

RVC OPEN ACCESS REPOSITORY – COPYRIGHT NOTICE

This author's accepted manuscript may be used for non-commercial purposes in accordance with [Wiley Terms and Conditions for Self-Archiving](#).

The full details of the published version of the article are as follows:

TITLE: Can malignant and inflammatory pleural effusions in dogs be distinguished using computed tomography

AUTHORS: Thom C. Watton, Ana Lara-Garcia, Christopher R. Lamb

JOURNAL TITLE: Veterinary Radiology & Ultrasound

PUBLISHER: Wiley

PUBLICATION DATE: 16 July 2017 (online)

DOI: [10.1111/vru.12534](https://doi.org/10.1111/vru.12534)

1 **Can malignant and inflammatory pleural effusions in dogs be distinguished using**
2 **computed tomography?**

3 Thom C. Watton, Ana Lara-Garcia, Christopher R. Lamb

4 Department of Clinical Sciences and Services, The Royal Veterinary College, University of
5 London

6

7 Address correspondence to: C. R. Lamb, Department of Clinical Sciences and Services, The
8 Royal Veterinary College, Hawkshead Lane, North Mymms, Hertfordshire AL9 7TA, UK.

9 Tel: 01707-666234

10 Email: clamb@rvc.ac.uk

11 Key words: computed tomography, chylothorax, dog, mesothelioma, pleural disease,
12 pyothorax

13 Running head: CT of pleural effusions

14 Funding Sources: The authors received no financial support for the research, authorship or
15 publication of this article.

16 Abstract

17 Computed tomography (CT) is the primary imaging modality used to investigate human
18 patients with suspected malignant or inflammatory pleural effusion, but there is a lack of
19 information about the clinical use of this test in dogs. In order to identify CT signs that could
20 be used to distinguish pleural malignant neoplasia from pleuritis, a retrospective case-
21 control study was done based on dogs that had pleural effusion, pre- and post-contrast
22 thoracic CT images, and cytological or histopathological diagnosis of malignant or
23 inflammatory pleural effusion. There were 20 dogs with malignant pleural effusion (13
24 mesothelioma, 6 carcinoma; 1 lymphoma), and 32 dogs with pleuritis (18 pyothorax; 14
25 chylothorax). Compared to dogs with pleuritis, dogs with malignant pleural effusions were
26 significantly older (median 8.5 years versus 4.9 years, $p=0.001$), more frequently had CT
27 signs of pleural thickening (65% versus 34%, $p= 0.05$), tended to have thickening of the
28 parietal pleura only (45% versus 3%, $p=0.002$) and had more marked pleural thickening
29 (median 3mm versus 0mm, $p=0.03$). CT signs of thoracic wall invasion were observed only in
30 dogs with malignant pleural effusions ($p= 0.05$). There were no significant differences in
31 pleural fluid volume, distribution or attenuation, degree of pleural contrast accumulation,
32 amount of pannus, or prevalence of mediastinal adenopathy. Although there was
33 considerable overlap in findings in dogs with malignant pleural effusion and pleuritis,
34 marked thickening affecting the parietal pleural alone and signs of thoracic wall invasion on
35 CT support diagnosis of pleural malignant neoplasia, and may help prioritize further
36 diagnostic testing.

37 Introduction

38 Pleural fluid accumulation may occur as a result of several different pathologic mechanisms
39 that determine the nature of the fluid.¹ Inspection of pleural fluid is the basis for tentative
40 diagnosis in many instances²; however, pleural fluid containing blood, moderate protein and
41 non-specific cellular content can occur with neoplasia, inflammatory or idiopathic
42 conditions^{3,4}, and fluid analysis alone may be insufficient for diagnosis. Although low in
43 prevalence, the neoplasms that most frequently cause pleural effusion in dogs by direct
44 seeding and invasion of the pleura are mesothelioma and carcinoma. Mesothelioma, a
45 primary malignant neoplasm of the pleura⁵⁻⁷, pericardium⁸⁻¹⁰ or peritoneum¹⁰⁻¹², can be
46 particularly difficult to diagnose on routine cytologic preparations because malignant
47 mesothelial cells may appear similar to the reactive mesothelial cells seen with
48 inflammatory pleural conditions.^{1,6,13,14} Carcinoma metastasis to the pleura can also be
49 difficult to diagnose cytologically and may require immunocytochemical analysis of the
50 effusion or histopathology.¹⁵ Metastasis to the pleura could occur with any type of
51 carcinoma, but in the dog this condition is mainly associated with primary epithelial lung
52 tumors, mammary carcinoma, prostatic carcinoma and transitional cell carcinoma of the
53 urinary bladder.¹⁶ Dogs with pleural carcinoma (or sarcoma) usually have a primary tumor
54 elsewhere, the detection of which aids diagnosis of the pleural effusion.

55 Diagnostic imaging is indicated for patients with pleural effusion of unknown cause.
56 Depending on clinical signs, ultrasonography and/or radiography may be performed first
57 and may enable detection of various well-recognized predisposing causes of pleural
58 effusion, such as thoracic masses, lung lobe torsion, pericardial disease, and cardiac failure.
59 When echocardiography and radiography are negative or findings are non-specific,

60 computed tomography (CT) is indicated to examine the thorax in more detail.¹⁷ CT is the
61 primary imaging modality used for humans with suspected pleural neoplasia.¹⁸⁻²¹ There have
62 been numerous studies of the CT features of pleural mesothelioma and other pleural
63 malignancies in humans.¹⁸⁻²⁴ CT features that support a diagnosis of pleural malignant
64 neoplasia rather than pleuritis include pleural thickening >1cm, nodular thickening,
65 interlobar distribution of thickening, and thoracic volume contraction.¹⁸⁻²⁶

66 There have been fewer reports of imaging findings in dogs with malignant neoplasia
67 affecting primarily the pleura. The radiographic signs primarily represent pleural or
68 pericardial fluid accumulation, although pleural masses due to mesothelioma may be visible
69 in radiographs made after fluid drainage.⁶ Few reports describe use of CT to examine the
70 pleura in dogs. Multifocal, irregular thickening of the parietal pleura on CT was illustrated in
71 a report of a dog with pleural mesothelioma.²⁷ Pleural thickening in CT images was also
72 reported in 8/12 (67%) dogs²⁸ and 3/10 (30%) dogs²⁹ with pyothorax, but was not described
73 in detail. A more recent study³⁰ described the CT findings in 7 dogs with various pleural
74 conditions including primary and metastatic neoplasia and pleuritis. Masses and nodular
75 lesions affecting the pleura were observed in 5/7 (71%) dogs, but there was no apparent
76 association between the morphologic features of pleural lesions and the specific diagnosis.³⁰

77 Even on gross inspection, pleural masses due to mesothelioma may resemble granulation
78 tissue.¹⁰ For patients in which pleural masses are suspected but not visualized clearly or
79 imaging findings are non-specific, thoracoscopy or thoracotomy for pleural biopsy is
80 indicated.

81 The aim of the present study was to compare the results of CT in a larger series of dogs with
82 pleural effusion secondary to pleural malignant neoplasia or pleuritis in order to identify
83 signs that could be used to distinguish these conditions.

84

85 **Materials and Methods**

86 Ethical approval was granted by the Clinical Research Ethical Review Board at the Royal
87 Veterinary College. For this retrospective case-control study, medical records from the
88 Queen Mother Hospital for Animals (QMHA) in the period 2010-2016 were searched by one
89 observer (TCW) for dogs that had pleural effusion, pre- and post-contrast thoracic CT
90 images, and cytologic or histopathologic diagnosis of pleural effusion secondary to pleural
91 malignant neoplasia or pleuritis. For the purposes of this study, pleuritis included pyothorax
92 and chylothorax. Although chylothorax has various primary causes, the effect of chyle on
93 the pleura is inflammatory.³¹ Dogs with primary neoplasia affecting non-pleural thoracic
94 structures were not included. Dogs in which a migrating thoracic foreign body was visible in
95 CT images were also not included.

96 Diagnosis of malignant pleural neoplasia was based on compatible cytologic, histologic
97 and/or immunohistochemical findings. Criteria for pleural malignant neoplasia were
98 characteristic cellular morphology on cytologic¹⁶ or histologic preparations and, when
99 diagnosis was uncertain, immunocytochemistry or immunohistochemistry for vimentin and
100 cytokeratin.¹⁵ Diagnosis of pyothorax was based on cytologic evidence of suppurative
101 bacterial infection of pleural fluid with or without positive culture. Diagnosis of chylothorax
102 was based on finding small lymphocytes to be the most numerous cell type and elevated

103 pleural fluid triglyceride concentration (>2.84mmol/L). In all instances, diagnosis by a board-
104 certified veterinary clinical pathologist was required for inclusion in the study.

105 As part of the inclusion criteria, all CT images were acquired using the same multi-slice
106 scanner (MX8000 IDT, Phillips Best, the Netherlands), and transverse images were reviewed
107 using a DICOM viewer (OsiriX version 7.01). Studies lacking pre- and post-contrast series
108 obtained with optimal settings for soft tissue examination were excluded. For the purposes
109 of this study, optimal settings were helical acquisition, slice thickness up to 3mm, medium
110 frequency ('soft tissue') reconstruction algorithm, and with post-contrast CT images
111 acquired 60 seconds after the start of intravenous injection of 2ml/kg of iohexol 300mg/ml
112 (Omnipaque 300, GE Healthcare, Oslo, Norway). Studies with evidence of excessive motion
113 blur were also excluded.

114 All CT studies were reviewed by a single board-certified radiologist (CRL) without
115 knowledge of signalment, clinical history or diagnosis. In cases where multiple CT studies
116 had been done, only the first CT study with evidence of pleural effusion was selected for
117 review. CT images were reviewed using soft tissue (width 320 HU; level 80 HU) and lung
118 (width 1500 HU; level -500 HU) windows with reference to several subjective and objective
119 criteria. The presence of pericardial, pleural or mediastinal fluid, the distribution of pleural
120 fluid (symmetrical or asymmetrical), presence of pleural thickening, presence of pannus,
121 mediastinal lymphadenopathy, and evidence of thoracic wall invasion were recorded.
122 Pleural fluid average attenuation measurements (Hounsfield units, HU) were made using a
123 single circular region of interest placed on the largest visible collection of pleural fluid in pre-
124 contrast images. Pleural thickening was defined as a hyperdense line at the border of
125 pleural fluid collections in post-contrast CT images, and was classified by site (visceral,

126 parietal or both) and morphology (diffuse, lobar, nodular, mass-like and/or calcified).
127 Attenuation measurements using a point region of interest and a thickness measurement
128 (mm) were recorded at the site of maximal pleural thickening where applicable. The term
129 pannus refers to fibrovascular tissue within the pleural cavity that tends to form sheets and
130 exhibits enhancement following intravenous contrast administration. Subjective assessment
131 of pleural fluid volume, amount of pannus, and degree of mediastinal lymphadenopathy
132 were recorded using an ordinal scale (0, none; 1, slight; 2, marked). Diagnosis of thoracic
133 wall invasion was based on observing thickening of intercostal muscles, loss of
134 intermuscular fat planes, streaking of intercostal or sub-cutaneous fat, periosteal reaction
135 on ribs or sternebrae and/or lysis of ribs or sternebrae.

136 Data were analyzed using a commercial statistical software package (SPSS 22, IBM). Fisher's
137 exact test was used to test differences in categorical data, and Mann-Whitney tests were
138 utilized to test differences in continuous data between dogs that had pleural malignant
139 neoplasia or pleuritis. Differences with $p < 0.05$ were considered significant. Binomial 95%
140 confidence intervals (CI) for estimates of likelihood ratios were determined using the
141 statistical calculator provided by the Centre for Evidence Based Medicine
142 (<http://ktclearinghouse.ca/cebm/practise/ca/calculators/statscalc>).

143

144 **Results**

145 Fifty-two dogs satisfied all criteria for inclusion in the study. There were 24 females (14
146 neutered) and 28 males (18 neutered) representing 22 different pedigree dog breeds plus 6
147 crossbred dogs. Twenty dogs had pleural malignant neoplasia (13 mesothelioma, 6
148 metastatic carcinoma, 1 lymphoma) and 32 had pleuritis (18 pyothorax, 14 chylothorax).

149 Diagnosis of mesothelioma was based on histology in 8 dogs, immunohistochemistry in one,
150 immunocytochemistry in one and cytology in 3 dogs. Diagnosis of carcinoma or lymphoma
151 was based on cytology in each instance. Median age of dogs that had pleural malignant
152 neoplasia was 8.5 years (range 4.0-12.8 years) compared to 4.9 years (range 1.3-13.0 years)
153 for dogs with pleuritis ($p=0.001$).

154 Results of CT are summarized in Table 1. Pleural thickening was the sign most frequently
155 observed in dogs with malignant pleural effusion (figure 1) whereas enlarged mediastinal
156 lymph nodes was the sign most frequently observed in dogs with pleuritis. Dogs with
157 malignant pleural effusion more frequently had CT signs of pleural thickening (65% versus
158 34%, $p=0.03$), tended to have thickening of the parietal pleura only (65% versus 13%,
159 $p=0.01$) and had more marked pleural thickening (median 3mm versus 0mm, $p=0.01$). CT
160 signs of thoracic wall invasion were observed only in dogs with malignant pleural effusions
161 ($p=0.05$) (figure 2). Likelihood ratios for pleural malignant neoplasia for categorical CT signs
162 of significance or borderline significance were: pleural thickening 1.9 (95% CI 1.1-3.0);
163 parietal pleural thickening only 5.2 (95% CI 2.0-13.7); and thoracic wall invasion 11.0 (95% CI
164 0.6-202.4). The likelihood ratio for visceral pleural thickening as a signs of pleuritis was 3.1
165 (95% CI 0.8-12.8). The criterion pleural thickening >1 cm was not significantly associated with
166 pleural malignant neoplasia. There were also no significant differences in pleural fluid
167 volume, distribution or attenuation, degree of pleural contrast accumulation, amount of
168 pannus (figure 3) or prevalence of mediastinal adenopathy or pulmonary nodules. Cause of
169 pulmonary nodules in dogs with pleuritis was not determined: none had signs of malignant
170 neoplasia affecting non-thoracic structures, but none were examined pathologically.

171

172 Discussion

173 In this study there was marked overlap in the CT signs observed in dogs with malignant
174 pleural effusion and dogs with pleuritis. As reported in humans¹⁸⁻²⁶, pleural thickening may
175 be observed in patients with either malignant effusion or pleuritis, hence although CT is
176 indicated as an aid to differential diagnosis of pleural effusion, it appears to be inaccurate.
177 In the dogs in the present series, the most discriminating CT sign (i.e. that with the highest
178 likelihood ratio for pleural malignancy) was thoracic wall invasion; however, this was
179 observed in only 15% dogs with mesothelioma, which suggests it is not a sensitive sign, and
180 was of borderline statistical significance because of the wide confidence interval associated
181 with small number of affected dogs. Parietal pleural thickening in the absence of visceral
182 pleural thickening also appears to be a useful discriminating sign. This was observed in 45%
183 dogs with malignant pleural effusion and only 3% dogs with pleuritis. Conversely, visceral
184 pleural thickening was observed in 10% dogs with malignant pleural effusion and 31% dogs
185 with pleuritis, although this difference was not significant. Malignant pleural effusion was
186 associated with a greater median pleural thickening than pleuritis, but there were no
187 significant differences in the prevalence of nodular thickening or calcified pleural lesions.
188 Foci of calcification or ossification in mesotheliomas has been reported infrequently in
189 dogs⁸, hence the potential diagnostic value of this sign appears to be limited.

190 The normal pleura of humans is too thin to be visible in CT images.²⁰ On the basis of
191 unpublished observations in a limited number of dogs with pleural transudates, we believe
192 the same is true in dogs; therefore, observing a hyperdense line in post-contrast CT images
193 at the border of a pleural fluid collection was considered to be evidence of pleural
194 thickening even if the line was too thin for accurate measurement of thickness or

195 attenuation value. Visceral pleural thickening is most clearly visible in animals that also have
196 pneumothorax (usually because of pleural drain placement).

197 The mechanisms that promote pleural effusion are similar in animals with neoplastic and
198 inflammatory pleural conditions, including increased permeability of the pleural
199 microvasculature and impaired lymphatic drainage from the pleural cavity because of tumor
200 or fibrosis obstructing lymphatic vessels.^{1,20} The presence of a thoracostomy tube can also
201 induce pleural effusion, with potential for secondary infection when tubes have been in
202 placed more than a few days.³²

203 Markedly asymmetrical (including unilateral) distribution of pleural fluid was observed in
204 the present study only in dogs with pleuritis, and has been noted in an earlier study of dogs
205 with pyothorax.²⁸ This finding could reflect restricted flow of pleural fluid by increased
206 viscosity and/or obstruction of normal routes by fibrin 'peel' that coats the pleura.

207 Organization of fibrin peel with ingrowth of capillaries and fibroblasts occurs within 7 days
208 of the onset of pleuritis.²⁰ Pannus is a term used for fibrovascular tissue that occurs in
209 inflammatory conditions that tends to form sheets over structures, such as the cornea.³³

210 This term is also applicable to the sheet- or mass-like tissue that replaces fibrin peel in dogs
211 with inflammatory or reactive pleural effusion.³⁴ In CT images, pannus may be distinguished
212 from fibrin peel because it enhances after intravenous contrast administration, and
213 distinguished from true pleural thickening when it occupies the pleural cavity with minimal
214 contact with the pleural surfaces; however, without detailed imaging-pathologic correlation,
215 it is possible that some masses due to pleural neoplasia in this series could have been
216 misinterpreted as pannus, and vice versa, particularly when pannus is thick and/or in broad
217 contact with the pleura. Compared to CT, ultrasonography may be advantageous in

218 distinguishing these entities because real-time imaging displaying motion of sheet-like tissue
219 would support diagnosis of pannus; however, sessile, immobile pleural masses may remain
220 difficult to diagnose on the basis of their imaging features alone.

221 Diagnosis of malignant pleural effusion is most challenging in patients in which no primary
222 neoplasm can be found elsewhere in the body. Whereas most dogs with pleural carcinoma
223 will have a primary neoplasm in the lung or abdomen, no other primary neoplasm will be
224 found in dogs with mesothelioma, hence mesothelioma is the more challenging diagnosis. In
225 the present study, only 3 dogs with mesothelioma were diagnosed on the basis of cytology
226 alone; most required immunological testing or histology. When mesothelioma is suspected
227 there is a need for detailed examination of the pleura. The importance of the present study
228 is that it provides new information about use of CT to examine the pleura, which should
229 help address this clinical problem.

230 To minimize bias, and to replicate the indication for detailed imaging examination of the
231 pleura, we did not include dogs in this study whose CT images contained signs that strongly
232 suggested either neoplasia or inflammatory conditions, such as intrathoracic masses or
233 foreign material. Presence of a pulmonary mass, for example, could bias an observer
234 towards an assumption of malignant pleural effusion, and to overemphasize related findings
235 such as adenopathy or pleural thickening. The occurrence of pulmonary nodules in a similar
236 proportion of dogs with malignant effusion and dogs with pleuritis emphasizes the non-
237 specific nature of that finding.

238 The main limitation of the present study is the small number of dogs included. This mainly
239 reflects the difficulty collecting larger numbers of dogs with primary pleural neoplasia, but is
240 problematic because it means that our estimates of the prevalence of various CT features

241 will be imprecise, which limits the statistical power of the tests done to compare the
242 neoplastic and pleuritis groups.

243 Neoplastic processes resulting in pleural effusion can present a significant diagnostic
244 challenge and have been associated historically with a poor prognosis.^{6,7,13} Recent advances
245 in malignant effusion management with pleural ports and intracavitary chemotherapy
246 appear to provide an improved prognosis.^{35,36} Definite diagnosis of mesothelioma
247 sometimes requires pleural biopsy via thoracoscopy or thoracotomy. Invasive procedures
248 such as these may not be favored by veterinarians or owners in the absence of supportive
249 imaging findings. On the basis of the present study, it may be concluded that CT signs of
250 marked thickening affecting the parietal pleural alone and signs of thoracic wall invasion
251 support diagnosis of pleural malignant neoplasia whereas visceral pleural thickening
252 supports a diagnosis of pleuritis. These results may help prioritize further diagnostic testing
253 of dogs with pleural effusion.

254

255 **List of Author Contributions**

256 Category 1

257 (a) Conception and Design

258 Author name(s) Thom C. Watton, Ana Lara-Garcia, Christopher R. Lamb

259 (b) Acquisition of Data

260 Author name(s) Thom C. Watton, Ana Lara-Garcia, Christopher R. Lamb

261 (c) Analysis and Interpretation of Data

262 Author name(s) Thom C. Watton, Christopher R. Lamb

263 Category 2

264 (a) Drafting the Article

265 Author name(s) Thom C. Watton, Ana Lara-Garcia, Christopher R. Lamb

266 (b) Revising Article for Intellectual Content Author name(s) Thom C. Watton, Ana Lara-

267 Garcia, Christopher R. Lamb

268 Category 3

269 (a) Final Approval of the Completed Article Author name(s) Thom C. Watton, Ana Lara-

270 Garcia, Christopher R. Lamb

271 **References**

- 272 1. Dempsey SM, Ewing PJ. A review of the pathophysiology, classification, and analysis of
273 canine and feline cavitory effusions. *J Am Anim Hosp Assoc* 2011;47: 1-11.
- 274 2. Tyler RD, Cowell RL. Evaluation of pleural and peritoneal effusions. *Vet Clin North Am-
275 Small Anim Pract* 1989;19: 743-768.
- 276 3. Nakamura RK, Rozanski EA, Rush JE. Non-coagulopathic spontaneous hemothorax in
277 dogs. *J Vet Emerg Crit Care* 2008;18: 292-297.
- 278 4. Vogtli T, Gaschen F, VogtliBurger R, Lombard C. Hemorrhagic pericardial effusion in the
279 dog: A retrospective study of 10 cases (1989-1994) with a review of the literature.
280 *Schweizer Archiv fur Tierheilkunde* 1997;139: 217-224.
- 281 5. Dubielzig RR. Sclerosing mesothelioma in 5 dogs. *J Am Anim Hosp Assoc* 1979;15: 745-
282 748.
- 283 6. Thrall DE, Goldschmidt MH. Mesothelioma in dog - 6 case-reports. *J Am Vet Radiol Soc*
284 1978;19: 107-115.
- 285 7. Morrison WB, Trigo FJ. Clinical characterization of pleural mesothelioma in 7 dogs.
286 *Compend Contin Educ Pract Vet* 1984;6: 342-348.
- 287 8. Yamamoto S, Fukushima R, Kobayashi M, Machida N. Mixed form of pericardial
288 mesothelioma with osseous differentiation in a dog. *J Comp Pathol* 2013;149: 229-232.
- 289 9. Ceribasi S, Ozkaraca M, Ceribasi AO, Ozer H. Pericardial mesothelioma in a German
290 Shepherd dog: a case report. *Vet Med* 2013;58: 594-598.
- 291 10. Smith DA, Hill FWG. Metastatic malignant mesothelioma in a dog. *J Comp Pathol*
292 1989;100: 97-101.

- 293 11. D'Angelo AR, Di Francesco G, Quaglione GR, Marruchella G. Sclerosing peritoneal
294 mesothelioma in a dog: histopathological, histochemical and immunohistochemical
295 investigations. *Vet Ital* 2014;50: 301-305.
- 296 12. Gumber S, Fowlkes N, Cho DY. Disseminated sclerosing peritoneal mesothelioma in a
297 dog. *J Vet Diagn Invest* 2011;23: 1046-1050.
- 298 13. Mott FE. Mesothelioma: a review. *Ochsner J* 2012;12:70-79.
- 299 14. Hirsch VM, Farrow CS. A scirrhous anaplastic carcinoma in two dogs resembling
300 mesothelioma. *Can Vet J* 1981;22:271-276.
- 301 15. Przeździecki R, Sapieryński R. Using of immunocytochemistry in differential diagnosis
302 of neoplasms of serosal cavities in dogs. *Pol J Vet Sci.*2014;17(1):149-59.
- 303 16. Rebar AH, Thopson CA. Body cavity effusions. In: RE Raskin, DJ Meyer (Eds.) *Atlas of*
304 *canine and feline cytology*. WB Saunders, Philadelphia; 2010: 185-187.
- 305 17. Prather AB, Berry CR, Thrall DE. Use of radiography in combination with computed
306 tomography for the assessment of noncardiac thoracic disease in the dog and cat. *Vet*
307 *Radiol Ultrasound* 2005;46:114-121.
- 308 18. Benamore RE, O'Doherty MJ, Entwistle JJ. Use of imaging in the management of
309 malignant pleural mesothelioma. *Clin Radiol* 2005;60:1237-1247.
- 310 19. Traill ZC, Davies RJO, Gleeson FV. Thoracic computed tomography in patients with
311 suspected malignant pleural effusions. *Clin Radiol* 2001;56:193-196.
- 312 20. Müller NL. Imaging of the pleura. *Radiology* 1993;186:297-309.

- 313 21. Metintas M, Ucgan I, Elbek O, Erginel S, Metintas S, Kolsuz M, et al. Computed
314 tomography features in malignant pleural mesothelioma and other commonly seen
315 pleural diseases. *Eur J Radiol* 2001;41:1-9.
- 316 22. Sahin AA, Çöplü L, Selçuk ZT, Eryilmaz M, Emri S, Akhan O, et al. Malignant pleural
317 mesothelioma caused by environmental exposure to asbestos or erionite in rural
318 Turkey: CT findings in 84 patients. *Am J Roentgenol* 1993;161:533-537.
- 319 23. Kawashima A, Libshitz HI. Malignant pleural mesothelioma: CT manifestations in 50
320 cases. *Am J Roentgenol* 1990;155:965-969.
- 321 24. Wang ZJ, Reddy GP, Gotway MB, Higgins CB, Fablons DM, Ramaswamy M, et al.
322 Malignant mesothelioma: evaluation with CT, MR imaging, and PET. *RadioGraphics*
323 2004;24:105-119.
- 324 25. Aquino SL, Webb WR, Gushiken BJ. Pleural exudates and transudates: diagnosis with
325 contrast-enhanced CT. *Radiology* 1994;192:803-808.
- 326 26. Waite RJ, Carbonneau RJ, Balikian JP, Umali CB, Pezzela AT, Nash G. Parietal pleural
327 change in empyema: appearances at CT. *Radiology* 1990;175:145-150.
- 328 27. Echandi RL, Morandi F, Newman SJ, Holford A. Imaging diagnosis – Canine thoracic
329 mesothelioma. *Vet Radiol Ultrasound* 2007;48:243-245.
- 330 28. Swinbourne F, Baines EA, Baines, SJ, Halfacree ZJ. Computed tomographic findings in
331 canine pyothorax and correlation with findings at exploratory laparotomy. *J Small Anim*
332 *Pract* 2011;52:203-208.

- 333 29. Caivano D, Biretoni F, Rishniw M, Bufalari A, De Monte V, Proni A, et al.
334 Ultrasonographic findings and outcomes of dogs with suspected migrating intrathoracic
335 grass awns: 43 cases (2010-2013). *J Am Vet Med Assoc* 2016;248: 413-421.
- 336 30. Reetz JA, Buza EL, Krick EL. CT features of pleural masses and nodules. *Vet Radiol*
337 *Ultrasound* 2012;53:121-127.
- 338 31. Fossum TW, Evering WN, Miller MW, Forrester SD, Palmer DR, Hodges CC. Severe
339 bilateral fibrosing pleuritis associated with chronic chylothorax in 5 cats and 2 dogs. *J*
340 *Am Vet Med Assoc* 1992; 201:317-324.
- 341 32. Hung GC, Gaunt MC, Rubin JE, Starrak GS, Sakals SA. Quantification and characterization
342 of pleural fluid in healthy dogs with thoracostomy tubes. *Am J Vet Res* 2016;77: 1387-
343 1391.
- 344 33. Bedford PGC, Longstaffe JA. Corneal pannus (chronic superficial keratitis) in the German
345 Shepherd dog. *J Small Anim Pract* 1979; 20:41-56.
- 346 34. Vansteenkiste DP, Lee KCL, Lamb CR. Computed tomographic findings in 44 dogs and 10
347 cats with grass seed foreign bodies. *J Small Anim Pract* 2014;55:579-584.
- 348 35. Charney SC, Bergman PJ, McKnight JA, Farrelly J, Novosad CA, Leibman NF, et al.
349 Evaluation of intracavitary mitoxantrone and carboplatin for treatment of
350 carcinomatosis, sarcomatosis and mesothelioma, with or without malignant effusions:
351 retrospective analysis of 12 cases (1997–2002). *Vet Comp Oncol* 2005;3:171-181.
- 352 36. Lara-Garcia A, Kosarek C, Hosoya K, Alvarez F, Smeak D, Pozzi A, et al. Palliative
353 management of malignant effusion with implantable vascular access ports in dogs.
354 (abstract) *Vet Comp Oncol* 2008;6: 69-70.

355 Table 1. Computed tomographic features of malignant and inflammatory pleural effusions in
 356 52 dogs

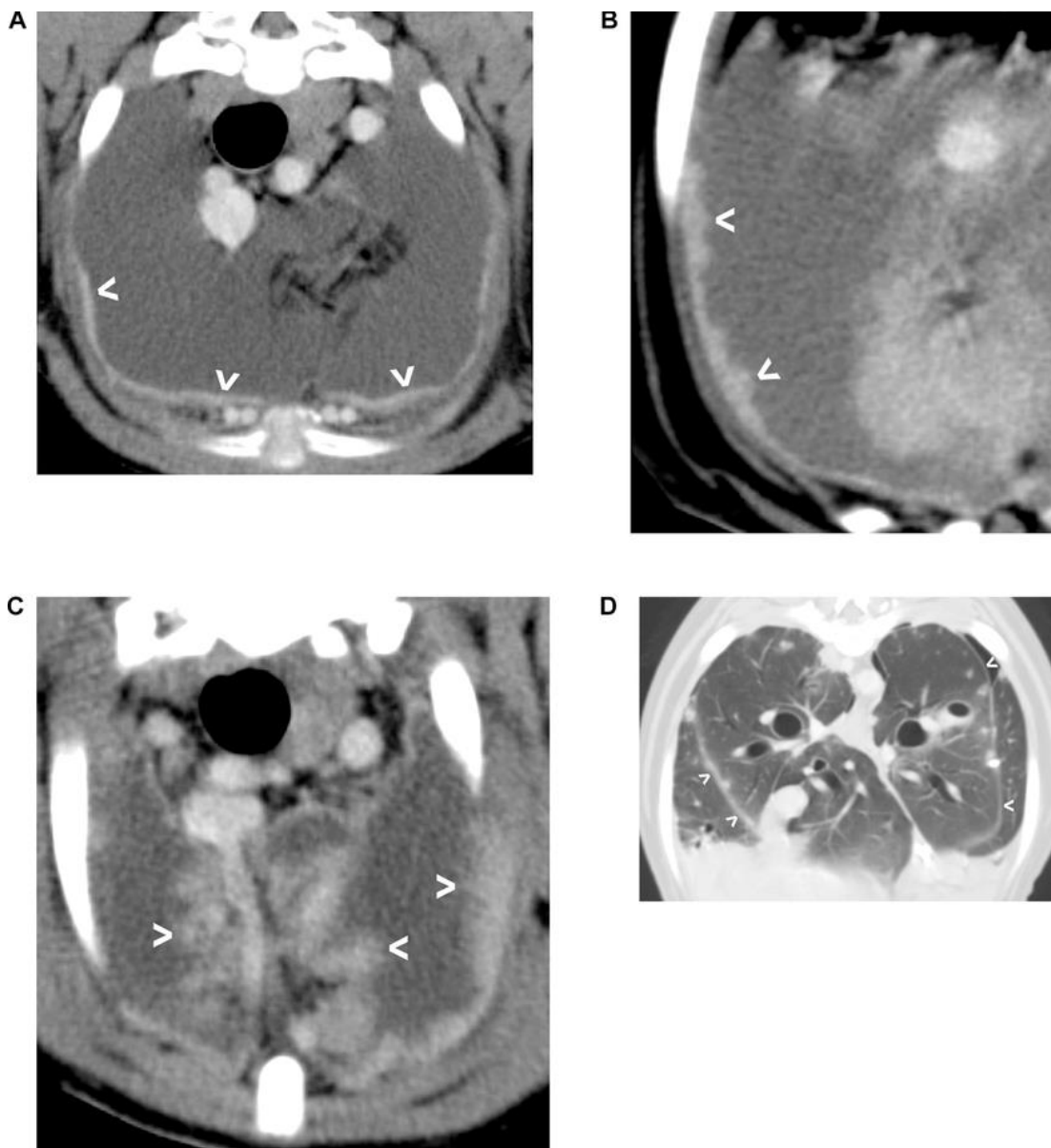
357		Malignant	Inflammatory	p-value
358		(n=20)	(n=32)	
359	Computed tomographic feature			
360				
361	Pleural fluid median (range) attenuation (HU)	19 (12-32)	20 (7-45)	NS
362	Asymmetrical distribution of fluid	0	5 (16%)	NS
363	Pleural thickening	17 (85%)	14 (44%)	0.03
364	Parietal/visceral/both	13/1/1	4/6/4	0.01
365	Diffuse	6 (30%)	7 (22%)	NS
366	Nodular	6 (30%)	7 (22%)	NS
367	Median maximal thickness (mm)	3 (0-40)	0 (0-38)	0.01
368	Pleura >1cm thick	6 (30%)	4 (13%)	NS
369	Median pre-/post-C (HU)	38/98	38/77	NS
370	Median difference	61 (12-98)	35 (10-66)	NS
371	Calcification of pleura	2 (10%)	0	NS
372	Pannus	5 (25%)	10 (31%)	NS
373	Thoracic wall invasion	3 (15%)	0	0.05
374	Pericardial fluid	1 (5%)	1 (3%)	NS
375	Mediastinal fluid	2 (10%)	3 (6%)	NS
376	Mediastinal adenopathy	11 (55%)	21 (66%)	NS
377	Pulmonary nodules	5 (25%)	4 (13%)	NS

378 _____

379 NS, not significantly different, p>0.05

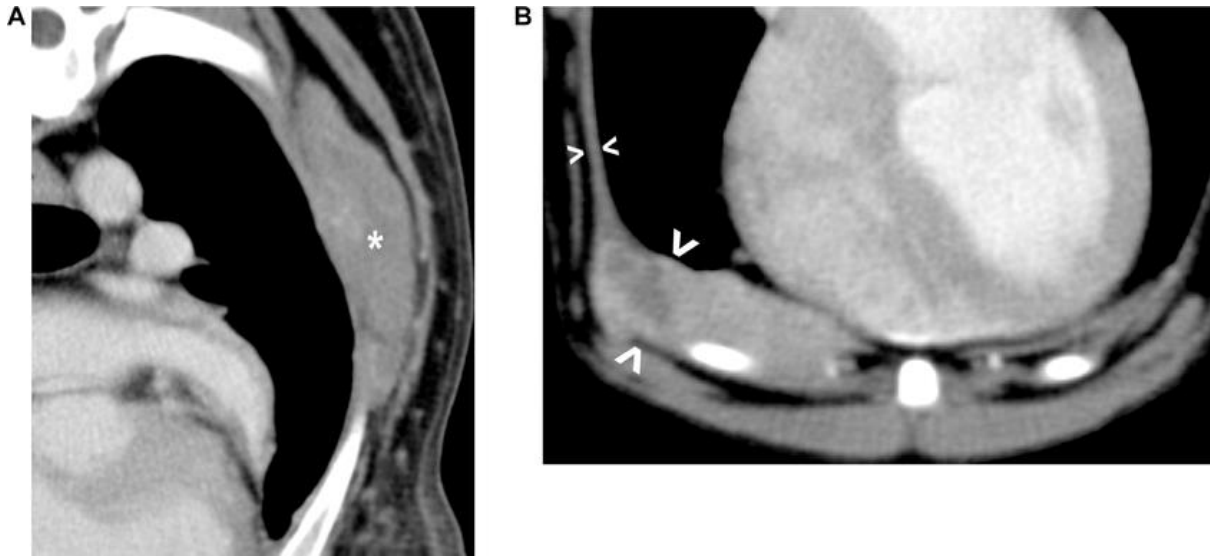
380 **Legends**

381 Figure 1. Examples of diffuse pleural thickening. A) Slight diffuse thickening of the parietal
382 pleura (arrowheads) in a dog with mesothelioma; B) Nodular thickening of the parietal
383 pleura (arrowheads) in a dog with mesothelioma; C) Marked irregular thickening of the
384 parietal and mediastinal pleura (arrowheads) in a dog with pyothorax; D) Slight diffuse
385 thickening of the visceral pleura (arrowheads) in a dog with pyothorax. A-C soft tissue
386 window (width 320 HU; level 80 HU); D lung window (width 1500 HU; level -500 HU).



387

388 Figure 2. Examples of thoracic wall invasion by mesothelioma. A) Broad mass (*) involving
389 parietal pleura and adjacent intercostal muscles; B) Locally invasive mass (large arrowheads)
390 thickening the inner layer of thoracic wall (small arrowheads) and obliterating the fat plane
391 between muscles of the thoracic wall. Both images displayed using a soft tissue window
392 (width 320 HU; level 80 HU).



393

394

395

396 Figure 3. Examples of pannus (A and B) in dogs with pyothorax. In each instance, the
397 morphology of pannus is a thick, folded sheet of tissue (arrowheads) that appears separate
398 from the pleura. An enlarged sternal lymph node (*) is visible in B. Both images displayed
399 using a soft tissue window (width 320 HU; level 80 HU).

