Stretched-exponential model DWI (SEM-DWI) as a potential imaging biomarker in grading gliomas and assessment of proliferative activity

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Introduction and Purpose: Diffusion Weighted Imaging (DWI) has been widely applied to characterize, to preoperative grading and to determine treatment response in glioma [1-4]. Traditional DWI applied in biological tissues is most commonly quantified using a mono-exponential model (MEM). However, the signal intensity attenuation does not follow a mono-exponential decay when b-factor exceeds 1000 s/mm^2. Stretched-exponential model DWI (SEM-DWI) was developed to overcome the short comings in assuming 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) and Ki-67 has been applied as typical biomarkers for proliferative activity in human gliomas [5].The purpose of this study was to evaluate the SEM-DWI in grading astrocytoma and to determine the correlation of its parameters with astrocytoma proliferative activity.

Materials and Methods: Both MEM-DWI and SEM-DWI technique were performed in 104 patients with histopathologically proven primary gliomas before surgery and chemoradiotherapy. The patients were divided into the training (n = 72) and the testing set (n = 32) according to the time of the imaging study. MEM-DWI derived apparent diffusion coefficient (ADC) and SEM-DWI derived distributed diffusion coefficient (DDC) and α values were measured were measured three times by placing free-hand regions of interest (ROI) on the solid parts of tumors. The DDC, ADC and α values which were determined to best differentiate the gliomas grade in the training data set were applied as the cut-off values. Then these cut-off values were applied to the test data set and check for predictive accuracy. Additionally, biopsies of 57gliomas (II/III/IV: n=28/12/17) out of the 72 cases in training set were performed for the evaluation of PCNA and Ki-67 expression and were correlated with that of DWI measurements.

Results: In the training patient data set: 1) 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 gliomas (LGG) than that in high-grade gliomas (HGG) (P < 0.05) (Figure 1). 2) There were statistically differences of α and ADC values between Ⅱ and III or IV gliomas (P < 0.05)，but they did not differ significantly between III and IV gliomas. 3) Significantly positive correlations were found between between PCNA LI and Ki-67 LI (P < 0.05）. 4) Statistically negative correlations were noted between DDC (ADC) values and PCNA (Ki-67) labeling index (LI)（P < 0.05）, but no statistical correlation was seen between α and Ki-67 LI values (P > 0.05). In the testing set: 1) In distinguishing HGG from LGG: the highest positive predictive values (PPV) and negative predictive values (NPV) (94.1%, 86.7%); the highest sensitivity and specificity (88.9%, 92.9%) ; and the highest diagnostic accuracy (90.6%) was all seen at DDC. 2) In discriminating between Ⅱ and III and between III and IV: the and NPV for DDC was respectively 87.5%, 92.9%; and 90.0%, 87.5%; the sensitivity and specificity was respectively 87.5%, 92.9%; and 90.0%, 87.5%; the diagnostic accuracy was 90.9% and 88.9%

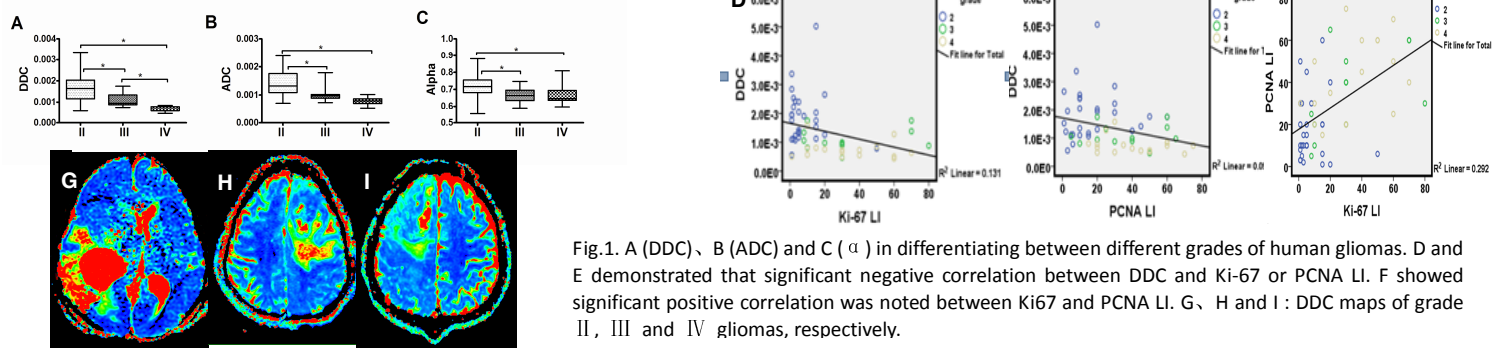

Fig.1. A (DDC)、B (ADC) and C (α) in differentiating between different grades of human gliomas. D and E demonstrated that significant negative correlation between DDC and Ki-67 or PCNA LI. F showed significant positive correlation was noted between Ki67 and PCNA LI. G、H and I : DDC maps of grade Ⅱ, Ⅲ and Ⅳ gliomas, respectively.

Conclusion: In this preliminary study, DDC was capable to differentiate the grade of human gliomas effectively, while ADC and α value could only distinguish LGG and HGG. Moreover, a significantly negative correlation was observed between DDC and PCNA (Ki-67) 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 gliomas.

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