing the TB technique?
21. Is there a significant difference in the pressure of injection (in PSI) between the BT and the TB techniques?

1.4 Hypotheses

For comparison of the theoretical mean for bolus tracking (μBT) with that of the theoretical mean for test bolus (μTB) with respect to:

1. the attenuation (in HU) in the descending thoracic Ao, CVC and rCPA
2. the mA, CTDI(vol) and DLP
3. the duration of the studies
4. the delays experienced during the CT scans
5. the volume of contrast agent used
6. the pressure of the injection (in PSI)

the null hypothesis is
H_o: μBT = μTB

and the alternative hypothesis is
H_1: μBT ≠ μTB

It is also hypothesised that for both techniques it is possible to subjectively evaluate the attenuation of the contrast agent in the smaller thoracic arteries (the brachiocephalic trunk, the left and right subclavian arteries, the common

carotid artery, the costocervical trunk, internal thoracic arteries and the vertebral arteries).

1.5 Objectives

The main objective is to determine if one CTA technique has significant benefits over the other, and should be chosen preferentially when performing thoracic CTAs in healthy medium sized dogs. Further objectives are to determine whether there is any difference in the radiation dose received by the patient during the two procedures and if one techniques is more time efficient and cost efficient (as evaluated by the dose of contrast agent used) than the other.

1.6 Benefits

A reliable standard technique to perform thoracic CTAs as well as developing empirical scan delays for future CTA studies in medium sized dogs will be established. This will allow CTAs to be carried out as time efficiently and cost effectively as possible as well as with the least risk to the patient, by minimising the radiation received and/or by minimising the amount of contrast agent used. Additionally, by choosing a technique which is more time efficient, the patient will be under general anaesthesia for a reduced period of time.

The results of this study can be used as a reference for future studies into the effect of technical and patient factors in veterinary CTA.

Future studies into the CTDI(vol) and DLP and organ doses in veterinary patients should be considered, as this data is lacking from the literature.

Future studies envisioned to benefit from this project include the study of the intra-thoracic pathology caused by *Spirocerca lupi* larval migration and adult worms aimed at improving the understanding of the pathophysiology of this condition, as well as for prognostication, treatment monitoring and surgical planning associated with such cases (currently a registered research project at the Faculty of Veterinary Science, University of Pretoria).

Chapter 2: Literature review

2.1 Introduction

Thoracic CT has become established as an increasingly important imaging procedure in human and veterinary medicine. Computed tomography is superior to conventional radiography of the thorax by eliminating superimposition and demonstrating enhanced resolution, thus being able to detect subtle changes in organ size, shape, margin, contour and position.[33] Except for some of the smaller vessels, nerves and details of the heart, most of the osseous, visceral and vascular structures of the dog thorax have been identified and described.[33,34,35]Although largely still in the infantile and explorative stages in veterinary medicine compared to human medicine, thoracic CT cannot only aid in improving diagnosis and pre-operative planning, but can also possibly aid in neoplasia staging and CT guided thoracic biopsies, which still need to be investigated. A report in 2008 highlighted the technique used and the information gained when using high resolution four dimensional *in vivo* CT in rats.[36] Additionally micro-CT is being used increasingly due to the high interest in animal models for human disease processes. One should expect that in future, this modality will move from a purely research tool to one used for clinical applications and diagnostics in veterinary medicine.

2.2 Application of computed tomography angiography

The use of contrast agents in conjunction with CT thoracic studies has been well described in the human literature and is also employed in veterinary science.[37]It has been well documented that the use of a bolus injection of contrast material is advantageous with respect to increasing the visibility of hypovascular tumours by maximising the difference in enhancement between

the tumour and the organ parenchyma.[38] Computed tomography angiography is the study of vascular structures by utilising contrast material during the tomographic study. Computed tomography angiography analyzes imaging data acquired during the first pass of a bolus of contrast material. Proper selection of acquisition timing is thus critical to optimize contrast medium enhancement.[39]This technology has effectively replaced arteriography in human medicine and is used extensively for the study of coronary pathology, pulmonary thromboemboli, pulmonary perfusion studies and the characterization of pulmonary nodules.[4,10,15,16,17,18] Additionally, any congenital or acquired vascular abnormalities and arterio-venous malformations are often diagnosed using CTA.[2] In veterinary medicine, all of the above applications are increasingly being used and employed as the need for quick, convenient and minimally invasive diagnostic modalities are sought.[14,24] Multi-phase angiographic studies can also be performed, to investigate arterial and venous phases as well as organ perfusion.[2]These studies are extensively used to investigate the characteristics of various thoracic and abdominal tumours, in the hope that the enhancement pattern for various tumours will be able to be characterised using CTA and thus minimise the need for biopsies.[19,21,26,37,40] When investigating the enhancement of pulmonary nodules with CTA, it has been shown that the average enhancement of malignant pulmonary nodules in humans was 38.1 HU compared to 10.0 HU in benign nodules ($P<0.001$) and that by using 15 HU as a cut-off, nodule enhancement was found to have a 98% sensitivity and 58% specificity for malignancy.[42]

An interesting application of CTA reported in the literature involves whole body post mortem angiography using a high viscosity contrast agent. A dissolver (polyethylene glycol) was used to facilitate distribution of the contrast agent. The study provided excellent visualisation of the human arterial anatomy.[43] Although this technique does not involve the temporal planning of the scan as is needed in live patients, it may become a feasible post mortem technique in certain cultures that prohibit invasive post mortems on pets.[44]

Many of the applications of CT which are utilised in veterinary science have been extrapolated from over 30 years of use of CT in human medicine. Similarly the use of contrast material with CT is very often adapted from the routinely performed human protocols. In order to overcome the limited

differences noted during CTA in humans, contrast material flow phantoms have been designed and investigated, comparing the enhancement in the aorta in a phantom to that in live human studies and the results have been promising, with good comparisons noted between the two.[7] Phantoms have been investigated in veterinary medicine in order to increase the operator expertise when doing Doppler ultrasonography,[45] but currently, there are no phantoms being used or studies being investigated for veterinary CTA to the authors knowledge. As this technique refers to the early haemodynamics after contrast injection, and utilises the compartment model for contrast enhancement initially developed in a porcine model,[7,46,47] this may be a promising field in the future. There are however limitations to using flow phantoms. The models do not take into account pulmonary circulation nor the equilibrium and secretory phases of haemodynamics of contrast material. Secondly, the cost of the contrast material used in such studies approximates those used in a clinical situation and thus financial constraints may be largely limiting in the veterinary world.

When viewing CT images in order to assist diagnostics, various software programs can be used including 3-D volume rendering techniques, maximum intensity projections (MIP) and reconstruction of images in different planes (multiplanar reformatting (MPR)).[48] An additional post processing technique post CT acquisition is virtual endoscopy, which can be used to evaluate an inflated oesophagus.

2.3 Contrast agents

The contrast agents used in CT and radiology are categorized according to their physical and chemical properties.[49] The water soluble contrast agents are divided into two major groups on the basis of dissociation in solution (ionic) or lack of dissociation (non-ionic). Ionic compounds dissociate into an iodinated molecule and the salt to which it is attached resulting in two particles from one molecule of contrast agent in solution. The non-ionic compounds do not dissociate and thus exist as one particle in solution.[50]As the radio-opacity of a contrast agentis directly related to the iodine content, the goal in developing successive generations of contrast agents has been to maximize the iodine content while minimizing the osmolarity of the resulting solution. The most

commonly used iodinated contrast agents are the second generation iodinated compounds.[49] These agents are low osmolar, non-ionic monomers which have improved vascular tolerability and thus fewer side effects. Third generation iodinated contrast agents are iso-osmolar, non-ionic agents and are reported to be the safest contrast agents to date. However their high cost currently limits their use largely to high risk patients only.[49-51]

2.4 Contrast agent bolus pharmacokinetics

In order to understand the distribution of the contrast agents used in CTA and the effects of various parameters on the distribution of the contrast agents, a basic understanding of the contrast agent dynamics and bolus geometry is required. Bolus geometry is defined as the pattern of enhancement, measured in a region of interest (ROI) plotted on a time(s)/attenuation (HU) diagram after intravenous injection of contrast material.[52]

Intravenously injected contrast agents travel via the arm (antebrachium) veins to the right heart, the lungs and the left heart before reaching the arterial system. This is termed the “first pass”. After the contrast medium is distributed through the organs and the interstitial spaces, it re-enters the right heart. This is termed “recirculation”. In the time frame of CTA, one will not only observe first pass of the contrast medium, but also recirculation.[13,53]

The relationship between the interval of contrast agent injection and the enhancement in the aorta is best explained as follows: (Fig.1)

After the start of the intravenous injection, the bolus is pushed towards the right heart. Once here, the right heart acts as a reservoir and a second pump which further pushes the contrast material towards the aorta. The time period from the start of injection to the peak aortic enhancement can thus be divided into three phases.

- The first interval is the injection phase, during which time there is a continuous increase in the attenuation within the aorta due to a consistent inflow of contrast material and a relatively small outflow to the visceral organs. The length of the first phase depends on the injection duration.
- During the second phase, although the injection process is complete, the flow of contrast agent from the right heart to the aorta

still continues and thus the attenuation within the aorta keeps increasing. The length of the second duration depends on the cardiac output of the patient.

- During the third phase there is no further inflow in the aorta but only outflow and the attenuation within the aorta decreases. [54]

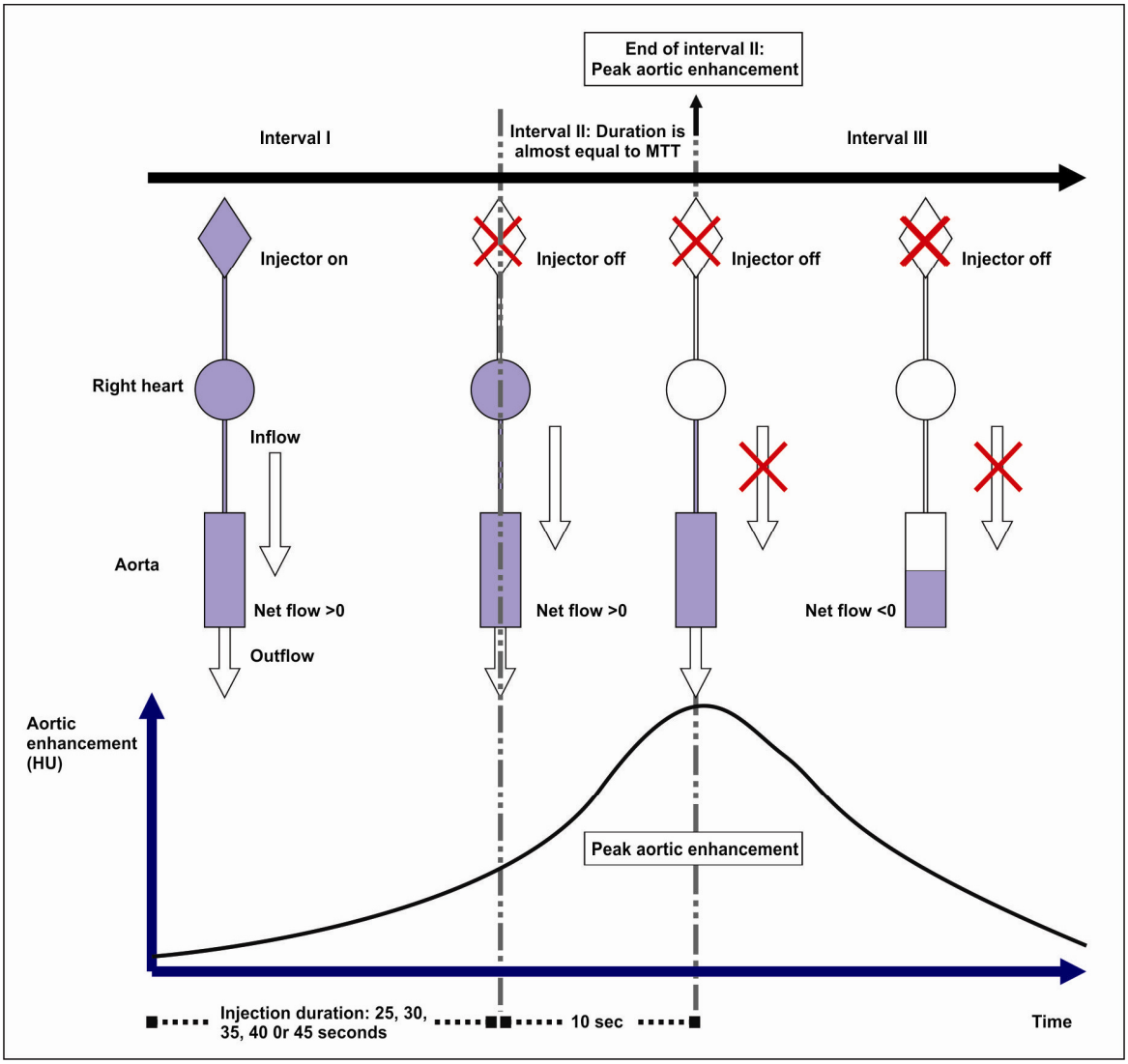

Fig. 1.**The relationship between the intervals of the contrast injection and the enhancement of the aorta. "MTT" is mean transit time in the blood from the right heart to the aorta.**[54]

2.5 Factors affecting angiographic studies

When performing any intravenous contrast study, there are several factors that need to be taken into account.

2.5.1 Physico-chemical factors

The first physico-chemical factor to consider is the concentration of the contrast agent being used. It has been reported that with a lower concentrations, a longer vascular transit time would result, due to the increased volume of the contrast agent required.[55] In addition, the higher the concentration of the contrast agent, the higher the residual iodine dose at the site of injection, in the absence of a saline flush.[55] Another important consideration arising from this study was that with increasing osmolality, there would be an increase in dilution of the contrast agent and this could decrease the enhancement provided by the bolus of contrast agent. This finding is in contrast to a study which found higher points of maximum enhancement (PME) with higher concentrations of iodine injected.[52] When injecting a higher concentration contrast agent, one can theoretically reduce the volume of contrast agent used, and by reducing the contrast volume the duration of contrast enhancement will be shortened, although the peak aortic contrast enhancement will be higher. This needs to be borne in mind, especially when using single, dual or four slice CT scanners as these machines will have a longer scan time over a specified scan length than higher capability scanners. Thus one would preferentially try and extend the duration of contrast enhancement using this principle.[9,56] Another study involving dogs showed that significantly higher aortic enhancement was obtained when injecting 150mgI/ml than when injecting 300mgI/ml.[57] This is in contrast to another study which showed higher aortic enhancement with 370mgI/ml than with 300mgI/ml.[27] In yet another study, no difference was noted in aortic enhancement when injecting 300mgI/ml and 370mgI/ml, although different injection rates were used (with a higher injection rate for 370mgI/ml protocol) and this was hypothesised to be the reason for the findings.[58]

A side effect to using a higher concentration contrast agent is the increased viscosity of the agent, which can hamper fast injection rates (especially when

small bore venous catheters are used).[9] In summary it is concluded that a higher concentration of iodinated contrast agent does not necessarily provide the best contrast effects.[55]

When evaluating parenchymal or organ perfusion, it has been shown that the more contrast agent that is injected, the more contrast will accumulate in the extravascular space of the target organ.[59]

2.5.2 Technical factors

The injection rate, injection duration, injection volume, use of a pressure injector, application of a saline flush and bolus shaping have all been identified as technical factors which influence the outcome of a contrast study, with injection duration being cited as the most important technical factor to consider when doing CTA.[9,60]

An inherent problem with CTA is the narrow temporal window in which vessel attenuation is adequate, if not optimal, after IV contrast administration. Injection duration will affect the degree of contrast enhancement and the timing of peak contrast enhancement, which is critical information for temporal planning. The rate of injection has an effect on the duration and degree of contrast enhancement, with the rate of enhancement being prolonged by slower injection rates – a method which is sometimes employed when older generation CT machines, with longer scan times, are used (Fig. 2).[56,60] Studies clearly demonstrate that an increase in the injection rate produces a higher PME in the time attenuation curves with a faster time to the peak maximal enhancement (tPME).[52] This relationship is independent on the volume of injection and the concentration of Iodine. Although very little difference was found in the aortic arrival times with an injection rate of 3ml/sec compared to 4ml/sec,[30] an approximate 15% increase in the peak aortic enhancement is seen when using an injection rate of 4ml/sec.[46]

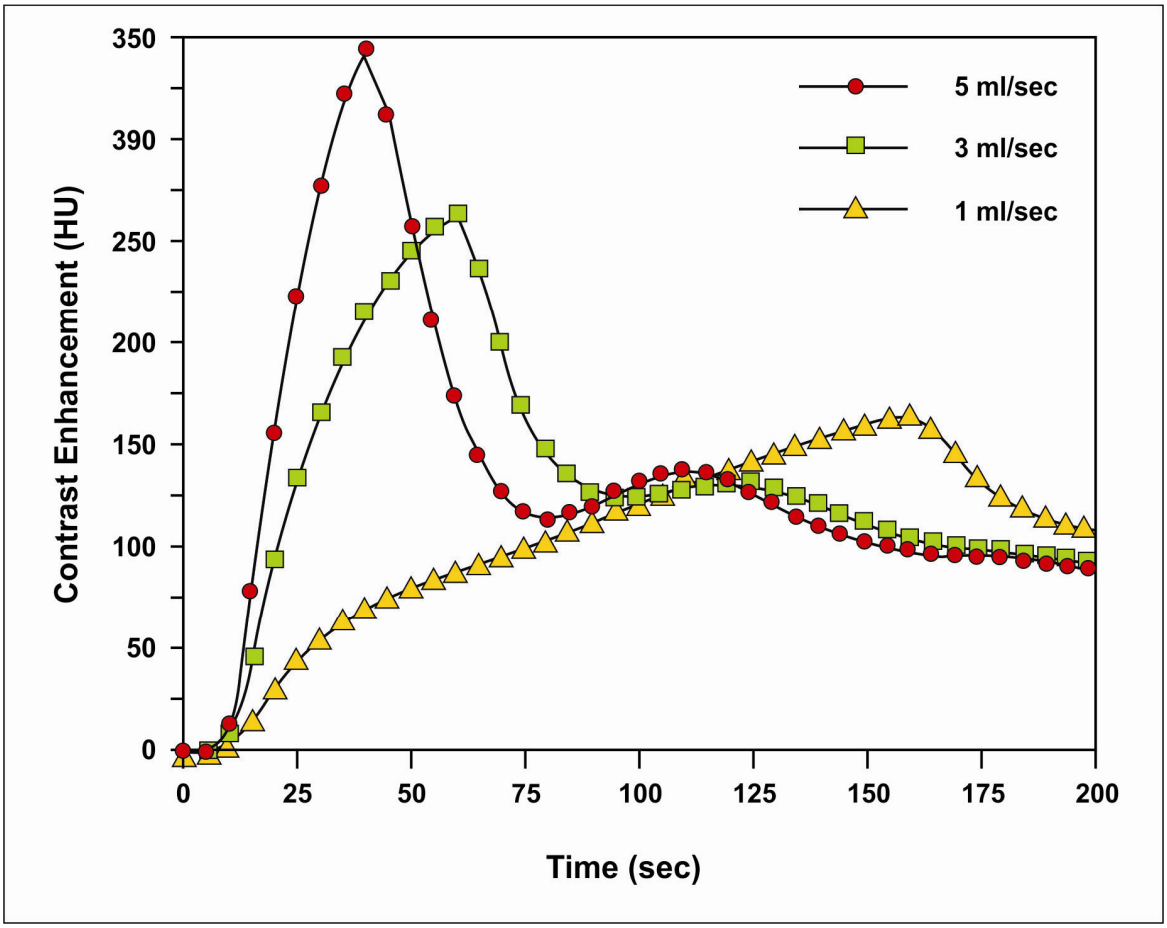

Fig. 2.**Effect of injection rate on arterial contrast enhancement. Three time-enhancement curves are created by simulating the injection of contrast material at rates of 1, 3, and 5mL/sec, while keeping the volume (150mL) and concentration (320mgI/mL) constant. The simulation model is based on an adult man with a body weight of 65 kg, a height of 1.72m and a normal cardiac output. Two trends are apparent from these time-enhancement curves: as the rate of injection increases, the degree of contrast enhancement increases and the duration of contrast enhancement decreases.**[46]

Canine and porcine studies show that with an increase in the volume of the contrast agent injected, independent on the injection rate and iodine concentration, the time attenuation curve is shifted upwards and to the right indicating a longer tPME and higher PME.[52]

It has also been shown that when performing dual phase CTA, high injection rates are preferred, as a higher injection rate magnifies the difference in the degree of enhancement during arterial and portal/venous phases. A faster injection rate also increases the temporal separation between the respective enhancement peaks.[9,56]

The use of a pressure injector for the administration of the contrast material is routinely used in CTA studies in order to achieve a tight bolus of contrast

material injected in as short a period of time. One of the side effects of using pressure injectors is an increase in the incidence of extravasation of the contrast agent.[13,61-64]The incidence of extravasation without the use of a pressure injector has been reported as being between 0.03% and 0.17%. This increased with the use of pressure injectors to between 0.25% and 0.9%.[65] However, another researcher stated that the incidence of contrast material extravasation does not significantly increase with the use of the automated pressure injector when used in conjunction with the low osmolar non–ionic contrast material.[64]

A bolus chaser or saline flush is a saline solution that is pushed through the injection line immediately after injection of the main contrast bolus. The use of a saline flush immediately following the intravenous injection of contrast material has been shown to lead to a statistically significant higher parenchymal and vascular enhancement as well as a more standardized and repeatable injection technique.[27,61,66] A study using a 20ml saline flush during single detector CT of the abdomen in humans demonstrated a prolonged period of aortic enhancement by up to 4 seconds.[38] Higher aortic enhancement during CTA increases detection of dissection flaps, thrombotic material and atherosclerotic plaques in the aorta.[38] Another study demonstrated that 75ml of contrast material in thoracic CTA followed by a saline flush was equivalent to using 125ml of contrast material without a saline flush.[62]The use of a saline flush also reduces the incidence of perivenous streak artifacts[38,52] and avoids pooling of contrast material in the peripheral veins following injection.[38] Saline flushes become increasingly important if small volumes, short injection durations and high iodine concentration contrast material are used.[53]

The administration of the saline flush is done in one of three ways. The saline flush can be injected manually, using a three-way stopcock valve.[53] A parallel power injector (also known as a double injector) can be used or the saline can be layered above the contrast agent within the same syringe.[52, 53] Due to the difference in osmolarity of the saline and the contrast agent and by careful loading of the syringe, these two agents can be present in the same syringe without significant mixing (a practice contra-indicated by the manufacturers of the contrast agents). The goal of this method is to use the unmixed layer of saline to clear the syringe, intravenous catheter, connecting tube and the patient's vein of the contrast material.[62] Advances in the development of

pressure or power injectors has led to programmable, double piston power injectors being utilized, with separate syringes for the contrast agent and saline flush. This injector provides the most practical solution to the use of a saline flush but can be quite costly.[13]

Generally, contrast is injected at a constant rate, also known as uniphasic injection and results in a peak in aortic enhancement at the end of injection.[53, 67] However, one can shape the way the bolus is delivered by altering the injection rate over time, during the injection. One method involves a fast injection of contrast material followed by a slow injection – a method which can prolong contrast enhancement. A third approach is the decelerated injection, which involves an exponential decline in injection rate over time.[68] A trial using this technique demonstrated uniform contrast enhancement while using less contrast agent. The aim of multiphasic injection techniques is to achieve a plateau of enhancement during the scan which will diminish the need to time the onset of scanning as precisely as one would need to, when using a uniphasic or biphasic injection protocol.[68]

Numerous human studies have also investigated the difference obtained when various injection sites (left antecubital *versus* right antecubital vein, venous *versus* arterial injection) are employed. Injection of the contrast into the central venous line can lead to lower vessel enhancement and image quality compared to contrast injection via a peripheral vessel. The reason is unclear but thought to be because that direct injection into a central venous line can lead to immediate circulation and pulmonary washout, resulting in low vessel contrast when image acquisition begins.[69] If a central venous line is utilised, it has been suggested to decrease or even erase the additional inherent delay after the bolus tracking has started. The problem with decreasing or removing the delay is that there may be no time for breath hold techniques to be employed and thus motion artifacts may result in reduced image quality. None of these factors have as yet been investigated in veterinary science.[13]

2.5.3 Patient factors

Patient factors that influence contrast enhancement in humans include the target organ of interest, the diagnostic application, the patient's body size, cardiac output, renal function, vascular access, age and gender. The cardiac output and weight have been shown to have a significant effect on the

distribution of the contrast agents.[23,70,71]One researcher stated that when disease states which are known to alter circulation are excluded, the most important patient factor to consider when using contrast agents in diagnostic studies is the body weight of the patient.[72] A higher body weight is generally associated with higher intravascular fluid volume, which results in a lower iodine concentration. Additional studies have suggested taking the body surface area (BSA) into account when calculating iodine dose as this had a higher correlation with aortic attenuation than when correlating it to body weight, height or body mass index.[68] It is thought that this improved correlation is due to the fact that BSA is a better indicator of metabolic weight than the other indicators of size.[56, 68] One caveat regarding this statement is that in obese patients increasing the iodine dose according to the body weight, can result in contrast enhancement higher than with that of non-obese patients. This is largely because the amount of metabolically active tissue as well as the size of the well perfused extracellular compartment is less in obese patients. For these patients a BSA scaling system is suggested.[68] Although not investigated in the above studies, obese patients may also have altered cardiac function which is also known to affect bolus pharmacokinetics. When cardiac output is reduced, the magnitude of peak contrast enhancement increases, and the times to contrast arrival and peak enhancement are delayed (Fig. 3). This is explained by the increase in circulation time and the lack of contrast agent dilution, which occurs during decreased cardiac output.[68]To summarise, aortic enhancement is decreased with increasing body weight, height, BSA and body mass index and thus the amount of contrast needs to be adjusted according to body weight or BSA.[68]

The age of the patient has also been shown to affect the transit time of a small amount of contrast agent through the pulmonary circulation. It becomes significantly longer in older patients. The study hypothesizes that the pulmonary blood pool in older patients may become sluggish. Contrast agents are better visualised in these patients when performing pulmonary CTA.[68]

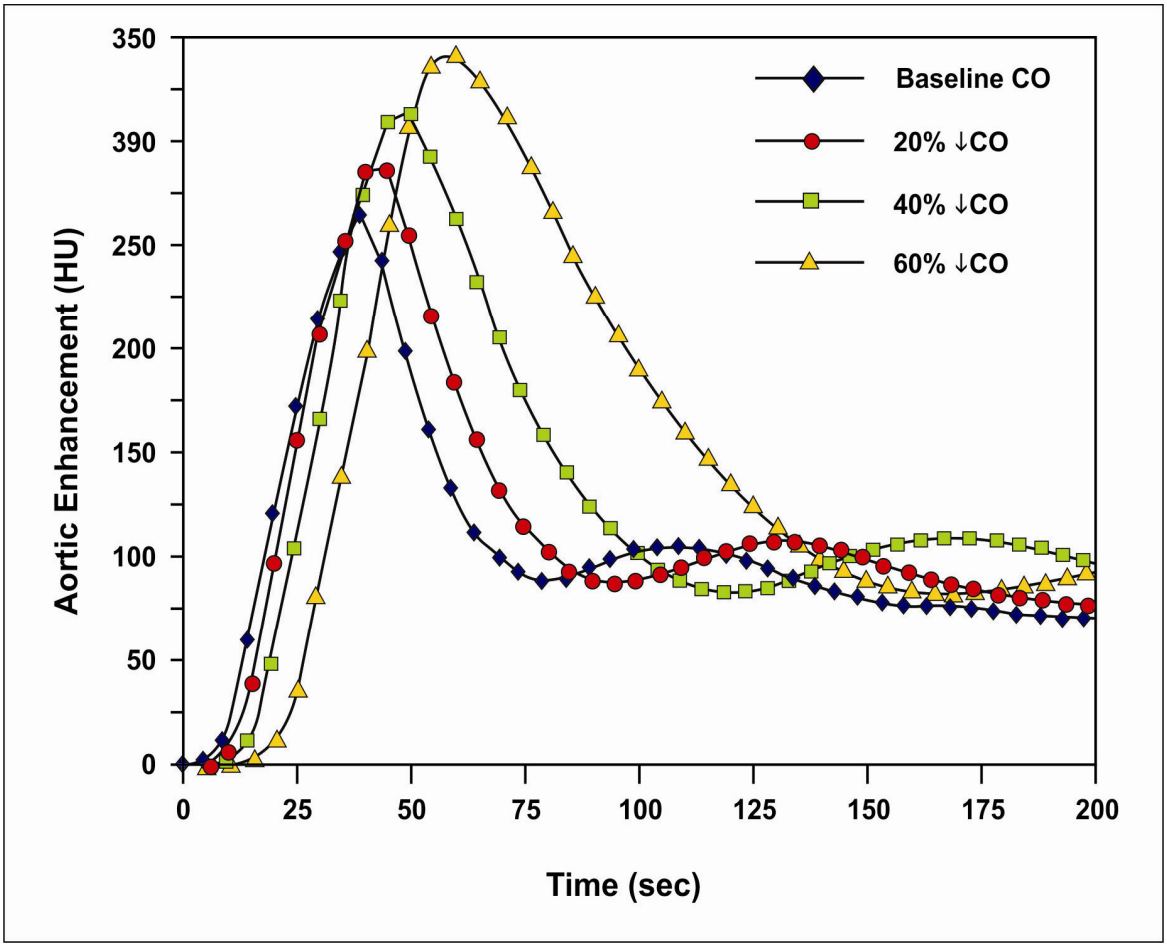

Fig. 3.**Effect of cardiac output (CO) on contrast enhancement. Time-enhancement curves simulate the effect of decreasing cardiac output, while holding contrast volume constant at 120mL and injection rate at 4mL/sec. When cardiac output is reduced, the magnitude of peak contrast enhancement increases, and the times to contrast arrival and peak enhancement are delayed.** [68]

2.6 Adverse effects of contrast agents

To complete the discussion on contrast agents, it is important to recognise and appreciate the adverse reactions that can be found using these agents in CTA. Adverse reactions to contrast agents have been extensively reported and investigated in human literature.[49,51,59,73-84] The side effects of the contrast agents are related to their physical and chemical properties.

The American College of Radiology classifies adverse reactions into three broad categories:[50] 1) Anaphylactoid (allergy like, non-dose dependant), 2) Dose dependant causing molecular damage, dependant on the osmolality and 3) Organ specific or local effects (contrast induced nephrotoxicity - CIN). The contrast agents are known to have cardiovascular effects such as increased

cardiac output, decreased haematocrit and decreased end diastolic left ventricular diameter. The contrast compounds also cause a direct effect on vascular permeability, platelet aggregation and echinocyte formation. A severe reaction to ionic intravenous contrast agents in two anaesthetised dogs has been reported. One dog had hypertension, bradycardia and apparent bronchospasm and the other dog became hypotensive, tachycardic and displayed erythema of the limbs.[85]

Despite the incidence of contrast induced nephrotoxicity (CIN) in the human population being low (<2%), regardless of the contrast medium used,[51]it is one of the leading complications of contrast use in human medicine and accounts for 10% of all causes of hospital acquired renal failure.[84]Contrast induced nephrotoxicity manifests as an abrupt decline in renal function as early as 24 hours and as long as 7 days following contrast administration in the absence of an alternative aetiology. In humans, CIN is characterized by an increase in serum creatinine level of at least 0.5mg/dl or 25% as compared to baseline values. In most cases this rise has been reported to occur 24-72 hours following exposure.[75, 83, 86-88] One publication cited that the creatinine levels have been shown to peak at 96 hours post contrast administration and thus CIN may be overlooked or underestimated in studies measuring creatinine concentrations at 48 hours or less.[80] Various risk factors, such as pre-existing renal impairment and diabetes mellitus, have been identified[51] and thus, contrast agents may be contributory rather than causative in CIN. Fortunately CIN is usually self limiting, with serum creatinine levels returning to near baseline values within 7 days. A recent report concluded that human patients receiving repeat contrast CT examinations within 24 hours, had an incidence of CIN of 12.4% and that an increase in the serum creatinine values between the first and second CT examination was highly associated with CIN.[74]Three decades ago, a study was done to determine the effect of multiple excretory urograms on glomerular filtration rate (GFR) in dogs. The contrast agent used in this study was sodium iothalomate and the results showed a significant reduction in the GFR following contrast urography.[89]

The mechanisms of CIN have been investigated during numerous *in vitro* and *in vivo* studies and three main mechanisms are implicated: oxidative stress, haemodynamic disturbances and hyperosmolar effects.[75, 81, 83]Low oxygen tension normally exists in the renal medulla and this region of the kidney has a

high metabolic rate and oxygen requirement, due to active salt reabsorption in the medullary thick ascending limbs of the loops of Henle. Contrast agents aggravate this outer medullary hypoxia as they cause enhanced metabolic activity and oxygen consumption as a result of osmotic diuresis.[83] As contrast agents may be uricosuric and may increase the excretion of both oxalate and Tamm-Horsfall proteins, there is a theory that contrast nephrotoxicity may be mediated by tubular obstruction.[83] Pathological studies of animal models of contrast nephrotoxicity often reveal vacuolisation of the proximal tubular epithelium.[90] Recent studies have also implicated a decrease in the antioxidant enzyme activity and/or an increase in oxygen free radicals as a putative mechanism for CIN.[83]During an *in vitro* study of the effect of contrast agents on various cell lines, the cytotoxic effect of the contrast agent was identified as early as 15 minutes of incubation, reaching a maximum at 3 hours.[84] Several studies have documented a contrast induced rise in various proteins and enzymes, which although non-specific for tubular damage, do support a theory of a direct toxic effect on the tubular epithelium.[90]Studies on the pathogenesis of CIN have focused on the ischaemic effects on the renal cells. It has been repeatedly demonstrated that when a contrast agent is injected directly into the renal artery of both dogs and humans, there is a biphasic response in the blood flow. There is an initial very brief increase in flow, followed by a period of reduced flow lasting several minutes in normal kidneys. This reduced flow is most likely due to intrarenal vasoconstriction. This vasoconstriction is then followed by an increased lipid peroxidation due to the increased production and decreased removal of free oxygen radicals, which correlates directly with a decrease in the GFR.[90]

2.7 Computed tomography angiography techniques

The variability introduced by varying patient factors is overcome in CTA by the application of either a BT or a TB technique or by using empirical scan delays.

2.7.1 Bolus tracking

A ROI with a desired HU is placed in a blood vessel of interest related to the study. The computer detects the contrast material by means of real time monitoring of the main bolus during injection by means of the acquisition of a

series of low-dose monitoring scans in the vessel of interest. The scan is initiated automatically when the desired HU in the ROI is met. One study showed that the BT technique (when compared with the TB technique) had better synchronization between the scanning and contrast agent enhancement, with a more homogenous and steady enhancement for coronary angiography.[91] This technique has been shown to have less scan time (and reduced radiation exposure) as well as requiring less contrast agent. Up to 20% less contrast agent can be used compared to the other techniques. A recent study on pulmonary angiography in beagles showed no advantage to using the TB technique above the BT technique, however a limitation to this study was that only one patient had both techniques performed and compared.[14]

Various factors can affect the outcome of the BT technique. Should the ROI not be accurately positioned, erroneous monitoring may lead to either the desired HU never being reached in the vessel of interest, or, if the ROI is placed in such a manner that it includes the vessel wall, the desired HU may be artifactually reached earlier than it actually should. These scenarios can result in a suboptimal CT scan. If the patient moves during the monitoring scans (such as would happen with respiratory motion), the ROI may move out of the vessel of interest and an unsuccessful scan may result. One can start the main scan manually should the scan not trigger automatically.

Factors to bear in mind when using the BT technique include the transition delay (delay between the time at which the threshold is reached and the start of the actual CT scan) and the interscan delay (time between the consecutive dynamic scans). Both delays are variable depending on the machine used but it has been reported than even machines from the same vendors can have different delays.[16]

Literature reviews suggest trigger thresholds inside the ROI in the aorta at levels of 100HU, 150HU and 200HU above the baseline.[23, 29, 52, 92] As soon as the trigger threshold is reached, the table or gantry is automatically moved into the start position (which is determined during the planning phase of the study) and a breath hold instruction is given to the patient. During this interval the contrast agent concentration increases to the desired level of enhancement and the scanning is initiated. Some authors justify the choice of a rather low threshold (100HU) based on the extra 4 seconds needed before scanning for

the table or gantry to move into the correct position.[52] Technical factors such as the use of a saline flush, the osmolality and ionicity of the contrast agent and the site of injection of the contrast agent will have a notable influence on the enhancement achieved in the vessel of interest, as previously discussed.

The BT technique has been reported to be particularly beneficial for patients with right heart failure or pulmonary hypertension.[69] BT techniques are preferred for CT angiography in children.[2] Recently an adapted BT technique has been proposed, aptly named the "adaptive bolus tracking technique". With this technique real time CT images are reconstructed whilst the intravascular bolus density information is fed into an adaptive controller, which aids in predicting the bolus peak time for the next position and in so doing sends a signal to the table driver to adjust the speed of the gantry accordingly. This adapted technique lowers radiation to the patient in two ways: by generally lowering the tube current and by tracking the bolus peak trajectory.[93]

2.7.2 Test bolus

A low dose of the contrast agent (usually 15 – 20% of the total dose of the contrast agent) is injected and low radiation dose, single slice, sequential images are obtained at a point containing the vessel of interest, to evaluate vascular contrast enhancement over time. Time attenuation curves are generated and the contrast agents arrival time and time of maximal enhancement of the vessel is determined.[52] From these graphs the time delays between the start of contrast agent injection and initiation of the scan are calculated automatically.[10,26,52] This method has a significant advantage of being specifically adapted to the patient being examined and the variability of the BT technique is removed. The technique has been advocated for use in human patients with compromised cardiac function or in debilitated patients.[94] A study in 1995 concluded that the injection of a test bolus improved the timing of spiral CT acquisition in human patients when evaluating the enhancement in the aorta.[25]When evaluating smaller vessels, the TB technique is validated and suggested.[94]The disadvantage of the TB method however, is an increased scan time, anaesthetic time and contrast agent dose.

2.7.3 Time delay studies

The time delay to peak enhancement in a desired ROI or vessel is standardised and utilized (mostly through the use of the TB technique and experience). Although the benefits of such a protocol include a reduced scan time, reduced radiation exposure and reduced time under anaesthesia for the patient, as well as a decrease in the amount of contrast agent required, this type of protocol has certain limitations; physiological factors such as cardiac output, blood pressure and size of the patient can all lead to marked variability of the time delays. The scan delay selected may be too early or too late if a fixed scan delay is used, particularly when acquiring the arterial phase images.[18]

In one study, using a single detector scanner for pulmonary CTA, no difference was noted between the BT and time delay techniques, however the study cautions that in patients with substantial cardiopulmonary impairment and low circulation rate, long scan delays may be needed and thus may be missed with a non variable, fixed scan delay.[69] Additionally, the inherent machine delays before scanning can begin, can differ even in machines from the same vendors, making the empirical scan delay technique even more variable.

2.8 Factors to consider for computed tomography angiography

2.8.1 Spatial resolution

This metric factor depends largely on the detector collimator and reconstruction kernel and measures the smallest high contrast object. The modulation transfer function of a system describes the spatial resolution of a system whereas the “spatial frequency” measures the line pairs per centimetre. Computed tomography angiography functions at largely 8 – 15 line pairs per centimetre when employing a single focal spot. Although this is inferior to conventional radiographic arteriography, it does detect vessels as small as 1mm and an additional benefit is the ability to perform post processing three dimensional evaluation.[4] It also eliminates superimposition, often noted with tortuous vessels.

2.8.2 Temporal resolution

This evaluation is particularly important in angiographic studies and superior temporal resolution is largely achieved by increasing tube rotation time. Other methods to increase temporal resolution include using dual source CT machines and multi-segment reconstruction, a method used mainly for cardiac CT. Multi-segment reconstruction increases patient radiation dose and is also prone to artifacts more so than single segment reconstruction.[4]

2.8.3 Z-axis coverage per tube rotation

This effectively affects how fast the scan takes place, as it takes into consideration how quickly the tube rotates whilst advancing in the direction of the scan (pitch). Scan time required to cover a present scan area will effectively be reduced if a higher detector row configuration is used. However, one must be aware, that with the multidetector row CT machines, having a higher detector row configuration (>4cm with larger detectors) one can actually run the risk of outrunning the contrast bolus.[4]

2.9 Radiation dose

One of the major disadvantages of thoracic CT is radiation exposure and the use of CTA has further raised concern regarding radiation dose incurred.[95]When an increased number of detectors are used, the radiation dose per detector decreases, but the overall radiation dose to the patient increases. Scanning parameters which affect radiation dose include the collimation, tube current, tube voltage, pitch, table speed and tube rotation time. Of these, tube current is the most important factor as the relationship between the tube current and radiation dose is linear.[69] An increase in the tube voltage (kV) will increase the patient dose in an exponential manner. The patient dose is inversely proportional to x-ray tube rotation speed and the CT pitch.[32]

As radiation safety is a primary concern, it is necessary to reduce the radiation dose as much as possible whilst acquiring CT images of diagnostic quality. This is largely accomplished by using automated exposure control, which is a technique where attenuation values, measured by special detectors, are used to down regulate the tube current in thinner parts of the patient in order to

reduce the beam intensity.[48] Recent studies have focused on changing scan parameters, such as the tube voltage, in order to reduce the radiation dose without affecting the image quality during CTA.[69, 96] This could possibly be due to the fact that at lower tube voltages, such as 80kV compared to 100kV or 120kV, relative contribution of the photoelectric effect is greater than the Compton effect, resulting in an increased iodine contrast and thus demonstrating higher contrast enhancement values.[95, 97, 98] This will however also result in a relative underestimation of tissue perfusion at lower tube voltages.[95] An added benefit to setting the tube voltage to 80kV has been the ability to use a reduced contrast dose, due to the increased photoelectric effect and the k-edge of the iodine resulting in a similar attenuation as is seen with an increased dose of iodine and a higher tube voltage. This will be particularly beneficial in those patients at risk of CIN.[99]

Investigations into the radiation dose acquired from several thoracic, abdominal and pelvic CT studies in humans have shown that doses for volumetric, helical CT studies exceed the recommended clinical reference dose levels.[95] Such studies have not been done in companion animal veterinary medicine. Radiation dose studies in animals have focused on experimental microCT doses in rats and mice.[100]

Various methods are used to quantify or calculate the radiation dose incurred during a CT examination. The CTDI is a unique dose metric which is measured in a cylindrical acrylic phantom at the scanner isocenter. It is obtained by using a 100mm long pencil shaped ionisation chamber in one of two phantom sizes (depending on which body part is being examined). The volume CTDI (CTDI(vol)) is the metric which is used by the American College of Radiology for CT practice accreditation.[31,32] This measure is independent of both patient size and scan length and is fixed for set protocols. Thus CTDI(vol) does not quantify how much radiation a patient receives but rather indicates the intensity of the radiation. When an adult patient undergoes the same technique and scan protocol as an infant or juvenile patient, the adult will receive less organ dose as the radiation will be attenuated to a larger degree than in juvenile and infantile patients.[31] Additionally the CTDI(vol) for two identical protocols will vary due to differences in the x-ray tube design, the beam-shaping filters and the tube filtration used.[31] CTDI(vol) is measured in microGray.

The DLP is the total amount of radiation incident on a patient and is the product of the CTDI(vol) and the scan length and is measured in microGray per centimetre. The amount of radiation used is directly proportional to the patient's effective dose (ED). Dividing the ED by the DLP gives the ED:DLP ratio which is used to convert DLP data into a corresponding estimate of ED. These conversion factors are, however, specific to a specific CT examination, such as a thoracic or abdominal CT, as well as for a specified patient size. Other factors to be taken into account when performing this conversion include phantom size, anatomic region, tube voltage, patient age and weighting factors (which take into account tissue weighting factors published by the International Commission on Radiation Protection).[31]

All CT scanners will display information on the protocol performed following the procedure and this includes information on the DLP and CTDI(vol),. These two measures are the only two dose parameters that can be interpreted universally and thus CT protocols should specify CTDI(vol) and DLP.[31] It is the responsibility of the radiologist to evaluate this information, interpret it and ensure that the scan protocols used follow the "as low as reasonably acceptable" (ALARA) principle. Since the above mentioned radiation dosage review is based solely on human studies, as none could be found for veterinary patients, the principles should currently be applied to all mammals and the veterinary radiologist should pay cognizance to this in order to practice good radiation safety.

2.10 Conclusions drawn from literature review

- no comparison has been done between the BT and TB techniques in veterinary literature
- various factors affect the bolus geometry of the contrast material when injected intravenously, the most important of which, in a healthy individual, is reported to be patient weight
- several scan parameters have an effect on the radiation dose
- no studies on the radiation dose during CT have been conducted in companion animals to date
- the use of the iodinated contrast agents have been reported to cause adverse reactions in humans and dogs

- no phantom studies on bolus geometry have been conducted in animals for the sole purpose of developing empirical scan delay in animal patients. However, porcine and canine species have been used as models for human studies
- there is a paucity of information regarding thoracic CTA in dogs in the literature

Chapter 3: Materials and methods

3.1 Experimental design

Screening procedure

Four adult purpose-bred research beagles from the University of Pretoria Biomedical Research Centre (UPBRC) and two adult beagles from the Onderstepoort Teaching Academic Unit (OTAU) were used. All the beagles were of average body condition score. There was no discrimination based on gender during the selection of the dogs. There were 3 spayed females and 3 castrated males varying in age between 34 – 69 months (appendix A). In order to ensure that all 6 animals were eligible to be included in the study, and because certain factors such as poor cardiac output, abnormal blood pressure and systemic disease could affect the rate at which contrast arrives in the aorta, all UPBRC beagles underwent a routine clinical examination 2 weeks prior to the start of the project. The two beagles from OTAU had their screening procedure done the day before the onset of the study. Screening included a full blood count (FBC), total serum protein and a full renal profile (urinalysis, urea, creatinine, urine gamma glutamyl transpeptidase (GGT) and urine protein to creatinine ratio). The reason a full renal profile was performed on all animals was due to the fact that another study was linked to this research project, evaluating the effect of repeated doses of iodinated contrast on renal function using scintigraphic glomerular filtration (GFR) determination. The urinalysis as well as a renal specific serum biochemistry panel (urea, creatinine, urine GGT: creatinine ratio, serum inorganic phosphate, sodium and potassium) was performed on all the dogs prior to the start of the project, 24 hours prior to and repeated 3 days after each CTA. The full renal profile (excluding the GFR scintigraphy) was also repeated 14 days after each CTA. Normal renal function was crucial to the additional study linked to this project.

Additional screening tests included thoracic auscultation and a series of 5 blood pressure readings to exclude cardiac pathology. The blood pressure

readings were done using a non invasive oscillometric technique using a Cordell Veterinary monitor (9403BP). A recommended method of blood pressure evaluation was used.[101]

Additionally, each animal had a right lateral recumbent and dorso-ventral thoracic radiograph taken to rule out radiologically visible thoracic pathology which would have affected the study. Each animal had a complete abdominal ultrasound examination, performed by the primary investigator and the radiographs and ultrasound images were assessed by the primary investigator.

The results arising from these screening procedures were assessed by the primary investigator and based on these findings the animals were declared fit to partake in the study. The GFR scintigraphies done prior to each CTA were also used as a screening procedure.

The animals were housed within the Onderstepoort Veterinary Academic hospital during the entire study period and were fed twice daily (Hills® maintenance, 86gram *bis in die*) and given *ad lib* water. The animals were fasted for 12 hours preceding the GFR scintigraphy and CTA studies as well as for the ultrasound examination. Water was withheld for 2 hours prior to anaesthesia or sedation.

Exclusion criteria included:

- An audible cardiac murmur.
- Hypertension or hypotension.
- Any indications of systemic disease identified on the FBC.
- Any radiologically visible thoracic pathology.
- Any abnormality detected on the abdominal ultrasound which may affect the study.
- An abnormal total serum protein level.
- Any indications of renal insufficiency/early renal tubular damage. As Certain factors evaluated for renal insufficiency/renal damage can Be abnormal in normal patients the following sub criteria were adopted: - any 2 of the following:
  - raised urea, creatinine, urine specific gravity and abnormal urine sediment
  - raised urine GGT : creatinine ratio

- abnormal kidneys on abdominal ultrasound
- a GFR less than 3.46 +/- 0.52ml/min/kg[102, 103] prior to each CTA and following the first CTA

3.2 Experimental procedures

Each animal underwent both the BT CTA and the TB CTA. The animals were randomly assigned into two groups by pulling the number of the dog 1 - 6 from a hat. Group 1 received the test bolus technique first, followed at least two weeks later by the bolus tracking technique. Group 2 had the studies conducted in the reverse order.

A 20 gauge intravenous catheter was placed in the cephalic vein of either the left or right thoracic limb and secured with tape. Patients were anaesthetised routinely and the patient was placed in sternal recumbency on the CT table to prevent dependant lung hypostasis and to minimise excessive motion artifacts during scanning. The anaesthetic protocol was standardised as follows:

- Premedication with diazepam (*Pax®, Pharmcare limited, Woodmead, Sandton, South Africa*) 0,2mg/kg i/v – wait 2 minutes
- Induction with Propofol 1% (*Fresenius Kabi SA (Pty) Ltd, Stand 7, Growthpoint Park 2 Tonetti Street, Halfway House, Midrand, South Africa*) at 5.5mg/kg i/v to effect.
- Endotracheal intubation
- Maintenance with isoflurane*(Forane® liquid, Abbott Laboratories Pty Ltd., Constantia Kloof, Roodepoort, South Africa)*
- Monitoring of anaesthesia.

During various stages of the CTAs, positive pressure ventilation with breath holding techniques, by means of manual rebreathing bag compression, were employed, to eliminate motion artifacts.

Subsequent to a planning topogram, a helical survey scan was done followed by an early arterial phase and a venous phase angiographic CT scan.

3.2.1 Protocol for the bolus tracking CTA

Step 1: Topogram

With the patient positioned in sternal recumbency on the CT table, a dorsal survey helical topogram was obtained from the level of the thoracic inlet to the most caudal extent of the diaphragm, in a cranio-caudal direction using a dual slice, 6th generation Siemens Emotion duo CT scanner with sliding gantry (*Siemens South Africa, 126, 14th road, Erand gardens, Halfway House, Midrand*).

Step 2: Pre-contrast survey thoracic CT

A collimated helical scan from the level of the seventh cervical vertebra (C7) to the level of the second lumbar vertebra (L2) was performed in a caudal to cranial direction.

Collimation was set at 2.5mm with a slice thickness of 3.0mm. A kV of 130, mA of 24 and a pitch of 1.65 was used. This survey scan was evaluated for any pathology or abnormalities not noted during the thoracic radiographic examination.

From this scan the image coinciding with the area of interest was obtained and a single axial scan at this site was obtained. A ROI was placed in the aorta at the level of eighth thoracic vertebra (T8)(Fig.4). This level was chosen as the Ao, CVC and rCPA were visualised on this single slice. The ROI occupied approximately ¾ of the vessel internal diameter and was placed clear of the vessel wall to prevent artifacts. The scan range and scan parameters used for the arterial and venous phase CTAs were planned using this survey pre-contrast scan.

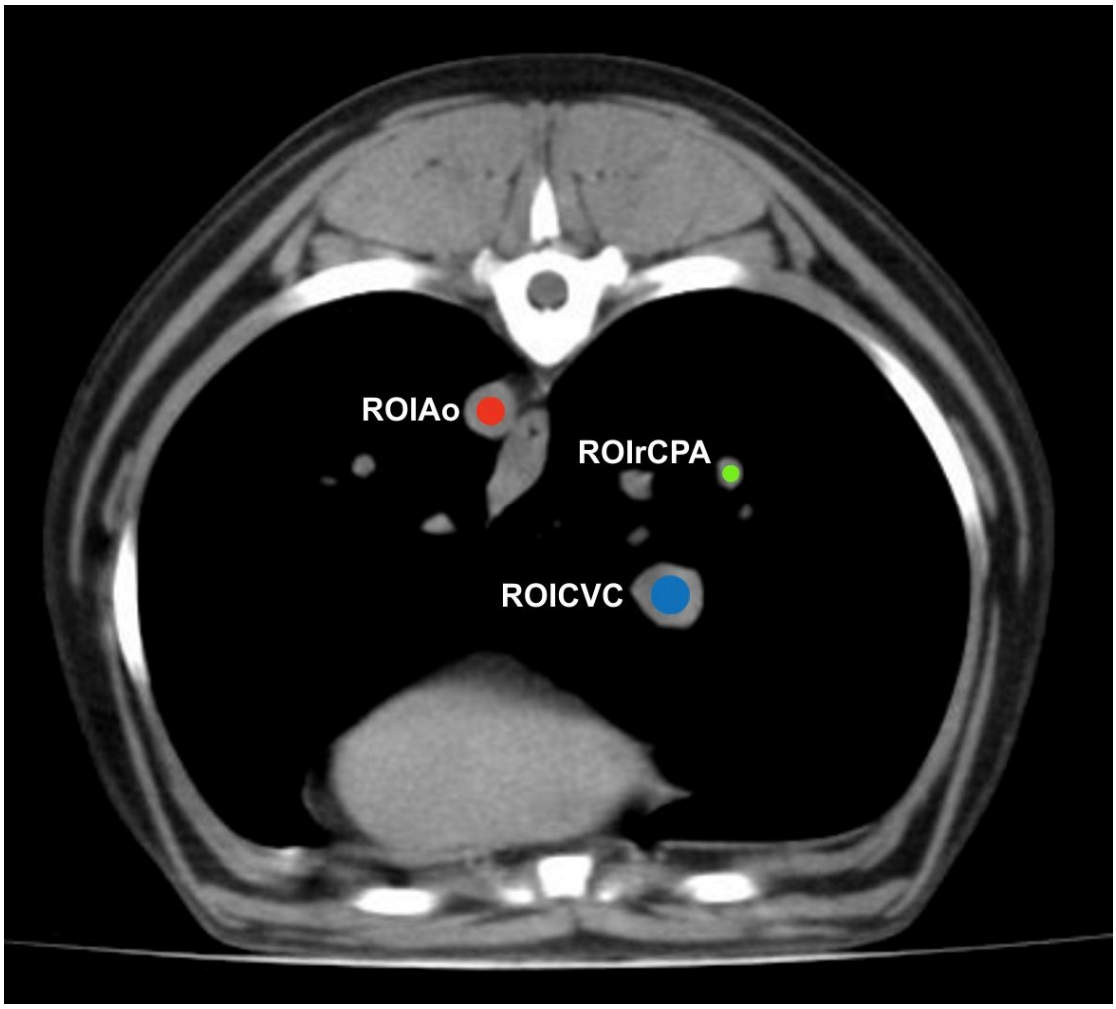

Fig.4: A transverse pre-contrast image of dog 5 at the level the eighth thoracic vertebra (T8). The aortic ROI (ROIAo)(red dot), the caudal vena cava ROI (ROICVC)(blue dot) and the right caudal pulmonary artery ROI (ROIrCPA)(green dot) are illustrated. Left of the dog is to the left of the image.

Step 3: CTA – Systemic arterial phase

A threshold of 150HU was set in the ROI to allow for triggered acquisition of the angiographic phase (pre-monitoring phase). This was chosen as a mean of the recommended thresholds mentioned in the literature review. These patients received the entire dose of the 2 ml/kg Iohexol *(Omnipaque™, GE Healthcare Pty Ltd., Weltevreden Park, South Africa, 1709)*(300mgI/ml) administered with a pressure injector set to inject at a rate of 3mls/sec, immediately followed by a manual saline chaser of 1ml/kg. The injection was started at the same time as the pre-monitoring phase. To facilitate the manual injection of the saline chaser, a three way stopcock valve was connected to the i/v catheter via an administration set. During the pre-monitoring phase, low dose sequential scans were performed at the pre-selected level. By means of

an inherent software programme, serial Hus received during each pre-monitoring scan, were acquired and plotted on a graph. When contrast reached the desired 150HU at this level, the machine automatically triggered the start of helical scanning of the systemic arterial phase (here after referred to arterial phase) in a caudal to cranial direction. The scan direction was chosen to limit motion artifacts from diaphragmatic movement. The scan was conducted from the level of T10 to the thoracic inlet. This range was chosen as the blood vessels of interest (Ao, CVC, rCPA and cranial thoracic arteries) were expected to lie in this scan range.

If it was noted that the attenuation in the Ao was rising to a subjective level of 150HU without automatic triggering the scan was triggered manually.

Scan parameters for the arterial phase were the same as for the pre-contrast survey helical scan. The kV ranged from 110 to 135 and the mA were chosen inherently by the Caredose® software.

Step 4: CTA – Systemic venous phase

Immediately following the arterial phase, a second helical scan was performed in the anticipated systemic venous phase (here after referred to as the venous phase). The scan was conducted in a caudal to cranial direction from the level of T13 to the thoracic inlet, with scan increments and parameters as for the arterial phase.

During both CTA helical scans, motion artifacts from respiration were minimised as much as possible by means of positive pressure breath hold applied manually with a rebreathing bag.

All the dogs were closely monitored during their recovery from anaesthesia in the CT room under direct veterinary supervision.

3.2.2 Protocol for the test bolus CTA

Step 1: Topogram

As for the bolus tracking technique

Step 2: Pre-contrast survey thoracic CT

As for bolus tracking technique

Step 3: Low dose sequential test bolus scan

The patient then received a test bolus of Iohexol 300mgI/ml at 15% of the full dose of 2ml/kg. This test bolus was administered manually. Based on the literature review on the human CTA protocols, the test dose should be administered with a pressure injector using the same injection rate as the full dose of contrast medium, however in this study, the volumes that were required for the test bolus did not justify the use of the pressure injector.

The test bolus injection was immediately followed by a manual saline flush at a dose of 1ml/kg. The manual saline flush was administered as for the bolus tracking group.

Forty serial sequential low dose scans followed with the onset of injection of the test bolus at the slice identified on the pre- contrast scan. A breath hold technique was once again employed to minimize motion artifacts from respiration. There was an unavoidable scan delay, inherent to the machine, of four seconds, following initiation of the scan.

Step 4: Dynamic evaluation

Using the dynamic evaluation software programme (DYNAEVA®), the 40 sequential scans obtained in the previous step, following intravenous administration of the test bolus, were evaluated and information regarding time to peak maximal enhancement (tPME) was obtained for the Ao and the CVC. The tPME obtained during dynamic evaluation were used as the time delays to plan the arterial and venous phases of the CTAs that followed.

Step 5: CTA – Arterial phase and venous phase

The dogs received the intravenous Iohexol (300mgI/ml) at a dose of 2ml/kg. The contrast was administered as for the BT technique, using a pressure injector operated at the same parameters, followed by a manual saline flush. Scanning was initiated at the start of injection with the unavoidable inherent four second scan delay as well as the time delays calculated during dynamic evaluation. The scan parameters were the same as for the BT technique with positive pressure breath hold techniques used to minimize motion artifacts. Arterial and venous phase scans were performed.

3.2.3 Observations and analytical procedures

The raw data was evaluated on the dedicated workstation by the primary investigator. Reconstruction increments were 50% (1.5mm). The images were viewed with a window width (WW) of 750 and a window level (WL) of 40, which is described in the literature as a "pleural" window,[104] as well as with a WW of 400 and WL of 40, which is termed a "mediastinal" window in the Siemens software. The investigator subjectively assessed the images viewed with the "mediastinal" window to be easier to interpret and all measurements were done in this window. Thoracic pre-contrast, arterial post-contrast and venous post-contrast images were evaluated on MPR images.

3.2.4 Data measurements

Three measurements of the attenuation, in HU, were taken for each of the following vessels:-Ao, CVC and the rCPA. The first measurement was taken at the level of T8, where all three vessels were well visualised on one slice. The second measurement was taken 3 slices (4.5mm) caudal to the first and the third measurement taken 3 slices (4.5mm) caudal to second measurement. The three measurements were then averaged and the mean obtained for each vessel.

The smaller cranial thoracic vessels were assessed subjectively, on a scale of 0 – 3 (0 = no post-contrast enhancement noted, 1 = mild post-contrast enhancement, 2 = moderate post-contrast enhancement, 3 = strong, homogenous post-contrast enhancement) for their attenuation and ease of identification as an individual vessel. The subjective assessment was then averaged.

The following vessels were assessed:-

- cranial vena cava
- brachiocephalic trunk
- left and right subclavian arteries
- carotid arteries
- costocervical trunk
- internal thoracic arteries
- vertebral arteries

If any of the above vessels were visualised and were large enough and adequately attenuating, the attenuation was measured objectively in HU.

Any side effects noted during the procedure were documented and the mA, CTDI(vol), DLP, the duration of the arterial and venous phases for each scan as well as the inherent delays experienced during the scans, was noted. Additionally the total amount of contrast injected, the average pressure obtained during pressure injection and the duration of the injection was recorded.

All measurements were entered into an Excel *spreadsheet (Microsoft Excel 2003, Microsoft Corp, Redmond, WA, USA) .The above data was* compared between the two groups.

3.2.5 Data and Statistical Analysis

Data analysis was done in conjunction with a statistician. In this within-subject study design, the BT and TB techniques were compared with respect to the HU in the Ao, CVC and the rCPA areas, both for the arterial and venous phases. The Shapiro-Wilks test was done for normality to assess whether differences (BT-TB) within parameters were normally distributed. The six comparisons, namely, the three areas each for the arterial and venous phases, were performed using the Students paired t-test. To facilitate the interpretation of the t-test results, the 95% confidence interval for difference of the means between the BT and the TB was rewritten to a 95% confidence interval for BT as a ratio of TB, where the latter was considered the gold standard. When evaluating the 95% confidence interval for the difference of the means, the closer the values are together, the more comparable they are to each other. For this data, only five of the dogs results were evaluated due to an error in timing with dog number 1 (see 4.2).

The assessment of the visualisation of the smaller cranial thoracic vessels was largely subjective in nature, however, a subjective grading score was used and these scores were average and compared between the two techniques (BT and TB). Once again, due to the timing error encountered with dog 1, only five of the six dogs' images were assessed for this data subset.

The radiation parameters (mA, CTDI (vol) and DLP), the duration of the studies, the dose of contrast used and the injection parameters were compared between the BT and TB techniques using the Students paired t-test

and significance was set at $P<0.05$. For this data, comparison was done between all six dogs.

3.3 Ethical considerations

The study was approved by the Animal use and care committee (V09/44). The animals used in this study were cared for in a manner approved by this committee. As they are owned by the UPBRC and OTAU and not client owned dogs, consent was obtained from this facility and the fate of the animals on completion of this study was decided upon by this facility. The project did not result in termination of any of the animals after the completion of the study.

The CT dose index was closely monitored for each patient throughout the study and if elevated levels were noticed, action was taken by the primary researcher. This entailed removing the patient from the trial with close monitoring for any side effects. A record of the number of studies containing ionising radiation each patient is involved in is kept. Such studies are kept to a minimum for each patient.

At all times, the number of people present in the CT scan room during radiation was limited as much as possible. Due to the need for manual breath holding during the scans, at least one person was required to be present in the CT room. A lead jacket and thyroid protector were worn during the procedures by any person in the room. Additional radiation safety precautions included a dosimeter to be worn at all times and these were evaluated monthly for radiation levels as per normal radiation monitoring procedures.

Chapter 4: Results

4.1 Study population

All the dogs were eligible to be included in the study based on the findings of the complete clinical examination, FBC, renal specific serum chemistry, urinalysis, blood pressure measurements, thoracic radiography and abdominal ultrasound. There were 3 males and 3 female dogs ranging in age from 34 – 69 months of age (appendix A). Body weight ranged from 10.4 kilograms to 16.10 kilograms (mean 14.06kg ± 2.25). None of the dogs were excluded based on the strict renal profile screening procedures instituted as a result of the second study being linked to this project.

4.2 Data acquisition

Each dog responded well to the chosen anaesthetic protocol, with none of the dogs requiring additional Propofol 1% ® for induction or maintenance of anaesthesia. The dogs all recovered well from the anaesthetic and no adverse reactions were noted.

All but one of the CT scans were diagnostic with adequate attenuation of the vessels of interest (Figs. 5 – 10). The TB technique conducted on dog 1 showed a very late time to peak arterial (Ao) enhancement (t = 49.1seconds), which was longer than the time to peak enhancement for the CVC (t = 23.5 seconds). The peak attenuation in the Ao (99.8 HU) was also lower than for the CVC (183.9 HU)(Fig 5) (appendix B and C). This made subjective attenuation in the aorta and arterial structures sub-optimal compared to other TB studies. Due to the late time to peak arterial enhancement and the obvious error in evaluating this patient during first pass bolus dynamics, this patient was excluded from all statistical analysis pertaining to bolus dynamics and post- contrast enhancement in the Ao, CVC, rCPA as well as subjective evaluation of attenuation in the smaller cranial thoracic vessels. However, as

the studies were conducted and completed in a comparable manner to the rest of the dogs studies, this patient's data was used for statistical evaluation of the mA, CTDI(vol), DLP, dose of contrast used and injection parameters.

DYNAEVA® data pertaining to peak attenuation and tPME during the TB technique from dog 4 and dog 6 was incorrectly archived and thus not available for statistical analysis appendix B and C). The data was however available at the time of the study and hence the delays acquired were successfully and correctly used during the planning stages of the CTAs.

The pressure injector was successfully utilised for all the scans (except the injection of the test boluses as mentioned previously). Motion artifacts were noted during one of the scans, the arterial phase of the bolus tracking scan for dog 3. However the scan was still considered diagnostic.

4.3 Data sets analysed

A complete data set of all measurements taken in the ROI for the aorta (ROIAo), the ROI for the CVC (ROICVC) and the ROI for the right caudal pulmonary artery (ROIrCPA) during the arterial and venous phases for both the BT and TB techniques is provided in appendices D - O. For the difference between the BT and TB technique, within our parameters, the results of the Shapiro-Wilks tests proved that none of the data sets deviated from normal distribution. (See 3.2.3 and 3.2.4).

For evaluation of attenuation in the CVC during the arterial phase of the bolus tracking technique (appendix H), two of the measures of HU for ROIb were negative values and this was most likely a partial volume artifact.

4.3.1 Attenuation in the Aorta

Observed data for attenuation (in HU) in the Ao in the arterial phase (Ao_{art}) are summarised in table 1.

Table 1: Mean and standard deviation (HU) in the Ao_{art}.

Technique	Observations	Mean	SD	95% CI
Bolus tracking	5	660.52	138.49	(488.5; 832.4)
Test Bolus	5	469.82	199.52	(222.1; 717.6)
Difference		190.66	227.07	(-91.2; 472.6)

(CI = confidence interval and SD = standard deviation).

Mean BT attenuation is not significantly different than the TB technique (p=0.13, paired t-test) when compared with respect to each other. To further facilitate interpretation the 95% confidence interval for the difference between BT and TB can be rewritten as a 95% confidence interval for the ratio of BT to TB where

$$80\% \leq \mu \text{ bolus tracking} / \mu \text{ test bolus} \leq 200\%$$

From the latter, with 95% confidence interval, the worst result we can expect for BT is 80% that of TB and the best is 200% that of TB, thus for all practical purposes BT can be regarded as superior to TB for this region in the arterial phase.

Observed data for attenuation (in HU) in the Ao in the venous phase (Ao_{ven}) are summarised in table 2.

Table 2: Mean and standard deviation (HU) in the Ao_{ven}.

Technique	Observations	Mean	SD	95% CI
Bolus tracking	5	190.6	28.29	(154.9; 225.2)
Test Bolus	5	188.8	21.9	(161.6; 216.07)
Difference		1.26	28.95	(-34.69; 37.21)

(CI = confidence interval and SD = standard deviation).

Mean BT and TB attenuation values do not differ significantly (p=0.92, paired t – test). The 95% confidence interval for BT as a ratio of TB is

81% ≤ μ bolus tracking/ μ test bolus ≤ 119%

The latter interval does not show any preference for a particular technique when evaluating the Ao_{ven}.

4.3.2 Attenuation in the caudal vena cava

Observed data for attenuation (in HU) in the CVC in the arterial phase (CVC_{art}) are summarised in table 3.

Table 3: Mean and standard deviation (HU) in the CVC_{art}.

Technique	Observations	Mean	SD	95% CI
Bolus tracking	5	37.84	20.8	(11.96; 63.79)
Test Bolus	5	91.48	66.54	(8.89; 147.1)
Difference		-53.62	48.58	(-113.94; 6.70)

(CI = confidence interval and SD = standard deviation).

Mean BT and TB attenuation values do not differ significantly (p=0.069; paired t-test). The confidence interval for the ratio of BT to TB is represented as

0% ≤ μ bolus tracking/ μ test bolus ≤ 107%

thus showing that BT is inferior to the TB technique when evaluating the CVC_{art}.

Observed data for attenuation (in HU) in the CVC in the venous phase (CVC_{ven}) are summarised in table 4.

Table 4: Mean and standard deviation (HU) in the CVC_{ven}.

Technique	Observations	Mean	SD	95% CI
Bolus tracking	5	171.3	32.36	(131.18; 211.5)
Test Bolus	5	191.08	22.00	(163.75; 218.4)
Difference		-19.72	19.59	(-44.05; 4.61)

(CI = confidence interval and SD = standard deviation).

Mean BT and TB attenuation values do not differ significantly (p=0.087; paired t-test). The 95% confidence interval for the ratio of BT to TB is

$$76.0\% \leq \mu \text{ bolus tracking} / \mu \text{ test bolus} \leq 102\%$$

The latter interval does not show any preference for a particular technique when evaluating the CVC_{ven}.

4.3.3 Attenuation in the right caudal pulmonary artery

Observed data for attenuation (in HU) in the rCPA in the arterial phase ($rCPA_{art}$) are summarised in table 5.

Table 5: Mean and standard deviation (HU) in the $rCPA_{art}$.

Technique	Observations	Mean	SD	95% CI
Bolus tracking	5	606.34	143.37	(428.37;734.38)
Test Bolus	5	413.72	174.99	(196.49;631.02)
Difference		192.62	287.52	(-164.4;549.63)

(CI = confidence interval and SD = standard deviation).

Mean BT and TB attenuation values do not differ significantly (p=0.208, paired t-test. The 95% confidence interval for the ratio of BT to TB is

$$60\% \leq \mu \text{ bolus tracking} / \mu \text{ test bolus} \leq 232\%$$

Thus for all practical purposes BT can be regarded as superior to TB for the $rCPA_{art}$

Observed data for attenuation (in HU) in the rCPA in the venous phase ($rCPA_{ven}$) are summarised in table 6.

Table 6: Mean and standard deviation (HU) in the $rCPA_{ven}$

Technique	Observations	Mean	SD	95% CI
Bolus tracking	5	174.34	27.25	(140.48;208.27)
Test Bolus	5	164.46	18.51	(1414.5;187.49)
Difference		9.87	30.26	(-27.69;47.46)

(CI = confidence interval and SD = standard deviation).

Mean BT and TB attenuation values do not differ significantly (p=0.505, paired t – test. Here the 95% confidence interval for BT as a ratio of TB is

$$83\% \leq \mu \text{ bolus tracking} / \mu \text{ test bolus} \leq 128\%$$

The latter interval does not show any preference for a particular technique when evaluating the $rCPA_{ven}$.

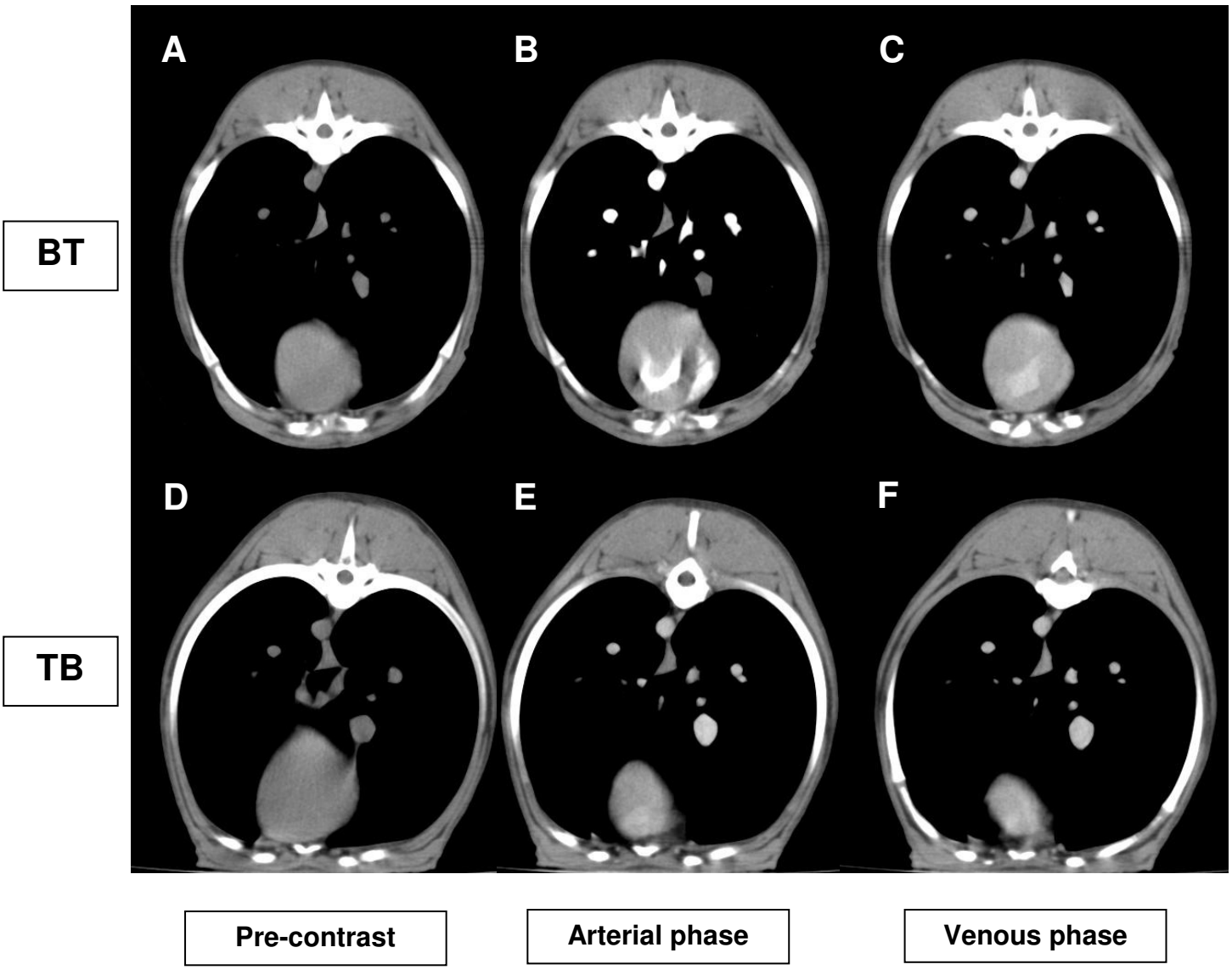

Fig.5.Transverse pre- and post-contrast images of dog 1 at the level of T8.A) pre-contrast image during the BT technique, B) BT arterial phase, C) BT venous phase, D) pre-contrast image during the TB technique, E) TB arterial phase, F) TB venous phase. Left of the dog is to the left of the image. Note the increased attenuation in the CVC compared to the Ao during the arterial phase for the test bolus technique.

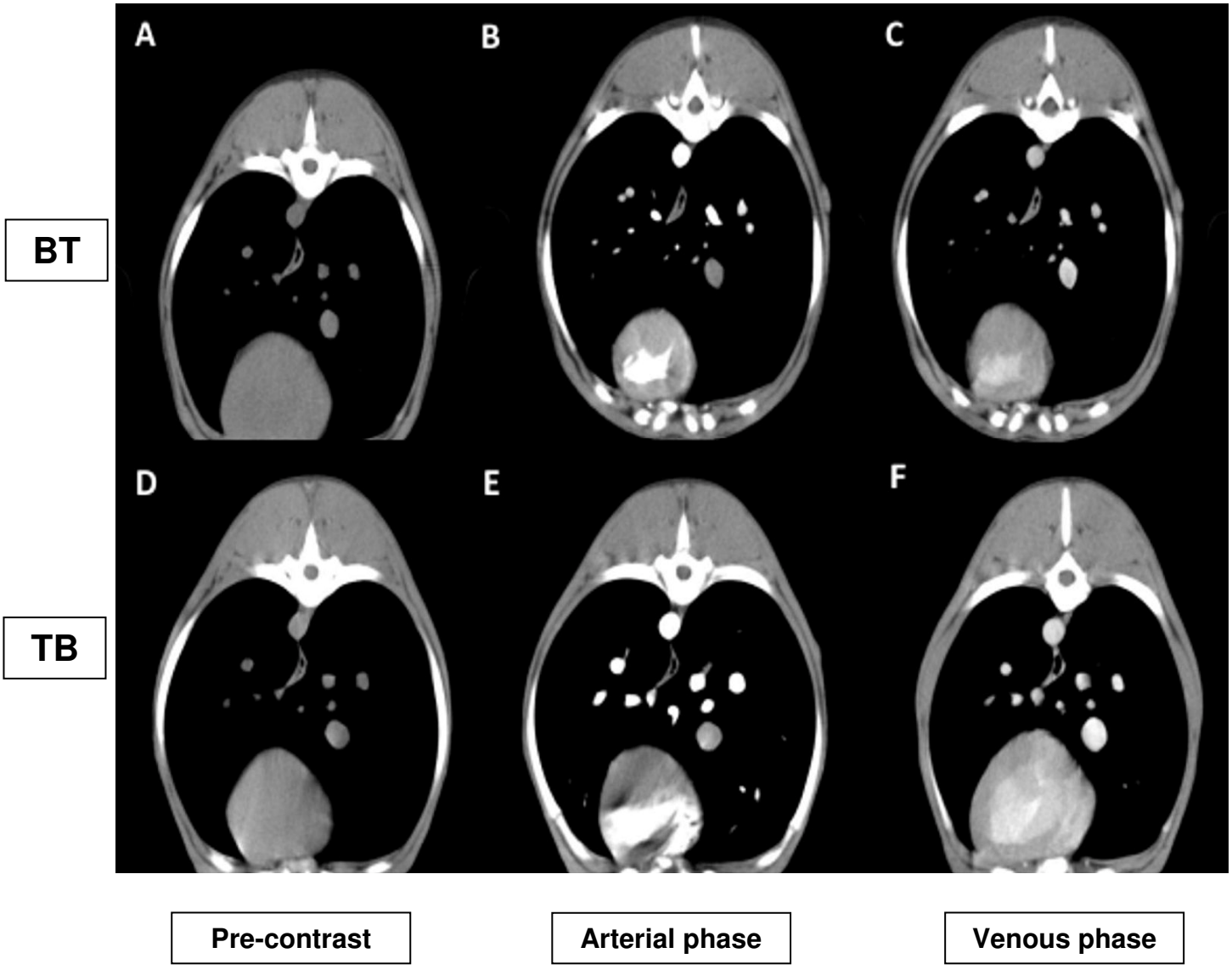

Fig.6.Transverse pre- and post-contrast images of dog 2 at the level of T8.A) pre-contrast image during the BT technique, B) BT arterial phase, C) BT venous phase, D) pre-contrast image during the TB technique, E) TB arterial phase, F) TB venous phase. Left of the dog is to the left of the image.

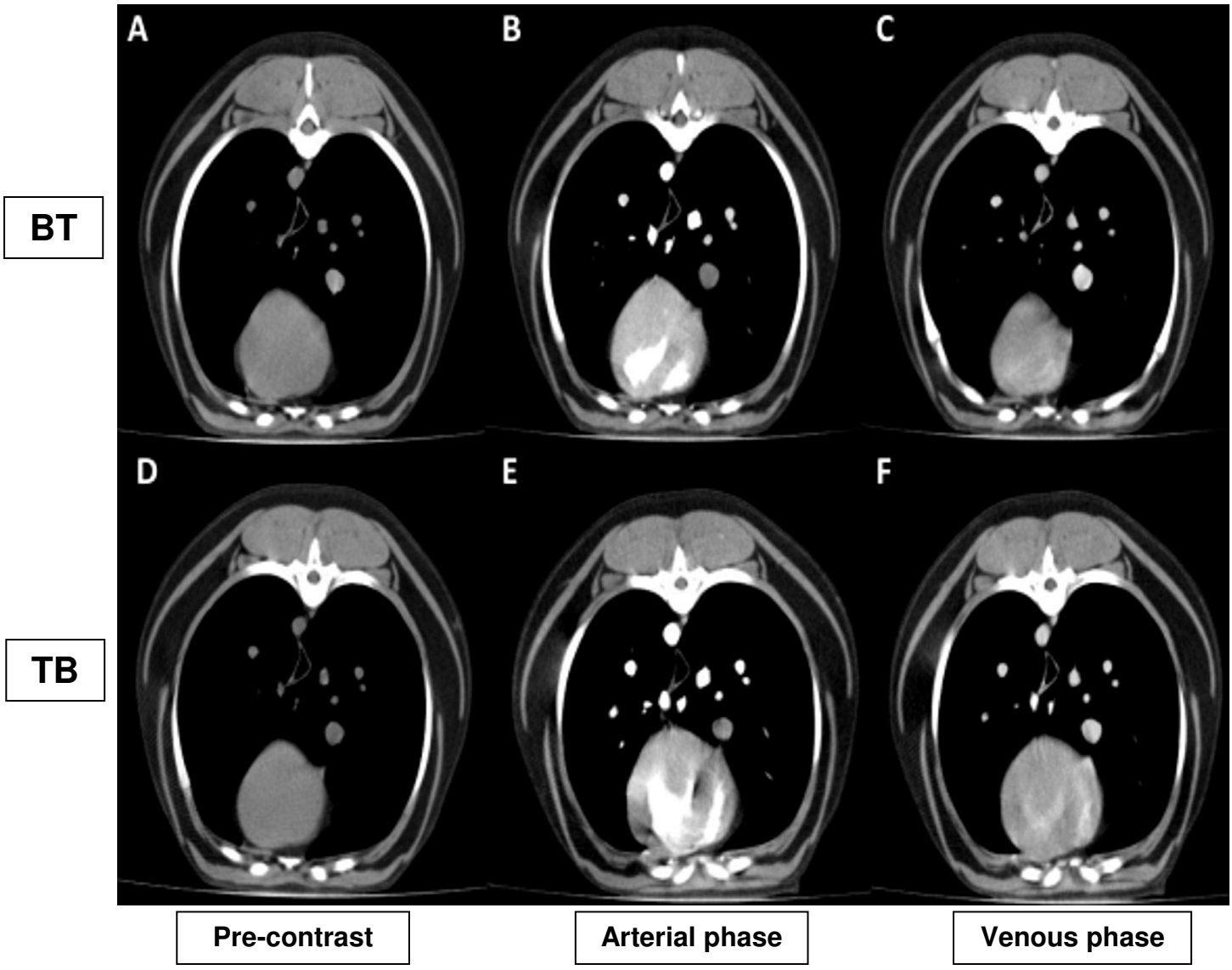

Fig.7.Transverse pre- and post-contrast images of dog 3 at the level of T8.A) pre-contrast image during the BT technique, B) BT arterial phase, C) BT venous phase, D) pre-contrast image during the TB technique, E) TB arterial phase, F) TB venous phase. Left of the dog is to the left of the image.

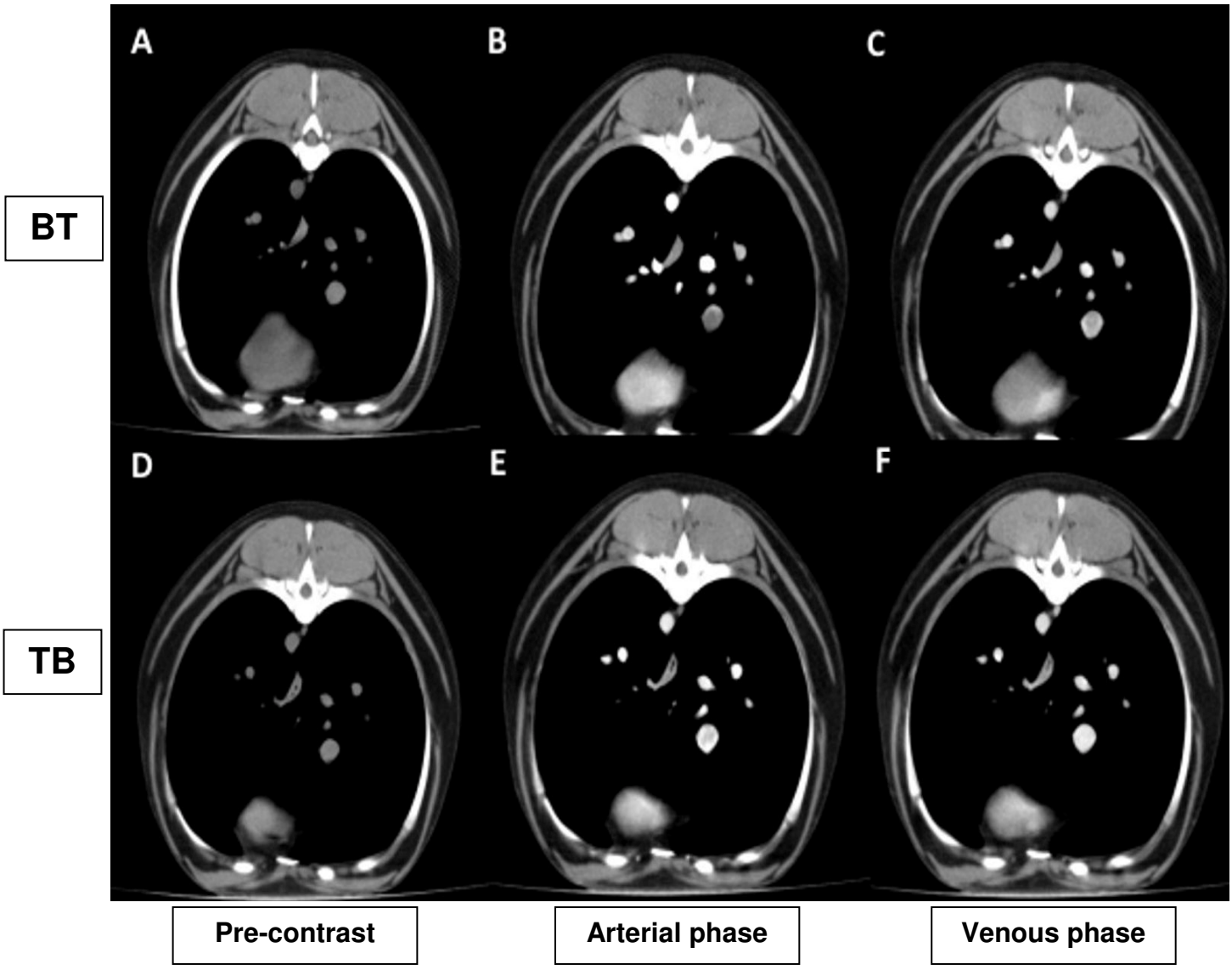

Fig.8.Transverse pre- and post-contrast images of dog 4 at the level of T8.A) pre-contrast image during the BT technique, B) BT arterial phase, C) BT venous phase, D) pre-contrast image during the TB technique, E) TB arterial phase, F) TB venous phase. Left of the dog is to the left of the image.

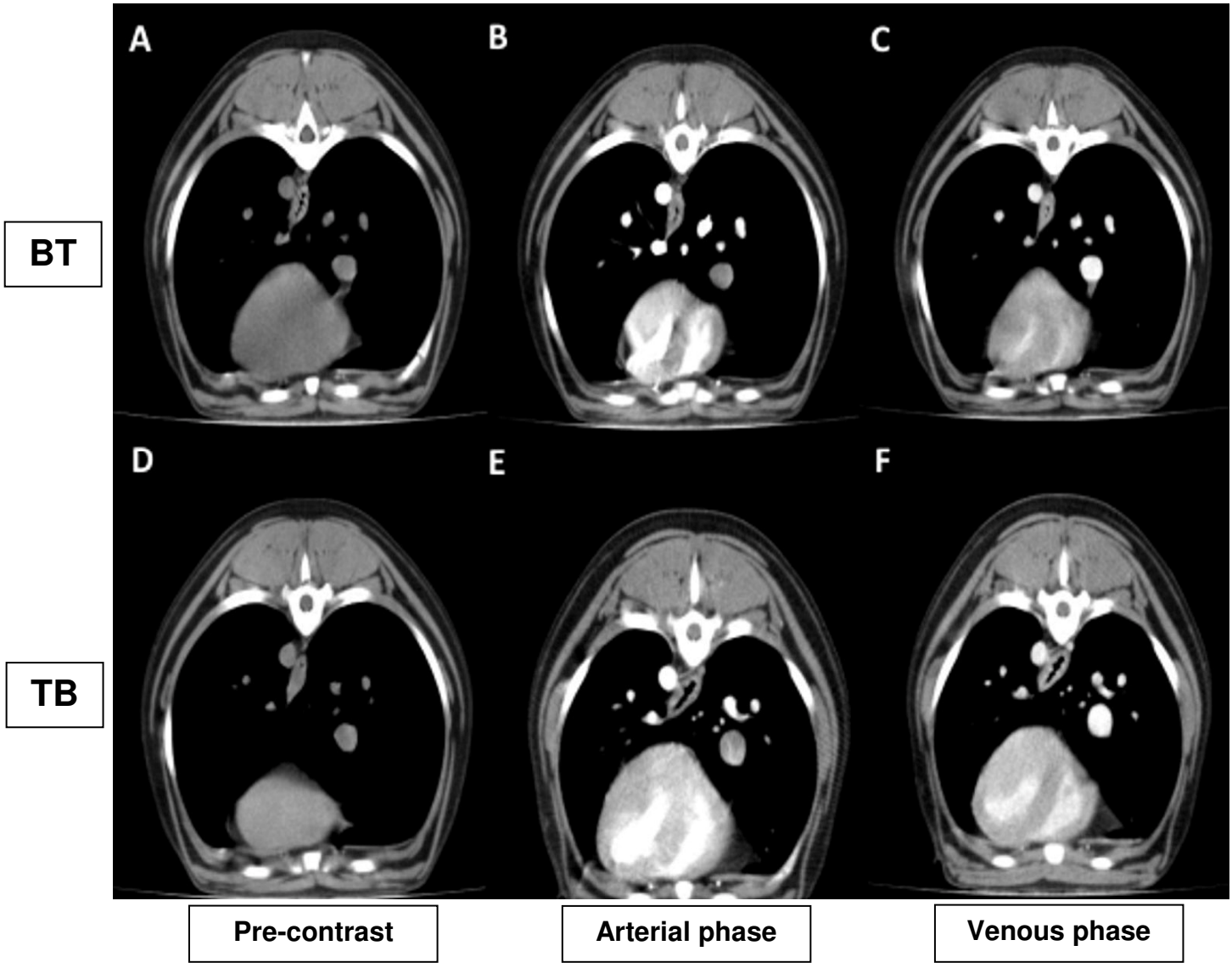

Fig.9.Transverse pre- and post-contrast images of dog 5 at the level of T8.A) pre-contrast image during the BT technique, B) BT arterial phase, C) BT venous phase, D) pre-contrast image during the TB technique, E) TB arterial phase, F) TB venous phase. Left of the dog is to the left of the image.

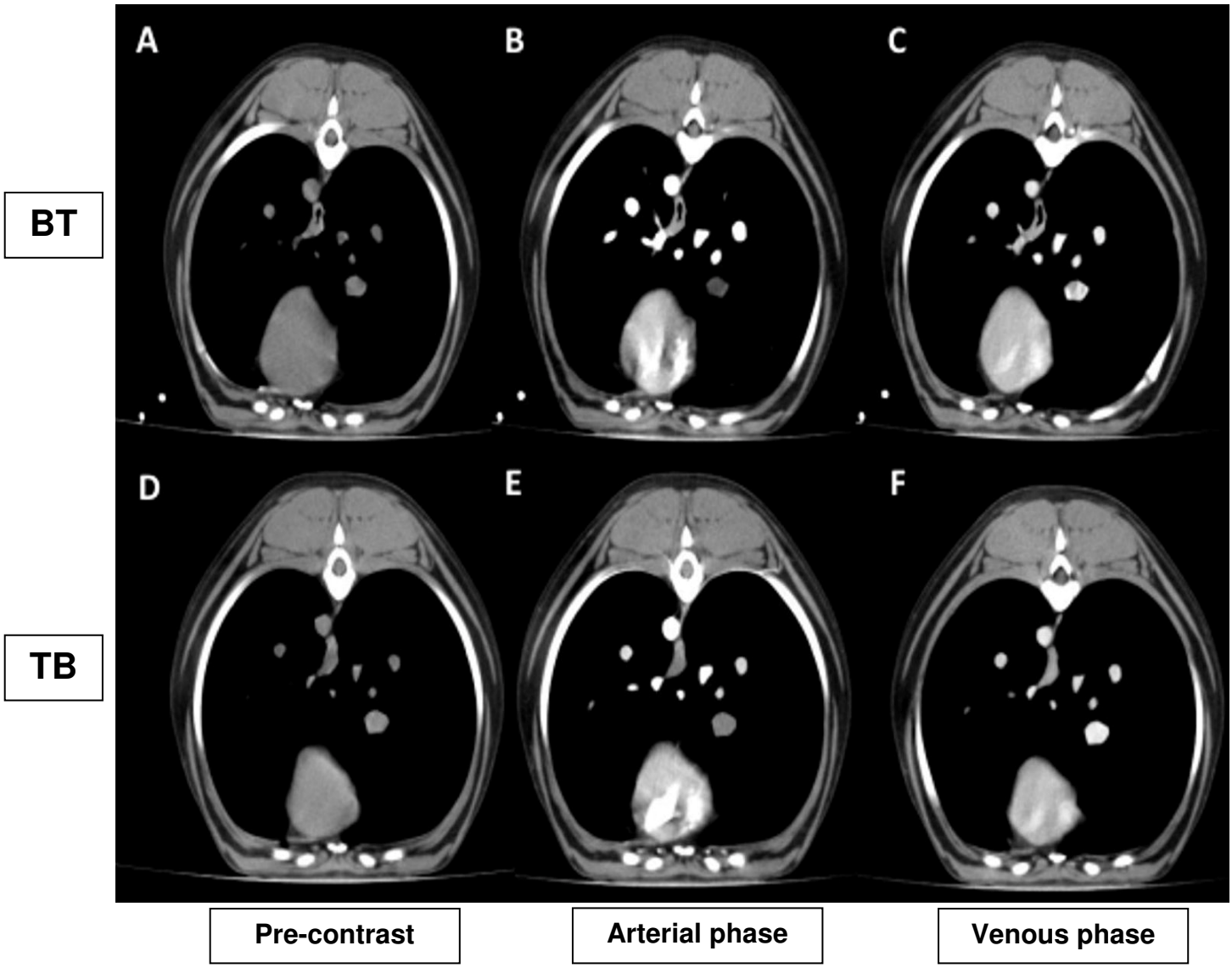

Fig. 10.Transverse pre- and post-contrast images of dog 6 at the level of T8.A) pre-contrast image during the BT technique, B) BT arterial phase, C) BT venous phase, D) pre-contrast image during the TB technique, E) TB arterial phase, F) TB venous phase. Left of the dog is to the left of the image.

4.3.4 Assessment of the smaller cranial thoracic vessels

The cranial thoracic vessels that were evaluated included the brachiocephalic trunk, the left and right subclavian, common carotids, the internal thoracic and the vertebral arteries as well as the costocervical trunk (appendix P and Q). The cranial vena cava and brachiocephalic vein was also evaluated in terms of its attenuation in HU, to assess how much of the injected contrast agent was still present in the first pass venous circulation, following intravenous injection, during the arterial and venous phases of the study (Fig. 11).

Images of the cranial thoracic arteries, during the arterial and venous phases are illustrated in Figs. 12-17. Most often the cranial thoracic arteries could be visualised with certainty and moderate attenuation during the arterial phases of the studies (grade 2.4 - 2.8 out of 3) with the internal thoracic artery and vertebral artery being the only smaller arteries that showed a lower grade of subjective enhancement during the arterial phase for both the BT (2.1 and 2.2 out of 3 respectively) and TB (2.2 and 2.3 out of 3 respectively) techniques. These two arteries also showed subjectively less attenuation during the venous phase for the test bolus studies (1.3, 1.1 out of 3 compared to 1.6 out of 3 for the rest of the arteries).However at all times the amount of attenuation was adequate to visualise and correctly identify the vessel.

The most striking finding during the assessment of the smaller cranial thoracic vessels was that the cranial vena cava and at times, the axillary vein as it as it merged with the brachiocephalic vein, on the side of injection, and at times bilaterally, was consistently visualised during the arterial and venous phases during both techniques (Fig 18). During the arterial and venous phase of dog 2 for the BT technique, there was inhomogeneous contrast filling of the cranial vena cava at the level of the thoracic inlet. No pre-contrast abnormalities were noted in the cranial vena cava at this region.

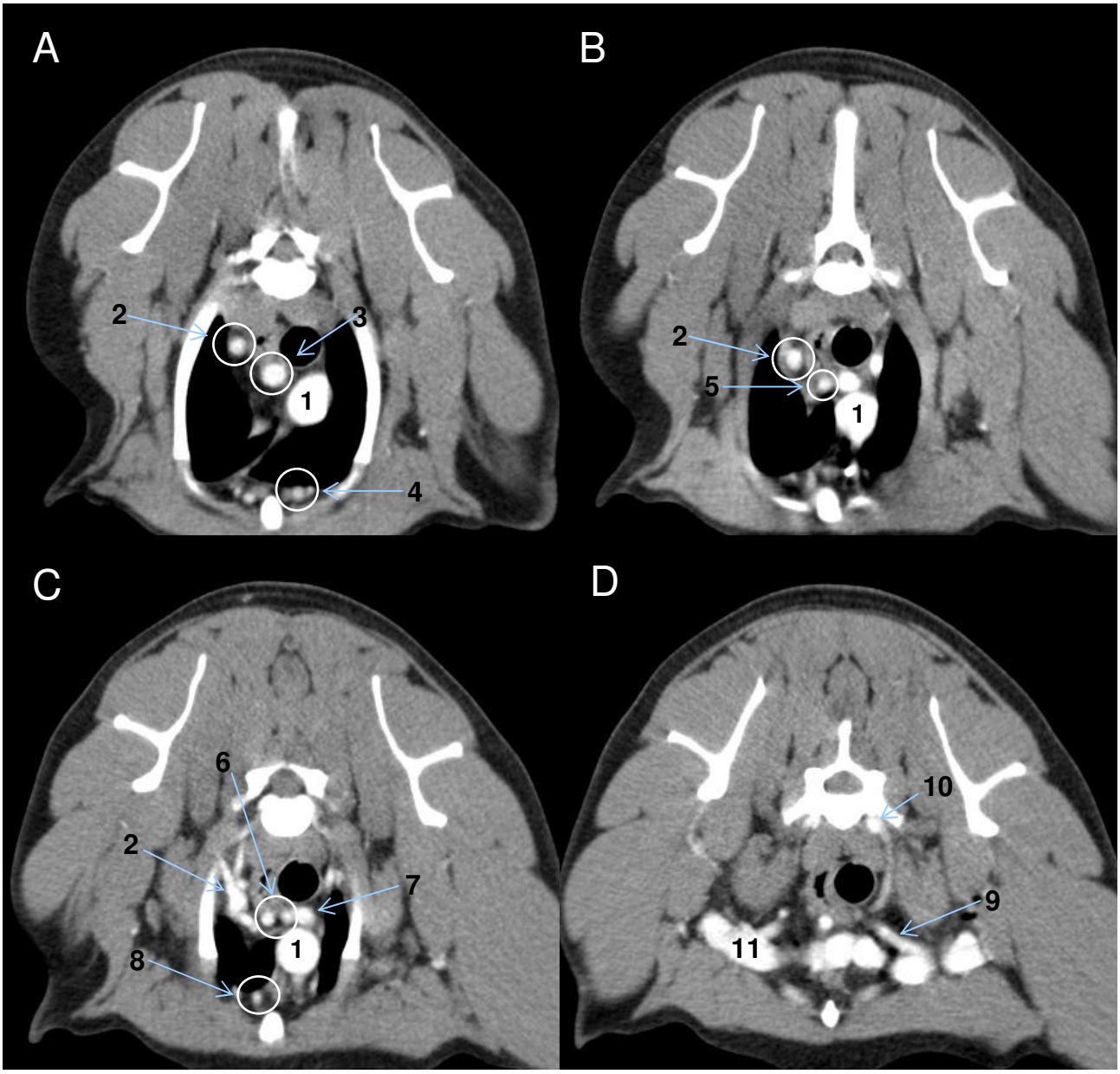

Fig. 11.Transverse post-contrast images of dog 5 during the arterial phase of the test bolus technique. Image taken from the level of the aortic bifurcation (A) moving cranially to (B)(C)(D). 1 = cranial vena cava, 2 = left subclavian artery, 3 = brachiocephalic trunk, 4 = internal thoracic veins, 5 = left common carotid artery, 6 = left and right common carotid arteries, 7 = right subclavian artery, 8 = internal thoracic artery, 9 = costocervical trunk, 10 = vertebral artery, 11 = confluence of the axillary vein into the brachiocephalic vein. Left of the dog is to the left of the image.

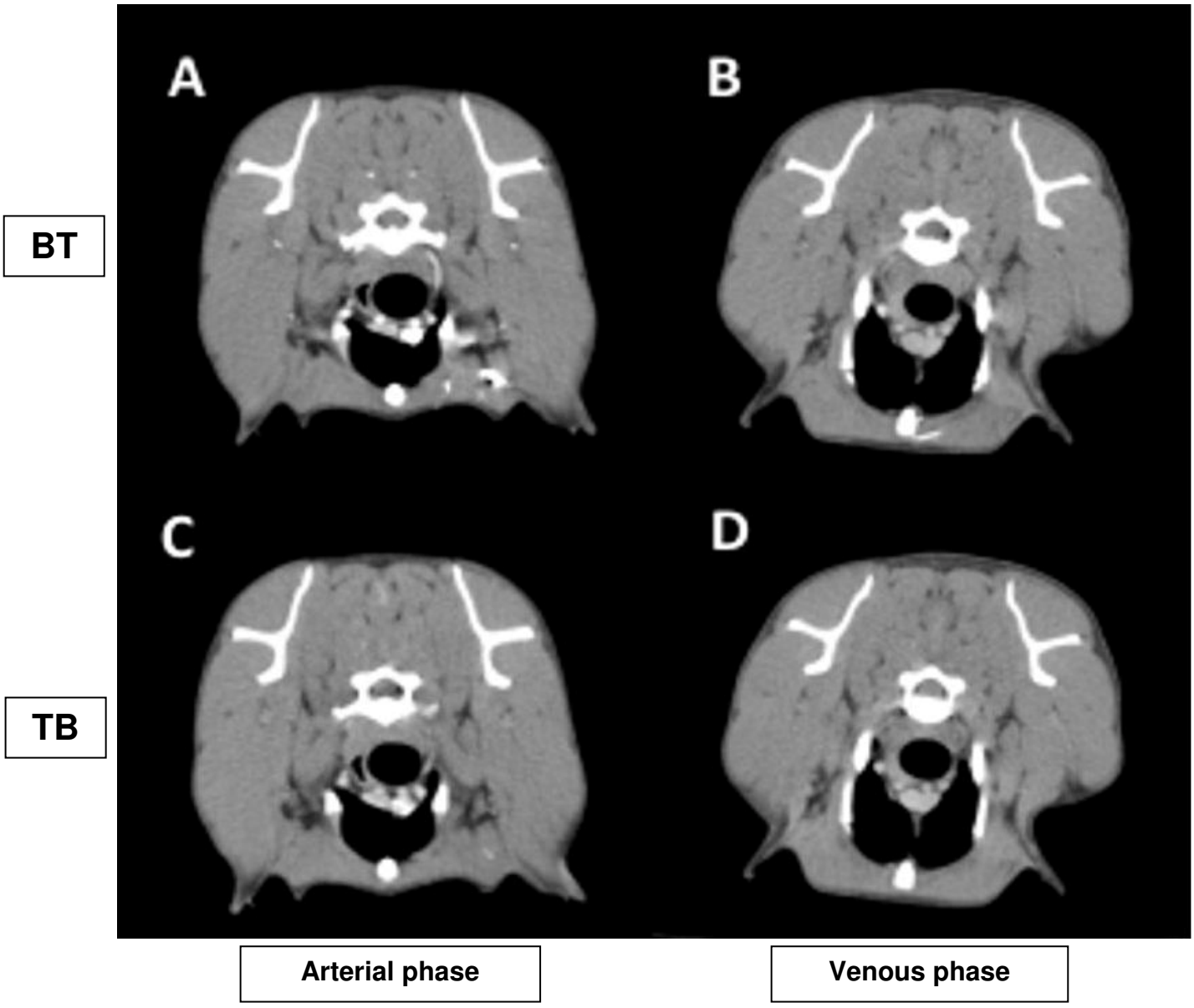

Fig. 12. The attenuation of the smaller cranial thoracic vessels of dog 1 during A)BT arterial, B) BT venous, C) TB arterial and D)TB venous phases. Left of the dog is to the left of the image.

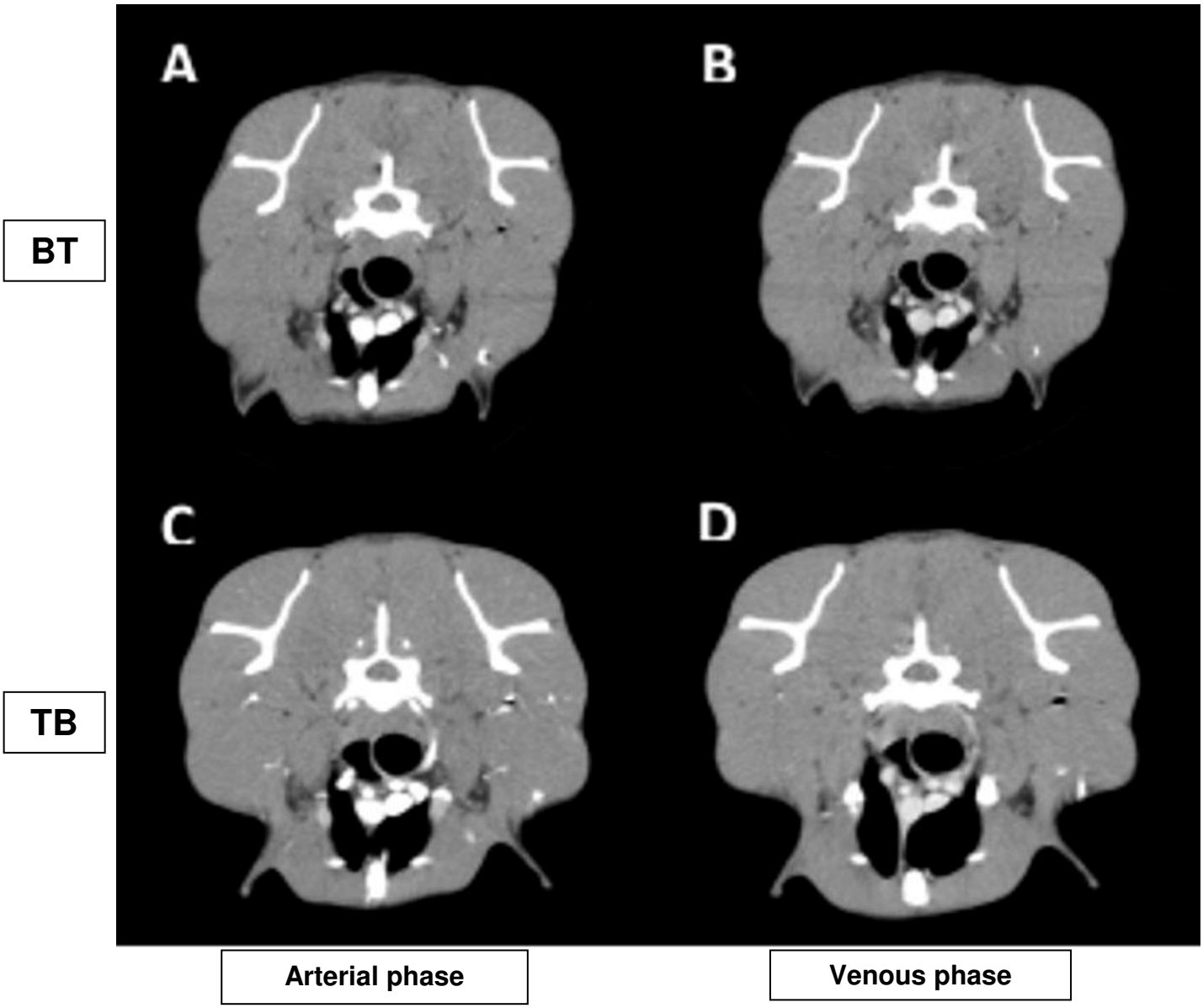

Fig. 13. The attenuation of the smaller cranial thoracic vessels of dog 2 during A)BT arterial, B) BT venous, C) TB arterial and D)TB venous phases. Left of the dog is to the left of the image.

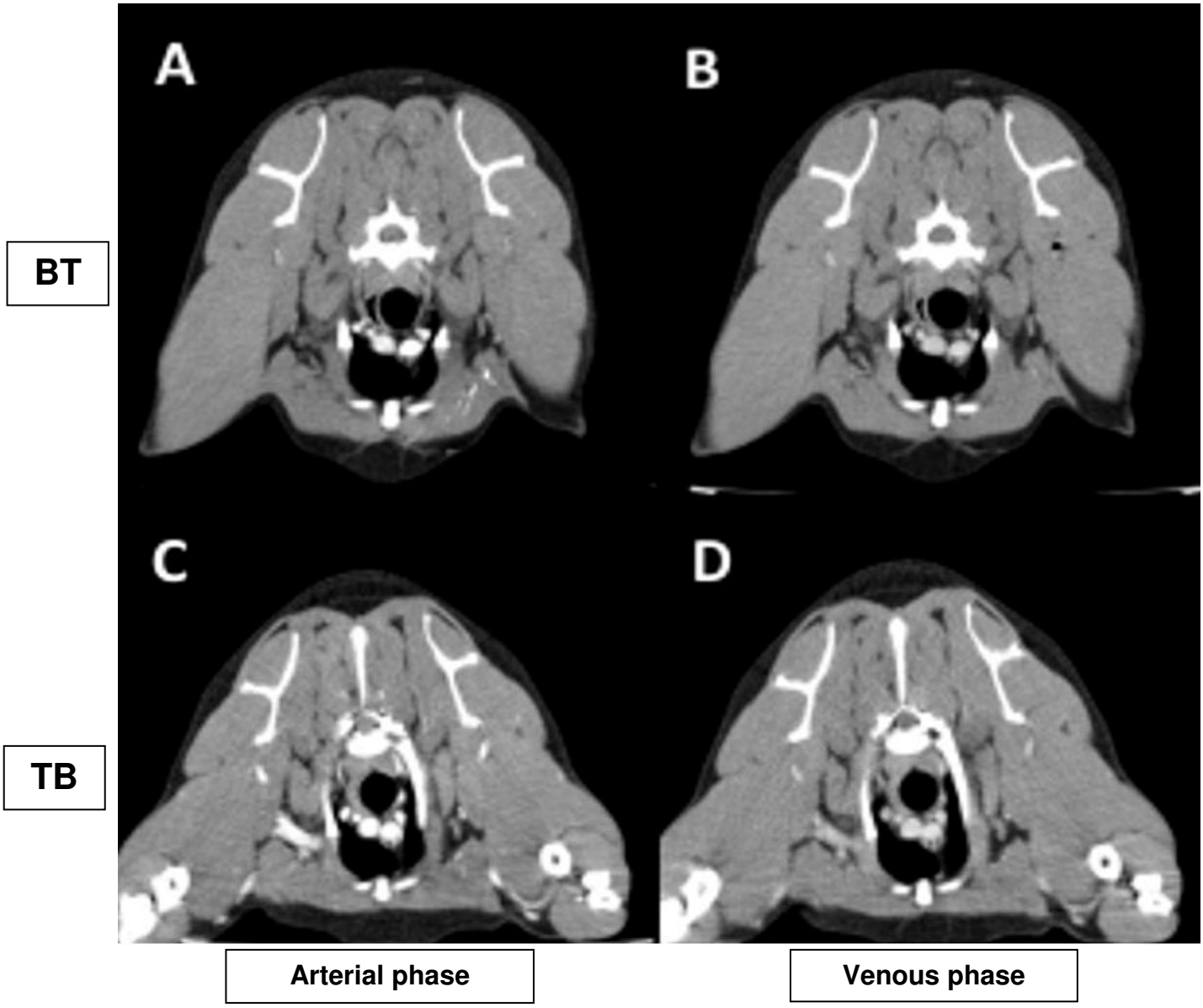

Fig. 14. The attenuation of the smaller cranial thoracic vessels of dog 3 during A)BT arterial, B) BT venous, C) TB arterial and D)TB venous phases. Left of the dog is to the left of the image.

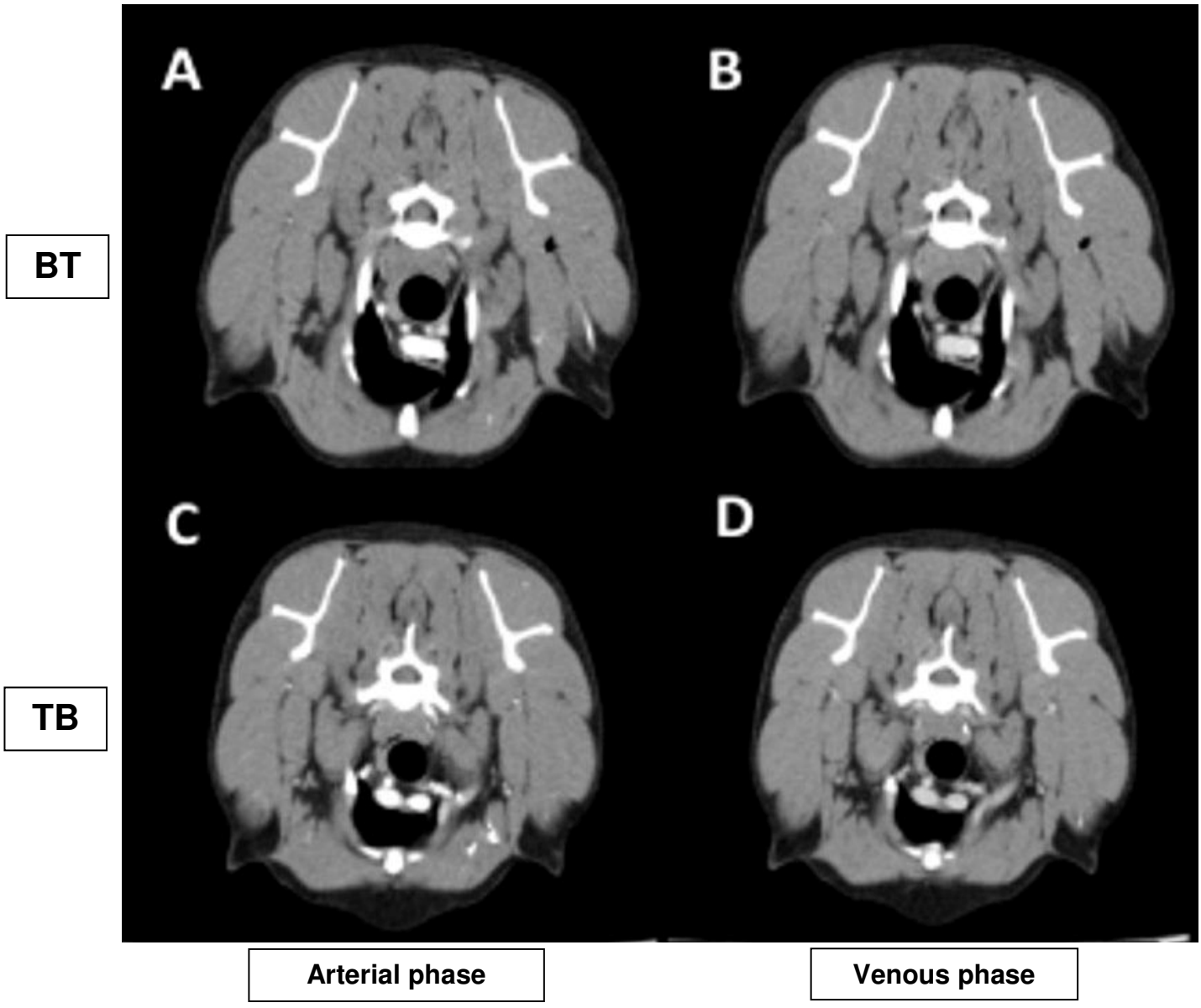

Fig. 15. The attenuation of the smaller cranial thoracic vessels of dog 4 during A)BT arterial, B) BT venous, C) TB arterial and D)TB venous phases. Left of the dog is to the left of the image.

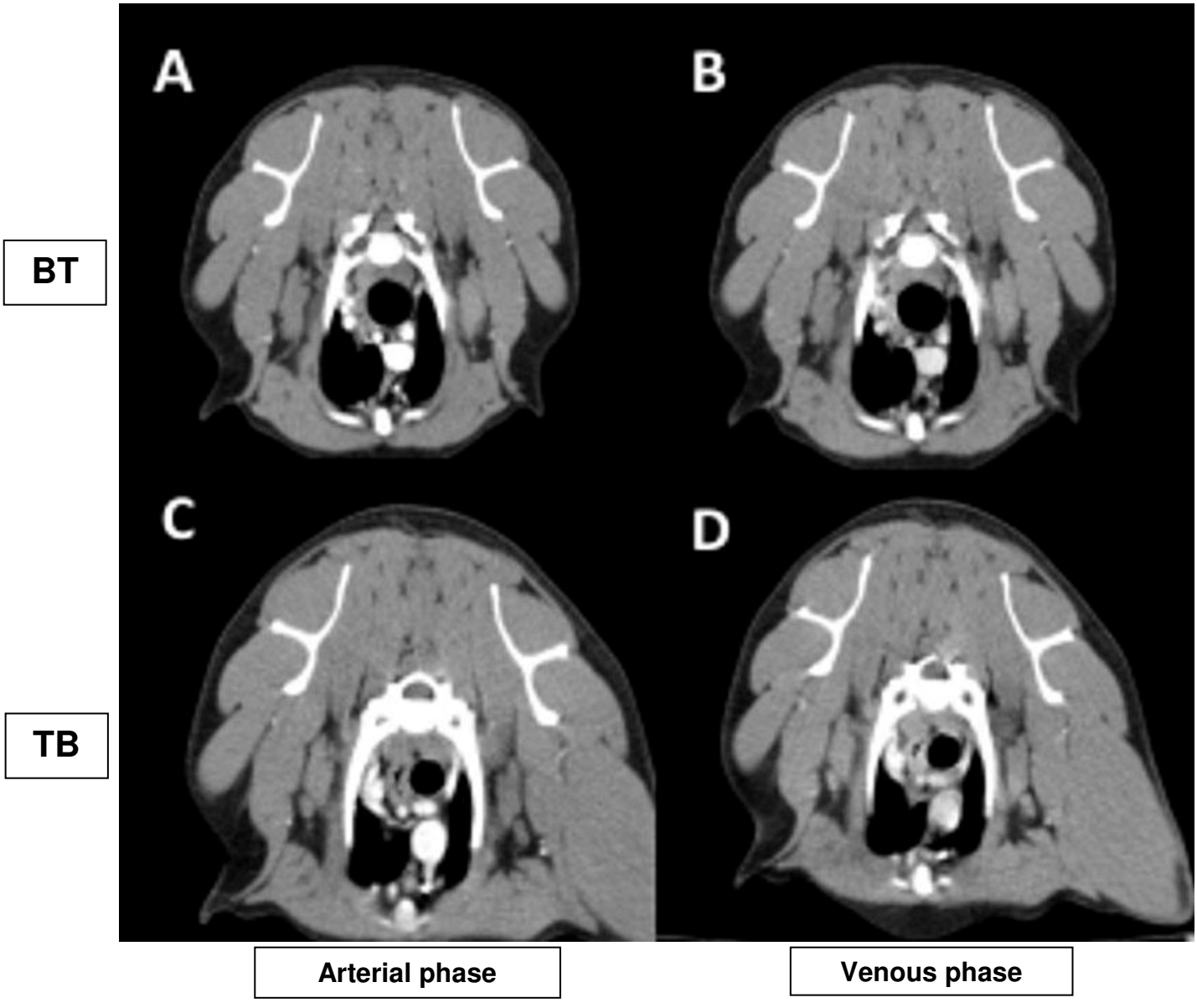

Fig. 16. The attenuation of the smaller cranial thoracic vessels of dog 5 during A)BT arterial, B) BT venous, C) TB arterial and D)TB venous phases. Left of the dog is to the left of the image.

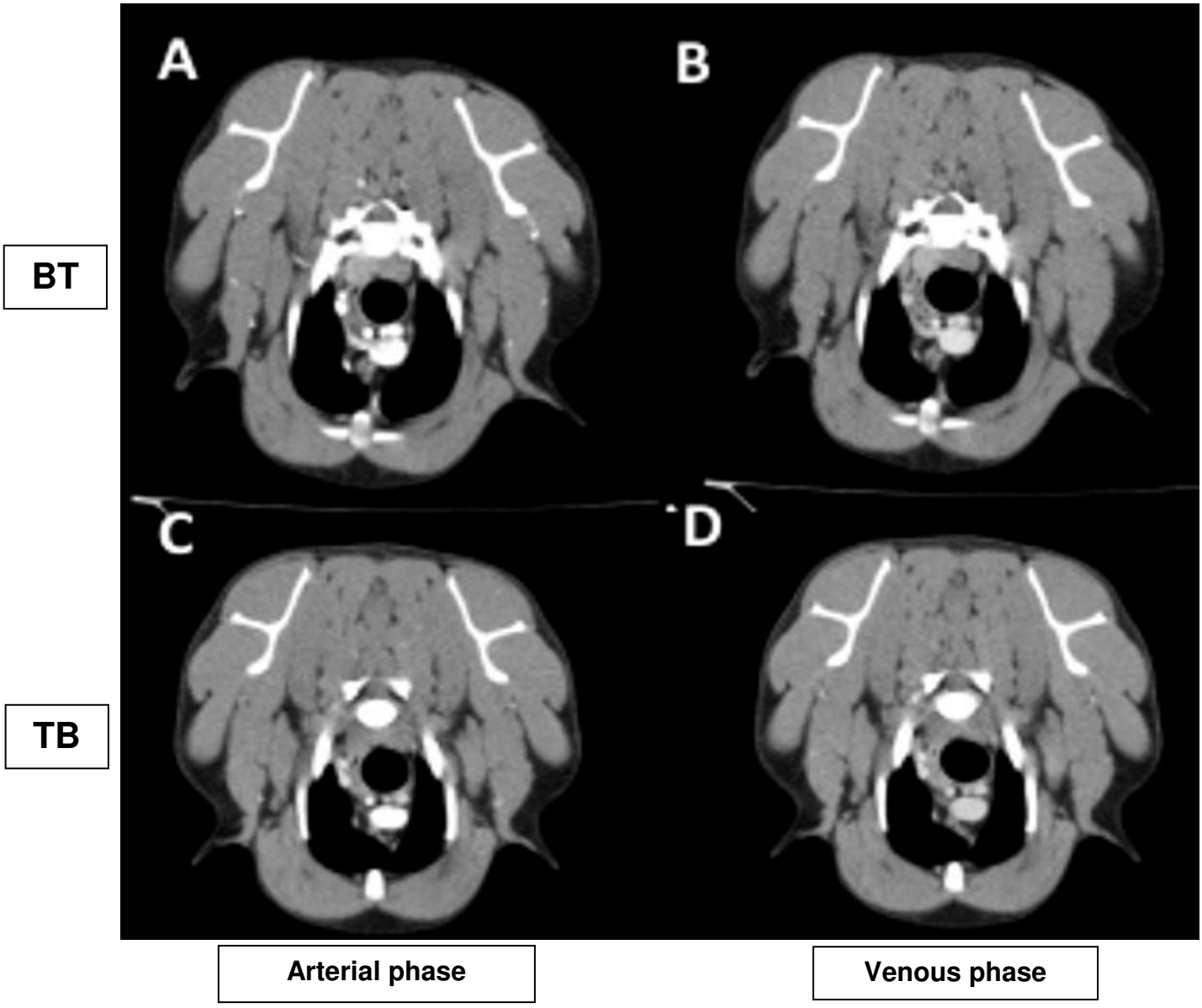

Fig 17. The attenuation of the smaller cranial thoracic vessels of dog 6 during A)BT arterial, B) BT venous, C) TB arterial and D)TB venous phases. Left of the dog is to the left of the image.

Fig. 16. The attenuation of the smaller cranial thoracic vessels of dog 5 during A)BT arterial, B) BT venous, C) TB arterial and D)TB venous phases. Left of the dog is to the left of the image.

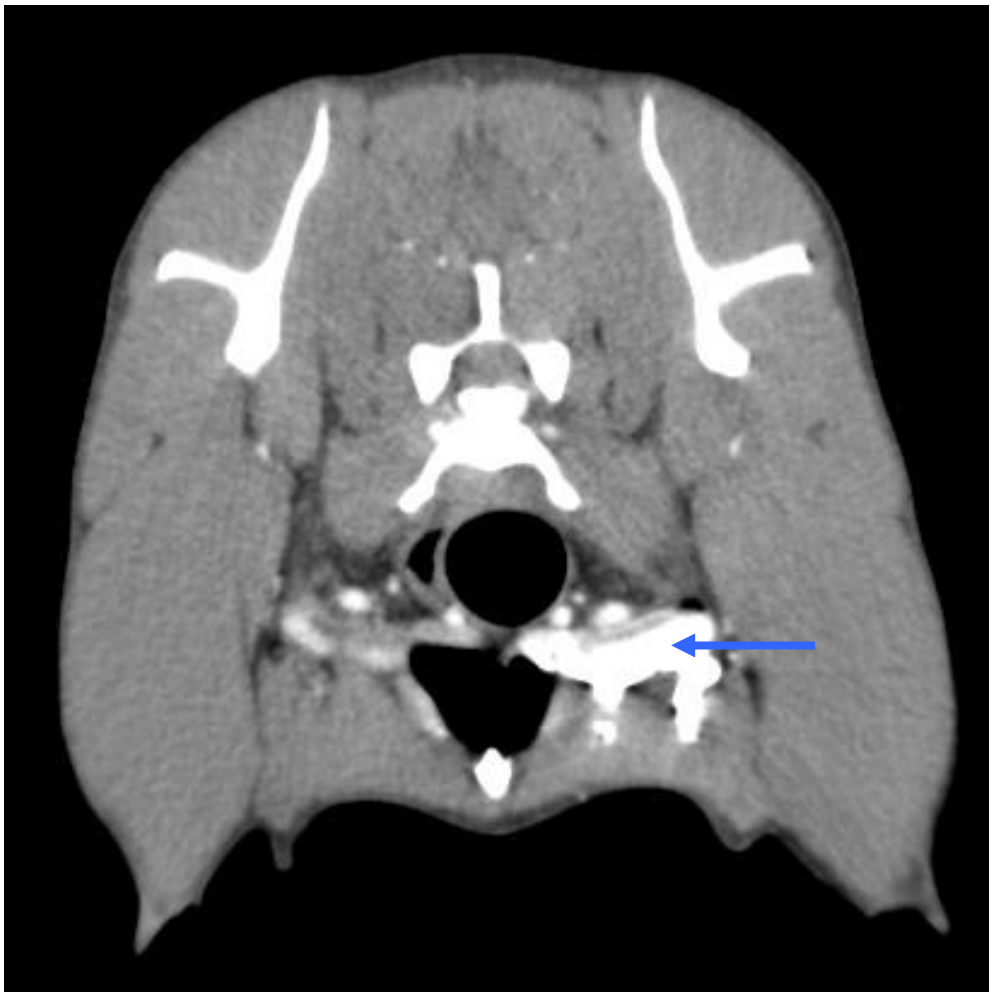

Fig.18. A transverse post-contrast image of dog 1 at the level of the cranial thoracic cavity, taken during the arterial phase of the BT technique. Note the homogenous attenuation in the confluence of the right axillary vein with the brachiocephalic vein (arrow). Left of the dog is to the left of the image.

4.3.5 mA, CTDI(vol) and DLP

Observed data for the mA, CTDI(vol) and the DLP is summarised in tables 7 - 9.

Table 7: The total mA for the bolus tracking and the test bolus techniques

Dog	Bolus tracking	Test Bolus
1	3304	3657
2	3601	4457
3	3458	4076
4	3575	3680
5	3428	3712
6	3760	3996
Mean	3538.5	3929.6
Standard deviation	**171.27**	**312.3**
p-value	**0.024***	

* = significantly different (P<0.05)

The mA during the BT is significantly lower than the TB technique (p=0.024; paired t-test). There is not sufficient evidence to reject the alternative hypothesis.

Table 8: The total CTDI (vol) for the bolus tracking and the test bolus technique

Dog	Bolus tracking	Test Bolus
1	32.68	44.72
2	19.17	47.23
3	13.31	45.2
4	9.02	44.84
5	17.38	44.91
6	31.18	45.07
Mean	**24.42**	**45.32**

Standard deviation	**11.89**	**0.94**
p-value	**0.013***	

* = significantly different (P<0.05)

The CTDI(vol) during the BT is significantly lower than the TB technique (p=0.013; paired t-test). There is not sufficient evidence to reject the alternative hypothesis.

Table 9: The total DLP for the bolus tracking and the test bolus techniques

Dog	Bolus tracking	Test Bolus
1	127	145
2	143	229
3	138	158
4	139	143
5	135	144
6	149	158
Mean	**139.1**	**162.8**
Standard deviation	**7.65**	**33.1**
p-value	**0.12**	

* = significantly different (P<0.05)

The DLP during the BT and TB technique do not differ significantly (p=0.12; paired t-test). There is not sufficient evidence to reject the null hypothesis, nor accept the alternative hypothesis.

4.3.6 Study Duration

The observed data for the average time taken for the two techniques, from the start of the CT scan to the end of the procedure (excluding anaesthetising the patient and patient positioning) is shown in table 10 (appendix R).

Table 10: Duration of the bolus tracking and test bolus techniques.

Dog	Bolus tracking	Test bolus
1	12.6	14.61
2	6.03	11.16
3	8.95	18.25
4	7.45	7.45
5	8.16	15.46
6	7.53	11.31
Mean	**8.4**	**13.04**
Standard deviation	**4.3**	**3.8**
p-value	**0.0216***	

* = significantly different (P<0.05). Time is measured in seconds.

The bolus tracking technique was thus significantly shorter than the test bolus technique (p-value= 0.0216, paired t-test). There is not sufficient evidence to reject the alternative hypothesis.

Observed data for the duration of the arterial and venous phases of the scans, as well as the time delays experienced during the scans for the bolus tracking and test bolus technique is found in tables 11 and 12, respectively.

Table 11: The duration of the arterial and venous phase scans and delays experienced prior to the scans for the bolus tracking technique

Dog	Delay prior to scan (s)	Arterial phase (s)	Delay until venous phase (s)	Venous phase (s)
1	5	18.23	6	20.93
2	4	19	6	24.6
3	4	16.9	7	26.2
4	5	23.1	7	30
5	4	16.75	7	24.25
6	4	16.13	7	27
Mean*	**4.2**	**18.37**	**6.8**	**26.41**
Standard deviation**	**0.4**	**2.85**	**0.44**	**2.3**

s = seconds

* Mean excluding dog 1

** Standard deviation excluding dog 1

Table 12: The duration of the arterial and venous phase scans and delays experienced prior to the scans for the test bolus technique

Dog	Delay prior to scan (s)	Arterial phase (s)	Delay until venous phase (s)	Venous phase (s)
1	49	17.23	7	23
2	13	16.95	15	20
3	10	17.3	50	26.6
4	15	16.85	29	24.7
5	15	15.84	7	15
6	10	16.27	26	27
Mean*	**12.6**	**16.6**	**25.4**	**22.6**
Standard deviation**	**2.5**	**0.58**	**16.3**	**5.1**

s = seconds

* Mean excluding dog 1

** Standard deviation excluding dog 1

There was no significant difference in the duration of the arterial phase scan (p-value = 0.22, paired t-test) nor the duration of the venous phase scan (p-value = 0.1, paired t-test) between the two techniques.

The BT technique showed a significantly shorter delay to the start of the arterial phase than the TB technique (p-value = 0.001, paired t-test). Thus there is not sufficient evidence to reject the alternative hypothesis. There was no significant difference between the two technique for the delay between the end of the arterial phase and the beginning of the venous phase (p-value = 0.06, paired t-test) between the two techniques. There is not sufficient evidence to reject the null hypotheses.

4.3.7 Total dose of contrast material used

The observed data for the volume of contrast material used during the bolus tracking technique is summarised in table 13.

Table 13: Contrast doses for the bolus tracking and test bolus techniques

	Bolus tracking	Test bolus		
Dog	**Dose of contrast (ml)**	**Dose of contrast(ml)**	**Test bolus dose (ml)**	**Total dose (ml)**
1	21	21	3.15	24.15
2	26	28	4.2	32.2
3	29	31.2	4.68	35.88
4	23	23	3.75	26.75
5	32	32	4.83	36.83
6	30	30	4.5	34.5
Mean	**26.8**	**27.5**	**4.19**	**31.7**
Standard deviation	**4.26**	**4.5**	**0.6**	**5.16**
p-value	**0.0004***			

* = significantly different (P<0.05). ml = millilitres

The amount of contrast used during the bolus tracking technique is significantly less than that used during the test bolus technique (p-value = 0.0004, paired t-test). There is insufficient data to reject the alternative hypotheses.

4.3.8 Injection parameters

The observed data for the injection parameters (injection rate, injection duration and injection pressure) during the bolus tracking and test bolus techniques are found in tables 14.

Table 14: Injection parameters for the bolus tracking and test bolus techniques

	Bolus tracking		Test bolus	
Dog	**Injection duration(s)**	**Injection pressure (psi)**	**Injection duration(s)**	**Injection pressure (psi)**
1	7	75	7	83
2	7	55	10	59
3	10	177	11	55
4	8	59	8	154
5	11	55	11	59
6	10	55	10	173
Mean	**8.83**	**79.3**	**9.95**	**97.1**
Standard deviation	**1.7**	**48.5**	**1.6**	**52.6**
p-value(injection duration)			**0.23**	
p-value(injection pressure)			**0.62**	

psi = pounds per square inch s = seconds

An injection rate of 3mls/sec was used for all procedures.

There was no significant difference in the duration of injection (p-value = 0.23, paired t-test) or the injection pressure (p-value = 0.62, paired t-test) for the two techniques. There is not sufficient evidence to reject the null hypotheses.

Chapter 5: Discussion

5.1 Introduction

Computed tomography thoracic angiographic studies were conducted in healthy adult beagle dogs using both the bolus tracking technique and the test bolus technique. This chapter discusses the technique, the attenuation in the aorta, caudal vena cava and the right caudal pulmonary artery for both an arterial and a proposed venous phase, the attenuation in the smaller cranial thoracic arteries, the mA, CTDI(vol), the total DLP, the dose of contrast used, the time taken and the injection parameters for both techniques. The pitfalls and limitations of the study, the clinical applications of the findings of this study, and suggestions of further research arising from this study are also discussed.

5.2 Data collection technique

The images were acquired using the technique described in Chapter 3 (Materials and methods).

5.3 Measurement technique

The measurement techniques were conducted successfully as described in Chapter 3 (Materials and methods).

5.4 Attenuation in the Aorta

During both the BT as well as the TB technique (n=5), adequate enhancement was achieved in the aorta at the level of T8, assessed as being adequate for diagnostic purposes.[104] With the p-value set at less than 0.05, there was no

significant difference noted between the two techniques, however if the p-value had been set at less than 0.1, BT would likely have been significantly higher than the TB technique. This trend would possibly have been more obvious if more dogs were included in the study, and for all practical purposes BT can be regarded as superior to the TB technique when assessing the $Ao_{art.}$

It is not surprising that the aorta showed good enhancement during the arterial phase, with a marginally higher attenuation noted during the BT technique, as the ROI was placed in the aorta at the level of T8 for both the triggered BT technique as well as during the low dose sequential scans during the TB technique. This is where subsequent measures of attenuation were made.

There was poor enhancement homogeneously noted in the Ao_{ven} for both techniques, however the levels of attenuation achieved were considered to be adequate.[14] With no significant difference in attenuation noted between the two techniques (p-value = 0.0.92) and when evaluating the 95% confidence interval for BT as a ratio of TB, the interval does not show any preference for a particular technique. This finding could possibly be explained as the contrast would have already undergone first pass bolus dynamics and would have already entered the venous circulation during this phase of scanning. The arterial phase scan during the BT technique had a mean duration of 18.37 ± 2.5 seconds with a mean 4.2 ± 0.44 second scan delay prior to the onset of the arterial phase scan as well as a mean 6.8 ± 0.44 second delay prior to the onset of the venous phase scan. Thus the mean time to the initiation of the venous phase scan for the BT technique was 29.37 seconds and 54.6 seconds for the TB technique. In a study evaluating normal canine portal and hepatic CT angiography, the time to peak enhancement for the portal vein was found to be 33.0 seconds.[26]

In a similar study, evaluating normal dogs and those with portosystemic shunts, the time to maximal portal vein enhancement ranged from 34.6 – 66.0 seconds.[37] In this current study, if one considers the delays calculated above, together with the additional scan time to reach the level of the aorta where attenuation was measured, the finding of poor attenuation during the proposed venous phase of the scan was not unexpected or surprising. This finding further justifies careful selection of the applicable slice as well as correct placement of the ROI in an appropriate vessel during either BT or TB angiographic study based on the suspected pathology.

5.5 Attenuation in the caudal vena cava

The mean attenuation (HU) in the CVC_{art} for the BT technique was 37.84± 20.8 compared to the mean attenuation for the TB technique, which was 91.48± 66.54 (n=5), a level considered to be below an adequate level.[14] The two techniques do not differ significantly (p-value = 0.069) and when the 95% confidence interval for the ratio of BT to TB is evaluated, it shows that BT is inferior to the TB technique when evaluating the CVC_{art}

Although the mean attenuation (HU) in the CVC_{ven} was slightly higher than results obtained for the CVC_{art}, the pattern of enhancement is similar and once again the two techniques do not differ significantly (p-value = 0.087). However, when evaluating the 95% confidence interval for the ratio of BT to TB, it does not show any preference for any technique when evaluating the CVC_{ven}. The levels obtained were considered to be adequately enhanced.[14]

The relatively low mean attenuation (HU) in the CVC_{ven} initially seemed surprising, with expected attenuation values higher than what was obtained. Although the study was designed with the ROI placed in the aorta it was anticipated that the contrast would reach the CVC during the proposed venous phase, following the first pass of contrast through the arterial system. Considering the time delays prior to the start of the venous phase for the BT technique, namely the arterial phase scan (18.37 ± 2.85 seconds), the delay prior to this scan (4.2 ± 0.44 seconds) and the interscan delay (6.8 ± 0.44 seconds) and taking into account the scanning time required to reach a level where attenuation was measured, together with the scan time required to reach the level of T8, it is hypothesised that the contrast had in fact not yet reached peak enhancement in the CVC at this level. As previously mentioned, CTA studies on portal vein dynamics in normal dogs and dogs with portosystemic shunts show the time to maximal peak enhancement for the portal vein ranged from 33 - 66 seconds.[26, 37] By extrapolating this data, the above explanation appears feasible.

The time delay prior to the start of the venous phase for the TB technique was approximately 54.64 seconds (viz. 12.6 ±2.5 seconds for the delay prior to the arterial phase, 16.64 ± 0.58 seconds for the arterial phase scan and 25.4 ± 16.18 seconds for the interscan delay). Using data from the published studies described above,[26, 37] in contrast to the attenuation of the CVC_{ven} for the BT

technique it is hypothesised that peak enhancement was in fact missed during the TB technique. This result was unexpected, as during the dynamic evaluation, a ROI was placed in the CVC and the time delays obtained during this assessment were used to calculate the time delays for the venous phase of the study. A possible explanation for the poor attenuation obtained in the CVC_{ven} for the TB technique, could be the direction in which the venous phase scan was conducted. All scans were done in a caudal to cranial direction, in an effort to minimise motion artefacts originating from respiration and diaphragmatic movement. In hindsight however, this was most likely the incorrect decision in this case, as the contrast may have been ahead of the scan during the venous phase. An additional method which could have been employed to limit this possible erroneous study design would be to reduce the scan area during the venous phase, thereby making the scan time shorter. This was not done as the study was designed in such a way that the entire thorax was examined during the venous phase.

Another explanation for the finding of poor attenuation in the CVC_{ven} of the TB technique may be as a result of a large scan area studied during the arterial phase. This would result in a long arterial scan time, thus resulting in the venous phase been missed.

However, one must once again be aware that during a CTA study, the success of the examination relies on correct slice selection and ROI placement in order to evaluate the vessel of interest during the correct phase.

In cases where there is suspected or known pathology in the venous system, such as Budd-Chiari like syndrome, it would make more scientific sense to place the ROI in the CVC (both during the BT technique and during the dynamic evaluation of the TB technique) and furthermore to evaluate the time to peak enhancement in this vessel and not use the aorta for such evaluations. However, with each dog used as its own control to compare the two angiographic techniques during this study, when evaluating the caudal vena cava, the TB technique proved superior.

5.6 Attenuation in the right caudal pulmonary artery

The mean attenuation (HU) for the $rCPA_{art}$ during the BT technique was 606.34 ± 143.37 compared with the mean attenuation (HU) of the TB technique (413.72 ± 174.99), levels which are considered to be adequate for diagnostic purposes.[14] This value did not differ significantly (p-value = 0.208). However the 95% confidence interval for the ratio of BT to TB indicates that preference may be given to the BT technique.

The findings during the venous phase of the studies show no significant difference between the BT and the TB techniques (p-value = 0.50) and both techniques showed attenuation levels above a recommended 150HU.[14] The 95% CI for the BT technique as a ratio of TB technique does not show any preference for a particular technique.

The attenuation of the $rCPA_{art}$ using both techniques showed good subjective attenuation, comparable to that achieved in the aorta during the studies. This is most likely due to the fact that during the arterial phase of the study, the blood has already entered the pulmonary system from the right heart prior to entering the systemic circulation. Based on the intervals of contrast injection as schematically illustrated in Fig. 1, it can be hypothesised that while the arterial phase scan was underway, there was still flow of contrast from the right heart (and pulmonary circulation) to the left heart and subsequently the aorta. In a recent study investigating pulmonary angiography in dogs, the initial pulmonary enhancement was noted at around 6 seconds following onset of contrast injection and the peak enhancement in the right caudal pulmonary artery was noted between 8 – 10 seconds.[14] In a more recent canine study comparing two injections protocols for CTA of the pulmonary arteries, the time to peak enhancement was 8.6±3.5 seconds for a fixed injection rate protocol.[60] Considering our injection duration ranged from 8.83 ± 1.7 seconds for the BT technique to 9.95 ± 1.6 seconds for the TB technique and our scan times ranged from 16.6 ± 0.58 seconds for the TB technique to 18.37 ± 2.85 seconds for the arterial phase during BT, as well as because the scans were conducted in a caudal to cranial direction, it can be concluded that although the attenuation in the right caudal pulmonary artery was good during the arterial phases, it was most likely obtained post peak enhancement. However

to confirm this speculation, specific studies into pulmonary enhancement would be needed.

The mean attenuation in the $rCPA_{ven}$ was comparable for both techniques with the attenuation (HU) for the BT technique being 174.34 ± 27.2 and 164.46 ± 18.5 for the TB technique. There was no significant difference between the two techniques (p-value = 0.5). The 95% CI for BT as a ratio of TB does not show any preference for a particular technique. This finding is similar to that obtained for the Ao_{ven} and the explanation for this finding would thus be similar, in that first pass bolus dynamics would have already occurred at this time and thus poor attenuation in this vessel would be expected. If the venous phase scan had occurred any later (by a matter of seconds) however, slightly higher attenuation values may be expected, due to second pass dynamics occurring at this later stage. However, there are many variables which would affect this finding, including contrast material variables (concentration, osmolality and osmolarity), patient variables (cardiac output and patient weight) as well as the various injection parameters (volume, rate and use of a saline flush). [13, 23, 46, 53-56, 58, 68, 71, 72, 105]

5.7 Assessment of the smaller cranial thoracic vessels

The visualisation of the cranial thoracic arteries was considered adequate for detection of gross pathology. For a specific study on pathology of any of the vessels evaluated under this heading, it is anticipated that the ROI for BT or the ROI for dynamic CT scanning for a time delay study would be placed in a more appropriate level of the aorta (most likely in the region of the ascending aorta or the aortic arch) and scanning would be done over a limited scan range over the region of interest.[106] If such a defined protocol is followed it is expected to obtain improved attenuation in the cranial thoracic arteries.

It is hypothesised that the reason there was visualisation of contrast consistently in all studies in the cranial vena cava (or at the confluence between the axillary veins into the brachiocephalic veins) on the side of injection, despite the use of a manual saline flush, was due to residual contrast remaining in the venous structures. The use a saline flush has been advocated to improve the bolus shape by “pushing” the bolus forward, to flush

out contrast remaining in the injection tubing and to eliminate the extra step required to clear the vascular access site of residual contrast. It has also been shown to be beneficial in reducing artifact formation, in particular streak or perivenous artifacts,[107] and increases the amount of contrast available which can be used for image acquisition.[56, 58] A saline flush is most often administered by means of a double barrel pressure injector. Due to the technical limitations of our pressure injector, the mode of administering the saline flush in this study was by manual injection. Thus the pressure attained during injection was most likely not adequate to fully achieve the benefits described above. In order to investigate this theory, the study should be repeated with a double barrel pressure injector. Another method which could have been employed in this study in order to achieve a saline chaser injected under pressure would have been to layer the contrast and saline in the same syringe. This was not done due to the technical difficulties and inexperience in performing such an injection protocol.

A previous study has shown that with a saline bolus chaser increased PME as well as increased tPME can be attained. Similarly, should a saline bolus chaser be employed, one can reduce the dose of contrast medium, whilst attaining similar peak enhancement values to those obtained with an increased dose and no saline chaser. The injection rates of the saline chaser mentioned in this study were as high as 10ml/s.[52] Should a pressure injector have been employed to administer the saline chaser, the results of our study may have been significantly affected. This is speculative and would need further investigation.

5.8 mA, CTDI(vol) and DLP

The radiation emitted by the CT x-ray tube is affected by the tube current (mA) and the tube voltage (kilovolt peak). However the total amount of radiation that is directed toward a given location within the CT gantry is also affected by the tube rotation speed and the pitch. The finding that the mA was significantly higher for the TB technique compared to the BT technique is due to the addition of a series of low dose sequential scans required for the TB technique. This consequently leads to a significant increase in the CTDI(vol)

for the TB technique compared to the BT technique as CTDI(vol) relates to the intensity of the x-ray beam incident on the patient and is measured from a single rotation of the x-ray tube. CTDI(vol) generally depends on the choice of kV and mA chosen to perform the examination.[31] However both the mA and the CTDI(vol) do not take into account the patient size and the scan length. The DLP was not significantly different between the two studies, although the BT technique had lower mean DLP values than the TB technique. This finding holds more weight than that of the other dose parameters evaluated (mA and CTDI(vol)), as the DLP can be used to estimate the effective dose for a CT examination by applying a DLP to E conversion factor (κ) which depends on the anatomic region examined.[31, 108] The effective dose takes into account the tissue being irradiated and permits comparisons between different forms of radiation as well as background radiation. It is agreed that the value calculated for effective dose in human studies is subject to many uncertainties and approximations[108] thus making the term a broad, generic estimate of risk. Although, to the best of my knowledge, there are no effective doses noted for animal studies, as the estimation of effective dose calculations in humans makes use of small anthropomorphic patient models, thus making these estimates applicable to small humans only, it would seem logical, albeit perhaps somewhere flippant, to associate this term with an estimate of dose to animal patients. Further work would be needed into defining animal equivalent models not only in CT but in other forms of diagnostic imaging involving ionising radiation. However to minimise radiation dose to a patient the BT technique is suggested.

5.9 Study duration

The finding that the duration of the BT study compared to the TB study was significantly shorter was not too surprising, as it was known that additional scans would be required during the TB technique. However, in some cases, the BT technique took half the time required for the TB technique and it was somewhat unexpected that the time difference would be significant. It is speculated that the significantly longer time to complete the TB studies was partly due to operator inexperience and the learning curve required to perform the TB technique in practice. One can expect the TB technique could be

conducted in a shorter time as experience with the technical aspects involved is gained. None the less, should one be dealing with a patient who is an anaesthetic risk or compromised in any way, it would be beneficial to choose a protocol which is known to be shorter in duration, whilst still providing diagnostic quality studies. For this reason, the BT technique would be desirable over the TB technique.

Surprisingly there was no significant difference noted in the durations and intervals of the arterial and venous phase scans between the two techniques. It was anticipated that the BT technique would result in different interscan delays, largely due to the fact that the protocol for the TB technique was designed to use the time to peak enhancement obtained in the aorta and caudal vena cava during dynamic evaluation. In comparison, the BT technique protocol took only the time to achieve an attenuation of 150 HU in the aorta prior to initiation of the scan into account, and did not evaluate the attenuation in the CVC during any stage of the study. By doing this, we were hoping to achieve the scans in the actual arterial as well as venous phases of the studies during the TB technique, whereas with the BT technique the proposed venous phase was performed following the completion of the arterial phase with no cognizance of the time taken for the arterial phase nor including an interscan delay to account for the completion of the arterial phase being earlier than a proposed venous phase. Despite this both methods gave similar attenuation in the CVC in the venous phase (BT mean HU =171.3 ± 32.36; TB mean HU = 191.08± 22), with both considered to be a level of adequate enhancement.[14] The attenuation noted was not statistically different between the two techniques (p-value = 0.087). However, as good practice, when evaluating multiple vessels during an angiographic procedure, the purpose of the study must be considered and during such CTAs a TB technique may be favoured.

5.10 Total dose of contrast material used

The finding that the dose of contrast material used during the BT technique was significantly less than the TB technique was expected. It is a characteristic of a TB technique, as the name implies, that an additional dose of contrast material be used to evaluate dynamic evaluation of enhancement

in the vessels of interest prior to planning the angiographic study. This may translate into increased costs incurred for the extra contrast material used, a factor that may need to be considered when cost sensitive cases are under study, as well as when there is a potential increase risk of contrast associated toxicities, such as patients with underlying renal pathology. Although this will most likely not be the major factor in the decision between performing a TB or BT technique in a patient, it may be a deciding factor to consider when all other factors prove equal.

5.11 Injection parameters

There was no significant difference in the injection duration or pressures used between the two techniques. This eliminates the injection protocol as a potential variable which may have affected the outcome of the study. However a recent study evaluating the effect of injection duration on peak enhancement and time to peak enhancement in the canine pulmonary arteries, has shown that there is a correlation between the injection duration and the time to peak enhancement which is a similar finding to human studies. [46, 56, 60] This becomes important when considering the varying weights of patients (as contrast dose is weight dependant) in the veterinary field as well as the temporal window of diagnostically adequate enhancement available during the scan. For example, if one has a small patient with a low body weight and a fixed injection rate is used (3ml/sec as in this study), the injection duration with be shorter than when a large breed dog is examined, using the same injection rate. A very narrow temporal window will be encountered in the small breed dog. Although the dogs in this study were of the same breed and similar weights (mean weight = 14.06 ±2.25 kg), this factor would need to be considered when examining dogs with varying weights and indeed, a similar study with dogs from different weight categories would be needed to validate the results obtained in this study.

The findings regarding the injection parameters cannot be viewed in isolation. The injection duration for the BT technique had a mean of 8.83 ±1.7 seconds. The delay prior to the onset of scanning during the arterial phase for this technique was 4.2 ± 0.44 seconds. This means that scanning would have started before the injection had ended and the peak enhancement would likely

have been caught during the scan. However when considering the injection duration (9.95 ± 1.6 seconds) and the delay prior to the start of the arterial phase (12.6 ± 2.5 seconds) for the TB technique, it is plausible to conclude that the peak contrast enhancement in the aorta for this technique was most likely missed, a factor which would not only affect the attenuation measured during the arterial phase, but also during the venous phase of the study. This could be part of the reason as to why the attenuation in the aorta during the arterial phase for the TB technique was marginally different. If the injection duration had been adjusted to accommodate the delays, perhaps the outcome of the results would have been different. In order to accommodate the prolonged delays prior to scanning during the TB technique, one could decrease the rate of injection to prolong the injection duration, however this has been shown to decrease arterial enhancement.[56] Another method which has been shown to facilitate a prolonged duration of injection (and a method which is used in small patients with low body weights) is to use an iodinated contrast material with a lower concentration of iodine (ie 180mgI/ml compared to 300mgI/ml).[56, 60]This will achieve a prolonged duration of enhancement but once again the net effect will be a decrease in aortic enhancement.

5.12 Limitations of the study

The main limitation to this study is the low number of animal investigated. Although each animal was used as its own control, statistically, the number of dogs was not adequate. For this reason the 95% confidence interval for the obtained data was rewritten as a 95% confidence interval for BT as a ratio of TB, with the latter being considered the gold standard.

The question arises whether the fact, that during this study, and for statistical evaluation, the TB technique was considered the gold standard can be considered a limitation to this study. When using the TB technique the scan is individualised for the patient under study, and takes into account the inherent factors that may affect the scan, such as CO, HR and blood pressure. However, the use of the TB technique presumes a relationship between the bolus geometry of the test bolus and the main bolus. The correlation between the test bolus tPME and the main bolus tPME has been found to be variable depending on which study is reviewed and can vary from none, to

moderate.[52]What has been found is a strong correlation between the test bolus tPME and the time to reach certain attenuation levels in the main bolus.[52] These findings indicate that the bolus geometry between the test bolus and the main bolus are, in fact, different and this may lead to the TB technique being demoted as a gold standard technique applied in this study.

As has been mentioned previously, the test dose during the TB technique was administered manually followed by a manual saline flush and thus the flow rates achieved during this administration would not have been close to the flow rate of 3ml/sec achieved during the injection of the full dose of contrast. One can expect that the test bolus was thus not delivered in a tight bolus and may have been diluted in the blood pool. This would affect not only the tPME but also the PME recorded and evaluated during the dynamic evaluation which would translate into potentially erroneous time delays used during the TB scan. In human studies comparing BT to TB techniques, the test bolus is injected using a pressure injector with the same injection rate as that used during injection of the main bolus.[91] In these studies the test bolus was 20ml, however in our studies due to the lower mean weight of the animals (14.06 ±2.25 kg) the test bolus injected was on average 4.2mls and injecting such a low dose under pressure, utilising the pressure injector currently in use at our facility, made this technically difficult.

Because the saline flushes were all manually injected the pressures obtained during manual injection are likely much less than those obtained when using a pressure injector and this may have negated the effects of a saline flush. However the influence of this variable was considered to be minimal, as each animal was used as its own control in this study.

One of the main variables which has been shown to affect the bolus geometry during CTA is cardiac output,[52, 56] with a decrease in cardiac output resulting in a longer tPME and a higher PME. Although the animals used in this study were deemed healthy based on routine clinical tests, cardiac output of the animals was not investigated. Another factor to consider is that the patients were placed under general anaesthetic which is known to affect cardiopulmonary parameters. The same anaesthetic protocol was used for each animal to limit this variable. Due to the fact that none of the animals showed a marked difference in any of the parameters measured it is unlikely that all the animals had reduced CO. Considering the design of the study,

where each animal acted as its own control, it can be concluded that CO did not affect the outcome of the study.

The animals were not monitored during the procedures to evaluate fluctuations in blood pressure and heart rate, which may be viewed as a limitation however several studies have documented that these variables have no effect on the tPME but may affect the PME.

Another limitation identified was the direction in which the scans were conducted, being caudal to cranial. This protocol was chosen purely to eliminate any potential motion artifacts which could have resulted from respiration. During manual breath hold (positive pressure breath hold) techniques, which were employed, there was a greater chance of the patient breathing over the positive pressure ventilation toward the end of the scan. If the scan was conducted in cranial to caudal direction, there would thus be more likelihood of diaphragmatic motion affecting the image acquisition. Similarly, should motion be encountered during the bolus tracking technique, there was a risk that the ROI positioned in the aorta would move out of the aorta and manual triggering would need to be instituted in order to initiate the scan, thus scan direction is likely to be more of a limitation of the study when evaluating the arterial phase of the angiographic study. It is speculated that if the scans were conducted in a cranial to caudal direction, then the visualisation of the smaller thoracic vessels, particularly the arteries in the arterial phase, would have been improved. This would need to be considered if any suspected pathology lies in this region and thus one would have to plan the study accordingly in a clinical setting.

Cognizance was made of the fact that the animals undergoing the TB technique received 15% more contrast medium than the BT group, however it is anticipated that this low dose of contrast was diluted by the blood pool and did not have an effect on the attenuation achieved following the bolus injection.

5.13 Clinical applications

The above study proves useful by giving the clinician the confidence to make an informed choice when choosing a CTA thoracic study protocol in a medium

sized, healthy patient. The limitations identified in this study can be taken into account during clinical CTAs and the variables kept to a minimum.

When evaluating the attenuation in the Ao_{ven}, CVC_{ven} and $rCPA_{ven}$ no preference was shown for either technique. However, when evaluating the Ao_{art} and $rCPA_{art}$ the BT technique is regarded as superior. The TB technique is however superior to the BT technique when evaluating the $CVC_{art.}$ The BT technique was shown to result in a shorter duration, less contrast and less mA and CTDI(vol). Thus for a general CTA of the thorax, taking all the above information into account, the BT technique should suffice, giving adequate attenuation in the vessels of interest.

In cost sensitive cases, the clinician can confidently decide on whether or not the test bolus technique may add benefit to the study at the risk of incurring extra cost, taking into account the suspected pathology and what pathology requires exclusion during the study.

Similarly, with the knowledge obtained from this research study, for patients who have sub-clinical renal disease, or are at higher risk of adverse reactions to the contrast material, the clinician can consider the benefit of using additional contrast to perform a TB CTA. This scenario would be applicable if he/she deems the procedure superior to the BT technique, such as when pathology of, or relating to the CVC is presumed or considered likely. However, for CTA evaluation of the arterial phase of the thorax, the risk and cost of using extra contrast can be eliminated and the BT technique can confidently be used, knowing that BT will give similar results to the TB technique.

5.14 Future studies

The following future studies have been identified based on this study

- The comparison of the PME and tPME in the Ao, CVC and rCPA obtained with the use of a double barrelled pressure injector (and thus pressure injection of the saline flush) versus the PME and tPME obtained with manual saline flushing.

- The effect of injection parameters (injection rate, duration and contrast material characteristics) on thoracic CTA in healthy dogs of different sizes (small, medium and large breed).

- The comparison of BT versus TB CTA of the thorax for dogs with known thoracic pathology.

- The comparison of BT versus TB CTA of the thorax for healthy domestic cats.

- The comparison of BT versus TB CTA of the thorax for domestic cats with known thoracic pathology.

- The effect of injection parameters (injection rate, duration and contrast material characteristics) on CTA in healthy cats.

- The development of animal models or phantoms for the calculation of the effective dose for ionising radiation.

Chapter 6: Conclusion

The following conclusions were deduced from this study:

- Adequate attenuation levels were achieved in the aorta, caudal vena cava and right caudal pulmonary artery during both the arterial and venous phases using the bolus tracking and test bolus techniques.

- There was a strong tendency for the attenuation in the aorta using the bolus tracking technique to be higher than using the test bolus technique in the arterial phase with preference given to the bolus tracking technique when evaluating the aorta.

- There was no statistically significant difference in the attenuation in the aorta during the venous phase for the two techniques.

- There was no statistically significant difference in the attenuation in the caudal vena cava obtained during both the arterial and venous phases for the two techniques. However, preference may be given to the TB technique when evaluating the caudal vena cava in the arterial phase.

- There was no statistically significant difference in the attenuation in the right caudal pulmonary artery during the arterial and venous phase for the two techniques. However, preference may be given to the bolus tracking technique when evaluating the right caudal pulmonary artery in the arterial phase.

- Subjectively, the cranial thoracic arteries could be adequately assessed with both the bolus tracking and test bolus techniques.

- The mA and CTDI(vol) values were significantly higher for the test bolus technique than the bolus tracking technique.

- There was no statistically significant difference for the DLP between the two techniques.

- Taking all the radiation exposure parameters into account (mA, CTDI(vol) and DLP), bolus tracking is superior to the test bolus technique, resulting in less radiation exposure.

- The bolus tracking technique was significantly shorter in duration than the test bolus technique.

- Significantly more contrast was used during the test bolus technique compared to the bolus tracking technique.

- There was no significant difference in the injection parameters used during the two CTA techniques.

- When performing a CTA, one must ensure correct placement of the ROI during the planning stages for both the bolus tracking and test bolus technique to obtain optimal CTA results.

- Taking all the evaluated variables into account, the bolus tracking technique is generally superior to the test bolus technique for thoracic CTA.

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Appendices

APPENDIX A
PATIENT DATA

DOG	AGE (months)	SEX	WEIGHT (kg)
1	62	female	10.40
2	69	male	15.10
3	34	female	15.60
4	37	female	12.20
5	39	male	16.10
6	37	male	15.00

APPENDIX B
DYNAEVA DATA SHOWING TIME TO THE POINT OF MAXIMAL ENHANCEMENT (tPME) AND MAXIMAL ENHANCEMENT (HU) IN THE AORTA DURING THE TEST BOLUS TECHNIQUE

	tPME	HU
Dog 1	49.1	99.8
Dog 2	13.2	88
Dog 3	10.2	200.7
Dog 4	Data missing	
Dog 5	15.3	131.9
Dog 6	Data missing	

APPENDIX C

DYNAEVA DATA SHOWING TIME TO THE POINT OF MAXIMAL ENHANCEMENT (tPME) AND MAXIMAL ENHANCEMENT (HU) IN THE CAUDAL VENA CAVA DURING THE TEST BOLUS TECHNIQUE

	tPME	HU
Dog 1	23.5	183.9
Dog 2	54.2	69.1
Dog 3	52.5	87.1
Dog 4	Data missing	
Dog 5	20.5	35.7
Dog 6	Data missing	

APPENDIX D

ATTENUATION (HU) IN THE AORTA DURING THE ARTERIAL PHASE FOR THE BOLUS TRACKING TECHNIQUE

BOLUS TRACKING arterial				
	ROI a (HU)	**ROI b (HU)**	**ROI c (HU)**	**Average ROI (HU)**
Dog 1	454.7	463.9	471	463.2
Dog 2	517	579.8	650.8	582.5
Dog 3	558.9	646.2	743.7	649.6
Dog 4	485	545	571.8	533.9
Dog 5	832.4	887.3	960.3	893.3
Dog 6	652.5	642.5	634.9	643.3
Sum*	3045.8	3300.8	3561.5	3302.6
Mean**	**609.16**	**660.16**	**712.3**	**660.52**

* Sum excluding dog 1

** Mean excluding dog 1

APPENDIX E

ATTENUATION (HU) IN THE AORTA DURING THE VENOUS PHASE FOR THE BOLUS TRACKING TECHNIQUE

BOLUS TRACKING venous				
	ROI a (HU)	ROI b (HU)	ROI c (HU)	Average ROI (HU)
Dog 1	136.5	138.4	132	135.6
Dog 2	157.7	161.7	146.7	155.3
Dog 3	177.2	139	190	168.7
Dog 4	183.3	204.7	201.9	196.6
Dog 5	230.9	209.4	239.1	226.4
Dog 6	193.9	211.5	204.6	203.3
Sum*	943	926.3	982.3	950.3
Mean**	**188.6**	**185.26**	**196.46**	**190.06**

* Sum excluding dog 1

** Mean excluding dog 1

APPENDIX F

ATTENUATION (HU) IN THE AORTA DURING THE ARTERIAL PHASE FOR THE TEST BOLUS TECHNIQUE

TEST BOLUS arterial				
	ROI a (HU)	ROI b (HU)	ROI c (HU)	Average ROI (HU)
Dog 1	114.9	132.6	136.9	128.1
Dog 2	461.5	445.9	379.9	429.1
Dog 3	596.2	595.3	595.5	595.6
Dog 4	181.1	214.2	209.3	201.5
Dog 5	308.9	388.2	499.2	398.7
Dog 6	637.9	727.2	807.6	724.2
Sum*	2185.6	2370.8	2491.5	2349.1
Mean**	**437.12**	**474.16**	**498.3**	**469.82**

* Sum excluding dog 1

** Mean excluding dog 1

APPENDIX G

ATTENUATION (HU) IN THE AORTA DURING THE VENOUS PHASE FOR THE TEST BOLUS TECHNIQUE

TEST BOLUS venous				
	ROI a (HU)	ROI b (HU)	ROI c (HU)	Average ROI (HU)
Dog 1	110	109.5	124.4	114.6
Dog 2	206.8	199.7	195.6	200.7
Dog 3	173	162.8	177.8	171.2
Dog 4	173.1	177	181.5	177.2
Dog 5	216.1	220.8	228.7	221.8
Dog 6	179.8	176.2	163.5	173.1
Sum*	948.8	936.5	947.1	944
Mean**	**189.76**	**187.3**	**189.42**	**188.8**

* Sum excluding dog 1

** Mean excluding dog 1

APPENDIX H

ATTENUATION (HU) IN THE CAUDAL VENA CAVA DURING THE ARTERIAL PHASE FOR THE BOLUS TRACKING TECHNIQUE

BOLUS TRACKING arterial				
	ROI a (HU)	ROI b (HU)	ROI c (HU)	Average ROI(HU)
Dog 1	35.1	42.2	26.6	34.6
Dog 2	2.7	38.8	27.1	22.8
Dog 3	65	-9.5	35.4	30.3
Dog 4	76	35.6	72.5	61.3
Dog 5	67	47.8	61.3	58.7
Dog 6	47.7	-13.7	14.4	16.1
Sum*	258.4	122.2	210.7	189.2
Mean**	**51.68**	**40.73**	**42.14**	**37.84**

* Sum excluding dog 1

** Mean excluding dog 1

APPENDIX I

ATTENUATION (HU) IN THE CAUDAL VENA CAVADURING THE VENOUS PHASE FOR THE BOLUS TRACKING TECHNIQUE

BOLUS TRACKING venous				
	ROI a (HU)	ROI b (HU)	ROI c (HU)	Average ROI (HU)
Dog 1	111.7	103.2	75.6	96.8
Dog 2	170.1	178.6	166.2	171.6
Dog 3	172.9	194.7	170.3	179.3
Dog 4	177.3	122.8	132.1	144.0
Dog 5	200.5	229.6	232.5	220.8
Dog 6	139.8	121.3	161.5	140.8
Sum *	860.6	847	832.6	856.5
Mean**	**172.12**	**169.4**	**172.52**	**171.3**

* Sum excluding dog 1

** Mean excluding dog 1

APPENDIX J

ATTENUATION (HU) IN THE CAUDAL VENA CAVA DURING THE ARTERIAL PHASE FOR THE TEST BOLUS TECHNIQUE

TEST BOLUS arterial				
	ROI a (HU)	ROI b (HU)	ROI c (HU)	Average ROI (HU)
Dog 1	143.9	168.5	132.5	148.3
Dog 2	83	34.9	36.4	51.4
Dog 3	87	87.4	42.3	72.2
Dog 4	240.1	153.3	200.4	197.9
Dog 5	107.6	106.7	111.6	108.6
Dog 6	7.3	44	30.8	27.3
Sum*	525	426.3	421.5	457.4
Mean**	**105**	**85.26**	**84.3**	**91.48**

* Sum excluding dog 1

** Mean excluding dog 1

APPENDIX K

ATTENUATION (HU) IN THE CAUDAL VENA CAVADURING THE VENOUS PHASE FOR THE TEST BOLUS TECHNIQUE

TEST BOLUS venous				
	ROI a (HU)	ROI b (HU)	ROI c (HU)	Average ROI (HU)
Dog 1	146.8	143.4	115.7	135.3
Dog 2	206	109.6	193.6	169.7
Dog 3	219.1	160.9	225.5	201.8
Dog 4	161.5	191.4	169.1	174
Dog 5	217.9	230.8	221.9	223.5
Dog 6	199	183.5	176.8	186.4
Sum*	1003.5	876.2	986.9	955.4
Mean**	**200.7**	**175.24**	**197.38**	**191.08**

* Sum excluding dog 1

** Mean excluding dog 1

APPENDIX L

ATTENUATION (HU) IN THE RIGHT CAUDAL PULMONARY ARTERYDURING THE ARTERIAL PHASE FOR THE BOLUS TRACKING TECHNIQUE

BOLUS TRACKING arterial				
	ROI a (HU)	ROI b (HU)	ROI c (HU)	Average ROI (HU)
Dog 1	310	321.2	362.3	331.1
Dog 2	399.9	540.3	644.3	528.1
Dog 3	137.9	619.8	717.2	491.6
Dog 4	455.2	629.9	674.3	586.4
Dog 5	762.6	887.5	911.9	854
Dog 6	450.7	589.3	674.8	571.6
Sum*	2206.3	3266.8	3622.5	3031.7
Mean**	**441.26**	**653.36**	**724.5**	**606.34**

* Sum excluding dog 1

** Mean excluding dog 1

APPENDIX M

ATTENUATION (HU) IN THE RIGHT CAUDAL PULMONARY ARTERYDURING THE VENOUS PHASE FOR THE BOLUS TRACKING TECHNIQUE

BOLUS TRACKING venous				
	ROI a (HU)	ROI b (HU)	ROI c (HU)	Average ROI (HU)
Dog 1	118.7	127.6	118.8	121.7
Dog 2	154.1	123	147.2	141.4
Dog 3	184.2	142.6	156	160.9
Dog 4	200.1	180.4	160.8	180.4
Dog 5	215.7	157.3	148.6	173.8
Dog 6	187.1	260.1	198.6	215.2
Sum*	941.2	863.4	811.2	871.7
Mean**	**188.24**	**172.68**	**162.24**	**174.34**

* Sum excluding dog 1

** Mean excluding dog 1

APPENDIX N

ATTENUATION (HU) IN THE RIGHT CAUDAL PULMONARY ARTERY DURING THE ARTERIAL PHASE FOR THE TEST BOLUS TECHNIQUE

TEST BOLUS arterial				
	ROI a (HU)	ROI b (HU)	ROI c (HU)	Average ROI (HU)
Dog 1	154.9	129.9	140	141.6
Dog 2	733.5	505.2	248.2	495.6
Dog 3	543.8	559.4	549.7	550.9
Dog 4	203	191	199.6	197.8
Dog 5	259.5	258.5	242.5	253.5
Dog 6	523	566.5	623	570.8
Sum*	2262.8	2080.6	1863	2068.6
Mean**	**452.56**	**416.12**	**372.6**	**413.72**

* Sum excluding dog 1

** Mean excluding dog 1

APPENDIX O

ATTENUATION (HU) IN THE RIGHTCAUDAL PULMONARY ARTERY DURING THE VENOUS PHASE FOR TEST BOLUS TECHNIQUE

TEST BOLUS venous				
	ROI a (HU)	**ROI b (HU)**	**ROI c (HU)**	**Average ROI (HU)**
Dog 1	106.7	108.8	95.5	103.6
Dog 2	173.2	105.3	150.8	143.1
Dog 3	166.7	175.8	168	170.1
Dog 4	142.6	162.1	167.8	157.5
Dog 5	190.9	228.9	158.6	192.8
Dog 6	173.7	162.9	140	158.8
Sum*	847.1	835	785.2	822.3
Mean**	**169.42**	**167**	**157.04**	**164.46**

* Sum excluding dog 1

** Mean excluding dog 1

APPENDIX P

SUBJECTIVE ASSESSMENT OF THE SMALLER CRANIAL THORACIC VESSELS DURING THE ARTERIAL PHASE

Vessel	Brachiocephalic trunk		Subclavian arteries		Common carotid arteries		Internal thoracic arteries		Vertebral arteries		Costocervical trunk	
Phase of study	BT	TB	BT	TB	BT	TB	BT	TB	BT	TB	BT	TB
Dog 2	2	3	2	3	2	3	2	3	1	3	2	3
Dog 3	2	3	2	3	2	3	1	3	2	3	2	3
Dog 4	3	2	2	3	2	3	2	1	2	2	2	3
Dog 5	3	3	3	3	3	3	2	2	3	3	3	3
Dog 6	3	2	3	2	3	2	3	2	3	2	3	2
Mean	**2.6**	**2.6**	**2.6**	**2.4**	**2.4**	**2.8**	**2**	**2.2**	**2.1**	**2.3**	**2.4**	**2.8**

Grade 0 = no post – contrast enhancement

Grade 1 = mild post – contrast enhancement

Grade 2 = moderate post – contrast enhancement

Grade 3 = strong, homogeneous post – contrast enhancement

APPENDIX Q

SUBJECTIVE ASSESSMENT OF THE SMALLER CRANIAL THORACIC VESSELS DURING THE VENOUS PHASE

Vessel	Brachiocephalic trunk		Subclavian arteries		Common carotid arteries		Internal thoracic arteries		Vertebral arteries		Costocervical trunk	
Phase of study	BT	TB	BT	TB	BT	TB	BT	TB	BT	TB	BT	TB
Dog 2	2	2	2	2	2	2	1	2	2	1	2	3
Dog 3	1	1	1	1	1	1	1	1	1	1	1	1
Dog 4	1	2	1	2	1	1	1	1	1	1	1	1
Dog 5	2	2	2	2	2	2	2	2	2	2	2	2
Dog 6	2	2	2	2	2	2	2	2	2	2	2	2
Mean	**1.6**	**1.6**	**1.6**	**1.6**	**1.6**	**1.6**	**1.6**	**1.3**	**1.6**	**1.1**	**1.6**	**1.6**

Grade 0 = no post – contrast enhancement

Grade 1 = mild post – contrast enhancement

Grade 2 = moderate post – contrast enhancement

Grade 3 = strong, homogeneous post – contrast enhancement

APPENDIX R

DURATION OF THE BOLUS TRACKING AND TEST BOLUS TECHNIQUES

	Bolus tracking			Test bolus		
Dog	**Time start (h:m:s)**	**Time end (h:m:s)**	**Time as decimal(min)**	**Time start (h:m:s)**	**Time end (h:m:s)**	**Time as decimal(min)**
1	10:52:28	11:05:04	12.6	09:18:48	09:33:25	14.61
2	11:28:40	11:34:42	6.03	09:56:11	10:07:21	11.16
3	11:09:51	11:18:49	8.95	11:05:47	11:24:02	18.25
4	10:07:53	10:15:20	7.45	10:07:53	10:15:20	7.45
5	11:35:40	11:43:50	8.16	11:31:26	11:46:54	15.46
6	10:38:15	10:45:47	7.53	10:04:00	10:15:19	11.31
Mean		**8.4**		**13.04**		
Standard deviation		**4.3**		**3.8**		
p-value		**0.0216**				