Evaluation of human brain metastases using molecular MRI based on endogenous protein-based amide proton transfer (APT) signals

Silun Wang[1], Zhibo Wen[2], Jing Gu[1], Ge Zhang[2], Xianlong Wang[2], Fanheng Huang[2], Peter C.M. van Zijl[1,3], and Jinyuan Zhou[1,3]

[1]Departments of Radiology, The Johns Hopkins University, Baltimore, MD, United States, [2]Department of Radiology, Zhujiang Hospital, Southern Medical University, Guangzhou, Guangdong, China, People's Republic of, [3]F.M. Kirby Research Center for Functional Brain Imaging, Kennedy Krieger Institute, Baltimore, MD, United States

Introduction

Brain metastases may develop in 20-40% adult cancer patients and are the most common complication of systemic cancer[1]. They show up as abnormalities on conventional MRI (e.g. T_2w and Gd-T_1w), but these image types have a limited capability to characterize tumors. Amide proton transfer (APT) imaging can generate molecular MRI signals that are based on the amide protons of endogenous mobile proteins and peptides[2,3]. Previous studies have shown that APT MRI can provide unique information about the presence and grade of malignant gliomas, separate edema from tumor[2], and differentiate between gliomas and radiation necrosis[3]. The aim of this study is to investigate APT image features of human brain metastases and compare the results with conventional MRI techniques.

Materials and methods

Nine patients (mean age ± SD = 54±16 years; 3 females; 6 males) who signed informed consent were recruited in this study. They had histologically confirmed brain metastases, including: seven lung carcinomas (four small cell lung cancer, three adenocarcinomas), one gastric adenocarcinoma, and one breast adenocarcinoma. Patients had no clinical history of previous surgery, chemotherapy, or radiotherapy. MRI was performed on a Philips 3T MRI scanner (Achieva 3.0 T) using a body coil for RF transmission and an eight-channel SENSE coil for reception. The APT imaging protocol was: RF saturation power = 3 μT; saturation time = 500 ms; slice thickness = 6 mm; matrix = 128×64; FOV = 240×240 mm^2. For quantitative analysis, ROIs were drawn according to Gd-enhanced T_1w images, and areas of signal enhancement were defined as the tumor core.

Results

Imaging characteristics of brain metastases: **Fig.1** shows the MRI results of a lung metastasis for a 58-year-old woman. T_2w MRI shows a large hyperintense lesion (compared to contralateral brain tissue) at the basal ganglia, with mass effects. The lesion is heterogeneous on T_1w MRI. Gd-T_1w imaging reveals an enhancing tumor core (red arrow). On the APT image, the most of the tumor visible on the conventional images is hyperintense (red arrow). **Fig.2** shows results for metastasis from a small cell lung cancer in a 61-year-old woman. The lesion is hyperintense on T_2w image with probable peritumoral edema (yellow arrow) and hypointense on T_1w image, with a Gd-enhancing tumor core (red arrow). APT image clearly identifies the tumor core as hyperintense (red arrow) and the peritumoral region as slightly hyperintense (yellow arrow), compared to contralateral brain tissue.

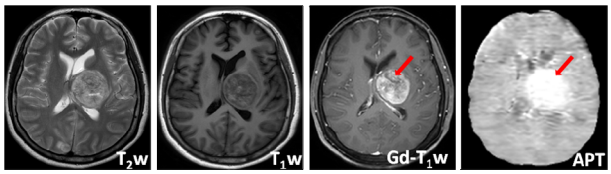

Fig. 1. Brain metastasis from lung adenocarcinoma. The Gd-enhancing tumor core (red arrow) has a mean APT signal intensity of 3.62%. The APT intensity is the percentage of the bulk water signal. The APT image was displayed using a window of -5% to 5%.

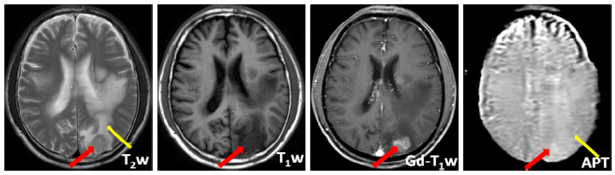

Fig. 2. A metastasis from small cell lung cancer. The Gd-enhancing tumor core (red arrow) and peritumoral T_2w-hyperintense edema (yellow arrow) have mean APT signal intensities of 2.87% and 1.76%, respectively.

Quantitative analysis of APT signal intensities: There are significantly higher APT signal intensities in the tumor core than in peritumoral regions ($p<0.01$), and than in the ipsilateral and contralateral normal appearing white matter (both $p<0.001$) (**Fig.3**). Metastases from small cell lung cancer have significantly lower APT signal intensities (2.5% ± 0.4%) than those of lung adenocarcinoma (3.3%±0.3%, $p=0.04$) and other adenocarcinomas (3.5%±0.2%, $p=0.029$) (**Fig.4**).

Conclusion

Our initial data show that APT imaging can separate tumor core and peritumoral areas (probable edema), as well as distinguish between biological features of various brain metastases (i.e., between metastases of small cell lung cancer and adenocarcinomas). Combining APT with standard MRI techniques may have potential improve the diagnostic accuracy.

References: 1. Land et al. CA Cancer J. Clin. 49, 8 (1999). 2. Wen et al. NeuroImage 51, 616 (2010). 3. Zhou et al., Nat. Med. 17, 130 (2011).

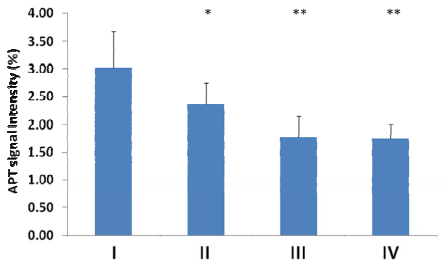

Fig. 3. Mean APT intensities plotted for several regions (n = 9). (I) Gd-enhancing tumor core; (II) peritumoral area with probable edema; (III and IV) ipsilateral and contralateral normal appearing white matter. Differences between the tumor core and other areas were compared using the one-way ANOVA test. *, $p<0.01$; **, $p<0.001$.

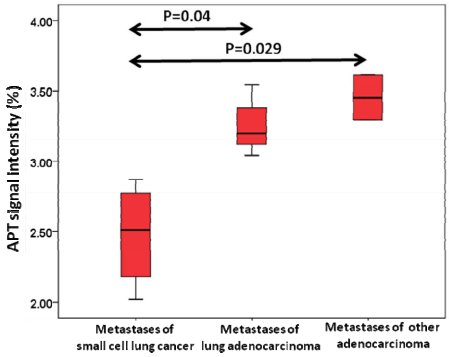

Fig. 4. Mean tumor core APT intensities plotted for different cancer types. Significant differences are found between metastases of small cell lung cancer and other brain metastases.