

Diagnosis of cerebral ventriculomegaly in felines using 0.25 Tesla and 3 Tesla magnetic resonance imaging

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ABSTRACT: Twenty European shorthair cats with neurological disorders, aged 1–3 years and with body weights of 2.6–4.05 kg, were studied in low-field and high-field magnetic resonance imaging systems. Aims of the study were to evaluate the dilation of lateral ventricles in the examined population of cats with the use of quantitative analysis methods and to identify any differences in the results of low- and high-field magnetic resonance imaging. The average brain height was determined to 27.3 mm, and the average volume of the brain was 10 699.7 mm³. Moderately enlarged ventricles were observed in 16 symptomatic cats. Moderate unilateral enlargement was observed in one cat. Mild ventricular asymmetry was described in four animals. The average difference in ventricular height between measurements obtained in low- and high-field magnetic resonance imaging was $0.37 \pm 0.16\%$ and for ventricular volume it was $0.62 \pm 0.29\%$. The magnetic resonance imaging scan did not reveal statistically significant differences in brain height or volume between healthy and cats with ventriculomegaly. The differences in the results of low- and high-field magnetic resonance imaging were not statistically significant. Described findings could facilitate the interpretation of magnetic resonance images in cats with ventriculomegaly or hydrocephalus.

Keywords: cat; brain; hydrocephalus; cerebrospinal fluid; dilation

Cerebral ventricular deformations which together with the compression of the white matter adjacent to the ventricles can cause serious neurological problems, including cognitive impairment, are associated with many diseases (Liu et al. 2009). Dilation of the ventricular system may be the result of obstruction of part of the ventricular system including the interventricular foramen, third ventricle, mesencephalic aqueduct, fourth ventricle or lateral apertures due to infection, neoplasia, injuries or haemorrhages (Przyborowska et al. 2013). Moreover, ventricular dilation may range from moderate to severe, and asymmetries between the lateral ventricles may develop (Vullo et al. 1997). Marked or progressive ventriculomegaly associated with changes in ventricular cerebrospinal fluid (CSF) pressure is described as hydrocephalus. In domestic animals, the condition is frequently secondary to obstruction causing blockage of CSF outflow in the

ventricles or the subarachnoid space (Przyborowska et al. 2013). External hydrocephalus is described as an accumulation of CSF between the cerebral hemispheres and the overlying arachnoid membrane; internal hydrocephalus is a term commonly used to describe abnormal dilatation of the ventricular system inside the cranium (Tani et al. 2001; Dewey et al. 2003). This condition may also result from CSF overproduction, congenital malformations blocking normal fluid drainage or from complications associated with head injuries and infections (Imamura et al. 2006; Klarica et al. 2009; Okada et al. 2009; Pattison et al. 2010; Woo et al. 2010; Eskandari et al. 2011; Przyborowska et al. 2013; Keating et al. 2016). Hydrocephalus was formerly considered to be a rare disease in veterinary medicine; however, the prevalence of the disease has increased in recent years due to the greater availability of magnetic resonance imaging. Magnetic resonance imaging (MRI) ex-

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aminations provide anatomical and morphological information, and they are performed to evaluate the soft tissue, joints, tendons, but especially the central nervous system (CNS) of humans and animals (Tani et al. 2001; Woo et al. 2010; Adamiak et al. 2012; Zhalniarovich et al. 2013; Hori et al. 2015; Skalec et al. 2016; Przyborowska et al. 2017a; Zhalniarovich et al. 2017a; Zhalniarovich et al. 2017b). In cats, viral infections such as parvoviral infections or feline infectious peritonitis (FIP) are common causes of hydrocephalus (Tani et al. 2001; Keating et al. 2016). In MRI examinations, symptoms of hydrocephalus that are visualised include enlargement of the ventricles.

The results of MRI examinations evaluating ventriculomegaly or hydrocephalus in animals have been discussed in several studies (Kii et al. 1997; Vite et al. 1997; Vullo et al. 1997; Kii et al. 1998; Esteve-Ratsch et al. 2001; Nykamp et al. 2001; Woo et al. 2010; Pivetta et al. 2013). Most studies were performed on dog breeds predisposed to ventriculomegaly, whereas cats have never been subjected to MRI exams. On the other hand, in many studies it has been shown that ventricular size is quite variable in healthy, asymptomatic dogs, and in many cases ventriculomegaly is accidentally diagnosed during neurological examination performed for other reasons (De Hann et al. 1994; Vullo et al. 1997; Pivetta et al. 2013).

In this study, MRI of the brain was performed on symptomatic European shorthair cats to determine the variance in lateral ventricular size in low- and high-field MRI systems. The aim of this study was to perform a quantitative evaluation of cerebral ventricular alterations in cats with ventriculomegaly. The results were compared with reference intervals for ventricular volume for cats obtained from a previously published study (Przyborowska et al. 2017b). A further goal was to determine the presence of any statistically significant differences between the results of the two MRI systems.

MATERIAL AND METHODS

Twenty adult European shorthair cats, with body weights ranging from 2.60 to 4.05 kg (mean weight of 3.22 kg), aged 1–3 years (mean age of 2.2 years), were studied without sex discrimination. All cats exhibited neurological signs specific for CNS disorders. The size of the examined

population guaranteed that the results would be statistically significant. The experimental animals were patients of the Department of Surgery and Radiology, Faculty of Veterinary Medicine, University of Warmia and Mazury, Olsztyn, Poland. The diagnostic and research protocols were consistent with the Guidelines for the Care and Use of Laboratory Animals. The animals were subjected to a full physical and neurological examination, and they were screened for metabolic diseases based on serum chemistry and complete blood count data. Cats were also screened for parvovirus, FIP (feline infectious peritonitis) and toxoplasma infections. The cats were subjected to MRI in a low-field magnetic resonance (MR) scanner with a 0.25 T magnet (Esaote Vet-MR Grande) and a high-field magnetic resonance scanner with a 3 T magnet (Siemens). The patients were under general anaesthesia during both examinations. A two-week break was taken between examinations in low-field and high-field MRI. The procedures were carried out with the owners' consent.

The cats were pre-medicated with atropine (Atropinum Sulfuricum[®], Polfa Warszawa) at 0.05 mg/kg body weight administered subcutaneously, medetomidine (Cepetor, ScanVet) at 0.1 mg/kg body weight, and midazolam (Midanium[®], Polfa Warszawa) at 0.1 mg/kg body weight administered by an intramuscular injection. General anaesthesia was induced with intravenous propofol (Scanofol, ScanVet) at 1 mg/kg body weight and maintained with the same drug administered intravenously as needed. The patients were intubated and oxygen was provided during intubation.

Magnetic resonance images were acquired with the use of a 0.25 T. The patients were positioned in sternal recumbency with the head centred in the head coil. Transverse and dorsal T1-weighted MR images were acquired using spin echo sequences with a repetition time (TR) of 650 ms and an echo time (TE) of 25 ms. T2-weighted images of the brain were obtained in transverse and sagittal planes. Transverse images of the head were acquired with T2-weighted fast spin echo sequences with a TR of 4010 ms and a TE of 90 ms. Sagittal T2-weighted images were acquired in fast spin echo sequences with a TR of 4290 ms and a TE of 120 ms. Transverse images were oriented in a position perpendicular to the hard palate. Sagittal images were acquired perpendicular to the transverse plane. Slice thickness was 2 mm with no gap. In the

high-field MRI system (3T) images were acquired by placing the animals in sternal recumbency with the head centred inside the human wrist coil. T1-weighted and T2-weighted images of the brain were obtained in identical planes in both systems. Slice thickness was 2 mm with no gap. Figure 1 and Figure 2 show representative T1-weighted and T2-weighted transverse images of a patient's brain.

Images were analysed across the region of interest. The parameters of the brain and ventricles were quantified using computer image processing algorithms. Firstly, ventricular height (VH) and brain height (BH) were measured in transverse images at the level of the interthalamic adhesion. The ventricular area of the lateral ventricle was manually outlined in the transverse plane and calculated by a computer. Lateral ventricular volume (VV) was

calculated as the sum of ventricular areas in each transverse image multiplied by slice thickness. The height and area of slit-like lateral ventricles were determined at 1 mm and 1 mm², respectively. In the following stage, the ventricular height-to-brain height ratio ($VH/BH \times 100\%$) and the ventricular volume-to-brain volume (BV) ratio ($VV/BV \times 100\%$) were calculated for both lateral ventricles. The symmetry and size of lateral ventricles were assessed in view of the degree of ventricular enlargement and asymmetry based on previously published data for dogs and cats (Kii et al. 1997; Vullo et al. 1997; Przyborowska et al. 2017b). The differences between cats with ventriculomegaly and normal cats were compared based on previously published reference intervals for ventricular volume for cats (Przyborowska et al. 2017b). The data were analysed in Statistica 12.5. Significant differences in brain and ventricle parameters were investigated using Student's two-tailed *t*-test. The results were regarded as statistically significant at $P \leq 0.05$. Finally, the data acquired in 0.25 T and 3 T were analysed with Student's paired *t*-test, in order to compare significant differences between the heights and volumes of the brain and ventricles. *P*-values ≤ 0.05 were considered as statistically significant.

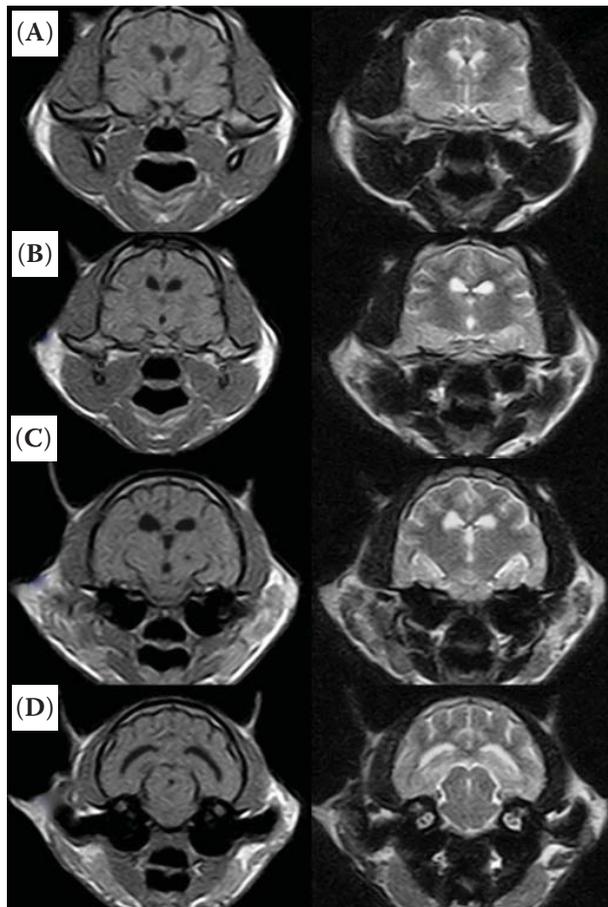


Figure 1. Transverse sections of a cat brain (C04) in low-field MRI. Transverse T1-weighted and T2-weighted images of the cat brain in low-field MRI in four sections: at the level of rostral thalamus (A), interthalamic adhesion (B), caudal thalamus (C) and occipital cortex (D). Lateral ventricles are moderately enlarged and symmetric

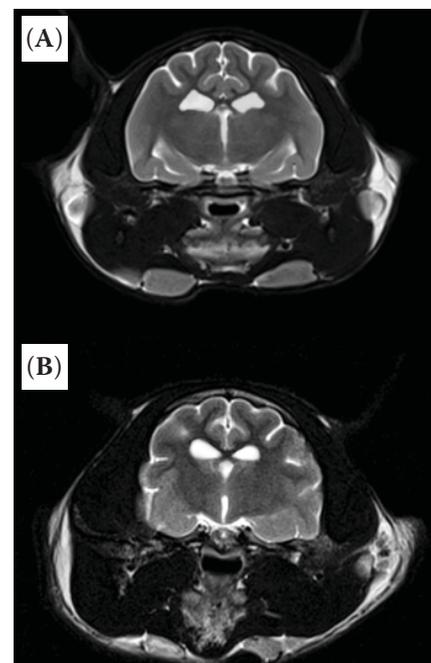


Figure 2. Transverse sections of brains of two cats (C19 and C05) at the level of interthalamic adhesion in high-field MRI. Both T2-weighted images (A) (cat C19) and (B) (cat C05) present moderate ventriculomegaly

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RESULTS

Twenty cats presented neurological signs, including depression, ataxia, strabismus and seizure, and one patient also exhibited circling behaviour and head tilting. In all cats, haemogram and blood chemistry values were consistent with the norm. In nine cases, serum samples were positive for parvovirus. In three cats, serum samples tested positive for FIP and in one patient serum samples were positive for Toxoplasma. In seven cases, serum samples tested negative for FIP, parvovirus and Toxoplasma. All cats were successfully examined by low- and high-field MRI. Body weight, ventricular height-to-brain height ratios (VH/BH) and ventricular volume-to-brain volume ratios (VV/BV) are presented in Table 1. In 0.25 T and 3 T MRI examinations, cerebral ventricles were enlarged in 17/20 cats. In the remaining animals with ventriculomegaly, all areas, i.e., frontal, parietal and temporal regions of lateral ventricles were affected. Lateral ventricles were classified as moderately bilaterally enlarged (VH/BH > 14%, VV/BV > 4.5%) in 16 cats. Lateral

ventricles were symmetric in 12 cases, and in four cats, lateral ventricles were mildly asymmetric. Moderate unilateral enlargement was observed in one cat, and in this case, ventriculomegaly was caused by a tumour. In one cat, measurements of ventricle height ratio based on 0.25 T MR images resulted in classification as enlarged, but the total ventricular volume ratio was within normal limits (VH/BH L = 14.2%, VH/BH R = 14.0%, VV/BV L = 3.2%, VV/BV 3.1%). In 3 T MRI in the same cat calculated ratios were lower and within normal limits (VH/BH L = 13.9%, VH/BH R = 13.8%, VV/BV L = 2.7%, VV/BV 2.9%). In two cats, the size of lateral ventricles was normal but atrophy of the cerebellum and enlargement of the fourth ventricle were observed (Figure 3). The average brain height was determined to be 27.3 mm, and the average volume of the brain to be 10 699.7 mm³. With reference to available data describing brain size in healthy cats (Przyborowska et al. 2017b), significant differences in brain height or volume were not observed between normal and examined cats (height: $P > 0.17$, volume: $P > 0.15$), but ventricular parameters

Table 1. Values obtained in low- and high-field MRI for all patients. The table presents values from low- and high-field MRI for all examined cats, including body weight (kg), results of serum screening and results of ventricular-to-brain height (VH/BH) and volume (VV/BV) ratios (%)

Cat	Serum screening	Body weight	0.25 Tesla				3 Tesla			
			VH/BH L	VH/BH R	VV/BV L	VV/BV R	VH/BH L	VH/BH R	VV/BV L	VV/BV R
C01	F	3.20	15.47	16.10	5.50	5.62	15.40	15.92	4.76	4.90
C02	F	2.90	16.87	16.57	7.77	6.54	16.52	16.36	6.80	5.70
C03	F	3.10	17.26	18.20	5.32	5.10	16.80	17.53	4.79	4.50
C04	O	2.80	18.52	19.20	6.64	6.83	18.13	18.40	6.00	6.15
C05	O	3.50	19.02	19.34	7.01	6.88	18.88	19.00	6.70	6.50
C06	O	3.20	16.88	17.09	6.76	6.89	16.56	16.70	6.00	6.20
C07	O	3.60	15.21	15.60	5.30	5.53	14.90	15.03	4.50	4.70
C08	O	3.70	17.54	19.48	5.15	6.75	17.05	18.90	4.58	6.00
C09	O	2.93	18.95	17.25	6.85	5.40	18.23	16.70	6.00	4.60
C10	O ^{Neo}	2.70	19.95	0.00	8.21	0.00	19.30	0.00	7.30	0.00
C11	P	2.75	9.29	6.43	0.46	0.49	9.00	6.10	0.30	0.34
C12	P	2.60	12.78	12.41	1.08	1.06	12.50	12.10	1.00	1.00
C13	P	3.60	17.36	15.09	5.39	5.49	17.00	14.90	5.10	5.20
C14	P	3.40	17.77	17.07	5.73	5.75	17.50	16.96	5.00	5.00
C15	P	3.20	16.23	15.41	6.83	5.91	16.03	15.19	6.12	5.71
C16	P	3.35	18.58	14.61	6.64	4.67	18.24	14.20	6.00	4.54
C17	P	3.70	19.06	17.55	8.19	6.16	18.50	17.26	7.20	5.67
C18	P	2.65	15.05	19.49	5.62	8.58	14.50	19.02	5.05	7.85
C19	P	3.45	18.59	19.31	7.87	8.91	18.17	18.90	7.15	8.38
C20	T	4.05	14.19	14.02	3.20	3.05	13.89	13.78	2.70	2.90

F = feline infectious peritonitis, Neo = neoplasia, O = other, P = parvovirus, T = toxoplasma

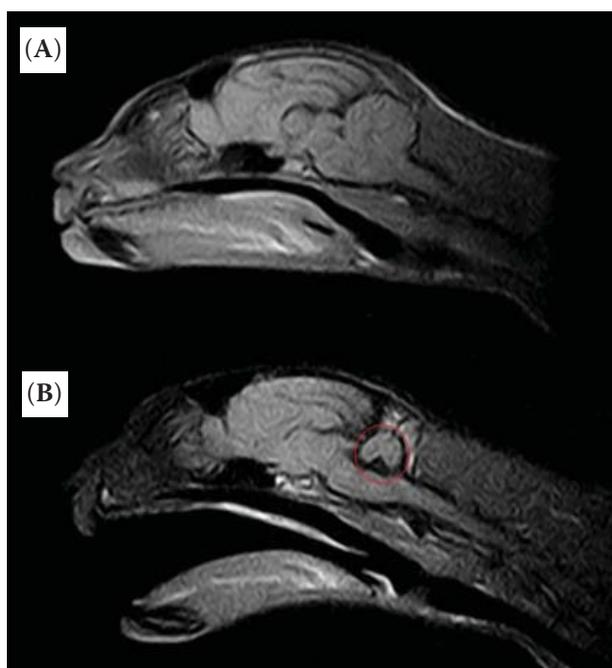


Figure 3. Sagittal T1-weighted image of cat brains (C01 and C11) in low-field MRI. Normal cerebellum and the fourth ventricle (A) and cerebellar atrophy and enlargement of the fourth ventricle are visible (red circle) (B)

differed significantly between groups ($P < 0.02$ for all cases) (Table 2).

The average difference between measurements obtained in low- and high-field MRI was under 0.5%, for ventricular height it was $0.37 \pm 0.16\%$, while the same average difference for ventricular volume was $0.62 \pm 0.29\%$. The statistical analysis of measured brain and ventricle values in 0.25 T and 3 T did not reveal any significant differences (all P -values > 0.05 ; Table 3).

Table 2. Heights (mm) and volumes (mm^3) of cat brains and the right and left ventricles. The table presents the mean values of normal cats ($n = 20$) and cats with ventriculomegaly ($n = 20$), and P -values of the Student t -test between groups. The results did not reveal any statistically significant differences in brain height or volume between healthy and cats with ventriculomegaly

		Normal	Ventriculomegaly	P -value	
Height	brain	27.79	27.32	0.16732	
	ventricle	left	2.98	4.8	< 0.00001
		right	2.89	3.89	0.018007
Volume	brain	9966.26	10699.72	0.154831	
	ventricle	left	134.12	706.21	< 0.00001
		right	130.49	530.43	0.020916

DISCUSSION

In cats, dilation of the cerebral ventricular system is frequently secondary to viral infection (Tani et al. 2001; Benigni and Lamb 2005; Hori et al. 2015; Keating et al. 2016). *In utero* infection with parvovirus can cause cerebellar hypoplasia which affects the external germinal layer of the cerebellum and prevents the formation of the granular layer. Hydrocephalus and hydranencephaly have been found to occur concurrently with parvovirus infection (Tani et al. 2001; Keating et al. 2016). Taga et al. (2000) reported acquired hydrocephalus and hydromyelia in a cat with FIP. Tani et al. (2001) described a cat with hydrocephalus and syringomyelia, which tested positive for the parvovirus antigen but negative for FIP antibodies. Hori et al. (2015) described several feline diseases that produce similar changes in MRI to those observed in hydrocephalus. In this study, in the examined population, nine cats tested positive for parvovirus antibodies. In this group, ventriculomegaly occurred more frequently than cerebellar hypoplasia; seven cats had moderate ventriculomegaly (approx. 78%), while only two presented with cerebellar hypoplasia (approx. 22%). Based on the information supplied by the owners, viral infection most probably occurred *in utero*.

MRI sequences are designed by exploiting differences in the behaviour of hydrogen protons in various tissues exposed to a changing magnetic field. To scan brain tissues, T1-weighted, T2-weighted and fluid attenuated inversion recovery sequences are used most frequently (Benigni and Lamb 2005; Cherubini et al. 2008; Hecht and Adams 2010; Hodshon et al. 2014). T1-weighted images are considered to be more useful in evaluations of brain anatomy while T2-weighted images better describe pathology (Benigni and Lamb 2005; Cherubini et al. 2008; Hecht and Adams 2010; Hodshon et al. 2014).

It has been reported that the ventricles of a healthy cat are too narrow to permit observations

Table 3. P -values from the Student t -test performed to analyse the differences between low- and high-field MRI

	P -value
Ventricular-to-brain height L	0.3210
Ventricular-to-brain height R	0.4045
Ventricular-to-brain volume L	0.1671
Ventricular-to-brain volume R	0.2549

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of ventricular walls in MRI (Hudson et al. 1995). In other studies, the authors were able to observe and/or measure the lateral ventricles of healthy cats in low- and high-field MRI (Gray-Edwards et al. 2014; Przyborowska et al. 2017a; Przyborowska et al. 2017b). In our study, ventricular volume was compared in different magnetic fields, and we were able to observe dilated ventricles in 17 cats and normal sized ventricles in three cats in both T1-weighted and T2-weighted images. However, a better visibility of ventricular borders was observed in high-field than in low-field MRI and was correlated with spatial and contrast resolution. Also, an accurate assessment of ventricular borders in T1-weighted images was more difficult than in T2-weighted images.

Comparing both MRI systems, measurements of brain and ventricular height differed slightly on average ($0.37 \pm 0.16\%$), while the difference between the results for brain and ventricular volume was higher (average value: $0.62 \pm 0.29\%$). In three cases (C02, C05, C17), the results differed by almost 1%. In one case (C20), ventricles were classified as dilated based on low-field MRI, while in high-field MRI values were within normal limits. In MR images, the signals produced by CSF and oedema can have similar intensity. In cases of hydrocephalus or ventriculomegaly, periventricular oedema is visualised in MRI. Thus, ventricular volume can be calculated incorrectly when marginal oedema surrounding cerebral ventricles is taken into consideration (Cherubini et al. 2008; Gray-Edwards et al. 2014). In our opinion, the difference in results may be the result of better visibility of the ventricular boundary in high-field MRI, while in low-field MRI the volume was miscalculated because marginal oedema was taken into consideration. In high-field MRI, the border between ventricles and surrounding brain tissue can be examined with greater precision, which lowers the risk of over calculation.

Due to the varying ventricular anatomy among animal breeds, comparative size analysis of these cavities is limited. In several studies of dogs, ventricular dilations were measured based on ventricular height, area and volume (De Hann et al. 1994; Kii et al. 1997; Vite et al. 1997; Vullo et al. 1997; Esteve-Ratsch et al. 2001; Woo et al. 2010; Pivetta et al. 2013). All three measurement methods have statistical significance. The parameters for comparison of ventricle size among cats have not been widely investigated (Przyborowska et al. 2017b).

The calculated ratios reached $VH/BH < 14\%$ and $VV/VB < 5\%$ in healthy cats. In this study, ventricular alterations were also evaluated with the involvement of analytical methods. Our work involving a population of cats with dilated lateral ventricles may confirm previously published findings. Based on resulting values, ventricles classified as dilated reached $VH/BH > 14\%$, and $VV/BV > 4.5\%$ in 17/20 cats (85%). Our findings could contribute to the development of reliable standards for the diagnosis of ventriculomegaly or hydrocephalus in cats. It should be noted, however, that the described values are not absolute because they can be influenced by breed, age and ventricular symmetry (Przyborowska et al. 2017b).

In the present study, ventricular alterations in European Shorthair cats with neurological disorders were evaluated using low-field MRI and high-field MRI. As physiological abnormalities were observed, the variations in the total ventricular volume in 85% of symptomatic cats were attributed to ventriculomegaly. The quantitative ratios of ventricular size in patients differed between the two examination methods. However, the differences between the results of low-field and high-field MRI were not statistically significant, and would not therefore influence the interpretation of results. Our findings could contribute to the better diagnosis of feline hydrocephalus; however, diagnosis of hydrocephalus in cats should not be only based upon the presence of large lateral ventricles.

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