An accurate and precise new method for measuring kurtosis of intravoxel incoherent motion

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Target Audience: Scientists and clinicians interested in kurtosis and intravoxel incoherent motion (IVIM) imaging.

Purpose: Recently, clinical usefulness of diffusional kurtosis has been reported, e.g., for distinguishing benign from malignant prostate tissues [1]. Measured diffusional kurtosis must contain a systematic error owing to two factors: approximations in method for kurtosis measurement and perfusion. The error is unclear because the true value of the kurtosis is unknown. Clarifying the error is important to improve the kurtosis measurement method and explore its clinical significance. We first investigate the systematic error in measured kurtosis by numerical experiments in which the true value is given. We then develop a new method for measuring kurtosis. Finally, we assess clinical significance of the kurtosis obtained by the new method with simulation.

Methods:

Numerical experiment: We made MR signals in case that the mono-exponential (exp.) perfusion mixes in the bi-exp. diffusion:

$S(b) = \tilde{S}(b)(f_p \cdot e^{-bD^*} + 1 - f_p)$, $\tilde{S}(b) = S_0\{fe^{-bD_f} + (1-f)e^{-bD_s}\}$, where b is b value, f_p is fractional ratio of perfusion, D^* is pseudodiffusion coefficient, f is fractional ratio of fast diffusion, $D_{f/s}$ is fast/slow diffusion coefficient and S_0 is a constant. Rician random noises were added to the MR signals. We targeted benign and cancerous prostate tissues. The diffusion parameters were determined so as to nearly realize the kurtosis reported in Ref. 1. The perfusion parameters were determined according to Ref. 2. We simulated the kurtosis measurement for the MR signals.

Theory of new method: Fourier transformation (F.T.) relation of q-space imaging (QSI) is $S(q)/S(0) = \int_{-\infty}^{\infty} P(R) \cdot \exp(iqR)\, dR$, where $S(q)$ is MR signal for QSI, $q = \gamma G\delta$ (γ: gyromagnetic ratio, G: motion probing magnetic gradient, δ: duration of the gradient) and $P(R)$ is probability density function (PDF) of spin displacement R. The F.T. relation means that the normalized MR signal of QSI is the characteristic function of PDF:

$$S(q)/S(0) = \sum_n^{0,2,4,\cdots,\infty} M_n\, q^n/n!\,, \qquad \cdots \ (1)$$

where we have expanded the right-hand side of the F.T. relation with respect to q, used the definition of moment $M_n = \int_{-\infty}^{\infty} P(R) R^n dR$ ($M_0 = 1$), and assumed that the PDF is an even function. We can obtain M_2 and M_4 by fitting MR signals to Eq. (1) truncated at q^4, and then kurtosis K from definition, $K = M_4/M_2^2 - 3$. We call this method[3] as characteristic function method (CFM) hereafter. On the other hand, logarithm of the characteristic function, $\log\{S(b)/S(0)\} = -bD + (bD)^2K/6 + \cdots$, is the cumulant generating function. Diffusional kurtosis imaging (DKI) uses the expansion truncated at b^2 to obtain kurtosis [4].

We propose a new method by improving CFM as follows. Note that moment M_n^G for a Gaussian PDF can be expressed as $M_n^G = c_n (M_2^G)^{n/2}$, where

$$c_n = n!/\{(n/2)!\, 2^{n/2}\}\,. \quad \cdots \ (2)$$

Since $M_2^G = (M_{n-2}^G/c_{n-2})^{2/(n-2)}$, we have $M_n^G = c_n (M_{n-2}^G/c_{n-2})^{n/(n-2)}$. Therefore, in non-Gaussian cases, moments for $n \geq 4$ can be expressed as

$$M_n = (c_n + K_n) \cdot (M_{n-2}/c_{n-2})^{n/(n-2)}, \quad \cdots \ (3)$$

where K_n's are new parameters that are zero for a Gaussian PDF and $K_4 = K$. If M_2 and K_n's are given, then M_n's are determined by Eq. (3) in succession. We then truncate the expansion of Eq. (1) at $n = 10$ and assumed a Gaussian form to M_n for $n > 10$:

$$S(q)/S(0) = \sum_n^{0,2,4,\cdots,10} M_n\, q^n/n! + \exp\left(-\tilde{M}_2 q^2/2\right) - \sum_n^{0,1,2,\cdots,5} (-\tilde{M}_2 q^2/2)^n/n!\,, \quad \cdots \ (4)$$

where $\tilde{M}_2 = (M_{10}/c_{10})^{1/5}$. We made a table of sample MR signal functions with Eqs. (2) - (4) by assigning various values to the parameters, M_2 and $K_{4,6,8,10}$. For all the sample MR signals, we calculated the 2nd and 4th moments using CFM, i.e., fitted the sample MR signals to Eq. (1) truncated at q^4. These results give tables of systematic errors for the 2th and 4th moments. We made calibration functions for the moments by interpolating the table data, i.e., for the measured 2nd and 4th moments m_2 and m_4, we made $m_2 - M_2$ and $m_4 - M_4$ as functions of m_2 and m_4. The calibration functions had been made as numerical interpolation functions. The new method gives the 2nd and 4th moments by using the calibration functions.

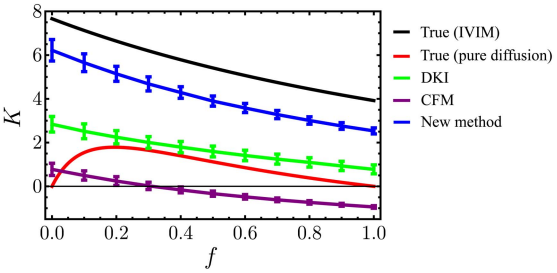

Figure 1: Variation of kurtosis with the fractional ratio of fast diffusion. Error bars indicate standard deviation. $b = 0, 50, 100, 200, 300, 400\ \mathrm{s/mm^2}$, $\mathrm{SNR} = 15$, $\mathrm{NAS} = 2$, and (number of voxcels in ROI) $= 5$ are assumed.

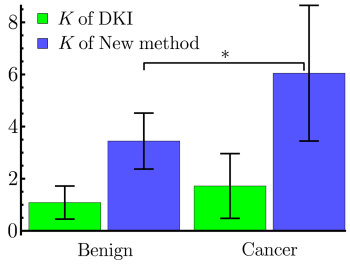

Figure 2: Simulated medians of K for benign and cancerus tissues obtained by DKI and the new method. Error bars indicate interquartile range. Significant differences ($P < 0.05$) are indicated by asterisks. $\mathrm{SNR} = 5$, $\mathrm{NAS} = 1$, (number of voxcels in ROI) $= 5$, $b = 0, 50, 100, 200, 300, 400\ \mathrm{s/mm^2}$, and (number of patients) $= 14$ are assumed. Note that parameters other than f also differ between benign and cancerus tissues.

Results: Figure 1 shows variation of kurtosis with the fractional ratio of fast diffusion. If perfusion mixes in diffusion, the true value of kurtosis becomes substantially large. Both DKI and CFM give greatly different results from the true value even though we use low b values to aim at measuring the IVIM kurtosis. The systematic error of the IVIM kurtosis is large especially in CFM, while the statistical error of CFM is smaller than that of DKI. Kurtosis obtained by the new method approached to the true value. Figure 2 shows a simulation result of IVIM kurtosis measurements for prostate cancer assessment. A significant difference between the benign and the cancerous tissues can be detected only by the new method for this small SNR.

Discussion: The systematic errors of kurtosis obtained by DKI and CFM are expected to be removed by a calibration because the errors are nearly constants when f varies. Therefore, we developed the new method by improving CFM in which the statistical error is small though the systematic error is large. The new method can provide IVIM kurtosis comparatively accurately. Although the calibration causes slight increase of the statistic error, the errors is the same level with that of DKI.

Conclusion: Value for IVIM kurtosis obtained by the new method is suggested in the simulation of prostate cancer assessment.

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