Quantifying Non-Gaussian Water Diffusion by Means of Pulsed-Field-Gradient MRI

J. H. Jensen[1], J. A. Helpern[1]
[1]New York University School of Medicine, New York, New York, United States

SYNOPSIS

The extent to which water transport in a tissue deviates from homogeneous, Gaussian diffusion can be quantified by a dimensionless statistical measure referred to as the excess kurtosis. By using pulsed-field-gradient spin echo MRI data acquired with large diffusion sensitizing gradients, we show how to estimate the excess kurtosis. In particular, the excess kurtosis can be approximately determined from the lower order terms of an expansion in the gradient strength of the logarithm of the signal intensity. This result is applied to estimate the excess kurtosis in healthy adult and newborn human brain and ischemic rat brain tissue.

INTRODUCTION

When water diffusion in a tissue is homogeneous and Gaussian, then the logarithm of the signal intensity obtained with a conventional diffusion-weighted imaging sequence depends linearly on the square of the strength of the diffusion sensitizing gradients. However, substantial departures from linearity are observed in the brain when large gradients are applied (1-3), suggesting a deviation from simple Gaussian diffusion. This deviation can be quantified with a standard, dimensionless statistical measure called the excess kurtosis (4,5). For Gaussian diffusion, the excess kurtosis vanishes. If the excess kurtosis is negative, the distribution of diffusion paths is more sharply peaked than for Gaussian diffusion, while a positive excess kurtosis indicates that the distribution is less sharply peaked. The excess kurtosis can be estimated from an expansion of the logarithm of the signal intensity in powers of the gradient strength. The excess kurtosis is therefore an experimentally measurable parameter that can be used to quantitatively characterize non-Gaussian water diffusion in tissues.

THEORY

For diffusion in one dimension, the excess kurtosis over a time interval t is defined by

$$K(t) = \left\{ \langle [x(t) - x(0)]^4 \rangle / \langle [x(t) - x(0)]^2 \rangle^2 \right\} - 3 \qquad [1]$$

where the angle brackets indicate an averaging over all the diffusion paths $x(t)$. Now consider a conventional pulsed-field-gradient spin echo sequence used for diffusion-weighted imaging (1-3). The logarithm of the signal intensity S has the expansion

$$\ln[S(b)] = \ln[S(0)] - bD_{\mathrm{app}} + (1/6)\, b^2 (D_{\mathrm{app}})^2 K_{\mathrm{app}} + O(b^3) \qquad [2]$$

with $b = (\gamma\delta g)^2 (\Delta - \delta/3)$. Here g is the gradient strength, γ is the proton gyromagnetic ratio, Δ is the time interval between the centers of the diffusion sensitizing gradient pulses, and δ is the duration of each pulse. In carrying out this expansion, Δ and δ are assumed to be fixed. Equation [2] defines the apparent diffusion coefficient D_{app} and the apparent excess kurtosis K_{app}.

If confounding effects, such as inhomogeneous T_2 relaxation, are negligible, then one can demonstrate that $K_{\mathrm{app}}(\Delta,\delta) = K(\Delta) + O(\delta)$, where K is the excess kurtosis in the direction of the diffusion gradients. This shows that K_{app} approaches the true excess kurtosis as δ goes to zero. In practice, K_{app} obtained with a small value of δ/Δ provides a good approximation for K. The dependence of K_{app} on the gradient orientation can be described by a tensor with 15 independent components.

RESULTS

By applying Eq. [2] to published data (1-3), the excess kurtosis can be estimated for various types of brain tissue (Table 1). These results indicate that water diffusion is less Gaussian in white matter (WM) than gray matter (GM), less Gaussian in adult brain than in newborn brain, and less Gaussian in ischemic brain than in normal brain. The large magnitudes of the variations suggest profound differences in tissue structure. Properties that affect the excess kurtosis include cell membrane permeabilities and intracellular water diffusion coefficients.

Table 1

	Apparent Excess Kurtosis in the Brain					
Reference	Adult GM	Adult WM	Newborn GM	Newborn WM	Normal Rat	Ischemic Rat
1					0.53 ± 0.05	1.42 ± 0.10
2	0.66 ± 0.28	1.03 ± 0.27				
3	0.78 ± 0.12	1.42 ± 0.11	0.29 ± 0.09	0.34 ± 0.09		

REFERENCES

1. Pfeuffer J, Provencher SW, Gruetter R. *MAGMA;* **8**:98-108 (1999).
2. Clark CA, Le Bihan D. *Magn Reson Med;* **44**:852-859 (2000).
3. Mulkern RV, Vajapeyam S, Robertson RL, Caruso PA, Rivkin MJ, Maier SE. *Magn Reson Imaging;* **19**:659-668 (2001).
4. *CRC Standard Math Tables, 25th Edition.* Beyer WH, ed. (West Palm Beach, FL: CRC Press, 1978) p 508.
5. Press WH, Teukolsky SA, Vetterling WT, Flannery BP. *Numerical Recipes in C: The Art of Scientific Computing.* (New York: Cambridge University Press, 1992) p 612.