Usefulness of advanced MR imaging in the canine and feline intracranial tumors

Summary of Doctoral Thesis

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The purpose of this study is to evaluate the usefulness of advanced MR imaging as a noninvasive diagnostic method to differentiate tumor type in canine and feline intracranial tumors, which are increasing to be diagnosed and treated in various ways. In the present study, the MRI data of a total 40 cases with intracranial tumors, that were presented to the Veterinary Medical Center of Nippon Veterinary and Life Science University and underwent brain surgery and obtained each definitive histopathological diagnosis from June 2011 to September 2019, were used. The obtained advanced MR imaging sequences included diffusion weighted imaging, diffusion tensor imaging, MR spectroscopy, and perfusion weighted imaging. This study evaluated whether each advanced MR sequences are useful to compare and/or characterize each tumor type, and then discussed those utilities comprehensively.

Diffusion weighted imaging (DWI) was performed in 35 cases and evaluated using apparent diffusion coefficient (ADC). At first, ADC values in the contralateral normal-appearing white matter (NAWM), that were used as a normal reference, were measured and compared between dogs and cats. As a result, ADC values of NAWM in dogs were significantly higher than those in cats. Therefore, in order to compare dogs with cats equivalently, evaluations were performed using the ADC ratio, which is a relative value obtained by dividing the tumor ADC value by the NAWM ADC value. In intratumoral regions, feline meningiomas and canine histiocytic sarcomas showed significantly lower ADC ratios compared to canine meningiomas. This finding is compatible with the actual clinical picture that histiocytic sarcoma is highly malignant and poorly prognosis. It is also consistent with the clinical fact that feline meningioma is a solid tumor. The ADC ratio for gliomas in this study was similar to the previous canine reports, and the ADC ratio for bone tumor was also identical to those of humans. In peritumoral areas, feline meningiomas had the lowest ADC ratio. This finding likely to be resulted from the strong displacement of the surrounding normal brain tissue by the tumor. However, the peritumoral ADC ratio in this study was not helpful to differentiate invasion in peritumor, and between vasogenic edema and cytotoxic edema in the area showing high signal intensity on T2-weighted images. Besides, regarding the method of setting a circular region of interest (ROI) when measuring ADC, we compared a large ROI that covers the entire tumor with a small ROI that is placed to avoid necrosis, bleeding, and calcification inside the tumor. No significant difference was found in meningiomas and bone tumor, but a significant difference was found in histiocytic sarcomas and gliomas. Therefore, when measuring intratumoral ADC, the method to setting the ROI would need to be considered depending on the tumor type.

Diffusion tensor imaging (DTI) was performed on 36 cases and evaluated using fractional anisotropy (FA). As well as DWI study, FA value of contralateral NAWM was compared between dogs and cats. The FA ratio (i.e., FA_{ROI}/FA_{NAWM}) was used for evaluation because canine FA values was significantly lower than those of cats. The intratumoral FA ratio was significantly higher in feline meningiomas than in canine meningiomas. Intratumoral FA ratio of histiocytic sarcomas was slightly lower, but was no significant difference compared to those of canine and feline meningiomas. The FA ratio of gliomas was the lowest among those of all tumors, while that of bone tumor was the highest. This finding suggests that feline meningioma and bone tumor are relatively solid tumors, and that canine and feline gliomas have variable directions of diffusion. In peritumoral areas, FA ratios of histiocytic sarcomas and gliomas were lower than those of canine and feline meningiomas. It is suspected that histiocytic sarcomas and gliomas would be infiltrating and/or destroying the surrounding brain parenchyma, while meningiomas compress surround tissues without nerve damage. Among them, peritumoral area of feline meningioma showed the highest FA ratio, because many compressed intact nerve fibers may present within the measuring ROIs. Taking the FA ratio and the ADC ratio into consideration, it might be associated with the brain remaining compressed after surgical removal of the feline meningiomas. The FA ratio in peritumoral bone tumor had the lowest value. Because bone tumor is surrounded by the cerebral cortex, the peritumoral FA ratio in bone tumor including cerebral cortex may be related to this lowest value. In the T2-weighted hyperintense region of the peritumoral area, histiocytic sarcomas showed a significantly lower FA ratio than those of canine meningiomas. Combined with the ADC ratio, it was considered that peritumoral T2 hyperintense region in histiocytic sarcoma had vasogenic edema. As with DWI study, the method of setting the ROI was examined, but there was no significant difference among all tumors. Therefore, it was suggested that both small ROI and large ROI methods are available in measuring FA values.

Magnetic resonance spectroscopy (MRS) is a specific MR sequence to measure metabolites *in vivo* non-invasively. At first, MRS of thalamus in normal dogs and cats were measured, and those results were used as the reference values for the following comparative MRS study of 15 cases with intracranial tumor. The metabolites measured in this study were lipid (Lip), lactate (Lac), alanine (Ala), N-acetyl-L-aspartate (NAA), glutamate (Glu), creatine (Cr), choline (Cho), and myo-inositol (Ins). Because Cr was reduced in all tumors, metabolites to Cr ratios were calculated using Cr value of contralateral NAWM or normal animals (if contralateral Cr measurement was not available) . Cr is absent in the meninges (meningiomas) and skulls (bone tumor), and it is considered that Cr is reduced in active cell division tissues (i.e., tumors). In addition, NAA is a neuronal marker, and glial cells and meningeal cells have little NAA originally, so NAA was reduced in all tumors of the present study. Cho was high in histiocytic sarcomas and gliomas and low in feline meningiomas and bone tumor. It was considered that all cases of glioma in this study were of high grade, and that Cho was elevated in association with active cell proliferation along with histiocytic sarcoma. Decreased Cr and NAA and increased Ala are common MRS findings in human meningioma, and those were also observed in canine and feline meningiomas in this study. However, the marked Cho peak seen in human meningioma was not observed in canine and feline meningiomas in this study, and especially, Cho was very low in feline meningiomas. The author speculates that this may be related to the prolonged growth rate of feline meningiomas. As well as human gliomas, elevated Lip and Lac were observed in canine gliomas in this study. Although this study included only malignant gliomas, this finding suggests the possibility that MRS is useful for glioma grading.

Perfusion weighted imaging (PWI) is a sequence to evaluate the hemodynamics of the brain using some parameters such as cerebral blood volume (rCBV), cerebral blood flow (rCBF), and mean transit time (MTT). In this study, PWI was performed by dynamic susceptibility contrast (DSC) method followed by intravenous administration of contrast media. Because underestimation of hemodynamics in the lesion has been reported in humans due to differences in the infusion rate (IR) of contrast media, therefore, the comparison of IR 1 ml/sec and 4 ml/sec was investigated using normal dogs and cats at first. Then, each parameter of PWI in 10 cases with intracranial tumors was evaluated. Also, in this study, each parameter was assessed as a relative value to NAWM. In normal animals, there was no difference between the left and right in each parameter, and the MTT ratio showed almost uniform values in each part of the brain. rCBV ratio and rCBF ratio showed high in the cortical area and tended to be lower in the thalamus, which was consistent with the result of the human normal brain. In normal dogs, the rCBV ratio and rCBF ratio in the hippocampus at IR 4 ml/sec were significantly increased as compared with those at IR 1 ml/sec. This finding was thought to be related to the fact that the hippocampus has abundant blood flow. Besides, the rCBV ratio in the thalamus and the MTT ratio in the cerebral cortex were significantly reduced at IR 4 ml/sec compared to IR 1 ml/sec. This result may be due to the fact the cerebral cortex has much more blood vessels than white matter. In normal cats, the rCBF ratio in the amygdala and the rCBV ratio in the thalamus and cerebral cortex significantly increased at IR 4 ml/sec compared to IR 1 m/sec. The rCBF ratio and rCBV ratio in normal cats in this study were generally lower than those of normal dogs. This finding suggested that cerebral perfusion in cats was challenging to obtain because feline cerebral blood vessels were very thin. The author supposes that fast IR may compensate poor cerebral perfusion in cats, and which could prevent underestimation of the lesion. In this study, 22 gauge and 24 gauge indwelling needles, that were placed on the cephalic vein, were tolerated to the injection at IR 4 ml/sec for dogs and cats, respectively. This suggests that PWI can be sufficiently performed during general MRI examinations in veterinary clinical practice. Among intracranial tumor cases, 6 meningiomas, 1 histiocytic sarcoma and 1 glioma were performed at IR 1 ml/sec, and 1 meningioma and 1 glioma were at IR 4 ml/sec. In the case of IR 1 ml/sec, the ratio of intratumoral rCBV and rCBF were highest in meningiomas and lowest in histiocytic sarcoma. There was no obvious difference in rCBV ratio and rCBF ratio between meningioma and glioma at IR 4 ml/sec, however, those of both tumors at IR 4 ml/sec were higher than those at IR 1 ml/sec. This result suggests that lesions may be underestimated at low IR as known in human medicine. Also, in all cases in this study, the values of each parameter were generally lower than those of humans. This fact suggests again that it is difficult to detect cerebral perfusion with PWI because the cerebral blood vessels in dogs and cats are thinner than those in humans. Also, it was challenging to assess tumor invasion or edema in the peritumoral region with PWI. Although the size of ROI was also examined in PWI, there was no significant difference in each parameter of any tumor. Therefore, it was suggested that both small ROI and large ROI methods were available in measuring PWI.

In human clinical practice, these advanced MR imaging techniques are using for tumor identification and grade classification. However, it is difficult to characterize the type of tumor using only one of these advanced MR imaging techniques, and it also has been reported that the diagnostic accuracy is improved by combining some specific sequences. In veterinary medicine where noninvasive histological diagnosis of brain tumor is difficult, the author considers that the development of these advanced MR imaging would greatly contribute to the progress of veterinary neuro-oncology and neurosurgery.