https://doi.org/10.17221/39/2019-VETMED

Transscleral ultrasonographic measurements of the optic nerve sheath diameter and a regression analysis with morphometric measures of the globe in dogs

Marta Vinas[1]*, Ulrich Zeyen[2], Nunzio D'Anna[1], Massimo Vignoli[3]

[1]CVRS – Policlinico Veterinario Roma Sud – Servizio di Oftalmologia, Roma, Italy
[2]Centro Veterinario Specialistico, CVS, Servizio di Ecografia, Roma, Italy
[3]Faculty of Veterinary Medicine, University of Teramo, Teramo, Italy

*Corresponding author: martavinasportillo@gmail.com

Citation: Vinas M, Zeyen U, D'Anna N, Vignoli M (2019): Transscleral ultrasonographic measurements of the optic nerve sheath diameter and a regression analysis with morphometric measures of the globe in dogs. Veterinarni Medicina 64, xx–xx.

Abstract: To describe transscleral ultrasonography as a novel alternative approach for visualising the optic nerve sheath and measuring its diameter and to analyse the linear regressions of the optic nerve sheath diameter value with the weights and morphometric measurements of the globe in dogs. Forty healthy dogs admitted for routine sterilisation were examined. Under general anaesthesia, a B-mode ultrasonography with a linear probe (9–18 MHz) was applied transscleral in the dorso-temporal quadrant. The optic nerve sheath diameter was measured 3 mm behind the caudal aspect of the globe. The morphometric measurements, including the axial globe, lens thickness and vitreous chamber, were estimated by two observers using the direct corneal approach. Univariate and multivariate multiple linear regression analyses were performed to explore the associations of the independent predictors with dependent variables. The optic nerve sheath diameter intraclass correlation coefficient (ICC) analyses revealed interobserver 0.91 (ICC = 0.83–0.95) and intraobserver 0.93 (ICC = 0.87–0.96) reliability. The multiple regression analysis revealed that the optic nerve sheath diameter was associated with the weight (R^2 = 0.60, P < 0.0001) but not with the axial globe (P = 0.48), the lens thickness (P = 0.73) or the vitreous chamber (P = 0.99). The findings of this study suggest that transscleral ultrasonography may be a valid alternative approach for the optic nerve visualisation and optic nerve sheath diameter measurements with excellent intra- and interobserver repeatability. The optic nerve sheath diameter was associated with the body weight, but not with the morphometric measurements of the globe.

Keywords: morphometry; canine; intracranial pressure; ocular ultrasound; body weight

High intracranial pressure (ICP) is a potentially life-threatening condition because of the associated progressive reduction in the cerebral arterial perfusion or brain injury secondary to herniation (Cooley et al. 2016). An increase above a certain threshold can result in the displacement of the cerebrospinal fluid (CSF) from the intracranial cavity into the perineural subarachnoid space due to direct continuity between these spaces. Increases in the CSF volume within the optic nerve sheath (ONS) results in the widening of its diameter (Padayachy et al. 2016). It has been recently postulated that with an ICP, the ONS size increases secondary to the structural changes in the trabecular fibres connecting the optic nerve to the optic nerve sheath diameter (ONSD), which can last for 30 days (East et al. 2019). Furthermore, the diagnosis of an elevated ICP is challenging and critical. The detection and subsequent prompt treatment are critical for the prevention of a secondary neu-

https://doi.org/10.17221/39/2019-VETMED

ronal ischemia, hypoxia, a functional brain disorder and even brain death (Ilie et al. 2015).

In humans, measuring the ONSD using a transorbital ultrasound has been described as a non-invasive alternative for assessing ICP in children and adults (Padayachy et al. 2016). In veterinary medicine, the ultrasonographic (US) measurement of the ONSD has been validated in two breeds of dogs (Lee et al. 2003) and in horses (Cooley et al. 2016). A recent publication proved a relationship between the ONSD-US and the body weight in healthy dogs by a transpalpebral approach, showing excellent inter- and intraobserver reliability (Smith et al. 2018). Notable variability in the ONSD can be present in canine populations and may be related to the heterogeneity of the canine populations. We hypothesise that the ONSD-US would linearly increase with the morphometric measurements of the globe.

The aims of this study were: a) a feasibility assessment of transscleral US measurements of the ONSD; b) analysis assessments of the relationships of the ONSD-US to the body weight, age, head conformation and morphometric measurements of the globe.

MATERIAL AND METHODS

This study was approved by the Ethics Committee of University of Padova (Project No. 63/2017). All the owners provided their informed consent.

This study was conducted on 40 dogs, including 24 males (22 intact and 2 neutered) and 16 females (11 spayed and 5 intact). Mixed breeds were over-represented at 16/40. The breeds included the following: mixed breed (16), Chihuahua (4), German Shorthaired Pointer (3) Beagle (2), Golden Retriever (2), Rough Collie (2), Springer Spaniel (2), and (1) of: Cavalier King Charles Spaniel, Cane Corso, Dachshund, English Cocker Spaniel, German Shepherd Dog, Spinone Italiano, Jack Russell Terrier, Newfoundland and Volpino Italiano.

No dogs were excluded from the analyses. The median age and weight were 66 months (10–180) and 16 kg (2–60 kg), respectively.

The study design was observational, prospective and cross-sectional. The sample population included clinically healthy dogs that were admitted as one-day patients for routine sterilisation or dental polishing. The study was performed at the Centro Veterinario Specialistico. The exclusion criteria for the study were as follows: any dogs diagnosed with any concurrent or previous systemic or ocular diseases, recent trauma, pregnancy or under any pharmacological treatment. The patients were included in the study only when their complete physical examinations and blood work results were within the normal limits. The recorded data included the age, breed, body weight, head conformation and ocular US measurements.

The complete ophthalmic examinations were performed by a resident of the European college of veterinary ophthalmology (ECVO) supervised by a board-certified veterinary ophthalmologist. The examinations included assessments of the palpebral reflex, menace response, pupillary light and dazzle reflexes, the Schirmer tear test I (Schering-Plough®, Animal Health, Union, NJ, USA), slit-lamp biomicroscopy (Keeler®, PSL Classic, Windsor, Berkshire, UK), fluorescein staining (Haag-Streit®, International, Koeniz, Switzerland), applanation tonometry (Tonovet®, Icare Mentor, Norwell, MA, USA), and indirect ophthalmoscopy (Omega® 2000, Heine, Herrsching, Germany). All the ocular signs were recorded.

B-mode ultrasonography. The ocular US was performed in the pre-treatment room immediately prior to moving the patient to the operating room theatre. The topical anaesthetic oxybuprocaine chloride (0.4%; Novesina®, Novartis, Origgio, VA, Italy) was placed on the corneal surface of both eyes, and a repeated dose was instilled 5 min later. A single dose of sterile ocular US gel (Ultrasound transmission gel, Parker Lab, Inc., Fairfield, N.J, USA) was placed on the corneal surface, then the scan was performed (Logiq E9, General Electric Company®, CA, USA). A 9–18 MHz linear probe was used for all the studies. The imaging depth on the US screen was between 3 and 4 cm. Two different projections for each eye were used for the study. The direct corneal contact was achieved by applying the probe in the horizontal projection at the centre of the cornea and used to record the images of the morphometric measurements of the globe. To improve the ONSD visualization, a transscleral projection was used. The transducer was applied at the dorso-temporal sclera in an oblique position, and it was then rotated ventrally to the caudal aspect of the eye with smooth and small ventral and dorsal oscillations until the ONSD was identified (Figure 1). The videos and images were recorded

https://doi.org/10.17221/39/2019-VETMED

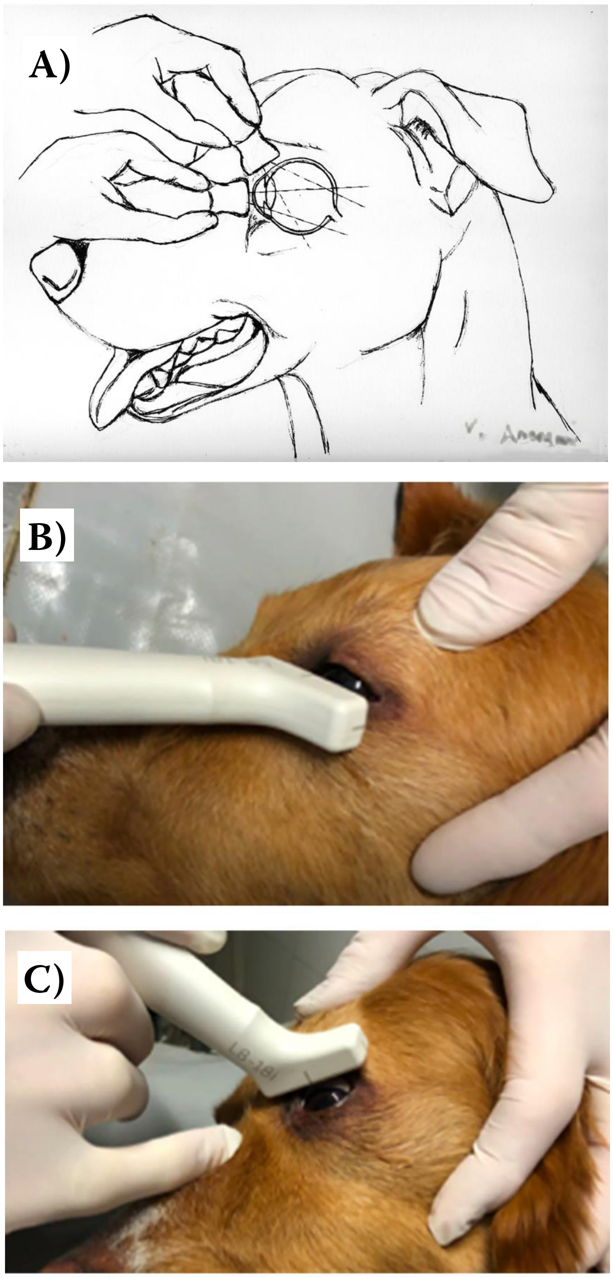

Figure 1. The two ultrasonography projections used for the study (**A**). Direct corneal contact approach (**B**). Transscleral approach (**C**)

for each patient, and the callipers on the US machine were used for the measurements. The axial globe measurement was determined by placing the callipers at the central cornea and tracing a straight line to the centre of the retina. The line from the centre of the anterior and posterior capsules was used for the lens thickness measurement. The vitreous chamber measurement was taken from the line traced from the centre of the posterior lens capsule to the centre of the retina (Figure 2).

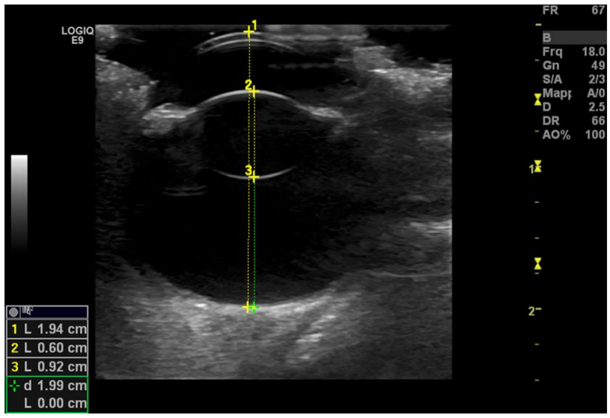

Figure 2. The direct corneal approach was used for the following measurements: 1 – axial globe, 2 – lens thickness and 3 – vitreous chamber

For consistency of the ONSD measurement, the callipers were placed at the maximum-width diameter, i.e., 3 mm behind the caudal aspect of the globe (Figure 3). The post hoc measurements were made with the imaging software provide with the US machine. To determine the test-retest reliability, i.e., the intraobserver variability, the ONSD measurement was performed twice by the same observer. To study the possible variability between the operators, an ECVO resident collected all the measurements while oblivious to the previously collected data. A total of eight measurements per patient were collected by each operator.

Statistical analysis. The continuous variables were analysed for normal distributions using bar graphs, histograms and the Shapiro-Wilk test. The normally distributed variables were reported as the mean and the standard deviation (SD), and the non-normally distributed variables were expressed as the median (range). The differences between the normally distributed data were analysed using an independent-samples *t*-test. The inter-rater reliability was assessed using the single-measure intraclass correlation coefficient (ICC) using a two-way mixed model (single measurements) with absolute agreement for the measurements. The intra-rater reliability was measured with a two-way mixed-effects single-measure ICC for the test-retest (repeated measurements), and the percentage of the coefficient of variation (CV) was calculated with the logarithmic method. An ICC value > 0.75 commonly indicates sufficient reliability. The minimum sample size needed for the ICC calculation was 14 patients (power 90%, alpha error 5%). A simple linear single regression model

https://doi.org/10.17221/39/2019-VETMED

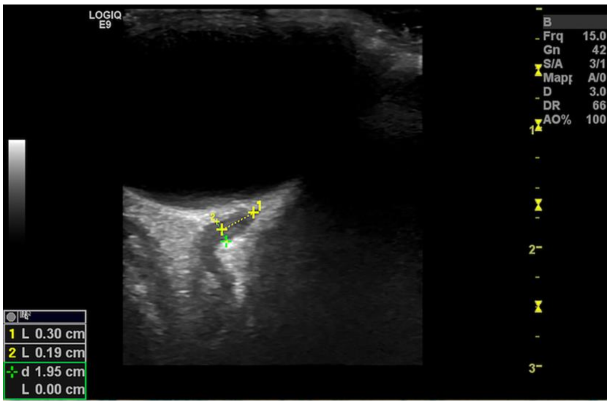

Figure 3. The transscleral approach was used to measure the optic nerve sheath diameter, which was 3 mm from the caudal aspect of the globe

Figure 4. The optic nerve (ON) is identified as a hypoechoic tubular structure surrounded by hyperechoic retrobulbar fat (F). The extraocular muscles (EOM) are identified as tubular hypoechoic structures, although they do not present a sigmoid shape and do not originate from the papilla. In the figure, the anterior is on the top, and the caudal is on the bottom

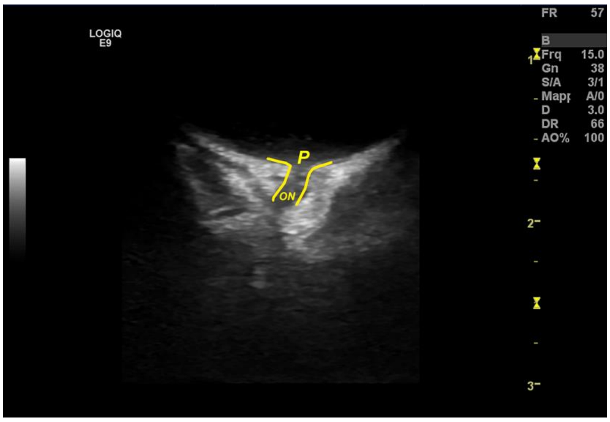

Figure 5. The transscleral approach for the visualisation of the papilla. In most cases, the papilla (P) and the sigmoid shape of the optic nerve (ON) cannot be visualised in the same plane

was used to determine the relationships of the body weight, age, head conformation and morphometric measurements of the globe with the ONSD. A multiple linear regression model was used to determine the best multivariate model for explaining the variability observed in the ONSD measurements. The required sample size for the multiple regression analysis using a model with 6 predictors with an assumed R^2 of 0.8, a power of 90%, and an alpha error of 5% was a minimum of 33 patients. The statistical significance was set to 5%, and a commercial software (MedCalc Statistical Software v.18.2.1, Ostend, Belgium) was used for the statistical analyses.

RESULTS

The head conformations were distributed as follows: 17 mesocephalic, 16 dolichocephalic, and 7 brachycephalic. The mesocephalic and dolichocephalic groups were overrepresented among the crossbreed dogs with seven and eight dogs, respectively. In the brachycephalic group, Chihuahuas (4/7) were overrepresented. The median time required to obtain the ON image was 60 sec (30–90). The optic nerve was identified as a well-demarcated hypoechoic tubular structure surrounded by hyperechoic retrobulbar fat (Figure 4). A physiological curvature of the ON was observed in dogs, therefore, the papilla and ON could be visualised on the same plane in most cases (Figure 5). No differences were found between the left and right ocular dimensions in the same dog ($P > 0.05$), see Table 1.

The single-observer (absolute agreement) ICCs, i.e., the intra-rater reliability, for the two observers, are reported in Table 2.

The univariate linear regression analyses of the body weight, age, head conformation and the mor-

Table 1. The ocular dimensions on the same dog. No differences were found between the left and right ocular dimensions in the same dog ($P > 0.05$)

	Right eye (mm)	Left eye (mm)
Optic nerve sheath diameter	2.1 (0.39)	2.06 (0.33)
Axial globe	20.7 (1.28)	20.6 (1.3)
Lens thickness	6.77 (0.35)	6.82 (0.29)
Vitreous chamber	9.51 (0.72)	9.40 (0.78)

https://doi.org/10.17221/39/2019-VETMED

Table 2. The intraclass correlation coefficient (ICC) reliability

	Inter-rater (95% CI)	Intra-rater (95% CI)	
		Observer 1	Observer 2
Optic nerve sheath diameter	0.91 (0.83–0.95)	0.93 (0.87–0.96)	0.95 (0.90–0.97)
Axial globe	0.98 (0.95–0.99)	0.95 (0.91–0.98)	0.95 (0.90–0.97)
Lens thickness	0.71 (0.52–0.84)	0.68 (0.47–0.82)	0.66 (0.45–0.80)
Vitreous chamber	0.89 (0.78–0.94)	0.88 (0.78–0.93)	0.88 (0.79–0.94)

phometric measurements of the globe (axial globe, lens thickness and vitreous chamber) as independent predictors of variations in the right ONSD were R^2 = 0.58 (P < 0.0001), R^2 = 0.008 (P < 0.585), R^2 = 0.11 (P < 0.036), R^2 = 0.44 (P < 0.0001), R^2 = 0.11 (P < 0.036), and R^2 = 0.32 (P < 0.0001) (Figure 6).

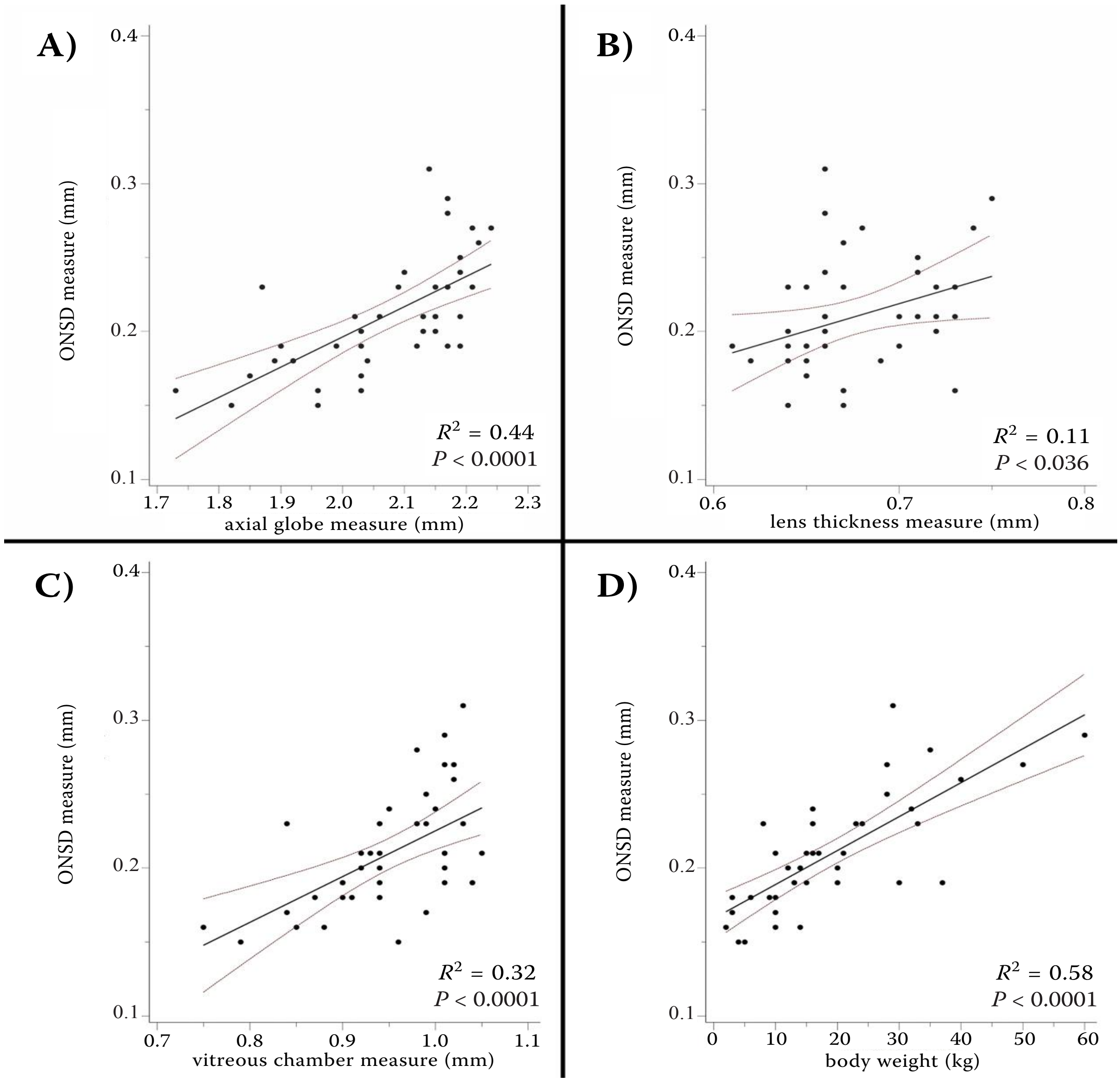

Figure 6. The linear regression analyses of the optic nerve sheath diameter versus the axial globe (**A**), lens thickness (**B**), vitreous chamber (**C**) and body weight (**D**) measurements. The solid line represents the regression line, and the dashed lines represent the 95% confidence interval

https://doi.org/10.17221/39/2019-VETMED

The corresponding values for the left ONSD were $R^2 = 0.62$ ($P < 0.0001$), $R^2 < 0.00001$ ($P < 0.985$), $R^2 = 0.12$ ($P < 0.026$), $R^2 = 0.51$ ($P < 0.0001$), $R^2 = 0.08$ ($P < 0.077$) and $R^2 = 0.51$ ($P < 0.0001$). The multiple regression analysis revealed that the right and left ONSD was associated with the body weight, but not with the age, head conformation or morphometric measurements of the globe.

DISCUSSION

The main goal of this study was to determine whether a plausible ONSD visualisation and measurement, which represents an optional indirect method for the diagnosis of intracranial hypertension in dogs, could be achieved by the transscleral US approach.

The canine optic nerve is a white-matter tract that originates from the diencephalon and is composed of retinal ganglion cell axons circumferentially surrounded by CSF within a peripheral sheath (Boroffka et al. 2008). The CSF of the optic nerve sheath is continuous with the CSF in the subarachnoid space around the brain (Ilie et al. 2015). A rise in the ICP is, therefore, transmitted to the optic nerve head and eventually results in swelling of the optic disc and papilledema. Although the development of the papilledema can require hours to many days, early human studies have shown that increases in the ICP result in the distension of the retrobulbar optic nerve sheath within seconds (Rajajee et al. 2011) and changes in the diameter of the nerve sheath can be visualised using transocular US (Raboel et al. 2012).

In veterinary medicine, the ONSD has been established in two breeds of dogs, and no significant differences in the ONSD values obtained from US and direct measurements have been found (Lee et al. 2003).

The corneal contact technique has been postulated to allow for the best visualization of the vitroretinal and retrobulbar structures (Gonzalez et al. 2001). In our study, we performed the ONSD-US visualisation via an alternative transscleral approach, as this approach avoids certain structures, such as the eyelids, cornea, anterior chamber and lens. In breeds such as a Shar Pei or St. Bernard where the eyelid is notably thick, or in cases of swelling eyelids, this approach allows a clear view of the ON sheath. Furthermore, in patients with keratitis (ulcerative or not) or uveitis, our technique can be beneficial because, in contrast to the corneal approach, it does not cause discomfort since it does not touch the cornea or exert pressure on the anterior chamber. In addition, in patients with a cataract, our approach evades this opacity providing an excellent view of the ON and its sheath.

In the present study, we agree that performing measurements at 3 mm behind the caudal aspect of the globe as previously described in human studies (Geeraerts et al. 2008; Bauerle et al. 2013; Padayachy et al. 2016; Raffiz and Abdullah 2017), and veterinary medicine (Smith et al. 2018) is the gold standard technique for ONSD measurements.

We found that the ONSD-US linearly increased with the body weight as recently described (Lee et al. 2003), although we found no benefits of applying a multiple linear model analysis compared with a simple model analysis using the body weight. In fact, the predictability of the observed ONSD variability does not increase when the vitreous chamber and axial globe measurements are included. The present study showed that the lowest intraobserver and interobserver reliabilities were obtained for the lens thickness measurement. This information, to our knowledge, has not been stated yet.

There was no correlation between the head conformation and the ONSD, and this finding could be explained by the small number of pure breed specimens in our population. In human medicine, ONSD decreases with the age (Cavallotti et al. 2002) and similar results have been reported in veterinary medicine, which leads to the hypothesis that the optic nerve could suffer a slight degeneration (Lee et al. 2003). In our population, an association was not observed between the ONSD and the age.

The limitations of this study include the collection of video clips by only a single observer. The second operator analysed the measurements from the registered videos, which could have induced errors in the measurements collected from the screen. Another limitation to consider is the relatively small number of dogs. Additional studies of the use of transscleral ONSD-US in dogs with a potential ICP are needed to confirm the accuracy of our study. However, we believe that the use of the transscleral US approach for the ONSD measurement in conscious dogs is possible, although we did not examine this possibility for ethical reasons. Transscleral US can be used as an alternative approach for ON visualisation, and ONSD measure-

https://doi.org/10.17221/39/2019-VETMED

ments exhibit excellent intra- and interobserver repeatability in dogs under anaesthesia. The present study demonstrates a positive relationship between the ONSD and the body weight, but not when a multiple liner model analysis also includes the morphometric measurements of the globe as independent predictors.

Acknowledgement

The authors would like to thank Valentina Andreani for her important contribution to the figures.

REFERENCES

Bauerle J, Schuchardt F, Schroeder L, Egger K, Weigel M, Harloff A (2013): Reproducibility and accuracy of optic nerve sheath diameter assessment using ultrasound compared to magnetic resonance imaging. BMC Neurology 13. doi: 10.1186/1471-2377-13-187.

Boroffka SA, Gorig C, Auriemma E, Passon-Vastenburg MH, Voorhout G, Barthez PY (2008): Magnetic resonance imaging of canine optic nerve. Veterinary Radiology and Ultrasound 49, 540–544.

Cavallotti C, Pacella E, Pescosolido N, Tranquilli-Leali FM, Feher J (2002): Age-related changes in the human optic nerve. Canadian Journal of Ophthalmology 37, 389–394.

Cooley SD, Scrivani PV, Thompson MS, Irby NL, Divers TJ, Erb HN (2016): Correlations among ultrasonographic measurements of optic nerve sheath diameter, age, and body weight in clinically normal horses. Veterinary Radiology and Ultrasound 57, 49–57.

East L, Lyon M, Agrawal P, Islam Z, Newell M, Hockman T, Heger IM, Xu H, Kuchinski AM, Gibson RW (2019): Increased intracranial pressure damages optic nerve structural support. Journal of Neurotrauma. doi: 10.1089/neu.2019.6490.

Geeraerts T, Merceron S, Benhamou D, Vigue B, Duranteau J (2008): Non-invasive assessment of intracranial pressure using ocular sonography in neurocritical care patients. Intensive Care Medicine 34, 2062–2067.

Gonzalez EM, Rodriguez A, Garcia I (2001): Review of ocular ultrasonography. Veterinary Radiology and Ultrasound 42, 485–495.

Ilie LA, Thomovsky EJ, Johnson PA, Bentley RT, Heng HG, Lee HC, Moore GE (2015): Relationship between intracranial pressure as measured by an epidural intracranial pressure monitoring system and optic nerve sheath diameter in healthy dogs. American Journal of Veterinary Research 76, 724–731.

Lee HC, Choi HJ, Choi MC, Yoon JH (2003): Ultrasonographic measurement of optic nerve sheath diameter in normal dogs. Journal of Veterinary Science 4, 265–268.

Padayachy LC, Padayachy V, Galal U, Pollock T, Fieggen AG (2016): The relationship between transorbital ultrasound measurement of the optic nerve sheath diameter (ONSD) and invasively measured ICP in children. Child's Nervous System 32, 1779–1785.

Raboel PH, Bartek Jr J, Andresen M, Bellander BM, Romner B (2012): Intracranial pressure monitoring: Invasive versus non-invasive methods. Critical Care Research and Practice. doi: 10.1155/950393.

Raffiz M, Abdullah JM (2017): Optic nerve sheath diameter measurement: a means of detecting raised ICP in adult traumatic and non-traumatic neurosurgical patients. The American Journal of Emergency Medicine 35, 150–153.

Rajajee V, Vanaman M, Fletcher JJ, Jacobs TL (2011): Optic nerve ultrasound for the detection of raised intracranial pressure. Neurocritical Care 15, 506–515.

Smith JJ, Fletcher DJ, Cooley SD, Thompson MS (2018): Transpalpebral ultrasonographic measurement of the optic nerve sheath diameter in healthy dogs. Journal of Veterinary Emergency Critical Care 28, 31–38.

Received: March 15, 2019
Accepted after corrections: September 10, 2019