Application of stretched-exponential model of intravoxel incoherent motion in grading astrocytoma and its correlation with astrocytoma proliferative activity

Jing-Jing Jiang\textsuperscript{1}, Ling-Yun Zhao\textsuperscript{1}, Wei Xiong\textsuperscript{2}, Yi-Hao Yao\textsuperscript{1}, Shun Zhang\textsuperscript{1}, Yan Zhang\textsuperscript{1}, Ri-Feng Jiang\textsuperscript{1}, Zhen-Yu Zhou\textsuperscript{3}, and Wen-Zhen Zhu\textsuperscript{1}

\textsuperscript{1}Tongji hospital, tongji medical college, huazhong university of science and technology, Wuhan, Hubei, China, \textsuperscript{2}MR modality, GE healthcare, Wuhan, Hubei, China, \textsuperscript{3}MR Research China, GE healthcare, Beijing, China

Introduction and Purpose: Diffusion Weighted Imaging (DWI) has been widely applied to characterize, to diagnose and to determine early assessment of the therapy effectiveness in glioma [1-4]. Traditional DWI applied in biological tissues is most commonly quantified using a mono-exponential model. However, the signal intensity attenuation of brain water molecules does not follow mono-exponential decay properly and will deviate from straightness when b-factor exceeds 1000 s/mm\textsuperscript{2}. Stretched-exponential model was developed to overcome the difficulties of making assumptions about the quantity of intravoxel proton pools with different diffusion coefficients in biological tissues. Proliferative activity of tumor cells is an essential parameter which determines the course of the disease as well as affects the prognosis. Cell Nuclear Antigen (PCNA) has been applied as a typical biomarker for proliferative activity in human astrocytomas[5]. The purpose of this study was to evaluate the performance of DWI using the stretched-exponential model of intravoxel incoherent motion (IVIM) in grading astrocytoma and to determine the correlation of astrocytoma with PCNA.

Materials and Methods: Patients (n=72, M/F: 43/29, age range: 6-64 years old) with histopathologically proved astrocytoma (WHO grades II/III/IV: n=34/15/23) underwent scanning for IVIM DWI with b value extending from 0 to 3000 s/mm\textsuperscript{2} at 3.0 Tesla MR system (GE, USA). Based on the stretched-exponential model, distributed diffusion coefficient (DDC) maps and \( \alpha \) maps were calculated three times to achieve an average value for further statistical analysis. Freehand regions of interest (ROI) was placed on the solid part of the tumors. Biopsies of 60 astrocytomas (WHO grades II/III/IV: n=29/13/17) were performed for the evaluation of PCNA expression.

Results: Mean DDC had significant difference between any two groups of grade II, III, and IV gliomas (P<0.05), which demonstrated higher values in low-grade group than that in high-grade group. Mean \( \alpha \) had significant difference among grade II and III and IV groups (P<0.05), while no significant difference was detected between grade III and IV groups (P>0.05). Statistical analysis demonstrated a threshold value of 1.065\( \times \)10\textsuperscript{-3}mm\textsuperscript{2}/s for DDC to provide a sensitivity of 94.1 and a specificity of 89.5%, in low- and high-grade astrocytomas differentiation (Figure 1 A). The area under the curve was 0.918. The observed correlation of DDC and PCNA expression was significantly negative (r=-0.363, P=0.004) (Figure 1 B).

Conclusion: In this preliminary study, DDC was capable to differentiate the grade of human astrocytoma effectively, while \( \alpha \) value could only distinguish low- or high-grade tumors. Moreover, a significantly negative correlation was observed between DDC and PCNA expression. Therefore, it was concluded that DDC value, which represented intravoxel distribution rates, might be applied as an effective biomarker for grading and monitoring the proliferative activity of human astrocytomas.