5-1-2020

Phase of enhancement and plane of reconstruction affect the appearance of the normal canine small intestine when utilizing triple-phase computed tomographic angiography

Jordan Taylor Hatfield

Phase of enhancement and plane of reconstruction affect the appearance of the normal canine small intestine when utilizing triple-phase computed tomographic angiography

By

Jordan Taylor Hatfield

A Thesis
Submitted to the Faculty of
Mississippi State University
in Partial Fulfillment of the Requirements
for the Degree of Master of Science
in Veterinary Medical Science
in the Department of the College of Veterinary Medicine

Mississippi State, Mississippi

May 2020

Phase of enhancement and plane of reconstruction affect the appearance of the normal canine small intestine when utilizing triple-phase computed tomographic angiography

By

Jordan Taylor Hatfield

Approved:

_____

Alison Lee
(Major Professor)

_____

Marc Seitz
(Committee Member)

_____

Alyssa Sullivant
(Committee Member)

_____

Larry Hanson
(Graduate Coordinator)

_____

Kent H. Hoblet
Dean
College of Veterinary Medicine

Name: Jordan Taylor Hatfield

Date of Degree: May 1, 2020

Institution: Mississippi State University

Major Field: Veterinary Medical Science

Major Professor: Alison Lee

Title of Study: Phase of enhancement and plane of reconstruction affect the appearance of the normal canine small intestine when utilizing triple-phase computed tomographic angiography

Pages in Study: 76

Candidate for Degree of Master of Science

The use of computed tomography in patients with gastrointestinal disease is increasing. However, the triple-phase computed tomographic angiographic appearance of the canine small intestine and the effects that phase of contrast enhancement and plane of reconstruction have on the appearance of the small intestine have not been fully evaluated. The purposes of this study were to investigate these effects on the appearance of the small intestinal wall. The minimal and maximal small intestinal diameter, wall thickness, number of wall layers identified, and degree of mucosal enhancement were recorded. The plane of reconstruction did not have any significant effects on wall thickness, diameter, degree of mucosal enhancement, or number of wall layers identified. There was a positive association between body weight and intestinal diameter. The arterial phase demonstrated the greatest mucosal enhancement and number of wall layers identified. The transverse plane was subjectively the most useful for evaluation of the small intestines.

DEDICATION

I would like to dedicate this research to my family, my friends, and my faith for without them I would not have accomplished what I have to this point in my career. My dad and my mom have been my greatest supporters throughout my veterinary education, internships, and residency. Both of you instilled in me a hard work ethic from an early age and pushed me to shoot for the stars. Without your consistent drive to push me, financial support, listening ears, and encouraging words this thesis would likely not have come to fruition.

To my brother, without the serious competitiveness between us I likely wouldn't have pursued becoming a veterinarian, much less a radiologist, at all. You have provided invaluable insight and much comic relief and been a pillar of support more times than I can count or remember. You likely didn't know how much influence you have had on all that I have accomplished in this process. Thank you for always being there for me and for being my best friend.

To my sisters, your support and comic relief pushed me through to finish this residency, even when I didn't think it was possible. Finally, to my grandparents, your influence on me at an early age by introducing me to farm animals, veterinary medicine, hard work, and the importance of obtaining higher education, pushed me to pursue my doctorate and this residency. I would like to thank all of them for pushing me to achieve what they knew I could even when I didn't think it was possible.

ACKNOWLEDGEMENTS

A special thank you to my committee members – Drs. Alison Lee, Marc Seitz, and Alyssa Sullivant – for all of your guidance and support throughout this research project, without you all this project would not have been possible. It would not have been completed without all of the time you put in into making the measurements, proofing the content, and providing additional insight.

I would also like to thank my resident mates, interns, the diagnostic imaging department, and the small animal internal medicine and surgery services. The support you all provided in recruiting case and acquiring studies is greatly appreciated.

Dr. Robert Wills, Isaac Jumper, and Cari Chisolm, thank you all, for the tireless work you performed while running statistics on the over 38,000 data points that I proved to you. I would also like to thank you for the 78 pages of results that you returned to me. Without your expertise and guidance, I would have been lost in all of the numbers and I would not have known where to start with the data analyses.

To my mentors at Washington State University – Drs. Tom Wilkinson, Greg Roberts, John Mattoon, Ashley Hanna, Pierre Burke, and Paige Coutu – I want to thank you for the wonderful guidance, leadership, and mentorship you provided during my internship year. You all are a large part of the reason that I pursued and was successful in obtaining a diagnostic imaging residency. You ignited in me the desire to perform this research. Without your presence none of this would have been feasible.

TABLE OF CONTENTS

DEDICATION ii

ACKNOWLEDGEMENTS iii

LIST OF FIGURES vi

CHAPTER

I. INTRODUCTION 1

Introduction to canine small intestinal disease 1
Gross anatomy of the canine small intestine 5
Arterial supply to the canine small intestines 7
Ultrasonographic appearance of the canine small intestine 10
Contrast enhanced ultrasonography of the canine small intestine 12
Normal duodenum 12
Normal jejunum 13
Abnormal canine small intestine 13
Computed tomographic appearance of the canine small intestine 14
Computed tomographic contrast agents 16
Ioversol 16
Contrast reactions in veterinary species 17
Inflammatory bowel disease in dogs 19
Pathogenesis of inflammatory bowel disease in dogs 19
Diagnosis of inflammatory bowel disease in dogs 21
Diagnostic imaging of IBD 21
Bloodwork, Intestinal Biopsy and Histopathology 23
Treatment of inflammatory bowel disease in dogs 24
Human abdominal imaging 24

II. STUDY 27

Study Objectives 27
Hypotheses 27
Materials and Methods 28
Study population 28
Imaging 29
Measurements 30

Statistical methods....34
Study results....35
Study population results....35
Transverse plane of reconstruction....36
Ascending duodenum....36
Descending duodenum....39
Jejunum....41
Ileum....44
Sagittal plane of reconstruction....47
Transverse Duodenum....47
Jejunum....50
Dorsal plane of reconstruction....53
Jejunum....53
Subjective evaluation....55

III. DISCUSSION....57

Discussion....57
Limitations....64
Future Studies....66
Synopsis....66

REFERENCES....68

LIST OF FIGURES

Figure 1.1 Ventral to dorsal view of the location of the canine abdominal viscera 6

Figure 1.2 Branching of the celiac and cranial mesenteric arteries (dorsal view).....9

Figure 1.3 Branching of the abdominal aorta and cranial mesenteric artery (dorsal view).....9

Figure 1.4 Ultrasonographic demonstration of normal wall layering in the descending duodenum (long axis).....11

Figure 1.5 Ultrasonographic demonstration of the normal wall layering of the descending duodenum (short axis).....11

Figure 2.1 Maximal and minimal wall measurements.....31

Figure 2.2 Maximal and minimal diameter measurements.....32

Figure 2.3 Transverse plane of reconstruction of the descending duodenum.....33

Figure 2.4 Enhancement pattern of the normal canine descending duodenum 34

Figure 2.5 Maximal diameter of the ascending duodenum.....37

Figure 2.6 Minimal diameter of the ascending duodenum 38

Figure 2.7 Average number of wall layers identifed in the ascending duodenum identified in a transverse plane of reconstruction.....38

Figure 2.8 Maximal diameter of the descending duodenum in a transverse plane of reconstruction 40

Figure 2.9 Minimal diameter of the descending duodenum in a transverse plane of reconstruction 40

Figure 2.10 Average number of wall layers identified in the descending duodenum in a transvers plane of reconstruction.....41

Figure 2.11 Maximal average jejunal diameter in a transverse plane of reconstruction 42

Figure 2.12 Average minimal jejunal diameter in a transverse plane of reconstruction 43

Figure 2.13 Average number of wall layers identified in the jejunum in a transverse plane of reconstruction 44

Figure 2.14 Average number of wall layers identified in the ileum in a transverse plane of reconstruction 45

Figure 2.15 Mucosal enhancement in dogs weighing less than 15.5 kilograms 46

Figure 2.16 Mucosal enhancement grade in dogs weighing between 15.5 kilograms and 31.0 kilograms 46

Figure 2.17 Mucosal enhancement grade in dogs weighing greater than 31.0 kilograms 47

Figure 2.18 Maximal Diameter of the transverse duodenum in a sagittal plane of reconstruction 48

Figure 2.19 Minmal diameter of the transverse duodenum in a sagittal plane of reconstruction 49

Figure 2.20 Average number of wall layers identified in the transverse duodenum in a sagittal plane of reconstruction 50

Figure 2.21 Average maximal overall jejunal diameter in a sagittal plane of reconstruction 51

Figure 2.22 Average overall minimal jejunal diameter in a sagittal plane of reconstruction 52

Figure 2.23 Average number of wall layers (averaged) identified in the jejunum in a sagittal plane of reconstruction 53

Figure 2.24 Maximal overall average jejunal diameter in a dorsal plane of reconstruction 54

Figure 2.25 Average number of wall layers identified in the jejunum in a dorsal plane of reconstruction 55

CHAPTER I

INTRODUCTION

Introduction to canine small intestinal disease

Clinical signs referable to the canine gastrointestinal tract are one of the most common presenting complaints to veterinary practitioners.[1] Prior studies[2–6] have demonstrated the prevalence of gastrointestinal signs as a cause for presentation to veterinary practitioners ranges from 1-17.8%. These clinical signs include, but are not limited to: vomiting, inappetence, anorexia, hyporexia, weight loss, lethargy, abdominal pain/discomfort, melena, hematochezia, and diarrhea. The cause of these clinical signs may be attributed to a singular disease process or may be multifactorial in nature.[7] There are a plethora of diseases that can affect the canine small intestine. These include inflammatory etiologies, infectious etiologies, parasitic etiologies, neoplastic etiologies, and pharmaceutical administration among others.[7] With the population of dogs presenting for clinical signs relatable to the gastrointestinal tract, the prevalence of chronic enteropathies has been reported to be 0.9-2.9%.[3,5,6]

In canine patients, the term chronic enteropathy is used to describe a disease in which mucosal inflammation is a hallmark feature and an etiologic agent is not identified.[2,7] This term encompasses a multitude of diseases including diet-, antibiotic-, and steroid- responsive diseases.[7] Of these, steroid-responsive diseases have been most commonly equated with inflammatory bowel disease.[7] There are a number of categories in which inflammatory bowel disease can be further characterized, which are based on the predominant cell type present. These

categories include: lymphocytic-plasmocytic enteritis, which is the most common, followed by eosinophilic enteritis, eosinophilic gastroenteritis, which occur less commonly, and lastly granulomatous enteritis, which is rarely identified.[7–9] The clinical signs and bloodwork abnormalities commonly associated with inflammatory bowel disease (IBD), such as vomiting, diarrhea, weight loss, hypocholesterolemia, hypocalcemia, and hypoalbuminemia, are nondescript and can be found in a multitude of disease processes.[7]

As with the diagnosis of any disease process, a thorough and complete physical examination is paramount to determining the most appropriate diagnostic steps. A complete blood count and serum chemistry profile are also typically performed and provide complementary diagnostic information to the physical examination, as well as, establish the patient's baseline status before more advanced diagnostics are obtained.

Regardless of the diagnostic work-up plan, diagnostic imaging is considered an integral part of the workup for these patients. Typical imaging modalities that are available to determine the cause of gastrointestinal disease include abdominal radiography, including positive and negative contrast radiographic studies, ultrasonography, fluoroscopy, and computed tomography. These modalities each have a number of advantages and disadvantages and a variable amount of availability (depending up on cost) within general practitioner and referral hospitals.

Of these, ultrasonography is often considered an integral imaging modality in the diagnostic work up of small intestinal disease as a large majority of diseases affecting the canine gastrointestinal tract cause abnormalities that can be identified ultrasonographically.[10–15] These changes typically manifest ultrasonographically as hyperechoic speckling or striations/stranding within the mucosal and muscularis layers, either segmental or diffuse thickening of portions of the small intestinal wall, abdominal effusion, or complete loss of normal wall layering.[10,13–17]

Even though these changes can be readily identified on ultrasonography, there is no single change that is characteristic of one disease process. It has been shown that dogs with small intestinal inflammatory disease processes may present with a normal overall wall thickness.[10,17–19] However, hyperechoic striations within the mucosal layer that are oriented perpendicular to the lumen are more commonly associated with protein-losing enteropathy than hyperechoic striations oriented parallel to the lumen or pinpoint hyperechogenicities throughout the mucosal layer.[10,13,14]

Furthermore, the diagnostic utility of ultrasound in achieving a diagnosis in gastrointestinal disease has been evaluated in dogs with chronic vomiting and diarrhea.[20,21] Leib and colleagues demonstrated that abdominal ultrasonography provided vital or beneficial diagnostic information that led to a correct diagnosis in 22.5% of cases which presented for chronic vomiting.[20] This study also showed that there are a number of patient factors which increased the diagnostic utility of abdominal ultrasound in these cases. These factors include increased age, greater number of vomiting episodes per week, presence of weight loss, a greater percentage of lost body weight, and a final diagnosis of gastrointestinal lymphoma or gastric adenocarcinoma. Leib and colleagues also concluded that in 9% of cases abdominal ultrasonography was marginally useful for the final diagnosis. While in the remaining 68.5.% of these cases, abdominal ultrasound did not provide information that changed the course of the medical work up or management.

In a separate study[21] performed by Leib and colleagues in dogs presenting for chronic diarrhea, abdominal ultrasound provided vital or beneficial diagnostic information for a correct diagnosis in 15% of cases.[21] In this study, abdominal ultrasound was especially beneficial in cases with weight loss, palpation of an abdominal or rectal mass, and a final diagnosis of GI

neoplasia. In 68% of cases with chronic diarrhea in this study, abdominal ultrasound did not provide information that changed the diagnosis or management of the case; however, in 15% of cases, findings from the ultrasound changed or altered the management of the case. In the remaining 17% of cases within this study, abdominal ultrasonography was of questionable benefit in the final diagnosis.[21]

While ultrasound may be employed in the diagnostic workup of dogs presenting for gastrointestinal signs due to its ability to reliably differentiate the small intestinal wall layering[10], there are a number of factors that affect the diagnostic quality of the ultrasound examination. These factors include patient preparation, obesity, body wall thickness, thoracic conformation, hair coat color, type of probe used for examination, frequency of probe, training of the examiner, and administration of certain medications.[11,12,22–24] Due to these limitations, computed tomography (CT) and more specifically, computed tomographic angiography (CTA), have been used more recently to gain additional clinical information in the evaluation of abdominal disease.[25–27] The increased use of this imaging modality can be attributed to its increasing availability, short image acquisition times, and increased contrast resolution compared with radiography and ultrasound.[25,28–31] Computed tomography of the canine abdomen has been shown to be sensitive and specific in the diagnosis of multiple disease processes such as small intestinal mechanical obstruction, extrahepatic portosystemic shunts, pancreatic insulinomas, and hemoabdomen.[25–28,32,33] However, one area in which computed tomography has not been routinely investigated is in the evaluation of infiltrative diseases that affect the small intestines.

Gross anatomy of the canine small intestine

The canine small intestine extends from the pylorus to the ileocolic orifice and is approximately 3.5 times the length of the body.[34] The canine small intestine is grossly divided into three segments: the duodenum, jejunum, and ileum. The duodenum is the most orad portion of the small intestine and in a normal dog is approximately 25 centimeters (or 10 inches) in length.[34] It begins at the level of the pyloroduodenal orifice. It runs a short distance cranially before turning caudally at the cranial duodenal flexure.[34] It the lies adjacent to the right abdominal body wall, runs caudally and makes a U-shaped turn medially at the caudal duodenal flexure, and runs obliquely cranially before terminating at the jejunum.[10–12,34]

The duodenum can be further subdivided into three parts: descending, transverse, and ascending.[34] The descending portion of the duodenum lies within the right cranial abdomen and is in contact with the right lateral and medial liver lobes, the dorsolateral abdominal wall, right lobe of the pancreas, right kidney, and large intestine.[11,12,34,35] The descending duodenum terminates at the caudal duodenal flexure.[10,34] The transverse duodenum connects the descending and ascending portions and lies caudal to the jejunum and ventral to the sixth lumbar vertebra.[34] The ascending portion of the duodenum runs cranially and to the left and lies ventral to the ureters, great abdominal vessels, and is near the descending colon. Its termination is the duodenojejunal flexure.[34]

The jejunum is the longest segment of the small bowel and begins at the duodenojejunal orifice and terminates at the ileum.[34] This segment of small intestine is located caudoventral to the stomach and ventral to the large intestine, duodenum, pancreas, and kidneys.[11,12,34,35] The jejunum takes a serpentine course through the abdomen and is surrounded by the greater

omentum.[11,12,34] Individual loops of jejunum are connected to each other by mesentery. The vascular supply to the jejunum is located within the mesentery.[34]

The ileum is the shortest segment of the small intestine and terminates at the ileocolic orifice. The ileum in a normal dog is approximately 15 cm in length and lies within the right cranial abdominal quadrant, medial to the right kidney.[11,12,34,35]

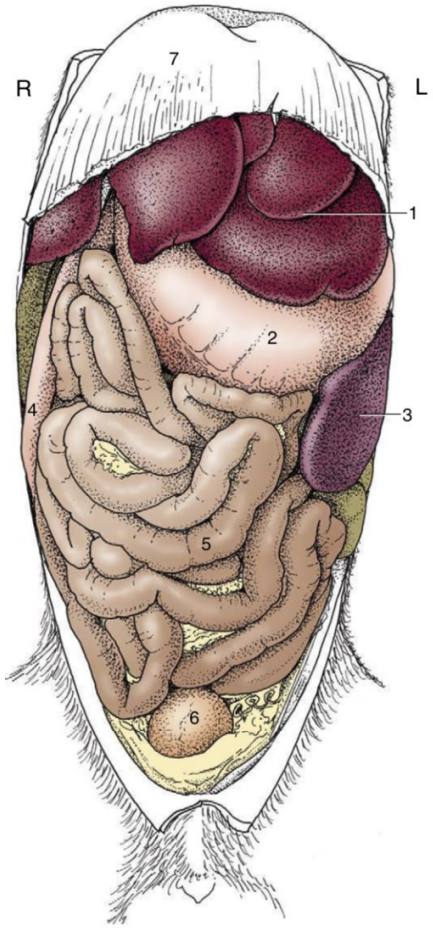

Figure 1.1 Ventral to dorsal view of the location of the canine abdominal viscera

1. Denotes the liver. 2. Denotes the stomach. 3. Denotes the spleen. 4. Donates the duodenum (descending portion). 5. Denotes the jejunum. 6. Denotes the urinary bladder. *Adapted from Miller's Anatomy of the Dog 4th edition.*

Arterial supply to the canine small intestines

The vascular supply to the canine small intestines originates from the first two major branches of the abdominal aorta: the celiac and cranial mesenteric arteries.[34] The first major branch of the abdominal aorta, the celiac artery, exits the ventral aspect of the abdominal aorta at the level of the first lumbar vertebra and first lumbar intervertebral disc space.[34,36] This artery immediately branches into the left gastric, hepatic, and splenic arteries.[34] The left gastric artery courses cranioventrally and supplies the left lateral aspect of the lesser curvature of the stomach and the caudal esophagus.[34] The splenic artery supplies the spleen, as well as the left greater curvature of the stomach. The hepatic artery courses cranioventrally, gives off 3-5 branches to the liver and a single branch to the right lateral aspect of the lesser curvature of the stomach (right gastric) before continuing on as the gastroduodenal. The gastroduodenal courses over the dorsal surface of the pylorus and terminates as the right gastroepiploic and cranial pancreaticoduodenal arteries. The cranial pancreaticoduodenal artery runs caudally medial to the right lobe of the pancreas and supplies the orad portion of the descending duodenum before anastomosing with the caudal pancreaticoduodenal artery.[34]

The second major branch of the abdominal aorta is the cranial mesenteric artery.[34,36] This artery is larger than the celiac artery and exits the ventral aspect of the abdominal aorta approximately 5 mm caudal to the celiac artery and at the level of the first lumbar intervertebral disc space and L2 vertebral body.[34,36] The cranial mesenteric artery terminates into three branches: a common trunk for the colic and ileocolic arteries, caudal pancreaticoduodenal artery, and 12-15 jejunal arteries.[34] The common colic trunk is the major vascular supply to the large intestines and ileum. The ileocolic artery originates from the common trunk and supplies the ascending colon, cecum, and ileum. This artery gives rise to the mesenteric ileal branch, which is

the major vascular supply to the terminal ileum. Additional vascular supply to the ileum is supplied through the antimesenteric ileal branch of the cecal artery.[34]

The jejunum receives the vast majority of its blood supply from the jejunal arteries in the form of jejunal arcades, which are direct branches from the cranial mesenteric artery.[34] These jejunal arteries form primary and secondary arcades by anastomosing with each other directly adjacent to the intestinal wall.[34,37] These arteries also give rise to the *vasa recti*, which are short, irregular arteries that go directly into the intestinal wall and enter the mesenteric border in the small intestine and antimesenteric border in the large intestines.[34,37]

Within the intestinal wall themselves there are two major arterial networks with the most well developed being the subserous network.[38] The subserousal network is well-developed in veterinary species as compared to humans and is a component of the mural network.[38] The mural network is a direct extension of the terminating arteries and plexiform anastomoses and mostly resides within the submucosa.[34,37]

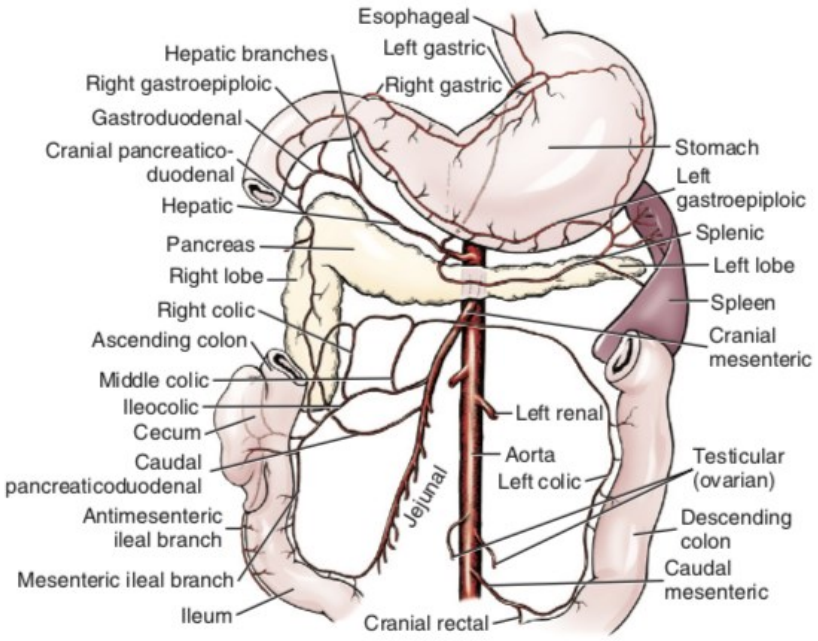

Figure 1.2 Branching of the celiac and cranial mesenteric arteries (dorsal view)

Adapted from Miller's Anatomy of the Dog 6th edition.

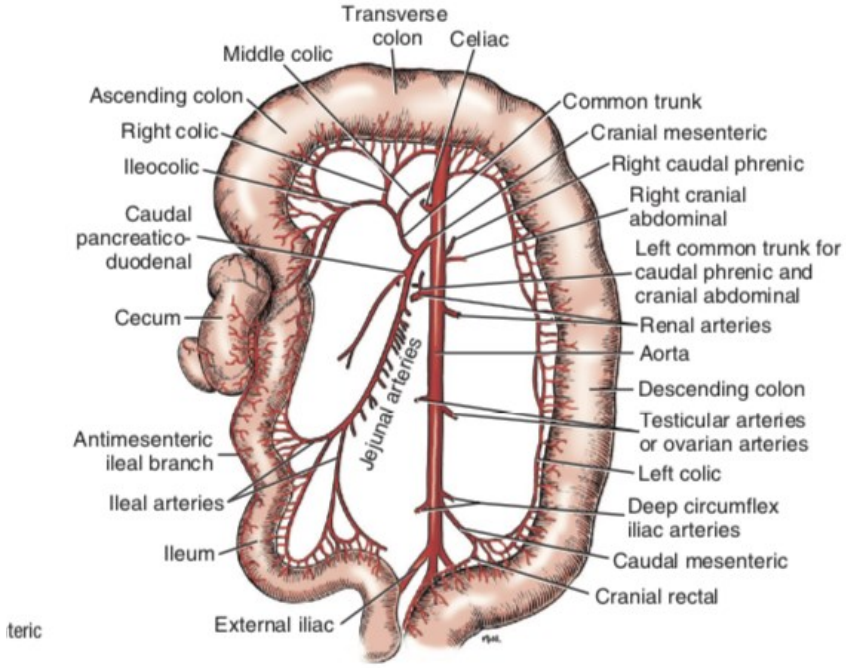

Figure 1.3 Branching of the abdominal aorta and cranial mesenteric artery (dorsal view)

Adapted from Miller's Anatomy of the Dog 6th edition.

Ultrasonographic appearance of the canine small intestine

In vivo the canine small intestine appears as five distinct ultrasonographic layers, which demonstrate an alternating hyperechoic and hypoechoic pattern. These layers starting from the most superficial and progressing to the deepest include the serosa, muscularis propria, submucosa, mucosa, and mucosal surface.[11,12,19,35] The ultrasonographic appearance has been demonstrated to have good to great correlation with the histologic layering of the small intestine.[12,35,39,40] The ultrasonographic thickness has also been shown to have good correlation with that identified on histology.[19,40]

The normal ultrasonographic thickness of the different segments of the gastrointestinal tract and a positive correlation of the thickness with body weight have been identified and described in dogs.[11,12,41] Dogs with body weights under 20 kilograms have a jejunal wall thickness of ≤4.1 mm, dogs between 20 and 39.9 kilograms have a thickness of ≤4.4 mm, and dogs over 40 kilograms having a thickness of ≤ 4.7 mm.[41] The duodenal wall thickness of normal dogs has also been described and a positive correlation with body weight identified.[41] In this study, normal dogs without clinical signs of gastrointestinal disease under 20 kilograms had a thickness of ≤5.1 mm, dogs between 20 and 29.9 kilograms had a thickness ≤5.3 mm, and dogs over 30 kilograms had a thickness of ≤6.0mm.[41] Additionally, age has been identified as having a significant effect on duodenal and jejunal wall thickness, with puppies having a thicker duodenal wall and thinner gastric wall. The wall layering in normal puppies without clinical signs associated with the gastrointestinal tract is also varied from that of adult dogs, with the mucosal, submucosal, muscularis all being of equal thicknesses.[11,12,39] In the adult, the mucosal layer is of equal to the combined thicknesses of the submucosa, muscularis, and serosa.[11,12]

Ex vivo studies of the canine small intestine have identified two additional ultrasonographic layers: a hyperechoic line within the muscularis layer and a dual echogenic mucosal layer.[19] Histologically, the hyperechoic line within the muscularis layer was shown to correlate with the junction of the muscularis longitudinal and circular layers, while the dual echogenicity of the mucosal layer was attributed to the intestinal villi and lamina propria.[19]

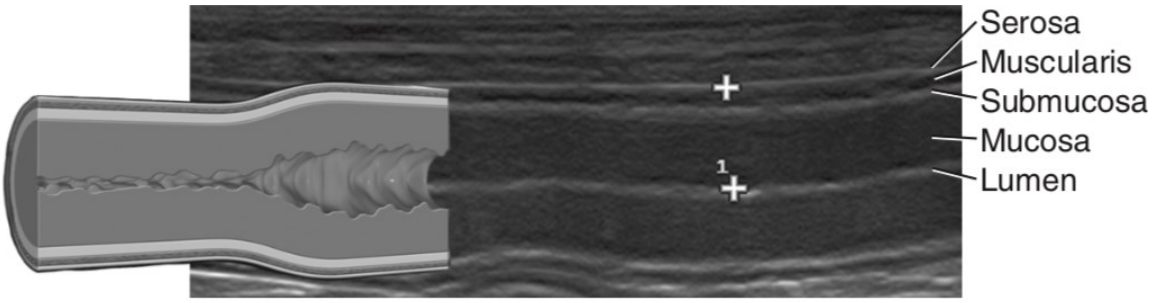

Figure 1.4 Ultrasonographic demonstration of normal wall layering in the descending duodenum (long axis)

Demonstration of normal wall layering. Note the alternating hyperechoic and hypoechoic layers. *Adapted from Small Animal Diagnostic Ultrasound 3rd edition.*

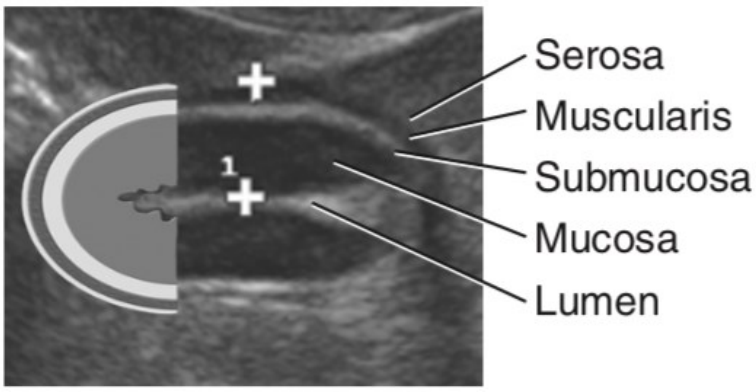

Figure 1.5 Ultrasonographic demonstration of the normal wall layering of the descending duodenum (short axis)

Demonstration of normal wall layering. Note the alternating hyperechoic and hypoechoic layers. *Adapted from Small Animal Diagnostic Ultrasound 3rd edition.*

Contrast enhanced ultrasonography of the canine small intestine

The evaluation of the canine small intestine using contrast enhanced ultrasonography is limited to four studies.[42–45] Two studies[42,43] evaluated the small intestines in normal dogs, while two other studies[44,45] evaluated the small intestines in abnormal dogs. Of the two studies involving normal dogs, one[43] evaluated the duodenum in eight healthy normal client owned Beagle dogs and the remaining study[42] evaluated the jejunum in nine healthy client owned dogs. Of the two studies[44,45] evaluating the small intestine in abnormal dogs, only one[45] looked at diseases that pertain to this discussion and thus this is the only study that will be discussed.

Normal duodenum

In a study[43] performed by Johnson-Neitman and colleagues, the duodenum in a set of eight healthy client owned dogs was evaluated using a right intercostal approach. After administration of a microbubble contrast agent[1], the microbubbles were first identified in the cranial pancreaticoduodenal artery. This was followed by a simultaneous contrast inflow and enhancement of the pancreatic parenchyma and serosal and mucosal layers of the duodenum. Peak intensity of the duodenal layers occurred after this and was characterized by homogeneous simultaneous enhancement of all of the duodenal layers. The contrast agent arrived at the duodenum approximately 6.95 ± 2.91 seconds following administration, the time to peak enhancement of the duodenum occurred at 13.08 ± 6.16 seconds following administration, and the outflow rate was -1.81 ± 1.62 decibels/second. These values were not statistically significant than those obtained for the pancreas.

[1] Definity, *Bristol-Myers Squibb Medical Imaging*, New York, New York

Normal jejunum

In a study[42] performed by Jiménez and colleagues, the contrast enhancement pattern in the jejunum in a set of nine client owned healthy dogs was described. In this study three serial doses of a microbubble agent were utilized in an incrementally, escalating dose protocol (0.007 ml/kg, 0.015 ml/kg, and 0.03 ml/kg). In this study the mean time to peak for each of these values were: 14.1, 19.6, and 21.9 seconds after contrast administration respectively. Peak intensity values for these doses were 38.3, 58, and 79.2 mean pixel values, respectively. In this study, the high dose subjectively revealed the clearest delineation of the jejunal arteries and enhancement of the jejunal wall. The enhancement of the jejunal wall occurred in a serosal to luminal direction and contrast enhancement was subjectively unsatisfactory in 77% of dogs with low dosing.

Abnormal canine small intestine

In a study[45] by Nisa et al, 47 client owned dogs with gastrointestinal signs and histopathology of the duodenum were enrolled and categorized into three separate groups: dogs with a histopathologically normal duodenum, which was used as a control group(14 dogs), chronic inflammatory enteropathy (26 dogs), and intestinal lymphoma (7 dogs). Dogs with chronic inflammatory enteropathy (CIE) were further subdivided into those that were in remission (16 dogs) and those that were symptomatic (10 dogs). A microbubble contrast agent[2] was administered intravenously at a dose of 0.01 ml/kg in all dogs. This study found that the peak intensity was significantly higher in dogs with symptomatic CIE than the control group, 105.4 mean pixel value and 89.9 mean pixel value respectively. The peak intensity in this study also positively correlated with the canine chronic enteropathy clinical activity index score of the

[2] Sonazoid®, *GE Healthcare*, Oslo, Norway

CIE group. The area under the curve was also significantly higher in symptomatic CIE dogs compared to the control group and those in remission. No significant differences were observed between the CIE group and the lymphoma group for any of the parameters evaluated.

Computed tomographic appearance of the canine small intestine

There are currently only four papers[46–49] that describe the appearance of the normal canine small intestines using contrast enhanced computed tomography.

In a study[46] performed by Hoey and colleagues, the appearance of the canine gastrointestinal tract was reported following the administration of a nonionic, iodinated contrast agent at 300 mg I/kg of patient body weight. In this study of healthy dogs, 62.8% of gastrointestinal segments were identified from serosa to serosa, while 77.7% of gastrointestinal walls were identified from serosa to mucosa on precontrast series. After administration of intravenous contrast, individual wall layering was identified in 21.8% of these intestinal segments when utilizing single phase angiography, with the majority of the wall layering being identified within the stomach and jejunum.

In a separate study[47] performed by Fitzgerald and colleagues, the appearance of the gastrointestinal tract using dual phase angiography (including portal and delayed venous phases) and normal attenuation value of the small intestinal mucosa during the portal phase of enhancement in healthy dogs was described. Fitzgerald and colleagues found that the gastrointestinal wall (serosa to mucosa) could be identified in 56.7% of segments prior to contrast administration, 84.5% of segments during the portal phase of enhancement, and 77.3% of segments during a late phase of enhancement. In this study, the enhancement of the mucosa was identified as being between 43-150 HU. Fitzgerald and colleagues concluded that, the portal

phase of enhancement was described as being the best phase for mucosal enhancement during this study.

A separate study[49] by Keh and colleagues, evaluated the clinical utility of computed tomographic enterography. In people, contrast enhanced computed enterography has been utilized to evaluate the gastrointestinal tract for inflammatory bowel disease.[50] This is a procedure in which1.0 – 1.5 liters polyethylene glycol solution or 0.1% barium sulphate and water-methylcellulose solution is administered orally 45-60 minutes prior to CT.[50] Keh and colleagues administered a 1:4 lactulose: water solution at a dose of 60 mL/kg as either a bolus or slowly over 45 minutes.[49] Noncontrast enhanced CT studies were then performed every 10 minutes for 1 hour. The constant infusion over 45 minutes resulted in good luminal distension of all intestinal segments, with the optimal distension occurring between 0 and 20 minutes.

The most recent paper[48] by Lee and colleagues identified the time of enhancement in which the arteries supplying the gastrointestinal tract could be identified the best and in which phase the wall of the gastrointestinal tract enhanced the most. In this study, a new phase of enhancement was identified and was termed the intestinal phase, which was defined as occurring at approximately 38.9 seconds after the administration of intravenous contrast. This study was performed by use of a small test-bolus and calculating time-to-attenuation curves of the major abdominal aorta and cranial mesenteric artery. This study found that the gastrointestinal wall enhancement was greatest during the intestinal phase and venous phases, with the attenuation values being 49.76 and 46.68 HU respectively. This study also found that there was no significant difference between these two phases in regards to degree of enhancement. This study did, however, identify a difference in the enhancement pattern between these two phases, with

the mucosal layer being predominately enhanced in the intestinal phase and transmural enhancement being predominant in the venous phase.

Computed tomographic contrast agents

Ioversol

There are a number of nonionic, iodinated contrast agents, available for use in veterinary medicine, of which Iohexol[3] and Ioversol[4] are two of the most commonly used and readily available intravenous contrast agents. These agents are non-ionic, tri-iodinated, monomeric contrast medium that are water soluble. At the author's institution, the most commonly used agent is Ioversol, therefore the following discussion will be limited to this contrast agent.

Ioversol contains 47.2% organically bound iodine and has a molecular weight of 807.11. The typical dose for Ioversol is based upon the age of the patient, patient body weight, and study being performed. At the author's institution, this contrast agent is most commonly used for procedures involving the nervous and musculoskeletal systems, thoracic cavity, and abdominal cavity, and is administered at a dose of 700-704 mg of iodine per kilogram of body weight (approximately one milliliter of Optiray 320 per pound of body weight). After administration, Ioversol demonstrates an open two-compartment model with first order elimination.

According to the pharmacokinetic data provided by the manufactor[51], there is an initial, rapid alpha phase in which the drug is distributed systemically, which is then followed by a slower beta phase in which the drug is eliminated. The biological half-life in human patients is approximately 1.5 hours with the vascular compartment half-life being 20 minutes. Blood levels

---

[3] Omnipaque, *GE Healthcare,* Oslo, Norway

[4] Optiray, *Liebel-Flarsheim Company LLC.,* Raleigh, North Carolina

typically reach their peak immediately after injection and fall with 5-10 minutes. The main route of excretion is through the kidneys and in humans greater than 95% of the administered dose is excreted in the first 24 hours.[51] The peak urine concentration typically occurs within the first two hours; however, this excretion rate is dependent on both the dose delivered and renal function in the patient. In humans, administration of larger doses of the agent resulted in shortened excretion times.

According to the manufacturer[51], adverse reactions following the administration of Ioversol are usually mild to moderate, occur for only a short duration of time, and resolve without treatment or therapeutic intervention. The most common adverse effect following the administration of Ioversol in humans is nausea, which occurs at a rate of greater than 1% in patients.[51] Other less common reactions have been noted and are included in the following table. These reactions have been documented in less than 1% of people.

Contrast reactions in veterinary species

A number of studies have evaluated the prevalence of contrast induced reactions in veterinary medicine.[52–54] There are also a number of case reports that have been documented.[55,56] In a study[55] performed by Pollard and colleagues a reaction rate (defined as a change in heart rate and blood pressure of 20%) of 7% after administration of iodinated, ionic contrast agents and 1% after administration of non-ionic, iodinated contrast agents were reported. In the most recent study[53] performed by Scarabelli and colleagues, 18% of patients had a mild reaction (indicated by a change in heart rate, respiratory rate, and mean arterial pressure of <10%), 18% experienced a moderate contrast reaction (defined as a change in heart rate, respiratory rate, or mean arterial pressure between 10-20%), and 1% of patients experienced a severe reaction (requiring intervention).

In veterinary patients, one of the most life-threating complications following administration of intravenous iodinated contrast agents is the development of acute anaphylactic reactions.[52–55,57,58] Additional systemic reactions that have been reported include contrast-induced nephropathy, cardiovascular alterations, and respiratory alterations.[52–54,57,58] The pathogenesis of anaphylactic reactions after administration of contrast media is unclear, but has been proposed to be due to the activation of the complement cascade. There have been a multitude of proposed mechanisms as to the pathogenesis of nephrotoxicity following administration of nonionic iodinated contrast agents. The two most prevailing theories include renal vasoconstriction, which results in medullary hypoxemia, and the direct cytotoxic effect of contrast media on renal tubular cells.[58,59]

A study[60] by Davenport and colleagues using human patients identified that patients with a serum creatinine of 1.6 g/dL or greater were at an increased risk of developing renal associated acute kidney injury. This study also demonstrated an odds ratio of 1.26, meaning for every 1.0 g/dL that the patient's serum creatinine levels rose above 1.5 g/dL the odds of developing acute kidney injury following contrast administration increased by 1.26.[60]

A separate study [61], also identified that the risk of contrast induced nephrotoxicity in humans increases with administration of a second dose of nonionic, iodinated contrast agents. In this study, patients who maintained normal renal function after an initial contrast-enhanced computed tomographic exam underwent a second contrast-enhanced computed tomographic examination and significant elevations of serum creatinine and decreased in the estimated GFR were identified, with four patients developing contrast induced nephropathy.

To date, there is only one publication reviewing contrast induced nephropathy (CIN) in dogs.[58] In this paper, CIN was defined as an increase in serum creatinine of 0.5 mg/dL from

baseline within 1 week following the administration of IV contrast. The rate of CIN in this study was found to be 7.6%, which mimics that which has been reported in the human literature of 0% to 33%.[58,62–64] The authors in this study did not identify a causal relationship between the administration of intravenous contrast and the occurrence of CIN.[58] In fact, none of the evaluated parameters (patient signalment, initial creatinine levels, number of total contrast administrations, dose of contrast received, duration of anesthesia, intravenous fluid administration, administration of additional nephrotoxic agents, or use of vasopressor therapy) were found to be different between the group that developed CIN following examination and those that did not.[58]

Inflammatory bowel disease in dogs

Pathogenesis of inflammatory bowel disease in dogs

Similar to that in humans, the exact mechanism of inflammatory bowel disease in dogs is not entirely known; however, it is thought that complex interactions between the intestinal microbes and dysregulated immune system responses occur within affected dogs.[65,66] A potential genetic predisposition has also been proposed and several dog breeds have been reported as being predisposed to the development of certain types of IBD.[9,67] Examples include protein-losing enteropathy in Soft-Coated Wheaten Terriers, immunoproliferative enteropathy in Basenjis, granulomatous colitis in Boxers, and lymphocytic-plasmacytic enteropathy in German Shephard Dogs (GSD).[9,17,67,68]

Genetic sequencing has identified alterations in the expression of pattern recognition receptors TLR4 and TLR5 in affected GSDs as compared to healthy Greyhound dogs.[69] Further studies investigated whether allelic variations of these pattern recognition receptors and that of TRL2 contributed to the abnormal response of the intestinal microbiota. Multiple non-synonymous single nucleotide polymorphisms (SNPs) were identified in the TLR5 and TRL4

genes, which were significantly associated with the development of IBD in dogs. Both GSD and non-GSD dogs with IBD also had alterations in the canine NOD2 gene, which suggests that these mutations may contribute to the development of IBD through the development of chronic mucosal inflammation.[70] Furthermore, up-regulation of the TLR2, 4, and 9 pattern recognition receptors has been identified in dogs with duodenal and colonic mucosal inflammation secondary to IBD, suggesting that there is derangement of the patient's innate immunity.[71] The degree of expression of TLR2 receptors has also been correlated to the clinically severity of disease in affected dogs.[72]

Specific local immune cell populations demonstrate alterations in dogs affected by IBD. These include an increase in the local concentration of lamina propria IgA^+ and IgG^+ plasma cells, $CD3^+$, $CD4^+$, and $CD8^+$ T cells, macrophages, and neutrophils and a decrease in the local mast cell population.[73–75] Mucosal cytokines profiles are also altered in affected dogs with mixed Th1/Th2 activation.[76–79] NFkB activation within the lymphocytes in the lamina propria of dogs with IBD has also been documented. NFkB in humans has been shown to influence the production of IL-23, which is related to mucosal inflammation, differentiation of novel $CD4^+$, and production of IL-17.[9,80]

The local microbiota have been shown to be an important contributor to the development and progression of chronic enteropathies. In particular, the association of dysbiosis, an imbalance or disruption of the GI microbiome, has been increasingly recognized and researched as of late.[9] A connection between chronic inflammatory bowel disease and a change within the normal small intestinal microbiota has shown that affected dogs have increased *Enterobacteriaceae, Clostridiaceae,* and *Escherichia coli* bacteria attached either to the mucosal epithelia or invading into the mucosa.[9] This alteration has also been identified in other forms of chronic enteropathies

and intestinal neoplasia. The number of bacteria adhered to the colonic mucosa has been positively correlated with disease severity in dogs with IBD.[68]

Diagnosis of inflammatory bowel disease in dogs

The diagnosis of inflammatory bowel disease (IBD) is complex, and usually involves synthesizing data from the patient's signalment, history, physical exam findings, diagnostic imaging, clinicopathologic testing, and histopathology of intestinal biopsies. The most common presenting complaints for dogs with IBD include vomiting, diarrhea, and weight loss.[9,67] These can occur in isolation, in combination, or in addition to lethargy, inappetence, tenesmus, melena, hematochezia, and peripheral edema.[8] When the clinical presentation includes diarrhea, every attempt must be made to characterize the diarrhea as small bowel or large bowel diarrhea. Small bowel diarrhea is commonly associated with IBD. In dogs with diarrhea, a diagnosis of IBD is typically considered after other etiologies have been excluded, such as infectious and parasitic agents, non-GI disorders, exocrine pancreatic insufficiency, pancreatitis, endocrinopathies (especially hypoadrenocorticism), and intestinal structural abnormalities. Because IBD is a diagnosis of exclusion, the standard diagnostic approach includes complete blood counts, serum chemistry, fecal analyses and floats, cobalamin and folate levels, screening for hyperadrenocorticism, ultrasonography and radiography of the abdomen, treatment trials with novel protein or hydrolyzed diets as well as endoscopy and histopathology if deworming and dietary trials fail.

Diagnostic imaging of IBD

Although abdominal radiographs are an important part of the diagnostic work up of IBD, they are limited in their evaluation of the small intestinal wall thickness due to the border

effacement that occurs from the similar opacities of the intestinal wall and the intraluminal ingesta. The degree of luminal distension and phase of peristalsis also play a role in limiting the diagnostic value of abdominal radiographs. The addition of barium can help delineate the thickness of the intestinal wall on radiographs. Findings that correlate with intestinal wall thickening and IBD on positive contrast abdominal radiographs include a rapid passage of contrast, a thickened wall, and an irregular mucosal margins.[10,81] These findings, however, are not pathognomonic for IBD and may be seen with a variety of disease.

As previously mentioned, ultrasonography is currently the imaging modality of choice for small animal patients with IBD. Common ultrasonographic findings include diffuse, moderate (<6 mm) intestinal wall thickening, hyperechoic mucosal striations/stranding/foci, retention of normal wall layering, and mesenteric lymphadenopathy.[10–14] These findings in combination with the presence of hypoalbuminemia and/or hypocobalaminemia should warrant the consideration of intestinal biopsies to confirm the presence of IBD. [8,10–12,16,17,40,82,83] Using imaging characteristics to differentiate IBD from neoplasia or infectious etiologies can be challenging due to an overlap of gross and visual changes.[10–12] A prior study,[82] has shown that the mean maximal wall thickness in dogs with nonspecific enteritis was significantly less than those dogs with intestinal neoplasms. However, in this study a small set of cases developed severe (>15 mm) wall thickening that was attributed to enteritis. This study also demonstrated that severe focal thickening (>15 mm) and loss of wall normal wall layering was more commonly associated with neoplastic etiologies than inflammatory etiologies. Intra-abdominal lymphadenopathy was reported in both populations within this study, but was more commonly identified and was more severe in patients with intestinal neoplastic etiologies than those with inflammatory etiologies.[82]

Other studies[17,18], however, have shown that the wall thickness between dogs affected by IBD and normal dogs is not significantly different. The authors in one of these studies[18] proposed that these dogs may have had disease that was sufficient to cause clinical signs, but not infiltrative enough to cause ultrasonographic abnormalities. In the remaining study[17], the authors found that a novel ultrasound score that evaluated the wall thickness of the duodenum and jejunum, mucosal echogenicity, lymph node size and appearance, and secondary changes was correlated with activity of clinical disease at presentation but not after initiation of treatment.

Bloodwork, Intestinal Biopsy and Histopathology

The complete review of bloodwork derangements, intestinal biopsy procedures, histopathologic appearance, and treatment for patients with IBD is beyond the scope of this thesis. However, a short synopsis is provided. The presence of hypoalbuminemia and the levels of folate and cobalamin can help direct the clinician to the need for intestinal biopsy, as well as, localizing the site of gastrointestinal tract in which biopsies need to be obtained, as cobalamin is preferentially absorbed in the ileum.[7,8] These parameters can also help establish a prognosis.[8,9,17,67]

Intestinal biopsies can be obtained either endoscopically or surgically. In some cases, endoscopically is the preferred choice, especially since prior studies have shown that the endoscopic appearance may correlate better with patient outcome than the histopathologic appearance.[8,84,85] Although, it has been inconsistently shown that endoscopic biopsies are less sensitive in the diagnosis of IBD and/or concurrent lymphangiectasia than full thickness biopsies.[17] With adequate sampling of the duodenum and ileum, and adequate skill of the endoscopist, biopsies obtained via endoscopy usually provide a diagnosis. New guidelines have been published recently[86] to maximize the usefulness of endoscopic pinch biopsies. Full

thickness biopsies of the duodenum, jejunum, and ileum do allow more thorough evaluation of the intestinal wall. However, the risk of surgical complications and dehiscence with hypoalbuminemia and/or colonic biopsies makes endoscopic biopsies in these scenarios more attractive to both clinicians and owners. Furthermore, IBD occurs in the mucosa, which is easily obtained via endoscopy.

The most common histopathologic finding in IBD is increased cellularity of the lamina propria. Both the degree and type of cellular accumulation can vary widely and can have a range of categories from normal to severe. In the presence of a large number of macrophages and neutrophils, infectious causes should be further pursued, while the presence of an increased number of lymphocytes and plasma-cells or eosinophils is more consistent with lymphocytic-plasmocytic enteritis or eosinophilic enteritis, respectively.[8,67]

Treatment of inflammatory bowel disease in dogs

Treatment of IBD in dogs is related to the underlying etiology and involves correcting any nutritional abnormalities and counteracting inflammation and dysbiosis. Typically, the cornerstone of treatment is considered to be the feeding of nutritionally balanced, highly digestible elimination diet. Additional treatments include administration of immunosuppressive doses of systemic glucocorticoids, other systemic immunosuppressive agents, and antibiotic therapy.[8,17,18,67] In some cases prebiotics and probiotics have also found to be beneficial.[9,67]

Human abdominal imaging

Traditionally, ultrasound was the primary imaging modality employed in the work up of inflammatory bowel disease in humans for the last 20 years.[87] This imaging modality has been shown to have moderate to high sensitivity and specificity for the diagnosis of mural enteric

inflammation caused by Chron's disease (CD), ranging from 75-94% and 67-100%, respectively.[87] Ultrasound, also has been proved to be an excellent modality in the diagnosis of strictures, identifying all strictures in a group of 22 patients and excluding strictures correctly in 10/11 patients.[87] However, these values have been shown to be dependent not only on the training of the operator, but also on the depth of the segment of bowel affected and the institution in which the examination was performed.[87,88]

In people, the current gold standard modality for the diagnosis of Crohn's Disease (CD) is cross-sectional imaging, specifically computed tomography and magnetic resonance imaging.[87,88] Typically, the first choice for imaging of the human abdomen is computed tomography or computed tomographic enterography due to its wide availability and quick acquisition times. Computed tomography has also been shown to be both highly sensitive and specific for mural enteric inflammation as well as for the diagnosis of small bowel stenosis, intraabdominal fistulas, and intraabdominal abscesses.[87,88] Perhaps the biggest disadvantage of computed tomography is that it uses ionizing radiation and is a major contributor to the total medical ionizing radiation dose a patient receives each year. Given that the age of diagnosis of most patients with CD is young to middle aged, clinicians should be mindful of this dose and subsequent doses of ionizing radiation in their patients.[87] Because of the received dose of ionizing radiation and the need for subsequent follow up imaging examinations, it has been suggested that computed tomographic enterography be used as the initial imaging examination for the diagnosis of CD with MRI being employed as a follow up and for recheck examination.[87]

Magnetic resonance imaging has also been shown to be highly sensitive and specific in the diagnosis of CD and is comparable to CTE in the identification of enteric mural inflammation and small intestinal stenosis.[87] MRI has also been shown to be more accurate than

other imaging modalities for the diagnosis of intraabdominal fistulas.[87] One of the biggest limitations of using MRI to evaluate the small intestines is motion artifact due to normal peristaltic activity. Studies have shown that this artifact can be reduced by using heavily T2 weighted sequences that are optimized to decrease motion and improve depiction of the perienteric mesentery.[89] The administration of Butylbromide and glucagon have also been shown to decrease the normal peristaltic activity prior to MRI evaluation.[87,89] Other limitations of MRI include lack of access, increased acquisition times, and increased time of image interpretation.[87]

Computed tomographic enterography (CTE) is typically performed as the prior imaging modality when IBD is suspected, although in some cases magnetic resonance imaging enterography (MRE) is considered an adequate alternative.[87] When comparing the two modalities, MRE and CTE were equally accurate for the assessment of enteroenteric fistulas; however, MRE identified more intestinal strictures. Moreover, MRE has better agreement for diagnosis of ileocolonic CD when compared to colonoscopy and CTE.[87] Computed tomographic enterography has been shown in a single study to be better able to distinguish perienteric features, such as mesenteric hypervascularity, edema, fibrofatty proliferation, and lymphadenopathy, better than MRE, while the two modalities have near agreement on the mural features associated with CD such as wall thickening >3mm, and mural hyperenhancement.[90] Future advancements and the addition of diffusion weighted imaging in MRI is likely to make to this modality the gold standard for the diagnosis of CD in humans.[87]

CHAPTER II

STUDY

Study Objectives

This study was performed with the following objectives:

1. To describe the maximum and minimum diameter of the normal canine small intestine in three groups of normal dogs, categorized by body weight during triple-phase computed tomographic angiography (CTA).
2. To describe the contrast enhancement pattern of the normal canine small intestine using triple-phase CTA.
3. To determine the relation between body weight and diameter of the normal canine small intestine.

Hypotheses

1. The arterial phase will be the most beneficial for evaluating the small intestinal mucosal layer, due to the greatest degree of mucosal enhancement in this phase.
2. Increasing body weight will be positively correlated with small intestinal diameter.
3. Increasing body weight will be positively correlated with small intestinal wall thickness.
4. Triple-phase CTA will be a reliable imaging modality to measure the normal canine small intestinal diameter and wall thickness and will allow assessment of wall layering.

Materials and Methods

Study population

Client owned dogs that were admitted to the primary small animal care services and were undergoing contrast-enhanced computed tomography examinations for problems unrelated to the gastrointestinal tract were prospectively recruited. Client consent for acquiring an additional computed tomographic examination of the abdomen was obtained prior to inclusion. The Institutional Animal Care and Use Committee (IACUC) approved this study prior to data collection, and the study was conducted in accordance with the IACUC protocols.[5] Inclusion criteria was limited to triple-phase CTA of the entire abdomen, defined as the cranial extent of the diaphragm to the coxofemoral joints, and a complete blood count and serum chemistry profile with no evidence of abnormalities referable to the gastrointestinal tract as determined by the attending clinician. Exclusion criteria included any clinical signs suggestive of gastrointestinal disease within the last 24 hours, such as vomiting, diarrhea, or inappetence, any history of exploratory laparotomy for suspected small intestinal disease (mechanical small intestinal obstruction, infiltrative disease, etc.), or active pancreatitis. Further exclusion criteria included a reported history of clinical signs related to the gastrointestinal tract within the last six months, any episode of vomiting or diarrhea within the last 48 hours, a history of prior laparotomy (excluding ovariohysterectomy procedures), or suspected pancreatitis (based on clinical or physical examination parameters consistent with pancreatitis, a positive canine pancreatic lipase immunoreactivity test, or abdominal ultrasound findings consistent with pancreatitis).

---

[5] IACUC-17-630

Imaging

Subjects were sedated using a protocol chosen by the attending primary clinician. An attempt was not made to standardize sedation protocols. Computed tomographic angiographic examination using a Toshiba Aquilion 16-slice multi-detector row CT scanner[6] was then performed using the following technical parameters: 16 x 0.5 or 16 x 1.5 mm collimation, tube rotation of 0.5 s, 100 or 120 kVp, variable mAs (range from 80-200 mAs), helical pitch of 1.5, and a field-of-view large enough to encompass the entire circumference of the abdomen. Positioning was based on the optimal positioning for the anatomic region of interest most pertinent to the patient's clinical signs. Examinations were performed as previously described. [25,27] Briefly, a pre-contrast scan was performed followed by injection of a non-ionic, organic, iodinated contrast agent, Ioversol[7] intravenously at a dose of 704 mg/kg body weight by a power-injection system[8] at a rate of 3 mL/seconds. The initial post-contrast scan was performed during the later arterial phase, 25s after initiation of contrast injection. The portal and venous phase scans followed at time intervals of 40s and 90s after initiation of injection. Once scanning was completed, reconstruction of the image data using a soft tissue kernel was performed with a variable slice thickness based on patient body weight (3mm for dogs <10kg and 5mm for dogs ≥10kg) in transverse, dorsal, and sagittal imaging planes.

---

[6] Toshiba Corporation, *Toshiba American Medical Systems Inc*., Tustin, California

[7] Optiray 320 mg/mL*, Liebel-Flarsheim Company, LLC*, Raleigh, North Carolina

[8] Medrad Stellant, *Bayer Healthcare LLC*, Whippany, New Jersey

Measurements

Image evaluation was performed using the open-source digital imaging and communication in medicine viewer, OsiriX 64-bit v.5.9.[9] Window and leveling was allowed to optimize the images based on evaluator preferences. The small intestinal diameter and wall thickness was measured using electronic calipers. Measurements were performed on small intestinal loops, as previously described[46] in a study by Hoey and colleagues. In short, measurements were acquired from small intestinal loops whose short axis was close to the plane of evaluation, and whose shape was not being altered by adjacent abdominal structures.[46] A board-certified radiologist and a second-year diagnostic imaging resident measured and recorded the maximum (Figure 2.1) and minimum (Figure 2.2) small intestinal diameter and wall thickness in all three planes (transverse, sagittal, and dorsal) and all three phases of contrast enhancement (arterial, portal, and venous).

The intestinal diameter was defined as the thickness from serosa to serosa, and intestinal wall thickness was defined as the thickness from mucosa-luminal interface to serosa. The small intestinal diameter and wall thickness were measured at one site in each of the following locations: ascending duodenum, descending duodenum, transverse duodenum, ileum, and ileocolic junction. These same measurements were obtained at three locations over the course of the jejunum. Distinction of individual wall layers was scored using a scale in which the number of wall layers identified corresponded with the numerical value recorded (0 given when no distinct layers are identified, 1 being only 1 layer identified, 2 being 2 distinct layers identified, 3 being 3 distinct layers identified, and 4 being each individual layer identified).

---

[9] *Pixmeo SARL*, Geneva, Switzerland

The same two individuals also subjectively graded the ability to identify the mucosal wall layer. The mucosal wall layer was subjectively identified in each of the regions measured and was graded using a scale previously described in the literature (Figure 2.3): 1 - good (defined as a distinct mucosal surface); 2-moderate (defined as a visible but indistinct mucosal surface); and 3-poor (defined as no viewable difference between the mucosa and remainder of the gastrointestinal wall).[47]

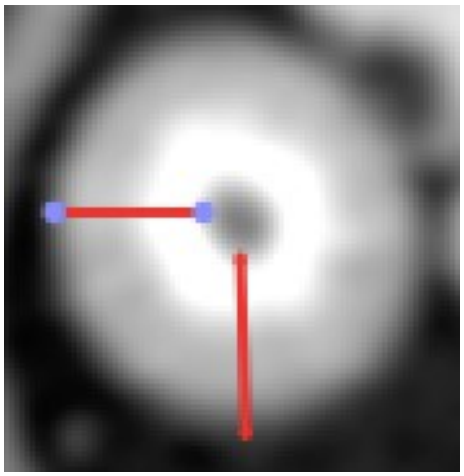

Figure 2.1 Maximal and minimal wall measurements

Demonstration of the measurements of the maximal and minimal wall thickness of the descending duodenum during a portal phase of enhancement in a transverse plane of reconstruction. Note the grade 2 mucosal enhancement.

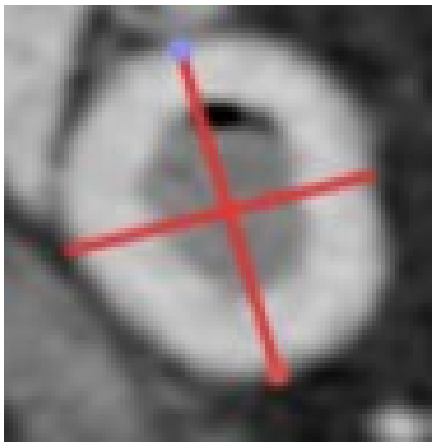

Figure 2.2 Figure 2.1

Demonstration of the maximal and minimal small intestinal diameter of the descending duodenum in a venous phase of contrast enhancement in a transverse plane of reconstruction. Note the grade 3 enhancement.

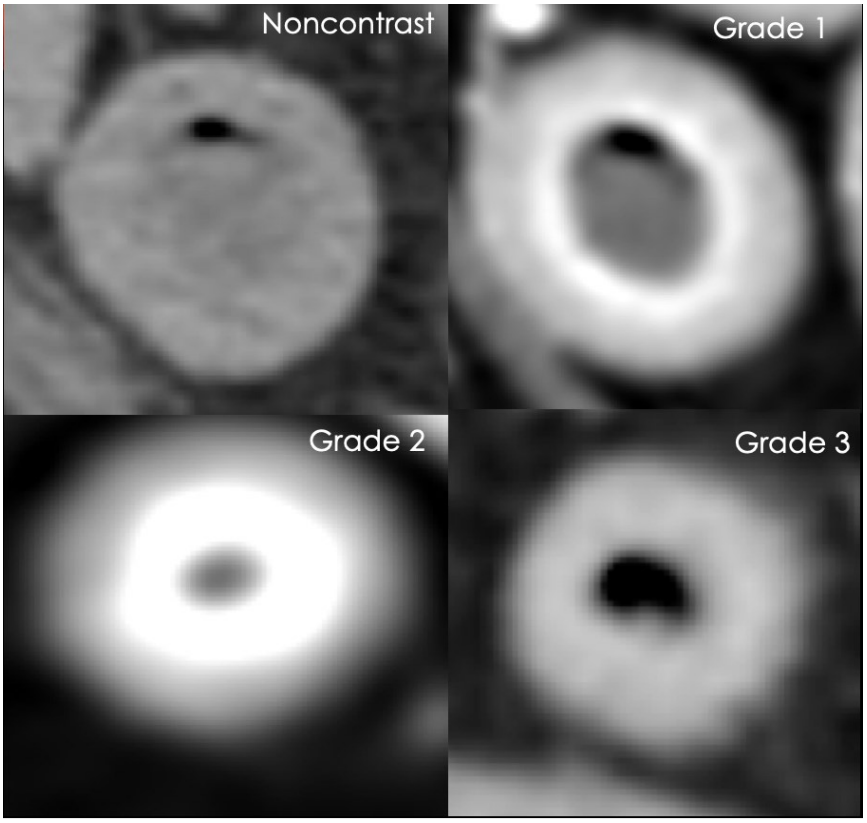

Figure 2.3 Transverse plane of reconstruction of the descending duodenum

Example of the grading scheme for mucosal enhancement. Note the thing ring of enhancement on the grade 1 image that progresses to the serosal surface in the grade 2 and grade 3 image

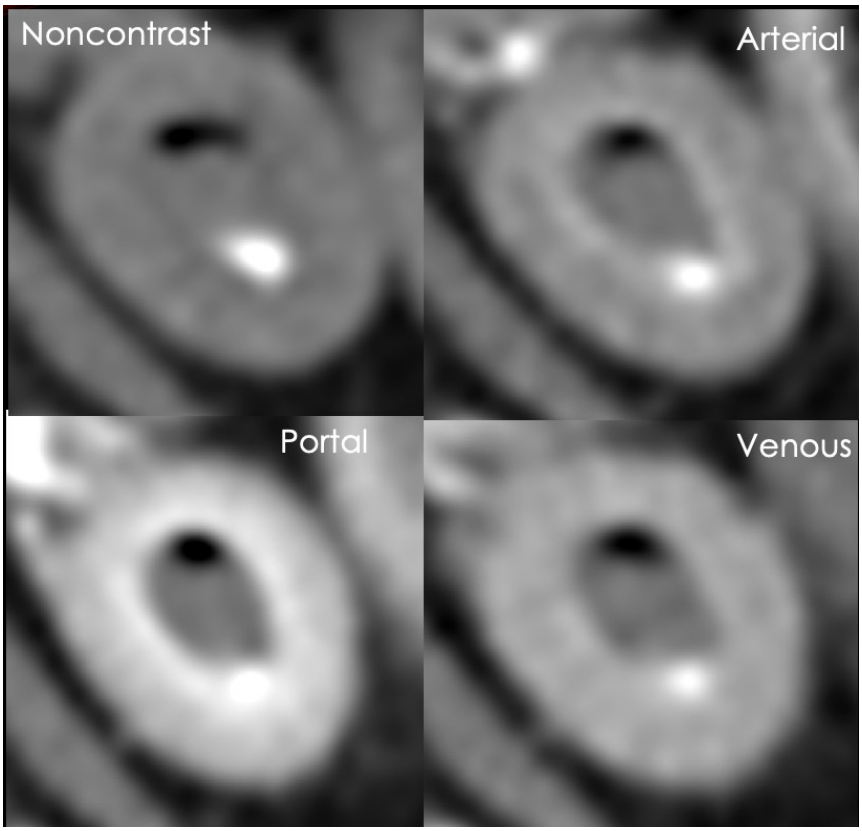

Figure 2.4 Enhancement pattern of the normal canine descending duodenum

Note the grade 1 mucosal enhancement in the arterial and poral phases and grade 3 enhancement in the venous phase. There is fluid attenuating material occupying approximately 95% of the lumen. There is also a small mineral attenuating object within the gravity dependent portion of the duodenal lumen.

Statistical methods

Analysis of small intestine diameter measurements in 30 dogs in three planes (transverse, sagittal, and dorsal) with four phases was determined with linear mixed models using PROC MIXED in SAS for Windows v9.4.[10] Outcomes included three measurements for the duodenum

[10] *SAS Institute*, Cary, NC

(ascending, descending, and transverse), the average of three measurements in the jejunum, and one measurement in the ileum. Measurements for each part of the small intestine included minimum diameter, maximum diameter, minimum wall thickness, maximum wall thickness, number of wall layers, and enhancement. Each dog's small intestine was measured by two investigators. The average of their measurements was used for further analysis. Separate models were used for each plane for each measurement that had supporting data. Fixed effects included phase, body weight, and the phase-body weight interaction. If the interaction term was not significant, it was removed and the model refitted. Dog ID was included as a random effect. Covariance structure in the model utilized that of variance components. Residual plots were used to ensure the assumptions of normality and homoscedasticity had been met for the statistical models. Significance of results was set at an alpha level of 0.05.

Study results

Study population results

During the study period, 30 dogs that met the inclusion parameters, were prospectively enrolled and included in the study. No dogs were excluded from the study. All 30 dogs underwent computed tomographic examination of the entire abdomen within the parameters described. The most represented breed was mixed breed dogs with a total number of seven included. Further breakdown of breeds included are as follows: mixed breed (7), Labrador retriever (4), terrier (4), German shepherd Dog(3), goldendoodle (2), dachshund (2), boxer (2), and one each of Pomeranian, Swiss mountain dog, Australian cattle dog, border collie, miniature schnauzer, and English bulldog. There were 20 (67%) females and 10 (33%) males included in the study. Of the 20 females included, 17 (85%) were spayed and three (15%) were intact. Of the 10 males included in the study, eight (80%) were neutered and two (20%) were intact. The

maximum included weight was 55.8 kilograms and the minimum included weight was 4.4 kilograms, which resulted in a range of 51.4 kilograms. Overall eight dogs that weighed less than 15.20 kilograms, 13 dogs between 15.20 and 31.00 kilograms, and nine dogs greater than 31.00 kilograms were included. The median weight was 24.75 kilograms and the mean weight was 24.17 kilograms.

Transverse plane of reconstruction

Ascending duodenum

Patient weight had a significant effect on both the maximal (Figure 2.5) and minimal (Figure 2.6) diameter of the ascending duodenum, with smaller dogs having significantly smaller values than larger dogs. Significant effects between the maximal and minimal thickness of the wall of the ascending duodenum and phase of enhancement, patient weight, nor weight and phase of enhancement were not identified.

The phase of enhancement had a significant effect on the number of wall layers identified (**Error! Reference source not found.**). Significantly more wall layers were identified in the arterial and portal phases compared to the venous and noncontrast phases of enhancement, with an average 1.900, 1.683, 1.466, and 1.333 wall layers being identified, respectively. No significant difference was identified between either the arterial or portal nor between the venous and noncontrast phases of enhancement.

A significant interaction between the degree of mucosal enhancement and body weight and phase interaction was identified (Figure 2.15, Figure 2.16, Figure 2.17). In all groups, the arterial phase had the greatest degree of mucosal enhancement, followed by the portal phase. There was also a significant difference between the arterial and portal phases in relation to the degree of mucosal enhancement with the arterial phase demonstrating greater significant

enhancement in dogs less than 15.20 kilograms and 15.20 to 31.00 kilograms. There was no significant difference between the arterial and portal phases in dogs greater than 31.00 kilograms. No significant effect was identified between the venous and noncontrast phases in any weight group.

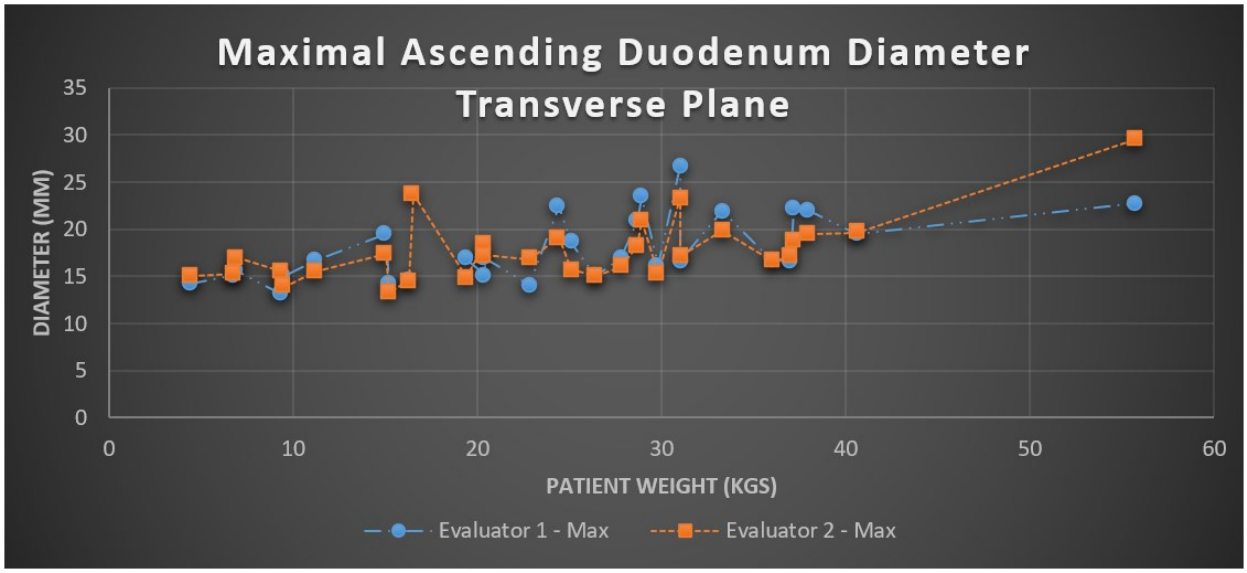

Figure 2.5 Maximal diameter of the ascending duodenum

Measurements from the noncontrast series were used for graph construction, as phase of enhancement did not have a significant effect on diameter.

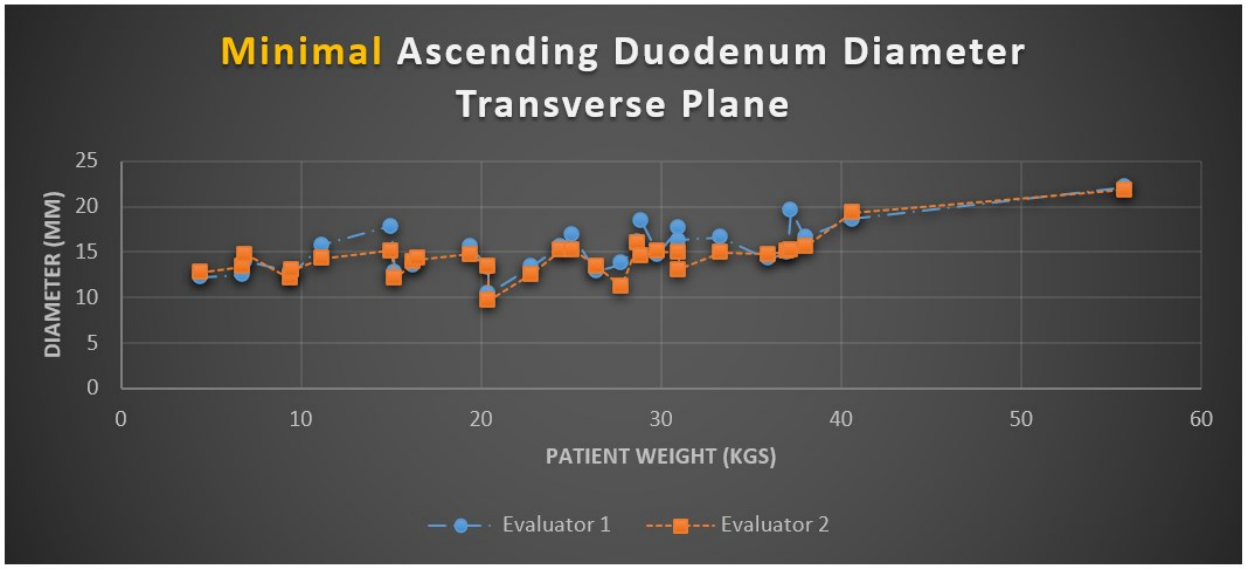

Figure 2.6 Minimal diameter of the ascending duodenum

Measurements from the noncontrast series were used for graph construction, as phase of enhancement did not have a significant effect on diameter.

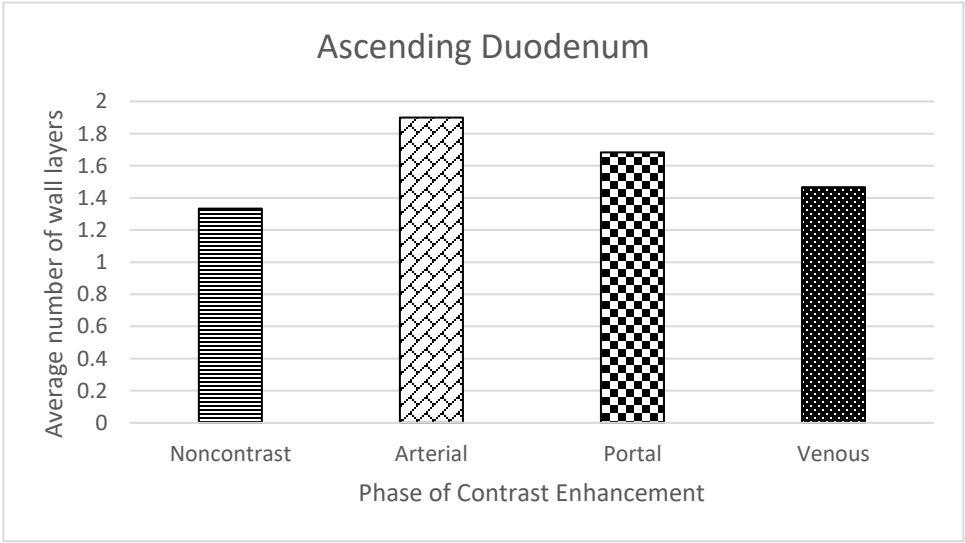

Figure 2.7 Average number of wall layers identifed in the ascending duodenum identified in a transverse plane of reconstruction

Note that the arterial and portal phases of contrast enhancement demonstrated the greatest number of average wall layers identified.

Descending duodenum

Patient weight had a significant effect on both the maximal (**Error! Reference source not found.**) and minimal (Figure 2.9) diameter of the descending duodenum, with smaller dogs having a significantly smaller diameter than larger dogs. Phase of enhancement did not affect the overall diameter nor wall thickness. No significant association between patient weight and the wall thickness of the descending duodenum (minimal or maximal) was identified.

Phase had a significant effect on the number of layers identified within the descending duodenum (Figure 2.10). There were significantly more wall layers identified in both the arterial and portal phases of enhancement compared to the venous and noncontrast phases, with an average of 2.250 wall layers, 1.883 wall layers, 1.300 wall layers, and 1.267 wall layers being identified respectively. There was no significant difference between the arterial and portal phases or between the noncontrast and venous phases.

Both phase and the weight-phase interaction had a significant effect on the mucosal enhancement of the descending duodenum (Figure 2.15, Figure 2.16, Figure 2.17). In all weight classes the arterial phase demonstrated the greatest mucosal enhancement followed by the portal phase. The greatest degree of mucosal enhancement was found in the arterial phase in dogs less than 15.20 kilograms. The difference between the arterial and portal phases in regard to mucosal enhancement, although not significant, was greatest in dogs less than 15.20 kilograms with dogs weighing over 15.20 kilograms having relatively symmetric enhancement during these two phases.

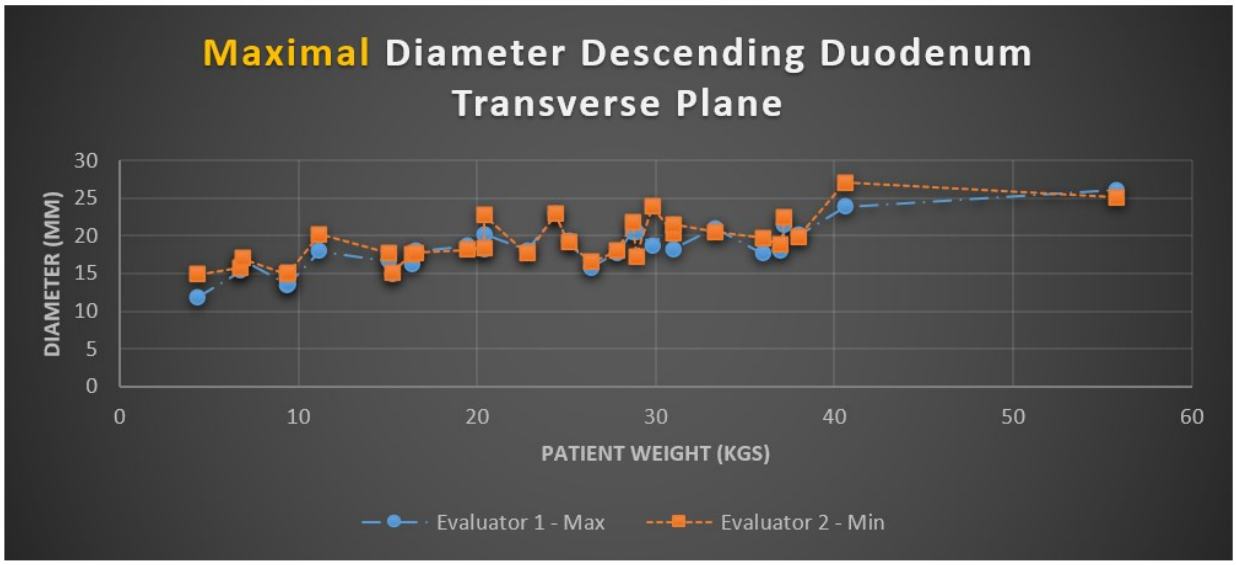

Figure 2.8 Maximal diameter of the descending duodenum in a transverse plane of reconstruction

Graphic demonstration of the positive association between patient body weight and maximal diameter of the transverse duodenum in a transverse plane of reconstruction. The noncontrast series was utilized for this graph, as the phase of contrast enhancement did not have an effect on the measured diameter.

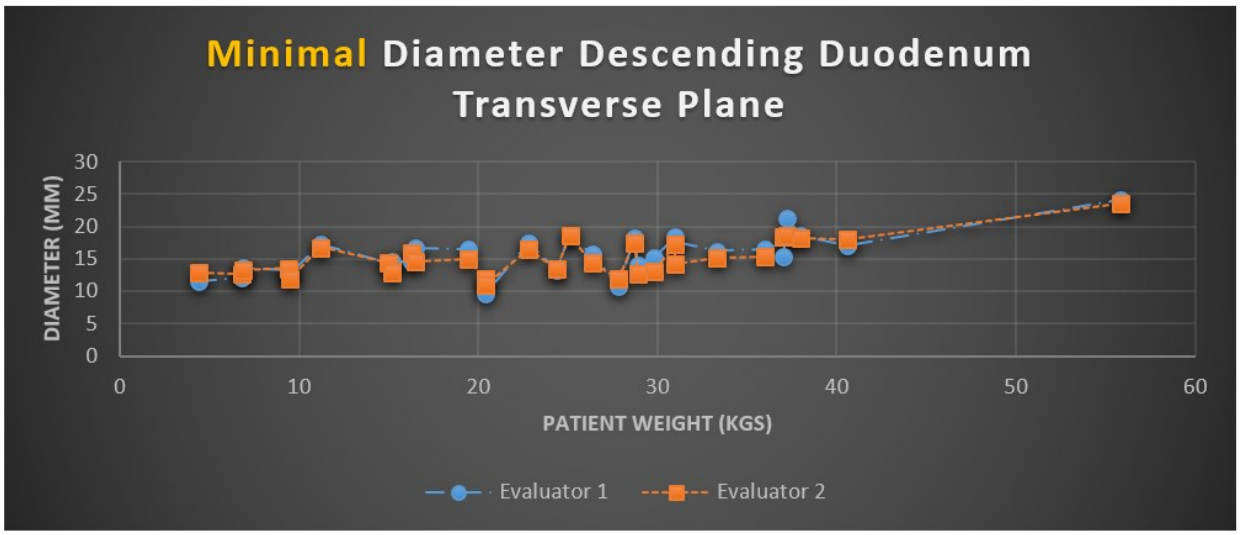

Figure 2.9 Minimal diameter of the descending duodenum in a transverse plane of reconstruction

Graphic demonstration of the positive association between patient body weight and maximal diameter of the descending duodenum in a transverse plane of reconstruction. The noncontrast series was utilized for this graph, as the phase of contrast enhancement did not have an effect on the measured diameter.

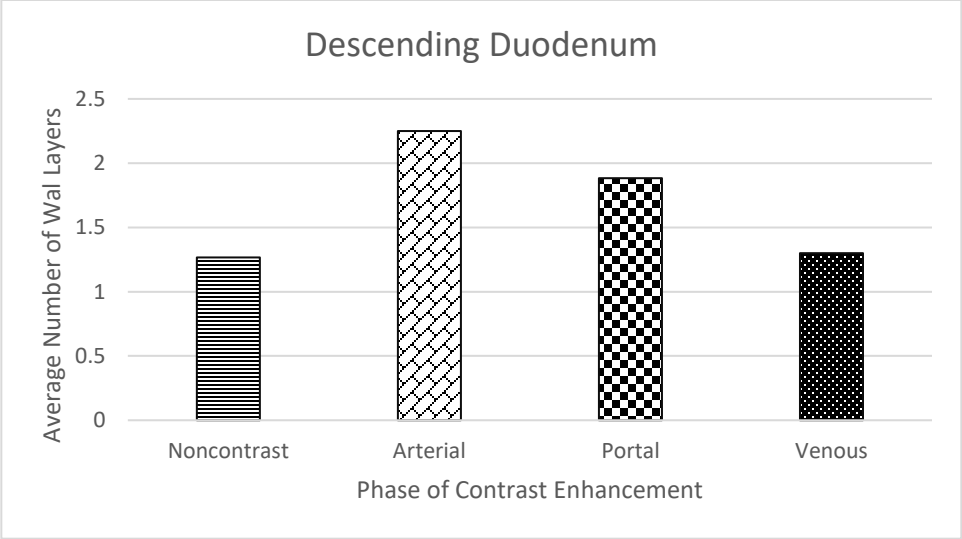

Figure 2.10 Average number of wall layers identified in the descending duodenum in a transvers plane of reconstruction

Note that the greatest average number of wall layers identified was in the arterial phase followed by the portal phase.

Jejunum

Patient weight had a significant effect on the overall maximal (Figure 2.11) and minimal (**Error! Reference source not found.**) diameter, with smaller dogs have significantly smaller overall diameter than larger dogs. Patient weight, phase of enhancement, and patient weight and phase of enhancement interaction did not have a significant effect on the maximal nor minimal thickness of the wall.

Phase of enhancement had a significant effect on the number of wall layers identified (**Error! Reference source not found.**) with the greatest average number of wall layers being identified in the arterial phase (1.711), followed by the portal phase (1.494), then the venous phase (1.306), and finally the noncontrast phase (1.206). There was also a significant difference

between the arterial and portal phases, with significantly more wall layers identified in the arterial phase. No significant difference was identified between the venous and noncontrast phases of enhancement.

The phase of enhancement had a significant effect on the degree of mucosal enhancement with a significantly greater degree of enhancement being identified in the arterial and portal phases (Figure 2.15, Figure 2.16, Figure 2.17). No difference between these phases nor between the venous and noncontrast phases was identified.

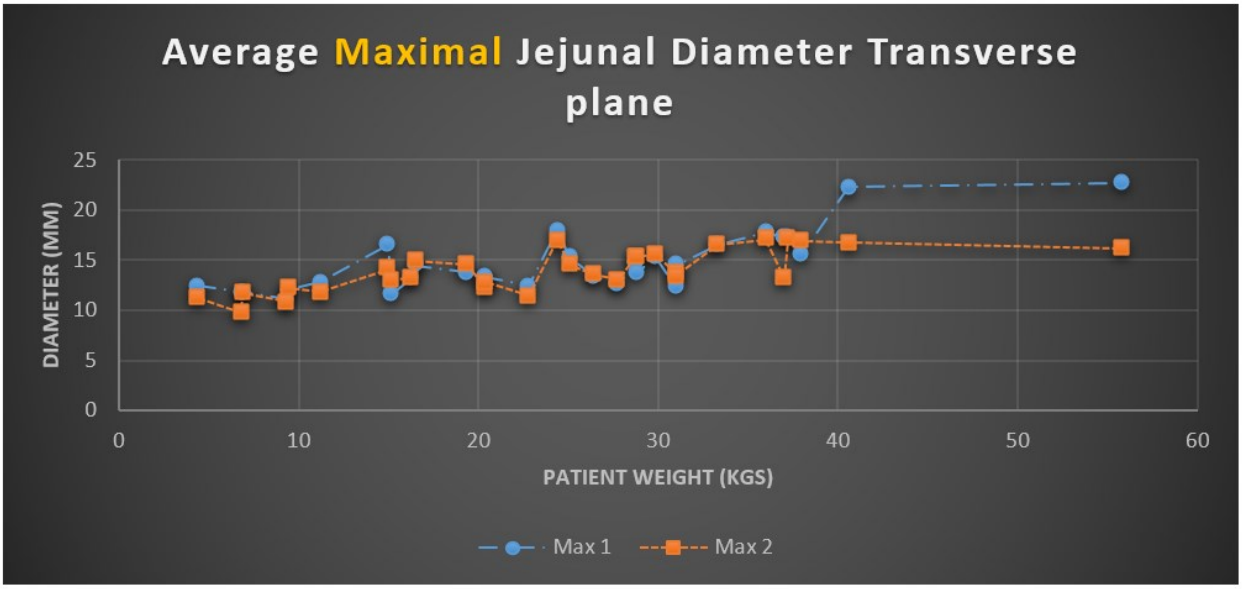

Figure 2.11 Maximal average jejunal diameter in a transverse plane of reconstruction

Graphic demonstration of the positive association between patient body weight and maximal average diameter of the jejunum in a transverse plane of reconstruction. The noncontrast series was utilized for this graph, as the phase of contrast enhancement did not have an effect on the measured diameter.

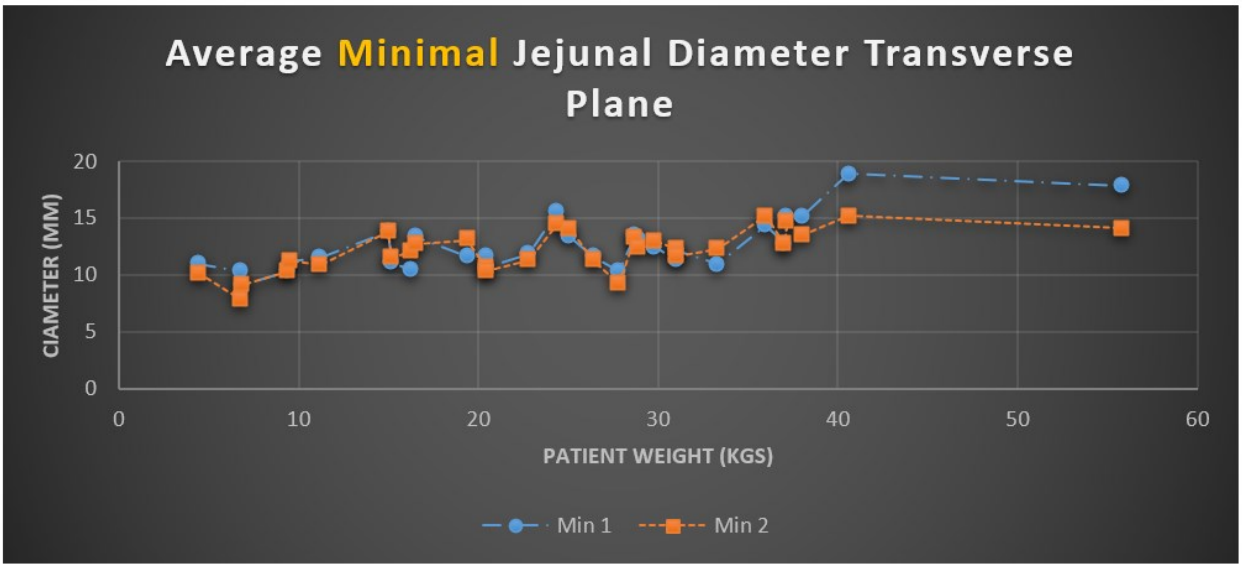

Figure 2.12 Average minimal jejunal diameter in a transverse plane of reconstruction

Graphic demonstration of the positive association between patient body weight and minimal diameter of the jejunum in a transverse plane of reconstruction. The noncontrast series was utilized for this graph, as the phase of contrast enhancement did not have an effect on the measured diameter.

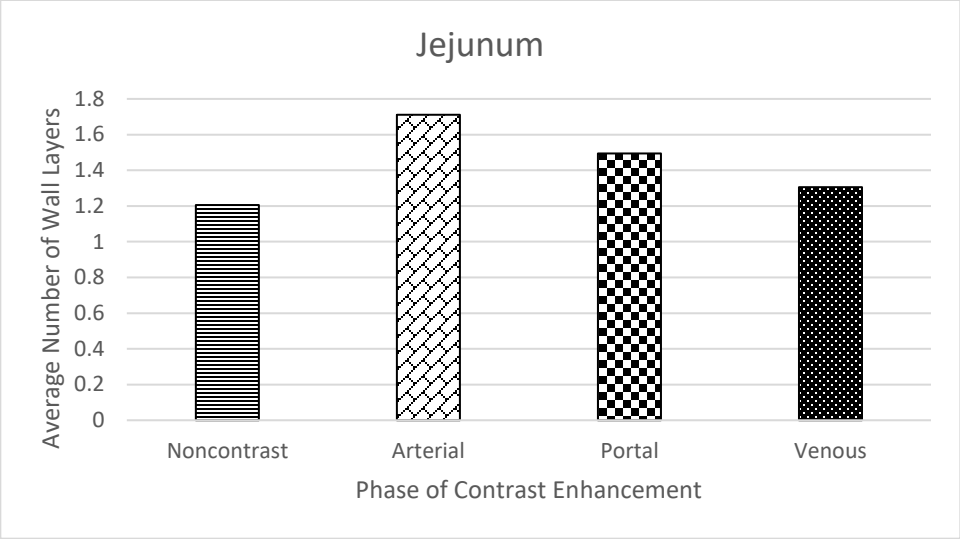

Figure 2.13 Average number of wall layers identified in the jejunum in a transverse plane of reconstruction

Note that the greatest average number of wall layers were identified within the arterial and portal phases of enhancement.

Ileum

A significant interaction between phase of enhancement and both the number of wall layers identified and the degree of mucosal enhancement were identified. A greater average number of wall layers were identified in the portal phase (1.4833) followed by the arterial phase (1.4333), then the venous phase (1.2500), and finally the noncontrast phase (1.0333). Significantly more wall layers were identified on both the arterial and portal phases than in the venous and noncontrast phases, with no significant difference between these two phases (Figure 2.14).

There was a significantly greater degree of mucosal enhancement in the portal phase compared to the remaining phases of enhancement (Figure 2.15, Figure 2.16, Figure 2.17). There

was no significant difference between the arterial phase and the venous phase nor between the arterial phase and portal phase. The arterial phase had significantly greater mucosal enhancement than the noncontrast series. There was also a significant difference in regard to the degree of mucosal enhancement between the venous and noncontrast phases of enhancement, with a greater degree of mucosal enhancement identified in the venous phase.

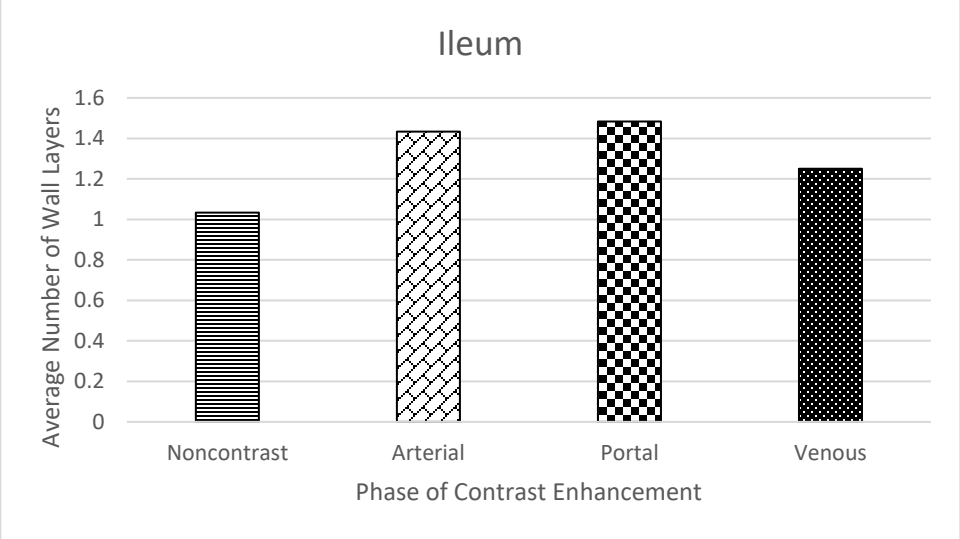

Figure 2.14 Average number of wall layers identified in the ileum in a transverse plane of reconstruction

Note that the greatest number of average wall layers was identified during the portal phase of enhancement followed by the arterial phase of enhancement.

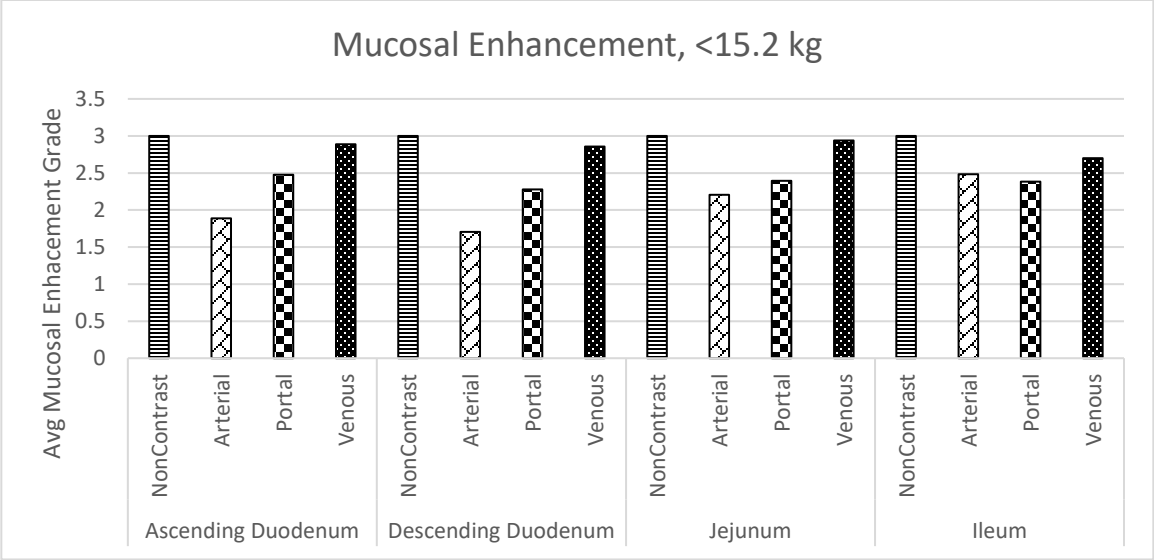

Figure 2.15 Mucosal enhancement in dogs weighing less than 15.5 kilograms

Note that the greatest degree of mucosal enhancement occurred in the arterial and portal phases for all segments. Also note that in the ileum the mucosal enhancement in the portal phase was significantly better than that in the arterial phase of enhancement.

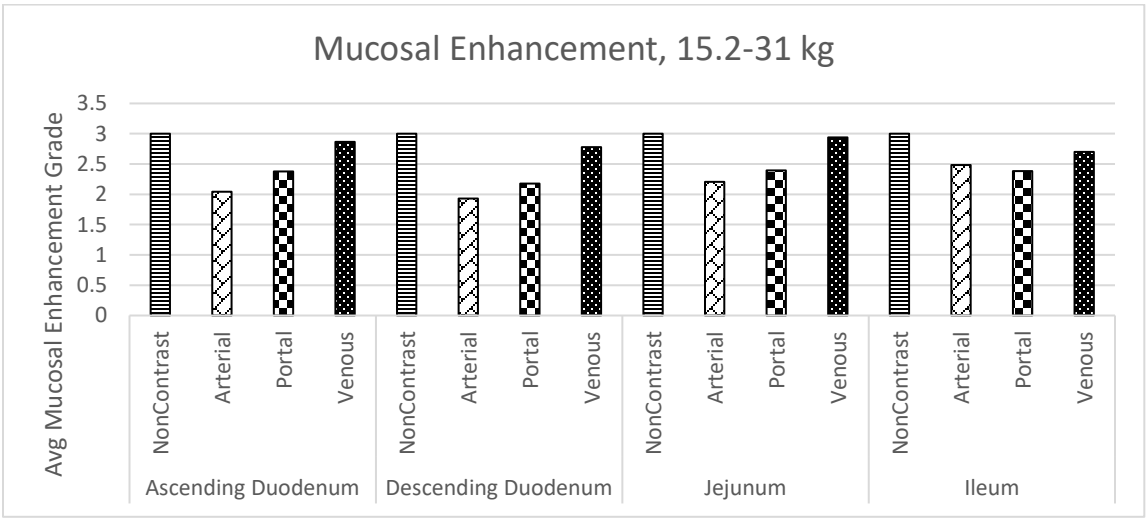

Figure 2.16 Mucosal enhancement grade in dogs weighing between 15.5 kilograms and 31.0 kilograms

Note that the greatest degree of mucosal enhancement occurred in the arterial and portal phases for all segments. Also note that in the ileum the mucosal enhancement in the portal phase was significantly better than that in the arterial phase of enhancement.

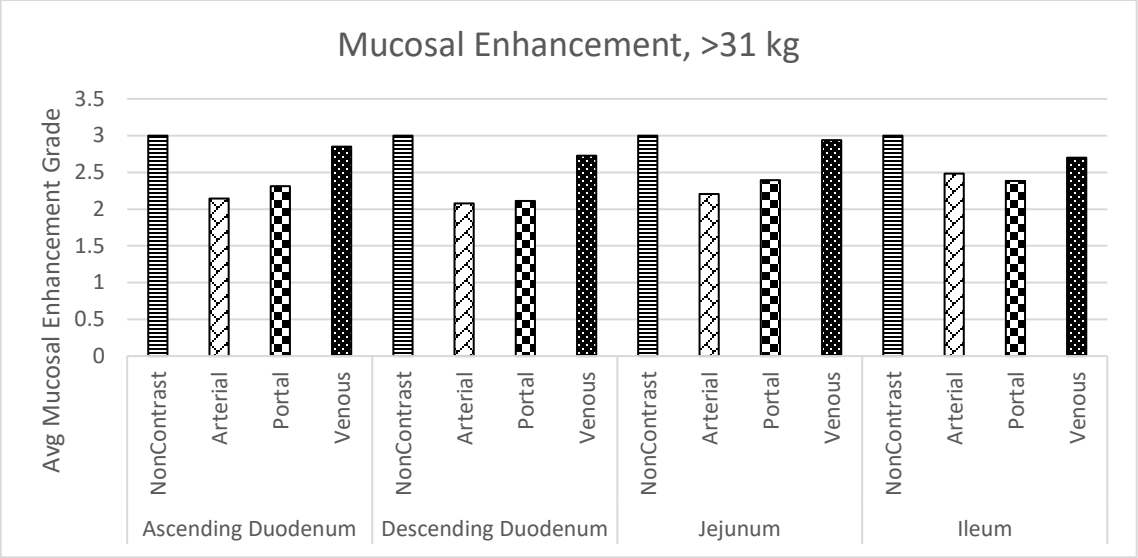

Figure 2.17 Mucosal enhancement grade in dogs weighing greater than 31.0 kilograms

Note the greatest degree of mucosal enhancement occurred in both the arterial and portal phases of enhancement. There was relatively symmetric mucosal enhancement in these two phases in all segments except for the ileum, in which significantly better mucosal enhancement was identified in the portal phase of enhancement than in the arterial phase.

Sagittal plane of reconstruction

Transverse Duodenum

In the transverse duodenum, weight had a significant effect on the maximal diameter, with smaller dogs having a significantly smaller overall diameter (Figure 2.18, **Error! Reference source not found.**). Phase of enhancement did not have a significant effect on either the maximal or minimal diameter or wall thickness.

Phase of enhancement had a significant effect on the average number of wall layers identified within the transverse duodenum with significantly more layers being identified in both the arterial and portal phases (Figure 2.20). In the arterial phase of enhancement there was an

average of 1.8833 wall layers identified and in a portal phase there was an average of 1.5833 wall layers identified.

Phase of enhancement also had a significant effect on the enhancement score of the transverse duodenum with the arterial and portal phases having significantly greater mucosal enhancement than the delayed venous and noncontrast series (Figure 2.15, Figure 2.16, Figure 2.17). No difference was identified between the arterial or portal phases. No significant interactions between weight and minimal diameter, minimal and maximal wall thickness, number of wall layers identified, and mucosal enhancement were identified.

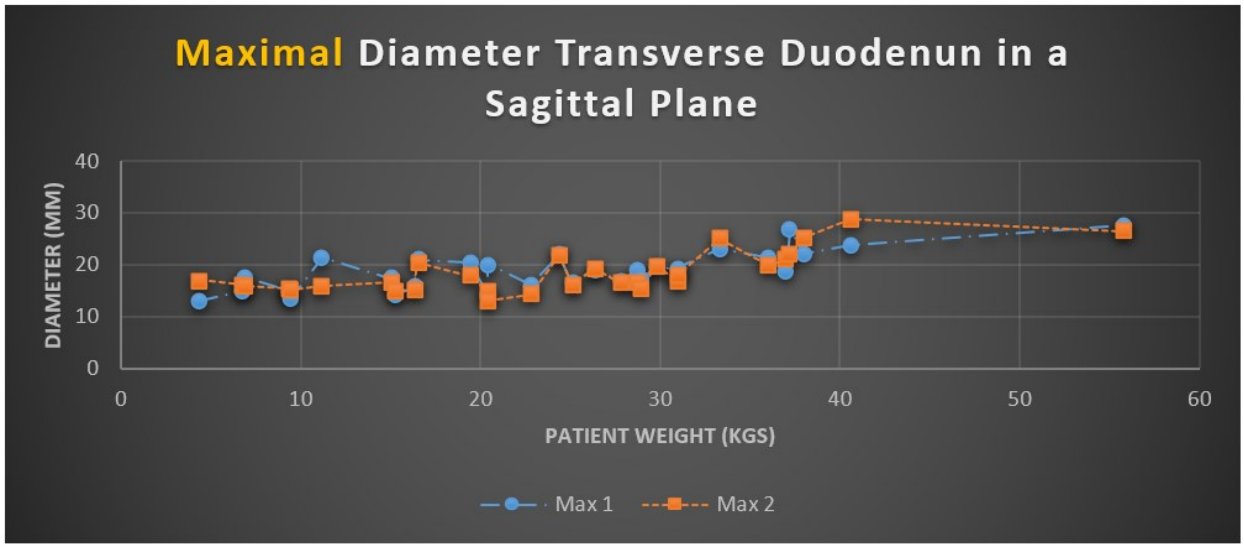

Figure 2.18 Maximal Diameter of the transverse duodenum in a sagittal plane of reconstruction

Graphic demonstration of the positive association between patient body weight and maximal diameter of the transverse duodenum in a sagittal plane of reconstruction. The noncontrast series was utilized for this graph, as the phase of contrast enhancement did not have an effect on the measured diameter.

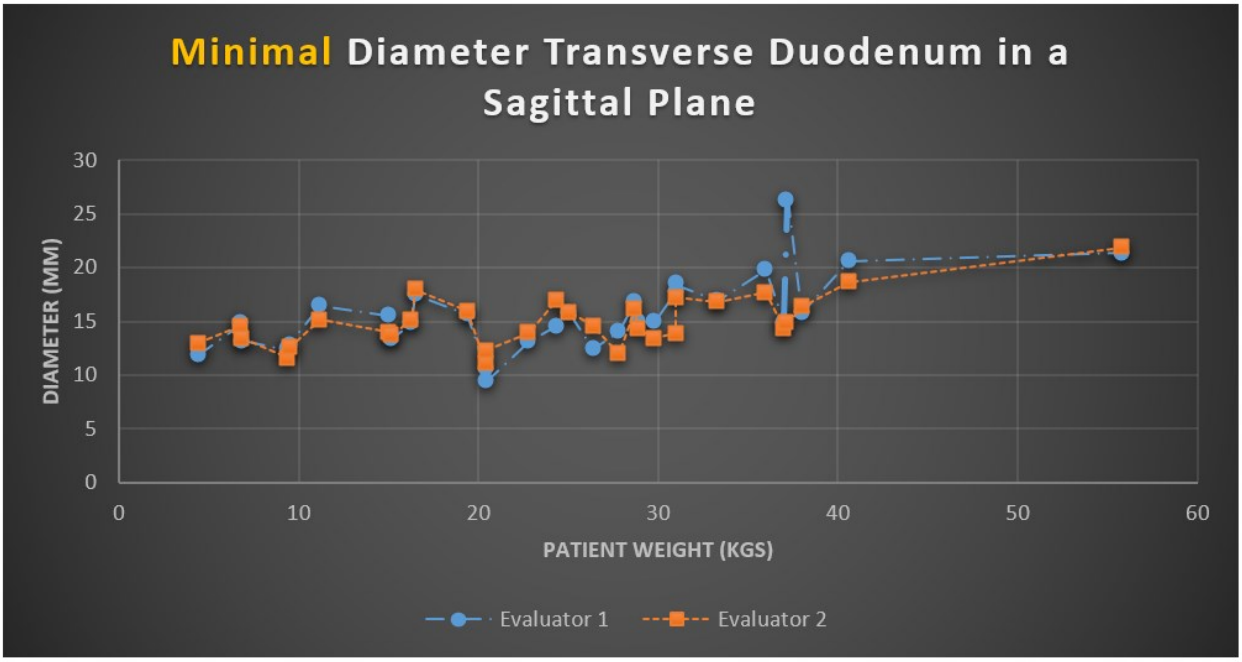

Figure 2.19 Minmal diameter of the transverse duodenum in a sagittal plane of reconstruction

Graphic demonstration of the positive association between patient body weight and minimal diameter of the transverse duodenum in a sagittal plane of reconstruction. The noncontrast series was utilized for this graph, as the phase of contrast enhancement did not have an effect on the measured diameter.

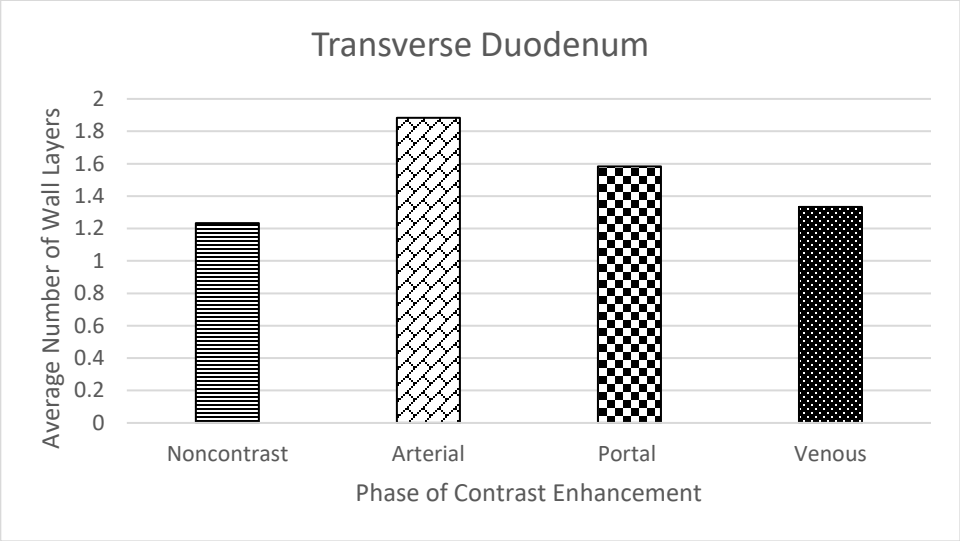

Figure 2.20 Average number of wall layers identified in the transverse duodenum in a sagittal plane of reconstruction

Note that the greatest average number of wall layers identified occurred in the arterial phase.

Jejunum

In regard to the jejunum, significant interactions were found between weight and the maximal (**Error! Reference source not found.**) and minimal (Figure 2.22) diameter, with smaller dogs having an overall smaller diameter. No significant interactions between weight and number of wall layers identified and degree of mucosal enhancement were identified. A significant interaction between phase of enhancement and the minimal jejunal wall thickness was identified.

A significant effect between phase of enhancement and average number of wall layers was also identified with the arterial and portal phases having significantly more wall layers identified, 1.600 and 1.5556 respectively (Figure 2.23).

Significant interactions between both weight and phase of enhancement and degree of mucosal enhancement were also found (Figure 2.15, Figure 2.16, Figure 2.17). In all weight groups (dogs less than 15.20 kilograms, between 15.21 kilograms and 31.00 kilograms, and those over 31 kilograms, the arterial and portal phases had the greatest degree of enhancement. No difference was identified between these two phases or between the delayed venous phase and the noncontrast series. In dogs over 31 kilograms, better mucosal enhancement was identified in the portal phase than in the arterial phase; however, this was not significant.

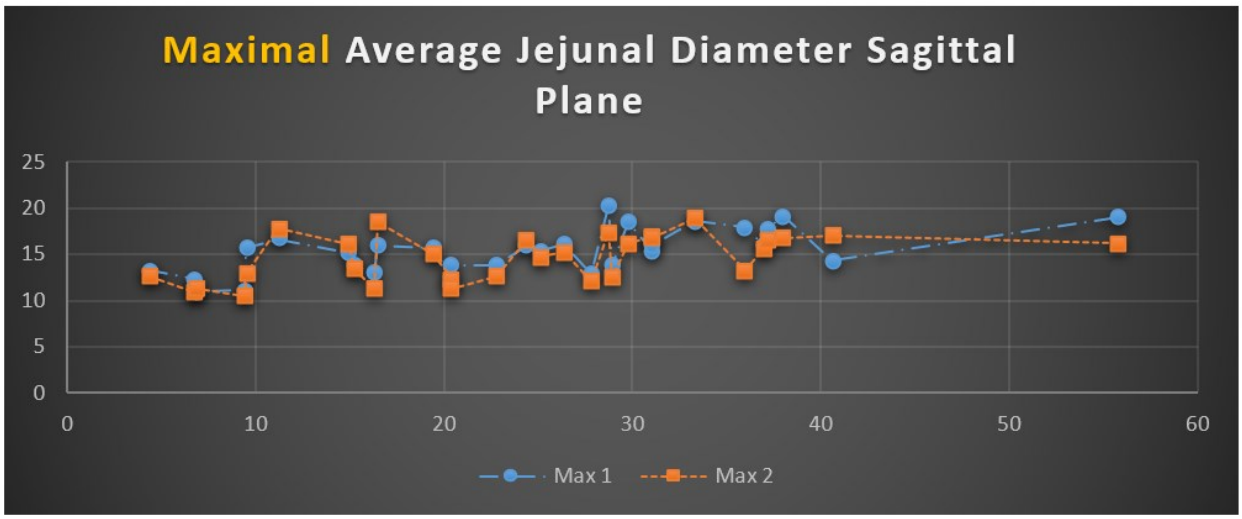

Figure 2.21 Average maximal overall jejunal diameter in a sagittal plane of reconstruction

Graphic demonstration of the positive association between patient body weight and maximal diameter of the jejunum in a sagittal plane of reconstruction. The noncontrast series was utilized for this graph as phase of enhancement did not have a significant effect on maximal diameter.

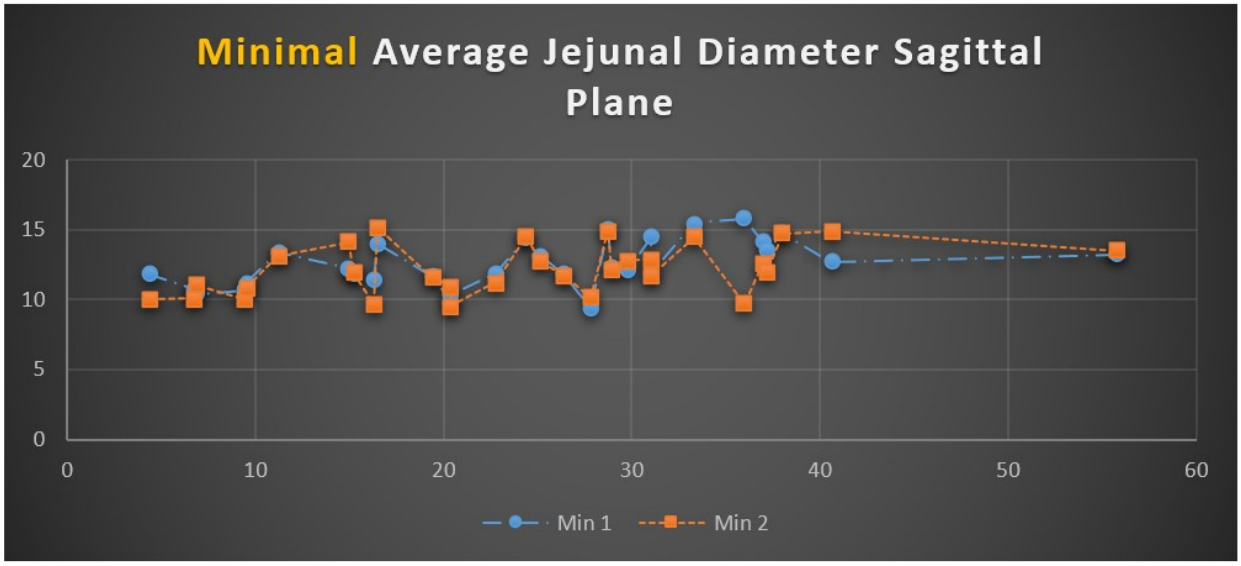

Figure 2.22 Figure 2.21 diameter in a sagittal plane of reconstruction

Graphic demonstration of the positive association between patient body weight and maximal diameter of the jejunum in a sagittal plane of reconstruction. The noncontrast series was utilized for this graph as phase of enhancement did have a significant effect on minimal diameter.

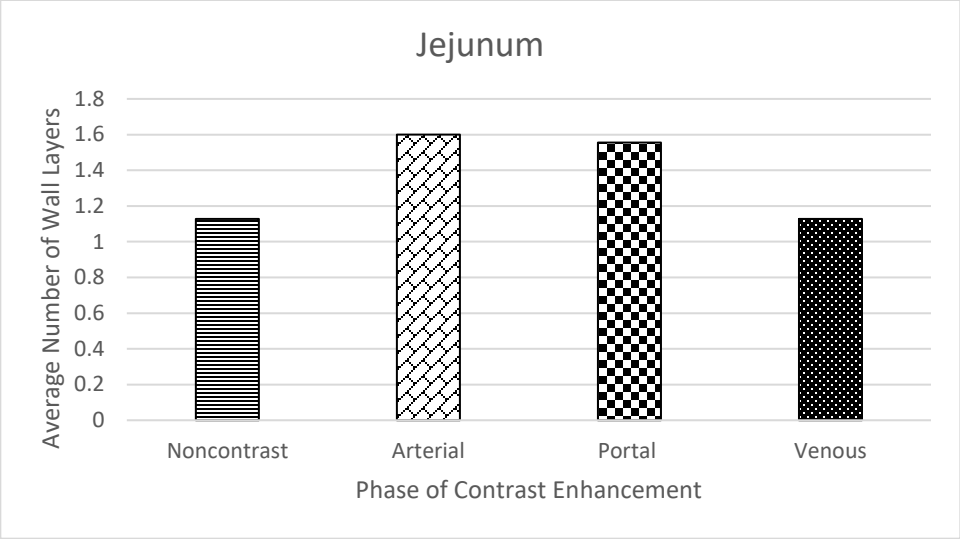

Figure 2.23 Average number of wall layers (averaged) identified in the jejunum in a sagittal plane of reconstruction

Note the greatest average number of wall layers was slightly higher in the arterial phase than in the portal phase of contrast enhancement. However, these two phases of contrast enhancement were similar.

Dorsal plane of reconstruction

Jejunum

Patient weight had a significant effect on the maximal diameter of the jejunum, with smaller dogs have an overall smaller diameter (Figure 2.24). An interaction between weight and minimal diameter was not identified in the jejunum. Patient weight nor phase of enhancement had an effect on the maximal and minimal jejunal wall thickness.

A significant interaction between phase of enhancement and average number of wall layers within the jejunum was identified, with more layers being identified in the arterial and portal phases than in the delayed venous and noncontrast phases (Figure 2.25). The most layers were identified within the portal phase (1.5944) followed by the arterial phase (1.5722).

Significant interactions were identified between both weight and phase and degree of jejunal mucosal contrast enhancement (Figure 2.15, Figure 2.16, Figure 2.17). For dogs 15.20 kilograms and less, the arterial phase had the greatest degree of mucosal enhancement. For dogs greater than 15.20 kilograms, the portal phase had the greatest degree of mucosal enhancement. For all weight groups, the arterial and portal phases had greater degrees of mucosal enhancement with no significant difference between these two groups. A significant difference was also not identified between the delayed venous and noncontrast series in regard to degree of mucosal enhancement.

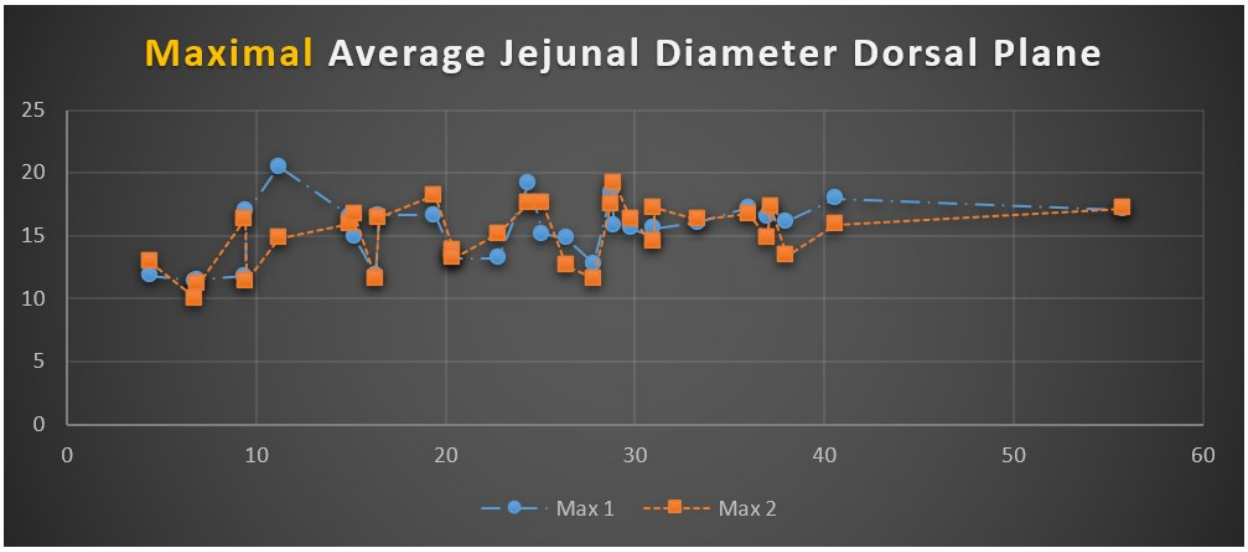

Figure 2.24 Maximal overall average jejunal diameter in a dorsal plane of reconstruction

Graphic demonstration of the positive association between patient body weight and maximal diameter of the jejunum in a dorsal plane of reconstruction. The noncontrast series was utilized for this graph as phase of enhancement did not have a significant effect on maximal diameter.

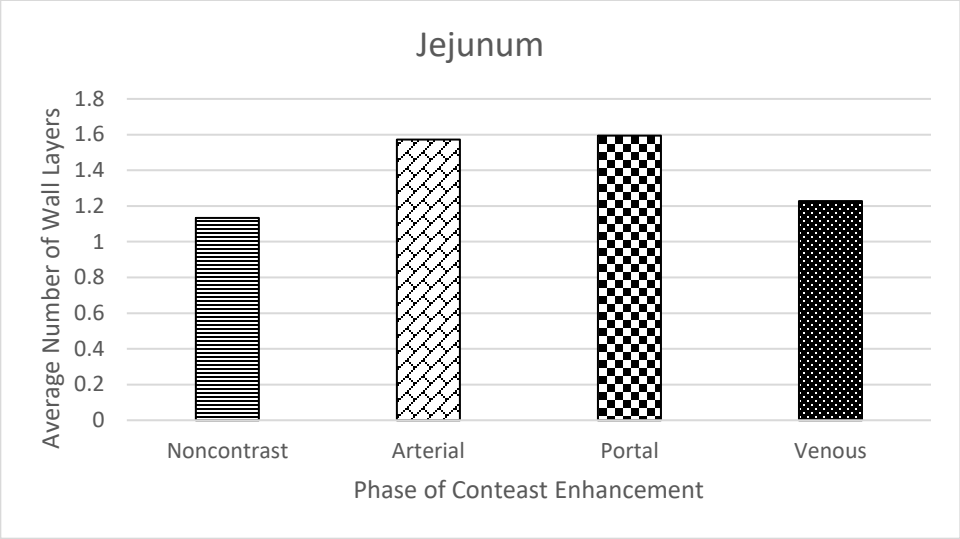

Figure 2.25 Average number of wall layers identified in the jejunum in a dorsal plane of reconstruction

The greatest average number of wall layers occurred within the arterial and portal phases of enhancement. Note that these two phases of enhancement demonstrated a similar number of wall layers identified.

In a dorsal plane of reconstruction, measurements were not obtained from the duodenum (any portion) or ileum, as these segments of the small intestine had their long axes oriented with the plane of reconstruction.

Subjective evaluation

In the author's opinion, the transverse plane was the most useful plane to identify each segment of small intestine measured. This is due to the perpendicular orientation of the majority of gastrointestinal tract to this plane of reconstruction. This orientation demonstrated the greatest number of small intestinal segments in cross section. Additional patient comorbidities that made it difficult to measure the small intestine were peritoneal effusion, which occurred in 2 dogs, and a thin body condition, which occurred in one dog. Increasing patient weight made identifying

and measuring each segment of small intestine subjectively easier. The presence of ingesta made measuring the overall diameter easier on all phases and the wall thickness easier on the postcontrast phases (arterial, portal, and venous). However, the presence of ingesta made it more difficult to measure wall thickness on the noncontrast series. The position of the patient during scanning (dorsal or ventral recumbency) did not subjectively have an effect on the ability to measure either the wall thickness or overall diameter of the small intestinal tract.

CHAPTER III

DISCUSSION

Discussion

The author was able to accept the first hypothesis in that the arterial phase in the majority of the small bowel segments demonstrated the greatest mucosal enhancement. In dogs less than 31.00 kilograms and in a transverse plane of reconstruction, the arterial phase demonstrated a significantly greater degree of enhancement in the ascending duodenum than the portal phase. In the remaining portions of the small bowel segments and for all weight groups the degree of enhancement in the arterial phase was not significantly greater than the degree of enhancement in the portal phase. However, for all weight classes in the ileum in a transverse plane of reconstruction, for the jejunum in a sagittal plane of reconstruction in dogs greater than 15.20 kilograms, and for the jejunum in a dorsal plane of reconstruction for dogs greater than 15.20 kilograms, the portal phase demonstrated the greatest degree of mucosal enhancement followed closely by the arterial phase, although the differences between these two phases were again not significant.

The degree of mucosal enhancement seen within the arterial phase is likely due to the vascular supply to the different layers of the canine small bowel. A prior study[91] by Delaney and colleagues showed that the canine small intestine receives approximately 6.48% of the cardiac output. The blood flow within the duodenum has been shown to be approximately 0.70 mL/min-

g of tissue while the remaining small intestinal tract has been shown to have a flow 0.72 mL/min-g of tissue.

The blood supply within the intestines is quite complex and is composed of two different parallel capillary beds: the mucous-submucous and muscular-serous plexi.[37,92] The arterial supply enters the mesenteric border through the serosal layer and arborizes in several splanchnic branches before entering the muscularis layering and forming a vast plexus within the submucosa. Two groups of arteries then exit the submucosa with one group giving off branches that surrounds the glands lining the crypt cells and the other continuing to course to the villi within the mucosa.[93] A larger portion of resting blood flow within the canine intestinal tract ends up within the mucosal and submucosal layers. In fact, 5-33% of blood flow within these two layers ends up within the submucosa, while 24-37% ends up in the mucosal villi and 21-27% end up in the intestinal crypts.[93] In the dog, approximately 65-92% of the blood flow to the small intestines ends up within the mucosa-submucosa plexus, while 8-35% ends up within the muscularis-serosa plexus. This distribution is similar to a feline model in which 62-85% was distributed to the mucosa-submucosa plexus, and 15-38% distributed to the muscularis-serosa plexus.[93–95]

The timing of the scan delays also likely played a role in this finding. A prior study[25] has described the arterial phase of enhancement occurring 5-10 seconds after initiation of injection and a portal phase of enhancement occurring 25-40 seconds after initiation of injection. Our arterial phase was defined as 25 seconds after initiation of injection and our portal phase was defined as 45 seconds after initiation of injection. These time points were selected due to technical parameters dealing with tube heat loading and cooling, scan parameter adjustments, and the fact that our patients were primarily undergoing computed tomography for a body region

not associated with the abdomen. The arterial phase of enhancement for the body region associated with the primary cause of scanning was preferentially acquired approximately 10 seconds after initiation of injection. After this acquisition was obtained, the CT scan parameters were reset and the abdomen was acquired in three sequential scans. This lack of a true arterial phase and instead acquisition during the early and late phases of the portal period of enhancement likely affected our results.

In addition, a prior study[48] performed in dogs found that the greatest degree of mucosal enhancement was observed approximately 38 seconds after initiation of contrast injection. In this study, a new phase of contrast enhancement of the canine small bowel was described and termed the intestinal phase. This phase is defined as the peak enhancement of the intestinal wall and occurred at 38.0 ± 4.2 s after initiation of injection. During this phase there was distinct enhancement of the intestinal wall, as well as, a distinguishable mucosal layer. This study however, did not find a difference between the enhancement of the intestinal wall in this phase compared to an early venous phase (55.3 ± 3.5 s after initiation of injection).[48] This study also did not attempt to evaluate the small intestines during a true arterial phase. The timing of this intestinal phase falls within the portal period of enhancement as previously described[25], so it is the author's opinion that this new term of enhancement is a simple misnomer for the previously described portal period. However, similar to our study, the study[48] by Lee and colleagues found that during the intestinal phase (portal period), the innermost layer of the intestinal wall was enhanced more than the remaining wall and the wall became more homogeneously enhanced on the venous phase. In fact, in this prior study, 22 out of 33 intestinal segments had distinct contrast enhancement in the innermost layer, which the authors described as the mucosa and submucosa.

A reason for the mucosal enhancement being greater in the portal phase in the ileum is not clear. However, it likely corresponds to the vascular supply to the ileum as well as the thickness of the mucosal layer in this segment. The ileum is the terminal segment of the intestinal tract and derives its blood supply from the terminal branches of the cranial mesenteric artery. The jejunum is also histologically composed of much denser tissue and contains a greater proportion of mucosal tissue than the ileum.[96] This study demonstrated that the jejunum is made up of approximately 82% mucosa, while the ileum only contains approximately 76% mucosa. There are also differences in the mucosal villi within these two segments with the jejunal mucosal villi having longer and wider villi, deeper crypts, and taller enterocytes than the ileal mucosal villi.[96] The jejunal villi are also more tightly packed than the ileal villi, which may have contributed to the increased conspicuity of the jejunal wall layer on the arterial phase.[97] The decrease in mucosal tissue and its associated vascular networks within the ileum likely resulted in a decrease in the identifiable contrast enhancement within this layer on the arterial phase. The ileum also has a thicker muscularis layer, which may be the layer identified on the portal phase of enhancement.[34] However, this finding needs to be verified with histopathology of full thickness biopsies.

An interesting finding in this current study is the thin, strongly contrast enhancing rim within the arterial phase in multiple segments of the small bowel. The grading system employed in this study was adapted from a prior study by Fitzgerald et al.[47] In that study, a thin rim of contrast enhancement within the inner most layer of the gastrointestinal tract was determined to be grade 1 mucosal enhancement and was thought to represent enhancement of only the mucosal layer. However, a prior study[40] using ultrasonography identified that the mucosal layer within the duodenum and jejunum is significantly thicker than the remaining layers, typically in the range

of being as thick as the remaining layers combined. The mucosal layer within the duodenum and jejunum in that set of dogs contributed to 63-64% and 57-60% of the overall wall thickness in those segments, respectively. Weight also had a significant effect on mucosal thickness, with smaller dogs having a thinner mucosal layer in both the duodenum and jejunum as compared to larger dogs. A significant difference between the remaining three layers was not identified.[40] A more recent ex vivo ultrasonographic study[19] also identified a dual echogenicity within the mucosal layer of the small intestines in normal dogs. The authors in this study[19] attributed this inner most hyperechoic layer to lacteal dilation within the tip of the intestinal villi. Given these studies, the inclusion of only clinically normal dogs in the present study, and the rich vascular network within the intestinal villi, the author proposes that this thin rim of enhancement during the arterial phase in the current study may in fact represent enhancement within the intestinal villi specifically as opposed to enhancement of the entire mucosal layer. In order to confirm this, full thickness biopsies followed by histopathology would be needed. This was not performed in the current study due to ethical constraints. If this thin contrast enhancing layer does represent the mucosal villi, then future work could be performed to determine if this layer becomes thickened or enlarged in dogs with lymphangiectasia.

The author was able to accept the second hypothesis in that body weight was positively correlated with small intestinal diameter. In the transverse plane of reconstruction, patient weight was positively correlated with both the maximal and minimal diameter of each segment of the small bowel. In a dorsal and sagittal plane of reconstruction, only the maximal small intestinal diameter was affected by patient body weight, with smaller dogs have significantly smaller overall diameters. The significance of this finding is hard to interpret, as no attempt was made to ensure that dogs had been fasted or feed the same amount of food prior to imaging. This

limitation may alter the significance of this finding as dogs that had been fed shortly prior to imaging would likely have had an overall greater diameter than those that had been fasted or not been fed recently. The clinical significance of this finding is also difficult to interpret. A prior study[28] has shown that computed tomography is 100% sensitive and specific for the diagnosis of a small intestinal mechanical obstruction, while ultrasound had a sensitivity of 100% and specificity of 67%. In this study a ratio of the largest intestinal diameter to smallest intestinal diameter of greater than 4.0 was consistent with a mechanical obstruction.[28] In other studies using abdominal radiography, multiple ratios have been proposed to identify cases with mechanical obstruction. Some of these ratios use the central height of the L5 vertebral body and range from 1.6 to 2.4, while others found a ratio of the maximal small intestinal diameter to minimal small intestinal diameter ≥3.4 and a ratio of the maximal small intestinal diameter to the average small intestinal diameter ≥1.9 were likely obstructed.[28,98–100] Ultrasonographically, a jejunal diameter >1.5 cm has been associated with small intestinal obstruction.[98] Given that ratios of the largest and smallest diameter were not performed in this study, the positive correlation between body weight and small intestinal diameter should be interpreted cautiously.

The hypothesis that intestinal wall thickness would be correlated to body weight was rejected for all segments of small bowel in all planes of reconstruction and all phases of contrast enhancement. This is in contrast to a prior ultrasonographic study[41], which demonstrated a positive correlation between body weight and duodenal and jejunal wall thickness. In that study both the duodenal and jejunal wall thicknesses was significantly greater in large dogs than in small dogs with the jejunum in small dogs being ≤4.4 mm and in large dogs ≤4.7 mm, while the duodenum in small dogs was ≤5.1 mm and in larger dogs it was ≤6.0 mm. A separate study[40] also showed that the thickness of the mucosal layer was also positively correlated with body

weight. In that study, small dogs had a mean jejunal mucosal thickens of 1.8 ± 0.4 mm, while large dogs had a thickness of 2.2 ± 0.5 mm. The duodenal mucosal thickness in this study for small dogs was 2.4 ± 0.5 mm, while in large dogs it was 2.8 ± 0.5 mm. It is not clear why a similar result was not found in this study. One possibility is that an insufficient number of dogs were sampled. Another possibility is the limitation of decreased spatial resolution using computed tomography compared to that of ultrasound.

The author was also able to accept the fourth hypothesis. The addition of arterial and portal phases resulted in significantly more wall layers being identified in these two phases than in the noncontrast and venous phases. This hypothesis held true for all segments of small bowel in all planes of reconstruction. The reason for this is also unclear. Prior studies[42,101] have been performed in both feline and canine patients using contrast enhanced ultrasonography that have identified the normal vascular pattern within the normal intestinal wall in both of these species. The vascular pattern within the canine intestinal wall has been described as a typical serosal to luminal enhancement direction, with radial enhancement of the jejunal wall also identified. No difference between the ingress and egress time between the mesenteric and antimesenteric sides of the small bowel was identified in this canine model.[42] In cats, the typical pattern of enhancement using contrast ultrasonography has been described as an initial rapid enhancement of the serosal and submucosal layers, which was followed by gradual enhancement of the entire wall. The washout phase was gradual, and the submucosal layer was the last to washout. During peak enhancement, the authors within this paper could identify the different wall layering.[101] One cause for the discrepancy between what was identified on contrast enhance ultrasound and this study is the improved spatial resolution of ultrasound compared to computed tomography. Given that ultrasound has increased spatial resolution as compared to CT, the smaller vessels within the

serosal layer are likely easier to identify on ultrasound compared to CT. The larger plexus within the mucosa and submucosa may also be easier to identify on CT, given its better contrast resolution as compared to ultrasound.

Lastly, the authors subjectively identified the transverse plane of reconstruction as the most useful plane of reconstruction for quantification of the canine small bowel. This is due to the orientation of the canine small bowel with the three planes of reconstruction: transverse, sagittal, and dorsal. The duodenum, for the most part, runs in a line parallel to the right lateral abdominal body, hindering the evaluation of it in cross-section on either the sagittal or dorsal planes. The ileum also lies in a plane that is parallel to the long axis of the abdominal cavity, which also hinders evaluation of it in cross section on both the sagittal and dorsal planes. The jejunum takes a more serpentine course through the abdominal cavity, which allows portions of it to be evaluated in almost any plane of reconstruction. Two prior studies have reported identification rates of 77% and 84.5% of a segment of the gastrointestinal tract in its transverse plane of reconstruction.[46,47]

Limitations

There were a number of limitations within this study. The first and most significant limitation is the lack of comparison between the obtained CT measurements and the gold standard imaging modality, ultrasound. The reasons for not pursuing this comparison are numerous, with the largest contributors being financial and clinical time constraints. Another major limitation of this study is the lack of histopathologic confirmation of normalcy for dogs included. However, in order to determine normalcy, histopathology of full or partial gastrointestinal biopsies would be required, and this procedure is neither benign nor ethical in clinically unaffected patients. This absence of histopathology may have allowed for the inclusion

of dogs with subclinical gastrointestinal disease. However, attempts were made to ensure that included patients had no abnormalities that could affect the gastrointestinal tract, including serum chemistry, clinical history, and a thorough physical exam.

Another limitation is that a standardized sedation protocol was not utilized. This was done to mimic a clinical setting and to make the obtained data more clinically applicable. Different sedatives affect the appearance and function of the small intestine differently. Specifically, administration of α-2 and opiate agonists have been shown to cause gastrointestinal stasis by increasing gastrointestinal sphincter tones and intestinal segmental tone, thereby causing functional ileus, which may lead to a falsely increased small intestinal diameter.[102] Additionally, patient parameters that may affect contrast distribution, such as cardiac output, systemic vascular resistance, and respiratory rate were not consistently monitored during the examinations.[103–105] The requirement for monitoring sedated patient parameters at the authors' institution is to record heart and respiratory rates every 5 minutes under sedation. Given that the majority of these computed tomographic examinations took between 5-10 minutes only a single monitoring event took place. The variability in sedative drug choice and dosing is also a confounding factor that likely contributed to the variability in patient parameters that affect contrast distribution.

Lastly, patient positioning (i.e., all in either sternal or dorsal recumbency) was not consistent. This was due to the inclusion of the abdomen as an additional site and not the patient's primary reason for imaging. The positioning of all patients was dictated by the optimal positioning for investigation of the anatomy related to the clinical problem. Respiratory induced motion has been shown to have a significant effect on evaluation of abdominal viscera in both sternal and dorsal recumbency.[106] This motion has also been shown to have differing effects on

the CT evaluation of abdominal viscera with less respiratory motion found within the liver and urinary bladder in sternal recumbency than in dorsal. In the remaining abdominal organs, dorsal recumbency was the optimal patient positioning.[106]

Future Studies

Future studies should be performed to compare measurements obtained on computed tomography and the gold standard of ultrasound, to determine if these two modalities show a degree of correlation. Additionally, the correlation between the identification and measurements of individual small bowel layers in dogs and histopathology of full thickness small bowel biopsies should be investigated. Given that all of the included dogs within this study were normal, future studies should also be performed in a subset of dogs effected with disease processes that have been shown to alter the small bowel wall thickness, such as inflammatory bowel disease, lymphangiectasia, neoplastic etiologies, and/or infectious etiologies.

Synopsis

This study identified that the addition of arterial and portal phases of contrast enhancement during computed tomography aided in the identification and evaluation of the wall layering, diameter, and thickness of the normal canine small bowel. Specifically, these two phases demonstrated the greatest degree of mucosal enhancement as well as the greatest number of wall layers identified. In addition, the overall small bowel diameter is positively correlated with patient weight, but small bowel wall thickness was not affected by patient weight. In this study, the transverse plane of reconstruction was the most useful plane when quantifying the thickness and overall diameter of the canine small bowel. The author recommends the inclusion

of both an arterial and portal phase when utilizing computed tomography angiography to evaluate the canine small bowel.

REFERENCES

1. Robinson NJ, Dean RS, Cobb M, Brennan ML. Investigating common clinical presentations in first opinion small animal consultations using direct observation. *Vet Rec*. 2015;176(18):463.

2. Dandrieux JRS, Mansfield CS. Chronic Enteropathy In Canines: Prevalence, Impact, And Management Strategies. *Vet Med Res Reports*. 2019;Volume 10:203-214.

3. Wiles BM, Llewellyn-Zaidi AM, Evans KM, O'Neill DG, Lewis TW. Large-scale survey to estimate the prevalence of disorders for 192 Kennel Club registered breeds. *Canine Genet Epidemiol*. 2017;4(1):1-18.

4. O'Neill DG, Church DB, McGreevy PD, Thomson PC, Brodbelt DC. Prevalence of disorders recorded in dogs attending primary-care veterinary practices in England. *PLoS One*. 2014;9(3).

5. Marchesi MC, Timpano CC, Busechian S, Pieramati C, Rueca F. Il ruolo della dieta nella gestione di cani affetti da malattie infiammatorie croniche intestinali: Studio retrospettivo su 76 casi. *Vet Ital*. 2017;53(4):297-302.

6. Kathrani A, Werling D, Allenspach K. Canine breeds at high risk of developing inflammatory bowel disease in the South-Eastern UK. *Vet Rec*. 2011;169(24):635.

7. Hall EJ, Day MJ. *Textbook of Veterinary Internal Medicine: Disease of the Dog and Cat*. 8th ed. (Ettinger SJ, Feldman E., Côté E, eds.). St. Louis: Elsevier; 2017.

8. Simpson KW, Jergens AE. Pitfalls and Progress in the Diagnosis and Management of Canine Inflammatory Bowel Disease. *Vet Clin North Am - Small Anim Pract*. 2011;41(2):381-398.

9. Jergens AE, Simpson KW. Inflammatory Bowel Disease in Veterinary Medicine. *Front Biosci (Elite Ed)*. 2012;4:1404-14149.

10. Thrall DE. *Textbook of Veterinary Diagnostic Radiology*. 6th ed. St. Louis: Elsevier Saunders; 2013.

11. Penninck D, D'Anjou MA. *Atlas of Small Animal Ultrasonography*. 1st ed. Ames: Blackwell Publishing; 2008.

12. Mattoon JS, Nyland TG. *Small Animal Diagnostic Ultrasound*. 3rd ed. St. Louis: Elsevier Saunders; 2015.

13. Pollard RE, Johnson EG, Pesavento PA, et al. Effects of corn oil administered orally on conspicuity of ultrasonographic small intestinal lesions in dogs with lymphangiectasia. *Vet Radiol Ultrasound*. 2013;54(4):390-397.

14. Sutherland-Smith J, Penninck DG, Keating JH, Webster CRL. Ultrasonographic intestinal hyperechoic mucosal striations in dogs are associated with lacteal dilation. *Vet Radiol Ultrasound*. 2007;48(1):51-57.

15. Malancus RN, Malancus CMT. Assessment of ultrasonographic and endoscopic changes in dogs with gastrointestinale disorders. *Arq Bras Med Vet e Zootec*. 2017;69(6):1451-1455.

16. Kull PA, Hess RS, Craig LE, Saunders HM, Washabau RJ. Lymphangiectasia in Dogs : 17 Cases (1996 – 1998). *J Am Vet Med Assoc*. 2001;219(2):197-202.

17. Gaschen L, Kircher P, Stüssi A, et al. Comparison of ultrasonographic findings with clinical activity index (CIBDAI) and diagnosis in dogs with chronic enteropathies. *Vet Radiol Ultrasound*. 2008;49(1):56-64.

18. Rudorf H, Van Schaik G, O'Brien RT, Brown PJ, Barr FJ, Hall EJ. Ultrasonographic evaluation of the thickness of the small intestinal wall in dogs with inflammatory bowel disease. *J Small Anim Pract*. 2005;46(7):322-326.

19. Le Roux AB, Granger LA, Wakamatsu N, Kearney MT, Gaschen L. Ex Vivo Correlation of Ultrasonographic Small Intestinal Wall Layering With Histology in Dogs. *Vet Radiol Ultrasound*. 2016;57(5):534-545.

20. Leib MS, Larson MM, Panciera DL, et al. Diagnostic Utility of Abdominal Ultrasonography in Dogs with Chronic Vomiting. *J Vet Intern Med*. 2010;24:803-808.

21. Leib MS, Larson MM, Grant DC, et al. Diagnostic Utility of Abdominal Ultrasonography in Dogs with Chronic Diarrhea. *J Vet Intern Med*. 2012;26(6):1288-1294.

22. Barberet V, Schreurs E, Rademacher N, et al. Quantification of the effect of various patient and image factors on ultrasonographic detection of select canine abdominal organs. *Vet Radiol Ultrasound*. 2008;49(3):273-276.

23. Garcia DAA, Froes TR. Importance of fasting in preparing dogs for abdominal ultrasound examination of specific organs. *J Small Anim Pract*. 2014;55(12):630-634.

24. Ponti F De, Giaroni C, Cosentino M, Lecchini S. Adrenergic Mechanisms in the Control of Gastrointestinal Motility : From Basic Science to Clinical Applications the sympathetic. *Science (80-)*. 1996;69(1):59-78.

25. Zwingenberger A. CT Diagnosis of Portosystemic Shunts. *Vet Clin North Am - Small Anim Pract*. 2009;39(4):783-792.

26. Nelson NC, Nelson LL. Anatomy of extrahepatic portosystemic shunts in dogs as determined by computed tomography angiography. *Vet Radiol Ultrasound*. 2011;52(5):498-506.

27. Fukushima K, Fujiwara R, Yamamoto K, et al. Characterization of triple-phase computed tomography in dogs with pancreatic insulinoma. *J Vet Med Sci*. 2015;77(12):1549-1553.

28. Winter MD, Barry KS, Johnson MD, Berry CR, Case JB. Ultrasonographic and computed tomographic characterization and localization of suspected mechanical gastrointestinal obstruction in dogs. *J Am Vet Med Assoc*. 2017;251(3):315-321.

29. Fields EL, Robertson ID, Brown JC. Optimization of contrast-enhanced multidetector abdominal computed tomography in sedated canine patients. *Vet Radiol Ultrasound*. 2012;53(5):507-512.

30. Fields EL, Robertson ID, Osborne JA, Brown JC. Comparison of abdominal computed tomography and abdominal ultrasound in sedated dogs. *Vet Radiol Ultrasound*. 2012;53(5):513-517.

31. Hammer MR, Podberesky DJ, Dillman JR. Multidetector computed tomographic and magnetic resonance enterography in children. State of the art. *Radiol Clin North Am*. 2013;51(4):615-636.

32. Fitzgerald E, Barfield D, Lee KCL, Lamb CR. Clinical findings and results of diagnostic imaging in 82 dogs with gastrointestinal ulceration. *J Small Anim Pract*. 2017;58(4):211-218.

33. Specchi S, Auriemma E, Morabito S, et al. Evaluation of the Computed Tomographic "Sentinel Clot Sign" To Identify Bleeding Abdominal Organs in Dogs With Hemoabdomen. *Vet Radiol Ultrasound*. 2017;58(1):18-22.

34. Evans HE, de Lahunta A. *Miller's Anatomy of the Dog*. 4th ed. St. Louis: Elsevier Saunders; 2013.

35. Penninck DG, Nyland TG, Fisher PE, Kerr LY. Ultrasonography of the Normal Canine Gastrointestinal Tract. *Vet Radiol*. 1989;30(6):272-276.

36. Culp WTN, Mayhew PD, Pascoe PJ, Zwingenberger A. Angiographic Anatomy of the Major Abdominal Arterial Blood Supply in the Dog. *Vet Radiol Ultrasound*. 2015;56(5):474-485.

37. Piasecki C, Wyatt C. Patterns of blood supply to the gastric mucosa. A comparative study revealing an end-artery model. *J Anat*. 1986;Vol. 149:21-39.

38. Noer R. The blood vessels of the jejunum and ileum: a comparative study of man and certain laboratory animals. *Am J Aanatomy*. 1943;(73):293-334.

39. Stander N, Wagner WM, Goddard A, Kirberger RM. Normal canine pediatric gastrointestinal ultrasonography. *Vet Radiol Ultrasound*. 2010;51(1):75-78.

40. Gladwin NE, Penninck DG, Webster CRL. Ultrasonographic evaluation of the thickness of the wall layers in the intestinal tract of dogs. *Am J Vet Res*. 2014;75(4):349-353.

41. Delaney F, O'Brien RT, Waller K. Ultrasound evaluation of small bowel thickness compared to weight in normal dogs. *Vet Radiol Ultrasound*. 2003;44(5):577-580.

42. Jiménez DA, O'Brien RT, Wallace JD, Klocke E. Intraoperative contrast-enhanced ultrasonography of normal canine jejunum. *Vet Radiol Ultrasound*. 2011;52(2):196-200.

43. Johnson-Neitman JL, O'Brien RT, Wallace JD. Quantitative perfusion analysis of the pancreas and duodenum in healthy dogs by use of contrast-enhanced ultrasonography. *Am J Vet Res*. 2012;73(3):385-392.

44. Shanaman MM, Schwarz T, Gal A, O'Brien RT. Comparison between survey radiography, b-mode ultrasonography, contrast-enhanced ultrasonography and contrast-enhanced multi-detector computed tomography findings in dogs with acute abdominal signs. *Vet Radiol Ultrasound*. 2013;54(6):591-604.

45. Nisa K, Lim SY, Shinohara M, et al. Evaluation of duodenal perfusion by contrast-enhanced ultrasonography in dogs with chronic inflammatory enteropathy and intestinal lymphoma. *J Vet Intern Med*. 2019;33(2):559-568.

46. Hoey S, Drees R, Hetzel S. Evaluation of the gastrointestinal tract in dogs using computed tomography. *Vet Radiol Ultrasound*. 2013;54(1):25-30.

47. Fitzgerald E, Lam R, Drees R. Improving Conspicuity of the Canine Gastrointestinal Wall Using Dual Phase Contrast-Enhanced Computed Tomography: a Retrospective Cross-Sectional Study. *Vet Radiol Ultrasound*. 2017;58(2):151-162.

48. Lee SK, Yoon S, Kim C, Choi J. Triple-phased mesenteric CT angiography using a test bolus technique for evaluation of the mesenteric vasculature and small intestinal wall contrast enhancement in dogs. *Vet Radiol Ultrasound*. 2019;(February):493-501.

49. Keh S, Sohn J, Choi M, et al. Evaluation of computed tomographic enterography with an orally administered lactulose solution in clinically normal dogs. *Am J Vet Res*. 2016;77(4):367-373.

50. Park MJ, Lim JS. Computed tomography enterography for evaluation of inflammatory bowel disease. *Clin Endosc*. 2013;46(4):327-336.

51. Liebel-Flarsheim. Optiray 320. *Ioversol Descr use*. 2017;240(March):1-24.

52. Vance A, Nelson M, Hofmeister EH. Adverse reactions following administration of an ionic iodinated contrast media in anesthetized dogs. *J Am Anim Hosp Assoc*. 2012;48(3):172-175.

53. Scarabelli S, Cripps P, Rioja E, Alderson B. Adverse reactions following administration of contrast media for diagnostic imaging in anaesthetized dogs and cats: a retrospective study. *Vet Anaesth Analg*. 2016;43(5):502-510.

54. Pollard RE, Puchalski SM, Pascoe PJ. Hemodynamic and serum biochemical alterations associated with intravenous administration of three types of contrast media in anesthetized dogs. *Am J Vet Res*. 2010;69(10):1268-1273.

55. Pollard RE, Pascoe PJ. Severe reaction to intravenous administration of an ionic iodinated contrast agent in two anesthetized dogs. *J Am Vet Med Assoc*. 2008;233(2):274–278.

56. Casoni D, Amen EM, Brecheisen M, Kuennecke B, Müggler T, Bergadano A. A combination of alfaxalone and medetomidine followed by an alfaxalone continuous rate infusion in cynomolgus monkeys (Macaca fascicularis) undergoing pharmacoMRS. *Vet Anaesth Analg*. 2015;42(5):552-554.

57. Pollard RE, Puchalski SM, Pascoe PJ, Res AJV. Hemodynamic and serum biochemical alterations associated with intravenous administration of three types of contrast media in anesthetized cats. *Am J Vet Res*. 2008;69(10):1274-1278.

58. Goic JB, Koenigshof AM, McGuire LD, Klinger AC, Beal MW. A retrospective evaluation of contrast-induced kidney injury in dogs (2006-2012). *J Vet Emerg Crit Care (San Antonio)*. 2016;26(5):713-719.

59. Rundback JH, Nahl D, Yoo V. Contrast-induced nephropathy. *J Vasc Surg*. 2011;54(2):575-579.

60. Davenport MS, Khalatbari S, Dillman JR, Cohan RH, Caoili EM, Ellis JH. Contrast material-induced nephrotoxicity and intravenous low-osmolality iodinated contrast material. *Radiology*. 2013;267(1):94-105.

61. Trivedi H, Foley WD. Contrast-induced nephropathy after a second contrast exposure. *Ren Fail*. 2010;32(7):796-801.

62. Arayan A, Nigogosyan MA, Van Every MJ. A retrospective review of contrast nephropathy in a general population. *Wis Med J*. 2015;114(3):95-99.

63. Kandzari DE, Rebeiz AG, Wang A, Sketch MH. Contrast Nephropathy: An Evidence-Based Approach to Prevention. *Am J Cardiovasc Drugs*. 2003;3(6):395-405.

64. Morcos S. Contrast Media-induced Nephrotoxicity - questions and answers. *Br J Radiol*. 1998;71:357-265.

65. Sartor RB. Mechanisms of disease: pathogenesis of Crohn's disease and ulcerative colitis. *Nat Clin Pr Gastroenterol Hepatol*. 2006;3(7):390-407.

66. Xavier R, Podolsky D. Unraveling the pathogenesis of inflammatory bowel disease. *Nature*. 2007;(448):427-434.

67. Hall EJ, Day MJ. *Textbook of Veterinary Internal Medicine*. 8th ed. (Ettinger SJ, Feldman EC, Cote E, eds.). St. Louis: Elsevier; 2017.

68. Cassmann E, White R, Atherly T, et al. Alterations of the Ileal and Colonic Mucosal Microbiota in Canine Chronic Enteropathies. *PLoS One*. 2016;11(2):1-18.

69. Littler RM, Batt RM, Lloyd DH. Total and relative deficiency of gut mucosal IgA in German shephard dogs demonstrated by faecal analysis. *Vet Rec*. 2006;11(158):334-341.

70. Kathrani A, House A, Catchpole B, et al. Polymorphisms in the TLR4 and TLR5 gene are significantly associated with inflammatory bowel disease in German shephard dogs. *PLoS One*. 2010;23(5(12)):e1540-e1540.

71. Burgener IA, König A, Allenspach K, et al. Upregulation of toll-like receptors in chronic enteropathies in dogs. *J Vet Intern Med*. 2008;22(3):553-560.

72. McMahon LA, House AK, Catchpole B, et al. Expression of Toll-like receptor 2 in duodenal biopsies from dogs with inflammatory bowel disease is associated with severity of disease. *Vet Immunol Immunopathol*. 2010;135(1-2):158-163.

73. German AJ, Hall EJ, Day MJ. Immune cell populations within the duodenal mucosa of dogs with enteropathies. *J Vet Intern Med*. 2001;15(1):14-25.

74. Stonehewer J, Simpson JW, Else RW, Macintyre N. Evaluation of B and T lymphocytes and plasma cells in colonic mucosa from heatlhy dogs and from dogs with inflammatory bowel disease. *Res Vet Sci*. 1998;65(1):59-63.

75. Jergens AE, Gamet Y, Moore FM, Niyo Y, Tsao C, Smith B. Colonic lymphocyte and plasma cell population in dogs with lymphocytic-plasmacytic colitis. *Am J Vet Res*. 1999;60(4):515-520.

76. Peters IR, Helps CR, Calvert EL, Hall EJ, Day MJ. Cytokine mRNA quantification in duodenal mucosa from dogs with chronic enteropathies by real-time reverse transcriptase polymerase chain reaction. *J Vet Intern Med*. 2005;19(5):644-653.

77. German AJ, Helps CR, Hall EJ, Day MJ. Cytokine mRNA expression in mucosal biopsies from German shephard dogs with small intestinal enteropathies. *Dig Dis Sci*. 2000;45(1):7-17.

78. Janeczko S, Atwater D, Bogel E, et al. The relationship of mucosal bacteria to duodenal histopathology, cytokine mRNA, and clinical disease activity in cats with inflammatory bowel disease. *Vet Microbiol*. 2008;128(1-2):179-193.

79. Jergens AE, Sonea IM, O'Connor AM, et al. Intestinal cytokine mRNA expression in canine inflammatory bowel disease: a meta-analysis with critical appraisal. *Comp Med*. 2009;59(2):153-162.

80. Atreya I, Atreya R, Neurath MF. NF-kappaB in inflammatory bowel disease. *J Intern Med*. 2008;263(6):591-596.

81. Kealy JK, McAllister H. *Diagnostic Radiology and Ultrasonography of the Dog and Cat*. 3rd ed. Philadelphia: Saunders; 2001.

82. Penninck D, Smyers B, Webster CRL, Rand W, Moore AS. Diagnostic value of ultrasonography in differentiating enteritis from intestinal neoplasia in dogs. *Vet Radiol Ultrasound*. 2003;44(5):570-575.

83. Manczur F, Voros K. Gastrointestinal Ultrasound of the dog. *Acta Vet Hung*. 1999;48(1):9-21.

84. Allenspach K, Culverwell C, Chan D. Long-term outcome in dogs with chronic enteropathies: 203 cases. *Vet Rec*. 2016;178(15):368.

85. Mandigers PJ, Biourge V, Van Den Ingh TS. A randomized, open-label positively controlled field trial of a hydrolyzed protein diet in dogs with chronic small bowel etneropathy. *J Vet Intern Med*. 2010;24(6):1350-1357.

86. Jergens AE, Willard MD, Allenspach K. Maximizing the diagnostic utility of endoscopic biopsy in dogs and cats with gastrointestinal disease. *Vet J*. 2016;214:50-60.

87. Pariente B, Peyrin-Biroulet L, Cohen L, Zagdanski AM, Colombel JF. Gastroenterology review and perspective: The role of cross-sectional imaging in evaluating bowel damage in Crohn disease. *Am J Roentgenol*. 2011;197(1):42-49.

88. Van Assche G, Dignass A, Panes J, et al. The second European evidence-based consensus on the diagnosis and management of Crohn's disease: Definitions and diagnosis. *J Crohn's Colitis*. 2010;4(1):7-27.

89. Maccioni F, Viscido A, Broglia L, et al. Evaluation of Crohn disease activity with magnetic resonance imaging. *Abdom Imaging*. 2000;25(3):219-228.

90. Gale HI, Sharatz SM, Taphey M, Bradley WF, Nimkin K, Gee MS. Comparison of CT enterography and MR enterography imaging features of active Crohn disease in children and adolescents. *Pediatr Radiol*. 2017;47(10):1321-1328.

91. Delaney J, Grim E. Relative blood flow to the gastric lesser curvature of the dog. *Dig Dis Sci*. 1965;10:201-204.

92. Lundgren O. Patterns of blood supply to the gastric mucosa: a comparative study revealing an end-artery model. *Acta Physiol*. 1967;72(s303):1-42.

93. Granger DN, Richardson PDI, Kvietys PR, Mortillaro NA. Intestinal blood flow. *Gastroenterology*. 1980;78(4):837-863.

94. Lundgren O. The circulation of the small bowel mucosa. *Gut*. 1974;15(12):1005-1013.

95. Washabau RJ. *Canine & Feline Gastroenterology*. 1st ed. (Washabau RJ, Day MiJ, eds.). Saunders; 2013.

96. Robinson JWL, Menge H, Sepulveda F V., Mirkovitch V, Robinson JWL. Functional and structural characteristics of the jejunum and ileum in the dog and the rat. *Digestion*. 1977;15(3):188-199.

97. Bleiberg H, Mainguet P, Galand P. Cell renewal in familial polyposis: comparison between polyps and adjacent healthy mucosa. *Gastroenterology*. 1972;(63):240-245.

98. Sharma A, Thompson MS, Scrivani P V., et al. Comparison of radiography and ultrasonography for diagnosing small-intestinal mechanical obstruction in vomiting dogs. *Vet Radiol Ultrasound*. 2011;52(3):248-255.

99. Finck C, D'Anjou MA, Alexander K, Specchi S, Beauchamp G. Radiographic diagnosis of mechanical obstruction in dogs based on relative small intestinal external diameters. *Vet Radiol Ultrasound*. 2014;55(5):472-479.

100. Ciasca TC, David FH, Lamb CR. Does measurement of small intestinal diameter increase diagnostic accuracy of radiography in dogs with suspected intestinal obstruction? *Vet Radiol Ultrasound*. 2013;54(3):207-211.

101. Diana A, Specchi S, Baron Toaldo M, Chiocchetti R, Laghi A, Cipone M. Contrast-enhanced ultrasonography of the small bowel in healthy cats. *Vet Radiol Ultrasound*. 2011;52(5):555-559.

102. Scrivani P V, Richarcl DVM, Dvm MB, Wendy CN. Effects of acepromazine and butorphanol on positive-contrast uppey gastrointestinal tract. 1998;(10).

103. Bae KT. Intravenous Contrast Medium Administration and Scan Timing at CT: Considerations and Approaches. *Radiology*. 2010;256(1):32-61.

104. Chu LL, Joe BN, Wesphalen AC., Webb EM, Coakley FV, Yeh BM. Patient-specific time to peak abdominal organ enhancement varies with time to peak aortic enhancment at MR imaging. *Radiology*. 2007;245(3):779-787.

105. Bae KT, Heiken JP, Brink JA. Aortic and hepatic peak enhancement at CT: effect of contrast medium injection rate - pharmacokinetic analysis and experimental porcine model. *Radiology*. 1998;206(2):455-464.

106. Oliveria CR, Henzler MA, Johnson RA DR. Assessment of respiration-induced displacement of canine abdominal organs in dorsal and ventral recumbency using multislice computed tomography. *Vet Radiol Ultrasound*. 2015;56(2):133-143.