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This is the **submitted version** of the journal article:

Mallol, Claudia; Gutierrez-Quintana, Rodrigo; Hammond, Gawain; [et al.].  
«MRI features of canine hemangiosarcoma affecting the central nervous system». *Veterinary Radiology and Ultrasound*, Vol. 63 Núm. 2 (2022), p. 185-196. 12  
pàg. DOI 10.1111/vru.13041

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1    **Magnetic resonance imaging features of canine haemangiosarcoma affecting the central**  
2    **nervous system**

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28 **Key Words:** hemangiosarcoma, spine, haemorrhage, hemorrhage, vertebra

29 **Conflict of interest diclosure:** The authors declare no conflict of interest. No third-party  
30 funding or support was received in connection with this study or the writing or publication of  
31 the manuscript.

32 **EQUATOR network disclosure:** EQUATOR network checklist was not used

33 **Abbreviations:** CNS, central nervous system; CSF, cerebrospinal fluid

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51 **ABSTRACT**

52 Haemangiosarcoma is the most common metastatic tumour involving the brain in dogs but a  
53 detailed description of its MRI features is lacking. The objective of this multicentre,  
54 retrospective study was to describe MRI characteristics of canine haemangiosarcoma affecting  
55 the central nervous system (CNS). Medical records of seven referral institutions were  
56 retrospectively reviewed. Dogs were included if they had an histopathologically confirmed  
57 diagnosis of haemangiosarcoma affecting the CNS and undergone an MRI of the brain and/or  
58 vertebral column. Lesions were independently evaluated by two observers. Twenty dogs met  
59 the inclusion criteria and one dog had both intracranial and intramedullary haemangiosarcoma.  
60 Consistent MRI features included heterogeneous (17/21) lesions in all sequences with mainly  
61 mixed signal intensity (12/21), presence of susceptibility artefact on T2\*w (15/16), associated  
62 moderate to severe perilesional oedema (21/21) and moderate to strong (20/21) heterogeneous  
63 (14/21) or ring-like (6/21) contrast enhancement. Intracranial haemangiosarcoma was  
64 frequently multiple and intra-axial, affecting consistently the telencephalon and no differences  
65 in MRI features were found between primary and metastatic haemangiosarcoma. This is the  
66 first MRI description of primary intracranial haemangiosarcoma and primary intracranial  
67 epithelioid haemangiosarcoma. Vertebral haemangiosarcomas were segmental poorly  
68 marginated polyostotic and highly aggressive lesions invading the thoracic vertebral canal and  
69 paraspinal tissues. Epidural haemangiosarcomas were single and well-marginated lesions in  
70 the thoracolumbar and/or lumbar region. Intramedullary haemangiosarcomas were cervical,  
71 metastatic in origin, and frequently (3/4) accompanied by intracranial lesions. These described  
72 MRI features will aid early identification of haemangiosarcoma guiding subsequent  
73 diagnostics and therapeutics.

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76 **INTRODUCTION**

77 Haemangiosarcoma is a highly malignant tumour derived from the endothelial cells.<sup>1</sup> It is  
78 common in dogs and comprises up to 5-7% of non-cutaneous primary malignant neoplasms  
79 and 12-21% of all mesenchymal neoplasms.<sup>2,3</sup> Typical primary sites in dogs include the spleen,  
80 liver and right atrium, but it can arise from any vascularised tissue.<sup>4,5</sup> Visceral  
81 haemangiosarcoma is characterized by its aggressive behaviour with rapid and widespread  
82 metastasis to the lungs, liver, peritoneum, and central nervous system (CNS) through the  
83 haematogenous route.<sup>4</sup>

84 At the time of presentation and based on a post-mortem study, 80% of dogs have metastases to  
85 distant organs and, in 14.2% of the cases, metastasis affects the brain.<sup>4,6</sup> In fact,  
86 hemangiosarcoma is the most common metastatic tumour involving the brain in dogs.<sup>6,1,7-11</sup>  
87 Primary haemangiosarcoma of the CNS is rare in dogs<sup>4,12</sup> and only approximately 30 cases  
88 have been reported in people.<sup>13</sup> No imaging description of primary intracranial  
89 haemangiosarcoma has been reported in dogs and a detailed magnetic resonance imaging  
90 (MRI) description of the metastatic form is only available for one dog.<sup>10</sup>

91 Spinal haemangiosarcoma has been reported mainly as extradural, arising from vertebrae<sup>14-19</sup>  
92 but also as primary epidural,<sup>20-22</sup> multicompartimental (extradural invading the  
93 leptomeninges),<sup>19</sup> metastatic intramedullary,<sup>23-26</sup> and intradural extramedullary.<sup>27</sup> It is  
94 estimated to comprise 2-3% of all primary bone tumours.<sup>17</sup> Descriptions of the MRI  
95 characteristics of the tumour affecting the vertebrae,<sup>15,19</sup> epidural space<sup>20,22</sup> and spinal  
96 cord<sup>24,25,28</sup> are sparse, with two, two and four cases respectively.

97 The aim of this study was to describe the MRI features of histopathologically confirmed canine  
98 haemangiosarcoma affecting the CNS.

99

100 **MATERIAL AND METHODS**

101 **Selection and description of subjects**

102 This was a multicentre, retrospective, descriptive study approved by the Research Ethics  
103 Committee of the School of Veterinary Medicine of the University of Glasgow (ref. EA46/20).  
104 Medical records of seven referral institutions were retrospectively reviewed to identify MRI  
105 studies of dogs with a diagnosis of haemangiosarcoma affecting the CNS confirmed by ECVP-  
106 certified veterinary pathologists. Dogs with confirmed haemangiosarcoma in distant organs,  
107 but without histopathological confirmation of the tumour affecting the CNS were excluded.  
108 Dogs were included if the MRI study included at least T2-weighted (T2w), fluid-attenuated  
109 inversion recovery (FLAIR), T1-weighted (T1w), T2\*-weighted gradient recall eco (T2\*w),  
110 and T1w post contrast images of the brain and/or at least T1w, T2w and T1w post contrast  
111 images of the vertebral column in any plane.

112 **Data recording and analysis**

113 A third-year ECVDI resident (C.M.) and an ECVN-certified veterinary neurologist (J.B.)  
114 reviewed medical records, and retrieved the following information: signalment (age, breed,  
115 sex), presenting complaint, general physical and neurological examination findings at  
116 presentation, neurolocalisation, laboratory findings, results of other imaging investigations  
117 (ultrasound, radiography, CT), histopathology results, and outcome. Median and range were  
118 used for descriptive statistics as most variables showed skewed distributions.

119 **MRI characteristics**

120 Magnetic resonance images were reviewed by an ECVDI-certified veterinary radiologist (GH)  
121 and an ECVN-certified veterinary neurologist (RG). Images were displayed using an open-  
122 source Workstation DICOM viewer (Osirix Imaging Sofware, version 3.9.2, Pixmeo, Geneva,

123 Switzerland). The evaluation of MRI studies included the CNS and all surrounding structures  
124 of the imaged area. Imaging characteristics of the lesion(s) were recorded based on a consensus  
125 opinion. Observers were asked to record the localisation of the lesion along the neuroaxis as  
126 precisely as possible and to record the axial origin as extra-axial or intra-axial (for intracranial  
127 lesions) and extradural, intradural-extramedullary, or intramedullary (for lesions affecting the  
128 vertebral column and/or spinal cord). The term intramedullary was only used to describe spinal  
129 cord lesions. Observers were also asked to specify if the lesions affected mainly grey matter,  
130 white matter or the transition zone between them. For extradural lesions, observers were  
131 specifically asked to record if the lesion was confined to the epidural space or if it involved the  
132 vertebrae and/or paraspinal soft tissues. They were also asked to record if the lesion was  
133 segmental (single abnormality even if spanning multiple vertebrae) or multifocal (separate  
134 abnormalities) and if it was monostotic (involving one vertebra) or polyostotic (involving  
135 multiple vertebrae). The number of lesions was recorded as single or multiple. In dogs with  
136 multiple lesions, observers were asked to describe the predominant pattern. The size of the  
137 biggest lesion was assessed measuring the maximum dimension in any direction on T2w  
138 images. This was done considering findings on other sequences, especially FLAIR, to avoid  
139 measuring perilesional oedema. For extradural lesions, size was measured as the length of the  
140 vertebral bodies along which the lesion extended. The signal intensity was recorded as  
141 hyperintense, hypointense, isointense, or mixed intensity compared to grey matter or to the  
142 adjacent tissue for extradural lesions on T2w, FLAIR and T1w images, and signal homogeneity  
143 of the lesion was categorized as homogeneous or heterogeneous. All mixed intensity lesions  
144 were considered heterogeneous. The presence of susceptibility artefact on T2\*w images was  
145 recorded. None, partial, or complete presence of hypointense peripheral rim on T2w and  
146 presence of non-haemorrhagic areas (lacking a susceptibility artefact) within the lesion were  
147 also recorded. The lesion was categorized as well or poorly marginated. Presence of

148 perilesional oedema was evaluated subjectively and classified as absent, mild, moderate, or  
149 severe. Mass effect was recorded in intracranial cases as absent or present and, when present,  
150 the type of mass effect (ventricular distortion, midline shift, foramen magnum and  
151 transtentorial herniation) was recorded. Presence or absence and subjective degree of spinal  
152 cord compression (none, mild, moderate, severe) was recorded in spinal cases. Contrast  
153 enhancement was classified as none, mild, moderate, or strong and the pattern of enhancement  
154 as homogeneous, heterogeneous, or ring-like.

## 155 **RESULTS**

### 156 **Subjects**

157 Twenty dogs met the inclusion criteria. Clinical signs, signalment, neurolocalisation, and MRI  
158 equipment details are summarized in Appendix 1.

159 The median duration of clinical signs before referral in dogs with intracranial  
160 haemangiosarcoma was 13 days (range, 2-120 days). The median duration of clinical signs  
161 before referral in dogs with spinal haemangiosarcoma was 7 days (range, 1-90 days).

### 162 **MRI characteristics**

163 Eight dogs underwent MRI of the brain only, one of the brain and vertebral column, and eleven  
164 of the vertebral column only.

#### 165 *Intracranial lesions*

166 MRI characteristics of intracranial lesions are summarized in Table 1.

167 All intracranial lesions were intra-axial. Most lesions were multiple (8/9) and all dogs had  
168 lesions affecting the telencephalon. The majority of lesions were heterogeneous in all

169 sequences (8/9), having a mixed signal intensity on T2w, FLAIR and T1w images, being either  
170 predominantly hypointense or hyperintense on T2w and FLAIR and predominantly isointense  
171 or hypointense on T1w (Figures 1, 2). Most lesions (8/9) showed a susceptibility artefact on  
172 T2\*w images, matching the location of a lesion observed on T2w images. Small susceptibility  
173 artefacts (microhaemorrhages) only visible on T2\*w images were present in five dogs (5/9).  
174 Multiple stages of the haemorrhage were recognized within most of the lesions (8/9). Most  
175 lesions were well-margined (8/9) and were surrounded by severe perilesional oedema in all  
176 dogs (Figures 1B, 2A). Mass effect was present in most dogs (7/9). In two dogs, invasion of  
177 the adjacent lateral ventricle was suspected, where loss of suppression of the cerebrospinal  
178 fluid (CSF) signal was noted on FLAIR (Figure 1F). Contrast enhancement was present in all  
179 dogs (and most lesions) and was predominantly moderate and heterogeneous (6/9) (Figure 1E,  
180 2E). Four dogs (4/9) had at least one lesion with ring-like contrast enhancement (Figure 3).  
181 Meningeal enhancement was present in four dogs (4/9) (Figure 3). Multifocal lesions in the  
182 masticatory muscles were present in three dogs (3/9).

183 *Spinal lesions*

184 MRI characteristics of spinal lesions are summarized in Table 2.

185 Spinal lesions were extradural in seven dogs (7/12) and intramedullary in five (5/12). All  
186 extradural lesions were single, four (4/7) arising from thoracic vertebrae, and three (3/7)  
187 confined to the thoracolumbar (2/7) or lumbar (1/7) epidural space. All vertebral lesions were  
188 segmental (4/4) and most were polyostotic (3/4). Invasion of the adjacent paraspinal soft tissues  
189 and vertebral canal was noted in all of them (Figure 4). Most intramedullary lesions (4/5) were  
190 single, and all were located in the cervical spinal cord.

191 All lesions were heterogeneous on T2w images, with a mixed signal intensity in eight (8/12),  
192 and hyperintense in four dogs (4/12). Most lesions (10/12) were heterogeneous on T1w images,

193 isointense in seven (7/12), mixed signal intensity in four (4/12) and hyperintense in one dog  
194 (1/12) (Figure 2, 4 and 5). A susceptibility artefact was present in all dogs where T2\*w images  
195 were available (Figure 5E). Five (5/7) dogs had non-haemorrhagic areas within the lesions.

196 All vertebral lesions (4/4) were poorly-margined and all epidural lesions (3/3) were well-  
197 marginated. All extradural lesions showed moderate perilesional oedema and caused moderate  
198 to severe spinal cord compression. Moderate to severe perilesional oedema was noted in all  
199 intramedullary lesions (Figure 2D).

200 Contrast enhancement was present in all lesions, being in most dogs (11/12) moderate to strong  
201 and heterogeneous (10/12). Two (2/5) intramedullary lesions showed ring-like contrast  
202 enhancement (Figure 2E).

### 203 **Additional imaging findings**

204 Fourteen dogs had other imaging investigations. All dogs had thoracic radiographs or CT, with  
205 no evidence of lung metastasis in 11 dogs and with multiple pulmonary soft tissue nodules  
206 compatible with metastasis in three. In one dog, CT revealed numerous soft tissue nodules in  
207 the left brachial plexus and left semimembranosus and gracilis muscles, histopathologically  
208 confirmed as metastatic haemangiosarcoma. Eleven dogs had abdominal imaging. Seven dogs  
209 had abdominal ultrasound, which was unremarkable or revealed minor unrelated changes in  
210 six dogs, and a large splenic mass histopathologically confirmed as haemangiosarcoma in one.  
211 Two dogs had abdominal CT, which revealed a splenic mass in one, and multiple peritoneal  
212 nodules in the other, both histopathologically confirmed as haemangiosarcomas. Two dogs had  
213 unremarkable abdominal radiographs. One dog had an unremarkable echocardiogram.

### 214 **Outcome and post-mortem examination**

215 Eleven dogs were euthanized during anaesthesia and eight dogs were euthanized within two  
216 weeks of diagnosis due to marked deterioration. One dog was lost from follow-up.

217 A full body post-mortem examination was performed in nine dogs (9/20), five intracranial  
218 haemangiosarcomas and four intramedullary spinal haemangiosarcomas. In the remaining 11  
219 dogs, the post-mortem was limited to the CNS in eight, and the diagnosis was confirmed by  
220 biopsy in three dogs. On post-mortem examination, haemangiosarcoma was found in other  
221 organs in six (6/9) dogs. Affected organs were the lungs (5/9), heart (4/9), spleen (4/9), liver  
222 (3/9), kidneys (3/9), pituitary gland (1/9), adrenal glands (2/9), muscles (1/9), pancreas (1/9),  
223 gastrointestinal tract (1/9), omentum (1/9), and urinary bladder (1/9). In the remaining three  
224 dogs with full body post-mortem examination, no evidence of haemangiosarcoma was found  
225 outside the CNS (three intracranial and one vertebral haemangiosarcoma).  
226 Immunohistochemistry was performed in three cases (including two primary intracranial, one  
227 of which was the epithelioid form, and one epidural) using CD3 or Factor 8 markers,  
228 confirming the endothelial cell origin of the neoplasia.

## 229 **DISCUSSION**

230 This study describes the MRI characteristics of dogs with primary and metastatic  
231 haemangiosarcoma affecting the CNS. Metastatic intracranial haemangiosarcoma has been  
232 scarcely described as multiple (rarely single) and mixed intensity masses in T2w and T1w,  
233 with associated mass effect, marked perilesional oedema and variable and often peripheral  
234 contrast enhancement,<sup>10</sup> resembling our results.

235 The telencephalon is the most common site for brain metastasis in dogs, including  
236 haemangiosarcoma,<sup>6,9</sup> and was affected in all dogs with intracranial haemangiosarcoma in our  
237 study. Only one case in this study had a single intracranial lesion, and although uncommon,

238 both primary<sup>4</sup> and metastatic<sup>6,9,29</sup> intracranial haemangiosarcomas can occur as a solitary  
239 lesion. Similarly to a previous MRI study, all dogs had at least one lesion that was bigger than  
240 4 mm.<sup>30</sup>

241 Intracranial haemorrhage associated with haemangiosarcoma can be expected due to the  
242 endothelial origin of the tumour and its friable consistency.<sup>6,7</sup> Different magnetic properties of  
243 haemoglobin products/metabolites may be used to determine the age of the haemorrhage.<sup>31</sup>  
244 Multiple haemorrhagic stages were recognized within most of the lesions in this study, and this  
245 was evident as a mixed signal intensity of the lesions in all sequences. The presence of a  
246 hypointense peripheral rim reflecting the conversion of the intracellular oxyhaemoglobin to  
247 deoxyhaemoglobin in the acute phase of the haemorrhage was also common. In people,  
248 multiple haemorrhagic stages within lesions has been used as a criteria to differentiate between  
249 neoplastic or spontaneous haemorrhages.<sup>32</sup>

250 Most lesions in this study had susceptibility artefact on T2\*w images, corresponding to the  
251 presence of haemorrhage. The only dog to have lesions with no susceptibility artefact had been  
252 examined with the lowest field MRI (0.2T) used in this study. Susceptibility artefact distortion  
253 is proportional to magnetic field strength<sup>30</sup>, so this can potentially explain the absence of  
254 susceptibility artefact in this case despite the presence of a haemorrhagic lesion. T2\*w is a  
255 sequence sensitive to haemorrhage given that haemoglobin derivates are paramagnetic and  
256 produce local magnetic field inhomogeneities<sup>31,33,34</sup> Similarly to a previous study in five dogs,  
257 the susceptibility artefact present on T2\*w images allowed visualization of small haemorrhagic  
258 lesions not seen in either T2w nor FLAIR images.<sup>34</sup> Reports of metastatic haemangiosarcoma  
259 and intracerebral haemorrhage described a susceptibility artefact on T2\*w images comprising  
260 the entire mass;<sup>34</sup> however, we found non-haemorrhagic areas (areas lacking susceptibility  
261 artefact) within lesions in four dogs. The presence of solid areas within haemorrhagic lesions

262 is a criteria in people to differentiate neoplastic from non-neoplastic intracerebral  
263 haemorrhage.<sup>32</sup>

264 Haemorrhages are often associated with perilesional vasogenic oedema in the acute phase,  
265 although perilesional oedema may persist even in the chronic phases or along multiple  
266 haemorrhagic stages, when an underlying neoplastic origin is present.<sup>32</sup> Oedema is also  
267 commonly associated with brain metastasis<sup>33</sup> and this is in agreement with our cases, where  
268 perilesional oedema was a consistent finding.

269 Contrast enhancement is often present in metastatic lesions<sup>33</sup> and was present in all dogs in this  
270 study. Breakdown of the blood-brain barrier and peripheral neovascularization are possible  
271 explanations for the enhancement,<sup>8</sup> the last explaining the ring-like enhancement in almost half  
272 of the dogs. Meningeal enhancement was present in four dogs. Histologically, neoplastic cells  
273 were found in the meninges of one dog, and another one showed multifocal accumulation of  
274 perivascular haemosiderophages and a small number of lymphocytes and plasma cells.

275 Haemangiosarcoma is the most common metastatic tumour involving the brain in dogs,  
276 compromising 29% of all secondary intracranial tumours.<sup>9</sup> Primary intracranial  
277 haemangiosarcoma is extremely rare in dogs, with only few cases reported, and no MRI  
278 descriptions.<sup>4,12</sup> Primary haemangiosarcoma was confirmed in two dogs, in which no evidence  
279 of haemangiosarcoma was found outside the CNS based on thoracic and abdominal imaging  
280 and their complete post-mortem examinations. One case was a haemangiosarcoma affecting  
281 the rostral cerebrum and invading the lateral ventricle, with haemorrhages identified in the  
282 diencephalon and meninges on histopathology. Invasion of a lateral ventricle also occurred in  
283 a dog with suspected (based on thoracic and abdominal imaging) primary haemangiosarcoma.  
284 Both cases had lack of suppression of CSF signal on FLAIR images inside the affected lateral  
285 ventricle due to the presence of histopathologically confirmed intraventricular haemorrhage.

286 The other confirmed primary case was an epithelioid haemangiosarcoma, in which neoplastic  
287 cells were found in the telencephalon, diencephalon, and mesencephalon. Epithelioid  
288 haemangiosarcoma is an uncommon histological variant of haemangiosarcoma that resemble  
289 tumours of epithelial origin. This variant has been poorly described in veterinary species and  
290 affects mostly the integument.<sup>35</sup> Case reports suggest a similar biological behaviour to the non-  
291 epithelioid visceral form,<sup>35,36</sup> but given its rarity in dogs and therefore the lack of studies, its  
292 biological behaviour is still to be determined. This is the first description of a primary  
293 intracranial epithelioid haemangiosarcoma, and the first description of the MRI features of  
294 primary intracranial haemangiosarcoma. In people, the MRI features of primary intracranial  
295 haemangiosarcoma are described as a single enhancing lesion with heterogeneous signal  
296 intensity on T1w and T2w images.<sup>37</sup> Interestingly, both confirmed primary  
297 haemangiosarcomas in this study had multiple intracranial lesions and their MRI features did  
298 not differ from metastatic haemangiosarcoma.

299 Skeletal muscle metastases occur in 24.6% of haemangiosarcomas, and always associated with  
300 involvement of other organs.<sup>38</sup> In people, muscle metastases are considered a late event in  
301 clinical progression and herald a poor prognosis.<sup>39</sup> Histopathology of the masticatory muscle  
302 lesions identified in this study was not available, although a metastatic origin was suspected.  
303 As opposed to previous studies,<sup>38</sup> these dogs had no evidence of other metastatic lesions on  
304 thoracic or abdominal imaging.

305 Extradural tumours represent approximately 50% of all spinal tumours<sup>26</sup> and were the most  
306 common type in this study (7/12). They can be conceptually classified as primary or secondary  
307 (metastatic), but in aggressive tumours such as haemangiosarcoma, it may be difficult to  
308 determine its origin because metastases are frequently encountered at the time of diagnosis.<sup>40</sup>  
309 Most primary vertebral tumours in dogs involve thoracic vertebrae; while most metastatic

310 vertebral tumours involve lumbar vertebrae.<sup>16</sup> All vertebral haemangiosarcomas in this study  
311 affected thoracic vertebrae and were suspected to be primary, based on thoracic and abdominal  
312 imaging (4/4) and a full body post-mortem examination (1/4). Osseous lesions are detected in  
313 21% of dogs with haemangiosarcoma, and in 9% of cases metastasis involve vertebrae.<sup>17</sup>  
314 Descriptions of haemangiosarcoma arising from the bone are in agreement with our study, and  
315 are predominantly lytic and highly aggressive lesions, often invading the paraspinal soft tissues  
316 and extending into the vertebral canal.<sup>15,18,41</sup> We found segmental, poorly marginated  
317 polyostotic highly aggressive large mass-like lesions. There is only one case report describing  
318 the MRI characteristics of canine primary vertebral haemangiosarcoma.<sup>15</sup>

319 Three cases of epidural haemangiosarcoma in dogs have been reported,<sup>21,20,22</sup> affecting the  
320 lumbar region in one dog and all suspected to be primary. In all cases herein the definitive  
321 diagnosis was reached by biopsy, and none underwent full body imaging or complete post-  
322 mortem examination, so we were unable to classify them as primary or metastatic.

323 The MRI features of epidural haemangiosarcoma are described<sup>20,22</sup> with similar findings to the  
324 ones we encountered. MRI findings of extradural hematoma in dogs are similar to epidural  
325 haemangiosarcomas. However, most reported canine extradural/epidural hematomas did not  
326 show contrast enhancement, although diffuse<sup>42</sup> and strong<sup>43</sup> contrast enhancement are reported.

327 Primary intramedullary tumours are more common than metastatic intramedullary tumours,  
328 and tend to be located in the cervical spinal cord.<sup>25</sup> Metastatic intramedullary  
329 haemangiosarcoma is reported to frequently affect the thoracolumbar spinal cord<sup>23,25</sup> often  
330 accompanied by brain metastasis.<sup>23</sup> Interestingly, all intramedullary lesions we identified on  
331 MRI were located in the cervical spinal cord, had disseminated disease involving multiple  
332 thoracic and abdominal organs and, in almost all dogs (4/5), the cerebrum was affected on  
333 histopathology.

334 The MRI findings of intramedullary haemangiosarcoma have been briefly described in  
335 dogs.<sup>24,25,28</sup> Our cases showed similarities in the signal intensity and contrast enhancement, but  
336 in contrast to previous reports, the presence of perilesional oedema was a consistent finding.  
337 The use of corticosteroids prior to imaging studies may be the reason behind the disparity,  
338 although this information was not available in previous reports. Interestingly, all dogs but one  
339 described hereby had a single intramedullary lesion identified on MRI despite being metastatic  
340 in origin.

341 MRI findings of an intradural extramedullary haemangiosarcoma (suspected metastatic) in a  
342 dog have recently been described as similar to those of intramedullary haemangiosarcoma, but  
343 with the presence of a “golf tee sign”.<sup>27</sup> No intradural extramedullary haemangiosarcomas were  
344 found in this study.

345 Non-neoplastic spontaneous haemorrhage (including coagulopathies, parasitic migration, and  
346 congenital or acquired vascular malformations, among others) and haemorrhagic tumours like  
347 haemangiosarcoma and haemangioma or often high-grade gliomas, may share similar  
348 characteristics on MRI and should be considered in the differential diagnosis of haemorrhagic  
349 lesions affecting the CNS.<sup>13,29,44</sup> This was a descriptive study, and further studies comparing  
350 haemangiosarcoma and other neoplastic or non-neoplastic haemorrhages are necessary to  
351 identify reliable MRI features that could aid in their antemortem differentiation.

352 Limitations of this study include its multi-institutional and retrospective nature leading to  
353 variability in the clinical, imaging and pathologic information available. Full body post-  
354 mortem examinations were only available for nine dogs and there was variability in the post-  
355 mortem report detail. Most patients with intracranial haemangiosarcoma had multiple lesions,  
356 of which the presence or absence of neoplastic cells in every lesion was only specified in some  
357 post-mortem reports. In a previous post-mortem study, 25% of dogs with haemangiosarcoma

358 and a grossly identifiable brain lesion were diagnosed with ischemic or haemorrhagic infarcts,  
359 all located in the cerebrum.<sup>6</sup> Therefore, some of the lesions described in this study could  
360 represent cerebrovascular accidents. MRI studies were performed with different machines and  
361 different field strengths, of which seven were a low field. Low field MRI machines provide  
362 less anatomical detail compared to high field MR imaging machines. Another limitation of this  
363 study is the small sample size. Despite involving seven referral institutions, only 20 patients  
364 were recruited.

365 Our study population probably had a strong bias towards cases with obvious neurological signs  
366 in which systemic signs might had been missed or not been present. Patients are more likely to  
367 have MRI if no evidence of neoplastic or metastatic disease is suspected or found elsewhere.

368 In conclusion, this study describes the MRI features of canine primary and metastatic  
369 haemangiosarcoma affecting the CNS. Consistent imaging features that can be employed for  
370 diagnosis include heterogenous and frequently mixed signal intensity lesions with the presence  
371 of susceptibility artefact on T2\*w, associated moderate to severe perilesional oedema and  
372 moderate to strong heterogeneous or ring-like contrast enhancement. Intracranial  
373 haemangiosarcomas were frequently multiple and intra-axial, affecting consistently the  
374 telencephalon. Vertebral haemangiosarcomas were segmental, poorly marginated, polyostotic,  
375 and highly aggressive lesions invading the thoracic vertebral canal and paraspinal tissues.  
376 Epidural haemangiosarcomas were single and well-marginated lesions in the thoracolumbar  
377 and/or lumbar region, and intramedullary haemangiosarcomas were metastatic in origin and  
378 always located in the cervical spinal cord.

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394 **ACKNOWLEDGEMENTS**

395 We thank Jaume Martorell for his assistance with figures, Dick White referrals for  
396 contributing with one case and Beto and Volea for providing the idea and the inspiration to  
397 write this manuscript.

398

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## Tables

**Table 1.** MRI characteristics of intracranial haemangiosarcoma

Axial origin	Haemorrhage
Intra-axial	9 (100%)
Extra-axial	0
	Present
	8 (89%)

<b>Topographical location</b>		Microhaemorrhages	5/8 (62%)
Telencephalon		Absent	1 (11%)
<b>Non-haemorrhagic areas</b>			
Present		4 (44%)	
Absent		5 (56%)	
<b>Hypointense rim T2w</b>			
None		2 (22%)	
Partial		6 (67%)	
Complete		1 (11%)	
<b>Haemorrhagic stages</b>			
Single		1 (11%)	
Multiple		8 (89%)	
<b>Number of lesions</b>		<b>Perilesional oedema</b>	
Single		Absent	
Multiple		0	
Median number		Present	
		9 (100%)	
<b>Size</b>		Mild, moderate	
Median		0	
Range		Severe	
		9 (100%)	
<b>Signal intensity</b>			<b>Mass effect</b>
<b>T2w, FLAIR</b>		Absent	
Hyperintense		2 (22%)	
Mixed		Present	
		7 (78%)	
<b>T1w</b>		<b>Type</b>	
Isointense		Ventricular distortion	
Mixed		7 (78%)	
Hyperintense areas		Herniation	
<b>Lack CSF signal suppression within ventricles on FLAIR</b>		Foramen magnum	
2 (22%)		0	
		Transtentorial	
		2 (22%)	
		Midline shift	
		5 (56%)	
<b>Signal homogeneity</b>			<b>Contrast enhancement</b>
Homogeneous		Mild	
Heterogeneous		0	
		Moderate	
		6 (67%)	
		Strong	
		3 (33%)	
		Meningeal enhancement	
		4 (44%)	
<b>Pattern of enhancement</b>			
<b>Margin distinction</b>		Homogeneous	
Well-margined		1 (11%)	
Poorly-margined		Heterogeneous	
		4 (44%)	
		Ring-like	
		4 (44%)	

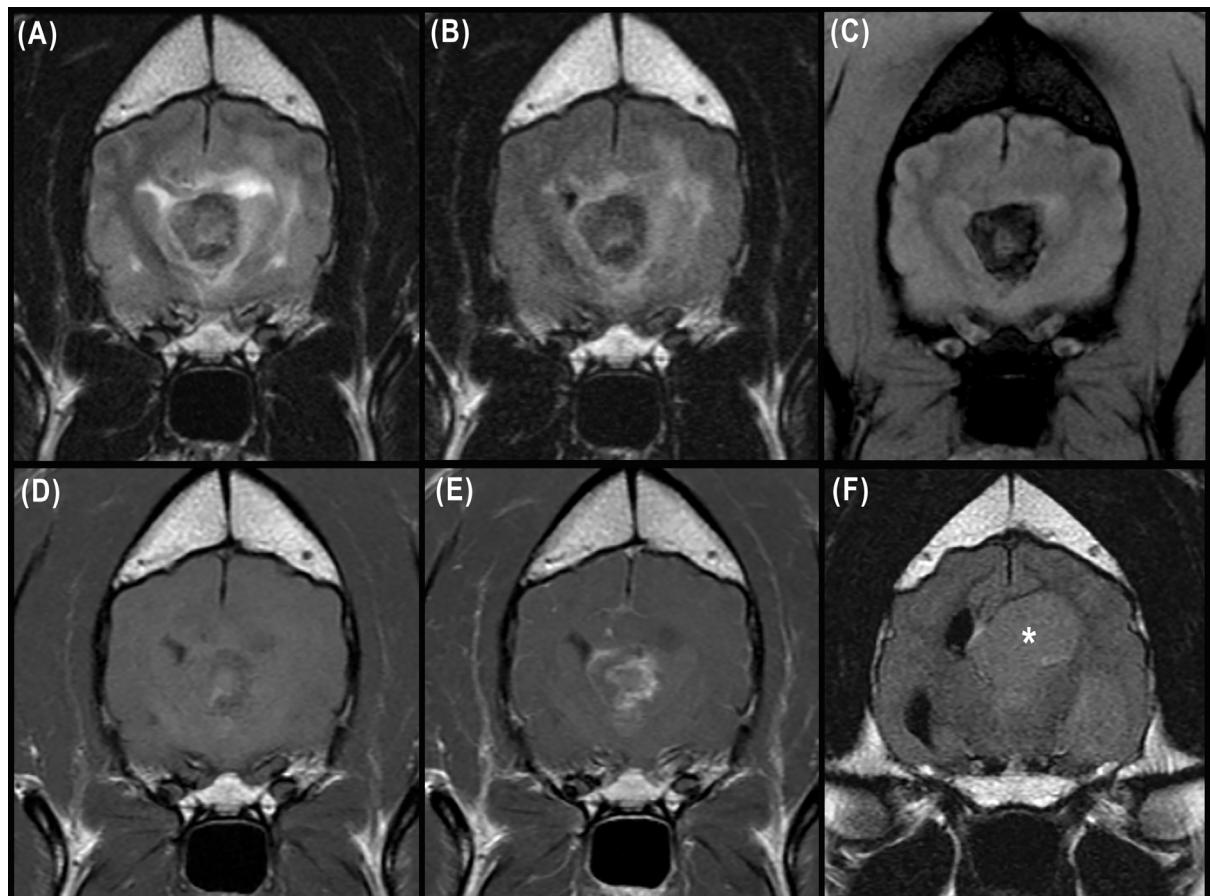
**Abbreviations:** CSF, cerebrospinal fluid

**Table 2.** MRI characteristics of spinal haemangiosarcoma

	<b>Extradural</b>		<b>Intramedullary</b>
	<b>Vertebral</b>	<b>Epidural</b>	
<b>Topographical location</b>			

Cervical	0	0	5/5 (100%)
Thoracic	4/4 (100%)	0	0
Thoracolumbar	0	2/3 (67%)	0
Lumbar	0	1/3 (33%)	0
<b>Number of lesions</b>			
Single (or segmental for vertebral)	4/4 (100%)	3/3 (100%)	4/5 (80%)
Multiple	0	0	1/5 (20%)
Monostotic	1/4 (25%)	N/A	N/A
Polyostotic	3/4 (75%)	N/A	N/A
<b>Median size</b>			
Length vertebral bodies and/or lesion length (cm)	2 vertebral bodies	2 vertebral bodies	2.1cm
<b>Signal intensity</b>			
<b>T2w</b>			
Hyperintense	2/4 (50%)	0	2/5 (40%)
Mixed	2/4 (50%)	3/3 (100%)	3/5 (60%)
<b>T1w</b>			
Hyperintense	0	1/3 (33%)	0
Isointense	2/4 (50%)	1/3 (33%)	4/5 (80%)
Mixed	2/4 (40%)	1/3 (33%)	1/5 (20%)
<b>Signal homogeneity</b>			
Homogeneous	0	1/3 (33%) T1w 0 T2w	1/5 (20%) T1w 0 T2w
Heterogeneous	4/4 (100%)	2/3 (67%) T1w 3/3 (100%) T2w	4/5 (80%) T1w 5/5 (100%) T2w
<b>Haemorrhage</b>			
T2*w available	1/4	2/3	4/5
Presence signal void	1/1 (100%)	2/2 (100%)	4/4 (100%)
<b>Non-haemorrhagic areas</b>			
Present	1/1 (100%)	1/2 (50%)	3/4 (75%)
Absent	0	1/2 (50%)	1/4 (25%)
<b>Margin distinction</b>			
Well-margined	0	3/3 (100%)	2/5 (40%)
Poorly marginated	4/4 (100%)	0	3/5 (60%)
<b>Perilesional oedema</b>			
Moderate	4/4 (100%)	3/3 (100%)	2/5 (40%)
Severe	0	0	3/5 (60%)
<b>Spinal cord compression</b>			
Moderate	1/4 (25%)	1/3 (33%)	N/A
Severe	3/4 (75%)	2/3 (67%)	N/A
<b>Contrast enhancement</b>			
Mild	0	0	1/5 (20%)
Moderate	2/4 (50%)	2/3 (67%)	2/5 (40%)
Strong	2/4 (50%)	1/3 (33%)	2/5 (40%)
<b>Pattern enhancement</b>			
Heterogeneous	4/4 (100%)	3/3 (100%)	3/5 (60%)
Ring-like	0	0	2/5 (40%)

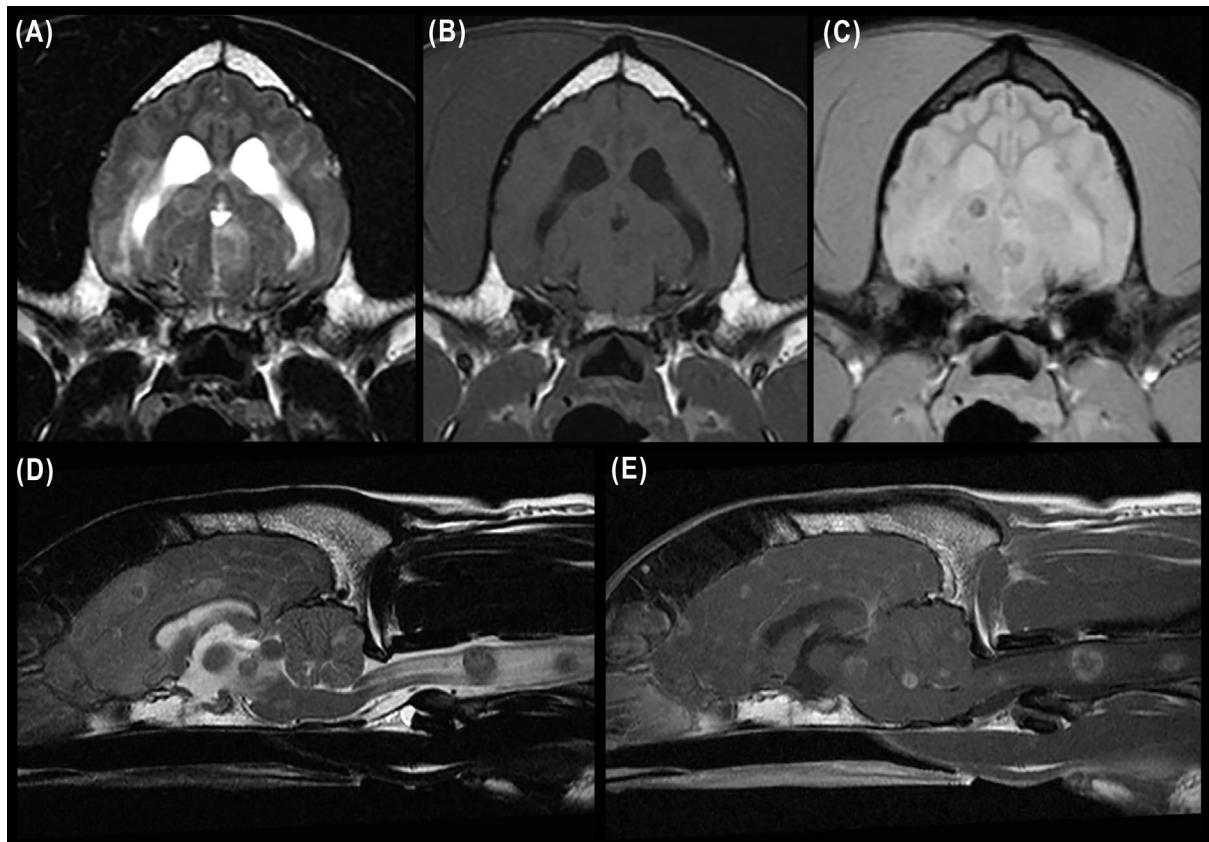
502 **Figure legends:**



503

504 **Figure 1** Primary intracranial haemangiosarcoma in an 11-year-old male neutered Golden  
505 Retriever at the level of the optic chiasm (A-E) and thalamus (F). A, Transverse T2w; B and  
506 F, FLAIR; C, T2\*w; D, T1w; and E, T1w post contrast images. Note the intra-axial, well-  
507 margined mass lesion in the telencephalon, heterogeneous with a mixed signal intensity  
508 (predominantly hypointense) on T2w, FLAIR and T1w images, with a susceptibility artefact  
509 on T2\*w, and with associated severe perilesional oedema and moderate heterogeneous contrast  
510 enhancement. Note the lack of suppression of CSF signal within the left lateral ventricle  
511 (asterisk, F) confirmed to be haemorrhage secondary to ventricular invasion.

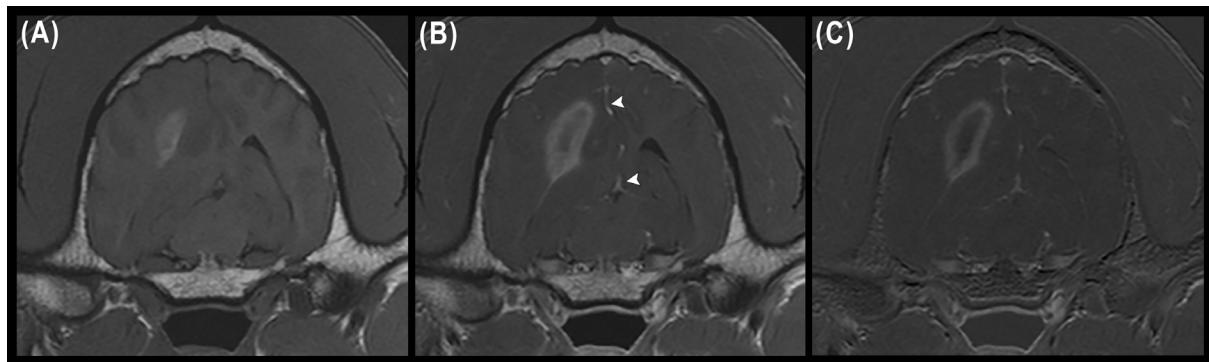
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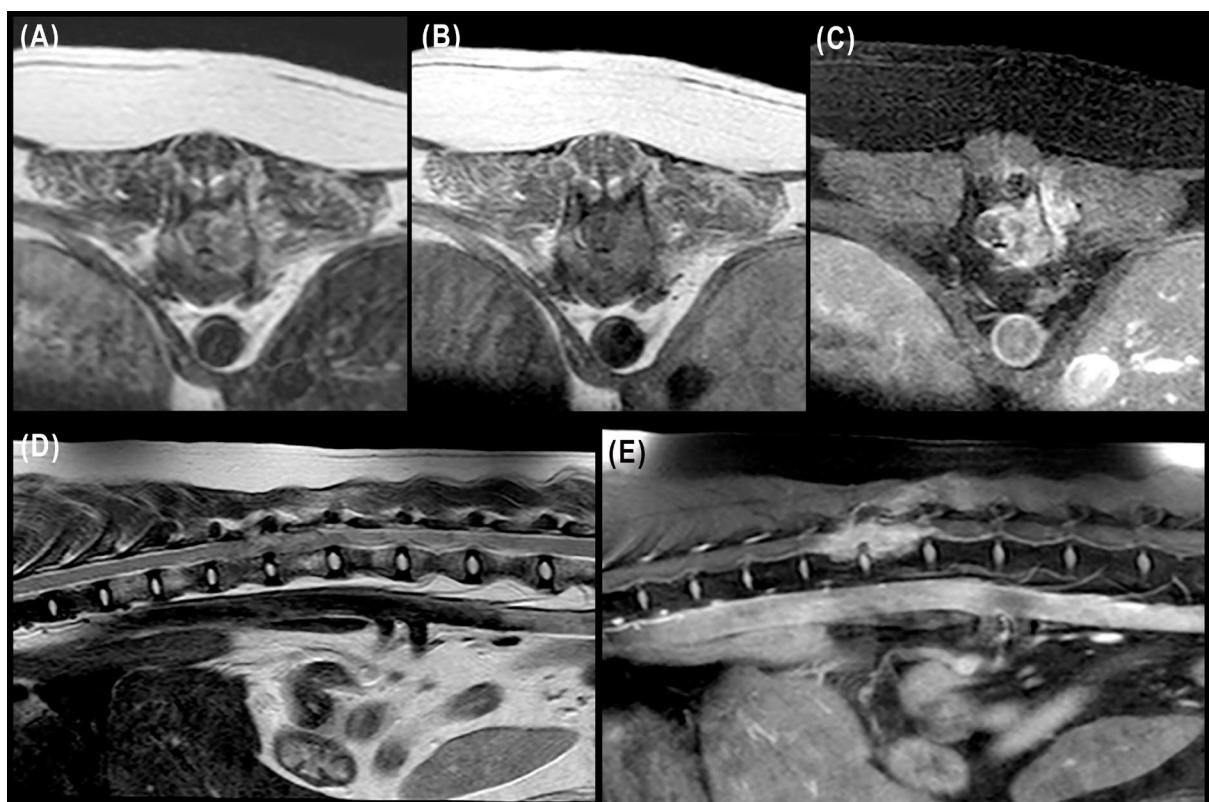
514 **Figure 2** Metastatic intracranial haemangiosarcoma in a 7-year-old male neutered Border  
515 Collie at the level of the rostral mesencephalon (A-C) and mid-sagittal plane (D-E). A,  
516 Transverse T2w; B, transverse T1w; C, transverse T2\*w; D, sagittal T2w; and E, sagittal T1w  
517 post contrast images. Note the multiple, intra-axial, well-margined lesions in the cerebrum,  
518 cerebellum and brainstem. Lesions were slightly heterogeneous and predominantly hypointense  
519 in all images, showing susceptibility artefact on T2\*w, severe perilesional oedema and  
520 moderate to ring-like contrast enhancement. Note the intramedullary lesions in the cervical  
521 spinal cord (D and E) showing similar characteristics.

522



523

524 **Figure 3** Haemangiosarcoma in the right parieto-temporal lobes in an 11-year old male  
 525 neutered mixed-breed dog. A, Transverse T1w; B, T1w post contrast; C, corresponding  
 526 Dynamic subtraction image. Note the meningeal (arrowheads, B) and ring-like contrast  
 527 enhancement of the mass. Meningeal metastases were found on histopathology.

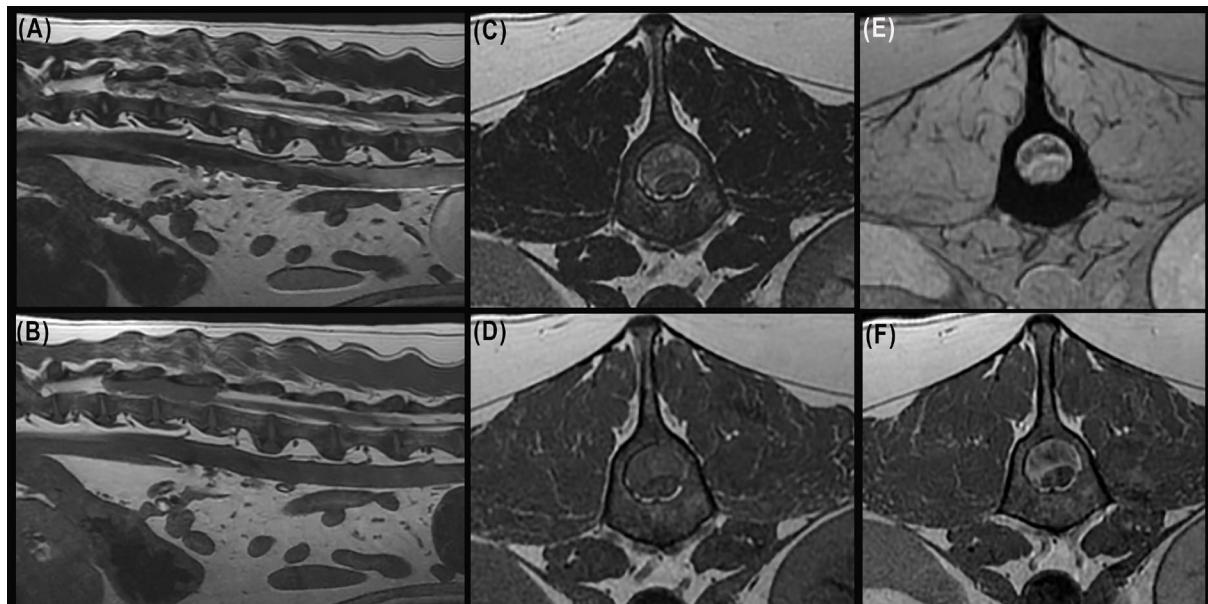


528

529 **Figure 4** Vertebral haemangiosarcoma in a 10-year old spayed female mixed-breed dog. A,  
 530 B, T1w; C, T1w fat sat post contrast images; D, Sagittal T2w; E, T1-weighted  
 531 fat sat post contrast images. Note the extradural, segmental, poorly marginated and polyostotic

532 aggressive lesion extending over the length of two thoracic vertebral bodies. It showed mixed  
533 signal intensity on T2w, iso- to hyperintense signal on T1w, and strong heterogeneous contrast  
534 enhancement. The mass was invading the adjacent paraspinal soft tissues and vertebral canal,  
535 causing severe spinal cord compression.

536



537  
538 **Figure 5** Epidural haemangiosarcoma in a 8-year old male neutered Labradoodle. A, Sagittal  
539 T2w; B, T1w images; C, Transverse T2w; D, T1w; E, T2\*w; F, T1w post contrast images.  
540 Note the single, epidural, well-margined thoracolumbar mass, extending over the length of  
541 two vertebral bodies, with T2w and T1w mixed signal intensity, susceptibility artefact on T2\*w  
542 and strong heterogeneous contrast enhancement, causing severe spinal cord compression.