Characterization of Non-Gaussian Water Diffusion in Humans using Diffusion Kurtosis Imaging

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INTRODUCTION: Recently, there has been growing interests in using MRI to study water diffusion properties in the brain. While the ADC and DTI can measure important diffusion parameters of the water molecules, they are based on the assumption that the water diffusion is perfectly Gaussian. However, water in biological structure often shows non-Gaussian diffusion patterns. This has been recognized by the non mono-exponential behavior of the MR signal as a function of b values. Here we propose a MR method to directly investigate the non-Gaussian properties of the water diffusion. This technique can measure the kurtosis of the displacement distribution function, which represents how much the diffusion pattern of the water deviates from a perfect Gaussian curve. We demonstrate that the 3D diffusion kurtosis characteristics, defined as the diffusion kurtosis tensor (DKT), can be quantified in humans within a clinically feasible time (about 10 minutes) on a clinical scanner. A method to present the DKT results is introduced. It is also shown that the DKT has the potential to provide different information from the conventional diffusion tensor (DT).

METHODS Theory: Kurtosis is a statistical term that defines how much a distribution is deviated from a Gaussian function. One can consider that ADC is a first-order approximation to the water displacement distribution function and Kurtosis is a second-order approximation. The kurtosis in a single direction, termed apparent kurtosis coefficient (AKC) or K_{app}, can be determined using conventional diffusion sequence but with 3 or more b values (including b=0) and fitting to the following equation (1): $\ln[S(b)] = \ln[S(0)] - b \cdot D_{app} + \frac{1}{6} b^2 \cdot D_{app}^2 \cdot K_{app}$, where D_{app} is ADC. For 3D kurtosis properties, it can be completely characterized by a four-dimensional tensor, *W*, which is a 3x3x3x3 matrix with 81 elements. Due to the full symmetry of the tensor, only 15 elements (see Eq. 1) are independent. Similar to the relationship between DT and ADC, the AKC at any direction can be calculated once the whole tensor, DK tensor, is known:

$$K_{app} = (n_1^4 \cdot W_{1111} + n_2^4 \cdot W_{2222} + n_3^4 \cdot W_{3333} + 4n_1^3 n_2 W_{1112} + 4n_1^3 n_3 W_{1113} + 4n_1 n_2^3 \cdot W_{1222} + 4n_2^3 n_3 W_{2223} + 4n_1 n_3^3 \cdot W_{1333} + 4n_2 n_3^3 \cdot W_{2333} + 6n_1^2 n_2^2 W_{1122} + 6n_1^2 n_3^2 W_{1133} + 6n_2^2 n_3^2 W_{2233} + 12n_1^2 n_2 n_3 W_{1123} + 12n_1 n_2^2 n_3 W_{1223} + 12n_1 n_2 n_3^2 W_{1233}) \cdot M_D^2 / D_{app}^2 \quad (1)$$

where n_i (*i*=1, 2 or 3) is the component of the direction unit vector, M_D is mean diffusivity. To facilitate the presentation of the 4D-matrix DK tensor, a mathematical tool called *spherical harmonics expansion* (2) was applied to reduce the tensor into simple indices, which describe the general features of the DK tensor, similar to the way that the trace and fractional anisotropy (FA) are used to describe the DT. A total of 3 indices, Q_0, Q_2 and Q_4, were calculated, where Q_0 represents the mean AKC averaged over all directions, Q_2 and Q_4 are related to the directional variation of the AKC.

Experiment: Studies (n=4, normal volunteers, with written consent) were conducted on a 3.0T clinical system (Siemens Medical Solutions). Diffusion experiment was performed using a dual spin-echo sequence with 30 directions (3) and 6 b values (0, 500, 1000, 1500, 2000, 2500s/mm^2). Other parameters were: TR=2s, TE=108ms, 13 slices, matrix 128x128, voxel size 2.5x2.5x2.5mm^3, total duration 10min20sec. A phantom experiment using fresh asparagus was also performed with similar parameters, except for a larger number of averages (NSA=32).

RESULTS and DISCUSSION: Fig. 1 shows the fitting results in a ROI containing corpus callosum for 4 representative gradient directions. A nonlinear signal decay of log(S) can be clearly seen, suggesting a non-Gaussian water diffusion. Note that the DT (4) and DK tensor can both be represented by a 3D surface plot, on which each point indicates the ADC (or AKC) in that particular direction. Fig. 2a and b show the surface plots for DK tensor and DT, respectively, in the same ROI as in Fig. 1. Black circles indicate the experimental points. The color encodes the amplitude of the ADC (or AKC). Blue=low value; red=high value. While the DT plot has the well-known dumb-bell shape (4), the DK tensor structure has dramatically different characteristics. In directions along the fiber orientation, the AKC appears to be very small, which is consistent with the expectation that the water diffusion is less hindered or restricted along the fiber. In directions perpendicular to the fiber, the AKC is much larger, presumably due to the axonal membrane and/or myelin restriction, causing the water diffusion pattern significantly deviating from a perfect Gaussian curve. This is further demonstrated in the phantom data, where the asparagus fibers mimic the white matter, showing a pancake-shaped 3D structure for the DK tensor. A simple demonstration using Monte-Carlo simulation (Fig. 2d) was also performed to show the theoretical predication of the DK tensor of a fiber bundle. Because the DK tensor has a higher degree of freedom compared to DT (15 versus 6), it has the potential to provide more information than conventional DT. This can be illustrated using the case of crossing fiber identification. We studied a synthetic voxel in which the raw data of a corpus callosum (single orientation left-right fiber) ROI and an occipital white matter (single orientation anterior-posterior fiber) ROI were combined to simulate the situation of a crossing-fiber. Fig. 3a and b show the DT and DK tensor, respectively, for this voxel. It can be seen that the DT surface plot still looks like a single-fiber structure with slight anisotropy, whereas the DK tensor plot clearly shows the superposition of two "pancakes". Fig. 4 shows the maps of (a) Q_0, (b) Q_2 and (c) Q_4 from the spherical harmonics expansion. Note that the averaged AKC map (Q_0) is quite different from the mean diffusivity map (Fig. 4d) which shows no contrast between gray and white matter. Table 1 shows the mean ADC and AKC values in typical brain regions. In summary, our results show that diffusion kurtosis imaging can measure the non-Gaussian characteristics of the water diffusion, and is capable of providing complementary information to DTI.

REFERENCES: 1) Jensen et al ISMRM Proc. 2154 (2003); 2) Jackson in "Classical Electrodynamics", John Wiley&Sons, New York (1975); 3) Jones et al MRM 42: 515 (1999); 4) Liu et al MRM. 51: 924 (2004).

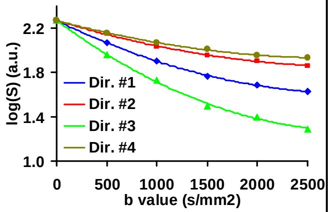

Fig. 1: Log of MR signal vs. b value at 4 gradient directions in one ROI containing corpus callosum. The symbols represent experimental data and solid lines are fitted curve. Such fitting results were routinely obtained in our data.

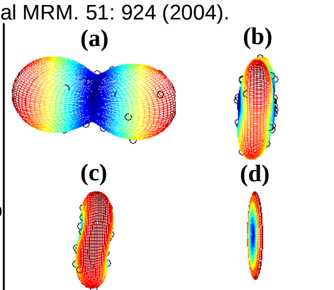

Fig. 2: Angular plots representing (a) DT of corpus callosum, (b) DKT of corpus callosum, (c)DKT of asparagus phantom, (d) DKT of simulation with a single fiber.

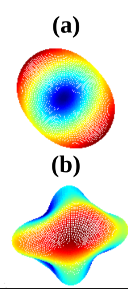

Fig. 3: (a) DT and (b) DKT angular plot of a synthetic crossing fiber that was obtained by combing two ROI with different fiber orientations.

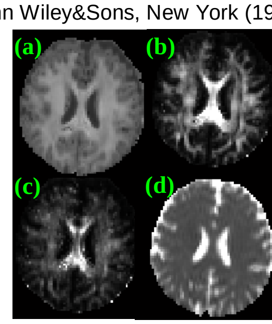

Fig. 4: DKT maps. (a) Q0, (b) Q2, (c) Q4. The trace of DT is also shown (d).

	gray matter	white matter	csf	thalamus
AKC	0.74±0.02	1.07±0.01	0.36±0.03	0.81±0.01
ADC (μm^2/ms)	1.00±0.04	0.93±0.01	3.87±0.12	0.90±0.03

Table 1: Averaged values of AKC and ADC in different brain regions. n=4, mean±SEM.