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Assessment of 3 bowel preparation protocols for computed tomography pneumocolonography in normal dogs

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ABSTRACT

Objective: To investigate the effects of different bowel preparation protocols on image interpretation of CT pneumocolonography (CTP) studies.

Study Design: Experimental crossover design

Animals: Intact male, hound-cross, research colony dogs (n=4)

Methods: All dogs received each of 3 different bowel cleansing protocols prior to CTP. For each segment of large bowel the subjective adequacy of bowel preparation was assessed, residual fecal and bowel volumes were calculated, and the density of fecal material in the bowel lumen was measured. Linear mixed effect models that included a random dog effect were used to evaluate mean differences in outcome measures among bowel cleansing protocols.

Results: No dogs experienced any clinical problems associated with the bowel cleansing protocols or CTP procedures. Bowel preparation was considered adequate for CTP interpretation for all 3 protocols evaluated. Preparation method did have a significant effect on residual fecal volumes and the fecal:bowel volume ratio, with protocols involving an extended fast producing the lowest total residual fecal volumes (False Discovery Rate <0.01). Maximum measured density of residual fecal material differed significantly among the 3 bowel preparation methods studied ($p < 0.001$).

Conclusions: Contrast-tagging of residual fecal material was successful with oral iopamidol administration. An at-home bowel preparation protocol may provide adequate bowel cleansing for CTP image interpretation. Further refinement and study on the use of outpatient bowel cleansing protocols for CTP imaging of dogs with large bowel disease is warranted.

INTRODUCTION

The large bowel can be a difficult anatomic region to image in the clinical setting. Computed tomography of the bowel has been described in the dog,[1,2] but it is not commonly recommended for imaging assessment of the colorectum, because if this organ is not evaluated while empty, the presence of fecal material can seriously limit the ability to identify and accurately describe mass lesions. Conversely, when the bowel is empty, collapse of the GI lumen and contraction of the muscular wall limits the information that can be derived about wall thickness and mass lesion extent on standard unenhanced and contrast enhanced CT. A non-invasive, low-risk technique of CT imaging of the large bowel during luminal insufflation of gas (CT pneumocolonography, CTP) is utilized in the human medial field to improve visual differentiation of lesions, and a technique for CTP has been previously described in a cohort of normal dogs.[3-8]

International consensus guidelines for humans recommend that CTP be performed following full cathartic bowel preparation, however many patients perceive laxative bowel preparation as the worst aspect of the test.[9] In an effort to avoid laxative bowel preparation, alternative methods such as a low-residue diet,[10,11] or a partial colonic preparation in conjunction with fecal tagging have been used.[12] Labeling stool in the non–cathartic prepared colon with an oral contrast agent is possible, and feasibility studies have shown that colorectal neoplasms can be discriminated from contrast-labeled stool.[10-15] It has been demonstrated in humans that the detection of large (≥ 1 cm) neoplasms can be performed in the presence of tagged stool, with performance characteristics similar to the cathartic-prepared colon.[10,13,15] Excellent results can be obtained for polyp detection and fecal tagging quality with a 2- or 1-day bowel preparation protocols.[13,16] A variety of orally administered agents including barium and iodinated-based contrast media have been described for use in fecal tagging in humans.[11,12,17] Although hospital-based protocols using fecal tagging with orally administered contrast medium has been found to be acceptable to human patients in terms of both discomfort and side effects, they reported dissatisfaction with the necessary postponement of imaging when this is initiated in hospital prior to CTP, and home-based protocols are more positively perceived.[9]

Bowel cleansing is most commonly recommended as preparation for colonoscopic procedures in veterinary medicine, and specific recommendations for bowel cleansing for the purposes of CTP do not currently exist in the veterinary literature. Recommendations for colonoscopic bowel preparation methods in veterinary medicine vary, but most commonly they employ a combination oral cleansing agents (+/- IV fluid administration), enemas, and fasting in order to cleanse the lumen of the large bowel of fecal material as much as possible for colonoscopic imaging and biopsy.[18] Bowel preparation, including the time and cost of additional pre-procedure hospitalization that is usually recommended, can be a problem for some pet owners. However it is not feasible to ask most owners to administer high-volume iso-osmotic lavage solutions or to perform enemas on their pets at home. An alternative protocol that could be administered at home prior to an imaging procedure is likely to be well received by clients. A tablet formulation of an osmotic phosphate colonic cleansing agent (Osmoprep, Salix

Pharmaceuticals, Raleigh NC) is available and easy to administer. While a hypertonic phosphate solution bowel preparation was demonstrated to be safe in a cohort of healthy dogs, the quality of colonic cleansing provided by the oral liquid cleansing agent used in that study was overall inferior to large-volume GI lavage solutions in those dogs, and was deemed inadequate for ideal colonoscopic evaluation.[19] A study of human patients receiving colonic preparations with a low-fiber diet, found that the major differences in the cathartic unprepared versus prepared colon were the amount of mucosal surface covered by stool, size of retained stool, and number of segments containing stool.[20] Luminal colonoscopic imaging differs from the three-dimensional data provided by CTP and as a result, minimal and/or optimal cleansing requirements for the two procedures may differ. However, because of the previously described inadequacies of a hypertonic phosphate-based bowel preparation protocol, we feel it is important to preliminarily assess the results of osmotic phosphate bowel preparation for CTP prior to recommending its use in clinical patients.

This study was undertaken to preliminarily evaluate components of possible bowel preparation methodologies for use in CTP in dogs that could offer the additional benefit of being administered at home by owners. The objectives of this study were to describe the measured residual fecal volumes of three different at-home bowel preparation methods and to document differences that might impact CTP interpretation in the clinical veterinary setting. We hypothesized that a colonic cleansing protocol utilizing a tableted phosphate cleansing agent that could be feasibly administered by owners at home would provide 1) lower residual fecal volumes than a low residue diet, and 2) would provide subjectively adequate luminal cleansing for CTP image interpretation. We additionally hypothesized that orally administered contrast would produce measureable differences in the density of fecal material in the large bowel, and if tagged with iodinated contrast, low volume residual fecal material would be easy to identify and differentiate from colonic wall tissue during CTP.

MATERIALS AND METHODS

This study was approved by and conducted in accordance with the Institutional Animal Care and Use Committee. Four healthy, purpose-bred male hound-mix research colony dogs were enrolled in this experimental study. All dogs received three different bowel cleansing protocols in a crossover design separated by ≥2 weeks, and were anesthetized three times for CTP following each bowel cleansing protocol. All dogs received the bowel cleansing protocols in the following order: Method 1, Method 2, Method 3. Dogs were anesthetized according to a standardized protocol of premedication with morphine (0.3 mg/kg) and atropine (0.02 mg/kg) subcutaneously, induction with propofol intravenously (5 mg/kg to effect), and maintenance on inhalant isoflurane in oxygen to effect. All dogs were recovered from anesthesia following image acquisition. Subcutaneous carprofen (2 mg/kg once) was administered for postoperative analgesia for any potential residual cramping or discomfort secondary to bowel distension. The CTP scan protocol was performed as previously described, with all scans of the abdomen and pelvis from the diaphragm to the anus performed under a positive-pressure breath-hold.[8] Carbon dioxide (CO_2) pneumocolon was established and maintained at 20mmHg using a mechanical insufflator (Endoflator , Karl Storz Veterinary Endoscopy, Goleta, CA), with initiation of the CTP scan 2 minutes after initiation of insufflation in all dogs, based on prior work.[8]

Bowel Preparation Method 1 (Cathartic, Extended Fast) - All dogs received a standard commercial diet (Adult Maintenance Dog Food, Eukaneuba , Proctor & Gamble, Cincinnati, OH) until commencement of bowel preparation on t=-2 days (approximately 36 hours prior to the scheduled CTP scan). Free access to water was provided at all times. The bowel preparation protocol used consisted of fasting for 36 hours (starting after an evening meal approximately 36 hours prior to the scheduled CTP scan) and 4 doses of a sodium phosphate monobasic monohydrate/sodium phosphate dibasic anhydrous tablet colonic cleansing agent (Osmoprep , Salix Pharmaceuticals, Raleigh, NC) at a dose of 6 grams PO q 8 hours, starting 32 hours prior to the scheduled CTP procedure). No enemas were administered. CT pneumocolonography was performed on day 0.

Bowel Preparation Method 2 (Low Residue, Tagged) - All dogs received a formulated low residue diet calculated to be calorically adequate according to body weight, consisting of 1.25 cups white rice, 1.25 cups cottage cheese, and 5 ml (1.85 grams I) iopamidol (Isovue 370, Bracco Diagnostics Inc., Princeton, US) twice daily for three meals (evening of day -2, morning and evening of day -1), initiation of a pre-procedural fast for approximately 12 hours (after the evening meal on day -1). Free access to water was provided at all times. No enemas were administered. CTP was performed on day 0.

Bowel Preparation Method 3 (Low Residue, Tagged, Extended Fast)- All dogs received the same formulated low residue diet, calculated to be calorically adequate according to body weight as in bowel preparation protocol 2, consisting of 1.25 cups white rice, 1.25 cups cottage cheese, and 5 ml (1.85 grams I) iopamidol (Isovue 370, Bracco Diagnostics Inc., Princeton, US) twice daily for three meals. In the third protocol, the timing of the diet and fast was altered such that meals were provided on the evening of day -3 and the morning and evening

of day -2, with initiation of a pre-procedural fast for approximately 36 hours (after the evening meal on day -2 and through day -1). Free access to water was provided at all times. No enemas were administered. CTP was performed on day 0.

CT Pneumocolon Procedure and Image Analysis – The CTP procedure was performed as previously described.[8] Prior to positioning in the CT scanner a purse string suture of 2-0 nylon was placed circumferentially in the anus at the mucocutaneous junction. Any fecal material palpated per rectum during catheter placement was digitally removed. A 10 French balloon-tipped Foley urinary catheter (SurgiVet , Smiths Medical ASD Inc., St. Paul, MN) was passed into the rectum, the catheter balloon was inflated with 5 mL of room air, and the purse string suture was tightened and tied. The Foley catheter was withdrawn until the balloon seated against the anus. An unenhanced scan of the abdomen and pelvis, from the diaphragm to the anus, was performed during a positive-pressure breath-hold. Following the initial scan, CO_2 pneumocolon was established and maintained, and two minutes after initiation of pneumocolon, an unenhanced scan of the abdomen and pelvis was repeated.

CT measurements/parameters evaluated – Images were acquired with a helical 16-slice CT scanner (Lightspeed 16 helical scanner, General Electric Co., Milwaukee, US) with a pitch of 1.375 and 2.5mm and 0.625mm collimation. Acquisition parameters were 120 kV and 150 mA with 1s tube rotation and contiguous reconstruction. Images were viewed in a soft tissue algorithm and soft tissue window, with manual adjustments to maximize conspicuity of the colon wall. Multiplanar reformatting was used to measure colon and fecal material volumes perpendicular to the long axis of the lumen (Osirix 64 bit v. 5.8.2, Pixmeo, Bernex, Switzerland; GE Advantage Workstation, 4.4, Milwaukee, WI). For each segment of large bowel (rectum, colorectal junction, descending colon, transverse colon, ascending colon) the following subjective assessments were performed: adequacy of bowel preparation, slice with largest % of bowel lumen filled with fecal material, and conspicuity of bowel wall. Minimum and maximum density of any fecal material in the colon in Hounsfield units (HU) was also recorded. A single board-certified radiologist (AZ) performed all subjective assessments and reviewed all measurements, and was blinded to bowel preparation method at the time of image review.

Statistical Analysis – Study data were collected and managed using REDCap electronic data capture tools[21] hosted at the University of California-Davis. Statistical analysis was performed by ST using SAS/STAT version 9.2 or later (SAS Institute, Cary NC) and R 2.15.2[22] or later.

Linear mixed effect models were used to test for mean differences of fecal minimum and maximum HU among bowel preparations. A random effect for each dog was included in the model. Values for max HU were log transformed because these values were strongly right-skewed. P-values < 0.05 were considered significant. Linear mixed effect models also were used to test for differences in mean bowel volume, fecal volume and the fecal:bowel volume ratio. Each bowel segment was evaluated individually as well as the total bowel. In these analyses, to account for multiple testing false discovery rates (FDR) were calculated across all bowel segments and volume measures. Values of FDR < 0.05 were considered significant. For

significant overall models, we compared all pairs of bowel preparations with a Tukey pairwise comparison procedure.

RESULTS

The median body weight of the four male hound-mix dogs enrolled in this study was 22.3 kg (range, 21.5-22.5 kg). The median subject age was 10 months (range, 9-11 months). All dogs were deemed to be systemically healthy based on the results of physical examination and pre-anesthetic hematologic evaluation of packed cell volume and serum total protein. All dogs ate the offered diets well; there were no problems with acceptance of the low-residue diet or with admixture of iopamidol. All dogs exhibited liquid diarrhea when receiving bowel preparation Method 1. During bowel preparation Methods 2 and 3, dogs exhibited soft, but not liquid stools. No dogs experienced any clinical problems associated with the bowel cleansing protocol or CTP procedure. Following insufflation, the conspicuity of the bowel wall was subjectively deemed to be good in all CTP studies, and that should a mass lesion have been present, it would likely have been identifiable with all preparation methods evaluated. While some segments clearly had more residual fecal material than others, bowel preparation was deemed adequate for CTP image interpretation in all bowel segments for all preparation methods. All dogs were recovered from anesthesia and received clinical follow-up for 14 days without any identified complications.

Measured Fecal And Bowel Luminal Volumes - The measured volumes of the bowel lumen and fecal material within the lumen are reported in Table 1. When the effect of bowel preparation method on measured bowel luminal volume was analyzed, no significant difference was found in preparation method of the various bowel segments except the rectum, in which bowel preparation Method 1 produced a higher mean measured bowel luminal volume than Method 2 or Method 3 (Table 1). However, when total measured bowel luminal volume was evaluated, there was no effect of bowel preparation method. When the calculated total large bowel volume was evaluated by individual dog, some intra-dog variation was noted, but it was inconsistent (Figure 1).

The bowel preparation method did have a significant effect on measured fecal volumes and the calculated fecal:bowel volume ratio for all segments of bowel in which fecal matter was identified (Table 1). Method 1 produced the lowest total residual fecal volumes, followed by Method 3 which both differed significantly from Method 2 (Table 1). Overall, while the calculated fecal volume to bowel luminal volume ratios were low for all segments of bowel (Table 1), this was occasionally observed as proportionally large focal accumulations of material within a small region of a bowel segment (Figures 2 and 3).

Fecal Tagging - Maximum measured HU values differed significantly among the three bowl preparation methods ($p < 0.001$). Figure 4 shows that the lowest values were associated with the standard bowel preparation (Method #1) and that tagging alone (Method #2) resulted in the highest maximum values. In contrast, minimum HU density did not differ significantly between the bowel preparation methods (Figure 3). Figure 3B demonstrates a representative CT image with iopamidol-tagged feces.

DISCUSSION

Findings from the current study indicate that effective bowel preparation for CTP imaging can be safely and effectively performed outside the hospital setting in healthy dogs. Low residual fecal volumes were obtained with either a cathartic preparation using an orally-administered tableted phosphate cleansing agent or with administration of a low residue diet for several days prior to the CTP procedure. In all dogs, the more aborad large bowel segments (descending colon and rectum) retained more feces than orad segments (ascending and transverse colon); this was reduced but not totally eliminated in protocols incorporating an extended fast. Additionally, contrast-enhanced identification of residual fecal material was successfully achieved using iopamidol mixed in with the administered low-residue diet, and iopamidol-tagged fecal material was easily distinguishable from the large bowel wall.

Currently, recommendations for minimum standard or optimized bowel preparation for CTP imaging studies do not exist in the veterinary medical literature. Even with a pneumocolon present, accurate clinical CT assessment of focal large bowel wall thickenings, polyps, or other mass lesions is likely to be compromised by the presence of large volumes of fecal material within the large bowel. Some level of pre-procedure bowel preparation to either minimize residual feces, differentiate residual feces from tissue, or both, is likely to optimize CTP interpretation. While a tableted formulation phosphate cathartic cleansing agent is more convenient and offers the option of at-home administration, hypertonic phosphate bowel preparation with and without enemas was previously deemed inadequate for ideal colonoscopic evaluation.[19] While all bowel preparation methods produced CTP images considered adequate for evaluation, the sodium phosphate tableted cathartic preparation used in our study (Method 1) did significantly reduce residual fecal volume compared to a low-residue diet alone (Method 2), exhibited a trend of lower fecal volumes compared to Method 3, and provided subjectively good assessment of the bowel.

Electrolyte imbalances and even renal failure have been identified in some humans after hypertonic phosphate bowel preparation, and the use in patients with pre-existing renal disease may be contraindicated.[18] Similar to the use of the tableted osmotic phosphate colonic cleansing agent in our study, hypertonic phosphate solution was shown to be safe in a group of healthy dogs undergoing colonoscopy.[19] Electrolyte and other serum chemistry parameter monitoring were not performed as part of this study but clinical signs of hypocalcemia or hyperphosphatemia (such as pre- or post-procedural weakness, muscle twitching, seizures, vomiting, fever, face-rubbing) were not observed. However, as CTP would likely be applied in a clinical setting to older patients with pre-existing comorbidities, pre-and post-bowel preparation serum biochemical monitoring might be advised, especially prior to induction of general anesthesia.

The CTP bowel preparation methods in this study were modified from existing colonoscopic bowel preparation recommendations at our institution. While recommendations for

colonoscopic bowel preparation methods in veterinary medicine vary, commonly food is withheld from the animal for 24-36 hours before the procedure.[18] However, this may not be optimal for some patients due to comorbidities or owner difficulties in administering a fast, and fecal tagging to better differentiate feces from bowel may offer an important alternative to patients for whom a cathartic colonic preparation is not elected. A wide range of iodinated contrast agents, iodine dosages, dose volumes (50-500 ml) and dose timing has been described in humans for fecal tagging in preparation for CTP studies.[12,13,20,23] In addition to the use of orally-administered iodinated contrast agents, oral barium administration may alternatively be used to tag fecal material in the colorectum. The advantage of barium tagging is that it does not induce diarrhea, which can result from the oral intake of larger volumes of high-osmolarity iodinated-based contrast media.[17] However, barium primarily tags the solid stool and not the liquid components, which can lead to inhomogeneous tagging.[11] A high osmolarity iodine-based contrast medium such as iopamadol was chosen for fecal tagging purposes in this study, as it softens the stool, causing a more homogeneous mixing with the iodine and thereby improving ease of CTP interpretation.[12] Higher doses of iodinated contrast media often result in diarrhea.[13,24] A much lower volume of contrast material was administered in our study than in previous human reports, which still resulted in acceptable fecal tagging, and liquid diarrhea was not observed. We additionally elected to combine fecal tagging with administration of a low residue diet, as prior research has demonstrated that a low-fiber diet can increase the quality of fecal tagging obtained with iodinated contrast.[25]

In humans a total of 45g iodine divided into three separate doses with meals, has been recommended in order to obtain optimal fecal tagging.[24] Our study cohort received a much lower total iodine dose (5.5 grams iodine) than in the reported human studies, but this was also administered in conjunction with a low-residue diet, so much less volume of residual stool was anticipated than in the human studies cited above. This dose was chosen in an effort to minimize iodine dose and account for not only the impacts of the low-residue diet administered, but also due to the lower body weights in our canine cohort compared to adult humans. In our dogs, this lower total dose (approximately 0.25 grams I/kg body weight) is approximately half of the total dose recommended for an adult human,[24] but still resulted in an acceptable quality of fecal tagging intensity, good homogeneity of tagging, and fecal material was easily differentiated from bowel wall. Interestingly, Method 3 (tagging + low residue diet + extended fast) resulted in a low mean maximum density of tagged feces, more similar to Method 1 in which iopamidol was not administered (cathartic + extended fast) than to Method 2 (tagging + low residue diet). This finding may be associated with the relatively greater degree of bowel cleansing achieved with Method 3 than Method 2, leaving less iopamidol in the bowel lumen. It may be that in bowel cleansing protocols that utilize an extended fast and are anticipated to result in low volumes of residual stool, larger doses of orally-administered iodine may provide improved fecal tagging, and this should be investigated further. Alternatively, the longer fast could have resulted in a greater proportion of the administered iodide being absorbed from the bowel lumen. Small amounts of iodine are absorbed in the colon, so the use of oral iodinated contrast agents can

result in mild allergic or rarely in severe anaphylactic reactions in humans[26], and this should be considered in veterinary patients if larger systemic doses of iodine may be a concern, or if an iodine allergy is suspected.

Measurement of residual fecal volume in the dogs of this study demonstrated some notable findings that may impact the refinement of CTP bowel preparation protocols for future use in clinical patients. Cathartic bowel preparation with a standard diet and an extended fast (Method 1) significantly reduced the residual fecal volume compared to dogs receiving a low residue diet and fecal tagging (Method 2). A low residue diet plus fecal tagging, combined with an extended fast (Method 3) also succeeded in reducing residual fecal volume compared to Method 2. Both Method 1 and Method 3 incorporated an extended fast, which did not completely ameliorate residual feces, but likely contributed to reduced residual fecal volumes in the aborad large bowel. Overall, while the total calculated fecal volume relative to bowel luminal volume was low for all segments of bowel, residual feces was occasionally observed as focal accumulations within a bowel segment which could theoretically obscure identification of a small clinical lesion in that segment. While not statistically significant, there was a trend for focal accumulations of feces in the caudal large bowel to be more of a concern with Method 3 than Method 1 (Figure 2). While the greater residual fecal volumes identified with Method 2 could be clinically significant in interpretation, especially with small polypoid lesions, fecal tagging is likely to allow sufficient differentiation to permit identification of even small clinical lesions. If orally-administered cathartic cleansing is not desired by the attending clinician, or if the patient has pre-existing comorbidities that would preclude cathartic administration, fecal tagging alone may still be sufficient. Further assessment of these factors in the framework of identifying and interpreting clinical disease is indicated.

The segment of bowel with the greatest residual fecal accumulation in our study, was generally the descending colon/rectum. This was much reduced, but not completely ameliorated, in protocols using an extended fast (Method 1 and Method 3), but an extended fast may not be desirable in the home setting, or for certain types of patients. While not assessed as part of this study, a single enema administered to a dog presenting for CTP by the veterinary staff prior to anesthesia on the night before or the morning of admission for the CTP procedure would likely further reduce any potentially lesion-obscuring bulky residual fecal accumulation in the more caudal large bowel segments, and could be considered as an alternative to an extended fast in future protocols. In general, digital extraction of any palpable fecal material on rectal exam prior to the CTP imaging procedure would be recommended. Further evaluation on the role of a single enema in the clinical setting would be warranted.

When the effect of bowel preparation method on measured bowel luminal volume was analyzed, no significant difference was found in the various bowel segments except the rectum, in which bowel preparation did have an impact, with Method 1 having a higher mean measured bowel luminal volume than Method 2 or Method 3. There is no obvious anatomic or physiologic

explanation for this, and as there was no difference in effect of bowel preparation method on total large bowel luminal volume, the identified impact on the rectum may represent a type II statistical error due to low dog numbers. Trends of lower calculated bowel volumes of transverse and ascending colon during assessment of Method 2 may also represent a type II statistical error, or could possibly have been associated with increased fecal material in the bowel lumen in this group in general, which may have inhibited diffusion of gas to the more orad sections of large bowel. Prior work has shown that large bowel luminal diameter did increase to a certain extent with time of insufflation.[8] As the order of bowel preparation method was not randomized, the crossover study design could have allowed for summative effects of bowel preparation, however as there was a delay of at least 2 weeks between initiation of each bowel preparation method, there was adequate time for the large bowel to return to baseline between studies.

A limitation of this study is the small sample size. This study was intended as a pilot study to determine factors that might or might not work in designing a clinical protocol that could be evaluated in a larger number of dogs. Because no work had been done in this area before we restricted our study to a small number of dogs while obtaining valuable information to support future studies in this area. As a result of the small sample size, we only had adequate power to detect large differences. We determined the minimum effect size that could be detected between any two bowel preparations at 80% power and a significance level of 0.05 with four dogs per group. Because the correlation among measurements on the same dog across the three bowel preparations varies depending on the outcome variable, we conservatively assumed independence and used a one-way ANOVA procedure. This analysis indicated that there was sufficient power to detect a difference between any two groups of at least 2.65 standard deviations. If measurements on the same dog are correlated, smaller effect sizes would be detectable at the same power. Large differences in means across bowel preparation methods were observed for fecal volume in all bowel sections and significant differences were found for these outcomes. However, the relative differences in bowel volume among the preparation methods were smaller than for fecal volume and except for the rectum, the study did not have sufficient power to detect differences this small.

At-home techniques of bowel preparation prior to CTP holds promise for application to clinical canine patients with focal colorectal disease in which precise anatomic characterization of the extent of mass lesions can be crucial to successful surgical planning. Based on experiences in humans and observations of the experimental dogs in our study, administration of an at home bowel preparation protocol as preparation for CTP in clinical veterinary patients is likely to be well-tolerated by patients and well accepted by clients. This study provides preliminary data on what level of residual feces may be expected in application of these three protocols in an at-home setting. However with the existing design, it is not possible to discern whether extended fast or cathartic alone would be effective as individual therapies, or whether a yet untested protocol where fecal volume is lessened but where increased contrast might remain in the colon due to lack of an extended fast might provide even more optimal imaging conditions. All three

protocols evaluated here were deemed to produce levels of bowel cleansing that are likely to allow interpretation of CTP studies in clinical canine patients presenting for assessment of large bowel disease. Protocols involving an extended fast resulted in the lowest residual fecal volumes in these dogs, and an extended fast may be an important component of optimized bowel cleansing. However depending on individual patient factors and comorbidities an extended fast may not be desirable for a given individual, and bowel preparation components of a low-residue diet, cathartic preparation, and/or fecal tagging with orally-administered iodinated contrast-enhanced may be successfully utilized in CTP studies in dogs. Individual protocol choices should be balanced against theoretical risks of allergic reaction to iodine, management challenges of diarrhea, potential electrolyte abnormalities or dehydration secondary to the cathartic effects, and other pre-existing comorbidities, especially in older patients. Further study involving larger numbers of animals and that allows for a factorial design to discern the optimal combination of preparation strategies is indicated.

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DISCLOSURE STATEMENT

The authors have no conflicts of interest to disclose.

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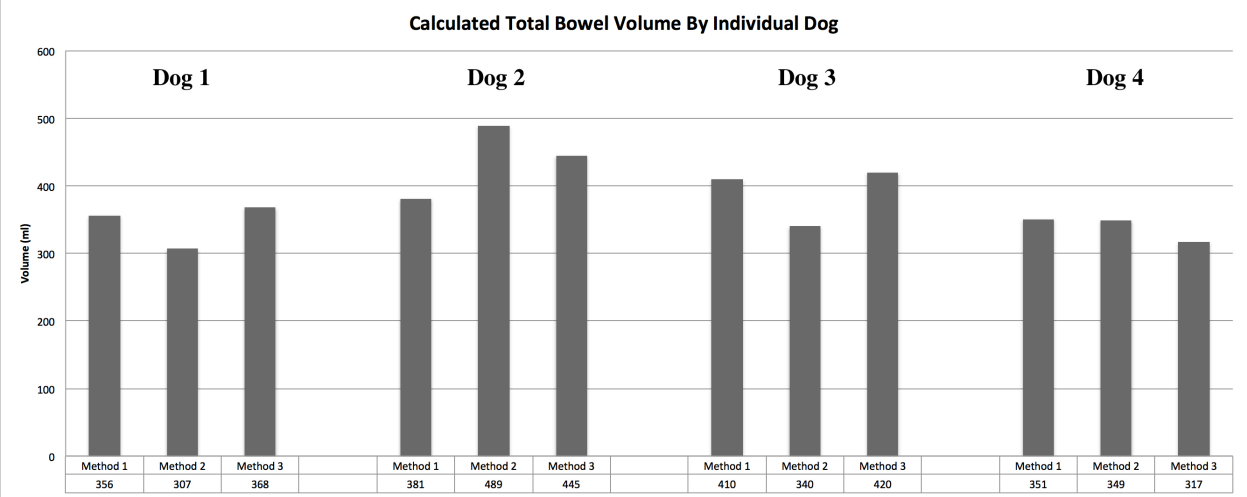

Figure 1: Calculated total large bowel luminal volumes in milliliters, as measured in each individual dog.

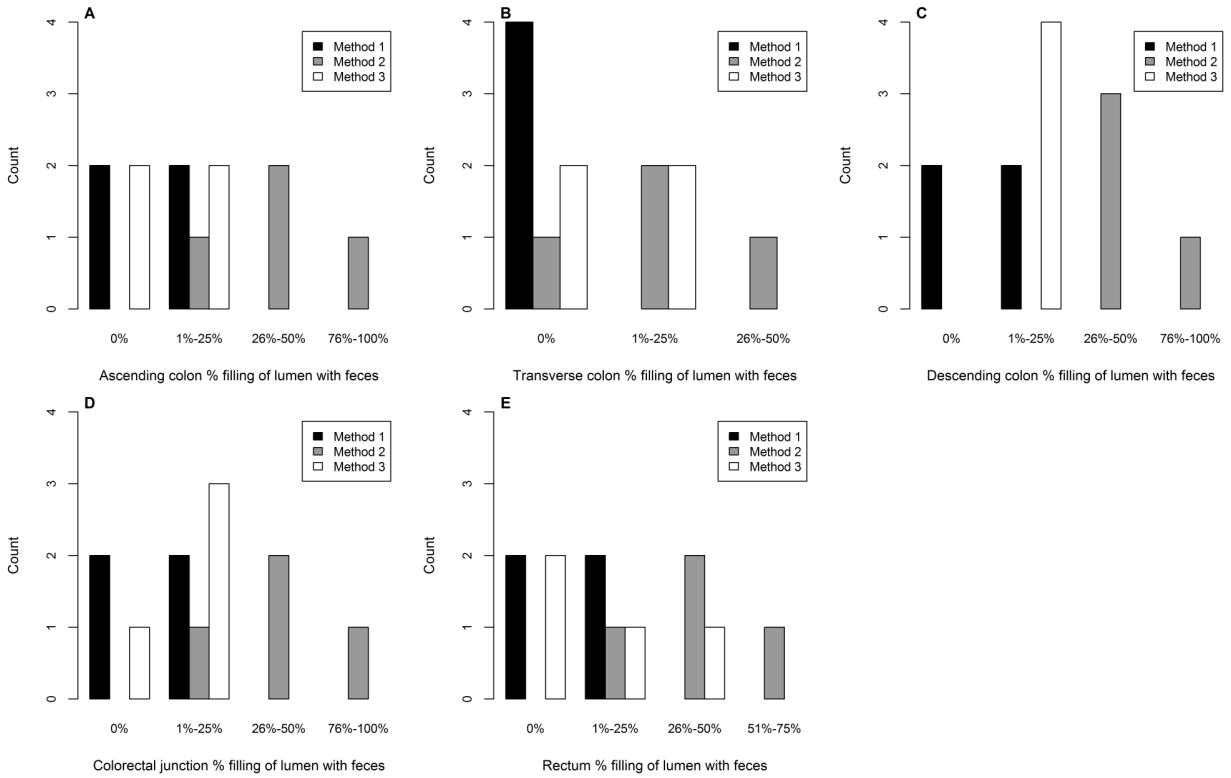

Figure 2: Distribution by bowel segment of the maximum cross-sectional filling percentage of the single transverse CT image most filled with feces within that bowel segment for the three bowl preparation methods. Bar height corresponds to the number of dogs with each filling level.

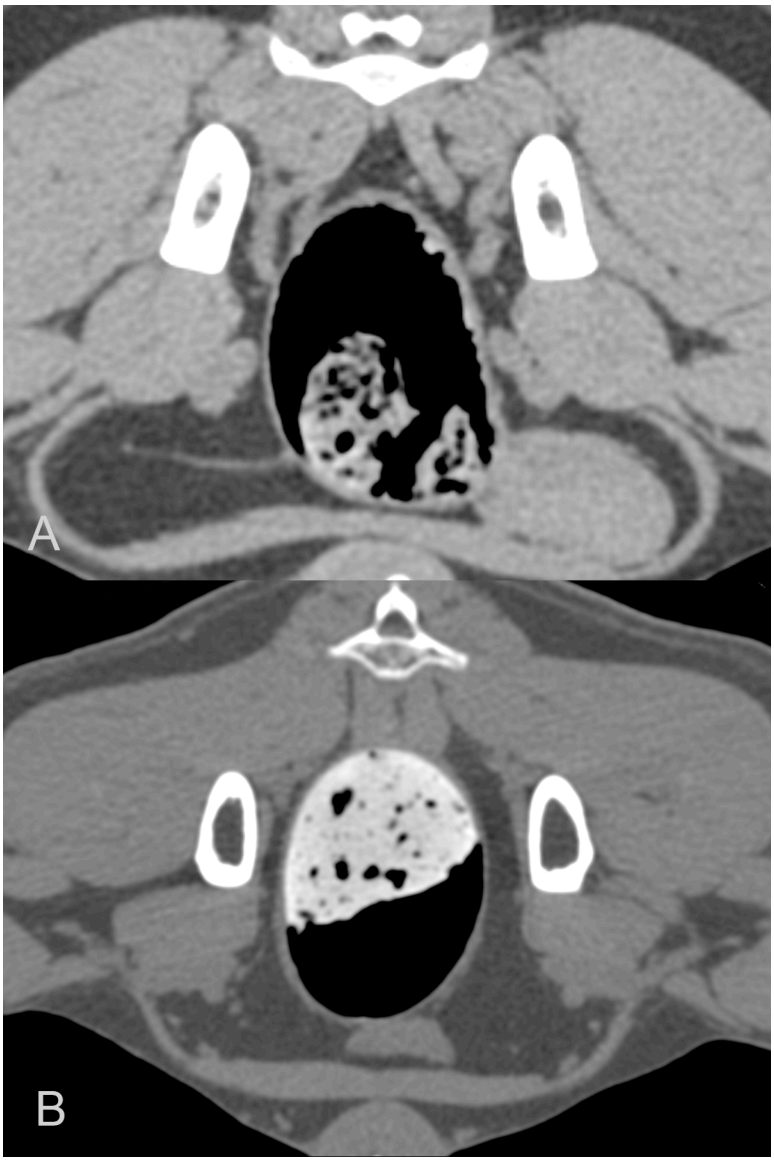

Figure 3: (A) Representative transverse CT image demonstrating a focal accumulation of un-tagged fecal material that could obscure a small luminal colonic lesion. (B) Representative CT image demonstrating successful identification of fecal material based on contrast-tagging with orally-administered iopamidol. Note the homogenous distribution of contrast in the tagged feces.

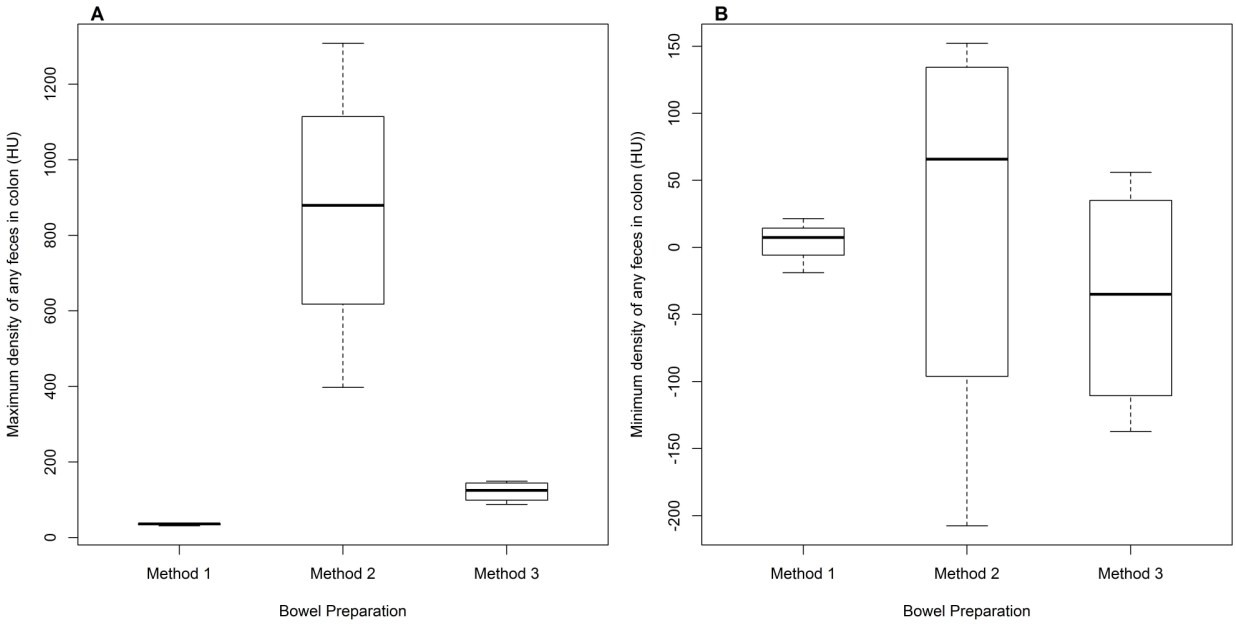

Figure 4: Distribution of maximum and minimum HU values for three bowl preparation methods

Table 1: Measured volumes of bowel lumen and fecal material within the lumen reported by bowel segment, expressed as mean ± SD below, and results of linear mixed effect models testing for any differences in mean bowel volume, fecal volume and the fecal:bowel volume ratio across the three bowl preparation methods. Pairwise-comparisons with Tukey's adjustment for multiple comparisons were conducted for significant tests (FDR < 0.05) to identify which bowl preparation methods differed from each other. For each outcome, bowel preparation methods with the same superscripts differed significantly (adjusted p-value < 0.05). (*)Fecal volume and the ratio of fecal volume:bowel volume were not analyzed separately for transverse and ascending colon sections because no fecal matter was present in these sections for Methods 1 and 3. LRD = low residue diet, EF = extended fast. FDR=False discovery rates.

Bowel Preparation	**Rectum to L7-S1 Bowel Volume (ml)**	**Descending Colon Bowel Volume (ml)**	**Transverse Colon Bowel Volume (ml)**	**Ascending Colon Bowel Volume (ml)**	**Total Large Bowel Volume (ml)**
Method 1 (Cathartic + EF)	100 ± 8[a,b]	183 ± 12	57 ± 13	34 ± 14	375 ± 27
Method 2 (LRD + Tagging)	74 ± 21[a]	226 ± 50	42 ± 6	30 ± 15	371 ± 81
Method 3 (LRD + Tagging + EF)	69 ± 17[b]	227 ± 55	57 ± 11	34 ± 10	387 ± 57
p value/FDR	p=0.015, FDR=0.024	p=0.052, FDR=0.072	p=0.130, FDR=0.159	p=0.892, FDR=0.892	p=0.578, FDR=0.636
Bowel Preparation	**Rectum to L7-S1 Fecal Volume (ml)**	**Descending Colon Fecal Volume (ml)**	**Transverse Colon Fecal Volume (ml)**	**Ascending Colon Fecal Volume (ml)**	**Total Fecal Volume (ml)**
Method 1 (Cathartic + EF)	0 ± 1[a]	5 ± 8[a]	0 ± 0	0 ± 0	6 ± 8[a]
Method 2 (LRD + Tagging)	31 ± 17[a,b]	69 ± 25[a,b]	4 ± 4	7 ± 6	112 ± 11[a,b]
Method 3 (LRD + Tagging + EF)	1 ± 2[b]	11 ± 5[b]	1 ± 1	1 ± 1	13 ± 6[b]

p value/FDR	p=0.012, FDR=0.022	p=0.002, FDR=0.007	*	*	p<0.0001, FDR=0.0001
Bowel Preparation	**Rectum to L7-S1 Fecal:Bowel Ratio (%)**	**Descending Colon Fecal:Bowel Ratio (%)**	**Transverse Colon Volume Fecal:Bowel Ratio (%)**	**Ascending Colon Volume Fecal:Bowel Ratio (%)**	**Total Fecal:Bowel Volume Ratio (%)**
Method 1 (Cathartic + EF)	0 ± 1[a]	3 ± 5[a]	0 ± 0	0 ± 0	2 ± 2[a]
Method 2 (LRD + Tagging)	40 ± 19[a,b]	32 ± 14[a,b]	9 ± 8	31 ± 32	31 ± 7[a,b]
Method 3 (LRD + Tagging + EF)	1 ± 3[b]	5 ± 4[b]	1 ± 2	2 ± 4	4 ± 2[b]
p value/FDR	p=0.007, FDR=0.015	p=0.004, FDR=0.0110	*	*	p=0.001, FDR=0.006