Characterization of water transportation via aquaporin using tri-exponential model in cerebral infarction and Parkinson's disease - preliminary study

Xueying Ling[1], Zhongping Zhang[2], Zhoushe Zhao[2], Lian Huang[3], Yusheng Zhang[4], Li Guo[5], Yongjin Shi[6], Changzheng Shi[6], Li Huang[6], and Hao Xu[6]

[1]medical imaging center, the first affiliated hospital of Jinan university, Guangzhou, Guangdong, China, [2]GE healthcare, China, Guangdong, China, [3]neurology, the first affiliated hospital of Jinan university, Guangzhou, Guangdong, China, [4]neurology, the first affiliated hospital of Jinan university, Guangdong, China, [5]the first affiliated hospital of Jinan university, Guangdong, China, [6]medical imaging center, the first affiliated hospital of Jinan university, Guangdong, China

Introduction and Purpose: Conventional diffusion weighted imaging (DWI) uses a simple mono-exponential model to calculate the apparent diffusion coefficient (ADC), which involved not only the water diffusion but also other physiological processes such as blood micro-circulation. To resolve this problem, Le Bihan et. al. proposed an intra-voxel incoherent motion (IVIM) theory which uses bi-exponential model to distinguish information of true diffusion and blood perfusion[1]. However, the diffusion-weighted signal decay may be also affected by the transportation of water molecules through the aquaporin (AQP) in cell membrane[2], which is usually ignored. The aim of our study was to separate the water transportation via AQP using a tri-exponetial model and evaluate its value in assessing the brain damage of patients with cerebral infarction and Parkinson's disease (PD).

Materials and Methods: This study was approved by local Institutional Review Board. Forty-two subjects including 16 subcortical infarction patients, 14 PD patients and 12 controls participated in this study. All subjects gave written informed consent forms. The conventional magnetic resonance imaging (MRI) and DWI (field of view: 240 × 240 mm; matrix: 128 × 128; section thickness: 3 mm; intersection gap: 0.3 mm; bandwidth, 250 kHz) with fifteen b-values (0, 30, 50, 100, 200, 300, 500, 800, 1000, 1500, 2000, 3000, 3500, 4000 and 5000 sec/mm^2) were applied on each subject and whole brain was imaged. We proposed a tri-exponential model to fit the DWI image set,

$$S_b / S_0 = (1- f - f_{AQP})\cdot\exp(-b\cdot D) + f\cdot\exp(-b\cdot D^*) + f_{AQP}\cdot\exp(-b\cdot D_{AQP}), \quad \text{(Eq. 1)}$$

where D, D* and f represent the true diffusion coefficient, pseudo-diffusion coefficient and perfusion fraction respectively which are IVIM measures, D_{AQP} represents the diffusion coefficient related to water transportation via AQP and f_{AQP} stands for its fraction of DW signal decay. These metrics were measured in the infarct foci and the mirror regions of the patients with infarction, and globus pallidus (GP), putamen (PUT), substantia nigra (SN) of PD patients and controls. To assess the differences of these measures between the infarct foci and mirror regions, between PD and controls, we used the Wilcoxon Mann Whitney U test to compare the medians. Receiver operating characteristic (ROC) curves were calculated to determine the diagnostic accuracy of the above metrics in infarct foci and PD.

Results: The median of D and D_{AQP} in the infarct foci were significantly lower than those in the mirror regions (P<0.05). D_{AQP} in GP, PUT and SN of PD patients was significantly lower than those in the controls (P<0.05), as shown in Fig. 1. In contrast, D and D* were not significantly different between PD patients and controls. Fig. 2A demonstrated a high diagnostic accuracy of D and D_{AQP} in differentiating the infarct foci from mirror regions (area under ROC curve (AUC) = 0.993 and 0.753; P < 0.001 and 0.035, respectively). In addition, for the PD patients, the diagnostic accuracy of D_{AQP} in GP was the highest (AUC = 0.855, P < 0.001), followed by D_{AQP} in SN and PUT (AUC = 0.795 and 0.753; P = 0.001 and 0.003, respectively).

Conclusion: Tri-exponential model based analysis of DWI images at multiple b-values can be a useful tool for demonstrating the brain damage from infarction and PD. D is the best index to describe the pathophysiological change in subacute subcortical infarction, while D_{AQP} in GP, PUT and SN may be a biomarker in differential diagnosis between PD and controls.

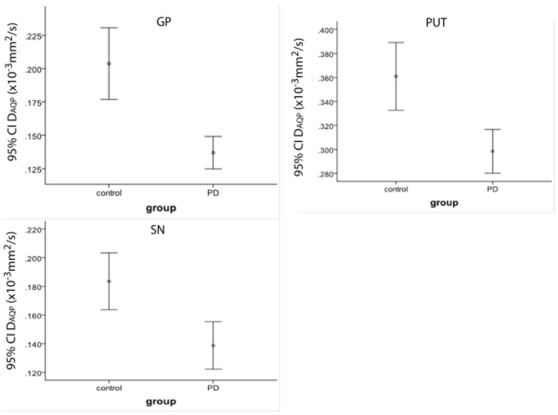

Figure 1. Comparisons of D_{AQP} in GP, PUT and SN between PD patients and the controls.

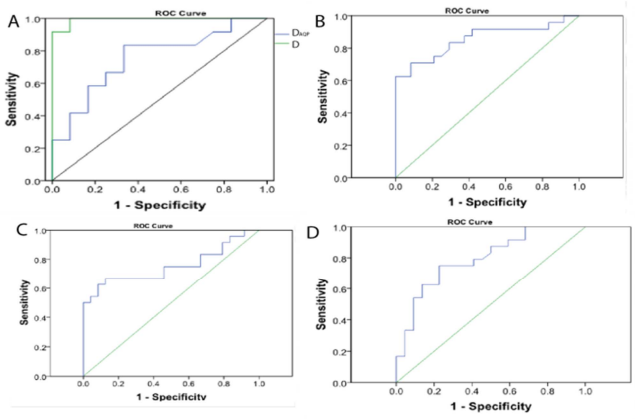

Figure 2. A: ROC curves of D_{AQP} and D in differentiating the infarct foci and the mirror regions; B, C and D: ROC curves of D_{AQP} in GP, PUT and SN to distinguish PD patients from controls.

References:

1. Le Bihan, D. et al. MR imaging of intravoxel incoherent motions: application to diffusion and perfusion in neurologic disorders. *Rad*iology 161, 401-7 (1986).

2. Badaut, J. et al. Brain water mobility decreases after astrocytic aquaporin-4 inhibition using RNA interference. J Cereb Blood Flow Metab 31, 819-31 (2011).