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ORIGINAL PAPER

Utility of a flexed neck sagittal magentic resonance imaging sequence for the assessment of cerebellomedullary cistern in dogs

Dafni Sivolapenko[1] | **Juliet Duncan**[1] | **Caroline Eivers**[2] | **Tiziana Liuti**[1] | **Katia Marioni-Henry**[1]

[1]Royal (Dick) School of Veterinary Studies and Roslin Institute, University of Edinburgh, Scotland, UK

[2]Department of Diagnostic Imaging, Veterinary Specialists Auckland, Auckland, New Zealand

Correspondence
Dafni Sivolapenko, Royal (Dick) School of Veterinary Studies and Roslin Institute, University of Edinburgh, Midlothian, Scotland EH25 9RG, UK.
Email: dsivolap@ed.ac.uk

Abstract

Cerebrospinal fluid (CSF) collection from the cerebellomedullary cistern (CM) of dogs with congenital or acquired cerebellar herniation could lead to serious complications. It is anecdotally more challenging in large brachycephalic breeds possibly due to the increased distance between the skin and CM. The first objective of this study was to assess whether flexed-neck sagittal magnetic resonance imaging (MRI) sequences would assist in the decision-making process of collecting CSF from the CM. The second objective was to examine the dimensions of the CM measured in extended and flexed views, and whether cranial index (CI), skull height and body weight correlated with the distance of the CM from the skin surface. Forty-one dogs of various breeds were included in the study. Measurements were performed on T2-weighted sagittal sequences acquired in extended and flexed-neck positions, and transverse sequences acquired in an extended-neck position. Mild cerebellar herniation was detected in 23/41 (56%) of the flexed-neck views versus none in the extended views. The CM area was significantly larger in flexed-neck views than in extended views ($p < 0.05$). In 29% of the cases (12/41), the trajectory of the needle intersected the cerebellar vermis. There was a positive correlation between the distance of the CM from the skin and body weight ($p < 0.05$) and skull height ($p < 0.05$), but not with the CI ($p = 0.23$). These findings suggest that a flexed-neck sagittal MRI sequence helps with assessment of the size of the CM and degree of cerebellar herniation, and that skull height and body weight, but not cranial index, affect the distance of the CM from the skin surface.

KEYWORDS
brachycephaly, cerebellar herniation, cerebellomedullary cistern, cerebrospinal fluid sampling, Chiari-like malformation, cisterna magna

1 | INTRODUCTION

Puncture of the cisterna magna (CM or cerebellomedullary cistern) for collection of cerebrospinal fluid (CSF) is a procedure commonly performed for diagnostic investigation of brain and spinal cord disease in dogs, especially when an inflammatory or infectious disease is suspected (Sturges, 2015). This procedure is carried out under general anesthesia, with the patient's neck flexed at approximately 90°–100°, in lateral recumbency (Sturges, 2015). CSF sampling is then performed by the introduction of a spinal needle on the midline, either halfway between the caudal aspect of the external occipital protuberance and the cranial aspect of the dorsal spinous process of the second cervical vertebra (axis) or in the center of a "triangle" formed by palpation of the caudal aspect of the external occipital protuberance and the wings of the first cervical vertebra (atlas) (Sturges, 2015). Due to the nature of this procedure, the presence or suspicion of cerebellar herniation through the foramen magnum constitutes a contraindication for cisternal puncture as it reduces patient safety (Vernau et al 2008). Cerebellar herniation through the foramen magnum can be acquired, associated with space-occupying or inflammatory intracranial disease causing increased intracranial pressure or it can be congenital, associated with an abnormal conformation of the caudal fossa (Carrera et al., 2009; Cerda-Gonzalez et al., 2009; Kornegay et al., 1983; Kromhout et al., 2015; Lewis et al., 2016). Cerebellar herniation is commonly reported in brachycephalic breeds as part of Chiari-like malformation (CLM), estimated to affect up to 95% of Cavalier King Charles Spaniels (CKCS) and 65% of Brussel Griffons (Freeman et al., 2014; Loughin, 2016). However, primary cerebellar herniation has also been reported in 16–28% of non-CKCS dogs without clinical signs of increased intracranial pressure or CLM (Harcourt-Brown et al., 2015).

Recent literature reported that cerebellar herniation was significantly increased in CKCS with CLM when the magnetic resonance imaging (MRI) was acquired in a flexed-neck position (Upchurch et al., 2011). We hypothesized that the same could occur also in dog breeds other than CKCS and in dogs without CLM. The first objective of this study was to assess whether flexed-neck sagittal sequences on MRI would assist in the decision-making process of collecting CSF from the CM of dogs, irrespectively of their breed. Flexed-neck sequences simulate the positioning of the patient for CM CSF puncture; therefore, we hypothesized that they may be useful to obtain more precise measurements of the dimensions of the CM, herniation of the cerebellar vermis, and assessment of the trajectory of the spinal needle (Sturges, 2015; Upchurch et al., 2011). The second objective was based on the anecdotal observation of one of the authors (K.M.-H.) that performing CM CSF taps appears to be more challenging in larger breed and brachycephalic dogs. We hypothesized that increase in body size, skull height and cranial index may lead to an increase in distance of the CM from the skin surface without a corresponding increase in the dimension of the CM itself, making the CM CSF more difficult to perform in large brachycephalic canine breeds.

2 | MATERIALS AND METHODS

A cross-sectional prospective study was performed. The study population consisted of 47 dogs of any breed, gender, age, and body weight that were presented to the Neurology Department of the Hospital for Small Animals, Royal (Dick) School of Veterinary Studies, University of Edinburgh between November 2013 and June 2016 and underwent MRI of the brain and/or cervical spinal cord as part of their diagnostic investigations. The study was conducted in compliance with the guidelines of the Veterinary Ethical Review Committee of the Royal (Dick) School of Veterinary Studies of the University of Edinburgh (Approval number 15.15).

All dogs were imaged using the same MRI unit (Philips Intera, 1.5T system; Philips Medical Systems), under general anesthetic, in dorsal recumbence, in both extended and flexed-neck position. For the extended-neck sequences, the patients were positioned as standard for canine head or neck MRI studies, in dorsal recumbency with the head rested directly on the gantry table. For the flexed-neck studies, the patients had their neck flexed at 90° angle based on visual assessment, to simulate the positioning for a cisternal spinal puncture (Sturges, 2015). This was achieved using a previously described technique by placing a 45° foam wedge behind the head, held secure with the use of sandbags (Gordon et al., 2017; Upchurch et al., 2011). Cases were excluded from the study if the angle between the basioccipital bone and the dorsal body of the axis was exceeding 140°, either due to the patient's conformation, body condition score (BCS), or suspected discomfort manifested by an increase in heart and/or respiratory rate. Images from patients with lesions that could affect brain morphology and the planned measurements in sagittal and transverse views were also excluded. Finally, studies in which the measurements could not be obtained from a midsagittal section due to poor visualization of bony structures were also excluded.

T2-weighted sequences were selected because CSF would appear hyperintense on these images and thus allow for more accurate measurements of the CM. T2-weighted sagittal and transverse sequences were obtained in an extended position, and a T2-weighted sagittal sequence was obtained in a flexed-neck position. The case numbers alone, and no other identifying information, were visible to the researcher performing the measurements. In an effort to standardize the process and reduce bias, all measurements were collected by one investigator (D.S.) who was unaware of the patients' signalment, history, presenting complaint, and clinical findings.

For sagittal sequences, the level at which the interthalamic adhesion and bony landmarks were visible was used for all measurements (Figure 1a,c). For transverse sequences, images at the level of the rostral colliculi were used for all measurements (Figure 1b). The measurements were performed as described in Figure 1a–c. The cranial index was then calculated using Stockard's cranial index calculation: (cranial width × 100)/cranial length (Mansour et al., 2018; Stockard, 1941). The weight of all the patients was noted from their anesthetic record after all measurements were collected. BCSs were not included as they were not available for all patients.

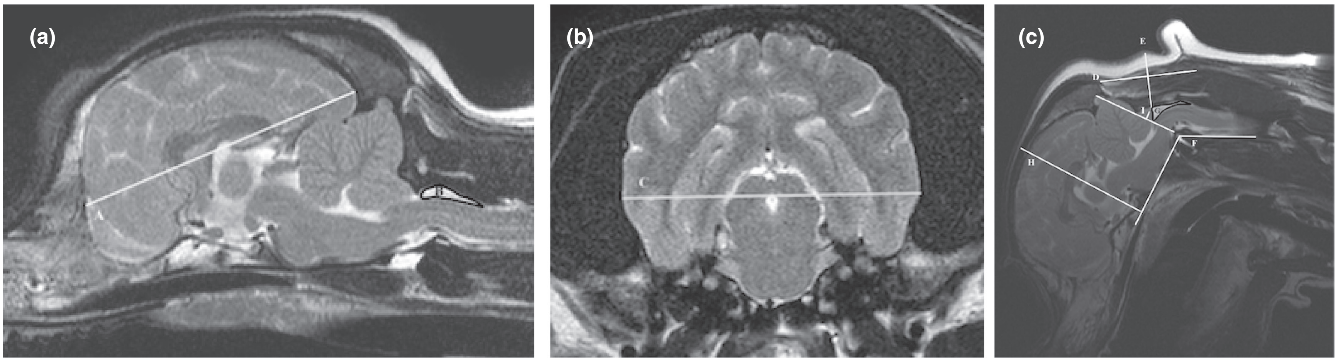

FIGURE 1 (a) Mid-sagittal T2-weighted image at the level of the interthalamic adhesion, demonstrating measurements A and B. Measurement A represents the cranial length, measured in millimeters, from the nasion at the nasofrontal suture to the inion at the central surface point of the external occipital protuberance. Measurement B represents the area of the cisterna magna in the extended-view; in cases where the occipital bone or dorsal atlanto-occipital membrane protruded into the cisterna magna, this area was virtually divided into two compartments, then added. (b) Transverse T2-weighted image at the level of the rostral colliculi, demonstrating measurement C; Measurement C represents the cranial width, measured in millimeters, from euryon to euryon. (c) Mid-sagittal T2-weighted image in flexed view at the level of the interthalamic adhesion, demonstrating measurements D–I. Measurement D represents the distance between the external occipital protuberance and the dorsal spinous process of the axis, measured in millimeters. Measurement E represents the distance between the skin and the cisterna magna, measured perpendicular to measurement A in millimeters. In this example, the trajectory of line E intersects the cerebellum. Measurement F represents the angle between a line tangent to the dorsal aspect of the basioccipital bone and a line tangent to the dorsal aspect of the body of the axis. Measurement G represents the area of the cisterna magna, in millimeters squared. Measurement H represents the height of the skull, measured on a line perpendicular to the basioccipital bone at the level of the clivus to the external aspect of the parietal bone, in millimeters. Measurement I represents the degree of cerebellar herniation in millimeters using a previously described technique (Freeman et al., 2014; Gordon et al., 2017)

All data were processed using R (R Foundation for Statistical Computing, http://www.R-project.org/). Descriptive statistics was used to describe the data; normality was assessed using a Kolmogorov–Smirnov test. A Wilcoxon signed-rank test was performed to compare non-parametric data such as the area of the CM in extended and flexed-neck position to assess if the position of the head would significantly affect the area of the CM. A Spearman correlation test was performed to assess correlation among parametric data such as the distance of the CM from the skin and body weight or skull height to assess if the larger body size and the increased height of the skull in brachycephalic dogs were significantly affecting the distance to the target area. A Spearman correlation test was also performed to assess whether the distance between the skin and the CM in flexed view correlated to the cranial index and if the cranial index would influence the degree of herniation of the cerebellar vermis. A Spearman correlation test was also used to assess if the area of the CM correlated to the body weight. Intra-observer variability was assessed using the intra-class correlation coefficient (ICC) with measurements repeated after an interval of 12 months (Ranganathan et al., 2017).

3 | RESULTS

Forty-seven patients underwent MRI in a flexed-neck position according to the protocol described during the period of this study. In this study, the angles of flexion between the basioccipital bone and the dorsal body of the axis ranged from 95.36° to 133.20°. Six cases were excluded, either because of insufficient neck flexion (three dogs) or because the measurements could not be obtained from the midsagittal section (three dogs). Therefore, a total of 41 dogs were included in this study. Fifteen dog breeds were included: 18/41 were CKCS, 5/41 were French Bulldog, 3/41 were Border Terrier, 2/41 were Boxer, 2/41 were Pug, 2/41 were Chihuahua, and 9/41 were other breeds (one of each of the following breeds: Nova Scotia Duck Tolling Retriever, Rhodesian Ridgeback, Miniature Schnauzer, Beagle, Staffordshire Bull Terrier, Basset, Papillon, Jack Russel Terrier, American Cocker Spaniel). Twenty-one (21/41) of the dogs were males, of which 10/21 were entire and the remaining were neutered. Twenty 20/41 dogs were females, of which 6/20 were entire and the remaining were neutered. Ages ranged from 0.3 to 14.6 years (median: 6.45 years). The body weights ranged from 3.9 to 36.4 kg, with a median of 13.38 kg.

When assessing the trajectory of the needle in the flexed view, in 61% of the cases (25/41), the needle did not intersect the cerebellar vermis; in 29% of the cases (12/41), the trajectory of the needle intersected the cerebellar vermis; and in 10% of the cases (4/41), it was considered subjectively too close to safely perform a cisternal spinal tap (Figure 2). All of the cases where the trajectory of the needle was either intersecting or was close to intersecting the cerebellar vermis were cases that exhibited cerebellar herniation. Cerebellar herniation was detected in the flexed-neck views in 23/41 (56%) of the cases; these were all cases that exhibited indentation of the caudal aspect of the cerebellum and impaction of the cerebellar vermis into the foramen magnum in the extended-neck images (Harcourt-Brown et al., 2015). Similarly, there were no cases that showed cerebellar indentation and impaction in the extended-neck images but did not show cerebellar herniation in the flexed-neck images. While there

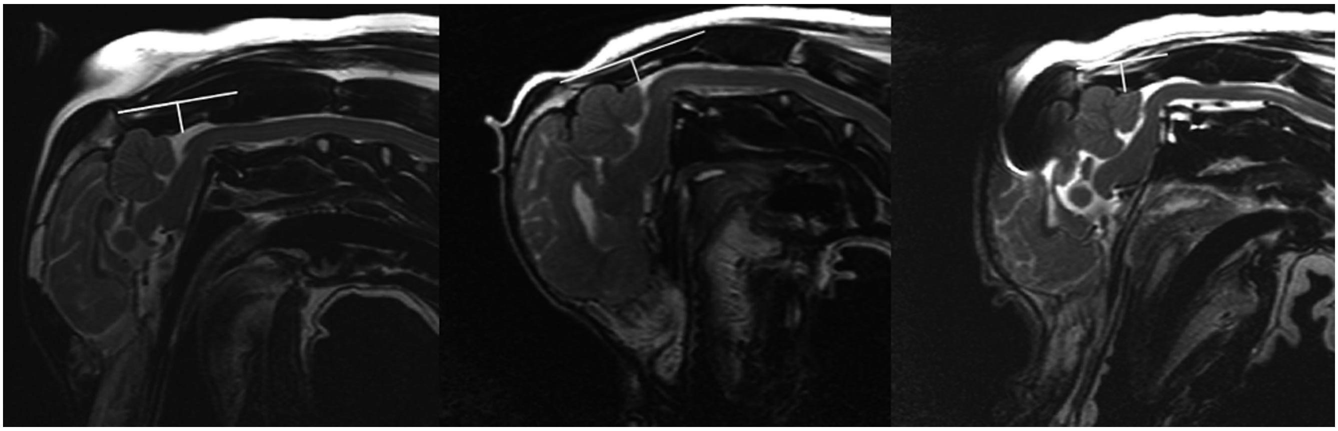

FIGURE 2 Mid-sagittal flexed T2-weighted images at the level of the interthalamic adhesion, demonstrating the simulated trajectory of the needle in flexed-neck views: "A" was considered safe for cisternal CSF sampling, "B" was considered close, and "C" was considered unsafe because the trajectory of the needle intersected the cerebellar vermis. CSF, cerebrospinal fluid

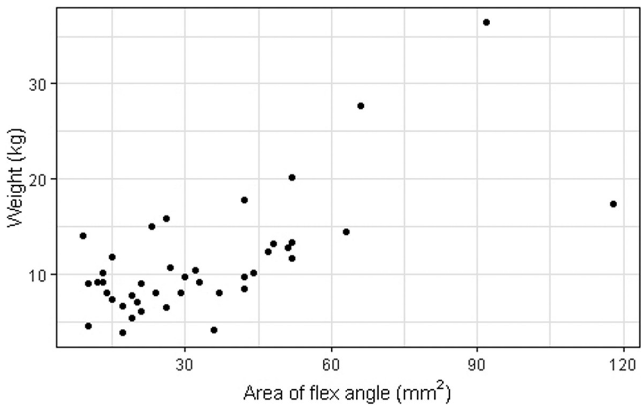

FIGURE 3 Area of the cisterna magna (mm^2) in flexion against body weight body weight (kg)

was cerebellar indentation and impaction noted in some extended-neck images, there was no herniation through the foramen magnum in any extended-neck images; herniation through the foramen magnum was only evident in the flexed-neck images. Cerebellar herniation measurements in the flexed-neck images ranged from 1.1 to 4.3 mm (median 1.6 mm).

We found that in the flexed-neck view, the CM area was significantly larger than in extended-neck view ($p < 0.05$). When examining if the distance of the CM from the skin would correlate to body weight, we found a positive correlation (0.6955416, $p < 0.05$). When examining if the distance of the cisterna from the skin would correlate to skull height, we found a moderately positive correlation (0.5495994, $p < 0.05$). When examining if the area of the CM in flexion correlated to the body weight, a moderately positive correlation was found (0.565926, $p < 0.05$, see Figure 3). The cranial index was not found to correlate with the degree of cerebellar herniation (−0.001562961), and this result was not clinically significant ($p = 0.9926$). The cranial indexes in dogs with cerebellar herniation were very similar to the cranial indexes of those without (mean 84.76, median 85.37 and mean 84.39, median 86.56, respectively). Finally, there was no correlation between the cranial index and the distance from the skin to the cisterna (0.2010865), and there was no statistical significance in this result, with $p = 0.23$.

Measurements were repeated for intra-observer variability 1 year apart, so the measurements were performed twice in total for area of the CM in flexion and extension, distance of the CM from the skin angle of flexion and skull height, and three times in total for cranial length and cranial width, due to data corruption being identified in one of the datasets for these measurements. For repeated measurements, ICC was considered good for the area of CM in extended view (ICC = 0.863, $p < 0.05$) and in flexion (ICC = 0.836, $p < 0.05$). ICC was considered good for cranial length (ICC = 0.863, $p < 0.05$) and excellent for cranial width (ICC = 0.913, $p < 0.05$). ICC was also considered excellent for repeated measurements for the distance of the CM from the skin (ICC = 0.999, $p < 0.05$) and for the angle of flexion (ICC = 0.912, $p < 0.05$). ICC was also considered moderate for skull height (ICC = 0.675, $p < 0.05$).

4 | DISCUSSION

The flexed-neck view was found to be useful in assessing the trajectory of the spinal needle based on the bony landmarks (occipital protuberance and dorsal spinous process of C2), which would in clinical practice be identifiable with palpation by the clinician performing the CSF puncture (Figure 2). The percentage of cases in this study where the trajectory of the needle was found to intersect the cerebellar vermis were surprisingly high, based on our clinical experience. This trajectory was calculated based on the current recommendations for performing cisternal CSF sampling, but it is possible that in clinical practice, the clinician may slightly deviate from this technique (Sturges, 2015).

Mild cerebellar herniation was evident in 56% of the cases; this was only detected in the flexed-neck images, consistent with previous studies (Upchurch et al., 2011). On review of the clinical information, we found that most of the cases that exhibited mild cerebellar herniation did not have a condition causing increased intracranial pressure but were diagnosed with CLM. Indeed, images from patients with large lesions that could affect brain morphology, but also lead to increased intracranial pressure, were excluded from this study. Also, CKCS were over-represented in our study, and nearly all of them (17/18) had CLM on imaging as expected based on recent veterinary literature (Loughin, 2016). While the over-representation of CKCS dogs is a limitation of our study, all of the cases where the trajectory of the needle was close to or was intersecting the cerebellum, including non-CKCS, exhibited cerebellar herniation in the flexed view. Therefore, we believe that the flexed view would be a useful addition to MRI protocols in CKCS and other dogs with CLM, as it offers further information that can assist in planning the procedure of CSF sampling in dogs of every breed and assessing its safety.

We were able to demonstrate that in the flexed-neck view, the CM area was significantly larger than in the extended-neck view. This is most likely due to the stretching of various soft tissue structures in the area, including the atlanto-occipital ligament, as reported in veterinary literature (Cerda-Gonzalez et al., 2015; Harcourt-Brown et al., 2015). Indeed, in some cases, in the extended-neck images the atlanto-occipital membrane was folded, creating a dorsal indentation and separating the CM in two compartments; these were measured separately then added in our study (Middleton et al., 2012). Instead, in the flexed-neck view, the altanto-occipital membrane did not separate the CM, as previously reported (Upchurch et al., 2011).

With regards to the body weight, we hypothesized that with increase in body weight, there would not be a corresponding increase in the area of the CM. Instead, the Spearman correlation test showed a monotonic relationship between body weight and area of the CM in flexion. However, when plotted on a graph, a linear relationship appeared evident for body weights under 10 kg; however, this relationship was not as well-defined for larger body weights (Figure 3). This suggests that while the area of the CM in flexion increases with an increase in body weight, this increase may not be directly proportional for larger dogs. A limitation of our study is that we had very few dogs in the body weight group of above 10 kg, so this relationship could not be explored further. Further research assessing this in a bigger population of dogs will be useful in clinical practice, since some breeds of dogs may have a small CM compared to their body weight and may be at higher risk of developing serious complications during a cisternal spinal tap. Various retrospective studies assessing complications following myelography reported a higher risk in large breed dogs and concluded that the adverse effects correlated to the volume of contrast injected calculated based on the body weight, hypothesizing that the volume of the subarachnoid space might not increase in a linear fashion with respect to body weight (Barone et al., 2002; da Costa et al., 2011, 2020).

We demonstrated that distance of the CM from the skin correlates with body weight and skull height in our population of dogs, confirming our hypothesis that a larger body size may lead to an increase in distance of the CM from the skin surface. We hypothesized that performing a cisternal CSF tap in brachycephalic dogs may be more challenging due to the increased height of the skull or their cranial index, as described by Stockard and used by other studies relating to brachycephalic dogs (Mansour et al., 2018; Schmidt et al., 2011; Stockard, 1941). The cranial index considers the length and width of the skull, but not the height of the skull; therefore, we elected to look at this variable in addition to the cranial index (Stockard, 1941). However, the cranial index, which is considered one of the best available indicators of brachycephaly in dogs did not correlate with the distance between the skin and the CM assessed in flexed-neck sagittal MRI sequences. We concluded that the body size and the height of the skull may affect the distance of the CM from the skin. This may lead to a more challenging CSF puncture in some dogs. In human literature, the distance from the skin to the CM was found to be associated with gender and age; these parameters were not assessed in our study (Cao et al., 2015). Further studies including a wider variety of breeds, and including gender and age in the analysis, would be useful.

In our study, we did not find a correlation between the cranial index and the degree of cerebellar herniation through the foramen magnum in flexed-neck images. In contrast, previous research has found that cerebellar impaction and indentation is associated with brachycephalic conformation (Harcourt-Brown et al., 2015). A possible explanation for this discrepancy is that there appeared to be a bias in our population with brachycephalic dogs being over-represented, both based on the breeds and on cranial index. As previously mentioned, cranial index has been used to assess conformation and divide dog breeds into brachycephalic, mesaticephalic and dolicocephalic in several studies, with brachycephaly defined as a cranial index of more or equal to 80 (Gordon et al., 2017; Harcourt-Brown et al., 2015; Knowler et al., 2018; Mansour et al., 2018; Schmidt et al., 2011; Sokołowski et al., 2018; Stockard, 1941). This appears to be extrapolated from human studies; however, there are no veterinary studies validating it in dogs (Harcourt-Brown et al., 2015).

The main limitations of this study are the small number of dogs included and the fact that CKCS dogs and brachycephalic dogs were over-represented. We were also planning to include BCS in the statistical analysis, but this information was only available for a few patients. Regarding the measurements performed, T2W images were selected to allow for better visualization of CSF for the measurements of the CM, but bone was less well-defined in these sequences, possibly reducing the accuracy of bone-related measurements. Transverse sequences were only obtained in the extended-neck view as this was a standard sequence in the diagnostic work-up for these patients. The only measurement performed on the transverse sequences was for cranial width, which was presumed to be unaffected by the patient's positioning, and therefore, it was deemed unnecessary to acquire additional transverse sequences in flexed-neck view. However, this assumption has not been investigated in our study or, to our knowledge, in other studies in published veterinary literature. Intra-observer reliability overall appeared to be good. These measurements could be affected by the level of experience of the person performing them and the scale of the measurements, which in this case were in the range of millimeters.

5 | CONCLUSION

In conclusion, we demonstrated that the flexed-neck view allows a more precise measurement of the CM and herniation of the cerebellar vermis, and it can be useful in the planning of CM puncture in dogs with cerebellar herniation or cerebellar indentation and impaction. We also showed that an increase in body size and skull height leads to an increased distance between the skin and the CM, and that the dimension of the CM correlates but is not proportional to the body size in all dogs. Further studies are necessary to prove that the distance of the CM from the skin and that differences in CM areas may lead to a more challenging CSF sampling. Based on our study, we propose that flexed-neck sagittal views will be useful in the planning of CM puncture, particularly in dogs with possible acquired or congenital cerebellar herniation, such as patients with CLM, in order to fully assess the potential risks.

AUTHOR CONTRIBUTIONS

Katia Marioni-Henry and Dafni Sivolapenko contributed to the concept and design of the study. Dafni Sivolapenko and Caroline Eivers contributed to data acquisition. Juliet Duncan, Dafni Sivolapenko and Katia Marioni-Henry contributed to data analysis and interpretation. Dafni Sivolapenko, Juliet Duncan and Tiziana Liuti contributed to creation of the figures and their corresponding legends. All authors contributed to critical revision of the manuscript.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Dafni Sivolapenko https://orcid.org/0000-0003-2584-8836

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