So you have got a brain mass …….

what do we have in the MRI toolkit to help determine what it is?

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1. A review of neuroanatomy

A sound working knowledge of neuroanatomy is the foundation for MRI interpretation of brain lesions. An accurate description of the lesion will provide you with a cognitive framework to form a ranked differential diagnoses list, and equip you with key words to search the published literature for correlative examples of similar disease. Also, an understanding of the functional context of neuroanatomy will help determine if a lesion could be responsible for the presenting complaint.

Generally, the brain can be divided into the supratentorial region, which is the area rostral to the tentorium cerebelli; and the infratentorial region, which is the area caudal to the tentorium cerebelli. The brain can also be subdivided into components based on embryologic development - the telencephalon, diencephalon, mesencephalon, mesencephalon and myelencephalon. These have corresponding components of the cerebrum; thalamus and associated structures; brain stem with the midbrain forming the upper part of the brainstem, and the lower part comprising pons and medulla oblongata; and the cerebellum. Terms are sometimes used interchangeably, which can be confusing - refer to Table 1. below for classifications.

Table 1. Anatomic components of the brain

Compartment	**Embryonic classification**	**Component**		
Supratentorial	Telencephalon	Cerebrum	Cerebral cortex	Frontal lobe (with olfactory bulbs)
				Temporal lobe (with hippocampus)
				Piriform lobes (with amygdala)
				Parietal lobes
				Occipital lobes
			Subcortical white matter	Commissural fibres
				Internal capsule

				Corona radiata
			Basal nuclei (basal ganglia)	Corpus striatum = caudate nucleus, lentiform uncle = putamen and globes pallidus; Subthalamic nuclei; substantial nigra
		Ventricles	Lateral ventriclels	
	Diencephalon		Thalamus	
			Hypothalamus	
			Epithalamus	
			Subthalamus	
		Ventricles	Third ventricle	
	Pituitary gland		Adenohypophysis	
			Neurohypophysis	
Infratentorial	Mesencephalon	Midbrain or upper brainstem	Cerebral peduncles	
			Tectum	Tectal (Quadrigeminal) plate
				Rostral and caudal colliculi
			Tegmentum	Cranial nerve nuclei
		Ventricles	Mesencephalic aqueduct	
	Metencephalon		Pons	Tegmentum
			Cerebellum	
		Ventricles	Fourth Ventricle	
	Myelencephalon		Medulla oblongata	Tegmentum

2. Features of a brain mass

When a mass is identified, consideration must be given to describing its appearance and location in order to form an appropriate ranked list of differential diagnoses. Begin with categorising it as intra-axial or extra-axial. Intra-axial structures include grey and white matter of the brain parenchyma itself. Extra-axial includes the skull and meninges, the ventricular system and the pituitary gland. Various disease processes and types of neoplasms have characteristic locations, distribution, shape and signal characteristics. While there is overlap, characterising these features will permit considerable progress in narrowing down a differential diagnosis list. For further information, the interested reader is directed to a publication of Bentley, 2015.

2.1 If intra-axial, consider the position and distribution:

- solitary or multifocal
- unilateral or bilateral
    - If bilateral, is it symmetric or asymmetric
- Does it involve white matter or grey matter?

2.2 If a lesion is extra-axial, where does it originate?

- meninges
- ventricular system
- sellar/parasellar region
- olfactory region
- cranial nerves

2.3 Characterise the signal intensity on various sequences

- Homogeneous or heterogeneous
- Hyperintense, isointense or hypointense (usually relative to cerebral grey matter)
- Presence of haemorrhage - refer to special sequences such as T2*GRE or SWI (with mag, phase and MIP images)
- Presence of abnormal restricted diffusion - refer to DWI and ADC map images
- Contrast-enhancement and pattern of contrast enhancement
- Changes to the surrounding tissue
    - Mass effect or lack thereof
    - Patterns of oedema
- Changes over time

3. The importance of clinical context

Lesion identification and characterisation is the first step; it's then important to consider the clinical context and whether the lesion fits the clinical picture.

Consider neurolocalisation; are the patient's neurologic abnormalities explained by the expected dysfunction produced by a lesion in that area? If the answer is no, then there may be another as yet unidentified lesion and closer scrutiny of the study is required. The interested reader is directed to the book by Christine Thomson, "Veterinary neuroanatomy: a clinical approach" for an in-depth discussion and review of the important concepts.

Consider the signalment. What diseases are common or expected given the species, breed and age of the patient? For example, an intra-axial peripherally enhancing cerebral mass in a 10-year-old Boxer might be expected to represent a glioma, while a peripherally enhancing cerebral mass in a 5-year-old Shi Tzu might be expected to represent meningoencephalitis of unknown origin.

Consider the expected onset and progression of signs; this can be valuable to help rank differential diagnoses. For example, acute onset but improving signs might support a cerebrovascular accident, while progressive deterioration in signs might indicate a progressive neoplastic or inflammatory disease.

4. Using standard MRI features to rank differential diagnoses

An excellent review of the literature is available, which presents the imaging characteristics of canine and feline brain tumours (May 2024). The interested reader is directed to this article for an in-depth review and analysis. Note that this review is restricted to brain tumours, so other mass lesions such as meningoencephalitis of unknown origin, granuloma, or abscess are not discussed.

Table 2. Provides some general differential diagnoses based on lesion location. Further prioritisation of differential diagnoses may be aided by patterns of signal intensity, contrast enhancement, and changes to surrounding tissue.

Table 2. Typical lesion location of canine and feline solitary brain masses (adapted from May 2024)

Lesion category	Lesion location		
Solitary brain mass	Extra-axial	Meningeal-based	Meningioma
			Histiocytic Sarcoma
			Lymphoma
		Sellar and Parasellar	Pituitary origin
			Non-pituitary origin
		Intra-ventricular	Choroid plexus carcinoma OR papilloma
			Ependymoma
			Rare such as intraventricular glioma or meningioma
	Intra-axial	Neuroepithelial tumours	Oligodendroglioma
			Astrocytoma
			Variations of these
		Other uncommon to rare neoplasms	Solitary metastases
			Lymphoma
			Histiocytic Sarcoma
			Embryonal tumours
		Inflammatory	MUO
			Infectious encephalitis (including abscesses)
		Vascular	Haemorrhagic infarct
			Ischemic infarct
Multifocal brain lesions	Multifocal	Neoplasia	Metastatic neoplasia (such as haemangiosarcoma, carcinoma or melanoma)
			Lympoma
			Histocytic sarcoma

Lesion category	Lesion location		
			Multiple meningioma
			Choroid plexus carcinoma with 'drop metastases'
			Distinct Synchronous tumours
		Inflammatory	MUO
			Infectious such as Neosporosis, Toxoplasmosis, Distemper, bacterial meningoencephalitis

These MRI features are not perfectly reliable in diagnosing brain disease however. In a study of 77 dogs with brain disease and 44 control animals with idiopathic epilepsy, investigators classified cases as the most likely etiologic category (neoplastic, inflammatory or cerebrovascular), and indicated the most likely specific diagnosis (Wolff, 2012). The authors found MRI performed well for classifying neoplastic and inflammatory disease, but had low sensitivity for cerebrovascular disease. In general, there was high specificity but not sensitivity for specific brain diseases. Importantly, haemorrhage-sensitive sequences and diffusion-weighted sequences were not employed, so this may explain the poorer result for cerebrovascular accidents, as supported by the results of an earlier study (Cervera 2010).

5. 'Novel' MRI techniques

Qualitative MRI features of various brain diseases often present with an overlap of features. Novel MRI techniques can provide quantitative data to improve the characterisation of lesions and improve the diagnostic yield or prognostic ability of neuroimaging.

5.1. Diffusion-weighted imaging (DWI) and Diffusion Tensor Imaging (DTI)

Diffusion Weighted Imaging (DWI) produces the metric of the 'apparent diffusion coefficient' or ADC, while Diffusion Tensor Imaging (DTI) produces the metric of Fractional Anisotropy or FA. In dogs, the ability of DWI to differentiate brain tumours from inflammatory or vascular brain lesions has been evaluated. There is an overlap of ADC and FA values across multiple types of brain tumours, cerebrovascular disease and MUO (Sutherland Smith 2011, MacLellan 2021). A high ADC cut-off value was identified as highly specific for the diagnosis of neoplastic lesions, but sensitivity and accuracy were low (Maclellan 2021). Thus, these metrics may be of limited use to aid differentiation of these lesion categories. Other work has evaluated the use of ADC in grading tumour types within one histological type. This work has found that in dogs with meningioma, ADC values were lower in malignant meningioma compared to benign meningioma (Fages 2020). However with oligodendroglioma, there was no difference in DWI features between grades II and III oligodendroglioma (Amphimaque

2022). Recently, DWI was useful in dogs with intracranial abscesses to distinguish from cystic or necrotic neoplasms (Scherf 2022).

5.2. Perfusion weighted imaging (PWI)

Dynamic contrast-enhanced MRI has been applied to evaluate the temporal enhancement pattern of lesions. The technique provides information on blood flow, tissue vascular density, integrity, and permeability. In humans, it has been used to investigate tumour angiogenesis, tumour type and grade, hypoxia, evaluation of blood-brain barrier disruption, and the effects of therapies on brain tumours. There has been one investigation of the use of this technique in canine brain tumours (Hanael 2023). There were some methodological issues with the study design, but results showed that blood-brain barrier disruption could be quantified, and that different patterns and distributions were identified for glioma compared to meningioma.

5.3. Magnetic Resonance Spectroscopy (MRS)

Proton-Magnetic resonance spectroscopy (H-MRS) is used to quantify the concentrations of various compounds in the brain based on the resonance of protons which are not bound up in water. The spectra produced provide a chemical 'fingerprint' for a lesion, and in some circumstances can improve the specificity of a diagnosis, and in humans may be useful to predict the histological grade of some brain tumours. In dogs, proton MRS has been applied in dogs with intracranial neoplasia and inflammatory brain disease (Stadler 2014, Carrera 2016). Both publications found differences in spectra between diseased and non-diseased brain, and differences between the two disease categories. In the publication by Stadler et al., no significant metabolite differences were found in meningioma versus glioma.

5.4. Radiomics and AI

There is emerging interest in the use of machine learning and AI algorithms to categorise and classify brain lesions. Publications so far address the use of AI for grade prediction for canine meningioma, grade prediction for canine glioma, distinguishing between meningioma and glioma, and neoplastic versus inflammatory brain disease. (Cere 2024) These studies encountered difficulty in obtaining large training datasets, due to the variability in MRI protocols, which reduces the robustness of the algorithms. A shift toward standardisation of veterinary brain MRI protocols is desirable (Packer 2018).

6. Summary

With good foundation knowledge of neuroanatomy and an understanding of the common distribution and imaging characteristics of brain lesions, a reasonable, if imperfectly accurate interpretation can be made to indicate the likely diagnosis. The incorporation of diffusion-weighted imaging sequences into a standard MRI protocol permits improved accuracy in the classification of lesions as neoplastic, inflammatory or cerebrovascular accident. Other novel

approaches to brain MRI are beginning to be employed. It is hoped they will improve the specificity of diagnosis. Of particular interest is the use of Radiomics and AI, which represents a rapidly developing technology which may gain clinical use in the future.

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