

Comparison of Three Non-Gaussian Diffusion Models for Differentiation of Pediatric Brain Tumors

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TARGET AUDIENCE: Radiologists would find useful information on pediatric brain tumor differentiation using high b-value diffusion-weighted images. Researchers who are interested in diffusion imaging would be provided with a comparison among three non-Gaussian diffusion models.

INTRODUCTION: Diffusion MRI has been increasingly used for brain tumor characterization and treatment assessment [1, 2]. A number of studies have demonstrated that apparent diffusion coefficient (ADC) can serve as an important imaging maker for brain tumor differentiation and treatment evaluation. ADC for clinical use is typically estimated using a mono-exponential model with one or very few diffusion-weighted images at moderate b-values (e.g., up to 1500 s/mm²). This simple approach, which assumes a Gaussian diffusion process and a homogenous tissue distribution for any given voxel, falls short at higher b-values (e.g., ≥ 2000 s/mm²), particularly in heterogeneous tumor tissues. Over the past few years, a number of non-Gaussian diffusion models have been developed, including bi-exponential [3], stretch-exponential [4], statistical [5], q-space [6], kurtosis [7], fractional order calculus (FROC) [8], and others. These models offer considerable advantages over the mono-exponential model by providing information related to tissue heterogeneity and microenvironment. Some of these models have been applied to differential diagnosis and tumor characterization [1, 9, 10]. To our best knowledge, a systematic comparison of these non-Gaussian models has not been reported in the context of differentiating pediatric brain tumors. In this study, we selected three non-Gaussian diffusion models - FROC, kurtosis and bi-exponential models - to evaluate the performance of each model for differentiating low-grade from high-grade pediatric brain tumors.

METHOD: The study was carried out on 53 children (4 mo to 13 yr) with histopathologically proven brain tumors (23 low-grade, 30 high-grade). Diffusion-weighted images were acquired using 12 b-values (0 - 4000 s/mm²) on a GE 3T scanner (Signa HDxt 3.0T, Waukesha, Wisconsin) within a scan time of 3 min. An ROI analysis was conducted on solid tumor regions for each patient, guided by T1+C, T2, and FLAIR images with input from radiologists. For each selected ROI, The three diffusion models (FROC, kurtosis, and bi-exponential) were used to fit to the experimental data on a voxel-by-voxel basis using customized software written in Matlab (Mathworks, Natick, MA). Mean absolute percentage error (MAPE) map was calculated and used as a measure of fitting accuracy. For each diffusion model, median values of the model parameters and MAPE were calculated over the entire tumor regions (3 to 5 slices) for each patient. With histopathology results as a gold standard, parametric values for the low-grade and high-grade groups were compared for each model using Mann-Whitney U test with statistical significance set at $p < 0.05$. In order to quantify the performance of each model for brain tumor differentiation, a receiver operating characteristic (ROC) analysis was applied to each individual parameter as well as the combination of all parameters (binary logistic regression) for each model. The MAPE and AUC (areas under the curves) were used to determine the merit of each model.

RESULTS: According to MAPE (0.041 ± 0.03 , 0.032 ± 0.03 , 0.031 ± 0.03 for the FROC, kurtosis and bi-exponential model, respectively), the bi-exponential model gave a slightly better fitting accuracy than FROC or kurtosis model, but the difference was not significant ($p = 0.23$, one-way ANOVA).

Figure 1 shows the mean and standard deviation of the parameters associated with each model in high-grade (left) and low-grade (right) brain tumors. The parameters of all three models exhibited a significant difference between low-grade and high-grade groups ($p < 0.005$; Fig. 1). **Figures 2 and 3** show the ROC curves and AUC values of the model parameters. For tumor differentiation, β (.928), K (.955), and D_s (.935) were the best individual markers in the FROC, kurtosis and bi-exponential models, respectively. When combining all parameters for each model, all three non-Gaussian models showed better performance than the mono-exponential model (i.e., using ADC as a single parameter), and FROC (AUC = .975) gave the best result (**Figure 3**).

DISCUSSION: Our results demonstrate that there is a significant difference in non-Gaussian diffusion parameters between the low-grade and high-grade pediatric brain tumors, irrespective of the three non-Gaussian diffusion models evaluated in this study. The performance of the three models was similar, but the FROC and kurtosis models produced images with better contrast between tumor and healthy tissues (images not shown) when compared with the bi-exponential model. The parameters obtained from high b-value diffusion dataset (e.g., β , K and D_s) have been related to tissue heterogeneity or micro-environmental changes that cannot be easily extracted using a mono-exponential diffusion model with a low to moderate b-value (e.g., < 1500 s/mm²) [6-10]. Our results suggest that non-Gaussian diffusion models with high b-values (up to 4000 s/mm²) can provide valuable and more reliable information for characterizing pediatric brain tumors.

REFERENCES: [1] Maier, et al., NMR Biomed, 2010. [2] Ross, et al., Mol Cancer Ther, 2003. [3] Niendorf, et al., MRM, 1996. [4] Bennett, et al., MRM, 2003. [5] Yablonskiy, et al., MRM, 2003. [6] Assaf, et al., MRM, 2000. [7] Jensen, et al., MRM, 2005. [8] Zhou, et al., MRM, 2010. [9] Rumboldt, et al., AJNR, 2006. [10] Sui, et al., ISMRM, 2012.

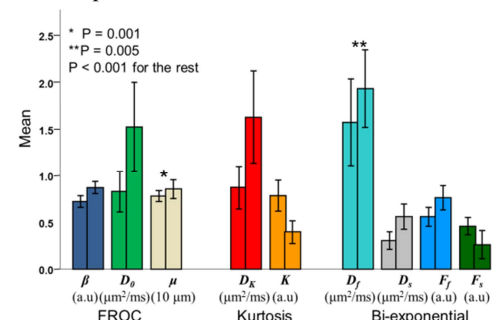


Fig. 1 Mean and standard deviation of the median values of the model parameters over tumor ROIs in high-grade (left) and low-grade (right) tumor groups for each of the three diffusion models as labeled in the figure.

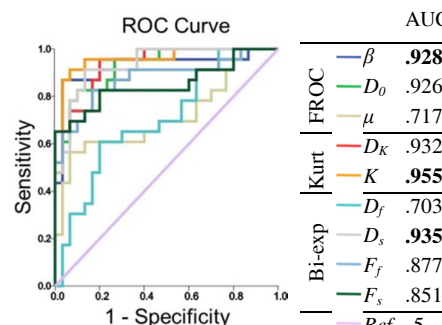


Fig. 2 ROC curves and AUC values for the parameters in the three models. The numbers in bold highlight the parameter with best performance in each model.

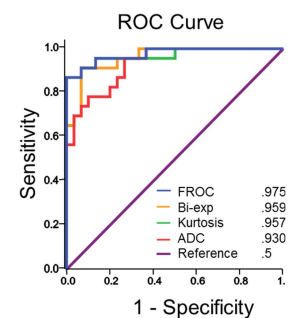


Fig. 3 ROC curves and AUC values after combining all parameters for each model.