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1 **A Simplified CT-Volumetry Method for the Canine Liver**

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14

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16 Running head 1: Israeliantz et al.

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21 Part of the results from this paper were presented as an abstract at the ECVDI Online
22 Conference, September 17-18, 2020.

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

26

27

28 **ABSTRACT**

29 Computed tomographic (CT) liver volumetry using the slice addition technique is an accurate,
30 but time-consuming method. Commonly used DICOM-viewing software only allow
31 contouring of one area per image, which can be troublesome in transverse plane as different
32 lobes are separated. In this prospective, experimental, methods comparison study, we aimed to
33 determine if hepatic contouring using sagittal reformatting and a reduced number of images
34 would yield accurate results. CT studies were performed in five canine cadavers and reviewed
35 using sagittal reformatting. For each dog, the number of images that included the liver was
36 used to create four stacks with progressively fewer images in which the liver would be
37 contoured, each with the following median number of images: A: 60, B: 31, C: 16, and D: 9.
38 Liver volume was calculated by three observers using the different stacks of images. After CT
39 examination, the cadavers were dissected, the liver was removed, and its volume determined
40 by water displacement. Single score intraclass correlation coefficient was calculated to assess
41 interobserver agreement. Kruskal-Wallis test was used to compare water displacement and CT-
42 based volumes. There was excellent agreement between observers (ICC= 0.957; 95% CI=
43 0.908-0.982, $p < 0.0001$). No significant difference was found between the volumes obtained by
44 CT-volumetry using each of the stacks and the volumes obtained by water displacement. Using
45 sagittally reformatted images and hepatic contouring in as few as nine images can be an
46 accurate and simple method for CT-volumetry of the canine liver.

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53 **Introduction**

54 There is great variation in liver size in dogs. Liver size is influenced by physiological factors
55 such as breed, body weight and age,¹ and by changes secondary to a variety of disorders which
56 can lead to organomegaly or microhepatia.² Furthermore, the liver has the capacity to
57 regenerate and increase its size as a response to certain therapies or after partial resection.³⁻⁶
58 Liver size is one of the principal diagnostic imaging criteria for assessment of dogs with
59 suspected hepatic diseases.⁷ Semiquantitative liver assessment can be performed using various
60 imaging modalities. However, the use of cross-sectional imaging, and particularly computed
61 tomography (CT), allows quantitative assessment with good results if a more accurate
62 assessment of liver volume is required.^{4-6,8}

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

70 Multiple studies in humans¹¹⁻¹⁶ and one in dogs¹⁷ have demonstrated good accuracy in the
71 measurement of liver volume by using the CT slice addition technique. This consists of
72 manually contouring the outline of the organ on each image slice, converting the contoured
73 areas into volume and summing the volumes obtained. This is, however, time-consuming and
74 cumbersome. Another drawback is that some of the most commonly used Digital Imaging and
75 Communications in Medicine (DICOM) viewing software in veterinary practice often only
76 allow contouring one area per image slice, and in the caudal aspect of the canine liver in a
77 transverse plane, the different liver lobes are separated (**Figure 1A**).

78 Horos (Purview, Annapolis MD, USA, version 3.3.6) is a free and readily available DICOM
79 viewer software program that is widely used in the veterinary imaging community and that
80 allows a simple sagittal reformatting from transversely reconstructed images. Empirical and
81 non-validated assessment showed that the area of the canine liver was continuous using sagittal
82 reformatting instead of a transverse reconstruction (**Figure 1**). According to our literature
83 search, no previously published studies have described using sagittally reformatted images to
84 calculate hepatic volume in dogs.

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

95

96 **Methods**

97 The study was a prospective, experimental, methods comparison design and was performed on
98 canine cadavers. The dogs were donated by their owners to the Hospital for Small Animals of
99 the University of Edinburgh via the Educational Memorial Programme for teaching and
100 research purposes after being euthanised for reasons unrelated to this study. The study was
101 approved by the Veterinary Ethical Review Committee of the Royal (Dick) School of
102 Veterinary Studies (Veterinary Ethical Review Committee reference 167.19). The cadavers

103 were preserved frozen and were chosen on the basis of availability and feasibility. Sample size
104 was determined based on convenience sampling. Clinical history and age were not available
105 for the subjects.

106 The inclusion criteria were dogs of any breed and size with no recent abdominal surgery
107 performed, based on the absence of a visible scar, and the absence of a hepatic mass. The latter
108 was verified on a preliminary assessment of the CT study by a diagnostic imaging intern (N.I.)
109 with knowledge of the CT anatomy of the liver, and a board-certified veterinary radiologist
110 (T.S., European College of Veterinary Diagnostic Imaging [ECVDI], American College of
111 Veterinary Radiology [ACVR]), and on visual inspection during liver dissection by the same
112 diagnostic imaging intern and a second-year veterinary internal medicine resident (G.W.,
113 European College of Veterinary Internal Medicine-Companion Animals [ECVIM-CA]). In
114 order to facilitate CT positioning and post-mortem dissection, the cadavers were thawed for 48
115 hours prior to procedures taking place. All cadavers were weighed prior the CT examination
116 and the weight was recorded. Breed and sex were identified and recorded.

117 All canine cadavers underwent a standardized abdominal CT examination with a third-
118 generation 64-row multidetector CT scanner (Somatom[®] Definition AS, Siemens AG,
119 Erlangen, Germany). The exams were performed by the same diagnostic imaging intern
120 assisted by an experienced radiographer. All dogs were positioned in ventral recumbency. The
121 abdominal CT images were acquired with the following settings: 100 kV, 0.33 s rotation time,
122 32 x 0.6 mm collimation configuration, 512 x 512 matrix and a collimator pitch of 1.4. The
123 current was automatically and individually selected by an automatic exposure control system
124 (Care Dose 4D, Siemens Medical Solutions, International) depending on the body size and
125 shape on the topogram scan. This resulted in different mAs between the dogs. The field of view
126 (FOV) was adapted to the size of each dog and ranged from 190 to 298 mm, mean 247 mm.
127 Transverse images were reconstructed with 1mm slice width at 0.5 mm interval using a

128 medium-frequency abdomen-specific soft tissue algorithm (Siemens proprietary iterative
129 kernel I40f) and stored in DICOM format on a local picture archiving and communication
130 system.

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

140 For each dog, four stacks of image slices in which the liver would be contoured were created.
141 Each stack included a different number of image slices, with different intervals between them.
142 In order to create these stacks, the two most lateral images that included the liver were
143 determined by consensus between a diagnostic imaging intern (N.I.) and a board-certified
144 veterinary radiologist (T.S.). The number of image slices between the two most lateral images
145 of the liver generated by the Sagittal Orientation tool was counted and recorded. The recorded
146 image number was divided by 64, and the result was rounded to the closest whole number. This
147 number was defined as the smallest interval and was used to create the first stack of image
148 slices on which the observers would contour the livers. For the purpose of this study, this was
149 defined as stack A, representing the largest group of image slices with the smallest intervals
150 between them. The interval used to create stack A was then multiplied by 2 (stack B), then 4
151 (stack C), and then 8 (stack D). This resulted in four image stacks with progressively fewer
152 image slices and progressively larger intervals between them (**Figure 2**). An observer-specific

153 spreadsheet was created, listing the exact locations of all image slices to be contoured (DICOM
154 annotation: image x / y, R → L) for each stack in each dog. The two lateralmost image slices
155 of the liver were included in all lists. Three observers with different grades of experience
156 independently performed liver contouring and CT-volume calculation: one final year
157 veterinary diagnostic imaging resident (J.L., ECVDI), and two diagnostic imaging interns (N.I.
158 and J.P.). All were familiar with the CT anatomy of the liver and the use of the DICOM viewer
159 software. Observers were familiarised with the contouring method and the use of the
160 spreadsheet in a training session on another dog, not included in the study. They were unaware
161 of the liver volumes prospectively obtained by water displacement, and of the volume results
162 of the other observers. Liver contouring was performed by manually drawing a region of
163 interest (ROI) on the pre-defined image slices using the pencil tool. The gallbladder was
164 excluded from the ROIs, as previously described.⁴ The caudal vena cava was not consistently
165 recognisable from the surrounding hepatic parenchyma, hence it was included in the ROIs.
166 After contouring the liver, volume was calculated for each stack using the volume computing
167 tool, and the result was recorded. The volume computing tool first fills in gaps between
168 contoured image slices by interpolating missing ROIs in the non-contoured image slices, and
169 then calculates the total volume of all areas of interest and generates a corresponding 3D model.
170 This interpolation process is done by a proprietary software of the DICOM viewer of which
171 the technical details have not been published.¹⁸ The combined contouring and liver volume
172 calculation session duration for each stack and dog was measured in minutes and the timing
173 was recorded.

174 Immediately after the CT examinations, an anatomical dissection was performed of the
175 cadavers, in which the livers were resected, and the gallbladders were removed. The livers were
176 visually examined by a diagnostic imaging intern (N.I.) and a second-year veterinary internal
177 medicine resident (G.W.) for any gross abnormalities. Each liver was then submerged in a

178 known volume of water within a calibrated measuring tube. The volume of water displaced
179 was recorded. Measurements were repeated three times and the mean value was calculated and
180 utilised in further analysis.

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

192

193 **Results**

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

198 In all dogs, it was possible to contour the liver with a single continuous ROI using sagittally
199 reformatted images. Hepatic volumes obtained by CT volumetry ranged from 336 ml to 410
200 ml (median 396 ml) for dog 1, from 339 ml to 441 ml (median 397 ml) for dog 2, from 198 ml
201 to 272 ml (median 239 ml) for dog 3, from 667 ml to 963 ml (median 780 ml) for dog 4, and
202 from 771 ml to 863 ml (median 831 ml) for dog 5. Hepatic volumes determined by water

203 displacement and the percentage of the CT volume measurements relative to the water
204 displacement volumes, together with dogs' breeds, weights and liver widths are summarised in
205 **Supplement 1**. No significant difference was found between the volumes obtained using each
206 of the stacks of image slices and the volumes obtained by water displacement when calculated
207 for all dogs jointly, nor when the comparison was done for each individual dog (**Figure 3**).
208 Slice thickness on sagittal orientation ranged from 0.371 mm to 0.582 mm (median 0.509 mm),
209 determined by variations in the reconstruction diameter between dogs. Liver width in mm
210 ranged from 100.94 to 218.84 (median 123.9 mm). Liver width in number of image slices
211 ranged from 236 to 376 (median 291 image slices). The number of image slices included in
212 stack A ranged from 58 to 65 (median 60), in stack B ranged from 30 to 33 (median 31), in
213 stack C ranged from 16 to 17 (median 16), and in stack D was 9 for all dogs. The intervals
214 between the contoured image slices for each stack and dog are detailed in **Table 1**.
215 There was excellent agreement between observers (ICC = 0.957; 95% CI = 0.908 – 0.982, $p <$
216 0.0001). The mean time employed to perform liver volumetry using stacks A was 21 min 19 s
217 (SD = 3 min 47 s), using stacks B was 11 min 35 s (SD = 2 min 14 s), using stacks C was 6
218 min 12 s (SD = 1 min 13 s), and using stacks D was 3 min 20 s (SD = 40 s). The more
219 experienced observer required less time to calculate liver volumetry using each stack compared
220 to the other two observers ($p < 0.05$).

221

222 **Discussion**

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

227 inconvenience of having separated hepatic lobes in the caudal aspect of the canine liver in
228 transverse reconstruction.

229 Liver volumetry has been established as a simple method for assessment of efficacy of both
230 intra- and extra-hepatic portosystemic shunt treatment in dogs, with increases in volume
231 documented after surgical attenuation of the shunting vessel.^{6,8} Other indicators of successful
232 shunt attenuation such as hepatic arterial perfusion require specific software, whereas hepatic
233 volumetry can be performed on free and commonly used DICOM viewing software such as
234 Horos. Studies comparing efficacy of different treatment options for dogs with portosystemic
235 shunts are currently lacking in the veterinary literature. Our findings may simplify the
236 methodology of further research in this field.

237 In our sample population, manually contouring the liver in as few as nine image slices did not
238 have a negative effect on the accuracy of the measurements. Experimental studies in human
239 medicine have shown similar results.¹⁹ Our search of the veterinary literature revealed no
240 studies evaluating the effect of reducing the number of contoured slice images over the
241 accuracy of hepatic CT volumetry using the slice addition technique. The few studies that have
242 utilised this technique in veterinary patients either have contoured every slice image where the
243 liver was visible, or have not detailed the method.^{4-6,8,17} It is important to note that the two
244 lateralmost image slices that included the liver were always manually contoured. Horos'
245 volume computing tool is able to automatically interpolate missing ROIs as long as they are
246 included between two image slices with manually contoured ROIs.

247 The principal inconvenience of manual liver CT volumetry methods is that they are time
248 consuming. In human medicine, this has been overcome by the use of semiautomated and
249 automated methods that are considerably more time efficient, but that often require specific
250 software.²⁰ We propose a simplified and time efficient semiautomated method that does not
251 require any software additional to what is usually available in clinical practice. Intuitively, and

252 as shown in our results, reducing the number of manual contours of the liver had a drastic
253 impact on the time required to perform CT liver volumetry, with a difference of almost 18
254 minutes between using stack A and using stack D. Our results show that this simplified
255 semiautomated method can be performed in less than 4 minutes. In our sample population, this
256 did not translate into a loss of accuracy. On the contrary, in the dogs with the largest errors
257 (dog 2 and 4), although not statistically significant, there was a greater discrepancy between
258 the liver volumes obtained by water displacement and CT using the stacks with the larger
259 number of image slices. These differences were of approximately 33% for stack A *versus* 12%
260 for stack D in dog 2; and of approximately 21% for stack A *versus* 15% for stack D in dog 4.
261 Similar discrepancies have been reported between CT liver volumetry and water displacement
262 measurements in human living patients, with overestimations of up to 34% possibly explained
263 by perioperative loss of blood, lack of perfusion and inaccurate contouring of the liver.¹¹ Given
264 that our study was performed in cadavers, loss of blood or lack of perfusion are not likely to
265 have had a significant impact in the total volume obtained, even if a small amount of blood
266 may have been lost during dissection due to the caudal vena cava not being tied off before
267 hepatic resection. However, inaccurate hepatic contouring in image slices only included in the
268 stacks the largest number of images could explain the slightly greater error when using these
269 stacks. We believe that the risk of inaccurate hepatic contouring would be minimised in living
270 dogs, for which our technique is intended, and in which the use intravenous contrast media is
271 common practice and facilitates the recognition of the borders of the organ. A study in sheep²¹
272 demonstrated that smaller livers (under 600 ml) are more likely to be overestimated when CT-
273 volumetry is performed. This might be of particular relevance in dogs with extra-hepatic
274 portosystemic shunts, where small breed dogs are overrepresented and small liver volumes are
275 expected.⁶ Further studies with larger samples representing this group of dogs would be needed
276 to assess the impact of this possible source or error.

277 Two of the observers in our study were less experienced than the third one. Our results indicate
278 that after a short training session, accurate liver volumetry can be performed adequately, even
279 by relatively inexperienced observers. Contrary to our hypothesis, the time employed by the
280 most experienced observer was significantly less, which can be explained by their greater
281 confidence in both the CT anatomy of the canine liver and use of the viewing software. Our
282 results are in agreement with what has been reported in human literature.¹⁶

283 There are several limitations to the study. The small sample size did not allow statistical
284 assessment of variations in body weight and hepatic volume, although dogs included in the
285 study had weights that are commonly seen within our hospital population. Additionally, we did
286 not aim to provide a cut-off minimum number of image slices that need to be contoured, but to
287 demonstrate that a simplified, time efficient semiautomated CT liver volumetry method is
288 possible. An additional limitation is that, due to our inclusion and exclusion criteria, only dogs
289 with grossly normal livers were included in our sample, preventing extrapolation of our results
290 to populations where the hepatic contour may be irregular due to chronic hepatic disease, or
291 distorted by the presence of space-occupying lesions. In human patients undergoing major
292 hepatic resection, approximately 25% of healthy liver parenchyma needs to be preserved in
293 order to prevent postresectional liver failure, and this percentage increases up to 50% if the
294 liver is cirrhotic.¹⁶ Equivalent data is lacking in the veterinary literature, but experimental
295 surgical models in dogs have attempted up to 90% hepatic resection with 7 days survivals
296 recorded after the procedure.²² Although the results of this experimental model are hardly
297 extrapolatable to a real clinical setting, they suggest that, as in human patients, major hepatic
298 resection is possible in dogs. Further studies in dogs with diffuse or focal changes in hepatic
299 contour are warranted to assess the accuracy of CT-volumetry and to establish if the margin of
300 error of this method is acceptable for determination of hepatic remnant volume prior to major
301 partial hepatectomy.

302 In our study, the thickness of the intervals used for the different stacks of contoured image
303 slices varied between dogs. This was the case because of the variability of the slice thickness
304 obtained in sagittally reformatted images, and because of the different liver widths between
305 dogs. Selecting a standardised image FOV for all cadavers would have eliminated differences
306 in sagittal image intervals between dogs in the same stack and strengthened the methodology.
307 However, a larger than necessary FOV would have reduced image resolution for the smaller
308 dogs and would have deteriorated the ability to trace the liver margins accurately. Although
309 accurate differentiation of hepatic margins in thawed cadavers is likely more challenging than
310 in vivo patients who often receive intravenous contrast medium, our proposed method was still
311 accurate in determining hepatic volume.

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

317

318

319 List of author contributions:

320 Category 1

321 (a) Conception and Design: Israeliantz, Schwarz

322 (b) Acquisition of Data: Israeliantz, Lodzinska, Woods, Pontes

323 (c) Analysis and Interpretation of Data: Israeliantz, Lodzinska, Woods, Pontes, Parys,
324 Schwarz

325

326 Category 2

- 327 (a) Drafting the Article: Israeliantz, Schwarz
328 (b) Revising the Article for Intellectual Content: Israeliantz, Lodzinska, Woods,
329 Pontes, Parys, Schwarz

330

331 Category 3

- 332 (a) Final Approval of the Completed Article: Israeliantz, Lodzinska, Woods, Pontes,
333 Parys, Schwarz

334

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401 **SUPPLEMENT 1. Summary of dogs' signalments, liver widths and hepatic volumes**
 402 **determined by water displacement.**

403

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

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405

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

408

	Interval stack A (N ^o images)	Interval stack A (mm)	Interval stack B (N ^o images)	Interval stack B (mm)	Interval stack C (N ^o images)	Interval stack C (mm)	Interval stack D (N ^o images)	Interval stack D (mm)
Dog 1	4	2.039	8	4.078	16	8.156	32	16.313
Dog 2	5	2.129	10	4.258	20	8.516	40	17.031
Dog 3	4	1.484	8	2.969	16	5.937	32	11.875
Dog 4	6	3.492	12	6.984	24	13.969	48	27.937
Dog 5	5	2.627	10	5.254	20	10.508	40	21.016
Median	5	2.129	10	4.258	20	8.516	40	17.031

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424 **Figures**

425

426 FIGURE 1. A, Transverse CT image and B, sagittally reformatted image of the cranial
427 abdomen of dog 2 from this study, acquired with a 1-mm slice thickness and soft tissue
428 algorithm (window width 350 HU; window level: 40 HU). The liver is contoured in white. In
429 A, the caudal aspects of the hepatic lobes are not continuous. In B, the entire liver can be traced
430 in a single region of interest.

431

432 FIGURE 2. Representation of the image slices selected for hepatic contouring planned over a
433 dorsally reformatted image in soft tissue algorithm (window width: 350 HU; window level: 40
434 HU) of the liver of dog 5 from this study. A represents the image slices contoured using stack
435 A (65 image slices), B represents the image slices contoured using stack B (33 image slices),
436 C represents the image slices contoured using stack C (17 image slices), and D represents the
437 image slices contoured using stack D (9 image slices).

438

439 FIGURE 3. Comparison of the hepatic volumes obtained by water displacement and by CT
440 volumetry using each of the image slice stacks. Water displacement volumes are always on the
441 left and stacks are ranged from A to D (left to right).