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1 **Appearance of the canine meninges in subtraction magnetic resonance images**

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10

11 Key words: anatomy, dog, gadolinium, magnetic resonance imaging, meninges, subtraction

12 Running head: Canine meningeal anatomy

13 Abstract

14 The canine meninges are not visible as discrete structures in non-contrast magnetic resonance
15 (MR) images, and are incompletely visualized in T1-weighted, post-gadolinium images,
16 reportedly appearing as short, thin curvilinear segments with minimal enhancement.
17 Subtraction imaging facilitates detection of enhancement of tissues, hence may increase the
18 conspicuity of meninges. The aim of the present study was to describe qualitatively the
19 appearance of canine meninges in subtraction MR images obtained using a dynamic
20 technique. Images were reviewed of 10 consecutive dogs that had dynamic pre- and post-
21 gadolinium T1W imaging of the brain that was interpreted as normal, and had normal
22 cerebrospinal fluid. Image-anatomic correlation was facilitated by dissection and histologic
23 examination of two canine cadavers. Meningeal enhancement was relatively inconspicuous in
24 post-gadolinium T1-weighted images, but was clearly visible in subtraction images of all
25 dogs. Enhancement was visible as faint, small rounded foci compatible with vessels seen end-
26 on within the sulci, a series of larger rounded foci compatible with vessels of variable caliber
27 on the dorsal aspect of the cerebral cortex, and a continuous thin zone of moderate
28 enhancement around the brain. Superimposition of color-encoded subtraction images on pre-
29 gadolinium T1- and T2-weighted images facilitated localization of the origin of enhancement,
30 which appeared to be predominantly dural, with relatively few leptomeningeal structures
31 visible. Dynamic subtraction MR imaging should be considered for inclusion in clinical brain
32 MR protocols because of the possibility that its use may increase sensitivity for lesions
33 affecting the meninges.

34 **Introduction**

35 The meninges (dura mater, arachnoid, and pia mater) are affected by a variety of
36 inflammatory and neoplastic conditions in dogs and, therefore, are tissues of importance for
37 radiologists interpreting magnetic resonance (MR) images of the canine head. The lack of a
38 blood-brain barrier in the meninges^{1,2} facilitates accumulation of gadolinium chelates, hence
39 use of post-gadolinium MR images has been emphasized for clinical examination of the
40 meninges.³⁻⁸ Numerous clinical reports include descriptions of meningeal lesions in post-
41 gadolinium T1-weighted MR images of dogs.⁹⁻¹⁴

42 In contrast, descriptions of the appearance of normal canine meninges in MR images are
43 relatively sparse. Based primarily on descriptions of humans, the meninges are not considered
44 to be visible as discrete structures in non-contrast MR images, but appear as short, thin
45 curvilinear segments with minimal enhancement in T1-weighted post-gadolinium
46 images.^{3,7,15} Meningeal enhancement may be divided into pachymeningeal (affecting the dura
47 and the periosteum on the inner aspect of the skull) and leptomeningeal (affecting the pia and
48 arachnoid).³ The pachymeninges appear continuous with the falx and/or tentorium and have
49 no sulcal indentations, whereas the leptomeninges occupy the spaces between sulci,
50 cerebellar folia and cisterns.³ A slight degree of enhancement of both the pachymeninges and
51 the leptomeninges is considered normal in dogs.⁷ Because the meninges are well-vascularized
52 and lack a blood-brain barrier, they may be expected to enhance much more than the brain;
53 however, the normal dura mater is said to have insufficient water content to allow the T1
54 shortening necessary for significant enhancement.^{3,15}

55 The conspicuity of enhancement in MR images may be increased by subtracting the T1-
56 weighted pre-gadolinium images from the post-gadolinium images.¹⁶⁻¹⁹ Subtraction imaging
57 facilitates detection of mild enhancement, particularly at tissue boundaries, areas of
58 complicated anatomy, or in tissues with high signal intensity pre-gadolinium

59 administration.^{16,18} In humans, subtraction MR images have been found to be useful in the
60 diagnosis and follow-up of patients with a variety of intra-cranial conditions.¹⁶⁻¹⁹ Sensitivity
61 of observers for detecting enhancement in MR images is higher when using subtraction
62 images than when making a comparison of a parallel (side by side) image pair.²⁰

63 Subtraction MR imaging has received little attention in veterinary medicine. We recently
64 compared the accuracy of T1-weighted pre- and post-gadolinium images, subtraction images,
65 T2-weighted images, and fluid-attenuated inversion-recovery (FLAIR) images for diagnosis
66 of meningeal conditions in a series of dogs.²¹ In that study, subtraction images had similar
67 accuracy to T1-weighted post-gadolinium images, but an advantage of subtraction images
68 may have been masked because of technical limitations, including misregistration in some
69 cases.²¹ Since then we have introduced a dynamic method for obtaining subtraction images,
70 based on a single T1W sequence that is paused halfway for injection of gadolinium. This
71 method minimizes misregistration due to patient movement and optimizes the image intensity
72 scale for subtraction.¹⁸ The aim of the present study was to describe qualitatively the normal
73 appearance of canine meninges in subtraction MR images obtained using this dynamic
74 technique.

75

76 **Methods**

77 Medical records were searched for 10 consecutive dogs that had dynamic pre- and post-
78 gadolinium T1-weighted imaging of the brain that was interpreted as normal, and had normal
79 cerebrospinal fluid. All MR studies were done with dogs under general anesthesia in dorsal
80 recumbency using flexible surface coils in a 1.5T magnet.* Spin-echo T1-weighted (TR
81 570ms, TE 15ms) pre- and post-gadolinium transverse images and T2-weighted (TR 4000ms,

* Intera Pulsar System, Philips Medical Systems, Reigate, UK

82 TE 110ms) transverse images were acquired with image slice thickness 3.5mm and inter-slice
83 gap 1mm. Field of view was adjusted individually; typical values for a medium-sized dog
84 were 120 x 120mm with a 224 x 224 image matrix, hence pixel size was approximately 0.5 x
85 0.5mm. Subtraction of pre- from post-gadolinium T1-weighted images was performed using
86 a dynamic study sequence comprising two T1-weighted image series separated by an interval
87 during which the sequence was paused, an intravenous bolus of 0.1mmol/kg gadobuterol[†]
88 was administered, and the sequence restarted within 1 minute.

89 Subtraction images were color-encoded using commercially available DICOM image
90 viewing software[‡], and superimposed on pre-gadolinium T1-weighted and T2-weighted
91 images. Evidence of misregistration of color-encoded subtraction images superimposed on
92 T1- and T2-weighted native images was judged subjectively by reference to anatomic
93 landmarks other than the meninges, including the interface between the calvaria and the
94 temporal muscles, nasopharyngeal mucosa, and large blood vessels. Misregistration was
95 characterized by malalignment of the color-encoded signal and corresponding anatomic
96 boundaries by the same distance and in the same direction across the entire image. When
97 necessary, misregistration was corrected manually.

98 Distribution of gadolinium in each dog was assessed by CRL on the basis of sequential side
99 by side viewing of T1-weighted pre- and post-gadolinium images, post-gadolinium and gray-
100 scale subtraction images, and pre-gadolinium T1-weighted and T2-weighted images with
101 well registered, superimposed color-encoded subtraction images. In post-contrast and
102 subtraction images, a curvilinear signal continuous with the falx and/or tentorium without
103 sulcal indentations was considered compatible with pachymeninges, whereas a curvilinear

[†] Gadovist 1.0mmol/ml, Bayer plc, Newbury, UK

[‡] OsiriX 64-bit, version 5.2.2, Pixmeo, Switzerland

104 signal superimposed on the sulci was considered compatible with leptomeninges. Emphasis
105 was on the cerebral cortex in the parietal and temporal regions, where the image plane was
106 approximately perpendicular to the calvaria. At least five consecutive images were assessed
107 for each dog.

108 To complement the imaging studies, dissection of two grossly normal 28kg and 30kg
109 mesaticephalic dogs (not subject to MR imaging) was performed by SF. A median section of
110 the head of one animal was made and the half brain removed from the cranium to visualize
111 the blood vessels on the surface of the cerebral cortex, leaving the dura mater in situ. The
112 dura mater was then reflected away from the cranial calvaria to examine the large dural
113 vessels. Sections of meningeal tissue of both dogs were prepared for histologic examination.
114 Serial sections of 6 μ m thickness were cut on a microtome, mounted on glass slides and
115 stained using Hematoxylin and Eosin.

116

117 **Results**

118 Median (range) age of dogs having MR imaging was 2.9 (1-11) years; there were 8 males (5
119 neutered) and 2 neutered females. Median (range) body weight was 17.3 (6.9-31.0) kg. Eight
120 different breeds were represented, including 6 mesaticephalic dogs (Beagle, German
121 shepherd dog, Labrador retriever, two Labradoodles, one mixed breed) and 4 brachycephalic
122 dogs (Boxer, Bichon frisé, two Staffordshire bull terriers). Clinical diagnoses were idiopathic
123 epilepsy in 7 dogs, vestibular syndrome in 2 dogs, and compulsive behavioral disorder in one
124 dog.

125 No signs of misregistration of color-encoded subtraction images on T1-weighted images were
126 evident in any dog. Slight misregistration (< 2 pixels) of color-encoded subtraction images on

127 T2-weighted images was identified in two dogs, probably reflecting patient movement
128 between image acquisitions.

129 On the basis of sequential side by side viewing of T1-weighted pre- and post-gadolinium
130 images, enhancement of tissues close to the surface of the brain was visible as faint, small
131 rounded foci compatible with vessels seen end-on within the sulci, a series of larger rounded
132 foci compatible with vessels of variable caliber on the dorsal aspect of the cerebral cortex,
133 and a continuous, but indistinct, thin zone of moderate enhancement on the dorsal aspect of
134 the cerebral cortex (figure 1). Linear foci of variable caliber compatible with vessels were
135 also visible within the diploë, in some places perforating the inner table of the calvaria and
136 communicating with the dorsal sagittal sinus. On the lateral aspects of the cerebral cortex,
137 where there was no diploë, the calvaria appeared relatively thicker and foci of enhancement
138 appeared smaller and less numerous.

139 On the basis of side by side viewing of T1-weighted post-gadolinium images and
140 corresponding gray-scale subtraction images, foci of enhancement were more conspicuous in
141 subtraction images in all dogs (figure 1). The continuous zone of enhancement around the
142 brain appeared thicker in subtraction images. Enhancement superimposed over the diploë was
143 also more conspicuous because of increased contrast with the bone marrow, which had
144 similar hyperintensity to gadolinium in native images.

145 When color-encoded subtraction images were superimposed on T1-weighted images, the
146 continuous zone of enhancement on the dorsal aspect of the cerebral cortex was
147 superimposed over the inner aspect of the broad zone of signal void around the brain (figure
148 2). When color-encoded subtraction images were superimposed on T2-weighted images, the
149 continuous zone of enhancement was dorsal to the hyperintense zone representing
150 cerebrospinal fluid in each dog, hence this zone of enhancement was interpreted as
151 representing the dura. Therefore, the broad zone of signal void normally observed around the

152 dorsal aspect of the brain in T1- and T2-weighted MR images appears to be formed by the
153 dura on its inner aspect and cortical bone on its outer aspect.

154 Based on dissection of two canine cadavers, the enhancement seen on the dorsal aspect of the
155 brain in MR images was thought to primarily represent gadolinium in meningeal veins within
156 the dura (figure 3) and in cerebral veins within the leptomeninges (figure 4).

157

158 **Discussion**

159 Meningeal enhancement following gadolinium administration was observed consistently in
160 this series of dogs likely to be free of meningeal disease. The degree of meningeal
161 enhancement observed in subtraction images was greater than expected based on previous
162 studies.⁷⁻¹⁰ Furthermore, the finding that the continuous zone of enhancement on the dorsal
163 aspect of the brain was consistently dorsal to the cerebrospinal fluid space when color-
164 encoded subtraction images were superimposed on T2-weighted MR images provides
165 evidence that meningeal enhancement in dogs is predominantly dural, with relatively few
166 leptomeningeal vessels visible. This observation could help explain why pachymeningeal
167 enhancement is observed more often than leptomeningeal enhancement in clinical patients
168 with meningeal disease.²¹

169 Dural enhancement is likely to predominantly represent gadolinium in meningeal veins,
170 which have larger caliber and slower flow rates than the corresponding arteries. Anatomic
171 studies of the intracranial vasculature of dogs have concentrated on the cerebral vessels and
172 venous sinuses²² with little emphasis on the blood supply to the dura. Although the meningeal
173 arteries and veins are described briefly in standard veterinary anatomy texts²³, they are
174 frequently omitted from diagrams illustrating meningeal anatomy.^{24,25} In humans, the degree
175 of dural enhancement in normal individuals is limited by vascularity and the amount of

176 extracellular fluid^{3,15}, but marked enhancement may occur when there is vascular congestion
177 and expansion of the extracellular fluid space, which occurs after craniotomy³ and in
178 association with various conditions affecting the meninges, including meningioma^{26,27} and
179 meningitis.²⁸

180 Small leptomeningeal vessels were mainly seen end-on within sulci, where they are
181 orientated perpendicular to the image plane. This distribution may reflect partial volume
182 averaging associated with use of 3.5mm image slices, which will tend to minimize visibility
183 of small contrast-containing vessels parallel to the image plane. In addition to limitations
184 associated with partial volume averaging, the relatively low in-slice spatial resolution of the
185 images in the present study, which is typical of clinical MR images, limited the precision of
186 image-anatomic correlations. Attempts to make measurements of meningeal vessels, the dura
187 and the calvaria in the present study were unsatisfactory because of low image resolution. In
188 MR images displayed at true size, curved interfaces appeared stepped because of the
189 relatively large size of pixels. In images displayed at greater than true size (and interpolated),
190 the interfaces between anatomic boundaries and enhancing structures were too blurred for
191 confident placement of calipers. Even if higher resolution MR images could be obtained,
192 attempted correlations between measurements of small anatomic structures in MR images
193 and in fixed specimens will tend to be undermined by post mortem changes in blood volume
194 of organs, which alter the diameter of vessels, and the effects of fixation, which causes
195 contraction of soft tissues.

196 Meningeal enhancement was relatively inconspicuous in native post-gadolinium T1-weighted
197 images, but was more clearly visible in subtraction images in all dogs. This finding is in
198 agreement with a previous study, which mentioned briefly the appearance of canine meninges
199 in subtraction MR images.⁷ Dynamic subtraction is a low-tech method for obtaining
200 consistently well-registered and optimally scaled MR images that clearly depict the

201 distribution of gadolinium-chelates.¹⁸ Improved registration reflects the minimal elapsed time
202 between pre- and post-gadolinium sequences when using a dynamic technique, which helps
203 avoid patient movement. Optimal gray-scale is possible when using a dynamic subtraction
204 technique because the pre- and post-gadolinium images are within the same series. In most
205 MR scanners, image scaling is automatically set by the workstation, and the software sets the
206 highest signal intensity in a series of images at white and the lowest at black, scaling all other
207 signal intensities relative to these levels. Fat normally corresponds to the highest signal in
208 pre-gadolinium T1-weighted images and is assigned white, but in post-gadolinium images
209 gadolinium is the highest signal so it is assigned white, and fat has a lower signal so is
210 assigned light gray. Thus the signal intensity gray scale of all tissues varies between the two
211 sequences. This difference may not be perceived by observers when examining pre- and post-
212 gadolinium images side by side; however, if these images are then subtracted, the resulting
213 images will include variations due to differences in image gray-scale as well as presence of
214 gadolinium. Dynamic acquisition of pre and post contrast T1W images ensures that the image
215 scale factors remain constant, thus enabling more accurate subtraction.¹⁸ Use of the term
216 ‘dynamic’ for this subtraction technique reflects a change in the state of the subject during the
217 acquisition. Another example of a dynamic technique is MR imaging performed throughout a
218 period of contrast infusion in order to estimate the kinetics of contrast uptake and wash-out
219 from tissues.²⁹

220 Alternatively, the conspicuity of meningeal enhancement may be increased by suppressing
221 the MR signals from fat. Similar to subtraction MR imaging, elimination of high intensity
222 signals from fat allows reassignment of high intensity signals from gadolinium to the highest
223 point in the greyscale spectrum.³⁰ Fat suppression is a useful additional MR sequence when
224 enhancing lesions are adjacent to fat³⁰, but it may not be necessary after post-gadolinium

225 subtraction imaging, which reduces the signal from all minimally-enhancing tissues,
226 including fat.

227 Color-encoding subtraction images helps observers distinguish the difference information
228 from the underlying anatomic information.²⁰ Although subtraction images do not capture
229 primarily anatomic information, the use of color-encoded subtraction images superimposed
230 on the native pre-gadolinium images in the present study, with corroborating evidence from
231 dissections, facilitated determination of the location of vascular structures, including the
232 meninges, relative to anatomic boundaries displayed in native images.

233 In summary, normal canine meningeal enhancement appears to be predominantly dural, with
234 relatively few leptomeningeal structures visible. Meningeal enhancement is more
235 conspicuous in dynamic subtraction than in native post-gadolinium T1-weighted images.

236 Dynamic subtraction MR imaging should be considered for inclusion in clinical brain MR
237 protocols because of the possibility that its use may increase sensitivity for lesions affecting
238 the meninges.

239

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318 **Legends**

319 Figure 1. Examples of native T1-weighted MR images of two dogs before (A, D) and after
320 (B, E) intravenous administration of gadolinium, and (C, F) corresponding gray-scale
321 subtraction image. Dog in A, B and C is a 7 year old male Labrador retriever with idiopathic
322 epilepsy; dog in D, E and F is a 1 year old male Boxer with idiopathic epilepsy. In each
323 instance, following gadolinium administration there is faint enhancement within the sulci
324 compatible with small leptomeningeal vessels (L), a series of rounded foci of variable caliber
325 compatible with vessels close to the gyri (arrows), a broad, indistinctly margined zone of
326 moderate enhancement superimposed on the broad zone of signal void around the brain
327 (between arrowheads), and curvilinear foci compatible with vessels within the diploë (D).
328 The dorsal sagittal sinus (S) is clearly visible in F.

329 Figure 2. Same dogs as in Figure 1. Examples of native T1-weighted (A and C) and T2-
330 weighted (B and D) MR images with superimposed color-encoded subtraction images. In
331 each instance, it is evident in both T1- and T2-weighted images that the majority of signal
332 from gadolinium is superimposed on the broad hypointense line around the dorsal aspect of
333 the brain, and that in T2-weighted images the gadolinium is predominantly dorsal to the
334 subarachnoid space. This distribution is compatible with dural enhancement. Multiple foci of
335 gadolinium are also visible superimposed on the diploë, compatible with diploic veins.

336

337 Figure 3. Dural vessels. A) Dissection of a canine head showing reflected from inner aspect
338 of the calvaria. Veins that bulge from outer aspect of dura (white arrow) normally lie in
339 superficial grooves in the bone (black arrow). B) Low magnification section through dura
340 showing a large meningeal vein (V) on its dorsal aspect. In this specimen, the diameter of the
341 vein is 1.4mm. The periosteum (small arrows) has become partly detached from the dura

342 during processing. C) High magnification section of dura showing blood vessels (large
343 arrows). The periosteum is visible as a thin layer of cells (small arrows) on the dorsal aspect
344 of the dura. Bar = 100 μ .

345

346 Figure 4. Leptomeningeal vessels. A) Left-dorsal aspect of the brain removed from the skull.
347 The largest vessels on the surface of the brain are the veins that lie along the gyral-sulcal
348 boundaries. Vessels over the surface of gyri are relatively fine. B) Low magnification section
349 through the leptomeninges showing veins (V) at the gyral-sulcal boundary. In this specimen,
350 the diameter of the larger vein is 1.2mm.