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## Die bregmatische Fontanelle allein ist ein unzuverlässiger Indikator für die Gesundheit von Zwergspitzen und anderen Zwerghunden

Die Schweizer Tierschutzverordnung verbietet die Zucht von Hunden mit persistierenden Fontanellen. Insbesondere bei Zwerghunden sind geschlossene Fontanellen für die Zuchtauswahl wichtig. Bei solchen Hunden werden in der Magnetresonanztomographie (MRT) häufig weitere Veränderungen am kraniozervikalen Übergang, am Hydrozephalus und an der Syringomyelie beobachtet. Ob solche Veränderungen mit persistierenden Fontanellen assoziiert sind, ist unklar. Ziel der Studie war es, zu untersuchen, ob persistierende Fontanellen mit anderen Anomalien des Kopfes und des Rückenmarks verbunden sind.

Für diese Querschnittsstudie wurden 41 Zwerghunde klinisch und neurologisch untersucht und einer 3T-MRT unterzogen. Die Hunde wurden anschliessend anhand des bregmatischen Fontanellenstatus im Ultraschall in Fälle und Kontrollen eingeteilt. Die Ergebnisse der beiden Gruppen wurden mittels des ungepaarten t-Tests, der linearen Regression und Korrelation sowie des Chi-Quadrat-Tests und des exakten Test nach Fisher verglichen.

Die Ergebnisse zeigten, dass 53,7 % der Hunde geschlossene Fontanellen hatten, während 46,3 % persistierende bregmatische Fontanellen hatten. Persistierende Fontanellen wurden häufiger bei Hunden mit geringerem Körpergewicht und kürzerem Schädel beobachtet, zeigten aber keinen Zusammenhang mit dem Alter. Es gab keine Hinweise darauf, dass der Fontanellenstatus das klinische oder neurologische Erscheinungsbild beeinflusst. Die MRT ergab bei 78,1 % der Hunde eine Chiari-ähnliche Missbildung, bei 56,1 % erweiterte Seitenventrikel und bei 41,5 % Syringomyelie. Bei Hunden mit persistierenden Fontanellen war die Wahrscheinlichkeit, an Syringomyelie zu erkranken, 3,7-mal höher (exakter Test nach Fisher; p-Wert 0,047). Erweiterte Seitenventrikel erhöhten das Risiko für

#### Summary

The Swiss Animal Welfare Ordinance prohibits the breeding of dogs with persistent fontanelles. Especially in toy-sized dogs, closed fontanelles are important for breeding selection. In such dogs, other alterations at the cranio-cervical junction, hydrocephalus and syringomyelia are frequently observed in magnetic resonance imaging (MRI). Whether such changes are associated with persistent fontanelles is unclear. The aim of the study was to investigate whether persistent fontanelles are associated with other abnormalities of the head and spinal cord.

For this cross-sectional study, 41 toy-sized dogs were clinically and neurologically examined and underwent 3T MRI. Dogs were then grouped into cases and controls, based on ultrasonographic bregmatic fontanelle status. Findings in the two groups were compared using the unpaired t-test, linear regression and correlation as well as Chi-square and Fisher's exact tests.

In result, 53,7% of the dogs had closed fontanelles, while 46,3% had persistent bregmatic fontanelles. Persistent fontanelles were more commonly observed in dogs with lower body weight and a shorter skull but showed no association with age. There was no evidence of an influence of fontanelle status on clinical and neurological presentation. MRI revealed Chiari-like malformation in 78,1% of dogs, dilated lateral ventricles in 56,1%, and syringomyelia in 41,5%. Dogs with persistent fontanelles were 3,7 times more likely to have syringomyelia (Fisher's exact test; p-value 0,047). Dilated lateral ventricles increased by 15 times the odds of syringomyelia (Fisher's exact test; p-value < 0,01). No association was found between persistent fontanelles and Chiari-like malformation, other cranio-cervical abnormalities, or ventriculomegaly.

Toy-sized dogs in this study frequently exhibited brain and spinal cord abnormalities on MRI, regardless of their fontanelle status. These findings suggest that presence or abSyringomyelie um das 15-Fache (exakter Test nach Fisher; p-Wert < 0,01). Es wurde kein Zusammenhang zwischen persistierenden Fontanellen und Chiari-ähnlichen Fehlbildungen, anderen kraniozervikalen Anomalien oder Ventrikulomegalie festgestellt.

Die in dieser Studie untersuchten Zwerghunde wiesen häufig Hirn- und Rückenmarksanomalien im MRT auf, unabhängig von ihrem Fontanellenstatus. Diese Ergebnisse legen nahe, dass das Vorhandensein oder Fehlen bregmatischer Fontanellen möglicherweise kein zuverlässiges Kriterium für die Zuchtauswahl zur Erhaltung einer gesunden Hundepopulation ist.

Schlüsselwörter: Chiari-ähnliche Fehlbildung, Magnetresonanztomographie, Rasseauswahl, Syringomyelie, Ventrikulomegalie, Zwergspitz

sence of bregmatic fontanelles may not be a reliable criterion for breeding selection aimed at maintaining a healthy dog population.

Keywords: Breed selection, Chiari-like malformation, Magnetic resonance imaging, Pomeranian, Syringomyelia, Ventriculomegaly

The bregmatic fontanelle alone is an unreliable indicator of health in Pomeranian and other toy-sized dogs

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#### Introduction

A persistent or open fontanelle is defined as a total lack of bone at a cranial suture<sup>11</sup> and is a common feature in toysized dogs.11,12 In Switzerland, affected individuals are generally excluded from breeding, except for Chihuahuas.2,32

Besides persistent bregmatic fontanelle (BF), toy-sized dogs are also commonly affected by ventriculomegaly, Chiari-like malformation (CM) and syringomyelia (SM).4,10,12,13,16,18,24, <sup>25,27</sup> CM is defined as «a malformation of the skull and cranio-cervical junction which compromises the neural parenchyma to cause pain and/or disrupt CSF circulation which can result in SM».<sup>13</sup> SM is described as «a condition that results in the development of fluid-containing cavities within the parenchyma of the spinal cord as a consequence of abnormal cerebrospinal fluid movement». The formation of SM is not completely understood yet and a possible relation between CM, SM and ventriculomegaly is suspected.  $^{13}$ These morphological changes may have an impact on the quality of life of affected animals.13,26 Common signs associated with CM and SM are phantom scratching, vocalization, spinal pain, reduced activity and jumping ability as well as touch aversion and changes in the emotional state. 13,26 A previous study showed that Chihuahuas with CM/SM-related clinical signs have more and larger persistent fontanelles.11 It is unclear whether persistent BF in toy-sized dogs is associated with neurological signs and other malformations of the head and spine. Therefore, the adequacy and reliability of selecting individuals for breeding based on BF status remain questionable.

The primary aim of this study was to evaluate whether persistent bregmatic fontanelles (BF) are associated with CM, SM, ventriculomegaly, and clinical or neurological findings. The hypothesis was that dogs with persistent BF are not more

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frequently affected by CM, SM, or ventriculomegaly, and do not exhibit more clinical or neurological signs. Secondly, the presence of CM and SM was compared with morphometric parameters derived from MRI. The hypothesis was that the presence of CM or SM is not associated with brain and skull morphology or morphometric measurements obtained via MRI. Thirdly, BF status as determined by ultrasound was compared to BF status assessed by palpation and MRI, with the hypothesis that all three methods would lead to the same conclusion regarding BF patency.

#### Material and Methods

#### **Patients**

This cross-sectional study was performed between March and December 2023 at the Division of Clinical Radiology Vetsuisse Faculty of Bern. Inclusion criteria for dogs were age older than one year and body weight less than 10 kg. Dog owners were asked to complete a questionnaire for presence or absence of the following clinical signs: scratching on shoulder and neck, scratching elsewhere, ear rubbing, mouth rubbing, neck pain, back pain, scoliosis, paresis of forelimbs, lameness of forelimbs, epilepsy, fly biting, pain/ screaming when scratching, pain/screaming when excited, pain/screaming when touched, pain when moving head, screaming when jumping, screaming, ataxia, paresis of hindlimbs, lameness of hindlimbs, collapse during exercise, cramps during exercise. Additional clinical signs and comorbidities reported by the owners at the time of presentation were documented.

The categorization of the dogs into cases and controls was based on BF status established by ultrasound examination. 6,15 Dogs with a persistent BF were categorized as cases, while those with closed BF were classified as controls.

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The study was in accordance with the local ethical regulations. Dogs that had neurological symptoms, suggestive of CM, SM, or ventriculomegaly, and therefore required an MRI were eligible to participate in the study. Clinically unaffected dogs that underwent MRI to test for these changes before breeding were also included with the owner's consent.

#### Clinical and neurological examination

All dogs were clinically examined including palpation of the BF.<sup>34</sup> Body weight and shoulder height were recorded. A neurological examination was performed by a board eligible or board-certified neurologist.

#### Anaesthesia

Dogs were fasted at least eight hours prior to anaesthesia. An intra venous catheter (jelco<sup>®</sup> 2 IV catheter Radiopaque, Smiths Medical ASD, Inc., 6000 Nathan Lane North, Minneapolis, MN55442 USA, 22G to 24G) was placed. A defined anaesthesia protocol was used with adaptions made for any contraindication. Premedication included butorphanol (Morphasol®-10, Dr. E. Graeub AG, Rehhagstrasse 83, 3018 Bern, Switzerland, 0,1 mg/kg i.v.) and medetomidine (Dormitor®, Orion Corporation, Orionintie 1 A, 02200 Espoo, Finland, 0,005 mg/kg i.v.), followed by preoxygenation. Induction was achieved with propofol (Propofol 1 % MCT Fresenius, Fresenius Kabi, Am Mattenhof 4, 6010 Kriens, Switzerland, titrated to effect i.v.). Dogs were intubated with an orotracheal tube, anaesthesia was maintained with sevoflurane (Sustane Sevoflurane ad us. vet., Piramal Critical Care, Inc., 3950 Schelden Circle, Bethlehem, PA 18017, USA, administered to effect). Ringer-Acetate solution (Ringer-Acetat Freseniusi.v., Fresenius Kabi, Am Mattenhof 4, 6010 Kriens, Switzerland, 5 ml/kg/h i.v.) was administered during anaesthesia. Monitoring of heart rate, non-invasive blood pressure, saturation by pulsoxymetry, spirometry, CO2 by capnography and analysis of the inhalant gas was performed. Perianesthetic complications were managed individually. Recovery period was managed by an anaesthetist.

#### Magnetic Resonance Imaging

MRI was performed using a 3 Tesla MRI scanner (Magnetom Vida, Siemens, Erlangen, Germany). For imaging the brain, dogs were positioned in sternal recumbency with the head in an 18-channel flex coil (Ultraflex Small 18, Siemens, Erlangen, Germany). A wedge-shaped cushion was put underneath the head to ensure a flexed head position and prevent pressure on the cephalic vein. <sup>22,23</sup> For MRI of the spine, dogs were then positioned in dorsal recumbency with the 18-channel flex coil placed underneath the dogs back. Table 1 lists the MRI parameters used for each region.

#### Ultrasonography

Ultrasound of the skull was performed under general anesthesia using a hockey stick probe (L8-18i-D) (Logiq E10s, GE HealthCare, GE Medical Systems (Schweiz) AG, Europastrasse 31, 8152 Glattbrugg, Schweiz) placed dorsally on the skull. If a full thickness loss of bone around the BF was visible, 11 the breadth of the interruption at its widest in mm was recorded.

#### Image analysis

Image analysis was performed in Deep unity (DeepUnity Diagnost 1.1.0.1, DH Healthcare GmbH, 53227 Bonn Germany).

The following parameters were evaluated on multiplanar reconstructions of the 3D T1 MPRAGE of the brain: breadth of persistent BF (in mm), presence and location of additional bone defects in the skull, evaluation of the foramen magnum (FM) as key hole shaped foramen (yes/no), <sup>14</sup> maximum

 Table 1: Overview of the Magnetic Resonance Imaging sequences, parameters and scanned regions.

MRI sequence	Region	MRI parameters		
Dorsal T1-W MPRAGE	Cranial border of brain to cranial end- plate of the third cervical vertebra (C3)	TR 2400 ms; TE 349 ms; Flip angle 8°; FOV 120×120 mm; Matrix 192; Voxel size 0,3×0,3×0,5 mm; NSA 1		
Sagittal T2-W TSE	Cranial border of brain to cranial endplate of C3	TR 6490 ms; TE 69 ms; Flip angle 120°; FOV 110×110 mm; Voxel size 0,1×0,1×2,5 mm; NSA 2		
Transverse T2-W TSE	Cranial border of brain to cranial endplate of C3	TR 7920 ms; TE 74 ms; Flip angle 150°; FOV 100×100 mm; Voxel size 0,2×0,2×2,5 mm; NSA 1		
Sagittal T2-W TSE	Adhesio interthalamica to first sacral vertebra (S1)	TR 3000 ms; TE 109 ms; Flip angle 120°; FOV 240×240 mm; Voxel size 0,2×0,2×1,6 mm; NSA 2		
Dorsal T1-W MPRAGE	Adhesio interthalamica to S1	TR 2500 ms; TE 3,39 ms; Flip angle 8°; FOV 400×400 mm; Voxel size 0,5×0,5×0,5 mm; NSA 2		
Transversal T2-W TSE	Over syrinx when present; otherwise, middle of the second cervical vertebra to the middle of the fourth cervical vertebra	TR 7420 ms; TE 118 ms; Flip angle 120°; FOV 75×75 mm; Voxel size 0,2×0,2×3,0 mm; NSA 2		

FOV = field of view; MPRAGE = Magnetization Prepared Rapid Acquisition with Gradient Echoes; NSA = number of signal averages; SNR = signal-to-noise ratio; TE = echo time; TR = repetition time; TSE = Turbo Spin Echo

height of the left and right ventricles (in mm) and brain (in mm) measured in the midline of the interthalamic adhesion<sup>35,37</sup> maximum cranial breadth (euryon to euryon)<sup>22,30</sup> (in mm), maximum cranial length (inion to nasion)<sup>30</sup> (in mm). The cephalic index (CI) [%] as indicator of «short headedness»<sup>30</sup> was calculated by dividing the maximum cranial breath by the maximum cranial length multiplied by 100.<sup>22</sup> Ventricular size was evaluated by comparison of the mean height of both ventricles to brain height. Ventricular to brain height ratio < 14 % was classified as normal-sized, 15–25 % was classified as moderately enlarged, > 25 % was classified as severely enlarged (Figure 1).<sup>9</sup> The grade of asymmetry of the lateral ventricles was subjectively assessed as absent, mild, moderate, or severe (Figure 2).<sup>21</sup>

Dilation of the fourth ventricle (yes/no) and presence of supracollicular fluid accumulation (yes/no) was subjectively assessed. The angle of head position [in degrees]<sup>22,36</sup> was assessed on T2 weighted images.<sup>23</sup> CM<sup>1</sup> was classified according to the British Veterinary Association (BVA) scheme as Grade 0, Grade 1 and Grade 2. The caudal cerebellar contour was categorized into three different patterns: convex/round shape, focal indentation by the occipital bone,

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no indentation but abnormal shape (Figure 3). The status of the spheno-occipital synchondrosis was assessed as open or closed.<sup>5,31</sup> The degree of SM<sup>1</sup> was examined in the T2 TSE transversal sequence according to the BVA scheme as Grade 0, Grade 1 or Grade 2.

#### Statistical methods

For continuous data, normality was tested with the Shapiro-Wilk test. An unpaired two-sample t-test was used to compare interval or ordinal data such as age, body weight, cephalic index and head angle alpha to BF status and presence of SM. Simple linear regression was used to evaluate the correlation between size, body weight and cephalic index. Nominal data such as sex, and all yes/no criteria defined on MRI were tested with Chi-Square test, or Fisher's Exact test, if less than 5 samples per cell. Spearman's rank correlation and Bland-Altman Plot assessed the agreement between BF opening in ultrasound and MRI. A p-value of < 0,05 was considered statistically significant.

Statistical analyses were performed using NCSS 2023 Statistical Software (NCSS, LLC. Kaysville, Utah, USA, ncss. com/software/ncss; 2023).

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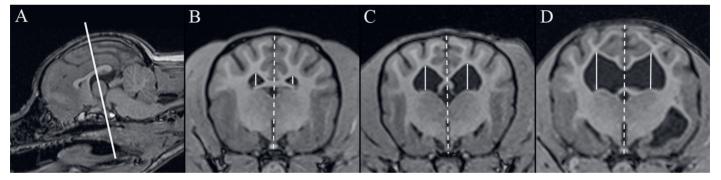


Figure 1: (A) Sagittal reconstruction of a 3D T1 MPRAGE dorsal sequence showing the level of the transverse images at the interthalamic adhesion (B-D). The solid lines in images B-D indicate ventricular height, which was evaluated in relation to brain height as marked by the dashed lines. (B) shows a dog with normal-sized ventricles (ventricular to brain height ratio < 14%), (C) a dog with moderate ventricular enlargement (ratio 15–25%), and (D) a dog with severe ventricular enlargement (ratio > 25%).

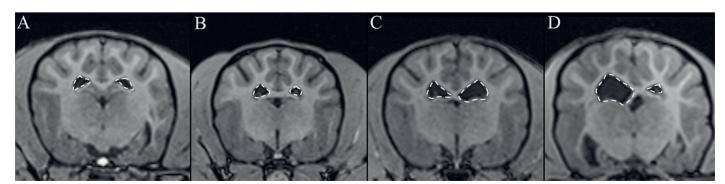


Figure 2: Transverse reconstructions at the level of the interthalamic adhesion of a 3D T1 MPRAGE dorsal sequence of different grades of asymmetry of the lateral ventricles in the brain from different dogs. The right and left ventricles are outlined with dashed lines to highlight the regions assessed for ventricular asymmetry: (A) indicates no asymmetry, (B) shows mild asymmetry, (C) represents moderate asymmetry, and (D) shows a severe asymmetry.

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#### Additionally

OpenAI's ChatGPT was used to assist with language refinement and rephrasing in the preparation of this manuscript.

#### Results

#### Study group

Forty-one client-owned dogs were included in the study, 33 due to neurological abnormalities and eight for breeding purposes. In two dogs, the detailed history was not docu-

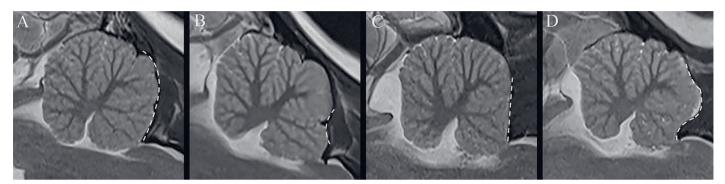


Figure 3: Different variations of the cerebellar shape are outlined with dashed lines in the midsagittal plane of the T2 weighted TSE sequence.

(A) shows a cerebellum with convex/round shape, (B) shows a cerebellum with focal indentation by the occipital bone, (C and D) show cerebella with no caudal indentation but an abnormal shape.

Table 2: Signalment split into case (persistent bregmatic fontanelle) and control (closed bregmatic fontanelle) group. Significant results are indicated with\*; level of significance was set to p < 0,05 (\*).

		Controls (n = 22)	Cases (n = 19)	Difference between both groups (p-value)	
Sex	Male	13	11	0,9382	
	Female	9	8		
Age [years]	Median	4,3	2,8		
	SD	3,5	1,6	0,29	
	Range	1,1–16,9	1,1–7,8		
	Median	3,9	2,7		
Body weight [kg]	SD	1,7	0,6	0,009*	
	Range	1,7–8,6	1,7–4,3		
	Median	80,3	83,7		
Cephalic index [%]	SD	6,5	3,1	0,036*	
[ /0]	Range	68,9 - 96,1	74,8–87,9		
Country resi-	Switzerland	15	13	0.00	
dence	Germany	7	6	0,99	
	Belarus	1	2		
	Germany	10	7		
	Italy	0	1		
	Kirgizstan	1	0		
Country of origin	Netherlands	0	1		
	Poland	1	0	_	
	Romania	1	0		
	Russian Federation	3	4		
	Switzerland	1	2		
	Unknown	4	2		
Pedigree	Yes	12	12	0.50	
	No	10	7	0,58	

n = number of dogs; SD = standard deviation

mented, and three owners did not complete the CM/SM questionnaire. Neurological examination was not performed in one postictal dog and one dog due to aggressive behaviour. Shoulder height was measured in 29 dogs.

#### Signalment of dogs

Of the total study group, 24 (58,5 %) dogs were male (twelve intact, eight neutered and four with hormone-chips) and 17 (41,5%) dogs were female (15 intact, two castrated). The median age was 3,1 years (range: 1,1 - 16,9 years). The median body weight was 3,6 kg (range: 1,7 - 8,6 kg). The median cephalic index was 83,3 % (range: 68,9 - 96,1 %). The study group consisted of 35 Pomeranians (85,4%), 3 Chihuahuas (7,3%), one Japan-Spitz (2,4%), and two mixed breed dogs (4,9%). A pedigree was available for 24 (58,5%) of the dogs examined.

Dogs were mostly bred in Germany (41,5%), other countries of origin are listed in Table 2. In six dogs (14,6%), the origin could not be determined based on microchip information. The majority of dogs resided in Switzerland (68,3%), while the remaining dogs lived in Germany (31,7%).

The BF was judged as persistent on ultrasound in 46,3% of dogs (19 cases), while 53,7 % exhibited a closed BF (22 controls). An overview of the characteristics of the study participants is presented in Table 2.

Dogs with a closed BF had a significantly higher body weight compared to those with a persistent BF (p = 0,01; Figure 4). The mean shoulder height measured in 29 dogs was 23,1 ± 4,0 cm (range: 17,5 - 31 cm), higher shoulder height was associated to higher body weight (r = 0,8; p < 0,01; Figure 6). The mean cephalic index over the whole study group was 81,8 ± 5,4% (range: 68,9 - 96,1%), with a significantly higher cephalic index in dogs with persistent BF (p = 0,036; Figure 5). A higher cephalic index and therefore a shorter skull was associated with lower body weight (r = -0.7; p < 0.01; Figure 6).

### Clinical signs and neurological examinati-

Of the 39 dogs with a documented clinical history, owners reported at least one clinical sign in 33 dogs (84,6%). Four dogs showed clinical signs that were potentially related to a neurological disorder, while nine dogs showed signs considered unlikely to be of neurological origin. In the remaining 20 dogs, a combination of neurological and non-neurological signs was noted (Table 3).

Thirty-eight owners (92,7%) completed the CM/SM questionnaire. 81,6% (31/38) dogs had at least one abnormal finding according to the CM/SM questionnaire. Of the 22 questions posed, a median of 2,5 «yes» responses were recorded (SD ± 2,8). Each dog exhibited between 0 and 10 of the 22 signs listed in the questionnaire. The most common

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abnormal finding according to the questionnaire was scratching on shoulder and neck (16), followed by rubbing of mouth (13) and signs of pain/screaming when touched (10). A neurological examination was performed in 39 (95,1%) dogs, with abnormalities noted in 30 dogs, the most common abnormality was back pain (19), decreased proprioception in one or more limbs (15), decreased menace response (7) and pacing (6). A summary of the clinical and neurological findings is also presented in Table 3.

Cases did not show more clinical signs in the history (p = 0,68), CM/SM questionnaire (p = 0,50), or in the neurological examination (p = 0.70) compared to controls.

#### MRI evaluation

The mean head angle ( $\alpha$ ) was 7,8° ± 11,5° (range: - 24° to 29°). No evidence of difference in head angle between cases and controls was found (p = 0,06) indicating no difference in positioning between dogs. The spheno-occipital synchondrosis was closed in 30 of the 41 patients (73,2%). In three dogs (7,3%), the bone was too thin to evaluate the synchondrosis status. A keyhole-shaped foramen magnum (FM) was observed in all but two dogs (95,1%). Additionally, 34 dogs The breamatic fontanelle alone is an unreliable indicator of health in Pomeranian and other toy-sized dogs

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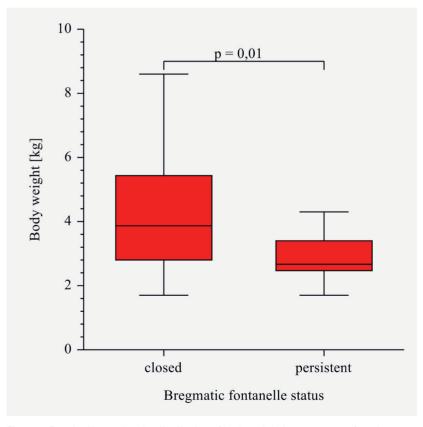
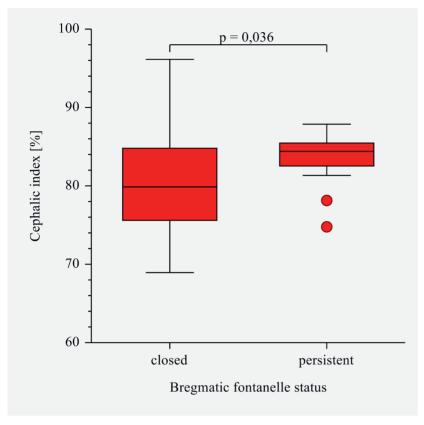


Figure 4: Boxplot illustrating the distribution of body weight between cases (persistent 1,5 times the interquartile range.

bregmatic fontanelle) and controls (closed bregmatic fontanelle). Controls tend to weigh more (p = 0,01) but also show a wider range in body weight. The length of the whiskers is

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**Figure 5**: Boxplot highlighting evidence of higher cephalic index in cases (persistent bregmatic fontanelle) compared to controls (closed bregmatic fontanelle) with a wider range in the control group (p = 0.036). The length of the whiskers is 1,5 times the interquartile range, with observations exceeding this distance considered outliers (dots).

(82,9%) exhibited skull bone defects, most commonly dorsal to the keyhole-shaped FM (n = 21). Other defects were identified at the mastoid fontanelles (n = 16), frontoparietal sutures (n = 8), squamosal suture (n = 3), adjacent to the interfrontal suture (n = 2), and at the sphenoid fontanelle (n = 2). One dog each had defects at the interfrontal suture and the spheno-occipital suture.

Regarding cerebellar morphology, eight dogs (19,5%) exhibited a convex or rounded cerebellum. Sixteen dogs (39,0%) displayed a focal indentation, while 17 (41,5%) had an abnormally shaped cerebellum without caudal indentation. The likelihood of an abnormal cerebellar shape did not differ significantly between dogs with persistent BF and those with closed BF (p = 0.70).

Within the study group, nine dogs (22,0%) were classified as CM grade 0; 28 dogs (68,3%) as CM grade 1, and four dogs (9,7%) as CM grade 2. Dogs with persistent BF did not have more often CM (grade 1 or 2) than dogs with closed BF (p = 0,26). For SM, 24 dogs (58,5%) were graded as SM 0, two dogs (4,9%) as SM 1, and 15 dogs (36,6%) as SM 2. The distribution of affected dogs between the case and control groups is presented in Table 4. The odds of dogs with a persistent BF and SM present (SM grade 1 or 2) were 3,7 times higher than in dogs with a closed BF (p = 0,047).

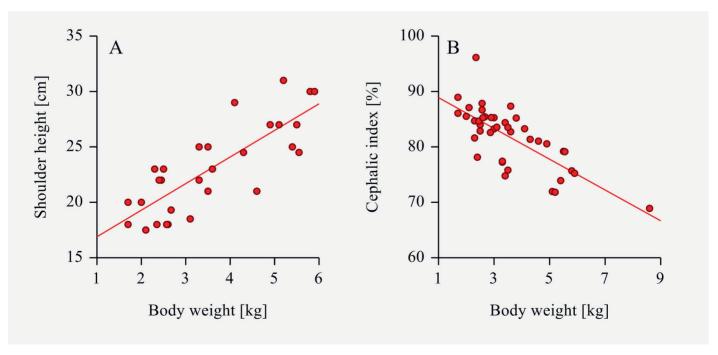


Figure 6: Scatter Plots illustrating the correlation between (A) body weight and shoulder height (r = 0.8; p < 0.01) and (B) body weight and cephalic index (r = -0.7; p < 0.01). The higher the shoulder height, the higher the body weight. The higher the body weight of the dog, the lower the cephalic index and therefore the longer the skull length.

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No significant differences were found in CM/SM questionnaire responses between dogs classified as having CM or SM and unaffected dogs (CM: p = 0.57; SM: p = 0.52).

Dilation of the fourth ventricle was observed in 38 of 41 (92,7%) dogs, without difference in BF status (p = 0,59; Table 4). Supracollicular fluid accumulation was present in 37 dogs (90,2%), with no difference in BF status (p = 1,00; Table 4). Lateral ventricles were normal-sized in 18 dogs (43,9%), moderately enlarged in 21 (51,2%), and severely enlarged in two (4,9%). Both dogs with severely enlarged lateral ventricles had a persistent BF (Table 4). Lateral ventricles were symmetric in 12 dogs (29,3%), mild asymmetry was present in 18 (43,9%), moderate asymmetry in nine (22,0%), and severe asymmetry in two (4,9%). No significant differences were observed between dogs with persistent and closed BF regarding lateral ventricle dilation (p = 0,83) or asymmetry (p = 0,10), see Table 4.

Dilation of lateral ventricles was associated with presence of SM (p = < 0,01). Dogs with enlarged lateral ventricles had 15 times higher odds of developing SM compared to those with normal lateral ventricle size. Additionally, a higher cephalic index (indicative of a shorter skull) and lower body

weight were both significantly associated with the presence of SM (p < 0,01 for both). No other MRI parameters were found to be associated with the presence of CM or SM.

#### BF status in ultrasound, palpation and MRI

A summary of the results when accessing the BF on palpation, ultrasound, and MRI is shown in Table 5. When classified as either persistent or closed, palpation and ultrasound findings were consistent in 80,5% of cases (33/41), with discrepancies observed in 19,5% (8/41). Fisher's Exact test yielded a p-value of < 0,01, indicating a statistical association between palpation and ultrasound findings. BF gaps of 4 mm and smaller in ultrasound were mostly classified as closed in palpation. Gaps of 5 mm and greater were always classified as persistent in palpation.

For the comparison between ultrasound and MRI, Spearman's rank correlation was 0,84, what represents a strong correlation. On average, the BF appeared  $3.3 \pm 1.7$  mm wider on MRI compared to ultrasound, with limits of agreement between -3.96 to 10.56 and differences in measurement between MRI and ultrasound ranged from 0 to 13.4 mm (Figure 7). The variability between the measurements was distributed randomly and did not increase with wider BF.

The bregmatic fontanelle alone is an unreliable indicator of health in Pomeranian and other toy-sized dogs

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Table 3: Overview of different clinical signs reported by the owners in history, CM/SM questionnaire and signs in neurological examination. The signs represent the range in the whole study group and was not differentiated for cases (persistent bregmatic fontanelle) and controls (closed bregmatic fontanelle) since signs do not occur more or less often in one of the groups. Signs are listed according to their frequencies.

Examination	Signs			
Clinical signs in history (n)	Rather non-neurological origin: alopecia (7), patellar luxation (7), food allergies (4), lameness (4), breathing problems (2), hypothyroidism (2), mitral valve disease (2), snoring (2), vomiting/nausea (2), abdominal hernia (1), air licking (1), asthma (1), licking of vagina until inflamed (1), mydriasis and cloudy eyes (1), mouth rubbing (1), scooting (1), teary eye (1), tracheal collapse (1)	Might be/is of neurological origin:  Paw licking/biting (12), Epilepsy (6), head rubbing/shaking (6), pain (6), scratching (5), sensitiveness to touch (5), aggressive behaviour (4), panic attacks (4), phantom scratching (4), ataxia (3), blepharospasm (3), licking on things in environment (3), compulsive tail chasing/circling (2), fly biting (2), discomfort with harness (2), suspected headache (2), discomfort and paddling before falling asleep (1), extremely fearful (1), reverse sneezing (1), rubbing body against things in environment (1), tensed cervical and lumbar area (1), trembling at excitement (1), unilateral twitching (1), very calm behaviour (1)		
Clinical signs in CM/SM questionnaire (n)	Scratching on shoulder and neck (16), rubbing of mouth (13), signs of pain/screaming when touching (10), scratching other body parts (8), epilepsy (8), back pain (8), neck pain (7), fly biting (6), rubbing of the ears (6), lameness of pelvic limbs (5), lameness thoracic limbs (4), pain/screaming when scratching (4), paresis pelvic limbs (4), paresis thoracic limbs (3), ataxia (3), collapse during exercise (3), screaming (3), cramps during exercise (2), pain when moving head (2), pain/screaming when excited (1), scoliosis (0), screaming when jumping (0)			
Neurological examination (n)	Mental status and behaviour: scratching (1)  Posture: varus (2), kyphosis (1), mildly reduced weight-bearing in one pelvic limb with severe muscle atrophy (1), steep pelvic limbs (1), valgus (1)  Gait: pacing gait (6), hypermetria (4), lameness (2), ataxia (1), circling (1), drifting to a side (1), intermittent hopping in pelvic limbs (1)  Cranial nerves: decreased menace response (7), strabismus (2), anisocoria (1), chronic eye problem (1), decreased direct and indirect pupillary light reflexes (1), decreased palpebral reflex (1), reduced ear sensibility (1)  Postural reactions: decreased proprioception in one or more limbs (15)  Spinal reflexes: panniculus absent (2), decreased flexor reflex in thoracic limbs (1), decreased tibialis cranialis reflex (1), decreased patellar reflex on the left hindlimb (1)  Sensibility: back pain (19), tension in the paraspinal muscles (1)			

n = number of dogs

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#### Discussion

This study investigated whether the status of the bregmatic fontanelle (BF) - open or closed - can serve as a reliable indicator of health in toy-sized dogs. We examined associations between BF status, clinical signs, and MRI findings, with a view toward evaluating its relevance for breeding selection.

Nearly half of the dogs presented for this study had a persistent BF. Many owners reported abnormal behaviours, clinical signs or other health concerns. However, we found no association between these reported issues and BF status. This finding contrasts with an earlier study, which reported that persistent fontanelles were more numerous and larger in Chihuahuas with clinical signs related to CM and SM.<sup>11</sup>

This discrepancy may be explained, by the difference in methodology, we evaluated only the presence or absence of an open BF, mirroring the approach used in breed selection-rather than assessing size and number of other open cranial sutures.

Regardless of BF status, MRI abnormalities such as CM, SM and ventriculomegaly were frequently observed. These changes are clinically relevant, as they are associated with phantom scratching, pain, and neurological deficits that impact quality of life.<sup>13,26</sup> Because such conditions cannot be diagnosed through clinical examination alone, MRI appears essential for assessing breeding suitability.<sup>10,17,19,20,26–28</sup> Only three dogs in our cohort were microchipped in Switzerland; the remainder were likely imported, possibly due to higher domestic demand for toy-sized dogs and the ease

Table 4: Magnetic resonance imaging parameters evaluated for cases and controls indicating the differences between both groups. Significant results are indicated with\*; level of significance was set to p < 0,05 (\*).

		Controls (n = 22)	Cases (n = 19)	Difference between both groups (p-value)	
Spheno-occipital synchondrosis status	Closed	15	15		
	Open	5	3	0,70	
	Not evaluable	2	1		
Keyhole shaped	Yes	22	17	0.04	
FM	No	0	2	0,21	
Further bone de-	Yes	19	15	0.00	
fects on skull	No	3	4	0,68	
	Convex/round	5	3		
Cerebellum shape¹	Focal indentation	7	9	0,70	
Shape	Abnormal shape	10	7		
	Grade 0	3	6		
CM <sup>1</sup>	Grade 1	16	12	0,26	
	Grade 2	3	1		
	Grade 0	16	8		
SM <sup>1</sup>	Grade 1	1	1	0,047*	
	Grade 2	5	10		
Fourth ventricle	Yes	21	17	0,59	
dilation	No	1	2	0,59	
Supracollicular	Yes	20	17		
fluid accumula- tion	No	2	2	1,00	
	Normal-sized	10	8		
Dilation of lateral ventricles <sup>1</sup>	Moderately enlarged	12	9	0,83	
	Severely enlarged	0	2		
Asymmetry of lateral ventricles <sup>1</sup>	Absent	9	3		
	Mild	6	12	0,1	
	Moderate	5	4	U, I	
	Severe	2	0		

 $n = number\ of\ dogs;\ 1 = for\ statistical\ analyses\ two\ categories\ normal/absent\ vs.\ present/abnormal\ (corresponding\ p-value)$ 

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of acquiring them from abroad. Future studies should include more Swiss-bred dogs to assess the prevalence of CM, SM, and related neurological signs in this population. This could help determine whether broader, cross-border regulations are needed.

According to Identitas - a national animal registry - toysized dog breeds are increasingly popular in Switzerland,8 making it crucial to understand how body size and weight influence congenital malformations. Our data showed that dogs with lower body weight and a higher cephalic index were more likely to have a persistent BF. No dog over 4,3 kg had a persistent BF; These findings suggest that smaller body size is a significant risk factor for persistent BF. Given the current Swiss breeding regulations allow breeding of dogs over 1.5 kg,<sup>2</sup> our results support reconsidering this threshold to reduce the risk of persistent BF in breeding lines. However, CM and/or SM were still diagnosed in several dogs above a body weight of 4.3 kg, and other than MRI, there are currently no other tools or morphological criteria to identify CM, SM or ventriculomegaly. 17,19,20,27

In line with our second study aim, ventriculomegaly was commonly observed. It is a common findings in toy-sized dogs and its clinical significance is still unclear with debates if it reflects a normal variant or a pathological condition.<sup>29</sup> We found that dogs with enlarged lateral ventricles on MRI had a 15-fold increased risk of developing SM Grade 1 or 2 (p < 0.01) which suggests that enlarged ventricles are indicators of a pathological condition, probably in the context of a «brachycephalic obstructive CSF channel syndrome» (BOCCS).<sup>13</sup> This syndrome takes the complex abnormalities of the cranio-cervical junction including the occipital area into account and seems therefore more suitable rather than talking about CM.

We also identified variability in the diagnostic accuracy of different methods used to assess BF status. Computed tomography (CT) is the gold standard for evaluating cranial suture gaps, but was not used in this study. Instead, we relied on ultrasonography, as it is the method used by the Swiss Pomeranian breeding club.<sup>33</sup> Although ultrasound has been proposed as a feasible tool for BF assessment, 6,15 its accuracy remains unvalidated. In this study, defects of 4 mm or smaller detected in ultrasound were classified as closed by palpation, while two BF closed on ultrasound were misclassified as persistent by palpation. These discrepancies may have resulted from challenges in detecting defects in very small skulls or from evaluator inexperience. MRI-based assessment of cranial sutures has also proven unreliable, with studies showing that MRI tends to overestimate suture width compared to histological measurements.<sup>5</sup> This aligns with our findings: MRI measurements yielded larger openings than ultrasound, potentially increasing false positives

and misclassifying closed BFs as persistent.

#### Limitations

One limitation of our study is the use of a clinical questionnaire originally designed for Cavalier King Charles Spaniels. This tool may not have captured all relevant signs in other breeds, particularly Pomeranians, which were overrepresented in our sample due to collaboration with the Swiss kennel club. Additionally, the lack of association between BF status and clinical or neurological signs may be partly due to the nonspecific nature of the questionnaire items, which could reflect unrelated conditions such as dermatologic issues or food allergies.

Owner perception and reporting biases also likely influenced results. Behavioural abnormalities like reduced play-

Table 5: The status of the bregmatic fontanelle in palpation, ultrasound and magnetic resonance imaging examination compared between cases (persistent bregmatic fontanelle) and controls (closed bregmatic fontanelle).

		Controls (n = 22)	Cases (n = 19)
Palpation	Closed	20	6
raipation	Persistent	2	13
	Mean	_	6,2
Largest width measured by ultrasound in [mm]	SD	-	3,4
	Range	_	2 - 14
	Number of dogs	5	19
Laurant wildelt and a second by MDI in Ferral	Mean	7,9	11,2
Largest width measured by MRI in [mm]	SD	4,4	4,4
	Range	4 - 13,4	5 - 21,6

MRI = magnetic resonance imaging; SD = standard deviation

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fulness or sleeping with the head elevated may have been long-standing and therefore perceived as normal. These biases are evident in discrepancies between clinical history and responses to the CM/SM questionnaire. Some owners mentioned clinical signs spontaneously during history-taking, while others only reported them when prompted by the questionnaire.

Another limitation concerns MRI positioning. While the BVA protocol recommends imaging with the head and neck extended, we positioned dogs with a flexed head angle to mimic the natural standing posture, in line with studies suggesting that extension can underestimate CM severity.<sup>36</sup> However, we did not consistently achieve the ideal head angle of 50°, which could have led to underestimation of CM grade.<sup>36</sup> Using the BVA classification for all toy-sized dogs presented challenges for us, as noted in other studies.<sup>13,17,27</sup>

#### Conclusion

This study revealed a high prevalence of morphometric abnormalities in the brain and spinal cord of toy-sized dogs,

regardless of whether the BF was open or closed. A closed BF alone is therefore not a sufficient indicator of neurological health and should not be used as a sole breeding selection criterion. As expected, no consistent association was found between BF status and clinical or neurological signs, or other MRI findings, apart from a modest link with SM. Importantly, enlarged lateral ventricles were identified as a significant risk factor for SM. Our findings underscore the need for further investigation into the pathogenesis of SM and its risk factors.

To preserve the health and welfare of toy-sized dog breeds, MRI evaluation of the brain and spinal cord should be considered essential prior to breeding. Currently, MRI is the only reliable method for detecting ventriculomegaly, CM, or SM in these dogs. <sup>17,20,27</sup>

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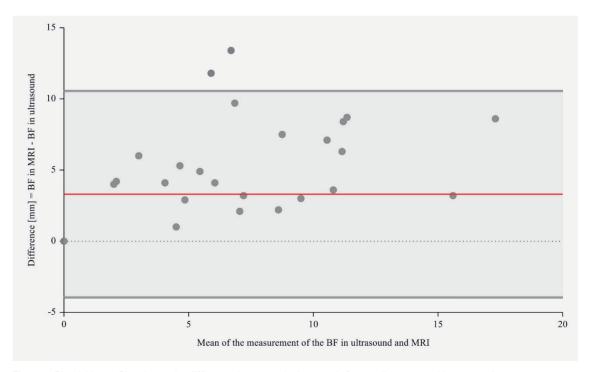


Figure 7: Bland Altman Plot shows the difference between the bregmatic fontanelle measured by magnetic resonance imaging (MRI) and ultrasound. On average, the bregmatic fontanelle was  $3.3 \pm 1.7$  mm larger when measured by MRI than when measured by ultrasound. The x-axis represents the mean of the measurement of the bregmatic fontanelle in ultrasound and MRI. The y-axis shows the difference between the measurement in MRI and ultrasound. Each dot in the plot represents one case. The red line indicates the average of 3.3 mm, the grey lines represent the limits of agreement set at -3.96 and 10.56. Differences in measurements between MRI and ultrasound ranged from 0 to 13.4 mm. In seventeen dogs, ultrasound and MRI showed both closed fontanelles.

#### La fontanelle bregmatique seule n'est pas un indicateur de santé fiable chez les spitz nains et autres chiens de petite taille

L'Ordonnance fédérale suisse sur la protection des animaux interdit l'élevage de chiens présentant des fontanelles persistantes. Chez les chiens de petite taille en particulier, la fermeture des fontanelles est importante pour la sélection génétique. Chez ces chiens, d'autres altérations au niveau de la jonction cranio-cervicale, une hydrocéphalie et une syringomyélie sont fréquemment observées à l'imagerie par résonance magnétique (IRM). On ne sait pas si ces changements sont associés à des fontanelles persistantes. L'objectif de l'étude était d'examiner si les fontanelles persistantes sont associées à d'autres anomalies de la tête et de la moelle épinière.

Pour cette étude transversale, 41 chiens de petite taille ont été examinés cliniquement et neurologiquement et ont subi une IRM 3T. Les chiens ont ensuite été répartis en deux groupes, cas et témoins, en fonction de l'état de la fontanelle brégmatique à l'échographie. Les résultats des deux groupes ont été comparés à l'aide d'un test t non apparié, d'une régression linéaire et d'une corrélation, ainsi que du test du chi carré et du test exact de Fisher.

Les résultats ont montré que 53,7 % des chiens avaient des fontanelles fermées, tandis que 46,3% avaient des fontanelles bregmatiques persistantes. Les fontanelles persistantes étaient plus fréquentes chez les chiens de faible poids et au crâne court, mais ne présentaient aucun lien avec l'âge. Aucune influence de l'état des fontanelles sur les manifestations cliniques et neurologiques n'a été mise en évidence. L'IRM a révélé une malformation de Chiari chez 78,1 % des chiens, une dilatation des ventricules latéraux chez 56,1 % et une syringomyélie chez 41,5 %. Les chiens présentant des fontanelles persistantes étaient 3,7 fois plus susceptibles d'être atteints de syringomyélie (test exact de Fisher ; valeur p = 0,047). La dilatation des ventricules latéraux multipliait par 15 le risque de syringomyélie (test exact de Fisher ; valeur p < 0,01). Aucune association n'a été trouvée entre la persistance des fontanelles et la malformation de Chiari, d'autres anomalies cranio-cervicales ou la ventriculomégalie.

Les chiens de petite taille de cette étude présentaient fréquemment des anomalies cérébrales et médullaires à l'IRM, quel que soit l'état de leur fontanelle. Ces résultats suggèrent que la présence ou l'absence de fontanelles brégmatiques ne constitue pas un critère fiable pour la sélection génétique visant à maintenir une population canine en bonne santé.

Mots clés: Sélection génétique, malformation de Chiari, imagerie par résonance magnétique, spitz nain, syringomyélie, ventriculomégalie

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#### La sola fontanella bregmatica non è un indicatore affidabile di salute nei cani di razza Pomerania e in altre razze toy

L'Ordinanza svizzera sul benessere degli animali vieta l'allevamento di cani con fontanelle persistenti. Soprattutto nei cani di piccola taglia (toy), la chiusura delle fontanelle è un aspetto importante nella selezione riproduttiva. In questi cani, alterazioni della giunzione cranio-cervicale, idrocefalo e siringomielia sono frequentemente osservati mediante risonanza magnetica (RM). Non è chiaro se tali alterazioni siano associate alla persistenza delle fontanelle. Lo scopo di questo studio era verificare se la presenza di fontanelle persistenti sia correlata ad altre anomalie della testa e del midollo spinale.

In questo studio trasversale, 41 cani di taglia toy sono stati sottoposti a esame clinico e neurologico e a RM a 3 Tesla. I cani sono stati quindi suddivisi in due gruppi, casi e controlli, in base allo stato della fontanella bregmatica valutata con ecografia. I risultati nei due gruppi sono stati confrontati utilizzando il test t di Student per campioni indipendenti, la regressione lineare e la correlazione, nonché i test Chi-quadro e di Fisher.

Dai risultati è emerso che il 53,7 % dei cani presentava fontanelle chiuse, mentre il 46,3 % presentava fontanelle bregmatiche persistenti. Le fontanelle persistenti sono state osservate più frequentemente nei cani con peso corporeo inferiore e cranio più corto, ma non sono risultate associate all'età. Non è emersa alcuna evidenza di un'influenza dello stato delle fontanelle sulla presentazione clinica e neurologica. La RM ha rilevato malformazione di tipo Chiari nel 78,1 % dei cani, dilatazione dei ventricoli laterali nel 56,1 % e siringomielia nel 41,5 %. I cani con fontanelle persistenti avevano una probabilità 3,7 volte maggiore di presentare siringomielia (test esatto di Fisher; p = 0,047). La dilatazione dei ventricoli laterali aumentava di 15 volte le probabilità di siringomielia (test esatto di Fisher; p < 0,01). Non è stata riscontrata alcuna associazione tra fontanelle persistenti e malformazione di Chiari, altre anomalie cranio-cervicali o ventricolomegalia.

I cani di taglia toy inclusi in questo studio presentavano frequentemente anomalie cerebrali e del midollo spinale alla RM, indipendentemente dallo stato delle fontanelle. Questi risultati suggeriscono che la presenza o l'assenza di fontanelle bregmatiche possa non essere un criterio affidabile per la selezione riproduttiva volta a mantenere una popolazione canina sana.

Parole chiave: selezione della razza, malformazione di Chiari, risonanza magnetica, Pomerania, siringomielia, ventricolomegalia The bregmatic fontanelle alone is an unreliable indicator of health in Pomeranian and other toy-sized dogs

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The bregmatic fontanelle alone is an unreliable indicator of health in Pomeranian and other toy-sized dogs

C. Mollet et al.

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