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

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27

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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 margined polyostotic and highly aggressive lesions invading the thoracic vertebral canal and
69 paraspinal tissues. Epidural haemangiosarcomas were single and well-margined 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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75

76 **INTRODUCTION**

77 Haemangiosarcoma is a highly malignant tumour derived from the endothelial cells.¹ 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.^{2,3} Typical primary sites in dogs include the spleen,
80 liver and right atrium, but it can arise from any vascularised tissue.^{4,5} 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.⁴

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.^{4,6} In fact,
86 hemangiosarcoma is the most common metastatic tumour involving the brain in dogs.^{6,1,7-11}
87 Primary haemangiosarcoma of the CNS is rare in dogs^{4,12} and only approximately 30 cases
88 have been reported in people.¹³ 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.¹⁰

91 Spinal haemangiosarcoma has been reported mainly as extradural, arising from vertebrae¹⁴⁻¹⁹
92 but also as primary epidural,²⁰⁻²² multicompartamental (extradural invading the
93 leptomeninges),¹⁹ metastatic intramedullary,²³⁻²⁶ and intradural extramedullary.²⁷ It is
94 estimated to comprise 2-3% of all primary bone tumours.¹⁷ Descriptions of the MRI
95 characteristics of the tumour affecting the vertebrae,^{15,19} epidural space^{20,22} and spinal
96 cord^{24,25,28} 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 Software, 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-marginated (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-marginated 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 gracillis 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,¹⁰ resembling our results.

235 The telencephalon is the most common site for brain metastasis in dogs, including
236 haemangiosarcoma,^{6,9} 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 primary⁴ and metastatic^{6,9,29} 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.³⁰

241 Intracranial haemorrhage associated with haemangiosarcoma can be expected due to the
242 endothelial origin of the tumour and its friable consistency.^{6,7} Different magnetic properties of
243 haemoglobin products/metabolites may be used to determine the age of the haemorrhage.³¹
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.³²

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 strength³⁰, 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 derivatives are paramagnetic and
256 produce local magnetic field inhomogeneities^{31,33,34} 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.³⁴ Reports of metastatic haemangiosarcoma
259 and intracerebral haemorrhage described a susceptibility artefact on T2*w images comprising
260 the entire mass;³⁴ 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.³²

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.³² Oedema is also
267 commonly associated with brain metastasis³³ and this is in agreement with our cases, where
268 perilesional oedema was a consistent finding.

269 Contrast enhancement is often present in metastatic lesions³³ 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,⁸ 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.⁹ Primary intracranial
277 haemangiosarcoma is extremely rare in dogs, with only few cases reported, and no MRI
278 descriptions.^{4,12} 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.³⁵ Case reports suggest a similar biological behaviour to the non-
291 epithelioid visceral form,^{35,36} 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.³⁷ 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.³⁸ In people, muscle metastases are considered a late event in
301 clinical progression and herald a poor prognosis.³⁹ 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,³⁸ these dogs had no evidence of other metastatic lesions on
304 thoracic or abdominal imaging.

305 Extradural tumours represent approximately 50% of all spinal tumours²⁶ 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.⁴⁰
309 Most primary vertebral tumours in dogs involve thoracic vertebrae; while most metastatic

310 vertebral tumours involve lumbar vertebrae.¹⁶ 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.¹⁷
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.^{15,18,41} 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.¹⁵

319 Three cases of epidural haemangiosarcoma in dogs have been reported,^{21,20,22} 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^{20,22} 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 diffuse⁴² and strong⁴³ 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.²⁵ Metastatic intramedullary
329 haemangiosarcoma is reported to frequently affect the thoracolumbar spinal cord^{23,25} often
330 accompanied by brain metastasis.²³ 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.^{24,25,28} 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”.²⁷ 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.^{13,29,44} 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.⁶ 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.

379 **LIST OF AUTHOR CONTRIBUTIONS**

380 **Category 1**

381 (a) Conception and Design: Mallol, Brocal

382 (b) Acquisition of Data: Mallol, Gutierrez-Quintana, Hammond, Schweizer-Gorgas, De
383 Decker, Novellas, Espada, Ortega, Parry, Oevermann, Coelho, Stalin, Gonçalves, Brocal

384 (c) Analysis and Interpretation of Data: Mallol, Gutierrez-Quintana, Hammond, Brocal

385 **Category 2**

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387 (b) Revising Article for Intellectual Content: Mallol, Gutierrez-Quintana, Hammond,
388 Schweizer-Gorgas, De Decker, Novellas, Espada, Ortega, Parry, Oevermann, Coelho, Stalin,
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390 **Category 3**

391 (a) Final Approval of the Completed Article: Mallol, Gutierrez-Quintana, Hammond,
392 Schweizer-Gorgas, De Decker, Novellas, Espada, Ortega, Parry, Oevermann, Coelho, Stalin,
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398

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Tables

Table 1. MRI characteristics of intracranial haemangiosarcoma

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

Topographical location		Microhaemorrhages	5/8 (62%)
		Absent	1 (11%)
Telencephalon	9 (100%)	Non-haemorrhagic areas	
Thalamus	3 (33%)	Present	4 (44%)
Cerebellum	3 (33%)	Absent	5 (56%)
Mesencephalon	2 (22%)	Hypointense rim T2w	
Pons	1 (11%)	None	2 (22%)
Medulla oblongata	2 (22%)	Partial	6 (67%)
Specific location		Complete	1 (11%)
White matter	1 (11%)	Haemorrhagic stages	
Grey matter	2 (22%)	Single	1 (11%)
Transition zone	2 (22%)	Multiple	8 (89%)
All or undetermined	4 (44%)	Perilesional oedema	
Number of lesions		Absent	0
Single	1 (11%)	Present	9 (100%)
Multiple	8 (89%)	Mild, moderate	0
Median number	4	Severe	9 (100%)
Size		Mass effect	
Median	1.7 cm	Absent	2 (22%)
Range	0.4-9.6 cm	Present	7 (78%)
Signal intensity		Type	
T2w, FLAIR		Ventricular distortion	7 (78%)
Hyperintense	1 (11%)	Herniation	
Mixed	8 (89%)	Foramen magnum	0
T1w		Transtentorial	2 (22%)
Isointense	1 (11%)	Midline shift	5 (56%)
Mixed	8 (89%)	Contrast enhancement	
Hyperintense areas	5 (56%)	Mild	0
Lack CSF signal suppression within ventricles on FLAIR	2 (22%)	Moderate	6 (67%)
Signal homogeneity		Strong	3 (33%)
Homogeneous	1 (11%)	Meningeal enhancement	4 (44%)
Heterogeneous	8 (89%)	Pattern of enhancement	
Margin distinction		Homogeneous	1 (11%)
Well-marginated	8 (89%)	Heterogeneous	4 (44%)
Poorly-marginated	1 (11%)	Ring-like	4 (44%)

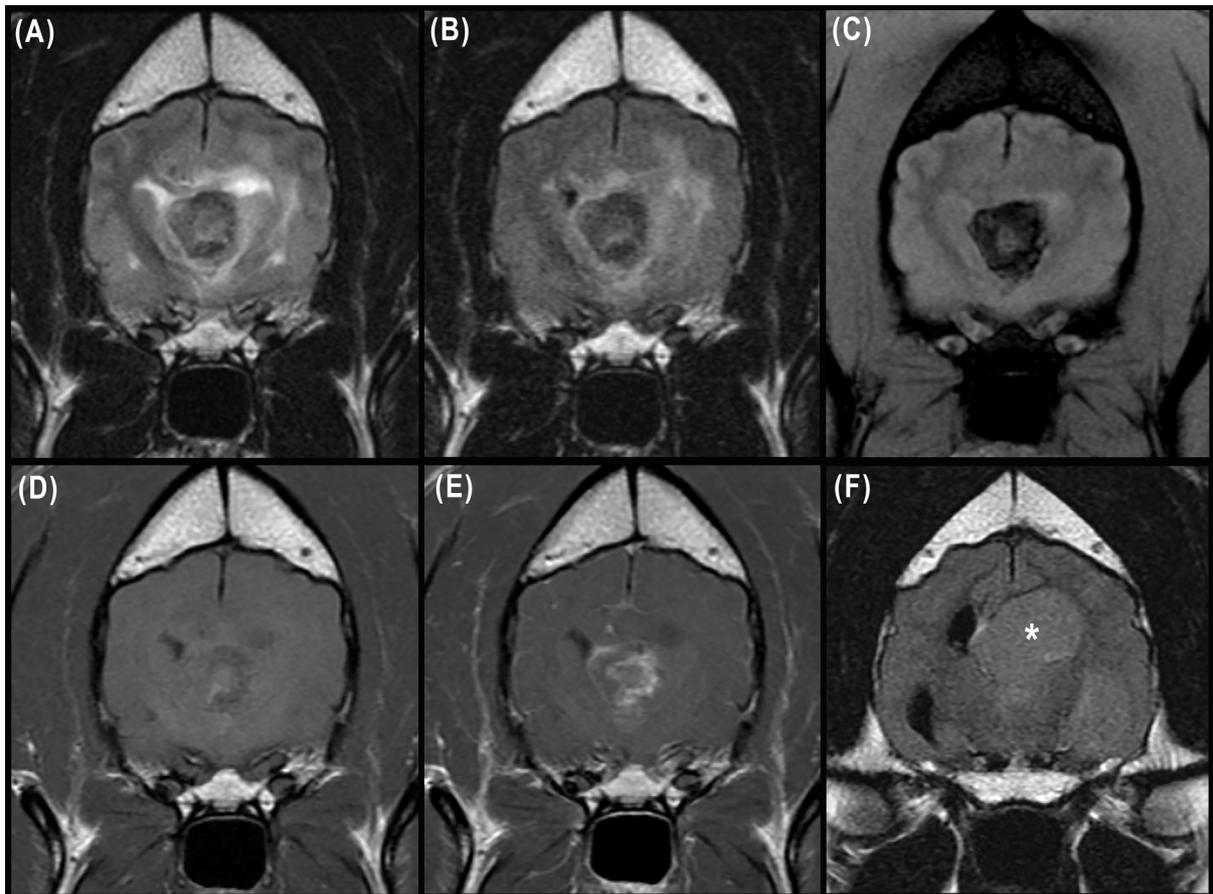
Abbreviations: CSF, cerebrospinal fluid

Table 2. MRI characteristics of spinal haemangiosarcoma

	Extradural		Intramedullary
	Vertebral	Epidural	
Topographical location			

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

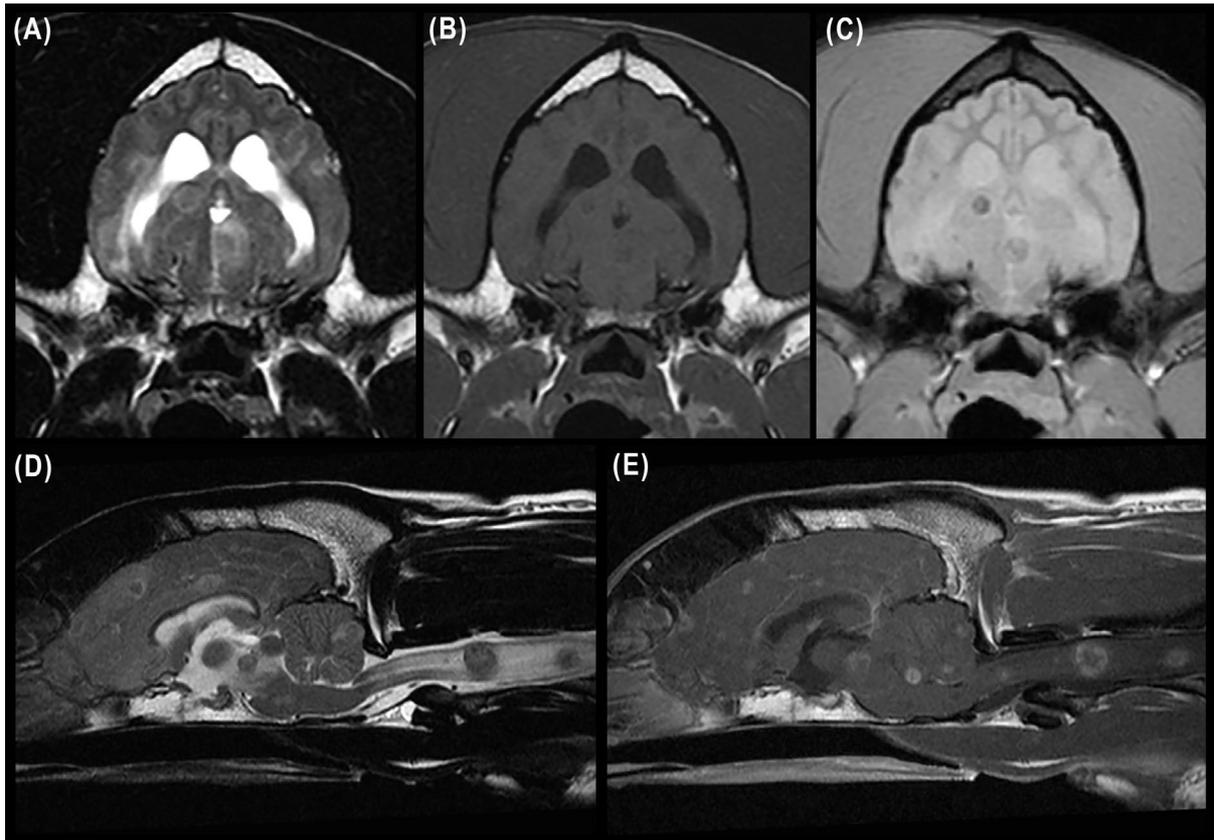
502 **Figure legends:**



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.

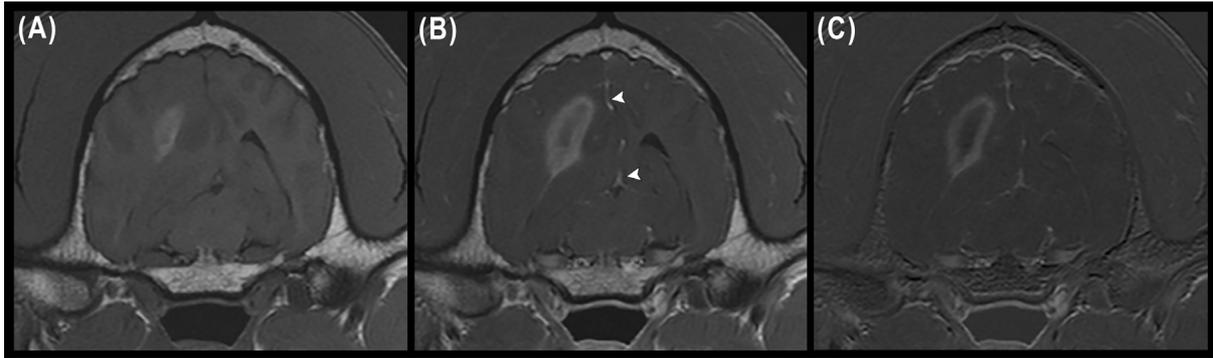
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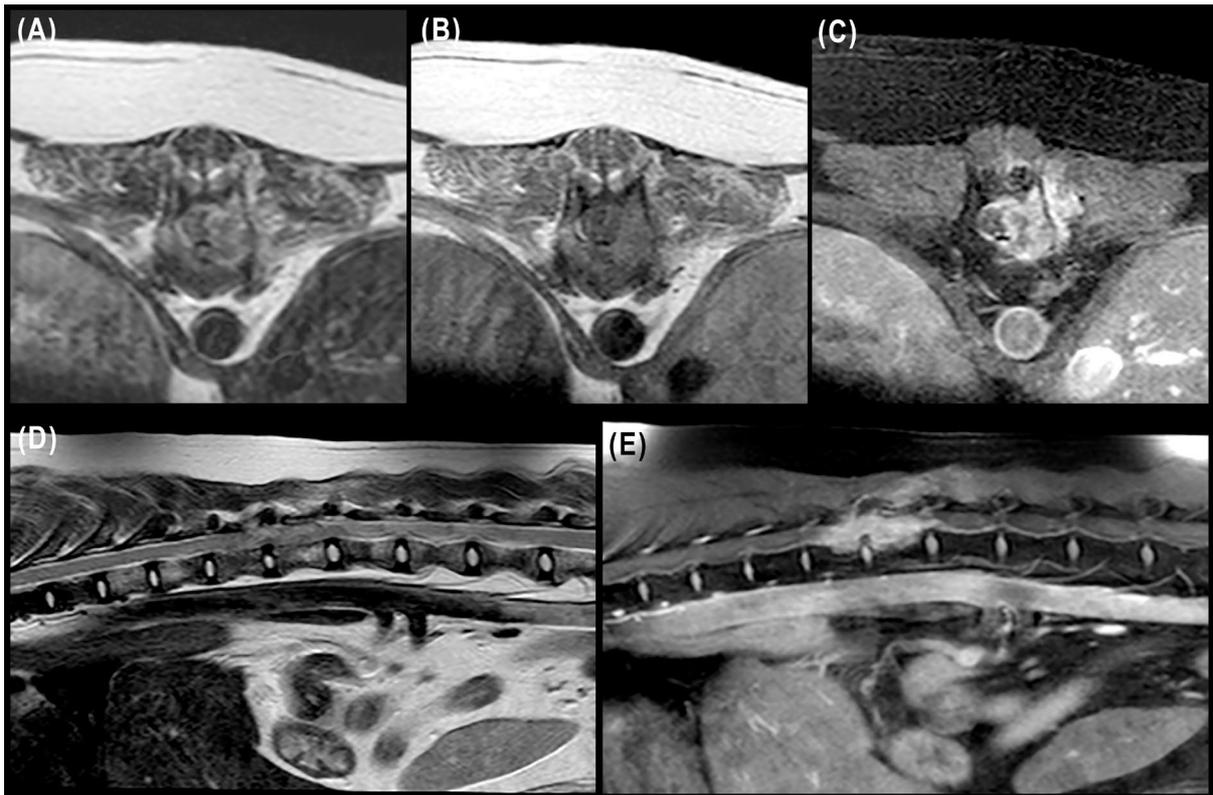
514 **Figure 2** Metastatic intracranial haemangiosarcoma in a 7-year-old male neutered Border
515 Collie at the level of the rostral mesencephalon (A-C) and mid-sagittal plane (D-E). A,
516 Transverse T2w; B, transverse T1w; C, transverse T2*w; D, sagittal T2w; and E, sagittal T1w
517 post contrast images. Note the multiple, intra-axial, well-marginated 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

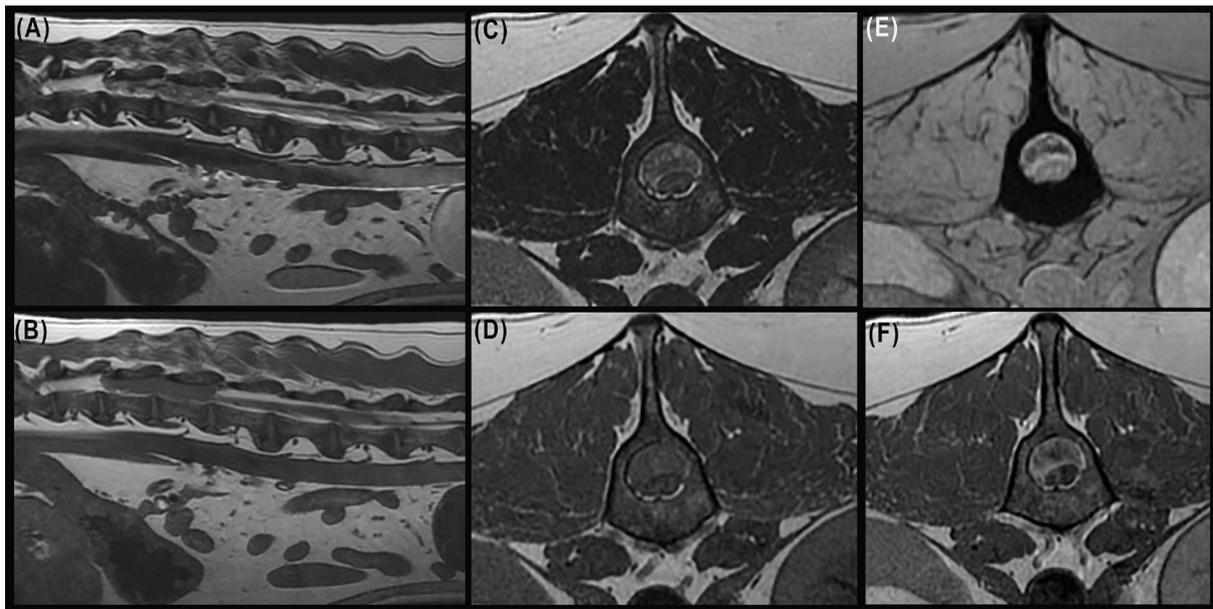
524 **Figure 3** Haemangiosarcoma in the right parieto-temporal lobes in an 11-year old male
 525 neutered mixed-breed dog. A, Transverse T1w; B, T1w post contrast; C, corresponding
 526 Dynamic subtraction image. Note the meningeal (arrowheads, B) and ring-like contrast
 527 enhancement of the mass.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



528

529 **Figure 4** Vertebral haemangiosarcoma in a 10-year old spayed female mixed-breed dog. A,
 530 Transverse T2w; 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 margined 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 paraspinous 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.