Towards imaging tumor cellularity: diffusion basis spectrum imaging (DBSI) and amide proton transfer (APT)

Chien-Yuan Eddy Lin[1,2], Bing Wu[2], Hung-Wen Kao[3,4], Peng Sun[5], Yong Wang[5], and Sheng-Kwei Song[5]

[1]*GE Healthcare, Taipei, Taiwan,* [2]*GE Healthcare China, Beijing, China,* [3]*Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan,* [4]*Department of Biomedical Imaging and Radiological Sciences, National Yang-Ming University, Taipei, Taiwan,* [5]*Department of Radiology, Washington University School of Medicine, St. Louis, MO, United States*

Purpose: Tumor cellularity is an important indicator of aggressiveness[1] and the efficiency of chemotherapy[2]. Amide proton transfer (APT) imaging detects the proton exchange between bulk water and the amide protons (-NH) in endogenous mobile proteins and peptides. Previous studies demonstrated that APT grading of diffuse gliomas might reflect tumor cellularity[3]. Recently, a newly developed diffusion basis spectrum imaging (DBSI) models tissue water diffusion as a linear combination of anisotropic and isotropic diffusion tensors[4], allowing the quantification of restricted and non-restricted isotropic diffusion tensor components reflecting the extent of cellularity and edema respectively. The aim of this study was to assess changes in APT and DBSI metrics in conventional MRI identified brain tumors.

Material & Methods: MRI acquisition was conducted at 3T clinical scanner (Discovery 750, GE Healthcare, Waukesha, WI, USA) using an 8-channel brain coil as the signal detection and whole body coil for RF transmission. APT imaging was obtained from a single shot, spin-echo EPI sequence with the following parameters: Saturation pulse: 100 ms × 20 fermi pulses, B1=1.6 μT. The image acquisition parameters were: TR/TE= 2500/24 ms, FOV= 20 cm, matrix size=128×128, slice thickness=4mm, 31 saturation images, S(w), w = 0, ±0.25, ±0.5, ±0.75, ±1, ±1.5, ±2, ±2.5, ±3, ±3.25, ±3.5, ±3.75, ±4, ±4.5, ±5, ±6 ppm, and S_0 (without saturation pulse), NEX=2. The APT map was calculated, with B_0 correction, as $[S(-3.5ppm) - S(+3.5ppm)]/S_0$. A spin-echo diffusion-weighted EPI sequence with a 99-direction diffusion weighting scheme was employed for DBSI acquisition: TR = 6 s, TE = 71 ms, maximal b-value = 1,000 s/mm^2, slice thickness = 4 mm, FOV = 24 cm. DBSI maps were computed as previously reported[4]. The cerebral blood flow (CBF) map was obtained from 3D pseudo-continuous arterial spin labeling MRI. In addition, standard imaging sequences such as T2WI and pre- and post-contrast T1W images were performed for identifying tumor.

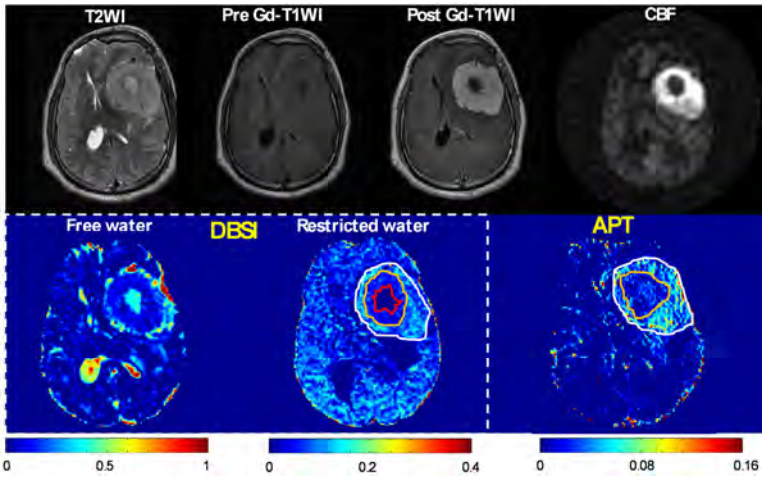

Fig. 1. MR images for a patient with brain tumor in the left frontal lobe.

Results & Discussions: Multi-parametric MR images on brain tumor are shown in Fig. 1. Tumor with clearly identified core was seen at left frontal lobe in conventional MRI, DBSI, and APT maps. Tumor core is hyperintense on T2W image, hypointense on pre and post Gd-T1W images, and CBF map, suggesting tissue necrosis. Outside the core, tumor is moderately hyperintense on T2W image, isointensity on pre Gd-T1W image, and significantly hyperintense on post Gd-T1W image and CBF map, suggesting increased angiogenesis. APT intensity increases in the entire Gd-enhancing tumor area and it is a typical feature of the tumor, suggesting increased content of mobile proteins and peptides. Tumor core was hyperintense on DBSI non-restricted isotropic diffusion fraction map (edema and necrosis) and is hypointense on DBSI restricted isotropic diffusion fraction map (cellularity). The DBSI non-restricted isotropic diffusion fraction map reveals elevated water content at tumor core and ventricles, consistent with the hyperintense T2W image. There is no signal in the core of tumor on the restricted isotropic diffusion fraction map, i.e., no cells seen in the necrotic core region. In the outer hyperintense region of restricted isotropic diffusion fraction map, increased cellularity coincides area of increased APT activity.

Conclusion: High APT signal has been suggested to be associated with tumor cellularity (3). Preliminary results suggested that increased restricted isotropic diffusion fraction paralleled increased APT activity in brain tumor.

Reference: 1. D.M. Koh, et al., AJR, 188: 1622-1635, 2007. 2. J. Zhou, et al., Nat. Med., 17: 130-135, 2011. 3. O. Togao, et al., Neuro-Oncology, 16: 441-448, 2014. 4. C.W. Chiang, et al., Neuroimage, 101:310-319, 2014.