



# Repeatability of ultrasound examination of the optic nerve sheath diameter in the adult cat: comparison between healthy cats and cats suffering from presumed intracranial hypertension

Journal of Feline Medicine and Surgery  
1–7

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DOI: 10.1177/1098612X19898006

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This paper was handled and processed by the European Editorial Office (ISFM) for publication in *JFMS*



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## Abstract

**Objectives** The objectives of this study were to test: (1) the repeatability of ultrasonographic examination of the optic nerve sheath diameter (ONSD) in the cat; (2) the association between the ONSD and age, sex and body weight in healthy cats; and (3) the difference in the ONSD between healthy cats and those suffering from presumed intracranial hypertension (ICH).

**Methods** This study had a prospective, blinded, observational cross-sectional study design. Two groups of animals were considered: healthy cats (group A) and cats with a diagnosis of presumed ICH (group B). The ONSD was evaluated, measured and compared between the two groups via an ultrasonographic transpalpebral approach. Repeatability of the procedure was evaluated through the intraclass correlation coefficient (ICC). Data were statistically compared using the Student's *t*-test and linear regression analysis.

**Results** A strong inter- and intraobserver ICC indicating good repeatability was observed. The interobserver ICC was 0.965 ( $P < 0.05$ ) for the right eye and 0.956 ( $P < 0.05$ ) for the left eye. The intraobserver ICC was 0.988 ( $P < 0.05$ ) and 0.984 ( $P < 0.05$ ), or the right and left eyes, respectively. In healthy cats the mean  $\pm$  SD ONSD was  $1.23 \pm 0.11$  mm (range 1–1.47 mm) and  $1.23 \pm 0.10$  (range 1–1.4 mm) for right and left eyes, respectively. The ONSD was not related to sex or weight; a weak relationship was observed with age. In group B, the mean ONSD was  $1.68 \pm 0.13$  mm (range 1.5–1.9 mm) and  $1.61 \pm 0.15$  mm (range 1.4–1.9 mm) for the right and left eyes, respectively. In group B, the ONSD was statistically significantly larger than in group A, the healthy cats ( $P < 0.001$ ).

**Conclusions and relevance** The transpalpebral ultrasonographic technique is a non-invasive, feasible and reproducible method to measure ONSD both in healthy cats and in cats suffering from suspected ICH.

**Keywords:** Intracranial hypertension; optic nerve sheath diameter; ultrasound; emergency

**Accepted:** 9 December 2019

## Introduction

The ability to diagnose intracranial hypertension (ICH) is an increasing necessity in emergency settings and in intensive care, both in human and veterinary medicine.<sup>1,2</sup> Catastrophic deterioration of brain function and/or death may occur if ICH is undetected and untreated; consequently, early detection can prompt more aggressive interventions optimising cerebral perfusion pressure and preservation of brain tissue.<sup>3,4</sup> Moreover,

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clinical diagnosis of ICH can be challenging in situations when the altered level of sensorium or administration of sedatives precludes assessment of the clinical signs typical of this condition.<sup>4,5</sup>

In humans, direct measurement through intraventricular intracranial pressure (ICP) devices is considered the 'gold standard' for measuring ICP.<sup>6</sup> There is no gold standard method to measure ICP in small animals in either clinical or research settings, but it is assumed that an intraparenchymal system would be the most precise.<sup>7</sup> Owing to its invasiveness, direct measuring procedures need specialised staff and centres; thus, there has been substantial interest in developing non-invasive techniques.<sup>8,9</sup> Ultrasonographic (US) measurement of optic nerve sheath diameter (ONSD) has been recently proposed as a feasible, sensitive screening test for ICH in emergency settings.<sup>1,10,11</sup> The rapid and non-invasive nature of ultrasonography has resulted in its increasing use for the detection of elevated ICP in emergency and critical care settings in humans. Transorbital ultrasonography offers the advantages of not requiring general anaesthesia, of being low cost and non-invasive, as well as usually needing short procedural times.<sup>12</sup>

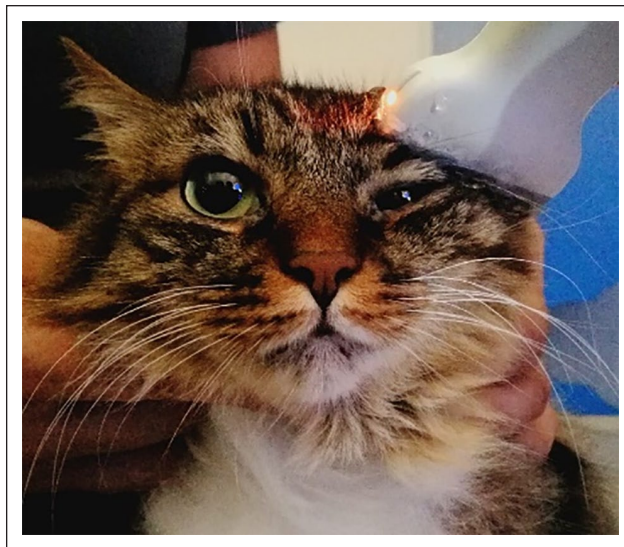
In the veterinary literature, a few studies describe ONSD measurement via the transpalpebral US approach in healthy dogs and horses.<sup>13–15</sup> To the best of our knowledge, there are no studies related to the ONSD in cats.

The aims of the present study were to test: (1) the repeatability of US examination of the ONSD in cats; (2) the association between the US examination of ONSD and age, sex and body weight in healthy cats; and (3) the difference in the ONSD between healthy cats and those with a presumed diagnosis of ICH based on clinical signs and MRI findings.

## Materials and methods

For this prospective, blinded, observational cross-sectional study, all healthy, privately owned cats presented to our institution between December 2017 and June 2019 for routine neuter were enrolled; a second pool of cases was obtained from patients with neurological signs attributable to ICH and with an MRI diagnosis of presumptive ICH. Written informed consent was obtained by the owners. Study approval was obtained from the University of Sassari Ethics Committee (project 72329). Age, sex, breed and weight were recorded for all cats.

The cats enrolled in the study were divided into two groups, as follows: healthy cats with no abnormalities identified on complete physical, neurological and ophthalmological examination, and no history of neurological or ophthalmological disease (group A); and cats with neurological signs attributable to ICH such as altered consciousness, reduced or absence of physiological nystagmus, anisocoria, reduction or absence of pupil response to light, and with an MRI diagnosis of presumed ICH (group B).

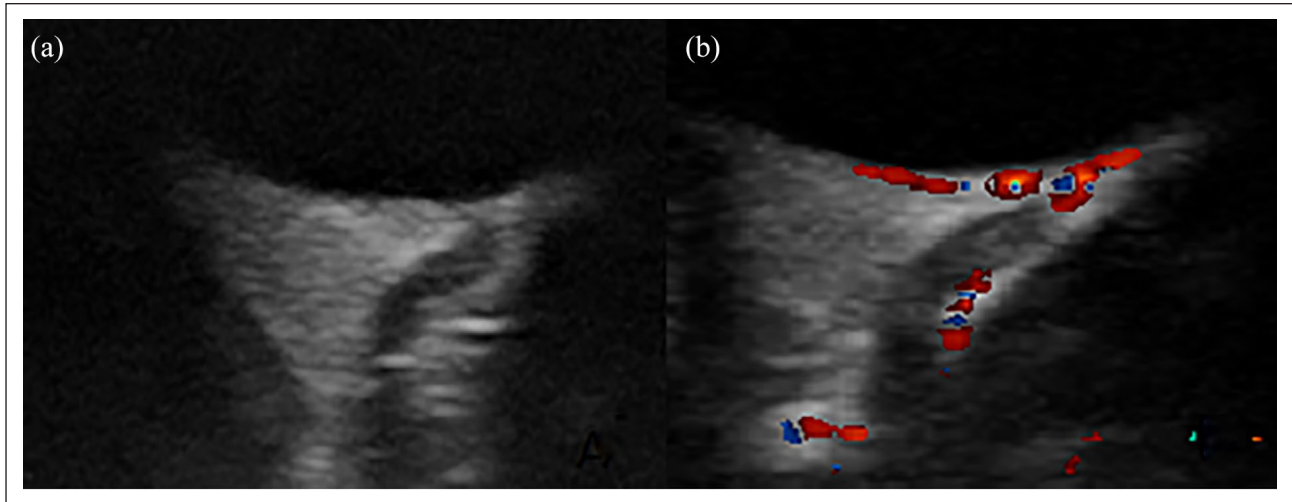


**Figure 1** Ultrasonographic assessment of the optical nerve sheath diameter: with the cat in sternal recumbency, the transducer was gently positioned on the most lateral aspect of the upper eyelid, perpendicularly to the sagittal axis of the head with the indicator pointing towards the medial canthus of the eye. The probe was then moved about 15° clockwise until the entry of the optic nerve into the globe was seen

Exclusion criteria for both groups included: age <1 year and >10 years; evidence of ocular trauma or other ophthalmological diseases; and any medical treatment with glucocorticoids, mannitol or hypertonic solution in the previous 10 days. Neurological and ophthalmological examinations were performed on all cats by the same author (MLM).

All US examinations were performed blind by two authors (MAE and GC); both had been trained in transpalpebral US scanning in a previous pilot study performed on five cadavers and 15 healthy cats. The training focused on ultrasonography and the eco-flow Doppler setting, globe and orbit anatomy, and measurement technique. In order to standardise the technique, the positioning of the examiner, patient and transducer were defined. At the end of this training period, the median length of time required to acquire ONSD images from both eyes was 151 s for each author.

US assessment of the ONSD was performed in B-mode via the transpalpebral approach, as described in humans and dogs.<sup>1,14</sup> Briefly, with the cat in sternal recumbency, the transducer was gently positioned on the most lateral aspect of the upper eyelid, perpendicularly to the sagittal axis of the head with the indicator pointing towards the medial canthus of the eye. The probe was then moved about 15° clockwise until the entry of the optic nerve into the globe was seen (Figure 1). Unlike in humans, the canine and feline optic nerves have a sigmoid shape, they do not possess a single central retinal artery, but rather several branches deriving from a



**Figure 2** Overview of the eyeball and the retrobulbar space. (a) The longitudinal section of the optic nerve appears as a thin, curvilinear, hypoechoic structure. (b) Colour flow Doppler image of the same eye

plexus of cilioretinal arteries. In contrast to the dog, the main retinal veins in the feline eye do not unite in the centre of the optic nerve head (ONH), but leave the eye parallel to the arteries as separate vessels at the lateral portion of the ONH.<sup>16</sup> Ultrasonographically, the optic nerve and its sheath appeared as a thin, curvilinear, hypoechoic structure with parallel linear borders, surrounded by fat and by the retrobulbar extraocular muscle cone, and extended caudally from just below the globe's posterior pole (Figure 2) (see supplementary material for a video of the ultrasound examination in a healthy cat). In challenging cases, colour flow Doppler was used to distinguish the optic nerve from other anatomical structures. Images were saved and the ONSD measured at a level 3 mm caudal to the papilla, with the optic nerve aligned and perpendicular to the probe. The ONSD was obtained by measuring the distance between the two outer hypoechoic borders of the nerve at the edge with the surrounding retrobulbar fat. Each eye was rinsed with sterile saline after completion of the examination.

In group A, all eyes were scanned using a 3–13 MHz linear ultrasound transducer (MyLab Alpha Esaote) before premedication to general anaesthesia for a routine ovariohysterectomy.

In group B, brain MRI with a low-field machine (0.23 T Paramed) was performed after the ONSD measurement in patients suspected of having increased ICP. The protocol included scans of the entire brain in a minimum of fast spin echo sequences with T2-weighted in sagittal and transverse planes, T1-weighted in a transverse and dorsal plane (pre- and post-contrast medium administration [Prohance; Bracco]) and dorsal T2-weighted fluid attenuation inversion recovery. All the MRI studies were reviewed by one author, a veterinary surgeon with experience in neurology

(MLM), blinded to the ONSD measurements. Images were evaluated for the presence or absence of MRI characteristics of presumed ICH, namely mass effect, substantial oedema, effacement of sulci, midline shift, or collapse of the ventricles or cisterns. The study was considered positive for raised ICP if at least two of these findings were present.<sup>17,18</sup>

#### Data analysis

Statistical analyses were performed using Stata 11.2 software.

All data were evaluated for normality using the Shapiro–Wilk's test. To test the repeatability of US examination of the ONSD in the cat, the intraclass correlation coefficient (ICC) was used as previously reported.<sup>14</sup> In particular, the ICC was used to assess the degree of agreement between measurements of the ONSD between the two observers (ie, interobserver) and between the three repeated measurements undertaken on each eye (ie, intraobserver).

In addition, the mean absolute difference in the measurements between the two observers and between the three individual measurements undertaken by each observer was calculated.

ONSD differences between affected and control animals were analysed using the Student's *t*-test. Linear regression analysis was used to evaluate the relationship between age, sex and weight and measurement of the mean left and right ONSD US measurement.

## Results

Fifty-seven cats were enrolled in the study: 50 in group A (healthy cats) and seven in group B (cats with suspected ICH).

**Table 1** Underlying diagnosis and optical nerve sheath diameter (ONSD) measurements in cats with presumed intracranial hypertension

Group B	Underlying diagnosis	Observer 1 mean right ONSD	Observer 1 mean left ONSD	Observer 2 mean right ONSD	Observer 2 mean left ONSD
ID 62	FIP	1.8	1.7	1.9	1.6
ID 63	FIP	1.7	1.9	1.9	1.8
ID 64	TBI	1.7	1.7	1.6	1.6
ID 65	Neoplasia	1.6	1.6	1.5	1.7
ID 66	Neoplasia	1.7	1.5	1.8	1.7
ID 67	Neoplasia	1.5	1.5	1.6	1.5
ID 68	Neoplasia	1.6	1.4	1.6	1.4

FIP = feline infectious peritonitis; TBI = traumatic brain injury

**Table 2** Optical nerve sheath diameter (ONSD) measurements from the two investigators

	Right ONSD observer 1 and 2 (mm)	Left ONSD observer 1 and 2 (mm)
Group A	1–1.47 (1.23 ± 0.11)	1–1.40 (1.23 ± 0.10)
Group B	1.5–1.9 (1.68 ± 0.13)	1.4–1.9 (1.61 ± 0.15)

In group B, ONSD was significantly larger than in group A ( $P < 0.001$ ). Data are range (mean ± SD)

In group A, 29 were intact females and 21 were intact males ( $n = 50$ ). They were all domestic shorthairs (DSH). Mean ± SD age was  $3.34 \pm 2.38$  years and mean ± SD weight was  $3.47 \pm 1.03$  kg.

Group B was composed of five intact DSH females and two intact DSH males ( $n = 7$ ). The mean ± SD age was  $5.14 \pm 2.79$  years and the mean ± SD weight was  $3.82 \pm 1.46$  kg. MRI diagnosed diffuse ICH owing to neoplasia ( $n = 4$ ), inflammation compatible with feline infectious peritonitis ( $n = 2$ ) and traumatic brain injury ( $n = 1$ ) (Table 1).

ONSD was identified and measured in all 57 animals and a total of 114 ONSDs were evaluated. Each ONSD was measured three times by the two authors for a total of 684 measurements.

#### *Intra- and interobserver repeatability*

The difference between the two observers was 0.007 and 0.008 mm, respectively, for right and left eyes. No difference was detected between the left and right sides for each observer ( $P > 0.05$ ) (Table 2).

Of the 57 cats scanned by both ultrasonographers, the ICC was 0.965 (95% confidence interval [CI] 0.940–0.979;  $P < 0.05$ ) for the right eye and 0.956 (95% CI 0.925–0.974;  $P < 0.05$ ) for the left eye. Of the 57 cats scanned by ultrasonographer 1, the ICC for the right eye across the three repeated measurements was 0.988 (95% CI 0.982–0.993) and 0.984 (95% CI 0.975–0.990) for the left, while for ultrasonographer 2, the ICC for the right eye across the three repeated measurements was 0.984 (95% CI 0.975–0.990) and 0.979 (95% CI 0.967–0.987) for the left.

Including measurements from both ultrasonographers, in group A the mean right ONSD was  $1.23 \pm 0.11$  mm (range 1–1.47 mm); the mean left ONSD was  $1.23 \pm 0.10$  mm (range 1–1.40 mm) (Figure 3a).

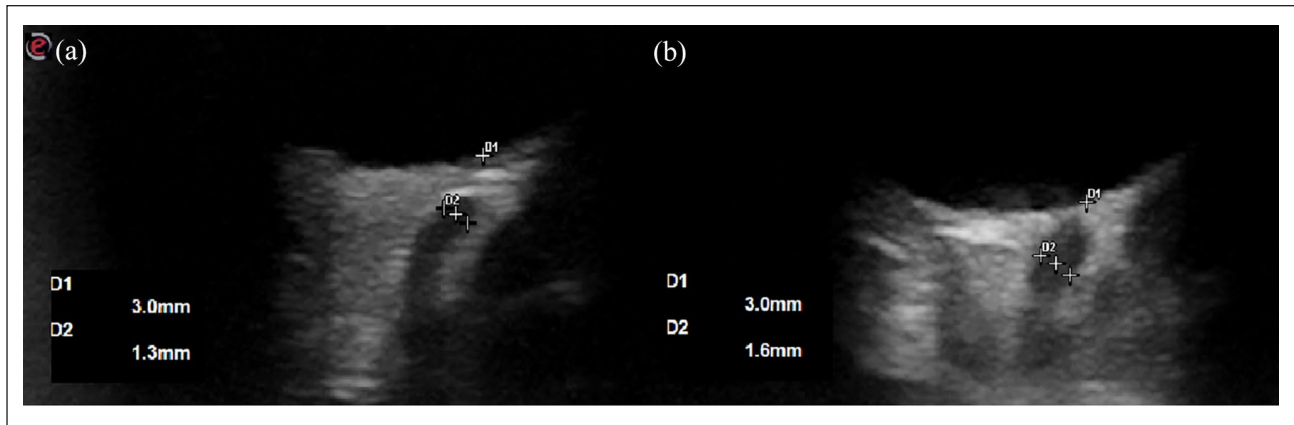
Including measurements from both ultrasonographers, in group B the mean right ONSD was  $1.68 \pm 0.13$  mm (range 1.5–1.90 mm); the mean left ONSD was  $1.61 \pm 0.15$  mm (range 1.40–1.90 mm) (Figure 3b).

Considering all the cats, regression analysis showed that age could statistically significantly predict ONSD, even with a limited  $R^2$ , ranging from 0.7 to 0.14, considering the different ultrasonographers' measurements of the left or right eye ([ONSD right ultrasonographer 1 =  $1.198 + 0.025 \times \text{age}$ ]  $F [1, 55] = 8.54$ ,  $P = 0.005$ ,  $R^2 = 0.13$ ); ([ONSD right ultrasonographer 2 =  $1.117 + 0.030 \times \text{age}$ ]  $F [1, 55] = 9.15$ ,  $P = 0.003$ ,  $R^2 = 0.14$ ); ([ONSD left ultrasonographer 1 =  $1.21 + 0.018 \times \text{age}$ ]  $F [1, 55] = 4.42$ ,  $P = 0.04$ ,  $R^2 = 0.07$ ); ([ONSD left ultrasonographer 2 =  $1.23 + 0.011 \times \text{age}$ ]  $F [1, 55] = 1.74$ ,  $P = 0.1$ ,  $R^2 = 0.03$ ), while weight and the sex were not significantly associated with ONSD ( $P > 0.05$ ).

Considering both eyes and both ultrasonographers, the ONSDs in group B were significantly larger than in group A ( $P < 0.001$ ).

## Discussion

The optic nerve sheath (ONS) is an anatomical extension of the dura mater and the subarachnoid space around the optic nerve is continuous with the intracranial subarachnoid space. An increase in ICP above a certain threshold can result in displacement of cerebrospinal



**Figure 3** (a) Healthy cat: optical nerve sheath diameter (ONSD) measured at a level 3mm caudal to the papilla (D1) with the optic nerve aligned and perpendicular to the probe. The ONSD was obtained by measuring the distance between the two outer hypoechogenic borders of the nerve at the edge with the surrounding retrobulbar fat (D2). (b) Cat with presumed intracranial hypertension – measurement of ONSD

fluid from the intracranial cavity into the perineural sub-arachnoid space owing to direct continuity between these spaces resulting in an increase of the ONSD and, in humans, also papilloedema.<sup>19–22</sup> As the feline (and canine and equine) eye differs from the human eye in not having a central retinal artery in the middle of the optic nerve, this changes the fluid dynamics so that papilloedema does not occur with elevated ICP in these species as it does in the human.<sup>23</sup> Dilatation of the ONS has been shown to be an earlier manifestation of ICP rise.<sup>24,25</sup> A strong relationship has been reported in humans between ONSD, as evaluated by ultrasonography, and ICP.<sup>1,26,27</sup>

To the best of our knowledge, this is the first study to ultrasonographically investigate the ONSD in cats and its possible relationship with ICH.

The first aim of this study was to test the repeatability of US examination of the ONSD in cats, using the transpalpebral approach.<sup>14,15</sup> The US window used was favoured by the fact that in carnivores the bony orbit is incomplete with the dorsolateral margin of the orbit closed by the orbital ligament, thus reducing possible acoustic shadowing artefacts. The transpalpebral approach was easily achieved in awake patients as there was no need to place gel or the transducer directly onto the cornea. ONSD was identified and measured in all the animals included in the study; it appeared as a hypoechoic sigmoid, thin structure. In contrast with what is seen in humans,<sup>1</sup> in the feline eyes examined, the margins of the ONS could not be differentiated from the optic nerve itself nor from the surrounding retrobulbar fat. Therefore, in order to reduce possible errors, we decided to measure the ONSD by placing the electronic calipers on the outer hypoechoic parallel margins of what was considered the optic nerve, including its sheath. The procedure was completed for both eyes in <3mins by the two veterinarians who had attended previous training aimed at standardising the technique.<sup>10</sup> The two observers were

considered interchangeable as the difference between their measurements was <0.01mm. Given the strong intra- and interobserver ICC reported in this study, the repeatability of US examination of the ONSD in cats can be confirmed.

The second aim of this study was to investigate the correlation of ONSD with the side of the eye, age, sex, body weight or breed in healthy cats. No statistical difference was detected between right and left eye ONSDs. A very weak correlation was found between age and ONSD; ONSD seemed to diminish with age, which is in concordance with a recent report by Chandrakumar et al in a study where feline intra-ocular structures were measured using CT,<sup>28</sup> and by Smith et al, who measured canine ONSDs by ultrasonography.<sup>14</sup> There was no correlation between ONSD and sex or weight. Finally, as the cats in the current study were all DSHs, no speculation can be made on the correlation between ONSD and breed. In healthy horses, ONSD was not related to age or body weight; however, normal reported ranges for ONSDs are <5mm in foals and ≤6.5mm in adults.<sup>15</sup> In healthy dogs, age and body condition score affected ONSDs, with the largest effect exerted by body weight. Multiple cut-off points were reported to account for a wide range of ONSDs observed between different breeds and ages.<sup>14</sup> In human adults, ONSD ranges from 5.0 to 6.0mm for predicting an ICP >20mmHg; multiple linear regression analysis found a significant relationship between ONSD and eyeball transverse diameter, but none with sex, height, weight or head circumference.<sup>29–31</sup>

The final aim of the study was to test the difference in ONSD between healthy cats and cats suffering from ICH presumptively diagnosed by clinical signs and MRI.

In the latter group, MRI studies showed signs consistent with ICH owing to intracranial pathologies, such as neoplasia, infection or trauma. With a mean ± SD ONSD of 1.67 ± 0.13mm, cats suffering from presumed ICH

had an ONSD significantly greater ( $P < 0.001$ ) than healthy ones, which had a mean  $\pm$  SD ONSD of  $1.23 \pm 0.11$  mm. As the cats examined did not suffer from concurrent ocular pathologies that could modify the ONSD, such as toxoplasmosis, cryptococcosis, systemic hypertension and lymphoma, we can deduce that the statistical difference between the two groups was due to ICH.<sup>32</sup> Given the strong intra- and interoperator repeatability, the low variability of the ONSD in healthy cats and the significant statistical difference observed between healthy cats and those with presumed ICH, we can reasonably state that in adult cats an ONSD of 1–1.4 mm indicated absence of ICH, while a value  $> 1.5$  mm suggested ICH. Future investigations including an appropriate number of patients belonging to different ages and breeds and suffering from different intracranial pathologies are required to confirm our results.

The present study had some limitations. First, ONSD US measurements were not compared with direct measurement of the ICP, as this would have been an invasive procedure and therefore correlation with the gold standard method for the diagnosis of ICH was missing. Second, the sample of patients presumably affected by ICH was too small to allow a more in-depth evaluation of the results. It would have also been interesting to compare ONSD in patients with chronic and acute ICH.

No adverse effects were reported in the present study; although, it is important to emphasise that optic nerve ultrasonography can potentially cause damage from inadvertent application of excessive pressure on the eye.<sup>33</sup>

The results of this study, if confirmed by future investigations, suggest that in cats, US measurement of the ONSD may serve as an additional diagnostic tool in the decision-making and monitoring of patients with ICH whenever invasive ICP evaluation is contraindicated and/or is not available.

## Conclusions

The present study provides baseline information for further investigations of US evaluation of ONSD in cats. The transpalpebral US examination is a feasible, reproducible and non-invasive method to measure ONSD in healthy cats, and might prove helpful in diagnosing raised ICP in emergency settings.

The preliminary results of this study suggest that ONSD in adult healthy cats measured, on average,  $1.23 \pm 0.11$  mm and was statistically different from cats with presumed ICH.

**Supplementary material** The following file is available online:

Video of US examination of the optic nerve in a healthy cat.

**Conflict of interest** The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

**Funding** The authors received no financial support for the research, authorship, and/or publication of this article.

**Ethical approval** This work involved the use of non-experimental animal(s) only (owned or unowned), and followed established internationally recognised high standards ('best practice') of individual veterinary clinical patient care. Ethical approval from a committee was not necessarily required.

**Informed consent** Informed consent (either verbal or written) was obtained from the owner or legal custodian of all animal(s) described in this work for the procedure(s) undertaken. For any animals or humans individually identifiable within this publication, informed consent for their use in the publication (verbal or written) was obtained from the people involved.

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