Detection of brain maturation - DTI with different B-values versus diffusion kurtosis imaging

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Introduction DTI offers an unprecedented capability to probe tissue microstructure in vivo and non-invasively. However, DTI indices obtained from different b-values may probe different information regarding the complex diffusion processes in vivo[1]. The non-monoexponential DW signal decay with b-value is largely attributed to the diffusion restriction due to underlying cellular microstructures[2]. Comparing diffusivities among DTI studies employing different b-values must therefore be done with great caution. To probe the apparent slow water diffusion, higher b-values must be used. Comparisons between the apparent fast and slow diffusion measurements in normal and pathological tissue have been reported previously in several studies, but little has been done in comparing the sensitivity of varying b-values during subtle neural tissue alternations. Brain development is known to be temporally accompanied by gradual and local tissue morphological changes in both WM and GM that can lead to subtle changes in water diffusion. This study aims to investigate the effects of different b-values in detecting the microstructural changes during well-controlled rat brain maturation, and compare the results to those obtained by diffusion kurtosis imaging (DKI).

Methods Three age groups of normal SD rats were scanned: postnatal day 13 (P13), 31 (P31) and 120 (P120). Sample size was 6 for each age group. All experiments were conducted using a Bruker PharmaScan 7T scanner. DW images were acquired with a respiration-gated 4-shot SE-EPI sequence with 5 different b-values (0.5, 1, 1.5, 2, 2.5 ms/μm^2) along 30 gradient encoding directions[5]. For P13 rats, the imaging parameters were TR/TE = 3000/33.3 ms, δ/Δ = 5/20 ms, slice thickness = 0.7 mm, FOV = 25 mm, data matrix=128x128 NEX = 4. For P31 and P120 rats, they were TR/TE = 3000/30.3 ms, δ/Δ = 5/17 ms, slice thickness = 1 mm, FOV = 30 mm, data matrix = 128x128, NEX=4. Three apparent diffusion coefficients (D_{app}) were computed for each direction using DW data with b=0 vs. 0.5 ms/μm^2, 0 vs. 1.5 ms/μm^2, and 0 vs. 2.5 ms/μm^2, respectively. FA, $\lambda_{//}$ and $\lambda_{\perp}$ were then calculated from the 2nd-order 3D diffusion tensor (DT) matrix. DKI measures the diffusion kurtosis that quantifies the extent of non-Gaussian diffusion due to restricted diffusion by fitting multiple b-value DW measurements to a quadratic exponential model[3,4]. In this study, DW images with all 5 b-values were fitted to the DKI model $\ln[S(b)]=\ln[S(0)]-bD_{app}+(1/6)b^2D_{app}^2K_{app}$ for D_{app} and apparent kurtosis (K_{app}) along 30 directions. Kurtoses along the 3 eigenvector directions of the 2nd-order DT were computed by transforming the 4th-order 3D kurtosis tensor. Subsequently, average kurtosis along all directions (mean kurtosis MK), kurtoses along the axial direction (axial kurtosis $K_{//}$) and radial direction (radial kurtosis $K_{\perp}$) were calculated[5]. ROIs were defined in 4 white matter (WM) and 3 grey matter (GM) structures. Note that identical ROIs were used to obtain various measurements from different parametric maps.

Results and Discussions FA, $\lambda_{//}$ and $\lambda_{\perp}$ measurements using 3 different b-values for WM and GM structures are shown in Fig. 1. It can be seen that the sensitivity of $\lambda_{\perp}$ increases with b-values. Changes of $\lambda_{\perp}$ in WM are likely contributed by the formation of myelin sheath and the restriction caused by myelin modification during development[6]. The formation of barrier around the axons shortens the diffusion distance in the radial direction. The apparent slow diffusion component represented by using b=2.5ms/μm^2 is shown to be more sensitive than using lower b-values. The decreasing $\lambda_{\perp}$ in WM with ages is not even seen in b=0.5ms/μm^2, but it becomes obvious and statistically significant as higher b-values are used. It is not surprising as higher b-value has been shown to be useful in some pathological studies[7,8]. Moreover, the sensitivity of $\lambda_{//}$ in characterizing the maturational process in different developmental stages also changes with the b-value used. In WM, there is an observed increase of $\lambda_{//}$ in WM with ages (except in CC). This may be due to the increase in microtubules and axoplasmic flow[9]. This increase in the apparent fast diffusion can be captured by using small b-values which some of the significant detections then vanish when higher b-values are used. Although the level of significance also changes in GM, it is not conclusive to judge the effect of different b-values. Maturation of the relatively isotropic GM is complex and it can be seen that the application of different b-values can affect the level of significance without changing the trend. Although the DTI-derived parameters are capable of detecting the developing changes in different structures in this study, the choice of b values should be optimized so to probe the desired microstructural changes. The corresponding ROI measurements of DKI-derived kurtosis parameters are shown in Fig. 2. The kurtoses generally increase with age, indicating increasing diffusion restriction in both axial and radial directions. It can also be seen that the kurtosis measurements are more sensitive and directionally specific. Therefore, DKI is potentially more robust in monitoring subtle tissue changes during brain development or pathologic progression.

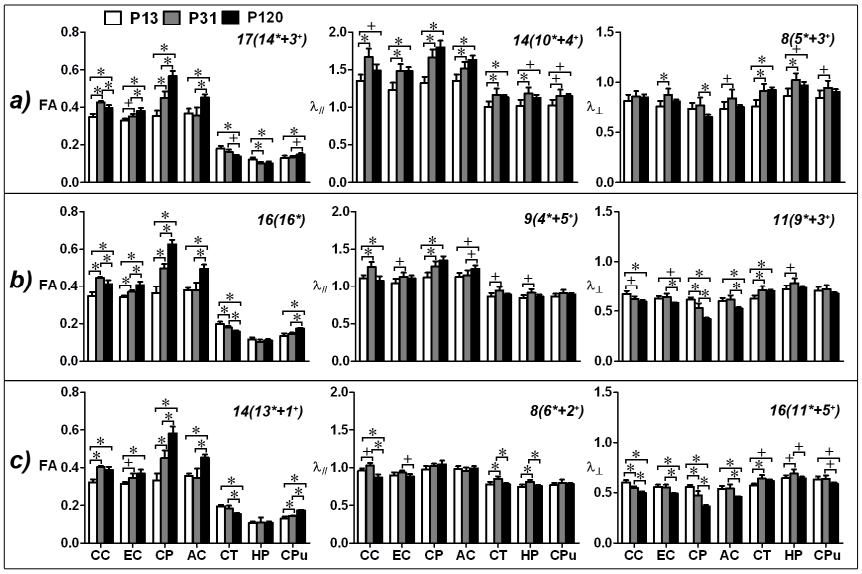

Figure 1. ROI measurements in different structures.**(a)** b=0.5 ms/μm^2.**(b)** b=1.5 ms/μm^2.**(c)** b=2.5 ms/μm^2. $\lambda_{//}$ and $\lambda_{\perp}$ are listed in μm^2/ms. (* p<0.01, $^+$ p<0.05 indicates significant difference between groups in Tukey's test) The total number of significant changes detected by each parameter is indicated in italics. corpus collosum (CC), external capsule (EC), cerebral peduncle (CP), anterior commissure (AC) cortex (CT), hippocampus (HP) and caudate putamen (CPu)

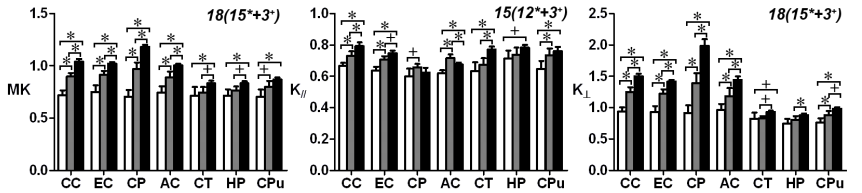

Figure 2. DKI-derived parameters. Mean kurtosis (MK), axial kurtosis ($K_{//}$) and radial kurtosis ($K_{\perp}$) are shown.

Conclusion The apparent fast and slow diffusion measurements by conventional DTI probe different microstructural information. Quantitatively, DTI-derived indices vary with the actual b-values used. The b-value for optimal DTI detection of microstructural changes depends on the specific physiological or pathological processes targeted. High-order diffusion approach, such as DKI, is therefore essential for more robust MR diffusion characterization of neural tissues.

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