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Exclusion of a Brain Lesion: Is Intravenous Contrast Administration Required after Normal Precontrast Magnetic Resonance Imaging?

E.J. Ives, N. Rousset, N. Heliczer, M.E. Herrtage, and A.E. Vanhaesebrouck

Background: No evidence-based guidelines are available for the administration of gadolinium-based contrast media to veterinary patients.

Objective: To investigate whether administration of intravenous (IV) contrast media alters the likelihood of identifying a brain lesion in dogs and cats.

Animals: Four hundred and eighty-seven client-owned animals referred for investigation of intracranial disease.

Methods: Two reviewers retrospectively analyzed precontrast transverse and sagittal T1-weighted (T1W), T2-weighted, and fluid-attenuated inversion recovery low-field MRI sequences from each patient for the presence of a clinically relevant brain lesion. All sequences subsequently were reviewed in the same manner with additional access to postcontrast T1W images.

Results: Of the 487 precontrast MRI studies, 312 were judged to be normal by 1 or both reviewers. Of these 312 studies, a previously undetected lesion was identified in only 6 cases (1.9%) based on changes observed on postcontrast sequences. Final diagnoses included meningoencephalitis of unknown origin (n = 1), feline infectious peritonitis (n = 1), and neoplasia (n = 2). All 4 of these cases had persistent neurological deficits suggestive of an underlying brain lesion. Contrast enhancement observed in the 2 other cases was considered falsely positive based on the results of further investigations.

Conclusions and Clinical Importance: In patients with normal neurological examination and normal precontrast MRI, the subsequent administration of IV gadolinium-based contrast media is highly unlikely to disclose a previously unidentified lesion, calling into question the routine administration of contrast media to these patients. However, administration still should be considered in animals with persistent neurological deficits suggestive of an underlying inflammatory or neoplastic brain lesion.

Key words: Gadolinium; Intracranial; Meningoencephalitis; Neuroimaging.

Chelates of gadolinium are the most commonly used IV contrast media in magnetic resonance imaging (MRI). Their administration has been widespread in both human and veterinary medicine since gadopentetate dimeglumine first became available for clinical use in 1988.[1] Gadolinium-based contrast media act as paramagnetic substances, shortening the T1-relaxation time of adjacent protons with resultant hyperintensity at regions of contrast media accumulation on subsequent imaging.[2] Contrast accumulation may occur in pathological tissues because of disruption of the blood–brain barrier, vasodilatation or neovascularization.[2,3]

The findings observed on postcontrast sequences may assist in the further characterization of a brain lesion observed on precontrast sequences.[3–5] However, the routine administration of gadolinium-based contrast media has been questioned for human patients, especially if no lesion is observed on precontrast sequences.[6] Suspected adverse reactions related to administration of these agents have been reported in humans and dogs,[7–12] and both increased scanning time and duration of general anesthesia, together with their associated costs, also should be considered.

Abbreviations:

CNS	central nervous system
CSF	cerebrospinal fluid
CT	computed tomography
FLAIR	fluid-attenuated inversion recovery
MRI	magnetic resonance imaging
T	Tesla
T1W	T1-weighted
T2W	T2-weighted
TE	echo time
TR	repetition time

No evidence-based guidelines currently exist for the IV administration of gadolinium-based contrast media to veterinary patients. The aim of this study was to determine whether the absence of a visible lesion on precontrast T1-weighted (T1W), T2-weighted (T2W), and T2W-fluid-attenuated inversion recovery (FLAIR) sequences can exclude the presence of MRI-detectable intracranial pathology, thus questioning routine IV administration of contrast media to these patients.

Materials and Methods

Case Selection

A retrospective search of the MRI database at The Queen's Veterinary School Hospital, University of Cambridge, United Kingdom was performed for all brain MRI scans of dogs or cats acquired between March 2004 and June 2012. Cases were

From The Queen's Veterinary School Hospital, Department of Veterinary Medicine, University of Cambridge, Cambridge, UK (Ives, Rousset, Heliczer, Herrtage, Vanhaesebrouck). Presented as a clinical research abstract at the European College of Veterinary Neurology Symposium September 27–28, 2013, Paris, France.

Corresponding author: E.J. Ives, The Queen's Veterinary School Hospital, Department of Veterinary Medicine, University of Cambridge, Cambridge CB30ES, UK; email: eji21@cam.ac.uk.

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included if precontrast transverse and sagittal T1W and T2W images, transverse FLAIR images, and postcontrast transverse and sagittal T1W images were acquired. Any additional image planes or sequences were excluded from the analysis.

To match the normal clinical environment at the authors' institution, clinical data for each patient were extracted from the original radiology request form and were available to each reviewer at the time of image analysis. These data included species, breed, age at the time of imaging, sex, and the indication(s) for imaging. The indications for imaging were grouped into categories of presenting clinical signs based upon the findings of complete general clinical and neurological examinations performed by a board-certified neurologist in all cases (Table 1).

All data were acquired and entered into a spreadsheet format using commercial software.[a] Case selection and data acquisition were performed by 2 investigators not involved in the image analysis (EI, NH).

Magnetic Resonance (MR) Imaging

All imaging was performed under general anesthesia at the authors' institution using a 0.2 Tesla (T) permanent magnet[b] before October 2008 and a 0.23 T permanent magnet after that time.[c] MR images of the brain were acquired using different transmitter-receiver coils dependent on the patient's head size. Acquisition parameters for each sequence were as follows: T1W repetition time (TR) 600–800 ms, echo time (TE) 18–26 ms; T2W TR 2,800–3,000 ms, TE 80 ms; FLAIR TR 5,840–7,000 ms, TR 80 ms. Slice thickness for all sequences was 4 mm. Contrast studies were performed immediately after IV bolus administration of 0.1 mmol/kg gadobenate dimeglumine[d] before October 2008 and 0.1 mmol/kg gadobutrol after that time.[e]

Image Analysis

For each case, precontrast sagittal and transverse T1W and T2W images and transverse FLAIR images were analyzed independently by a board-certified neurologist (AV) and a third-year European College of Veterinary Diagnostic Imaging residency-trained radiologist (NR) using digital imaging software.[f] If a lesion was identified, each reviewer was asked to specify in which sequence(s) it was visible. A clinically relevant lesion was defined as a structural abnormality, mass lesion, abnormal signal intensity or some combination of these that could account for the indication for imaging. At the reviewer's discretion, changes observed could be classified as incidental if deemed artifactual, breed-related or incompatible with the presenting signs. These changes included mild ventricular asymmetry in the absence of a mass effect, bilateral T2W hyperintensity of the piriform lobes if deemed postictal, and mild cerebellar herniation in conjunction with Chiari-like malformation in breeds such as the Cavalier King Charles Spaniel. A case was determined to have a normal precontrast MRI study if no lesion was observed on T1W, T2W, and FLAIR sequences to account for the indication for imaging. If a clinically relevant lesion was observed on ≥1 of the sequences above, then the precontrast assessment was classified as abnormal by that reviewer.

Three months after initial assessment, a second analysis was performed for all cases by the same reviewers, but with the additional inclusion of sagittal and transverse T1W images acquired after administration of gadolinium-based contrast media. Contrast enhancement of the pituitary gland, choroid plexus or trigeminal nerves could be rated as nonpathologic if deemed within normal limits.[13,14] Reviewers were asked to indicate if any abnormal contrast enhancement was visible on postcontrast sequences and to classify the entire study, with access to all sequences, as either normal or abnormal based on the presence of a clinically relevant brain lesion.

Table 1. Categorized indications for imaging.

Indication for Imaging	Number of Dogs	Number of Cats	Total Number (% of Total)
Seizures	227	20	247 (51)
Behavior change	65	12	77 (16)
Vestibular signs	59	12	71 (15)
Ataxia	39	9	48 (10)
Reduced level of mentation	36	4	40 (8)
Cranial nerve deficits	38	1	39 (8)
Paresis	24	6	30 (6)
Blindness	22	7	29 (6)
Polyuria/polydipsia	21	2	23 (5)
Collapsing episodes	12	1	13 (3)
Anisocoria	8	3	11 (2)
Cerebellar signs	7	1	8 (2)
Tremors	6	2	8 (2)
Postural reaction deficits	5	2	7 (1)
Multifocal central nervous system signs	3	–	3 (1)

Acquisition of Additional Clinical Data

The results of further investigations (including hematology, serum biochemistry, cerebrospinal fluid analysis [CSF] and histopathologic data when available), follow-up information, and the final presumptive or definitive clinical diagnoses, were retrieved from the clinical records for all MRI studies that either reviewer had rated as normal during the first assessment, but had subsequently rated as abnormal after additional access to postcontrast images.

Results

Study Population

The initial database search identified 551 brain MRI studies that fulfilled the inclusion criteria. Sixty-four studies subsequently were excluded because of inadequate medical records or lack of access to all sequences. Four hundred and eighty-seven cases were available for complete analysis, comprising 433 dogs and 54 cats.

Median age for the dogs was 6 years (range, 3 months to 15 years), with 247 male (57%) and 186 female (43%) dogs. Breeds represented included Labrador Retriever (n = 56, 13%), Boxer (n = 36, 8.3%), mixed breed (n = 34, 7.9%), German Shepherd (n = 25, 5.8%), Border Collie (n = 22, 5.1%), and 60 other breeds with ≤20 dogs each.

Median age for the cats was 7 years (range, 4 months to 16 years) with 31 male (57%) and 23 female (43%) cats. Breeds represented included Domestic Shorthair (n = 26, 48%), Domestic Longhair (n = 7, 13%), British Shorthair (n = 7, 13%), and 9 other breeds with ≤2 cats each.

The categorized indications for imaging and the numbers of animals for which each category was applicable are summarized in Table 1.

Precontrast Assessment

A total of 281 cases (58%) were deemed to have normal precontrast MRI studies by both reviewers. A clinically relevant lesion was observed in 175 cases (36%) by both reviewers. A single reviewer reported a normal precontrast MRI study in an additional 31 cases (6%), resulting in overall interobserver agreement of 94%.

Assessment after Inclusion of Postcontrast Sequences

A total of 288 cases (59%) were deemed to have a normal complete MRI study by both reviewers. A clinically relevant lesion was identified in 177 cases (36%) by both reviewers. A single reviewer reported a normal MRI study in the additional 22 cases (5%), resulting in interobserver agreement of 95%.

Identification of a Lesion Only on Postcontrast Images

Of the 312 cases rated as normal by either 1 (31 cases) or both reviewers (281 cases) at precontrast assessment, a previously undetected lesion was observed in only 6 cases (1.9%) on postcontrast sequences (in 5 cases by a single reviewer and in 1 case by both reviewers). Four of these cases had persistent neurological deficits on examination consistent with the lesion identified on postcontrast images. Diagnoses in these cases included meningoencephalitis of unknown origin in a 2-year-old dog with a mononuclear CSF pleocytosis, and a suspected basal meningioma in a 10-year-old dog with blindness. Feline infectious peritonitis and cranial nerve T-cell lymphoma in an 8-year-old dog were confirmed by postmortem histopathology and CSF flow cytometry, respectively, in 2 additional cases. Based on results of CSF analysis and subsequent disease course, the remaining 2 cases appeared to represent false positives after observed meningeal contrast enhancement. Final clinical diagnoses included idiopathic epilepsy in a cat and suspected cerebellar cortical degeneration in a young dog.

Identification of a Previously Undetected Lesion on Precontrast T1W, T2W, or FLAIR Images

In 3 dogs (1%), a lesion was identified subsequently by 1 reviewer on precontrast T1W, T2W, or FLAIR sequences (with no visible contrast enhancement) that had not been identified previously during the first assessment. The final clinical diagnoses for these cases were suspected neuraxonal dystrophy based on signalment, presenting clinical signs and MRI appearance; a small suspected forebrain glioma; and L-2-hydroxyglutaric aciduria confirmed by genetic testing.

Discussion

The results of this study indicate that if no brain lesion is observed on routine T1W, T2W, and FLAIR sequences, then the likelihood of identifying an abnormality on postcontrast sequences is low (1.9%). This questions the routine IV administration of contrast media in this situation.

Whereas this is the first study to specifically assess this dilemma for MRI in veterinary medicine, a number of studies have investigated the diagnostic role of gadolinium-based contrast media in human medicine. These studies report similar findings to the present study, with a previously unidentified lesion seen in only 3% of human patients after contrast administration when compared to precontrast T1W and T2W images.[15] When MRI was used to investigate seizure etiology in children <2 years of age, contrast media was judged essential in only 1.8% of cases, with intracranial infectious processes demonstrated or highly suspected in all cases.[16] Another report stated that IV administration of gadolinium-based contrast media may be unnecessary in human patients after negative precontrast FLAIR imaging.[6] This conclusion was based upon improved sensitivity of MRI for lesion detection from 99.5% using FLAIR images alone to 99.6% after inclusion of postcontrast sequences. Previous studies in humans also have suggested that negative FLAIR images may eliminate the need for gadolinium-enhanced T1W images in the diagnosis of intracranial infections,[17] leptomeningeal disease,[18] and in the detection of intracranial tumors.[19,20] However, a critical review of the human literature concluded that despite the widespread use of MR contrast media, no rigorous studies existed to establish a solid evidence base for their application in human medicine.[1]

The findings of this study also are similar to those reported for computed tomography (CT) of the brain in both human and equine patients. It has been reported that if the unenhanced CT scan is normal, then subsequent contrast administration may result in identification of an abnormality in only 0.5–2.7% of cases.[21–24] Published guidelines for cranial CT in human medicine conclude that it is reasonable not to administer IV contrast if there are no persistent neurological deficits and if the unenhanced scan is normal.[22]

The cases for which a brain lesion was identified only on postcontrast images in this study warrant further discussion. Although the small number of cases for which contrast was essential for lesion detection precluded statistical analysis, there was no suggestion that patient signalment should influence the decision on whether or not to administer IV contrast. However, the results show support for the administration of contrast media to patients with persistent neurological deficits that are consistent with the presence of a central nervous system (CNS) inflammatory or infectious disease.

The recommendation for the routine use of contrast media in the suspicion of CNS inflammatory disease still would apply if CSF sampling were planned

because CSF analysis may be normal in up to 10% of patients with an underlying CNS inflammatory disorder.[25] A previous veterinary study compared the sensitivity of different MRI sequences for the detection of multifocal intracranial disease and found FLAIR sequences to be the most sensitive when compared to T1W, T2W, and contrast-enhanced T1W sequences. However, the study also showed support for continued use of contrast-enhanced sequences in the investigation of this subset of patients, with 4% of dogs having MRI changes visible only after contrast administration.[26] Another study of 25 dogs with an inflammatory CSF sample reported that contrast administration identified the presence of a previously occult lesion in 8 of these cases.[27]

The results of this study also suggest that gadolinium-based contrast media may be of benefit in the identification of certain intracranial neoplasms, especially if involving the cranial nerves or if too small to result in appreciable mass effect, as seen for the case with a suspected meningioma in this study. In agreement with these findings, several authors continue to support the use of MRI contrast media in the detection of cerebral metastasis in humans.[28,29] However, lack of contrast enhancement does not exclude the presence of metastatic disease, as recently reported in a dog with metastatic cerebral adenocarcinoma.[30] The reason for lack of enhancement in this case was unknown, but suggestions included a combination of prior corticosteroid administration and increased intracranial pressure, in the presence of highly differentiated metastases.

Excluding the cat with a final diagnosis of suspected idiopathic epilepsy, all cases for which contrast administration was essential for lesion detection had neurological deficits on initial examination suggestive of an underlying pathologic lesion. It would appear therefore that for animals with neurolocalization of intracranial disease, but without persistent neurological deficits on examination, the IV administration of contrast media to patients with negative precontrast imaging is highly unlikely to identify a previously undetected abnormality. However, lesion localization and determination of both a normal neurological examination and negative precontrast imaging should be based upon careful examination of the animal and precontrast images by suitably trained and experienced neurologists and radiologists before the decision not to administer contrast is made. This approach will avoid, wherever possible, a situation where a repeated MRI scan may be required at a later date, with associated costs and the risk of repeated general anesthesia. This approach requires real-time review of precontrast imaging by a radiologist, which may not be possible in all situations.

Two of the cases for which a previously undetected lesion was observed after contrast administration appeared to represent false positives. Diffuse meningeal enhancement was observed during analysis in both cases, resulting in suspicion of meningitis to explain the indication for imaging. The subjective nature in differentiation between pathologic and nonpathologic meningeal enhancement is likely to account for these false positive results.

The purpose of this study was to compare the likelihood of lesion identification before and after IV administration of contrast media, and it does not challenge the view that the degree or pattern of contrast uptake may assist in the further characterization of a lesion already observed on precontrast images. In both human and veterinary medicine, the pattern of contrast enhancement has been used to evaluate tumor type,[4,5] predict seizure risk in cases of intracranial neoplasia,[31] and differentiate neoplastic from non-neoplastic lesions, such as postoperative scar tissue, irradiation injury, inflammation or cerebrovascular lesions.[3,32,33] However, contrast enhancement patterns do not consistently reflect the histologic features of an intracranial lesion, with no association between MR images and histologic findings in approximately 25% of cases in 1 veterinary study.[34]

An important factor to consider before administration of any substance is the potential for adverse effects. The reported incidence of adverse reactions after administration of gadolinium-based contrast agents to humans ranges from 0.004 to 5%.[7–11] The most frequent complaints include rashes, abnormal sensations at the injection site, nausea or vomiting, anxiety and headaches.[7–11] However, severe late reactions, such as nephrogenic systemic fibrosis, also may be seen.[35] Severe anaphylactoid reactions are estimated to occur in approximately 0.01% of human patients,[7] with a mortality rate of 0.0007–0.0019%.[10,36] Many of the more frequent, mild reactions may be difficult to recognize in veterinary patients, especially given the routine use of general anesthesia for MRI in veterinary medicine. There are few reports on the incidence of gadolinium-associated adverse reactions in veterinary medicine. One report described suspected anaphylactoid reactions in 3 dogs, comprising 0.2% of animals given contrast over this time period.[12] Other studies assessing the potential cardiovascular[37–39] and serum biochemical effects[40,41] of contrast administration to dogs have found no clear association between administration of these agents and adverse effects. In addition to the potential for adverse reactions, the prolongation of both scanning time and general anesthesia associated with the acquisition of postcontrast sequences also should be considered. This consideration is likely to be more relevant for low-field MRI, given the longer scan times when compared to high-field imaging.

Limitations of this study include the use of previously acquired scans rather than a randomized prospective study. However, the analysis of scans acquired during a time when gadolinium-based contrast media were routinely used at the authors' institution decreases the potential for case selection bias. The inclusion of clinical data for each case may have biased reviewer expectation as to the potential for a lesion to be present. However, a recent study found equivalent interreviewer agreement with or without

provision of clinical data for detection of brain lesions in dogs.[33]

The lack of a histopathologic diagnosis for every case means that sensitivity and specificity for contrast administration cannot be determined. For this reason, a definitive diagnosis was available only for 2 of the cases in which a lesion was observed only on contrast-enhanced sequences. The final diagnoses in the other 4 cases were suspected based upon the results of further investigations and the subsequent disease course. However, the purpose of the present study was to mimic a clinical situation and provide data to guide clinicians at the time of imaging as to whether IV administration of contrast media to patients with negative precontrast imaging will increase the likelihood of identifying a previously undetected lesion. Reviewer consensus on the presence of a lesion was not determined at the end of analysis in this study. Consideration was given to any case in which either reviewer had identified a previously undetected lesion. This approach was used in an attempt to present the most realistic scenario as to the proportion of cases for which a lesion may be missed should contrast not be administered. In this study, there was only a single case for which both reviewers independently identified a previously undetected lesion (0.4%). This case appeared to represent a false positive, with a final diagnosis of feline idiopathic epilepsy.

Although the results of this study are similar to those reported in human medicine, conclusions can only be drawn for low-field brain MRI in dogs and cats. Results may be dependent on magnetic field strength and sequence parameters.[42,43] The use of contrast-enhanced FLAIR images,[44] digital subtraction images, delayed image acquisition,[14,45–47] different doses[47,48] or other types of gadolinium-based contrast media[49] also may influence lesion detection. In this study, there was no suggestion that the utility of postcontrast sequences for lesion detection is dependent on low field magnet strength (0.2 T versus 0.23 T) or the use of different contrast agents (gadobenate dimeglumine versus gadobutrol). A previous study in the human medical literature also concluded that whereas higher field strength magnets offer greater lesion enhancement for a given dose of gadolinium-based contrast media, this does not result in a clinically relevant difference in lesion detection.[50] The possibility that previous corticosteroid administration could have resulted in a reduction in blood-brain barrier permeability and thus decreased the number of cases with observed contrast enhancement also cannot be excluded.[51,52]

In conclusion, results of this study call into question the IV administration of gadolinium-based contrast agents to patients with a normal neurological examination and no visible lesion on precontrast imaging. However, the authors recommend that contrast administration still be considered if there are persistent neurological deficits on examination consistent with the presence of underlying pathology, such as CNS inflammatory or neoplastic disease.

Footnotes

[a] Excel 2010; Microsoft Corp, Redmond, WA
[b] Esaote VetMR spa, Genova, Italy
[c] Esaote VetMR Grande, Genova, Italy
[d] MultiHance 0.5 mol/L, Bracco spa, Milan, Italy
[e] Gadovist 1 mol/L; Bayer plc, Newbury, Berkshire, UK
[f] Visbion, Surrey, UK

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References

1. Breslau J, Jarvik JG, Haynor DR, et al. MR contrast media in neuroimaging: A critical review of the literature. Am J Neuroradiol 1999;20:670–675.

2. Sage MR, Wilson AJ, Scroop R. Contrast media and the brain–The basis of CT and MR imaging enhancement. Neuroimaging Clin N Am 1998;8:695–707.

3. Smirniotopoulos JG, Murphy FM, Rushing EJ, et al. Patterns of contrast enhancement in the brain and meninges. Radiographics 2007;27:525–551.

4. Kraft SL, Gavin PR, DeHaan C, et al. Retrospective review of 50 canine intracranial tumours evaluated by magnetic resonance imaging. J Vet Intern Med 1997;11:218–225.

5. Ródenas S, Pumarola M, Gaitero L, et al. Magnetic resonance imaging findings in 40 dogs with histologically confirmed intracranial tumours. Vet J 2011;187:85–91.

6. Saleh A, Wenserski M, Cohnen M, et al. Exclusion of brain lesions: Is MR contrast medium required after a negative fluid attenuated inversion recovery sequence? Br J Radiol 2004;77:183–188.

7. Li A, Wong CS, Wong MK, et al. Acute adverse reactions to magnetic resonance contrast media: Gadolinium chelates. Br J Radiol 2006;79:368–371.

8. Dillman JR, Ellis JH, Cohan RH, et al. Frequency and severity of acute allergic-like reactions to gadolinium-containing IV contrast media in children and adults. Am J Roentgenol 2007;89:1533–1538.

9. Abujudeh HH, Kosaraju VK, Kaewlai R. Acute adverse reactions to gadopentetate dimeglumine and gadobenate dimeglumine: Experience with 32,659 injections. Am J Roentgenol 2010;194:430–434.

10. Prince MR, Zhang H, Zou Z, et al. Incidence of immediate gadolinium contrast media reactions. Am J Roentgenol 2011;196:138–143.

11. Carollo BR, Runge VM, Price AC, et al. The prospective evaluation of Gd-DPTA in 225 consecutive cranial cases: Adverse reactions and diagnostic value. Magn Reson Imaging 1990;8:381–393.

12. Girard NM, Leece EA. Suspected anaphylactoid reaction following intravenous administration of a gadolinium-based contrast agent in three dogs undergoing magnetic resonance imaging. Vet Anaesth Analg 2010;37:353–356.

13. Pettigrew R, Rylander H, Schwarz T. Magnetic resonance imaging contrast enhancement of the trigeminal nerve in dogs without evidence of trigeminal neuropathy. Vet Radiol Ultrasound 2009;50:276–278.

14. Joslyn S, Sullivan M, Novellas R, et al. Effect of delayed acquisition times on gadolinium-enhanced MRI of the presumably normal canine brain. Vet Radiol Ultrasound 2011;52:611–618.

15. Elster AD, Moody DM, Ball MR, Laster DW. Is Gd-DPTA required for routine cranial MR imaging? Radiology 1989;173:231–238.

16. Petrou M, Foerster B, Maly PV, et al. Added utility of gadolinium in the magnetic resonance imaging (MRI) workup of seizures in children younger than 2 years. J Child Neurol 2007;22:200–203.

17. Tsuchiya K, Inaoka S, Mizutani Y, Hachiya J. Fast fluid-attenuated inversion recovery MR of intracranial infections. Am J Neuroradiol 1997;18:909–913.

18. Singer MB, Atlas SW, Drayer BP. Subarachnoid space disease: Diagnosis with fluid attenuated inversion recovery MR imaging and comparison with gadolinium-enhanced spin-echo MR imaging blinded reader study. Radiology 1998;208:417–422.

19. Husstedt HW, Sickert M, K stler H, et al. Diagnostic value of the fast-FLAIR sequence in MR imaging of intracranial tumours. Eur Radiol 2000;10:745–752.

20. Essig M, Knopp MV, Schoenberg SO. Cerebral gliomas and metastases: Assessment with contrast-enhanced fast fluid-attenuated inversion recovery MR imaging. Radiology 1999;210:551–557.

21. Demaerel P, Buelens C, Wilms G, Baert AL. Cranial CT revisited: Do we really need contrast enhancement? Eur Radiol 1998;8:1447–1451.

22. Cowan I, MacDonald S. How useful is contrast enhancement after a normal unenhanced computed tomography brain scan? Australas Radiol 1999;43:448–450.

23. Branson HM, Doria AS, Moineddin R, Shroff MM. The brain in children: Is contrast enhancement really needed after obtaining normal unenhanced CT results? Radiology 2007;244:838–844.

24. Lacombe VA, Sogaro-Robinson C, Reed SM. Diagnostic utility of computed tomography imaging in equine intracranial conditions. Equine Vet J 2010;42:393–399.

25. Tipold A. Diagnosis of inflammatory and infectious diseases of the central nervous system in dogs: A retrospective study. J Vet Intern Med 1995;9:304–314.

26. Cherubini GB, Platt SR, Howson S, et al. Comparison of magnetic resonance imaging sequences in dogs with multi-focal intracranial disease. J Small Anim Pract 2008;49:634–640.

27. Lamb CR, Croson PJ, Cappello R, Cherubini GB. Magnetic resonance imaging findings in 25 dogs with inflammatory cerebrospinal fluid. Vet Radiol Ultrasound 2005;46:17–22.

28. Singh SK, Agris JM, Leeds NE, Ginsberg LE. Intracranial leptomeningeal metastases: Comparison of depiction at FLAIR and contrast-enhanced MR imaging. Radiology 2000;217:50–53.

29. Russell EJ, Geremia GK, Johnson CE. Multiple cerebral metastasis: Detectability with Gd-DTPA-enhanced MR imaging. Radiology 1987;165:609–617.

30. Singh JB, Oevermann A, Henke D, et al. Imaging diagnosis—Lack of contrast enhancement in metastatic cerebral adenocarcinoma. Vet Radiol Ultrasound 2012;53:193–196.

31. Schwartz M, Lamb CR, Brodbelt DC, Volk HA. Canine intracranial neoplasia: Clinical risk factors for development of epileptic seizures. J Small Anim Pract 2011;52:632–637.

32. Cherubini GB, Mantis P, Martinez TA, et al. Utility of magnetic resonance imaging for distinguishing neoplastic from non-neoplastic brain lesions in dogs and cats. Vet Radiol Ultrasound 2005;46:384–387.

33. Wolff CA, Holmes SP, Young BD, et al. Magnetic resonance imaging for the differentiation of neoplastic, inflammatory, and cerebrovascular brain disease in dogs. J Vet Intern Med 2012;26:589–597.

34. Singh JB, Oevermann A, Lang J, et al. Contrast media enhancement of intracranial lesions in magnetic resonance imaging does not reflect histopathologic findings consistently. Vet Radiol Ultrasound 2011;52:619–626.

35. Marckmann P, Skov L, Rossen K, et al. Nephrogenic systemic fibrosis: Suspected etiological role of gadodiamide used for contrast-enhanced magnetic resonance imaging. J Am Soc Nephrol 2006;17:2359–2362.

36. Jung JW, Kang HR, Kim MH, et al. Immediate hypersensitivity reaction to gadolinium-based MR contrast media. Radiology 2012;264:414–422.

37. Bøkenes J, Hustvedt SO, Refsum H. Comparison of cardiovascular changes after administration of gadodiamide injection and gadopentetate dimeglumine in dogs. Acad Radiol 1997;4:204–209.

38. Wible JH Jr, Galen KP, Wojdyla JK. Cardiovascular effects caused by rapid administration of gadoversetamide injection in anaesthetised dogs. Invest Radiol 2001;36:292–298.

39. Mair AR, Woolley J, Martinez M. Cardiovascular effects of intravenous gadolinium administration to anaesthetised dogs undergoing magnetic resonance imaging. Vet Anaesth Analg 2010;37:337–341.

40. Pollard RE, Puchalski SM, Pascoe PJ. Haemodynamic and serum biochemical alterations associated with intravenous administration of three types of contrast media in anaesthetised dogs. Am J Vet Res 2008;69:1268–1273.

41. Carotenuto AM, Borghi L, Paltrinieri S, et al. Serum biochemical response to contrast media administration in anaesthetised dogs. Vet Rec 2013;172:101.

42. Robertson I. Optimal magnetic resonance imaging of the brain. Vet Radiol Ultrasound 2011;52:S15–S22.

43. Konar M, Lang J. Pros and cons of low-field magnetic resonance imaging in veterinary practice. Vet Radiol Ultrasound 2011;52:S5–S14.

44. Falzone C, Rossi F, Calistri M, et al. Contrast-enhanced fluid-attenuated inversion recovery vs. contrast-enhanced spin echo T1-weighted brain imaging. Vet Radiol Ultrasound 2008;49:333–338.

45. D'Anjou M, Carmel EN, Blond L, et al. Effect of acquisition time and chemical fat suppression on meningeal enhancement on MR imaging in dogs. Vet Radiol Ultrasound 2012;53:11–20.

46. Schorner W, Laniado M, Niendorf HP, et al. Time dependent changes in image-contrast in brain-tumours after gadolinium-DTPA. Am J Neuroradiol 1986;7:1013–1020.

47. Mathews VP, Caldemeyer KS, Ulmer JL, et al. Effects of contrast dose, delayed imaging, and magnetization transfer saturation on gadolinium-enhanced MR imaging of brain lesions. J Magn Reson Imaging 1997;7:14–22.

48. Runge VM, Kirsch JE, Burke VJ, et al. High-dose gadoteridol in MR imaging of intracranial neoplasms. J Magn Reson Imaging 1992;2:9–18.

49. Colosimo C, Ruscalleda J, Korves M, et al. Detection of intracranial metastases: A multicenter, intrapatient comparison of gadobenate dimeglumine-enhanced MRI with routinely used contrast agents at equal dosage. Invest Radiol 2001;36:72–81.

50. Davis MC. High- vs. low-field MR: What's the difference? Diagn Imaging 1998;20:28–30.

51. Ostergaard L, Hochberg FH, Rabinov JD, et al. Early changes measured by magnetic resonance imaging in cerebral

blood flow, blood volume, and blood–brain barrier permeability following dexamethasone treatment in patients with brain tumours. J Neurosurg 1999;90:300–305.

52. Zaki HS, Jenkinson MD, Du Plessis DG, et al. Vanishing contrast enhancement in malignant glioma after corticosteroid treatment. Acta Neurochir 2004;146:841–845.