Use of Contrast-Enhanced Fluid-Attenuated Inversion Recovery Sequence to Detect Brain Lesions in Dogs and Cats

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Background: The diagnostic value of a contrast-enhanced T2-weighted FLAIR sequence (ceFLAIR) in brain imaging is unclear.

Hypothesis/Objectives: That the number of brain lesions detected with ceFLAIR would be no greater than the sum of lesions detected with nFLAIR and ceT1W sequence.

Animals: One hundred and twenty-nine animals (108 dogs and 21 cats) undergoing magnetic resonance imaging (MRI) of the head between July 2010 and October 2011 were included in the study.

Methods: A transverse ceFLAIR was added to a standard brain MRI protocol. Presence and number of lesions were determined based on all available MRI sequences by 3 examiners in consensus and lesion visibility was evaluated for nFLAIR, ceFLAIR, and ceT1W sequences.

Results: Eighty-three lesions (58 intra-axial and 25 extra-axial) were identified in 51 patients. Five lesions were detected with nFLAIR alone, 2 with ceT1W alone, and 1 with ceFLAIR alone. Significantly higher numbers of lesions were detected using ceFLAIR than nFLAIR (76 versus 67 lesions; $P = 0.04$), in particular for lesions also detected with ceT1W images (53 versus 40; $P = .01$). There was no significant difference between the number of lesions detected with combined nFLAIR and ceT1W sequences compared to those detected with ceFLAIR (82 versus 76; $P = .25$).

Conclusion and Clinical Importance: Use of ceFLAIR as a complementary sequence to nFLAIR and ceT1W sequences did not improve the detection of brain lesions and cannot be recommended as part of a routine brain MRI protocol in dogs and cats with suspected brain lesions.

Key words: Contrast enhancement; Intracranial lesions; Magnetic resonance imaging.

The acquisition of a fluid-attenuated inversion recovery sequence (FLAIR) is essential in brain magnetic resonance imaging (MRI) because heavy T2 weighting in combination with suppression of the cerebrospinal fluid signal improves lesion detection, especially in the vicinity of cerebrospinal fluid spaces.[1–5] The signal intensity in FLAIR depends on both T1- and T2 relaxation times. As paramagnetic contrast media result in shortening of T1- and, to a lesser extent, T2 relaxation times, enhancement of lesions may be seen in contrast-enhanced FLAIR sequences (ceFLAIR).[6,7] However, as the T2 relaxation time of the lesion itself also influences signal intensity in ceFLAIR, lesion visibility might be reduced in some cases.[8] As a result, the diagnostic value of ceFLAIR to detect brain disease in human medicine is controversial.[9–17] In veterinary medicine, ceFLAIR is superior to precontrast FLAIR sequences (nFLAIR) and contrast-enhanced T1-weighted (ceT1W) sequences for the detection of brain lesions.[5] Lesion detection with

Abbreviations:

ceFLAIR	contrast-enhanced fluid-attenuated inversion recovery sequence
ceT1W	contrast-enhanced T1-weighted
FLAIR	fluid-attenuated inversion recovery sequence
MRI	magnet resonance imaging
nFLAIR	precontrast fluid-attenuated inversion recovery sequence
T	tesla
T1W	T1-weighted
T2W	T2-weighted

ceFLAIR depends on both the visibility of lesions with nFLAIR and contrast enhancement. The extent to which lesion detection can be improved by ceFLAIR compared to the combined evaluation of nFLAIR and ceT1W sequences is therefore unclear. If ceFLAIR does not improve lesion detection, it might prove to be a time-consuming procedure with little additional diagnostic benefit.

The objective of this study was to evaluate the diagnostic value of ceFLAIR as a supplementary sequence to nFLAIR and ceT1W sequences for the detection of brain lesions in dogs and cats. Our hypothesis was that the number of lesions detected with ceFLAIR would be no greater than the sum of lesions detected with nFLAIR and ceT1W images. We further hypothesized that when lesions are detected with ceFLAIR but not with nFLAIR, this is because of T1-dependent contrast enhancement, and these lesions are detected with ceT1W sequences.

Materials and Methods

Dogs and cats undergoing MRI of the head between July 2010 and October 2011 were included in the study. Of 129 animals

(108 dogs and 21 cats), 13 were examined for disorders unrelated to the central nervous system (aural, ocular, or nasal disease) and 116 were examined for suspected brain disease.

Forty animals were examined in a low-field MRI scanner (0.3 tesla [T])[a] and 89 animals in a high-field scanner (1.5 T[b]) because the magnet was changed during the study period. The mean acquisition time of FLAIR was 6.2 minutes (range 5–10 minutes) in the low-field scanner and 3.9 minutes (range 3–5 minutes) in the high-field scanner. The standard brain MRI protocol used consisted of T2-weighted (T2W) spin-echo sequences in sagittal and transverse planes (echo time 100–125 ms, repetition time 1,845–8,048 ms), nFLAIR in transverse and dorsal planes (echo time 90–125 ms, repetition time 6,000–8,031 ms, inversion time 2,000 ms), and T1W spin-echo sequences in transverse and dorsal planes (echo time 12–15 ms, repetition time 30–600 ms).[18] After intravenous administration of 0.15 mmol/kg gadodiamide,[c] ceT1W sequences in transverse and dorsal planes were performed, followed by a ceFLAIR in a transverse plane and, finally, a delayed ceT1W sequence in a dorsal plane. The presence and number of lesions was evaluated on all MRI sequence by 3 examiners (K.M., J.L., and D.G.) in consensus. The examiners were unaware of animal information, including signalment, history, physical, and complete neurologic examination.

Lesions were classified as intra- or extra-axial. Lesions with both extra- and intra-axial components were considered extra-axial. Lesions were further defined as focal or multifocal. Diffuse lesions were considered as a single lesion. Enlargement of internal and external cerebrospinal fluid spaces and lesions outside of the brain cavity were not evaluated. Contrast enhancement on all ceT1W images (2 sequences before ceFLAIR and 1 after) was evaluated as present or absent with the help of subtraction images. Finally, the visibility of each lesion identified on any sequence was assessed on the transverse images of nFLAIR, ceFLAIR, and ceT1W images.

Data were analyzed by statistical software.[d] Lesion visibility within the different sequences was considered as dependent data. Differences in the number of detected lesions among the sequences were tested using McNemar's test using the R-function McNemar exact.[19] The level of significance was set to $P \leq 0.05$.

Results

MRI evaluation of all available sequences revealed lesions in 51 of 116 animals evaluated for suspected brain disease and 0 of 13 animals evaluated for other reasons. Of the 51 animals with lesions, 40 had a single lesion and 11 had 2 or more lesions. A total of 83 lesions (58 intra-axial and 25 extra-axial) were identified in 51 animals in at least 1 of the sequences (Table 1). Contrast enhancement was visible on ceT1W images in 55 lesions (30/58 intra-axial and 25/25 extra-axial) (Table 1, Fig 1). The enhancement was detected in 41/55 (75%) lesions with the high-field magnet and 14/28 (50%) lesions with the low-field magnet. A histopathologic diagnosis was available in 16 animals (3 biopsies and 13 necropsies).

One lesion was detected only with ceFLAIR and was not visible on nFLAIR and ceT1W images (Fig 1). Regarding all cases, no significant difference in lesion detection was found between ceFLAIR and the combination of nFLAIR and ceT1W images ($P = .25$). The sole lesion detected only with ceFLAIR was 1 of 10 multifocal lesions in a Maltese dog. This lesion was visible on T2W images. Five lesions were detected only

Table 1. Brain lesions detected with magnetic resonance imaging based on sequence type, field strength, location, and contrast enhancement.

	Number of Lesions	Number of Lesions Detected in		
		ceT1W	nFLAIR	ceFLAIR
Total	83	55	67	76
Field strength				
Low field	28	14	27	25
High field	55	41	40	51
Location				
Extra-axial	25	25	17	23
Intra-axial	58	30	50	53
Contrast enhancement				
Nonenhancing	28	0	28	23
Enhancing	55	55	40	53

ceT1W, contrast-enhanced T1-weighted; nFLAIR, precontrast fluid-attenuated inversion recovery sequence; ceFLAIR, contrast-enhanced fluid-attenuated inversion recovery sequence.
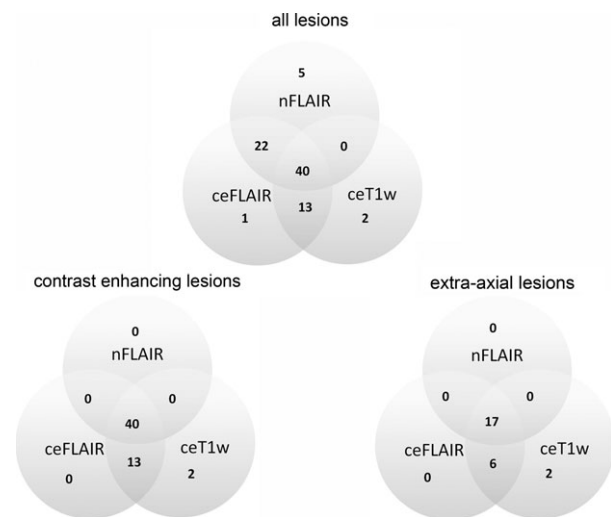

Fig 1. Magnetic resonance imaging detection of all lesions, contrast-enhancing lesions, and extra-axial lesions. nFLAIR, precontrast fluid-attenuated inversion recovery sequence; ceFLAIR, contrast-enhanced fluid-attenuated inversion recovery sequence; ceT1W, contrast-enhanced T1-weighted.

with nFLAIR (Fig 1). These were all intra-axial lesions in 3 small-breed dogs (Jack Russell Terrier, Yorkshire Terrier and Brittany Spaniel) with multifocal brain disease. These lesions were all small but visible on T2W images. Two lesions were detected only with ceT1W images (Fig 1). These lesions were extra-axial and visible with low signal intensity on T2W images.

A significantly higher number of lesions was detected with ceFLAIR compared to nFLAIR ($P = .04$) (Table 1, Fig 1). This difference was more obvious for lesions detected with ceT1W images ($P = .01$), but not for lesions undetected with ceT1W images ($P = 1.00$). Also, this difference was significant for extra-axial lesions ($P = .03$), all of which were contrast enhancing,

but not for intra-axial lesions ($P = 1.00$). Lastly, this difference was significant for animals examined with the high-field scanner ($P = .02$), but not for animals examined with low-field scanner ($P = 1.00$).

Discussion

Findings of the present study suggest that ceFLAIR does not significantly improve lesion detection beyond that of both ceT1W sequence and nFLAIR in combination. In the present study, ceFLAIR was superior to either ceT1W sequence or nFLAIR in detecting brain lesions in dogs and cats, corroborating findings of a previous study in which 48 lesions were detected with ceT1W, 71 with nFLAIR, and 81 with ceFLAIR in 46 dogs and cats, but the superiority of ceFLAIR above a combination of both nFLAIR and ceT1W was not evaluated.[5] The advantages of ceFLAIR are disputed in human neuroradiology, in part because the sequence combines the effects of ceT1W images and T2W nFLAIR such that the observed hyperintensity may be because of lengthening of T2- or shortening of T1 relaxation times.[8,9,20,21] The latter could be greater in ceFLAIR than ceT1W sequences as some evidence suggests a greater sensitivity of ceFLAIR to gadolinium.[22] However, as the effects of lengthening of T2- and shortening of T1 relaxation times interact and can even cancel each other out, ceFLAIR should not be performed in isolation.[8] Instead, ceFLAIR is generally considered an additional supplementary sequence. If a standard protocol is to be supplemented with an additional sequence, the extra cost and time for this should be justified by clinically useful information conferred only by the additional sequence.

In the present study, only 1 lesion was detected with ceFLAIR but not with nFLAIR or with ceT1W images and several lesions were detected with nFLAIR alone although these lesions were all detected with T2W images. Furthermore, several lesions were detected with either ceFLAIR or nFLAIR, but not with both. Possible reasons for the discrepancy between findings with nFLAIR and ceFLAIR include differences in sequence parameters, such as spatial resolution, slice alignment, imaging plane, or contrast resolution. A higher signal-to-noise ratio might explain differences in spatial resolution between T2W sequences and FLAIR, but spatial resolution of nFLAIR and ceFLAIR was identical. However, small differences in slice alignment among the sequences because of breathing or movement cannot be fully ruled out. In addition, small lesions could be affected by partial volume averaging rendering them indistinct or invisible, especially when only a single plane is evaluated. In the present study, nFLAIR and ceT1W sequences were performed in 2 planes, but ceFLAIR was only performed in a transverse plane because of time restrictions and this may have decreased the sensitivity of lesions detection on ceFLAIR. However, the transverse plane in which ceFLAIR was performed is considered to be the most informative in assessing meningeal enhancement in dogs and cats.[23]

Greater numbers of lesions were detected with ceFLAIR compared to nFLAIR. This was found to be true for lesions displaying contrast enhancement with ceT1W images and those with extra-axial location. Contrast enhancement occurs in lesions with high vascularization or when the blood–brain barrier is disrupted, enabling contrast to enter the interstitial space.[24] The resulting shortening of T1 relaxation time explains the hyperintensity of these lesions in ceFLAIR and its superiority over nFLAIR for lesion detection. As contrast enhancement is also a feature of structures located outside of the blood–brain barrier, it is expected in extra-axial lesions.[9,25] This was also found in the present study, in which extra-axial lesions all showed enhancement on ceT1W images and were more often detected with ceFLAIR than with nFLAIR. As lesions with both extra-axial and intra-axial components were at least partially outside of the blood–brain barrier and were expected to show contrast enhancement, these were grouped with extra-axial lesions for data analysis.

One advantage of ceFLAIR compared to ceT1W images in extra-axial lesions is better differentiation of enhancing meninges from cortical veins because slow-flowing blood is usually not hyperintense on ceFLAIR.[9,10,13,15,16,26] This could be an argument for a supplemental ceFLAIR sequence, but recent studies have shown that a ceT1W sequence with fat suppression is superior to ceFLAIR for meningeal lesions because it combines the advantages of suppression of the fat signal with shortening of T1 relaxation time.[23,27] A ceFLAIR is, however, still justified for these lesions when using low-field systems that may suffer from unsatisfactory quality of ceT1W sequences with fat suppression. Moreover, 2 extra-axial lesions in the present study were seen exclusively on ceT1W images. These lesions had low signal intensity on T2W images. These may have been undetectable because signal intensity in FLAIR depends in part on T2 relaxation time, which may be short in some lesions, including meningiomas. Given that these lesions may be missed, ceFLAIR cannot replace ceT1W images.[11,12,14] Another potential advantage of ceFLAIR compared to ceT1W sequences described in humans is a better delineation of cerebral tumors as well as a better delineation of enhancing and nonenhancing tumor parts.[20,21] This was not evaluated in the present study as only lesion detection was assessed. However, previous studies have not corroborated this finding in veterinary medicine.[5]

As contrast enhancement of intracranial lesions is a dynamic process, detection of enhancement is influenced by the time between contrast administration and sequence acquisition. To diminish the effect of time after contrast administration, ceFLAIR was performed after a transverse and dorsal ceT1W sequence, but before a delayed ceT1W sequence. This may, however, have increased the relative sensitivity of the ceT1W sequence compared to ceFLAIR.

The replacement of the 0.3-T by a 1.5-T magnet during the study period limited homogeneity within

the study population. The higher number of contrast-enhancing lesions detected with the high-field magnet may be because of greater shortening of T1 relaxation time in the presence of gadodiamide in high-field scanners, which may improve contrast enhancement and lesion detection.[28] However, it is also possible that differences in detection were merely because of different types of lesions between animals evaluated in the low- and high-field scanners. Low-field scanners are still widely used in veterinary medicine, especially in private veterinary centers.[29] The main concern of lower field strength is a lower signal-to-noise ratio and the accompanying longer sequence acquisition time, which was evident in the present study.

One limitation to this study was that the true number of lesions was not known and a gold standard was therefore lacking. Moreover, a histopathologic diagnosis was available in so few cases that this was not further evaluated. Including only cases with histologically confirmed lesions may have introduced a bias regarding etiology or severity of brain disease. MRI sequences were evaluated in consensus and not independently by the 3 observers. Independent evaluation would have increased the objectivity of the results and might have resulted in valuable information regarding the reliability of the assessed sequences. However, evaluation of a diagnostic test in absence of a true gold standard limits interpretation of interrater agreement.

The evaluation was done on isolated sequences followed by evaluation of each lesion identified in all other sequences. Only those lesions in which the 3 examiners came to a consensus as being true lesions and not artifact were evaluated. This is important as image artifacts and hyperintensities at the ventricular border are commonly reported findings in ceFLAIR.[8,17,30,31] Therefore, inclusion of a control group is important, however, in the present study, a group of 13 animals presented because of disorders unrelated to the central nervous system served as control group without histologically confirmation of normal brain tissue.

In conclusion, findings of the present study suggest that inclusion of ceFLAIR in a MRI brain protocol in which nFLAIR and ceT1W sequence are performed does not significantly increase lesion detection. Moreover, contrast enhancement, and therefore also extra-axial location, may be useful to predict lesion visibility with ceFLAIR. Further studies are necessary to evaluate to what extent supplementary ceFLAIR confers clinically useful information above that of nFLAIR and ceT1W in certain types of brain lesions in small animals.

Footnotes

[a] Hitachi AIRIS II, Hitachi Medical Systems, Düsseldorf, Germany
[b] Phillips Interna 1.5T, Phillips Medical Systems, Best, Netherlands
[c] Omniscan, GE Healthcare, Munich, Germany
[d] R Development Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria, URL http://www.R-project.org/

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