Analysis of Effect of Short Diffusion Time in Diffusion Kurtosis Imaging using Oscillating Gradient

Matthew M. Cheung[1,2], Leon C. Ho[1,2], Abby Y. Ding[1,2], Condon Lau[1,2], and Ed X. Wu[1,2]

[1]Biomedical Imaging and Signal Processing, The University of Hong Kong, Pokfulam, Hong Kong SAR, China, People's Republic of, [2]Department of Electrical and Electronic Engineering, The University of Hong Kong, Pokfulam, Hong Kong SAR, China, People's Republic of

Introduction Kurtosis estimated from diffusion kurtosis imaging (DKI) describes the non-Gaussian diffusion in neural tissues[1]. It has been known that kurtosis measurements are dependent on the diffusion time (Δ), due to restricted diffusion, heterogeneity of diffusion compartments or water exchange between different compartments[2,3]. Previous studies have investigated the effect of long Δ on diffusion weighted (DW) signal decay in rats[4-6] and human brains[7]. These studies showed that kurtosis generally decreases with prolonged Δ, and such change may provide additional clinically relevant information[7]. However, there has been no report of the Δ dependency of kurtosis in the short Δ regime. It is possible to probe microstructure with short effective diffusion time (Δ_{eff}) using oscillating diffusion gradients[8] and we apply this technique to investigate the Δ effect to DKI measurements in rat brain tissues *in vivo* in this study.

Methods All experiments were performed on normal male Sprague Dawley rats (n=6, 250-300g) using a Bruker PharmaScan 7T scanner. DW images were acquired using 4-shot SE-EPI sequence with seven different b-values (0.3, 0.6, 0.9, 1.2, 1.5, 1.8, 2.1ms/μm²) along 30 gradient encoding directions. The experiments were repeated with effective diffusion time Δ_{eff} = 4.75, 9.5ms using oscillating gradient spin-echo (OGSE) with cosine waveform[8] and Δ_{eff} = 19, 38ms using pulsed gradient spin-echo (PGSE). The imaging parameters were: TR/TE=3000/93ms, δ=38ms for OGSE and 4.5ms for PGSE, slice thickness=1.5mm, FOV=36x36mm², data matrix=128x128 and NEX=2. DWIs were first coregistered using AIR5.2.5. DW signals as a function of b-value for each Δ_{eff} were non-linearly fitted to the DKI model $\ln(S/S_0)=-bD+(1/6)b^2D^2K$. Fractional anisotropy (FA), mean diffusivity (MD) and mean kurtosis (MK) maps were computed. Regions of interest (ROIs) were defined in 2 gray matters (GM): hippocampus (HP); caudate putamen (CPu) and 2 white matters (WM): corpus callosum (CC); internal capsule (IC). The measurements in each ROI were compared by Friedman test, followed by Dunn's post-hoc test.
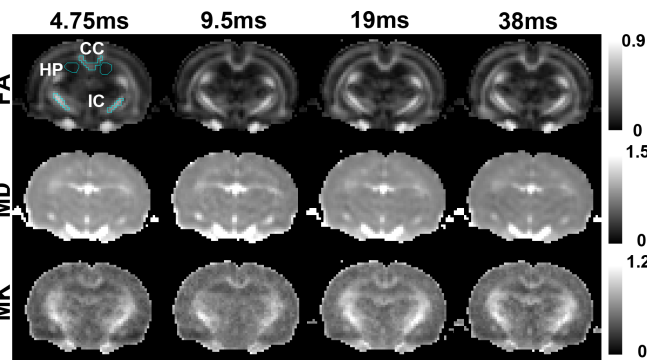
Results Fig.1 shows the parametric maps with different Δ_{eff} from single slice of a normal animal. The ROI definitions of CC, HP and IC are shown on the FA map with Δ_{eff}=4.75ms. CPu was defined on another slice that was not shown. Fig. 2 shows the corresponding log mean signal decay of different ROIs against Δ_{eff}. The slopes of the signal decays apparently decreased with Δ_{eff}, suggesting an increase in diffusivity. The measured parameters are plotted in Fig. 3. There was no statistical significant change in FA among all the structures studied. The decrease of MD or increase of MK, however, shows statistical significance in CC, IC and CPu.

Discussions This is the first study that examined the Δ dependency on DKI measurements in brain tissues *in vivo* with diffusion time <20ms. In long Δ regime, decrease of MD with Δ, which is likely caused by the increased restriction over long observation time, was consistent with previous reports that employed conventional DTI models[8]. Such increased restricted is also reflected in the kurtosis measurements that increase. In theory, kurtosis change is not sensitive to water exchange in short Δ regime[3]. The pre-exchange lifetimes for intra- and extra-cellular water of *in vivo* rat brain, which were estimated to be 500 and 120 ms respectively[9], are relatively long compared with the Δ_{eff} in this study. The observed kurtosis change therefore likely reflects the tissue complexity and cellular dimension. Combining other preliminary reports that showed kurtosis decreases in prolonged Δ[4-7], our results suggested that kurtosis maxima in rat brain tissue exist at around 10-40ms. This timing and the Δ dependency of diffusivity or kurtosis may provide microstructural information at the cellular level. It should be noted that there also exists rapid water exchange among different intra-cellular compartments, which can be as fast as 15ms[9]. Also, the gradient pulse duration (δ) in this study is not identical for PGSE and OGSE scans but this effect should be negligible from previous theoretical[2] and experimental[5] analyses.

Conclusions DKI measurements with short Δ_{eff} were studied and analyzed. The Δ dependency of diffusivity and kurtosis may provide insights into the complex cellular properties in normal and diseased neural tissues.

References 1. Jensen JH, et al. Magn Reson Med 2005. 2. Jensen JH, et al. J Magn Reson 2011. 3. Jensen JH, et al. NMR Biomed 2010. 4. Hui ES, et al. ISMRM 2010;4027 5. Minati L, et al. Magma 2010. 6. Wu EX, et al. NMR Biomed 2010. 7. Latt J, et al. ISMRM 2009;40 8. Does MD, et al. Magn Reson Med 2003. 9. Quirk JD, et al. Magn Reson Med 2003.

Fig.1 Fractional anisotropy (FA), mean diffusivity (MD) and mean kurtosis (MK) maps with different diffusion times from single slice of a normal animal.
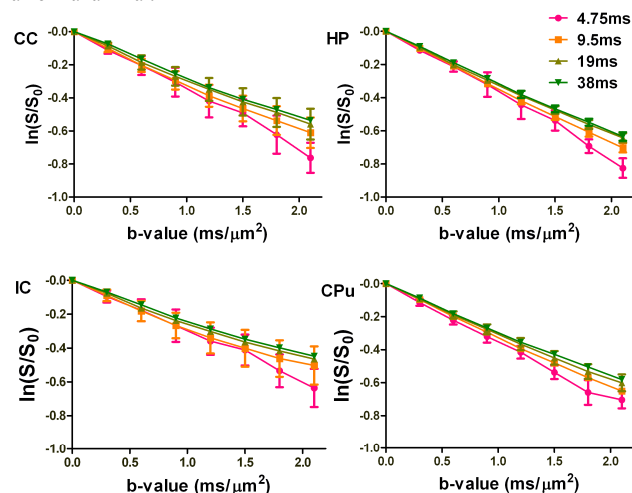

Fig.2 Normalized signal decays (S/S_0), computed as the average of DW signal (mean±SD) along 30 diffusion encoding directions.
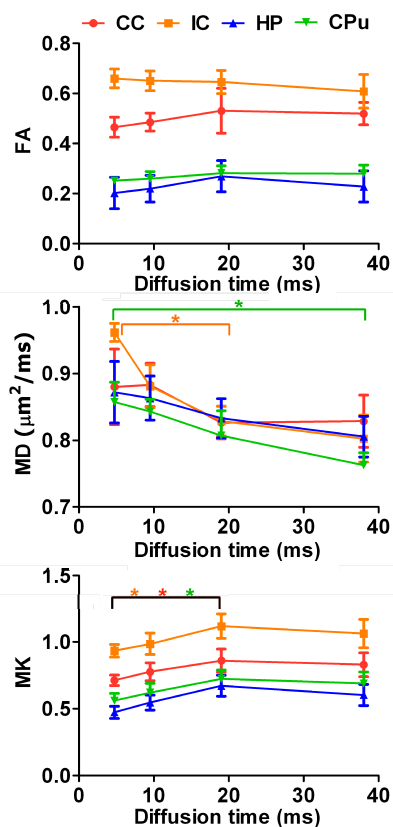

Fig.3 ROI quantifications of FA, MD and MK vs Δ_{eff}. The error bar indicates the SD of measurements across all animals. (*: p<0.05)