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A Simplified CT-Volumetry Method for the Canine Liver

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Abbreviations: CT, computed tomography; DICOM, digital imaging and communications in medicine; FOV, field of view; HU, Houndsfield units; ICC, intraclass correlation coefficient; ROI, region of interest; SD, standard deviation.
ABSTRACT

Computed tomographic (CT) liver volumetry using the slice addition technique is an accurate, but time-consuming method. Commonly used DICOM-viewing software only allow contouring of one area per image, which can be troublesome in transverse plane as different lobes are separated. In this prospective, experimental, methods comparison study, we aimed to determine if hepatic contouring using sagittal reformatting and a reduced number of images would yield accurate results. CT studies were performed in five canine cadavers and reviewed using sagittal reformatting. For each dog, the number of images that included the liver was used to create four stacks with progressively fewer images in which the liver would be contoured, each with the following median number of images: A: 60, B: 31, C: 16, and D: 9. Liver volume was calculated by three observers using the different stacks of images. After CT examination, the cadavers were dissected, the liver was removed, and its volume determined by water displacement. Single score intraclass correlation coefficient was calculated to assess interobserver agreement. Kruskal-Wallis test was used to compare water displacement and CT-based volumes. There was excellent agreement between observers (ICC= 0.957; 95% CI= 0.908-0.982, p<0.0001). No significant difference was found between the volumes obtained by CT-volumetry using each of the stacks and the volumes obtained by water displacement. Using sagittally reformatted images and hepatic contouring in as few as nine images can be an accurate and simple method for CT-volumetry of the canine liver.
Introduction

There is great variation in liver size in dogs. Liver size is influenced by physiological factors such as breed, body weight and age,\(^1\) and by changes secondary to a variety of disorders which can lead to organomegaly or microhepatia.\(^2\) Furthermore, the liver has the capacity to regenerate and increase its size as a response to certain therapies or after partial resection.\(^3\)-\(^6\)

Liver size is one of the principal diagnostic imaging criteria for assessment of dogs with suspected hepatic diseases.\(^7\) Semiquantitative liver assessment can be performed using various imaging modalities. However, the use of cross-sectional imaging, and particularly computed tomography (CT), allows quantitative assessment with good results if a more accurate assessment of liver volume is required.\(^4\)-\(^6,8\)

In the veterinary literature, CT liver volumetry has been performed in patients with portosystemic shunts before and after surgical attenuation of the shunting vessel\(^4\)-\(^6,8\) and volumetric assessment of liver tumour volume has been used for objective assessment of treatment response in dogs.\(^9\) Determination of hepatic remnant volume is not currently common practice in veterinary patients prior to partial hepatectomy.\(^10\) However, in humans it is an essential step to determine the remnant liver volume and assess the viability of the procedure prior to living donor transplantation or in patients in need of major liver resection.\(^11\)

Multiple studies in humans\(^11\)-\(^16\) and one in dogs\(^17\) have demonstrated good accuracy in the measurement of liver volume by using the CT slice addition technique. This consists of manually contouring the outline of the organ on each image slice, converting the contoured areas into volume and summing the volumes obtained. This is, however, time-consuming and cumbersome. Another drawback is that some of the most commonly used Digital Imaging and Communications in Medicine (DICOM) viewing software in veterinary practice often only allow contouring one area per image slice, and in the caudal aspect of the canine liver in a transverse plane, the different liver lobes are separated (Figure 1A).
Horos (Purview, Annapolis MD, USA, version 3.3.6) is a free and readily available DICOM viewer software program that is widely used in the veterinary imaging community and that allows a simple sagittal reformatting from transversely reconstructed images. Empirical and non-validated assessment showed that the area of the canine liver was continuous using sagittal reformatting instead of a transverse reconstruction (Figure 1). According to our literature search, no previously published studies have described using sagittally reformatted images to calculate hepatic volume in dogs.

The aim of this study was to determine if contouring the liver using simple sagittal reformatting would yield accurate results for CT volumetry of the canine liver. We also aimed to determine if contouring the liver in fewer slice images would reduce the time required to do so, and whether this would result in a loss of volumetric accuracy. We hypothesized that (1) sagittal reformatting would allow accurate measurement of liver volume, and (2) that reducing the number of slice images in which the liver would be contoured (by increasing the intervals between them) would not result in a significant loss of accuracy, but (3) would reduce the time needed to estimate liver volume by means of CT. We also hypothesized that (4) there would be no significant differences in the volumes obtained and time employed by different observers using the same intervals.

Methods

The study was a prospective, experimental, methods comparison design and was performed on canine cadavers. The dogs were donated by their owners to the Hospital for Small Animals of the University of Edinburgh via the Educational Memorial Programme for teaching and research purposes after being euthanised for reasons unrelated to this study. The study was approved by the Veterinary Ethical Review Committee of the Royal (Dick) School of Veterinary Studies (Veterinary Ethical Review Committee reference 167.19). The cadavers
were preserved frozen and were chosen on the basis of availability and feasibility. Sample size was determined based on convenience sampling. Clinical history and age were not available for the subjects. The inclusion criteria were dogs of any breed and size with no recent abdominal surgery performed, based on the absence of a visible scar, and the absence of a hepatic mass. The latter was verified on a preliminary assessment of the CT study by a diagnostic imaging intern (N.I) with knowledge of the CT anatomy of the liver, and a board-certified veterinary radiologist (T.S., European College of Veterinary Diagnostic Imaging [ECVDI], American College of Veterinary Radiology [ACVR]), and on visual inspection during liver dissection by the same diagnostic imaging intern and a second-year veterinary internal medicine resident (G.W., European College of Veterinary Internal Medicine-Companion Animals [ECVIM-CA]). In order to facilitate CT positioning and post-mortem dissection, the cadavers were thawed for 48 hours prior to procedures taking place. All cadavers were weighed prior to the CT examination and the weight was recorded. Breed and sex were identified and recorded. All canine cadavers underwent a standardized abdominal CT examination with a third-generation 64-row multidetector CT scanner (Somatom® Definition AS, Siemens AG, Erlangen, Germany). The exams were performed by the same diagnostic imaging intern assisted by an experienced radiographer. All dogs were positioned in ventral recumbency. The abdominal CT images were acquired with the following settings: 100 kV, 0.33 s rotation time, 32 x 0.6 mm collimation configuration, 512 x 512 matrix and a collimator pitch of 1.4. The current was automatically and individually selected by an automatic exposure control system (Care Dose 4D, Siemens Medical Solutions, International) depending on the body size and shape on the topogram scan. This resulted in different mAs between the dogs. The field of view (FOV) was adapted to the size of each dog and ranged from 190 to 298 mm, mean 247 mm. Transverse images were reconstructed with 1mm slice width at 0.5 mm interval using a
medium-frequency abdomen-specific soft tissue algorithm (Siemens proprietary iterative kernel I40f) and stored in DICOM format on a local picture archiving and communication system.

All images were reviewed on a computer workstation (Imac 27-inch, Apple, USA) with a calibrated LCD flat screen monitor (retina display), using a dedicated, readily available open-source DICOM viewer software (Horos, Purview, Annapolis MD, USA, version 3.3.6). For analysis, the study was only reviewed using the Sagittal Orientation tool of the viewing software, with a window width of 350 Hounsfield units (HU) and a window level of 40 HU. The Sagittal Orientation tool displays sagittally reformatted images with a thickness and interval determined by dividing the image reconstruction diameter by the matrix size. For example, a CT image series acquired with a 300 mm display FOV and a 512-image matrix would result in a 0.585 mm sagittal image thickness and interval.

For each dog, four stacks of image slices in which the liver would be contoured were created. Each stack included a different number of image slices, with different intervals between them. In order to create these stacks, the two most lateral images that included the liver were determined by consensus between a diagnostic imaging intern (N.I.) and a board-certified veterinary radiologist (T.S.). The number of image slices between the two most lateral images of the liver generated by the Sagittal Orientation tool was counted and recorded. The recorded image number was divided by 64, and the result was rounded to the closest whole number. This number was defined as the smallest interval and was used to create the first stack of image slices on which the observers would contour the livers. For the purpose of this study, this was defined as stack A, representing the largest group of image slices with the smallest intervals between them. The interval used to create stack A was then multiplied by 2 (stack B), then 4 (stack C), and then 8 (stack D). This resulted in four image stacks with progressively fewer image slices and progressively larger intervals between them (Figure 2). An observer-specific
spreadsheet was created, listing the exact locations of all image slices to be contoured (DICOM annotation: image x / y, R → L) for each stack in each dog. The two lateralmost image slices of the liver were included in all lists. Three observers with different grades of experience independently performed liver contouring and CT-volume calculation: one final year veterinary diagnostic imaging resident (J.L., ECVDI), and two diagnostic imaging interns (N.I. and J.P.). All were familiar with the CT anatomy of the liver and the use of the DICOM viewer software. Observers were familiarised with the contouring method and the use of the spreadsheet in a training session on another dog, not included in the study. They were unaware of the liver volumes prospectively obtained by water displacement, and of the volume results of the other observers. Liver contouring was performed by manually drawing a region of interest (ROI) on the pre-defined image slices using the pencil tool. The gallbladder was excluded from the ROIs, as previously described. The caudal vena cava was not consistently recognisable from the surrounding hepatic parenchyma, hence it was included in the ROIs. After contouring the liver, volume was calculated for each stack using the volume computing tool, and the result was recorded. The volume computing tool first fills in gaps between contoured image slices by interpolating missing ROIs in the non-contoured image slices, and then calculates the total volume of all areas of interest and generates a corresponding 3D model. This interpolation process is done by a proprietary software of the DICOM viewer of which the technical details have not been published. The combined contouring and liver volume calculation session duration for each stack and dog was measured in minutes and the timing was recorded. Immediately after the CT examinations, an anatomical dissection was performed of the cadavers, in which the livers were resected, and the gallbladders were removed. The livers were visually examined by a diagnostic imaging intern (N.I.) and a second-year veterinary internal medicine resident (G.W.) for any gross abnormalities. Each liver was then submerged in a
known volume of water within a calibrated measuring tube. The volume of water displaced was recorded. Measurements were repeated three times and the mean value was calculated and utilised in further analysis.

Statistical analysis was performed by an observer with statistical training as part of their PhD coursework (M.P.) using a commercially available software (Graph Pad Prism, Graph Pad, San Diego, CA, USA and R Studio Version 1.0.143, irr library). A p-value of less than 0.05 was considered significant. Kruskal-Wallis test was used to compare the differences between the water displacement and CT-based volumes in all animals investigated. When each of the dogs was compared, the water displacement volume was compared to the mean of the volumes calculated by the three observers using a Wilcoxon signed-rank test. Single score intraclass correlation coefficient was calculated to assess agreement between observers. Agreement was deemed poor for ICC < 0.50; moderate for ICC = 0.50 – 0.75; good for ICC = 0.76 – 0.90, and excellent for ICC > 0.90. Kruskal-Wallis test was used to compare the time employed by observers to complete stack A, and a one-way ANOVA was used for stacks B, C and D.

**Results**

Five dog cadavers were included in the study. A sixth dog was excluded due to the presence of a hepatic mass. Represented breeds were two Whippets, two crossbreeds and one English Bulldog. Three were females, and two were males. Weights ranged from 6.7 kg to 28.2 kg (median 14 kg).

In all dogs, it was possible to contour the liver with a single continuous ROI using sagittally reformatted images. Hepatic volumes obtained by CT volumetry ranged from 336 ml to 410 ml (median 396 ml) for dog 1, from 339 ml to 441 ml (median 397 ml) for dog 2, from 198 ml to 272 ml (median 239 ml) for dog 3, from 667 ml to 963 ml (median 780 ml) for dog 4, and from 771 ml to 863 ml (median 831 ml) for dog 5. Hepatic volumes determined by water
displacement and the percentage of the CT volume measurements relative to the water displacement volumes, together with dogs’ breeds, weights and liver widths are summarised in Supplement 1. No significant difference was found between the volumes obtained using each of the stacks of image slices and the volumes obtained by water displacement when calculated for all dogs jointly, nor when the comparison was done for each individual dog (Figure 3).

Slice thickness on sagittal orientation ranged from 0.371 mm to 0.582 mm (median 0.509 mm), determined by variations in the reconstruction diameter between dogs. Liver width in mm ranged from 100.94 to 218.84 (median 123.9 mm). Liver width in number of image slices ranged from 236 to 376 (median 291 image slices). The number of image slices included in stack A ranged from 58 to 65 (median 60), in stack B ranged from 30 to 33 (median 31), in stack C ranged from 16 to 17 (median 16), and in stack D was 9 for all dogs. The intervals between the contoured image slices for each stack and dog are detailed in Table 1.

There was excellent agreement between observers (ICC = 0.957; 95% CI = 0.908 – 0.982, p < 0.0001). The mean time employed to perform liver volumetry using stacks A was 21 min 19 s (SD = 3 min 47 s), using stacks B was 11 min 35 s (SD = 2 min 14 s), using stacks C was 6 min 12 s (SD = 1 min 13 s), and using stacks D was 3 min 20 s (SD = 40 s). The more experienced observer required less time to calculate liver volumetry using each stack compared to the other two observers (p < 0.05).

Discussion

In this study we propose a novel, simplified approach to hepatic CT-volumetry in dogs. Our hypothesis that using sagittally reformatted images would allow accurate measurement of liver volume was confirmed. This validates the use of widely available and free software that only allows contouring one ROI per image slice for volume calculations, hence overcoming the
inconvenience of having separated hepatic lobes in the caudal aspect of the canine liver in transverse reconstruction.

Liver volumetry has been established as a simple method for assessment of efficacy of both intra- and extra-hepatic portosystemic shunt treatment in dogs, with increases in volume documented after surgical attenuation of the shunting vessel. Other indicators of successful shunt attenuation such as hepatic arterial perfusion require specific software, whereas hepatic volumetry can be performed on free and commonly used DICOM viewing software such as Horos. Studies comparing efficacy of different treatment options for dogs with portosystemic shunts are currently lacking in the veterinary literature. Our findings may simplify the methodology of further research in this field.

In our sample population, manually contouring the liver in as few as nine image slices did not have a negative effect on the accuracy of the measurements. Experimental studies in human medicine have shown similar results. Our search of the veterinary literature revealed no studies evaluating the effect of reducing the number of contoured slice images over the accuracy of hepatic CT volumetry using the slice addition technique. The few studies that have utilised this technique in veterinary patients either have contoured every slice image where the liver was visible, or have not detailed the method. It is important to note that the two lateralmost image slices that included the liver were always manually contoured. Horos’ volume computing tool is able to automatically interpolate missing ROIs as long as they are included between two image slices with manually contoured ROIs.

The principal inconvenience of manual liver CT volumetry methods is that they are time consuming. In human medicine, this has been overcome by the use of semiautomated and automated methods that are considerably more time efficient, but that often require specific software. We propose a simplified and time efficient semiautomated method that does not require any software additional to what is usually available in clinical practice. Intuitively, and
as shown in our results, reducing the number of manual contours of the liver had a drastic impact on the time required to perform CT liver volumetry, with a difference of almost 18 minutes between using stack A and using stack D. Our results show that this simplified semiautomated method can be performed in less than 4 minutes. In our sample population, this did not translate into a loss of accuracy. On the contrary, in the dogs with the largest errors (dog 2 and 4), although not statistically significant, there was a greater discrepancy between the liver volumes obtained by water displacement and CT using the stacks with the larger number of image slices. These differences were of approximately 33% for stack A versus 12% for stack D in dog 2; and of approximately 21% for stack A versus 15% for stack D in dog 4. Similar discrepancies have been reported between CT liver volumetry and water displacement measurements in human living patients, with overestimations of up to 34% possibly explained by perioperative loss of blood, lack of perfusion and inaccurate contouring of the liver. Given that our study was performed in cadavers, loss of blood or lack of perfusion are not likely to have had a significant impact in the total volume obtained, even if a small amount of blood may have been lost during dissection due to the caudal vena cava not being tied off before hepatic resection. However, inaccurate hepatic contouring in image slices only included in the stacks the largest number of images could explain the slightly greater error when using these stacks. We believe that the risk of inaccurate hepatic contouring would be minimised in living dogs, for which our technique is intended, and in which the use intravenous contrast media is common practice and facilitates the recognition of the borders of the organ. A study in sheep demonstrated that smaller livers (under 600 ml) are more likely to be overestimated when CT-volumetry is performed. This might be of particular relevance in dogs with extra-hepatic portosystemic shunts, where small breed dogs are overrepresented and small liver volumes are expected. Further studies with larger samples representing this group of dogs would be needed to assess the impact of this possible source or error.
Two of the observers in our study were less experienced than the third one. Our results indicate that after a short training session, accurate liver volumetry can be performed adequately, even by relatively inexperienced observers. Contrary to our hypothesis, the time employed by the most experienced observer was significantly less, which can be explained by their greater confidence in both the CT anatomy of the canine liver and use of the viewing software. Our results are in agreement with what has been reported in human literature.\textsuperscript{16}

There are several limitations to the study. The small sample size did not allow statistical assessment of variations in body weight and hepatic volume, although dogs included in the study had weights that are commonly seen within our hospital population. Additionally, we did not aim to provide a cut-off minimum number of image slices that need to be contoured, but to demonstrate that a simplified, time efficient semiautomated CT liver volumetry method is possible. An additional limitation is that, due to our inclusion and exclusion criteria, only dogs with grossly normal livers were included in our sample, preventing extrapolation of our results to populations where the hepatic contour may be irregular due to chronic hepatic disease, or distorted by the presence of space-occupying lesions. In human patients undergoing major hepatic resection, approximately 25\% of healthy liver parenchyma needs to be preserved in order to prevent postresectional liver failure, and this percentage increases up to 50\% if the liver is cirrhotic.\textsuperscript{16} Equivalent data is lacking in the veterinary literature, but experimental surgical models in dogs have attempted up to 90\% hepatic resection with 7 days survivals recorded after the procedure.\textsuperscript{22} Although the results of this experimental model are hardly extrapolatable to a real clinical setting, they suggest that, as in human patients, major hepatic resection is possible in dogs. Further studies in dogs with diffuse or focal changes in hepatic contour are warranted to assess the accuracy of CT-volumetry and to establish if the margin of error of this method is acceptable for determination of hepatic remnant volume prior to major partial hepatectomy.
In our study, the thickness of the intervals used for the different stacks of contoured image slices varied between dogs. This was the case because of the variability of the slice thickness obtained in sagittally reformatted images, and because of the different liver widths between dogs. Selecting a standardised image FOV for all cadavers would have eliminated differences in sagittal image intervals between dogs in the same stack and strengthened the methodology. However, a larger than necessary FOV would have reduced image resolution for the smaller dogs and would have deteriorated the ability to trace the liver margins accurately. Although accurate differentiation of hepatic margins in thawed cadavers is likely more challenging than in vivo patients who often receive intravenous contrast medium, our proposed method was still accurate in determining hepatic volume.

In conclusion, this simplified method of CT liver volumetry is accurate and time efficient in this small sample of dogs with normal appearing livers. Hepatic volume determination can be performed in less than four minutes using widely available software by a trained observer even with limited imaging experience. Our findings may facilitate hepatic volumetry in clinical practice, as well as simplify further research that requires hepatic volume determination.

List of author contributions:

Category 1

(a) Conception and Design: Israeliantz, Schwarz
(b) Acquisition of Data: Israeliantz, Lodzinska, Woods, Pontes
(c) Analysis and Interpretation of Data: Israeliantz, Lodzinska, Woods, Pontes, Parys, Schwarz

Category 2
References


SUPPLEMENT 1. Summary of dogs’ signalments, liver widths and hepatic volumes determined by water displacement.

<table>
<thead>
<tr>
<th>Breed</th>
<th>Weight (kg)</th>
<th>Liver width (mm)</th>
<th>Water displacement liver volume (ml)</th>
<th>Median CT liver volume (% of water displacement volume)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dog 1 Whippet</td>
<td>12.8</td>
<td>120.3</td>
<td>390</td>
<td>102 (86 – 105)</td>
</tr>
<tr>
<td>Dog 2 Whippet</td>
<td>14</td>
<td>123.9</td>
<td>330</td>
<td>120 (102 – 133)</td>
</tr>
<tr>
<td>Dog 3 Crossbreed</td>
<td>6.7</td>
<td>100.94</td>
<td>240</td>
<td>100 (83 – 113)</td>
</tr>
<tr>
<td>Dog 4 English Bulldog</td>
<td>28.2</td>
<td>218.84</td>
<td>675</td>
<td>116 (99 – 143)</td>
</tr>
<tr>
<td>Dog 5 Crossbreed</td>
<td>26.8</td>
<td>168.12</td>
<td>850</td>
<td>98 (91 – 102)</td>
</tr>
</tbody>
</table>

**TABLE 1.** Details of the intervals utilised between contoured image slices for each stack and dog in mm and in number of image slices.

<table>
<thead>
<tr>
<th>Breed</th>
<th>Interval stack A (N° images)</th>
<th>Interval stack A (mm)</th>
<th>Interval stack B (N° images)</th>
<th>Interval stack B (mm)</th>
<th>Interval stack C (N° images)</th>
<th>Interval stack C (mm)</th>
<th>Interval stack D (N° images)</th>
<th>Interval stack D (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dog 1 Whippet</td>
<td>4</td>
<td>2.039</td>
<td>8</td>
<td>4.078</td>
<td>16</td>
<td>8.156</td>
<td>32</td>
<td>16.313</td>
</tr>
<tr>
<td>Dog 2 Whippet</td>
<td>5</td>
<td>2.129</td>
<td>10</td>
<td>4.258</td>
<td>20</td>
<td>8.516</td>
<td>40</td>
<td>17.031</td>
</tr>
<tr>
<td>Dog 3 Crossbreed</td>
<td>4</td>
<td>1.484</td>
<td>8</td>
<td>2.969</td>
<td>16</td>
<td>5.937</td>
<td>32</td>
<td>11.875</td>
</tr>
<tr>
<td>Dog 4 English Bulldog</td>
<td>6</td>
<td>3.492</td>
<td>12</td>
<td>6.984</td>
<td>24</td>
<td>13.969</td>
<td>48</td>
<td>27.937</td>
</tr>
<tr>
<td>Dog 5 Crossbreed</td>
<td>5</td>
<td>2.627</td>
<td>10</td>
<td>5.254</td>
<td>20</td>
<td>10.508</td>
<td>40</td>
<td>21.016</td>
</tr>
<tr>
<td>Median</td>
<td>5</td>
<td><strong>2.129</strong></td>
<td><strong>10</strong></td>
<td><strong>4.258</strong></td>
<td><strong>20</strong></td>
<td><strong>8.516</strong></td>
<td><strong>40</strong></td>
<td><strong>17.031</strong></td>
</tr>
</tbody>
</table>
FIGURE 1. A, Transverse CT image and B, sagittally reformatted image of the cranial abdomen of dog 2 from this study, acquired with a 1-mm slice thickness and soft tissue algorithm (window width 350 HU; window level: 40 HU). The liver is contoured in white. In A, the caudal aspects of the hepatic lobes are not continuous. In B, the entire liver can be traced in a single region of interest.

FIGURE 2. Representation of the image slices selected for hepatic contouring planned over a dorsally reformatted image in soft tissue algorithm (window width: 350 HU; window level: 40 HU) of the liver of dog 5 from this study. A represents the image slices contoured using stack A (65 image slices), B represents the image slices contoured using stack B (33 image slices), C represents the image slices contoured using stack C (17 image slices), and D represents the image slices contoured using stack D (9 image slices).
FIGURE 3. Comparison of the hepatic volumes obtained by water displacement and by CT volumetry using each of the image slice stacks. Water displacement volumes are always on the left and stacks are ranged from A to D (left to right).