

1 **Agreement between transverse T2W and 3D-CISS sequences in the evaluation of**
2 **spinal cord disease in dogs**

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24 **ABSTRACT**

25 The constructive interference in steady state (CISS) sequence has been widely used in
26 human neuroimaging. It has been shown to be advantageous in the evaluation of intra- and
27 extra-axial cystic abnormalities, arteriovenous and dysraphic malformations and
28 disturbances of cerebrospinal fluid circulation. To assess the utility of this technique in
29 small animals, interpretations based on this sequence were compared with those based on
30 T2-weighted (T2W) sequences in 145 dogs that underwent MRI of the spine for suspected
31 spinal cord disease. Two sets of images (T2W and CISS) were reviewed separately by three
32 observers in random order and intra and inter observer agreements between both sequences
33 were evaluated for several categorical variables. The overall agreement between T2W and
34 CISS sequences was good. The highest agreement was observed for lesion diagnosis
35 ($0.739 < k < 0.928$), treatment recommendation ($0.715 < k < 0.833$) and degree of spinal cord
36 compression ($0.772 < k < 0.952$). The agreement for intramedullary intensity change
37 ($0.192 < k < 0.332$) was lower compared to the other variables. Lesions that were
38 predominantly characterised by focal hyperintense parenchymal changes on T2W were in
39 some instances undetected on the CISS sequence whilst lesions consistent with spinal
40 arachnoid diverticula on CISS sequences were occasionally missed on T2W. CISS enabled
41 demonstration that lesions were directly affecting associated spinal nerves in some cases
42 where T2W sequence was equivocal. Although CISS does not replace standard spin echo
43 sequences, the results support inclusion of this sequence in small animal spinal MRI studies
44 when subarachnoid diverticula or spinal nerve compression are suspected.

45

46 INTRODUCTION

47 Three-dimensional (3D) constructive interference in steady state (CISS) is a fully refocused
48 steady-state gradient-echo magnetic resonance imaging (MRI) sequence. In human
49 medicine, this sequence is now widely available and frequently used to investigate a varied
50 range of pathologies, particularly when routine MRI sequences do not provide the desired
51 anatomic information (Ramli 2001, Kulkarni 2011). The image contrast in CISS is
52 determined by the T2/T1 ratio of the tissue with tissues that have long T2 relaxation times
53 and short T1 relaxation times showing increased signal intensity. Because of high T2/T1
54 ratio, water has high signal on this sequence resulting in excellent contrast between
55 cerebrospinal fluid (CSF) and other structures (Chavhan and others 2008). The other tissues
56 have poor contrast though, and the gray-white differentiation is also not well visualized
57 (Chavhan and others 2008). Other advantages are the high signal-to-noise ratio (Scheffler
58 2003) and better contrast-to-noise ratio (Roser and others 2008) relative to other routine
59 imaging sequences (Scheffler and others 2003). Furthermore, CISS images do not present
60 significant susceptibility, motion, or flow-related artifacts (Gonçalves and Amaral 2011).

61 In people CISS is mainly used to image the central nervous system, but it is also used to
62 assess the abdomen, the musculoskeletal system and the breast. It has also become the
63 sequence of choice for evaluating the cranial nerves in human patients due to its high
64 spatial and contrast resolution between the cerebrospinal fluid and the nerve (Gonçalves
65 and Amaral 2011, Kulkarni 2011, Besta and others 2016, Tsutsumi and others 2016). The
66 use of CISS for visualisation of spinal abnormalities is a more recent development. It has
67 been shown to be advantageous in the evaluation of intra- and extra-axial cystic
68 abnormalities, arteriovenous and dysraphic malformations and disturbances of CSF
69 circulation (Chavhan and others 2008, Gonçalves and Amaral 2011, Kulkarni 2011). It has

70 also been shown to better characterise syringomyelia in humans, as it delineated the
71 extension of the syrinx better, had higher contrast-to-noise ratio and less CSF flow artifact
72 and allowed better visualisation of septation and communication between the syringomyelia
73 cavities (Hirai and others 2000).

74 To our knowledge, there have been no clinical reports of the use of CISS sequences in
75 dogs. The purpose of this retrospective cross-sectional study was to evaluate the usefulness
76 of CISS in various spinal pathologies and to discuss its potential role in the canine spinal
77 imaging protocol.

78

79 **Materials and Methods**

80 The imaging database of the Small Animal Teaching Hospital of the University of
81 Liverpool was searched from October 2013 to June 2015. All MRI studies of the spine
82 performed in dogs during this period were included if both T2-weighted (T2W) and 3D-
83 CISS sequences in the transverse plane were available for review. All studies were
84 performed with a 1.0 Tesla MRI scanner (Siemens Magnetom, Erlangen, Germany), using
85 an integrated spine coil or an extremity coil in small patients. Sequences were variable but
86 included sagittal, dorsal (both used exclusively for localisation of the lesion) and transverse
87 T2W and transverse CISS images for all patients. Imaging parameters varied based on
88 patient size (T2W sequence: TR = 2750-6200ms, TE = 90-110ms, slice thickness 2.5–3.0
89 mm; CISS sequence: TR = ~6-6.8ms, TE = ~12-13.6ms, slice thickness 1-1.2mm).

90 Studies meeting the inclusion criteria were exported to a picture archiving and
91 communication system for evaluation (Visbion PACS 4.1, Visbion Limited, Surrey, UK).

92 The T2W and CISS images were randomized and reviewed by a neurology resident in
93 training (MO), a board-certified veterinary neurologist (RG) and a board-certified

94 veterinary radiologist (FM) who were unaware of the patient information. Evaluation was
95 performed independently for each sequence. All images were interpreted with the same
96 software (OsiriX 7.5, Pixmeo, Geneva, Switzerland), which allowed adjustment for
97 brightness, contrast, window width, and magnification.

98 Images were evaluated for spinal cord lesions and the following was determined for each
99 sequence: presence or absence of a notable lesion (the largest was considered if multiple
100 lesions were present), extradural, intradural extramedullary or intradural intramedullary
101 location, degree of spinal cord compression (1 = none, 2 = mild, 3 = moderate, 4 = severe),
102 degree of spinal cord signal changes (1 = none, 2 = mild, 3 = moderate, 4 = severe) and
103 whether the lesion was directly affecting an associated spinal nerve (i.e. if the spinal nerve
104 was enlarged or directly compressed by the lesion). The number of slices in which the
105 lesion could be visualised was recorded for each sequence. The reviewers recorded the
106 most likely diagnosis for each sequence and the two reviewers with neurosurgical
107 experience (MO and RG) also recorded their treatment recommendation based on the
108 imaging findings: 0 = no surgery, 1 = equivocal for surgery, 2 = surgery. Image quality was
109 evaluated for each study and graded as follows: 1 = poor, 2 = fair, 3 = good, 4 = excellent.
110 Artifacts (motion artifacts and those induced by pulsatile CSF flow) were also documented
111 for each study and ranked as 1= absent, 2 = mild, 3 = moderate and 4 = severe. The
112 different categorical variables used in image evaluation are summarised in Table 1.

113 The medical records were reviewed and data regarding breed, sex, age, bodyweight and
114 duration of the clinical signs (recorded as the number of days between manifestation of the
115 initial clinical sign and MRI) was collected for each patient.

116

117 *Statistical analysis*

118 All statistical analyses were performed with SPSS (SPSS 22.0 for Windows, SPSS Inc,
119 Chicago, Illinois, USA). Independent variables were generated from the signalment data
120 and clinical records (breed, sex, age, weight and duration of clinical signs) and the results
121 from the observers on reviewing the MRI studies. Descriptive statistics were calculated for
122 each variable; normally distributed continuous data were summarised as means and
123 standard deviation and non-normally distributed as medians and interquartile ranges. The
124 distribution of continuous variables was assessed through graphical analysis and the
125 Kolmogorov-Smirnov test. Categorical data for breed and diagnosis were amalgamated into
126 appropriate groups and expressed as frequencies with 95% confidence intervals (95% CI)
127 as applicable as there were too many categories with small numbers to allow analysis;
128 groupings were made on the basis of clinical judgement. A total of 46 different dog breeds
129 were grouped into Crossbreed, Dachshund, French Bulldog, Jack Russell Terrier, Labrador
130 Retriever, Pug, ShihTzu, Spaniel breed, Staffordshire Bull Terrier, Toy breed and Other.
131 Fifteen different diagnoses were grouped into 11: acute non-compressive nucleus pulposus
132 extrusion (ANNPE), spinal arachnoid diverticula, bony malformations (including articular
133 process malformation, osseous-associated cervical spondylomyelopathy, atlantoaxial
134 instability and vertebral stenosis secondary to hemivertebra), foraminal stenosis causing
135 nerve root compression, ischaemic myelopathy, degenerative intervertebral disc disease
136 (including intervertebral disc extrusion and protrusion), neoplasia, neuritis, Chiari-like
137 malformation and syringomyelia or no abnormalities identified.

138

139 Intra- and inter-observer agreement of categorical variables was assessed through
140 calculation of Cohen's Kappa (κ) for intra-observer (comparing T2W and CISS sequences)

141 for two observers (comparing treatment recommendation) agreements or Fleiss' Kappa for
142 three observer agreement (presence of lesion, lesion diagnosis, anatomical location and
143 nerve root compression). The intra- and inter-observer agreement of ordinal variables
144 (degree of spinal cord compression, spinal cord intensity change, image quality and image
145 artifacts) was assessed through calculation of intraclass correlation coefficients (ICC, two-
146 way single measure for absolute agreement) with 95% confidence intervals. An adaptation
147 of the κ evaluation grid by Landis and Koch (Landis and Koch 1997) was used to qualify
148 the level of inter- and intra-observer agreement (Appendix).

149 Responses of the three observers for image quality and image artifacts were summarised as
150 medians and associations between these and independent variables (breed, sex, age, weight
151 and duration of clinical signs and lesion location) were assessed through ordinal logistic
152 regression analysis. Validity of the ordinal logistic regression assumption of proportional
153 odds was tested with the test of parallel lines (Brant 1990). Any independent variable
154 demonstrating some association with image quality or artifacts on preliminary univariable
155 analysis (a P-value <0.25) was considered for inclusion in a multivariable model. For any
156 variables having a pair-wise correlation coefficient of >0.70 , only the variable with the
157 smallest univariable P-value was selected for incorporation in the multivariable analysis.
158 All multivariable models were constructed with a manual backwards stepwise removal
159 approach; variables with Wald and likelihood ratio test $P < 0.05$ were retained. Confounding
160 factors were detected by assessing parameter estimates for substantial changes ($>20\%$)
161 following removal from the models. Model goodness of fit was assessed using the
162 Pearson's chi-square statistic for the model.

163

164 **Results**

165 A total of 145 dogs were included in the study. Breeds included dachshunds (14), spaniel
166 breeds (14), crossbreeds (14), pugs (11), toy breeds (9), French bulldogs (8), Jack Russell
167 terriers (8), Staffordshire bull terriers (7), Labrador retrievers (6), Shih Tzus (6) and five or
168 fewer of 31 other pedigree breeds (48). Neutered male dogs were most frequent (37.2%),
169 followed by entire males (33.8%), neutered females (23.4%) and entire females (5.5%).
170 The median age of dogs was 78 months (interquartile range [IQR]: 49.5-101.4) and median
171 weight 12.0kg (IQR: 8.0-24.5). The median duration of clinical signs was 10 days (IQR: 3-
172 42). The areas imaged included the cervical region in 52 cases, the thoracic region in 64
173 cases and the lumbar region in 29 cases. The diagnosis was confirmed through surgery on
174 70 cases (62 with degenerative intervertebral disease, 5 spinal arachnoid diverticula, 1
175 ANNPE, 1 atlantoaxial instability and 1 osseous-associated cervical spondylomyelopathy).

176

177 *Intra- and inter-observer agreement for presence of lesion, lesion diagnosis and treatment*
178 *recommendation*

179 Kappa agreement and intraclass correlations coefficients for agreement are presented in
180 Tables 2. There was variability in the intra-observer agreement between T2W and CISS
181 sequences for presence of a lesion: substantial agreement was seen in observer 1, moderate
182 agreement was seen in observer 2 and slight agreement was seen in observer 3. The inter-
183 observer agreement for this categorical variable was fair for T2W and moderate for CISS
184 sequence. Both T2W and CISS sequences were considered unremarkable in two studies
185 interpreted by observer 1, in five studies evaluated by observer 2 and in one study assessed
186 by observer 3. A lesion was detected on T2W images that was not perceived on
187 corresponding CISS in two studies evaluated by observer 1, in five studies assessed by
188 observer 2 and in eight studies interpreted by observer 3. The lesions that were undetected

189 on the CISS sequences were predominantly characterised by focal hyperintense
190 parenchymal changes on T2W that in some cases were associated with reduced volume of
191 nucleus pulposus of the intervertebral disc ventral to the area of hyperintensity, consistent
192 with ANNPE or ischaemic myelopathy (2/2 in observer 1, 3/5 in observer 2 and 6/8 in
193 observer 3) (Fig 1). In the remaining studies, the abnormalities detected on T2W were
194 interpreted as intramedullary neoplasia (1) by observer 2, foraminal stenosis (1) by
195 observer 2 and 3 and intervertebral disc protrusion (1) by both observer 2 and 3. A lesion
196 was detected on CISS that was unrecognized on corresponding T2W in two studies
197 evaluated by observer 2 and in four studies interpreted by observer 3. On CISS sequences
198 these lesions were mainly described as focal dilatations in the subarachnoid space filled
199 with CSF compatible with arachnoid diverticulum (2/2 in observer 2 and 3/4 in observer 3)
200 (Fig 2). In the remaining study evaluated by observer 3, the abnormalities in CISS images
201 were consistent with foraminal stenosis. There was substantial to almost perfect intra-
202 observer agreement between T2W and CISS sequences concerning imaging diagnosis and
203 treatment recommendation for a given patient. The inter-observer agreement between these
204 sequences was substantial for imaging diagnosis and moderate for treatment
205 recommendation.

206

207 *Intra- and inter-observer agreement for parenchymal change and spinal corf compression*

208 Kappa agreement and intraclass correlations coefficients for agreement are presented in
209 Table 3. There was slight to fair intra-observer agreement between both sequences for
210 detection of spinal cord intensity changes. The inter-observer agreement for this variable
211 was moderate to substantial for each sequence. A degree of spinal cord intensity changes
212 was identified on T2W but undetected on CISS sequences in 47% (68/145) of the studies

213 evaluated by observer 1, in 44% (64/145) of the studies assessed by observer 2 and in 31%
214 (46/145) of the studies interpreted by observer 3.

215 There was substantial to almost perfect intra-observer agreement between T2W and CISS
216 sequences regarding degree of spinal cord compression. The inter-observer agreement
217 between sequences was substantial for this variable.

218

219 *Intra- and inter-observer agreement for anatomical location and nerve root involvement*

220 Kappa agreement and intraclass correlations coefficients for agreement are presented in
221 Table 4. The intra-observer agreement concerning anatomical location was moderate to
222 almost perfect between sequences and the inter-observer agreement for this categorical
223 variable was substantial for both sequences. The intra-observer agreement for nerve root
224 compression was moderate to substantial between T2W and CISS sequences and the inter-
225 observer agreement was fair for each of them. CISS images clearly demonstrated that the
226 lesion was directly affecting an associated nerve root while no root involvement was visible
227 on corresponding T2W sequence in 21 studies evaluated by observer 1, in 6 studies
228 assessed by observer 2 and in 24 studies interpreted by observer 3. This finding was
229 predominantly observed in cases of disc herniation. With exception of one study interpreted
230 by observer 3, all the remaining cases where nerve root involvement was detected on T2W
231 images were also visible on corresponding CISS image.

232

233 *Association of image quality and image artifacts with independent variables*

234 The inter-observer agreement of image quality and artifact severity recorded by three
235 observers reviewing the two MRI sequences are presented in table 5. On univariable
236 analysis, age, duration of clinical signs, weight, breed and sex and lesion location showed

237 some evidence of association ($P < 0.25$) with both image quality and image artifacts for the
238 T2W and CISS sequences. However, on multivariable analysis only weight and lesion
239 location remained in the final models (Table 6). Associations for weight were similar, with
240 increasing weight being associated with higher image quality for T2W and CISS sequences
241 ($P = 0.001$ and 0.03 respectively) and with decreasing severity of artifacts in the T2W and
242 CISS sequences ($P = 0.01$ and 0.048 respectively). For the CISS sequences, location other
243 than the thoracolumbar spine was associated with higher image quality ($P = 0.005$ for
244 cervical and $P < 0.001$ for lumbar) and decreasing severity of artifacts ($P = 0.011$ for
245 cervical and $P = 0.009$ for lumbar), whilst for the T2W sequence only location within the
246 lumbar spine was associated with higher image quality ($P = 0.021$).

247

248 **Discussion**

249 Recent developments in MRI technology and pulse sequences have refined this imaging
250 technique further. Newer sequences are being developed constantly and the CISS, with its
251 high spatial and contrast resolution between the cerebrospinal fluid and the nervous tissue
252 offers certain advantages in terms of anatomical detail (Ramli 2001, Gonçalves and Amaral
253 2011). Pulsatile cerebrospinal fluid flow is minimized by acquiring the sequence with flow
254 compensation applied over each TR cycle, rather than over each echo as in the case of
255 conventional compensation techniques (Ramli and others 2001). Turbulent flow, however,
256 is not suppressed, with phase dispersion resulting in signal loss (Ramli and others 2001).
257 Two data sets are acquired successively with alternating and non-alternating radio
258 frequency pulses, which are subsequently combined in a maximum intensity projection to
259 produce an image with excellent CSF-to-spinal cord (Casselmann and others 1993, Ramli
260 and others 2001). To our knowledge, there have been no clinical reports of CISS images in

261 dogs although its use has been described for imaging of the cranial nerves in the horse
262 (Gonçalves and others 2015). Here, we describe the use of this MR sequence, with respect
263 to its utility for the diagnosis of different spinal cord pathologies.

264 In our study, the overall agreement between T2W and CISS sequences was good. The
265 highest agreement was observed for lesion diagnosis, treatment recommendation and
266 degree of spinal cord compression for both inter- and intra-observer assessments. The intra-
267 observer agreement for spinal cord intensity changes was lower compared to the other
268 variables and the inter-observer agreement for this variable was substantial to almost
269 perfect for each sequence. In our study, spinal cord intensity changes were more likely to
270 be detected on T2W images than on CISS images. Lesions that were predominantly
271 characterised by focal hyperintense parenchymal changes on T2W consistent with
272 ANNPE/ischaemic myelopathy were in some instances undetected on the CISS sequence
273 by all three observers. The morphological characteristics of spinal cord abnormalities with
274 ill-defined margins and variable signal characteristics on T2W images typical of these
275 conditions can be difficult to evaluate on CISS sequences, due to the intrinsic lack of
276 contrast between such structures.

277 On the other hand, a lesion consistent with spinal arachnoid diverticula on CISS sequences
278 was in some occasions missed on T2W images by two observers. In people, the use of
279 CISS was shown to be useful for characterising both intra- and extramedullary cystic
280 abnormalities (Gonçalves and Amaral 2011). The increased sensitivity of this sequence is a
281 consequence of the accentuation of the T2 values between CSF and abnormal structures
282 due to the higher intrinsic resolution between neural structures, CSF and lesions surrounded
283 by CSF. Consequently, the extremely thin wall of diverticulum or cystic structures, which
284 may easily evade detection with conventional sequences can be resolved using CISS. In

285 people, the anatomical information provided by CISS is of particular value in planning
286 surgical interventions, most notably determining the spatial relationship between intradural
287 extramedullary masses and affected spinal nerve roots (Zhu and others 2015) as well as in
288 the management of intraaxial and extraaxial cystic abnormalities, dysraphic malformations
289 and disturbances of cerebrospinal fluid circulation (Ramli and others 2001).

290 The inter-observer agreement for presence of a lesion varied between observers. This range
291 of results is likely representative of the different levels of radiological experience and
292 different backgrounds between the participating observers. Investigations on inter-observer
293 variability, which have become more common in recent years, demonstrated that reading
294 agreement can vary among tests in veterinary medicine, including MRI (Leclerc and others
295 2013).

296 In people, the CISS sequence has been shown to be highly sensitive and specific in the
297 evaluation of lumbar disc herniations, especially for the extruded and sequestered discs
298 (Aydin and others 2011). Although this sequence cannot differentiate properly disc material
299 from osteophytes, it easily revealed the site of injury and relationship of the herniated
300 fragment to the dural sac, nerve roots and bulged discs (Ramli and others 2001). In our
301 study, although the intra-observer agreement between T2W and CISS sequences for nerve
302 root compression was moderate to substantial, in some studies the T2W was insufficient for
303 detailed analysis of nerve roots, especially in cases of disc herniation. In contrast, the slice
304 thickness of the CISS enabled the nerve roots to be identified in cases where conventional
305 T2W sequence was equivocal (although in most cases this could not be further confirmed
306 by surgery or post-mortem examination and false positive findings on the CISS sequence
307 may have occurred). Due to the thin slices used by the CISS, neurographic images can be
308 obtained, improving the spatial resolution and enabling good definition of the spinal and

309 neuroforaminal canal dimensions and nerve root compression. Therefore, CISS sequence
310 should be considered in cases of suspected radiculopathy not explained by routine
311 sequences.

312 Our study did not investigate sensitivity or specificity of T2W or CISS sequence in the
313 diagnosis of different pathologies. Our purpose was solely to evaluate agreement between
314 those two sequences and identify possible discrepancies between them. An accuracy study
315 was not possible because not all patients underwent surgery or had histopathology
316 performed.

317 Weight and lesion location were the only factors affecting imaging quality in both
318 sequences. Increasing weight was associated with higher image quality and with reduced
319 severity of artifacts for both T2W and CISS sequences. For both sequences the
320 thoracolumbar spine was associated with worse image quality. This likely reflects motion
321 related artifact associated with respiration (particularly for the CISS sequence) and possibly
322 because some parts of the spine in this region may be further from the coil, due to longer
323 spinous processes.

324 Artifacts in CISS images are considered to be banding artifacts caused by susceptibility
325 variation and/or motion artifact (Hashiguchi and others 2007, Ramli and others 2001).
326 Additional reported disadvantages of CISS images include a long acquisition time and their
327 lack of contrast between soft tissues and neuronal tissues. Generally, there is no marked
328 difference in acquisition times between CISS and T2W sequences, with both typically in
329 the order of 4-5 minutes; therefore, no significant time-saving is achieved using either
330 sequence.

331

332 In conclusion, overall there was a good agreement between T2W and CISS images for

333 evaluating spinal cord diseases in dogs. Acquiring additional CISS images after normal
334 T2W images is likely to result in detection of otherwise occult spinal lesions in only a small
335 proportion of patients, such as those with small lesions close to the CSF pathways. As for
336 humans, this sequence showed to be beneficial in identification of arachnoid diverticulum,
337 which may evade detection with conventional sequences. CISS can also allow visualisation
338 in fine detail of the spinal nerves and may be able to identify structural abnormalities
339 affecting these or compression of nerve roots. Although CISS does not replace standard
340 spin echo sequences, the results support inclusion of this sequence in small animal spinal
341 MRI studies, mainly when imaging cystic lesions or those thought to affect nerve roots.
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419 Table 1. Summary of categorical variables used in evaluation of each set of images

Presence of lesion	Present/absent
Anatomical location	Extradural, intradural extramedullary or intramedullary and corresponding intervertebral disc space or vertebra
Nerve root compression	Present/absent
Lesion diagnosis	e.g. no abnormalities, nucleus pulposus extrusion, spinal arachnoid diverticula, bony malformations, foraminal stenosis, Chiari-like malformation and syringomyelia.
Treatment recommendation	0 (no surgery), 1 (equivocal), 2 (surgery)

420

421

422 Table 2. Kappa values (with 95% confidence intervals in parenthesis) for intra- and inter-
 423 observer agreement for presence of lesion, lesion diagnosis recorded and treatment
 424 recommendation by three observers reviewing two MRI sequences from 145 dogs. Cohen's
 425 kappa was calculated for intra-observer agreement and inter-observer agreement where
 426 there were only two observers (treatment recommendation), with Fleiss' kappa calculated
 427 for all remaining agreements with three observers.

	Intra-observer agreement for T2W versus CISS sequences			Inter-observer agreement	
	Observer 1	Observer 2	Observer 3	T2W sequence	CISS sequence
Presence of lesion	0.66 (0.221-1.000)	0.493 (0.205-0.777)	0.131 (0.001-0.423)	0.351 (0.257-0.445)	0.449 (0.354-0.544)
Lesion diagnosis	0.928 (0.867-0.989)	0.739 (0.649-0.829)	0.782 (0.698-0.866)	0.772 (0.724-0.821)	0.794 (0.743-0.845)
Treatment recommendation	-	0.833 (0.755-0.911)	0.715 (0.617-0.813)	0.477 (0.359-0.595)	0.500 (0.378-0.622)

428

429

430 Table 3. Intraclass correlation coefficients (with 95% confidence intervals in parenthesis)
 431 for intra- and inter-observer agreement for intramedullary change and spinal cord
 432 compression recorded by three observers reviewing two MRI sequences of 145 dogs.

	Intra-observer agreement for T2W versus CISS sequences			Inter-observer agreement	
	Observer 1	Observer 2	Observer 3	T2W sequence	CISS sequence
Spinal cord compression	0.952 (0.933-0.965)	0.862 (0.774-0.911)	0.772 (0.691-0.833)	0.694 (0.522-0.799)	0.711 (0.639-0.778)
Intramedullary intensity change	0.192 (-0.040-0.396)	0.390 (0.104-0.588)	0.332 (-0.036-0.586)	0.658 (0.548-0.744)	0.471 (0.372-0.567)

433

434

435 Table 4. Kappa values (with 95% confidence intervals in parenthesis) for intra- and inter-
 436 observer agreement for anatomical location and nerve root compression recorded by three
 437 observers reviewing two MRI sequences of 145 dogs.

	Intra-observer agreement for T2W versus CISS sequences			Inter-observer agreement	
	Observer 1	Observer 2	Observer 3	T2W sequence	CISS sequence
Anatomical location	0.952 (0.889-1.015)	0.621 (0.498-0.744)	0.596 (0.463-0.729)	0.609 (0.544-0.674)	0.745 (0.675-0.815)
Nerve root compression	0.491 (0.052-0.930)	0.794 (0.649-0.939)	0.608 (0.481-0.735)	0.349 (0.251-0.441)	0.342 (0.248-0.436)

438

439 Table 5. Intraclass correlation coefficients (with 95% confidence intervals in parenthesis)
 440 for inter-observer agreement of image quality and artifact severity recorded by three
 441 observers reviewing two MRI sequences of 145 dogs.

	Intra-observer agreement for T2W versus CISS sequences			Inter-observer agreement	
	Observer 1	Observer 2	Observer 3	T2W sequence	CISS sequence
Image quality	-	-	-	0.291 (0.185-0.400)	0.317 (0.201-0.432)
Artifact severity	-	-	-	0.095 (-0.010-0.214)	0.111 (-0.013-0.254)

442

443 Table 6. Multivariable ordinal logistic regression analysis of variables affecting image
 444 quality and severity of artifacts on review of two MRI sequences (T2W and CISS) of 145
 445 dogs.

Outcome	Variable	Category	Odds Ratio	95% CI	P-value
T2W artifact severity	Weight	(kg)	0.96	(0.93-0.98)	0.01
	CISS artifact severity	Weight	(kg)	0.97	(0.94-1.00)
	Lesion location	Thoracolumbar	(ref)	-	-
		Cervical	0.34	(0.15-0.78)	0.011
		Lumbar	0.27	0.10-0.72)	0.009
T2W image quality	Weight	(kg)	1.07	(1.03-1.11)	0.001
	Lesion location	Thoracolumbar	(ref)	-	-
		Cervical	1.44	(0.60-3.46)	0.42
Lumbar		3.34	(1,20-9.31)	0.021	
CISS image quality	Weight	(kg)	1.03	(1.00-1.06)	0.03
	Lesion location	Thoracolumbar	(ref)	-	-
		Cervical	3.38	(1.44-7.95)	0.005
Lumbar		7.47	(2.78-20.1)	<0.001	

446 Ref = reference category, CI = confidence intervals, *P*-Values are from the Wald Chi-
 447 squared test

448

449

450 **Appendix** Scale used to qualify the level of inter- and intra-observer agreement determined
451 on the basis of the κ statistic.

κ	Agreement
>0.80	Almost perfect
>0.60 to 0.80	Substantial
>0.40 to 0.60	Moderate
>0.20 to 0.40	Fair
>0.00 to 0.20	Slight
0	Poor

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