

Carloni, A. et al. (2022) Can MRI differentiate between ring-enhancing gliomas and intra-axial abscesses? *Veterinary Radiology and Ultrasound*, 63(5), pp. 563-572.

The material cannot be used for any other purpose without further permission of the publisher and is for private use only.

There may be differences between this version and the published version. You are advised to consult the publisher's version if you wish to cite from it.

This is the peer reviewed version of the following article:

Carloni, A. et al. (2022) Can MRI differentiate between ring-enhancing gliomas and intra-axial abscesses? *Veterinary Radiology and Ultrasound*, 63(5), pp. 563-572, which has been published in final form at: 10.1111/vru.13098

This article may be used for non-commercial purposes in accordance with <u>Wiley Terms and Conditions for Self-Archiving</u>.

https://eprints.gla.ac.uk/271038/

Deposited on 18 May 2022

Enlighten – Research publications by members of the University of Glasgow http://eprints.gla.ac.uk

1	TITLE: Can MRI differentiate between ring-enhancing gliomas and intra-axial abscesses?
2	
3	AUTHORS: Andrea Carloni <sup>a</sup> , Marco Bernardini <sup>a,b</sup> , Chiara Mattei <sup>a</sup> , Angela Vittoria De
4	Magistris <sup>a</sup> , Francisco Llabres-Diaz <sup>c</sup> , Jonathan Williams <sup>d</sup> , Rodrigo Gutierrez-Quintana <sup>e</sup> , Anna
5	Oevermann <sup>f</sup> , Daniela Schweizer-Gorgas <sup>f</sup> , Cyrielle Finck <sup>g</sup> , Isabelle Masseau <sup>g</sup> , Valentina
6	Lorenzo <sup>h</sup> , Annalisa Sabatini <sup>i</sup> , Barbara Contiero <sup>b</sup> , Swan Specchi <sup>a</sup>
7	
8	AFFILIATIONS:
9	<sup>a</sup> Diagnostic Imaging department, Veterinary Hospital "I Portoni Rossi" Anicura Italy, Zola
10	Predosa (BO), Italy.
11	<sup>b</sup> Department of Animal Medicine, Production and Health, Clinical Section, University of
12	Padua, Legnaro, Padua, Italy.
13	<sup>c</sup> Department of Clinical Science and Services, Royal Veterinary College, Hatfield, UK
14	<sup>d</sup> Pathobiology and Population Sciences, Royal Veterinary College, Hatfield, UK
15	<sup>e</sup> School of Veterinary Medicine, College of Medical Veterinary and Life Sciences, University
16	of Glasgow, UK.
17	<sup>f</sup> Division of Neurological Sciences, Vetsuisse Faculty, University of Bern, Bern, Switzerland.
18	<sup>g</sup> Department of Clinical Sciences, Faculty of Veterinary Medicine, University of Montreal,
19	Saint-Hyacinthe, Qc, Canada.
20	<sup>h</sup> Neurología Veterinaria, Getafe, Madrid, Spain.
21	<sup>i</sup> Veterinary Hospital "Gregorio VII", Roma, Italy.
22	
23	CORRESPONDENCE: swan.specchi@anicura.it
24	
25	KEYWORDS: brain; neoplasia; infection; dog; cat;

- 26
- 27 CONFLICT OF INTEREST DISCLOSURE: The authors have no conflict of interest to28 declare.
- 29
- 30 PRESENTATION DISCLOSURE: The preliminary results of this manuscript have been
- 31 presented at the online 2021 Annual EVDI Conference.
- 32
- 33 EQUATOR NETWORK DISCLOSURE: Relevant details described in the Strobe Vet-
- 34 statement checklist were included in this manuscript.

35 ABSTRACT

36 Gliomas of the brain may appear as expansile ring-enhancing masses in magnetic resonance 37 imaging (MRI) studies, mimicking the appearance of intra-axial abscesses. The aims of this study were to compare the MRI features of ring-enhancing gliomas and intra-axial brain 38 39 abscesses in dogs and cats and to identify the characteristics that might help differentiate them. For this multicenter, retrospective, and observational study, inclusion criteria were the 40 41 following: a) a definitive diagnosis of glioma or abscess based on cytological or histopathological examination following CSF collection or surgical biopsy/necropsy, 42 respectively; b) MRI study performed with a high or low field MRI scanner, including a same 43 44 plane T1W pre- and post-contrast, a T2W and a T2 FLAIR sequence in at least one plane. If 45 available, delayed T1W post-contrast, T2\*W GE, DWI/ADC and SWI sequences were also evaluated. Sixteen patients were diagnosed with ring-enhancing gliomas and 15 with intra-46 47 axial abscesses. A homogenous signal on T1W (P = 0.049) and T2W (P = 0.042) sequences, a T2W (P = 0.005) or T2\*W GE (P = 0.046) peripheral hypointense halo and an even 48 49 enhancing capsule (P = 0.002) were significantly associated with brain abscesses. A progressive central enhancement on delayed T1W post-contrast sequences was correlated 50 51 with ring-enhancing gliomas (P = 0.009). The combination of the following features was 52 suggestive of brain abscess: homogeneous T1W or T2W signal intensity, a T2W or T2\*W GE 53 peripheral hypointense halo and an evenly enhancing capsule. Central progression of 54 enhancement on delayed T1W post-contrast sequences was suggestive of glioma.

### 55 INTRODUCTION

56 Gliomas are primary neuroepithelial tumors accounting for approximately 35–37% of all primary brain tumors in dogs.<sup>1,2</sup> Glial tumors are less common in cats, representing 57 approximately 8% of feline primary brain tumors.<sup>3</sup> Commonly reported MRI features of 58 gliomas have included single, intra-axial, T1-weighted (T1W) iso- to hypointense and T2-59 weighted (T2W) iso- to hyperintense to normal brain parenchyma lesions, with cyst-like or 60 necrotic areas and variable distribution and degree of contrast enhancement.<sup>1,4-7</sup> An 61 intratumoral hemorrhagic component has also been reported.<sup>6</sup> Brain abscesses are uncommon 62 in companion animals and may develop via a hematogenous spread of bacteria, direct 63 invasion/contiguity, or contamination of cerebrospinal fluid.<sup>8-15</sup> A brain abscess originates as 64 a localized area of neutrophilic cerebritis which, if untreated, may progress into liquefactive 65 necrosis containing viable and degenerate neutrophils (pus) surrounded within 1 to 2 weeks 66 by a well-vascularized fibrovascular capsule.<sup>8,9</sup> On MRI, a brain abscess has been reported as 67 a focal, T2W hyperintense and T1W hypointense lesion compared to normal brain 68 69 parenchyma, with a necrotic non-enhancing center, surrounded by a thick and strongly contrast-enhancing peripheral rim.<sup>11-13,15,16</sup> 70 A recent review in the veterinary literature reports up to 45% of gliomas having partial or 71 complete ring-enhancement;<sup>17</sup> therefore, gliomas may appear as expansile ring-enhancing 72 masses, mimicking the radiological appearance of intra-axial abscesses.<sup>18</sup> In human medicine, 73 multiple MRI studies using specific sequences have attempted to find unique characteristics 74 to distinguish between ring-enhancing gliomas and abscesses. A hypointense peripheral 75 76 capsule on T2W images caused by paramagnetic free radicals within phagocytic

77 macrophages, often associated with susceptibility artifact in T2W gradient echo (T2\*) and

78 with a "double rim sign" in susceptibility-weighted imaging (SWI), is considered a

79 distinguishing feature of brain abscesses in humans.<sup>19,20</sup> Abscesses commonly show restricted

diffusion in diffusion weighted imaging (DWI) while gliomas usually do not.<sup>18, 21-23</sup> However,
overlapping imaging features have been reported.<sup>24-26</sup> Since the two diseases require very
different treatment and have a different prognosis, a correct imaging interpretation is
paramount.<sup>13,17,27,28</sup>

The aims of the current study were to compare the MRI features of confirmed ring-enhancing gliomas and intra-axial brain abscesses in dogs and cats and to identify the imaging features that might help to differentiate them. Authors hypotheses were 1) some MRI qualitative characteristics would be associated with brain abscess/glioma classification and, 2) a threshold value for the ratio between lesion diameter and capsule thickness in T1W postcontrast sequences could be used as a cut-off for discriminating between brain abscesses and gliomas.

91

#### 92 MATERIALS AND METHODS

93 CASE SELECTION CRITERIA

94 This was a multicenter, retrospective, observational study. All animals included were client-

95 owned and underwent MRI examinations of the brain as part of their clinical workup.

96 Previous informed written consent was obtained from all dog owners. All the procedures

97 performed complied with the European legislation "on the protection of animals used for

98 scientific purposes" (Directive 2010/63/EU).

99 The databases of the Veterinary Hospital "I Portoni Rossi" Anicura Italy, the Veterinary

100 Teaching Hospital of the University of Bern, the Royal Veterinary College, the University of

101 Glasgow, the University of Montreal, the Veterinary Clinic "Neurología Veterinaria" and the

102 Veterinary Hospital "Gregorio VII" were searched for dogs and cats diagnosed with a single

103 ring-enhancing intra-axial lesion. All hospitals approved the use of their imaging data for this

104 project.

106 Inclusion criteria for this study were the following: (1) a definitive diagnosis of glioma or

107 abscess based on cytological or histopathological examination following CSF collection or

108 surgical biopsy/necropsy, respectively; (2) a MRI study performed with a high or low field

109 MRI scanner, including at least a same plane pre- and postcontrast T1W and a T2W sequence

in at least one plane as well as a T2 FLAIR sequence in any plane. If available, T2\*W GE,

111 DWI/ADC, SWI and delayed postcontrast T1W sequences were analyzed. The final decisions

112 for subject inclusion or exclusion were made by an ACVR board-certified radiologist (SS)

and a second-year ECVDI resident (AC).

114

115 MEDICAL RECORD DATA RECORDING:

Medical record entries were retrieved and evaluated by an ACVR board-certified radiologist (SS) and a second-year ECVDI resident (AC). The reports of necropsy, surgical biopsy and/or CSF analysis along with patients' age, sex, and breed were recorded. Because the aim of the study was to describe the MRI features of brain abscesses and to compare them with ringenhancing gliomas in doubtful cases, the presence of MRI changes related to bite wounds were recorded, but not considered as imaging criteria for including subjects in the study.

122

## 123 IMAGE ANALYSIS

124 Images were analyzed by an ACVR board-certified radiologist (SS), a ECVN board-certified

neurologist (MB) and a second-year ECVDI resident (AC) not blinded to the final diagnosis.

126 The final decision on the imaging characteristics was reached on a consensus basis. The

127 studies were randomly reviewed using a DICOM (i.e., Digital Imaging and Communications

128 in Medicine) viewer program (OsiriX DICOM viewer, Pixmeo, Geneva, Switzerland). The

129 three observers were asked to fill in a pre-defined standardized commercially available

spreadsheet (Microsoft Excel 2020, Microsoft, Redmond, Wash). The following MRI features 130 131 were assessed: T1W and T2W signal heterogeneity/homogeneity as well as the intensity (hypo-, iso-, hyper-) of the signal compared to normal gray matter on the same sequences; 132 presence of a peripheral hypointense halo on T2W sequences compared to contents of the 133 lesion;<sup>13</sup> presence of a T2 FLAIR attenuated component within the lesion; presence and grade 134 135 (0, no; 1, mild; 2, moderate; 3, severe) of perilesional white matter edema based on a 136 subjective evaluation; pattern of ring enhancement (even/uneven); presence of progressive 137 central enhancement on delayed post-contrast sequences (delayed post-contrast enhancement was assessed in different planes if the same plane was not available)<sup>29</sup> and the ratio between 138 139 lesion diameter and maximum capsule thickness in the immediate T1 post contrast images. In cases in which T2\*W GE sequences, DWI or SWI were available, additional data were 140 141 collected such as the presence of susceptibility artifact (i.e., hemorrhage) and a hypointense peripheral halo compared to lesion content in T2\*W GE sequences;<sup>16</sup> the presence of 142 abnormal diffusion restriction in DWI/ADC;<sup>18,21</sup> the presence of "dual-rim sign" (defined as 143 144 two concentric rims at the margins of the lesion with the outer one being hypointense and the 145 inner one hyperintense relative to cavity contents) on SWI images as described previously.<sup>20</sup> 146

# 147 STATISTICAL ANALYSIS

All analyses were performed with commercial software (MedCalc, Software Ltd, Ostend,
Belgium) by an experienced statistician (BC). Count data regarding the abscess/glioma
diagnosis were crossed referenced with the MRI findings to obtain contingency tables. Chisquare test was applied to analyse data, using Yates correction for 2x2 contingency tables and
Fisher's exact test when frequencies inside tables were less than 5. When a significant
association (P<0.05) was found between an MRI qualitative predictor and abscess/glioma</li>
classification, the relative risk and 95% confidence interval (95%CI) were calculated.

155 The ratio between the lesion diameter and capsule thickness in the immediate T1 post-contrast

sequences was analyzed using a receiver-operating characteristic (ROC) approach to identify

the cut-off that could best discriminate between abscesses and gliomas. The threshold was

158 calculated using the Youden criterion.<sup>30</sup>

159

## 160 **RESULTS**

161 A total of 31 cases met the inclusion criteria. Sixteen patients were diagnosed with ring-

162 enhancing gliomas through necropsy (15/16) or surgical biopsies (1/15); Intra-axial abscesses

163 were diagnosed in 15 patients through necropsy (5/15), CSF analysis (7/15) and surgical

164 biopsies (3/15). Within the abscess group, 6/15 had evidence of bite wounds/penetrating

165 lesions visible as temporal muscle myopathy and calvarial focal defects in

166 continuity/contiguity with the intra-axial mass.

167

168 In the ring-enhancing glioma group there were 13 dogs and 3 cats. The canine breeds

169 represented in the study were Boxer (n = 3), French Bulldog (n = 2), Labrador Retriever (n = 1)

170 2), Jack Russell terrier (n = 2), Lhasa Apso, Boston Terrier, Springer Spaniel and mixed-

171 breed (n = 1 each). Two Domestic short-haired and 1 Sacred Birman cat represented the feline

group. Of the 13 dogs, 6 were males (4 neutered) and 7 females (3 spayed). The 3 cats were 2

spayed females and 1 male. The median age was 8 years (range: 5-12) for dogs and 8 years

174 (range: 5-15) for cats.

175 In the intra-axial abscess group, there were 10 dogs (3 mixed-breed, 1 Boxer, 1 Staffordshire

176 Bull Terrier, 1 West Highland White Terrier, 1 Border Terrier, 1 Miniature Schnauzer, 1

177 Chihuahua and 1 Golden Retriever) and 5 cats (4 Domestic short-haired and 1 Domestic long-

haired cat). Of the 10 dogs 4 were males (1 neutered) and 6 females (3 spayed). The 5 cats

were 4 neutered males and 1 spayed female. The median age was 4 years old (range: 1-11) for

180 dogs and 9 years old (range: 5-12) for cats.

181

182 The MRI technical parameters for each institution are listed in Supplement 1 and 2, 183 respectively. The radiofrequency coil selections varied based on patient sizes and availability. 184 All the animals were imaged in sternal recumbency, under general anesthesia. MRI studies 185 were acquired with both low- and high-field MRI scanners. T2\*W GE sequences were 186 available in 13 cases of ring-enhancing glioma and in 9 cases of intra-axial abscessation. DWI 187 sequences were obtained in 6 cases with ring-enhancing glioma and in one patient with a 188 brain abscess. SWI was available in only one patient with ring-enhancing glioma. Delayed 189 T1W post-contrast sequences performed at least 5 minutes after the first "immediate" post-190 contrast sequence were available in 12 glioma cases and in 10 intra-axial abscess cases.

191

#### **192** RING-ENHANCING GLIOMAS *vs.* BRAIN ABSCESSES

193 MRI findings of ring-enhancing gliomas and brain abscesses are summarized in Table 1. 194 Comparisons between groups for MRI characteristics are provided in Table 2. Overall, brain 195 abscesses showed a more homogeneous signal on T1W and T2W sequences compared to 196 ring-enhancing gliomas. A peripheral hypointense halo on T2W and T2\*W GE sequences 197 was significantly associated with brain abscesses rather than ring-enhancing gliomas (Figure 198 1). On postcontrast T1W sequences, abscesses showed a more even ring-enhancing capsule 199 compared to the ring-enhancing gliomas (figure 2), while ring-enhancing gliomas were more 200 likely to have a progressive central enhancement on T1W delayed postcontrast sequences 201 (figure 3). Based on the ROC analysis, a cut-off value of >12 in the ratio between lesion 202 diameter and capsule thickness in the immediate T1 post contrast sequences had a 43.75% 203 sensitivity and 85.71% specificity for the detection of ring-enhancing gliomas. The details of the obtained measurements are provided in supplement 3. The intensity of the lesions 204

(hyperintense, isointense or hypointense) compared to the gray matter, the presence of a T2 205 206 FLAIR attenuating component within the mass, the presence and grade of T2 FLAIR 207 perilesional vasogenic edema, and the presence of intralesional susceptibility artefacts were 208 not statistically significant. The unrestricted or decreased diffusion in DWI/ADC sequence 209 was not statistically evaluated due to the low number of patients where this sequence was 210 available. However, 6/6 patients with ring-enhancing glioma and DWI/ADC available showed 211 unrestricted diffusion; whereas the lesion in the only patient with DWI/ADC available images 212 within the brain abscesses group was characterized by restriction to diffusion (figure 2).

- 213
- 214

#### 215 **DISCUSSION**

216 Our study showed that ring-enhancing gliomas share several MRI features with intra-axial 217 brain abscesses. However, findings supported our first hypothesis in that some qualitative 218 MRI characteristics were significantly associated with brain abscess or ring-enhancing 219 glioma: a homogenous signal on T1W and T2W sequences, a T2W and T2\*W GE peripheral 220 hypointense halo, and an even enhancing capsule were more likely associated with brain 221 abscesses. Progressive central enhancement on T1W delayed postcontrast sequences was 222 strongly associated with ring-enhancing gliomas while this feature was only present in a 223 single dog with a brain abscess. Findings also supported our second hypothesis in that a threshold value of >12 for the ratio between lesion diameter and capsule thickness in T1 post-224 225 contrast sequences was found to be a cut-off for discriminating between abscesses and 226 gliomas. The presence of bite wounds/penetrating lesions in continuity/contiguity with an 227 intra-axial mass makes a brain abscess the most likely differential diagnosis. However, we did 228 not consider them as imaging criteria because we aimed to focus on those MRI findings that 229 can help the clinician in a doubtful clinical situation.

In our cohort of patients, brain abscesses had a significantly more homogeneous signal on 230 231 T1W and T2W sequences, likely reflecting the presence of necrotic/fluid content in the abscess.<sup>11-13,15,16</sup> In contrast, ring-enhancing gliomas usually showed a more heterogeneous 232 233 T1W or T2W signal due to the presence of variable content in these tumors, including hemorrhage, necrotic tumor tissue, cysts or altered cellular density.<sup>5-7,17,31</sup> 234 235 There was absence of statistical significance in the evaluation of the type of T1W and T2W 236 signal compared to the grey matter in both gliomas and abscesses. This is related to the tumor 237 heterogeneity in gliomas and the variable ratio between cellular/protein content in abscesses 238 depending on their chronicity stage, respectively. During their development, abscesses begin 239 as a focal area of cerebritis histologically defined by a perivascular infiltration of neutrophils, 240 lymphocytes, and plasma cells within the brain parenchyma with an ill-defined central 241 necrotic zone composed of inflammatory cells, cellular debris, and microorganisms. In human 242 literature, cerebritis is used to denote brain parenchymal inflammation secondary to infection with bacteria or other non-viral pathogens. In contrast, encephalitis is typically viral in 243

244 origin.<sup>32</sup>

Subsequently, the necrotic center increases in size and becomes more well defined. As the
abscess becomes more chronic, the central necrotic area regresses and, if the patient survives
without treatment, the abscess will heal as a collapsed fibrotic glial scar.<sup>12</sup>

Our study demonstrates a significant correlation between a peripheral hypointense halo on T2W and T2\*W GE sequences and brain abscesses. This halo is due to paramagnetic free radicals within phagocytic macrophages and it has already been described in both human and veterinary medicine.<sup>8,13,15,16,19,21,33</sup> However, although seen in most abscesses in our study, this halo was not detected on all abscesses; moreover, it was also visible in the MRI study of one patient with a glioma. A T2W and T2\*W GE peripheral hypointense halo has been described in both veterinary and human literature in several conditions such as gliomas, chronic hematomas, metastases, granulomatous lesions, infarctions, meningiomas, and radiation
 necrosis.<sup>12,19</sup> Despite its statistical significance, it cannot therefore be regarded as
 pathognomonic for brain abscesses.

258 Another MRI finding that statistically correlated with brain abscesses was the presence of an 259 even enhancing capsule. This may be explained by the pathophysiology of brain abscess formation, which includes four different stages: the first two stages represent the "early" and 260 261 "late cerebritis" phases without collagenous capsule; during stage 3, called "early capsule", 262 there is an initial deposition of collagen at the periphery of the necrotic center and it is followed by ingrowth of granulation tissue and neovascularization; in the fourth or "late 263 capsule" stage there is complete formation of the capsule surrounding the necrotic center.<sup>12</sup> 264 265 Ring enhancing gliomas are not truly encapsulated, and the peripheral enhancing portion of 266 the lesion represents expanding neoplastic tissue with microvascular proliferations surrounding a central necrotic core.<sup>31</sup> The intrinsic neoplastic nature of this tissue may explain 267 both its uneven peripheral enhancement pattern and the progressive central enhancement 268 269 noted in 9 out of the 12 T1W delayed postcontrast sequences that correlated with ring-270 enhancing gliomas. In both veterinary and human literature, intra-axial lesions usually show progressively increased conspicuity on delayed postcontrast sequences.<sup>4,29,34</sup> Moreover, the 271 272 presence of tumor angiogenesis along with poorly vascularized peripheral neoplastic tissue 273 surrounding the necrotic center may play a role in the delayed central progression of the enhancement.<sup>31</sup> 274

In one brain abscess a very mild progressive central enhancement was seen. In this case,
immediate and delayed postcontrast T1W sequences were acquired in different planes and the
progressive central enhancement may therefore not be real. Other possible explanations
include a partial volume artifact due to the capsule's thickness or the presence of a very thick
capsule that necessitated more time to enhance completely.

When evaluating the ratio between the lesion diameter and the capsule's thickness in the
immediate postcontrast T1W sequences, a cut-off >12 (43.75% sensitivity and 85.71%
specificity) can be proposed for the detection of ring-enhancing gliomas. The uneven
peripheral enhancement pattern of ring-enhancing gliomas due to the presence of
microvascular proliferation compared to the more even and smooth capsule of brain
abscesses<sup>12,31</sup> would explain why ring-enhancing gliomas had higher lesion diameter:capsule
thickness ratio than abscesses.

T2 FLAIR sequences have been proposed to characterize fluid collections and differentiate fluid-cavitary lesions from other parenchymal T2 high signal lesions.<sup>6</sup> Cystic regions are typical of canine glioblastoma but can also occur in approximately one-third of low-grade canine gliomas;<sup>6,31</sup> on the other hand, brain abscesses are associated with a necrotic core during their development which may mimic the signal intensity and the cellular density of a ring-enhancing glioma.<sup>12,31</sup> This may explain the lack of statistical significance of an intralesional T2 FLAIR attenuating component in our study.

294 The grade of the perilesional vasogenic edema was not statistically significant; vasogenic 295 edema is secondary to the disruption of the blood-brain-barrier (BBB) and represents a nonspecific feature of several brain diseases including neoplastic and infectious disorders.<sup>35,36</sup> 296 297 In humans, two patterns of vasogenic edema have been described: type 1 is seen in the 298 immediate vicinity of low-grade and nonglial tumors and is thought to be secondary to 299 parenchymal compression with secondary ischemia and necrosis; type 2 occurs with high-300 grade glial tumors and is characterized by fingerlike projections reflecting tumor microinvasion causing additional derangements of the BBB.<sup>35</sup> Further studies are needed to 301 302 investigate the relationship between the severity of perilesional vasogenic edema, brain 303 abscesses and low- and high-grade gliomas.

304 The presence of intralesional T2\*W GE susceptibility artifact was observed in 4/13 patients 305 with ring-enhancing gliomas and only in 1/9 with brain abscesses, failing to achieve statistical significance, probably due to the small sample of patients. These susceptibility artifacts were 306 likely consistent with hemorrhage, which is more commonly reported in gliomas.<sup>5-7,31,37</sup> A 307 recent article in veterinary medicine recommends the use of SWI because it allows better 308 definition of intracranial hemorrhage.<sup>37</sup> In the same study, the presence of intra- and 309 310 extralesional fine, linear, and continuous susceptibility SWI artefacts was identified in 74.1% 311 of intracranial tumors and was interpreted as neovascularization.<sup>37</sup> In our study population, SWI images were only available for a single glioma patient, showing some intralesional 312 313 foci/tubular susceptibility artifacts that were not visible on the T2\*W GE sequence. In the 314 brain abscess group, T2\*W GE intralesional susceptibility artifacts were seen in one feline patient. These artifacts were attributed to hemorrhagic foci secondary to the recent bite wound 315 316 reported in the medical record.

317 Only seven MRI studies included a DWI/ADC sequence. This sequence was not included as 318 part of the standard MRI brain protocol for many of the institutions. All ring-enhancing 319 glioma patients for whom a DWI/ADC sequence was available (n=6), showed an unrestricted 320 diffusion of the lesion whereas the only patient with a brain abscess showed an abnormal 321 restriction to diffusion. These findings agree with what is reported in human and veterinary 322 medicine<sup>21,23, 33, 38,39</sup> In humans, atypical diffusion (e.g., restriction to diffusion in gliomas and unrestricted diffusion in brain abscess) is reported in 5-21% of the cases.<sup>24-26</sup> In veterinary 323 medicine, restriction to diffusion in glial cell tumors has been described<sup>40</sup> while there are no 324 325 reports about unrestricted diffusion in brain abscesses.

In humans, the "dual rim sign" in SWI is the most specific imaging feature to distinguish
gliomas and abscesses.<sup>20</sup> This sign is typically seen in pyogenic abscesses while it has never
been reported in gliomas.<sup>20</sup> In our study, only one patient with glioma had SWI images

available, without evidence of "dual rim sign". The lack of visualization of "dual rim sign" in
this patient agrees with what is reported in human medicine. Unfortunately, due to the
retrospective nature of our study, a SWI sequence was not included in the MRI protocol of
any patient of the abscess group. Future studies are needed to investigate the utility of the
SWI sequence in veterinary medicine.

The major limitation of this study is the use of different MRI equipment and protocols. Lowfield MRI might have failed in detecting small lesions. The different planes in some studies between the immediate and the delayed postcontrast T1W sequences might have caused incorrect interpretation of the effective progression of the central enhancement.

Another limitation is that, due to the retrospective and multicenter nature of the study over a
long period, different histological classification systems were used from different veterinary
pathologists with different backgrounds. For this reason, we decided not to make a distinction
between high- and low-grade ring-enhancing gliomas.

342 A potential source of bias was that the authors were aware of the final diagnosis at the time of 343 image interpretation. However, we did not consider it a major concern because the study 344 aimed to describe the MRI features of brain abscesses and ring-enhancing gliomas and not 345 test the diagnostic accuracy of MRI. In conclusion, even if several overlapping MRI features 346 between ring-enhancing gliomas and brain abscesses do exist, some features can help to prioritize the MRI diagnosis. The presence of a homogeneous T1W or T2W signal intensity, a 347 T2W or T2\*W GE peripheral hypointense halo and an even enhancing capsule may indicate a 348 349 brain abscess. The central progression of the enhancement on delayed postcontrast T1W 350 sequences is indicative of glial neoplasia. The addition of DWI and SWI sequences on highfield MR scanners should be considered for assessment of intra-axial brain lesions which 351 352 cannot be easily discriminated using standard MRI sequences.

#### 354 LIST OF AUTHOR CONTRIBUTIONS

- 355 Category 1
- 356 (a) Conception and Design: Swan Specchi, Andrea Carloni, Chiara Mattei, Marco Bernardini.
- 357 (b) Acquisition of Data: Andrea Carloni, Swan Specchi, Marco Bernardini, Chiara Mattei,
- 358 Angela Vittoria De Magistris, Francisco Llabres-Diaz, Jonathan Williams, Rodrigo Gutierrez-
- 359 Quintana, Anna Oevermann, Daniela Schweizer-Gorgas, Cyrielle Finck, Isabelle Masseau,
- 360 Valentina Lorenzo, Annalisa Sabatini.
- 361 (c) Analysis and Interpretation of Data: Andrea Carloni, Swan Specchi, Marco Bernardini,
- 362 Chiara Mattei, Barbara Contiero.
- 363
- Category 2
- 365 (a) Drafting the Article: Andrea Carloni, Swan Specchi, Marco Bernardini, Chiara Mattei,366 Barbara Contiero.
- 367 (b) Revising Article for Intellectual Content: Swan Specchi, Andrea Carloni, Marco
- 368 Bernardini, Chiara Mattei, Angela Vittoria De Magistris, Francisco Llabres-Diaz, Jonathan
- 369 Williams, Rodrigo Gutierrez-Quintana, Anna Oevermann, Daniela Schweizer-Gorgas,
- 370 Cyrielle Finck, Isabelle Masseau, Valentina Lorenzo, Annalisa Sabatini.

- 372 Category 3
- 373 (a) Final Approval of the Completed Article: Andrea Carloni, Swan Specchi, Marco
- 374 Bernardini, Chiara Mattei, Angela Vittoria De Magistris, Francisco Llabres-Diaz, Jonathan
- 375 Williams, Rodrigo Gutierrez-Quintana, Anna Oevermann, Daniela Schweizer-Gorgas,
- 376 Cyrielle Finck, Isabelle Masseau, Valentina Lorenzo, Annalisa Sabatini, Barbara Contiero.
- 377

- 378 Category 4
- 379 (a) Agreement to be accountable for all aspects of the work in ensuring that questions related
- to the accuracy or integrity of any part of the work are appropriately investigated and
- 381 resolved: Andrea Carloni, Swan Specchi, Marco Bernardini, Chiara Mattei, Angela Vittoria
- 382 De Magistris, Francisco Llabres-Diaz, Jonathan Williams, Rodrigo Gutierrez-Quintana, Anna
- 383 Oevermann, Daniela Schweizer-Gorgas, Cyrielle Finck, Isabelle Masseau, Valentina Lorenzo,
- 384 Annalisa Sabatini, Barbara Contiero.

# 385 REFERENCES

386	1.	Snyder JM, Shofer FS, Van Winkle TJ, Massicotte C. Canine Intracranial Primary
387		Neoplasia: 173 Cases (1986–2003). J Vet Intern Med 2006;20:669–75.
388	2.	Song RB, Vite CH, Bradley CW, Cross JR. Postmortem Evaluation of 435 Cases of
389		Intracranial Neoplasia in Dogs and Relationship of Neoplasm with Breed, Age, and
390		Body Weight. J Vet Intern Med 2013;27:1143–52.
391	3.	Troxel MT, Vite CH, Van Winkle TJ, et al. Feline Intracranial Neoplasia:
392		Retrospective Review of 160 Cases (1985–2001). J Vet Intern Med 2003;17:850–59.
393	4.	Hecht S. Brain neoplasia. In: Mai W eds. Diagnostic MRI in dogs and cats, 1 <sup>st</sup> ed.
394		Boca Raton, FL: CRC press;2018:211-40.
395	5.	Wisner ER, Dickinson PJ, Higgins RJ. Magnetic resonance imaging features of canine
396		intracranial neoplasia. Vet Radiol Ultrasound 2011;52:S52–S61.
397	6.	Bentley RT, Oberb CP, Andersonb KL, et al. Canine intracranial gliomas:
398		Relationship between magnetic resonance imaging criteria and tumor type and grade.
399		Vet J 2013:463–71.
400	7.	Young BD, Levine JM, Porter BF. Magnetic resonance imaging features of
401		intracranial astrocytomas and oligodendrogliomas in dogs. Vet Radiol Ultrasound
402		2011;52:132–41.
403	8.	Thomas WB. Nonneoplastic Disorders of the Brain. Clin Tech Small Anim Pract
404		1999;14:125–47.
405	9.	Sonneville R, Ruimy R, Benzonana N, et al. An update on bacterial brain abscess in
406		immunocompetent patients. Clin Microbiol Infect 2017;23:614-20.
407	10.	Radaelli ST, Platt SR. Bacterial Meningoencephalomyelitis in Dogs: A Retrospective
408		Study of 23 Cases (1990–1999). J Vet Intern Med 2002;16:159–63.

11. Mateo I, Lorenzo V, Munoz A, Pumarola M. Brainstem Abscess Due to Plant Foreign 409 410 Body in a Dog. J Vet Intern Med 2007;21:535–38. 411 12. Klopp LS, Hathcock JT, Sorjonen DC. Magnetic resonance imaging features of brain 412 stem abscessation in two cats. Vet Radiol Ultrasound 2000;41:300-307. 413 13. Costanzo C, Garosi LS, Glass EN. Brain abscess in seven cats due to a bite wound: 414 MRI findings, surgical management and outcome. J Feline Med Surg 2011;13:672-80. 415 14. Rosenblatt AJ, Scrivani PV, Caserto BG et al. Imaging diagnosis -416 meningoencephalitis secondary to suppurative rhinitis and meningoencephalocele infection in a dog. Vet Radiol Ultrasound 2014;55:614–19. 417 418 15. Seiler G, Cizinauskas S, Scheidegger J, Lang L. Low-field magnetic resonance 419 imaging of a pyocephalus and a suspected brain abscess in a German Shepherd dog. 420 Vet Radiol Ultrasound 2001;42:417–22. 421 16. Bach JF, Mahony OM, Tidwell AS, Rush JE. Brain abscess and bacterial endocarditis in a Kerry BlueTerrier with a history of immune-mediated thrombocytopenia. J Vet 422 423 Emerg Crit Care 2007;17:409–15. 424 17. Miller AD, Ryan Miller C, Rossmeisl JH. Canine Primary Intracranial Cancer: A 425 Clinicopathologic and Comparative Review of Glioma, Meningioma, and Choroid 426 Plexus Tumors. Front Oncol 2019; 9:1151. doi: 10.3389/fonc.2019.01151. 427 18. Huisman T. Tumor-like lesions of the brain. Cancer Imaging 2009;9: S10-S13. 19. Haimes BA, Zimmerman RD, Morgello S, et al. MR imaging of brain abscesses. Am J 428 429 Roentgenol 1989;152:1073-85. 430 20. Toh CH, Wei K-C, Chang C-N, et al. Differentiation of pyogenic brain abscesses from necrotic glioblastomas with use of Susceptibility-Weighted Imaging. Am J 431 432 Neuroradiol 2012;33:1534–38.

433	21.	Kim YJ, Chang K-H, Song IC, et al. Brain abscess and necrotic or cystic brain tumor:
434		discrimination with signal intensity on Diffusion Weighted MR Imaging. Am J
435		Neuroradiol 1998;171:1487–90.
436	22.	Toh CH, Wei K-C, Ng S-H. Differentiation of brain abscesses from necrotic
437		glioblastomas and cystic metastatic brain tumors with diffusion tensor imaging. Am J
438		Neuroradiol 2011; 32:1646–51.
439	23.	Chiang I-C, Hsieh T-J, Chiu M-L, et al. Distinction between pyogenic brain abscess
440		and necrotic brain tumour using 3-tesla MR spectroscopy, diffusion and perfusion
441		imaging. Br J Radiol 2009;82: 813-20.
442	24.	Reddy JS, Mishra AM, Behari S, et al. The role of diffusion-weighted imaging in the
443		differential diagnosis of intracranial cystic mass lesions: a report of 147 lesions. Surg
444		Neurol 2006;66:246–51.
445	25.	Reiche W, Schuchardt V, Hagen T et al. Differential diagnosis of intracranial ring
446		enhancing cystic mass lesions-Role of diffusion-weighted imaging (DWI) and
447		diffusion-tensor imaging (DTI). Clin Neurol Neurosurg 2010;112:218-25.
448	26.	Hakyemez B, Erdogan C, Yildirim N, Parlak M. Glioblastoma multiforme with
449		atypical diffusion-weighted MR findings. Br J Radiol 2005;78:989–92.
450	27.	Bersan E, Maddox T, Walmsley G, et al. CT-guided drainage of a brainstem abscess
451		in a cat as an emergency treatment procedure. J Feline Med Surg Open Reports.
452		January 2020. doi:10.1177/2055116919896111.
453	28.	Bilderback AL, Faissler D. Surgical management of a canine intracranial abscess due
454		to a bite wound. J Vet Emerg Crit Care 2009; 19(5): 507–12.
455	29.	Carmel EN, d'Anjou M-A, Blond L, Beauchamp G, Parent J. Effect of acquisition
456		time on observer variability and qualitative characterization of gadolinium-enhancing

457		brain lesions in dogs and cats. Abstracts from the annual meeting of the American
458		College of Veterinary Radiology. Vet Radiol Ultrasound 2010;51: 221-35.
459	30.	Youden WJ."Index for rating diagnostic tests". Cancer 1950;3:32–35.
460	31.	Lipsitz D, Higgins RJ, Kortz GD. Glioblastoma Multiforme: Clinical Findings,
461		Magnetic Resonance Imaging, and Pathology in Five Dogs. Vet Pathol 2003;40:659–
462		69.
463	32.	Rath TJ, Hughes M, Arabi M, Shah GV. Imaging of Cerebritis, Encephalitis, and
464		Brain Abscess. Neuroimag Clin N Am 2012;22:585–607.
465	33.	Nagendran A, McConnel JF. Diffusion- and perfusion-weighted imaging
466		characteristics of an intracranial abscess in a cat. J Small Anim Pract. 2021
467		Aug;62(8):714. doi: 10.1111/jsap.13322. Epub 2021 Mar 23. PMID: 33759197.
468	34.	Song GJ, Chang K-H, Na DK, et al. Delayed Effect of Contrast Enhancement in Brain
469		Tumors on MRI. J Korean Soc Radiol 1995 32(3):383-88.
470	35.	Ho M-L, Rojas R, Eisenberg RL. Cerebral Edema. Am J Roentgenol 2012;99:W258-
471		W273.
472	36.	Patel K, Clifford DB. Bacterial Brain Abscess. Neurohospitalist 2014;4(4):196-204.
473	37.	Weston P, Morales C, Dunning M, et al. Susceptibility weighted imaging at 1.5 Tesla
474		magnetic resonance imaging in dogs: Comparison with T2*-weighted gradient echo
475		sequence and its clinical indications. Vet Radiol Ultrasound. 2020;61:566-76.
476	38.	Desprechins B, Stadnik T, Koerts G, et al. Use of Diffusion-Weighted MR Imaging in
477		Differential Diagnosis Between Intracerebral Necrotic Tumors and Cerebral
478		Abscesses. Am J Neuroradiol 1999;20:1252–57.
479	39.	Scherf G, Sutherland-Smith J, and Uriarte A. Dogs and cats with presumed or
480		confirmed intracranial abscessation have low apparent diffusion coefficient values.
481		Vet Radiol Ultrasound. 2022; https://doi.org/10.1111/vru.13064.

482 40. Sutherland-Smith J, King R, Faissler D, et al. Magnetic resonance imaging apparent
483 diffusion coefficients for histologically confirmed intracranial lesions in dogs. Vet
484 Radiol Ultrasound. 2011;52:142–148.

# 485 Table 1: Qualitative MRI features of ring-enhancing gliomas and brain abscesses in dogs and

486 cats.

			Glioma (n = 16)	Abscess (n = 15)
Signal homogeneity	T1W	Homogeneous	4/16 (25%)	10/15 (66%)
		Heterogeneous	12/16 (75%)	5/15 (33%)
		Homogeneous	0/16 (0%)	5/15 (33%)
		Heterogeneous	16/16 (100%)	10/15 (66%)
Signal intensity	T1W	Hypointense	Hypointense 11/16 (69%)	
		Isointense	4/16 (25%)	1/15 (6%)
		Hyperintense	1/16 (6%)	0/15 (0%)
	T2W	Hypointense	0/16 (0%)	3/15 (20%)
		Isointense	0/16 (0%)	1/15 (6%)
		Hyperintense	16/16 (100%)	11/15 (73%)
T2W peripheral hypointense halo	Presence		1/16 (6%)	9/15 (60%)
	Absence		15/16 (93%)	6/15 (40%)
T2*W GE peripheral hypointense halo	Presence		1/13 (8%)	5/9 (55%)
	Absence		12/13 (92%)	4/9 (44%)
T2 FLAIR intralesional attenuating component	Presence	•	10/16 (62%)	9/15 (60%)
			6/16 (37%)	
T2 FLAIR white matter perilesional edema	Grade 0-	-1	8/16 (50%)	2/15 (13%)
	Grade 2-	-3	8/16 (50%)	13/15 (86%)
Pattern of ring-enhancement	Even		1/16 (6%)	10/15 (66%)
	Uneven		15/16 (93%)	5/15 (33%)
Progressive central enhancement on delayed T1W post-	Presence	•	9/12 (75%)	1/10 (10%)
contrast	Absence		3/12 (25%)	9/10 (90%)
Susceptibility artifacts on T2*W GE <del>SWI</del>			4/13 (31%)	1/9 (11%)
			9/13 (69%)	8/9 (89%)
Signal on DWI/ADC	Unrestrie	cted diffusion	6/6 (100%)	0/1 (0%)
	Decrease	ed diffusion	0/6 (0%)	1/1 (100%)
"Dual rim sign" on SWI	Presence		0/1 (0%)	N/A
	Absence		1/1 (100%)	N/A

# 491 Table 2: Comparison between MRI findings in ring-enhancing gliomas and brain abscesses in

dogs and cats.

	Gliomas	Abscesses	Chi-square	Р	Relative	95%CI
	N=16	N=15	test		risk	
T2W homogeneous lesion	0	5	4.13	0.042	2.6	1.6-4.23
T1W homogeneous lesion	4	10	3.87	0.049	2.4	1.08-5.45
Intensity of the lesion on T2W sequences			4.90	0.050		
- hyper	16	11	2.81	0.093		
- iso	0	1	0.001	0.974		
- hypo	0	3	1.62	0.202		
Intensity of the lesion on T1W sequences			3.13	0.251		
- hyper	1	0	0.001	0.974		
- iso	4	1	0.81	0.369		
- hypo	11	14	1.63	0.202		
T2 FLAIR intralesional attenuating component	10	9	0.05	0.821		
T2 FLAIR white matter perilesional edema			5.56	0.162		
- grade 2-3	8	13	3.23	0.072		
- grade 0-1	8	2	1.63	0.202		
Peripheral T2 hypointense halo	1	9	7.92	0.005	3.15	1.55-6.39
Peripheral T2*W GE hypointense halo	1	5	3.97	0.046	3.33	1.33-8.37
Susceptibility artifacts on T2*W GE sequences	4	1	0.32	0.572		
Even ring-enhancing pattern on T1W + C sequences	1	10	9.85	0.002	3.64	1.66-7.95
Progressive central enhancement on delayed T1W	9	1	6.86	0.009	0.13	0.02-0.88
post-contrast						



494

Figure 1: Transverse T2W FSE image (1.5 T, TR 2500, TE 15) of a one-year-old, neutered
male, American Staffordshire Terrier with left thalamic abscess. Note the peripheral

- 497 hypointense halo (arrow) surrounding a homogeneous hyperintense center. There is a
- 498 moderate mass effect on the third ventricle (arrowheads) along with moderate T2
- 499 hyperintense vasogenic edema surrounding the lesion.



Figure 2: (A-C; 1.5 T, transverse T1W FSE TR 500, TE 13 and transverse DWI/ADC TR 502 503 4233, TE 110, B value 1000) 9-year-old, male neutered, DSH cat with a right parietal lobe abscess secondary to a bite wound. An even, well-defined ring-enhancing lesion with 504 505 hypointense center (arrow) is visible on the T1 post-contrast sequence (A); right temporal 506 myopathy and a calvarial defect are also visible (dashed arrow). On the transverse DWI (B) 507 the central portion of the abscess is strongly hyperintense to normal brain parenchyma (black 508 asterisk) while it shows low values (white asterisk) on the ADC map (C), consistent with 509 restriction to diffusion. (D-F; 1.5 T, transverse T1W FSE TR 465, TE 11 and transverse 510 DWI/ADC TR 4288, TE 94, B value 1000) 5-year-old, male, French Bulldog with ringenhancing glioma of the right fronto-parietal lobe. The T1W post-contrast sequence shows an 511 512 unevenly marginated ring-enhancing glioma (arrowheads) (D). On the transverse DWI (E) the 513 central portion of the lesion is hypointense (white §) to normal brain parenchyma while on the 514 ADC map (F) it shows high signal (black §), consistent with unrestricted diffusion.

- 515 Note the difference between the even enhancing capsule of the brain abscess (A) compared to
- 516 the unevenly marginated ring-enhancing glioma (D).
- 517



Figure 3: Immediate post-contrast T1W transverse (A) and dorsal delayed post-contrast T1W 519 (B) images (1.5 T, transverse T1W FSE TR 500, TE 13) of a 9-year-old, male neutered, DLH 520 521 cat with a right temporo-parietal lobe abscess secondary to a bite wound with temporal 522 myopathy (arrows). Despite the different acquisition planes, the thickness of the abscess' 523 capsule does not increase over time (white arrowheads). Immediate post-contrast T1W 524 FLAIR (C) and delayed post-contrast T1W FLAIR (D) transverse images (1.5 T, transverse 525 T1W FLAIR FSE TR 2560, TE 26, TI 1013) of a 9-year-old, female spayed, Labrador 526 Retriever with a left cerebellar ring-enhancing glioma. Note the conspicuous central 527 progression (black arrowheads) of the enhancement on the delayed post-contrast sequence.