Towards Better Understanding of Brain Tissue using Directional Kurtoses by Orthogonal Transformation of Diffusion Kurtosis Tensor D (K_DT)

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Introduction

It has been demonstrated recently that diffusion kurtosis imaging (DKI), a 4th order diffusion analysis that characterizes the restricted non-Gaussian diffusion based on the non-monoexponential diffusion-weighted (DW) signal decay versus b-value, is capable of providing extra information regarding biological systems in addition to conventional DTI, a 2nd order diffusion analysis [1-6]. While the average kurtosis along all gradient directions have been used in these studies so far, such mean kurtosis (MK) approach may reduce the DKI sensitivity to probe changes along the direction parallel (axial) or perpendicular (radial) to the dominant diffusion direction. Intuitively, more information should be available from kurtosis along these specific diffusion directions. An orthogonal transformation of the 4th order diffusion kurtosis tensor (K_DT) is proposed here to compute the projection of K_DT on the eigenvectors of 2nd order diffusion tensor (DT), thereby obtaining directional kurtoses. Because histological fixation alters the cellular structures and diffusion restrictions in brain tissue [7], it may serve as an effective manipulation for evaluating the efficacy of directional kurtosis analysis. Therefore, DKI experiments were performed on *in vivo* and *ex vivo* fixed rat brains in this study, and DKI-derived parameters were compared with the conventional DTI parameters.

Theory

2nd order DT can be characterized by matrix diagonalization [8], thereby obtaining eigenvalues, λ_i, and eigenvectors of the DT, and thus $E=(e_{ij})$, an orthogonal matrix whose columns consist of the 3 orthonormal eigenvectors. From [1,2], apparent diffusion kurtosis (K_{app}) in a particular direction is related to 4th order K_DT by: $K_{app}=(MD^2/D_{app}^2)\cdot\sum\sum\sum\sum n_i n_j n_k n_l W_{ijkl}$, where $MD=(\lambda_1+\lambda_2+\lambda_3)/3$, n_i is the component of the encoding gradient and W_{ijkl} is individual element of K_DT. We recently showed that K_DT can be transformed to a coordinate system in which the 3 DT eigenvectors are the base vectors [9], i.e. $\hat{W}_{ijkl}=\sum\sum\sum\sum e_{i'i}e_{j'j}e_{k'k}e_{l'l}W_{i'j'k'l'}$. Therefore, kurtosis along each eigenvector is: $K_i=(MD^2/\lambda_i^2)\cdot\hat{W}_{iiii}$. Assuming $\lambda_1>\lambda_2>\lambda_3$, axial kurtosis ($K_{//}$) and radial kurtosis ($K_\perp$), defined as the kurtosis along axial and radial direction are: $K_{//}=K_1$ and $K_\perp=(K_2+K_3)/2$, respectively.

Methods

All experiments were performed on a 7T Bruker scanner. ***In vivo:*** 7 normal adult SD rats. DW images were acquired with a respiration-gated SE 4-shot EPI with encoding scheme of 30 gradient directions [10] using: TR/TE=3000/30.3ms, δ/Δ=5/17ms, image resolution=234x234x1000μm^3, 5 b-values of 500, 1000, 1500, 2000 and 2500s/mm^2, and NEX=4. ***Ex vivo:*** 5 normal adult SD rat brain fixed with the standard formalin fixation procedure. The pulse sequence and encoding scheme were the same as *in vivo* experiments except for TE=34.3ms, δ=9ms, and b-values of 1000, 2000, 3000, 4000 and 5000s/mm^2. Multi-slice ROIs were manually drawn based from the FA and MK maps of each animal. 5 white matter (WM), namely, corpus callosum (CC), external capsule (EC), cerebral peduncle (CP), anterior commissure (AC) and medial lemniscus (ML), and 3 gray matter (GM), namely, cerebral cortex (CT), hippocampus (HP) and cauduate putamen (CPu) were defined.

Results

Fig.1 shows FA, $\lambda_{//}$, $\lambda_\perp$, MK, $K_{//}$ and $K_\perp$ map of a typical *in vivo* and *ex vivo* rat brain, noting the substantial difference between the $K_{//}$ map of *in vivo* and *ex vivo* brain. The ROI measurements are shown in Fig. 2. Under *ex vivo* condition, diffusivities are lower as expected. Water diffusion is more restricted in terms of non-Gaussian diffusion as shown by the increase in $K_{//}$, $K_\perp$ and MK. Also note from Fig.2(c) and (d) that there is a substantial increase in $K_{//}$, $K_\perp$ and MK from *in vivo* to *ex vivo* for WM while there is relatively less increase for GM, implying that structural changes caused by fixation produce more diffusion restriction in WM than in GM.

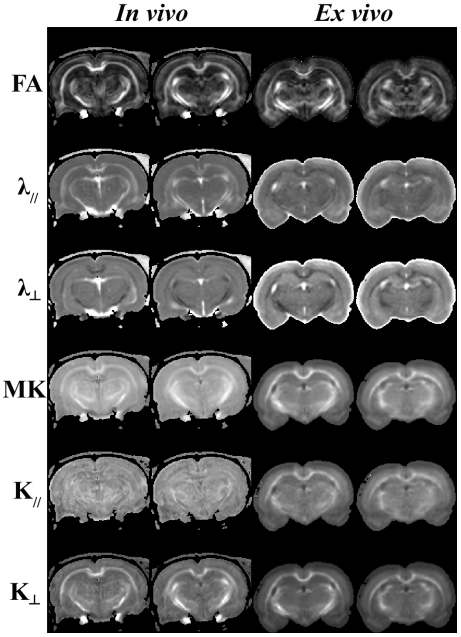

Figure 1. FA, $\lambda_{//}$, $\lambda_\perp$, MK, $K_{//}$ and $K_\perp$ map of a typical *in vivo* and *ex vivo* rat brain

Discussions and Conclusions

In vivo $K_{//}$ is largely the same for WM and GM while there is substantial difference between the two for $\lambda_{//}$. The structure of *in vivo* WM is often regarded as ordered axons containing neurofibrils and wrapped around by myelin [11]. Therefore, one expects that the *in vivo* axial diffusion environment would be rather homogeneous and exhibits relatively less diffusion restriction. However, this is not the case, as revealed by the similar $K_{//}$ values measured for WM and GM. *In vivo* axial diffusion restriction in WM is likely attributed to the presence of glial cells, astrocytes and oligodendrocytes [12]. Another important observation is that the intrinsic structure along the axonal direction in WM is severely altered under *ex vivo* condition, as shown by the large increase in $K_{//}$ (up to 80%) and relatively less increase in $K_\perp$ (up to 41%). Meanwhile, only similar percentage changes were observed for $\lambda_{//}$ (-68%) and $\lambda_\perp$ (-54%) from *in vivo* to *ex vivo*, suggesting the excellent sensitivity of directional kurtoses to changes in water diffusion environment. It is also worth noting that despite the general increase for all kurtosis indices, MK lacks the directional information that is useful in differentiating specific diffusion environment changes along axial and radial directions, .e.g., as revealed by the $K_{//}$ and $K_\perp$ above. Multi-dimensional cluster analysis is presently under way to evaluate whether, with directional kurtoses or combined with the conventional directional diffusivities, DKI can provide improved differentiation and characterization of various brain tissue structures and specific pathologies.

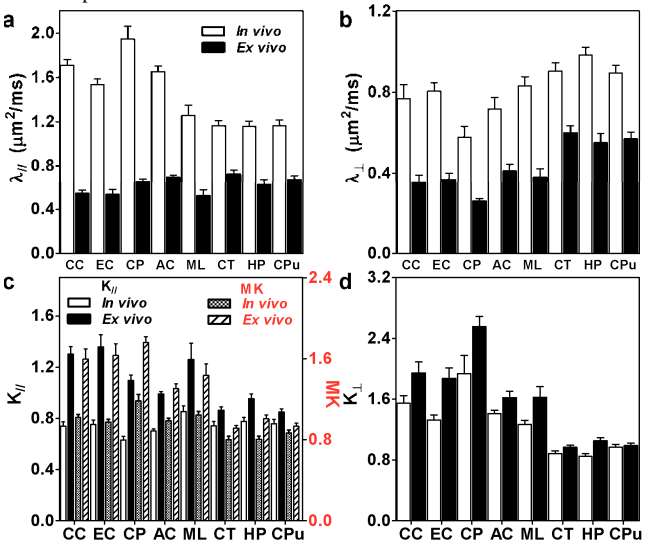

Figure 2. ROI measurement of *in vivo* (N=7) and *ex vivo* (N=5) rat brains. ROIs include corpus callosum (CC), external capsule (EC), cerebral peduncle (CP), anterior commissure (AC) and medial lemniscus (ML), cerebral cortex (CT), hippocampus (HP) and cauduate putamen (CPu)

References [1] Jensen JH et al. MRM 2005. [2] Lu H et al. NMR Biomed 2006. [3] Falangola MF et al. ISMRM2007. [4] Falangola MF et al. ISMRM2007. [5] Helpern JA et al. ISMRM2007. [6] Ramani A et al. ISMRM2007. [7] Schwartz ED et al. AJNR Am J Neuroradiol 2005. [8] Basser PJ et al. Biophys J 1994. [9] Qi L et al. J Comput Appl Math (*in press*). [10] Jones DK et al. MRM 1999. [11] Beaulieu C. NMR Biomed 2002. [12] Waxman SG et al. The Axon: structure, function, and pathophysiology. 1995.