

## Prevalence of Chiari-like Malformations in Clinically Unaffected Dogs

T.R. Harcourt-Brown, J. Campbell, C. Warren-Smith, N.D. Jeffery, and N.P. Granger

**Background:** The importance of Chiari-like malformation (CM) in the generation of clinical signs or the formation of syringomyelia in dogs is incompletely understood, partly because the prevalence of various CM definitions in unaffected dogs is unknown.

**Hypothesis/Objectives:** The aims were: to estimate the prevalence of CM in dogs asymptomatic for CM or syringomyelia, according to 3 currently used definitions; and, to investigate the effect of brachycephaly and head position during magnetic resonance (MR) imaging on estimates of the prevalence of CM.

**Animals:** One ninety-nine client-owned dogs without apparent signs of CM or syringomyelia.

**Methods:** Blinded, retrospective analysis. Archived MR images were analyzed for evidence of cerebellar indentation and impaction into or herniation through the foramen magnum. Logistic regression analysis was used to investigate the relationship of CM diagnosis with head position and the cranial index (a measure of brachycephaly).

**Results:** In 185 non-Cavalier King Charles Spaniel (CKCS) dogs, indentation was identified in 44% (95% CI, 47–51%) and impaction in 22% (95% CI, 16–28%). No asymptomatic, non-CKCS dogs showed herniation. Regression analysis showed a significant increase in the odds of indentation and impaction in an extended head position and as the cranial index increased (became more brachycephalic).

**Conclusions and Clinical Importance:** The high prevalence of cerebellar indentation and impaction suggests that they may be normal anatomical variations and therefore unsuitable as definitions of CM. We suggest that future research into CM in dogs should define cases and controls more strictly so that overlap between normal and abnormal animals is minimized.

**Key words:** Canine; Chiari-like malformation prevalence; Definition.

Chiari-like malformation in dogs (CM) is thought to be analogous to human Chiari-I malformation<sup>1</sup> in which a portion of the cerebellum herniates through the foramen magnum. In dogs, CM has been linked to various clinical signs (eg, scratching of the head and neck, apparent pain, cranial nerve abnormalities)<sup>2,3</sup> and the development of fluid filled cavities within the spinal cord (syringomyelia) that may themselves also cause similar clinical signs.<sup>4,5</sup> An enigmatic feature of both CM and syringomyelia is that both can and, commonly do, occur in dogs that have no apparent clinical signs.<sup>6,7</sup>

In an attempt to clarify the clinical relevance of CM, many studies have sought correlations between morphometry of the skull and development of syringomyelia or typical clinical signs.<sup>2,3,7–20</sup> CM has been recognized most commonly in the Cavalier King Charles Spaniel (CKCS) and so most investigations have either solely investigated this breed<sup>7,9,11–13,16,21,22</sup> or included non-CKCS as de facto normal dogs.<sup>8,10,14,17,18,20</sup> It

### Abbreviations:

BVA	British Veterinary Association
CI	confidence interval
CKCS	Cavalier King Charles Spaniel
CM	Chiari-like malformation
Exp( <i>B</i> )	exponential of the <i>B</i> statistic
MR	magnetic resonance

also has been suggested that CM is a feature of extreme brachycephaly in the CKCS, so that comparisons between the CKCS and other brachycephalic breeds should be favored.<sup>23</sup>

Despite finding some statistically significant differences within their study groups, these studies have not provided a unifying explanation for the role of CM in the development of syringomyelia or clinical signs or both. One potential explanation is that the criteria used to differentiate dogs with CM from those without CM are not defined explicitly or consistently enough to allow valid comparisons among studies.

This current study attempts to address this problem by determining the prevalence of CM, according to 3 previously established definitions, in a group of dogs asymptomatic for CM and syringomyelia. Secondly, we considered that the prevalence of CM according to some definitions might be susceptible to variation associated with head position during MR scanning or non-specifically associated with brachycephaly. Therefore, we also tested the hypotheses that CM (using 3 definitions) was variably associated with brachycephaly; and the angle at the atlanto-occipital region during MR scanning.

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## Materials and Methods

Archived MR image series<sup>a</sup> of brains of dogs from 2009 onwards (Langford Veterinary Services, University of Bristol, UK) were retrieved in the order of acquisition, regardless of the reason for MR examination. These studies subsequently were analyzed if they included a midsagittal T2-weighted sagittal turbo spin echo image that extended from the cribriform plate to the second cervical vertebra and a T1-weighted dorsal spin echo image of the skull. Scan series were excluded if there was evidence of disease that could increase intracranial pressure (eg, a space-occupying mass).

Imaging was performed using either a 1 Tesla (Gyroscon Intera NT<sup>b</sup>) or 1.5 Tesla unit (Gyroscon Intera<sup>b</sup>). There were slight differences in the parameters used between machines and sequences but typical values were as follows: for the 2D, turbo spin echo, T2-weighted images, time to repeat (TR) was 3,500 milliseconds, time to echo (TE) was 125 milliseconds, echo train (ET) duration was 15 milliseconds, slice thickness was 3 mm, interslice gap was 0.3 mm, matrix size was 256 × 256 (interpolated to 512 × 512), flip angle was 90° and voxel size was 0.55 mm × 0.5 mm × 3 mm. For the 2D, spin echo, T1-weighted images, TR was 600 milliseconds, TE was 12 milliseconds and ET duration was 4 milliseconds. Slice thickness, interslice gap, flip angle, matrix, and voxel size were as described for the T2-weighted sequences.

### Definitions of Chiari Malformation

Midsagittal MR images were graded positive or negative for any or all of the following possible definitions of CM (Fig 1) by an observer blinded to breed and clinical status:

- 1 Indentation of the caudal aspect of the cerebellum<sup>c</sup> [10,17,20,22]—defined as a concave, rather than flattened or convex, caudal border of the cerebellum.
- 2 Impaction of the cerebellar vermis into the foramen magnum<sup>d</sup>—defined as deformation of the shape of caudo-ventral vermis into a point such that the angle between lines drawn along the caudal and ventral borders of the cerebellum meet at an acute, rather than an obtuse, angle. This definition was considered analogous to descent into the foramen magnum that has been used previously.<sup>17,20</sup>
- 3 Herniation of the cerebellar vermis through the foramen magnum<sup>7,10,22</sup>—defined as extension of the cerebellar vermis caudal to a line drawn between the ventral aspect of the supraoccipital bone (opisthion) and the caudal border of the basioccipital bone (basion).

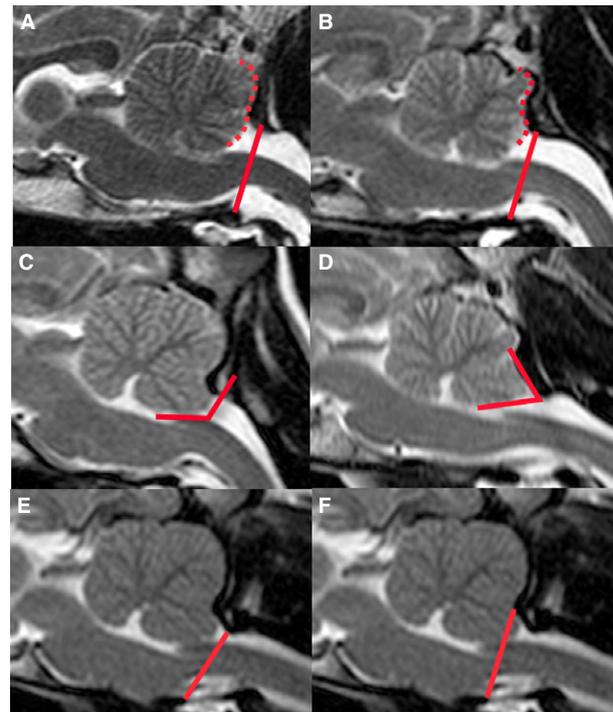
If the cerebellum had a straight or convex caudal border and was entirely rostral to the foramen magnum, the dog was classified as having no changes suggestive of CM.

### Quantification of Brachycephaly

The cranial index was used as a measure of head shape. This index was defined as the skull breadth (measured at its widest point on dorsal T1-weighted images) divided by the skull length (measured from the nasion toinion) and multiplied by 100. This ratio is thought to increase with increasing brachycephaly (ie, shorter, wider skulls).<sup>23,24</sup>

### Quantification of Neck Flexion

Neck flexion for each dog was measured as the angle between a line connecting the dorsum sellae to the ventral foramen



**Fig 1.** Definitions of Chiari-like malformation. (A) Normal cerebellum with a flat caudal border (dotted line) entirely rostral to the foramen magnum (solid line). (B) Mildly indented cerebellum; the caudal border (dotted line) is concave. (C) Another indented cerebellum with an obtuse (>90°) angle to the caudo-ventral border (solid lines); therefore this was not considered to be impacted. (D) Cerebellum that is both indented and impacted; it has an acute (<90°) angle to its caudo-ventral border (solid lines). (E, F) Cerebellum from the same dog that is both indented and impacted with two definitions of the foramen magnum. Our definition (E) considered the opisthion to be the ventral-most extent of a continuous hypointense line caudal to the cerebellum. Therefore, we defined this dog as not showing herniation. Other researchers<sup>7,22</sup> illustrated definitions of the foramen magnum more similar to (F) which would suggest they would define this cerebellum to be herniated.

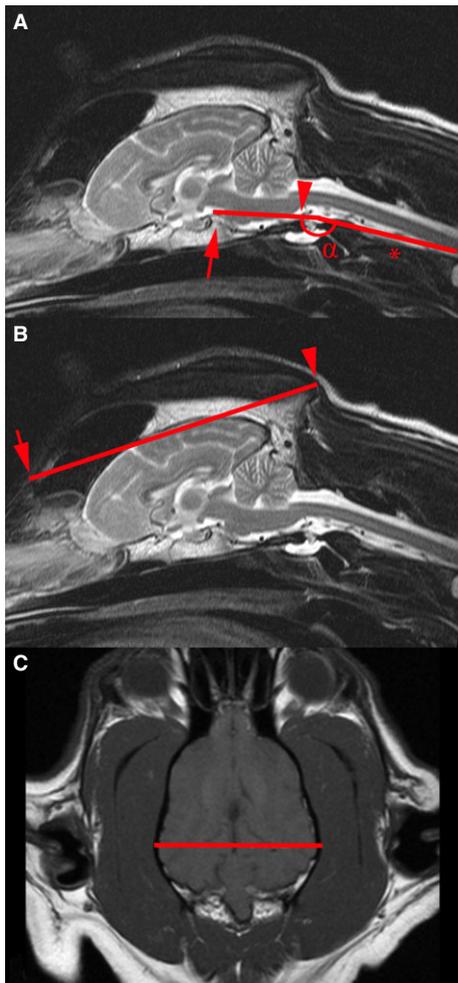
magnum and a line along the floor of the vertebral canal within the second cervical vertebra; similar to that previously described in the CKCS.<sup>22</sup> This variable was called the head angle and decreased as the occipital-atlanto-axial region was flexed (Fig 2).

### Data Collection

Images from 200 dogs were assessed blinded to breed. After the data had been collected, clinical information was obtained from the case notes and each animal's breed recorded. Animals with clinical signs potentially attributable to CM (eg, neck scratching, spontaneous vocalizing, central vestibular abnormalities) for which no other cause had been identified were excluded. Dogs that displayed seizures alone were not excluded because seizures are generally not regarded as related to CM or syringomyelia.<sup>11</sup>

### Statistical Analysis

All analysis of the data was performed by the same author (TRHB). The prevalence and 95% confidence interval (CI) of



**Fig 2.** Measurements used to calculate head angle and cranial index. **(A)** head angle ( $\alpha$ ) as the angle between a line connecting the dorsum sellae (arrow) to the caudal basioccipital bone (basion; arrowhead) and the floor of the vertebral canal within C2 (\*). **(B)** Cranial length measurement used to calculate the cranial index. This line connected the nasion (arrow) to the caudal supraoccipital bone (inion; arrowhead). The frontal/nasal suture that defines the nasion was not clear on all sagittal T2-weighted images so its location was estimated as the ventral-most extent of the frontal sinuses on para-sagittal images. **(C)** Cranial width measurement used to calculate the length to width ratio (solid line). This line was drawn across the widest part of the cranial cavity (euryon to euryon) on a dorsal T1-weighted MR sequence. All other measurements were made on midsagittal T2-weighted MR images.

each malformation across all dogs (excluding CKCS) and within any breed in which  $\geq 10$  dogs were scanned was calculated by the modified Wald method using an online resource.<sup>d</sup> The data from CKCS were excluded from further logistic regression analysis as our primary aim was to establish the prevalence of CM in non-CKCS dogs.

To investigate the effect of head angle and brachycephaly (cranial index) on the odds of showing indentation or impaction, 2 logistic regression models were constructed: 1 with impaction and 1 with indentation as dependent variables.<sup>e</sup> After testing for multicollinearity using multiple regression, head angle and cranial index both were used as predictor variables.

Univariable logistic regression analysis was performed on the datasets with cranial index and head angle as predictor variables. Variables with a univariable Wald statistic  $P < .2$  were carried forward into the multivariable model and their exponential of the  $B$  statistic ( $\text{Exp}[B]$ ) was calculated along with its 95% CI to indicate the change in odds ratio for expressing each malformation with a unit change in the variable. The multivariable models were built using a forced entry method, and variables were retained as significant predictors with Wald  $P < .05$ . Goodness-of-fit for the multivariable models was estimated using the omnibus test of model coefficients. The amount of variance explained by each model was estimated using Nagelkerke's  $R^2$ .

## Results

One dog (a Pomeranian) was excluded because it showed signs of apparent pain and neck scratching for which no other cause could be found, thus data from 199 dogs were analyzed. The most common breeds that met the inclusion criteria were Cocker Spaniel ( $n = 11$ ), Golden Retriever ( $n = 11$ ), Labrador Retriever ( $n = 22$ ), Jack Russell Terrier ( $n = 12$ ), Staffordshire Bull Terrier ( $n = 12$ ), Springer spaniel ( $n = 14$ ) and CKCS ( $n = 14$ ; Table 1). The medians and ranges of cranial index for these 10 breeds are shown in Figure 3.

Excluding the CKCS, indentation of the cerebellum was found in 82/185 (44%; 95% CI, 37–51%) and impaction was found in 40/185 (22%; 95% CI, 16–28%) of all dogs scanned. All dogs that were impacted also were indented aside from one mixed breed dog. Herniation was recorded in the Pomeranian excluded from the study.

All 14 included CKCS had a diagnosis other than CM: noninfectious meningoencephalitis (5/14); idiopathic facial paralysis (3/14); seizures (2/14), and 1 each of masticatory myositis, generalized tremor, idiopathic peripheral vestibular disease and cardiogenic collapse. All 14 CKCS had indentation, 86% (12/14) had impaction and 29% (4/14) had herniation of the cerebellum.

No dogs other than CKCS showed herniation, and thus data for this malformation were not analyzed. The head angle and cranial index for non-CKCS dogs with impaction and indentation are shown in Table 1. No significant collinearity (tolerance statistic  $>0.2$ ) was found between head angle and cranial index.

### *Relationship Among Cerebellar Indentation, Brachycephaly and Neck Angle During Scanning*

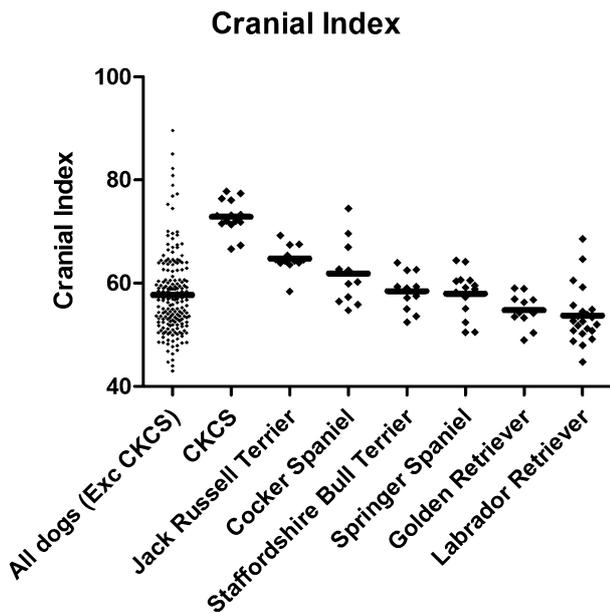
Cranial index ( $P < .001$ ) and head angle during scanning ( $P = .080$ ) showed a positive association with indentation during univariable analysis and thus both were included in the multivariate model. When they were entered into the regression model together, both measures were significantly associated with increased odds of indentation (cranial index [ $P < .001$ ] and head angle [ $P = .046$ ]). The odds ratio for displaying indentation increased by 1.014 (95% CI, 1.000–1.028) for each 1 degree increase in head angle and by 1.143 (95% CI, 1.084–1.206) for each unit increase in cranial

**Table 1.** Prevalence of each definition of CM and mean estimates of brachycephaly in the seven most frequently scanned canine breeds ( $n > 10$ ).

Breed	Indented <sup>a</sup>	Impacted <sup>a</sup>	Herniated <sup>a</sup>	Head Angle <sup>b</sup>	Cranial Index <sup>b</sup>
All Dogs (excluding CKCS)	44% (37–51%) 82/185	22% (16–28%) 40/185	0% (0–2%) 0/185	173° (170–177°)	57.7 (56.6–58.8)
CKCS	100% (75–100%) 14/14	86% (58–97%) 12/14	29% (11–55%) 4/14	170° (157–183°)	72.9 (71.0–74.7)
Staffordshire Bull Terrier	83% (54–97%) 10/12	50% (25–75%) 6/12	0% (0–28%) 0/12	174° (160–189°)	58.5 (56.2–60.7)
Jack Russell Terrier	75% (46–92%) 9/12	50% (25–75%) 6/12	0% (0–28%) 0/12	184° (164–203°)	64.8 (63.1–66.5)
Cocker Spaniel	64% (35–85%) 7/11	18% (4–49%) 2/11	0% (0–30%) 0/11	177° (160–194°)	61.9 (57.7–66.1)
Labrador Retriever	27% (13–48%) 6/22	5% (<1%–24%) 1/22	0% (0–18%) 0/22	174° (162–186°)	53.7 (51.3–56.2)
Springer Spaniel	21% (7–48%) 3/14	7% (<1%–34%) 1/14	0% (0–25%) 0/14	182° (169–194°)	58.0 (55.4–60.5)
Golden Retriever	18% (4–49%) 2/11	0% (0–30%) 0/11	0% (0–30%) 0/11	173° (160–186°)	54.8 (52.3–56.9)

<sup>a</sup>Data expressed as percentage followed by 95% CI in parentheses then proportion.

<sup>b</sup>Data expressed as mean followed by 95% CI of the mean in parentheses.



**Fig 3.** Cranial indices for the seven most frequently scanned canine breeds. Horizontal lines represent median values.

index. This multivariate model also indicated that, together, these 2 variables accounted for 24.6% of variability in indentation status (Nagelkerke's  $R^2 = 0.246$ ).

#### ***Relationship Among Cerebellar Impaction, Brachycephaly and Neck Angle During Scanning***

As with indentation, both cranial index ( $P < .001$ ) and head angle ( $P = .017$ ) showed a significant influence on the odds of impaction in univariable analysis and thus were included in the multivariate model. When they were entered into the regression model

together, both measures were significantly associated with increased odds of impaction (cranial index [ $P < .001$ ] and head angle [ $P = .012$ ]). The odds ratio for displaying indentation increased by 1.022 (95% CI, 1.005–1.040) for each 1 degree increase in head angle and by 1.154 (95% CI, 1.090–1.222) for each unit increase in cranial index. This multivariate model also indicated that, together, these 2 variables accounted for 29.8% of variability in indentation status (Nagelkerke's  $R^2 = 0.298$ ).

#### **Discussion**

The 95% CI of our prevalence data suggest that 37–51% of non-CKCS dogs without clinical signs associated with CM had indentation of their cerebellum and 16–28% had impaction. Because so many apparently normal dogs have these purported abnormalities, we would consider that neither of these definitions of CM is useful. We found that brachycephaly is associated with impaction and indentation of the cerebellum. This suggests that detection of those features in CKCS should not be considered abnormal, but more likely a consequence of their brachycephalic conformation. The association of neck extension with increasing odds of indentation and impaction indicates that MR should be carried out in standardized position if the morphology of the cerebellum is investigated (as suggested by the British Veterinary Association [BVA]<sup>c</sup>).

If indentation and impaction are common anatomical variations rather than a reflection of a disease process, this finding has major implications for breeding strategies that depend on these definitions to identify diseased dogs. For example, the BVA and UK Kennel Club have published guidelines to screen dogs by MR imaging for CM, syringomyelia or both.<sup>f</sup> They define CM as grade 1 if there is indentation by the supraoccipital bone (alongside signal consistent with

cerebrospinal fluid between the caudal vermis and the foramen magnum) and grade 2 if the cerebellar vermis is impacted into or herniated through the foramen magnum. Based on these definitions, our data suggest that 44% of normal dogs may be considered grade 1 and 22% grade 2. Their current breeding recommendations do not take into account the presence of CM, but do imply that these recommendations may change in the future as data are collected to derive estimated breeding values for individual dogs.<sup>25</sup> Our data suggest that the current definitions used for CM would not be appropriate to include in these breeding values.

In humans, diagnosis of symptomatic Chiari-1 malformation is dependent on herniation of the cerebellar tonsils through the foramen magnum because clinical signs (typically headaches) are associated with herniation greater than 3–5 mm.<sup>26,27</sup> In dogs, clinical signs of CM alone have been suggested to include subclinical vestibular disturbances (eg, ventral positional strabismus, decreased menace response with apparently normal vision); cervical pain; and apparent pruritus of the head, neck, and shoulder regions.<sup>2,3</sup> However, these signs have more commonly been described as being secondary to the cervical syringomyelia that often accompanies CM<sup>28</sup> and appear unassociated with extent of herniation.<sup>9,16</sup> In our study, no asymptomatic, non-CKCS dog showed herniation, which implies it is unlikely to represent normal variation in canine caudal cranial fossa morphology and may therefore be a better indication of abnormality.

We may have underestimated the prevalence of herniation because of how we defined the foramen magnum. We defined the dorsal part (opisthion) as the most ventral aspect of the hypointense line caudal to the cerebellum.<sup>16</sup> Other researchers<sup>22</sup> identified a hypointense structure in this area on T2-weighted images that changed shape in flexion and extension and considered it to be the atlanto-occipital ligament. As a result, they measured the opisthion more rostrad than we did (Fig 1). We chose our definition because it seemed that dynamic imaging<sup>22</sup> or concurrent computed tomography<sup>7,29</sup> would be necessary to conclusively distinguish ligament from bone in this area. We believe our definition was more objective and applicable to each MR image. We detected herniation in 29% (11–55%) of our CKCS. Other researchers have reported herniation in 7–100% of asymptomatic CKCS<sup>7,8</sup> without explicit definition of the foramen magnum's boundaries.

Because of this potential for bias, we remeasured the foramen magnum in all images using a less objective definition for the opisthion (dorsal foramen magnum). On this occasion, we attempted to differentiate which hypointense structure(s) formed the caudo-ventral boundary to the cerebellum (either the supraoccipital bone, the atlanto-occipital ligament, or the dorsal lamina of C1 in cases of atlanto-occipital overlapping) and defined the opisthion as the point at which we considered the supraoccipital bone to end. This location was not clear in some dogs. This new definition suggested that 5/185 (3%) of non-CKCS dogs showed herniation

(3/5 by <1 mm and all <2 mm) whereas 11/14 (79%) of the CKCS now showed herniation. Because our analysis concentrated mainly on non-CKCS dogs, and herniation was very uncommon with either definition, we did not feel that any bias from this imprecision was clinically relevant. This reanalysis did emphasize the need for additional anatomical studies of the ability of MR images to accurately define the bony structure of the caudal cranial fossa.

We found that the odds of showing impaction or indentation significantly increased as dogs' skulls became shorter and wider (ie, increase in cranial index). The clinical importance of the influence of cranial index is hard to quantify. The measure of effect size used in the logistic regression models (Nagelkerke's  $R^2$ ) showed the predictive influence of cranial index and head angle combined to show indentation or impaction was approximately 25–30%. The range of cranial index for non-CKCS dogs was 47. Using the equation Odds ratio =  $\text{Exp}(B)^{\text{magnitude of unit change}}$ , this suggests the dog with the highest cranial index (ie, shortest, widest head) had 10.84 (95% CI, 1.69–68.44) times higher odds of indentation and 19.85 (95% CI, 1.79–218.69) higher odds of impaction than the dog with the longest, narrowest head. This effect seems large, but without knowing the odds for impaction or indentation in a dog with a long narrow head it is difficult to establish clinical relevance. What it does show is that cranial index has a similar influence on both indentation and impaction as  $\text{Exp}(B)$  values because both were similar with overlap of their 95% CI.

It has been suggested that CKCS should be compared only with brachycephalic dogs, because comparison with mesaticephalic dogs could be misleading.<sup>23</sup> The significant influence we found on indentation and impaction from cranial index appears to support this suggestion because we would argue that previous abnormalities used to define CM (indentation and impaction) may be consequences of short, wide skulls and not necessarily an indication of a disease process.

One problem with using brachycephaly to define control groups is that there is no universally agreed upon measure for the term. We selected cranial index as it was measurable from MR sequences routinely obtained and has been suggested to accurately categorize dogs.<sup>23</sup> Other measures also have been described<sup>23,24</sup> that take into account such factors as facial bone involution (craniofacial angle) or the relative length of the entire skull to the interzygomatic distance (skull index). During these previous investigations of brachycephaly, dogs were subjectively divided into brachycephalic and mesaticephalic groups before making skull measurements. These data then were analyzed to determine which best fulfilled the a priori definition of brachycephaly, meaning they were always only proxy measures of the initial grouping.

Another problem is that different measurements categorize dogs inconsistently. For example, previous data<sup>30</sup> show that the English bulldog is similar to the Pekingese if a ratio of head length (including snout) to width is used (skull index). If the cranial index is used,

which does not take into account the snout, the bulldog is more similar to the purported dolicephalic saluki than the Pekingese. Finally, these data for the ranges of cranial indices show that there is overlap between the CKCS and other dogs that typically would be considered mesaticephalic, particularly the Labrador retriever and cocker spaniel (Fig 3).

These problems with defining brachycephaly highlight that using arbitrarily defined control groups of non-CKCS dogs (brachycephalic or not) may be inappropriate because there is little evidence that this adequately distinguishes them from dogs with CM. Previous studies using non-CKCS dogs as controls have explicitly stated that no indentation or herniation was seen in their groups of small breed dogs,<sup>10</sup> brachycephalic dogs,<sup>17</sup> or French Bulldogs.<sup>18</sup> This suggests that they may be appropriate to use as controls, but is not consistent with our finding that 37–51% of dogs will show some degree of cerebellar indentation. Other studies have not stated how many non-CKCS controls showed indentation or impaction<sup>8,20</sup> but show cerebellar indentation (a definition of CM used in both studies) in their illustrations of normal dogs. This supports our hypothesis that indentation and impaction may be underrecognized in previously used control groups.

Another secondary aim of our study was to investigate the influence of head position. We found that the odds for both indentation and impaction significantly increased with a more extended head position (increasing head angle). Previous research<sup>22</sup> found that herniation was more severe in a flexed position. Extending the head may have caused rostral bulging of the atlanto-occipital ligament or displacement of the dorsal lamina of C1, if there was occipital dysplasia and atlanto-occipital overlap. This possibly explains our findings because either of these structures could contact and deform the caudo-ventral vermis and cause indentation or impaction.

This significant association provides further evidence that indentation and impaction are poor definitions for CM, because they may change depending on how a dog is positioned for MR imaging. There is no evidence from our data or previous studies that flexion or extension can induce indentation, impaction or herniation in dogs that do not otherwise have these features. Until this is known, our data suggest that prospective studies investigating CM should standardize head position.

We conclude there is a high prevalence of cerebellar indentation and impaction in the normal canine population, suggesting they are unreliable as defining factors for CM. Our data supported the hypothesis that some measures of brachycephaly are associated with indentation or impaction, but the overlap in these measurements among breeds showed that construction of control groups based on subjective assessment of skull type could be inappropriate. Instead, it may be better for future studies investigating the relationship between abnormalities of the caudal cranial fossa and clinical signs or syringomyelia to define control groups based on the absence of specific anatomical features

considered important (eg, cerebellar herniation, obstruction to CSF flow at the foramen magnum).

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## Footnotes

<sup>a</sup> PACS; Visbion Ltd, Surrey, UK

<sup>b</sup> Philips Medical Systems, Surrey, UK

<sup>c</sup> BVA/Kennel Club Chiari Malformation/Syringomyelia (CM/SM) scheme—procedure notes (Accessed June 2013 at [http://www.bva.co.uk/public/documents/CM\\_SM\\_Procedure\\_Notes.pdf](http://www.bva.co.uk/public/documents/CM_SM_Procedure_Notes.pdf))

<sup>d</sup> <http://graphpad.com/quickcalcs/ConfInterval1.cfm> (Accessed 18th November 2013)

<sup>e</sup> SPSS Statistics, Version 21, IBM, Hampshire, UK

<sup>f</sup> British Veterinary Association/Kennel Club Chiari malformation/Syringomyelia (CM/SM) Scheme Appendix 1 (last accessed November 2013 at [http://www.bva.co.uk/public/documents/CM-SM\\_breeding\\_recommendations.pdf](http://www.bva.co.uk/public/documents/CM-SM_breeding_recommendations.pdf))

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*Conflict of Interest Declaration:* The authors disclose no conflict of interest.

*Off-label Antimicrobial Declaration:* The authors declare no off-label use of antimicrobials.

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