Comparison of Results Obtained by Fitting DWI Data to a Model Including IVIM and Kurtosis using Nonlinear Least Squares and Maximum Likelihood Estimation

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Purpose: This study investigates the accuracy and precision of diffusion parameters derived from fitting MR diffusion weighted data. A five parameter diffusion model was fit to simulated data using a non-linear least squares fit and through maximum likelihood estimators to compare the results obtained using two fitting methods. The repeatability of diffusion estimates for data collected from a phantom which incorporates diffusion and flow was investigated and compared to the precision of diffusion values calculated for the simulations.

Methods: Simulations of diffusion weighted MR signal were generated using a model that incorporates a diffusion compartment, a fast exponential decay compartment, kurtosis in the diffusion compartment, and noise. The expected MR signal was calculated using the equation $S = S_0\left((1-f)e^{(-bD_t+b^2D_t^2K/6)} + fe^{-bD_p}\right)$ where S_0 is the signal at b=0, D_t is the diffusion coefficient, K is kurtosis in the diffusion compartment, D_p is the fast exponential decay coefficient for perfusion, and f is the fraction of S_0 from the fast decay compartment. Independent Gaussian noise was added to a real and an imaginary channel before computation of the signal magnitude. 10,000 simulations of noisy data were performed by adding noise to simulate signal to noise ratios (SNR) of 40, 10 and 5 in the b=0 signal. The values of D_t, D_p, K, and f used in the simulations were 0.001 mm^2/s, 0.015 mm^2/s, 1.0, and 0.1 respectively. The signal with noise at b=0 was used for S_0. B values of 0, 10, 25, 50, 100, 250, 450, 1000, 1500, and 2000 were used. The data for each simulation were fit to the model using two methods; 1) non-linear least squares fitting (NLS), and 2) through maximum likelihood estimators (MLE). A Rician distribution for the noise was fit to the data after extreme outliers were removed. Diffusion images of a phantom were acquired at 3T (Philips Ingenia) using the b values used in the simulations. The phantom consisted of a sponge in a PVC nipple submerged in a water bath and water was forced through the sponge similar to a phantom in the literature (Cho et al., 2012). The water was pumped at three rates; 1, 2, and 3 mL/min. The reproducibility of the phantom was investigated by making multiple measurements on three days.

Results: The deviation of the mean D_p, K and f from the true values and the standard deviations of the estimates were normalized by the true value and are reported in Figure 1. D_p was overestimated by both fitting approaches with large standard deviations. The quality of the fit was independent of SNR. The distributions for f also had large standard deviations at lower SNR with MLE producing estimates closer to the true value than NLS. The quality of the estimates improved as the SNR increased. The estimates of K also improved with increasing SNR with MLE giving better estimates than NLS. At lower SNR, MLE produced a greater number of extreme outliers than NLS and the number of simulations that needed to be removed increased. Phantom data collected on three days are presented in Figure 2. The SNR of the b=0 image was greater than 200. The data from similar flow rates are grouped with the variation between days being less than the difference between flow rates. The standard deviation of the calculated parameters was smaller than the variation for simulations with SNR of 40.

Discussion: The influence of noise on diffusion parameter estimation is parameter dependent with some parameters being difficult to measure in the presence of noise. The diffusion coefficient was fairly robust at the SNR values tested with the distribution of D_t having a mean within 20% of the true value and fairly tight standard deviation (data not shown). The fast decay compartment was included to simulate perfusion. The influence of noise makes D_p and f more difficult to estimate than D_t for the parameter values simulated here. Further simulations are being carried out to test parameter sensitivity to noise for other combinations of values of the parameters. It is important to note that the uncertainty of estimated diffusion parameters may be much greater than the SNR of the acquired data. Simulations are an important tool for characterizing the uncertainty of derived diffusion parameters. At very high SNR, the parameter distributions are much tighter as seen with the small variation of parameters calculated for the phantom. The phantom data also shows the possibility of adjusting the diffusion and perfusion compartments to develop phantoms which mimic specific tissues.

Conclusion: The accuracy and precision of model parameters derived from MR diffusion weighted data are greatly influenced by SNR. Understanding this relationship can be important in power calculations for diffusion experiments and in assessing the reliability of conclusions. A diffusion model which includes perfusion and kurtosis has been fit with NLS and MLE with the conclusion that improved SNR allows for improved parameter estimation. It seems that at lower SNR the MLE method produces more reliable results than NLS.

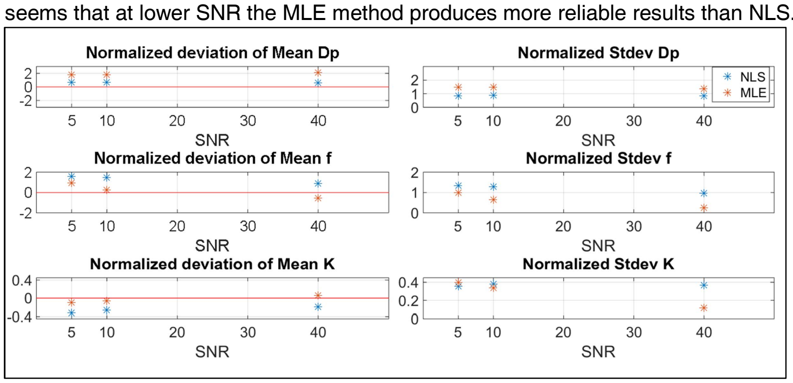

Figure 1

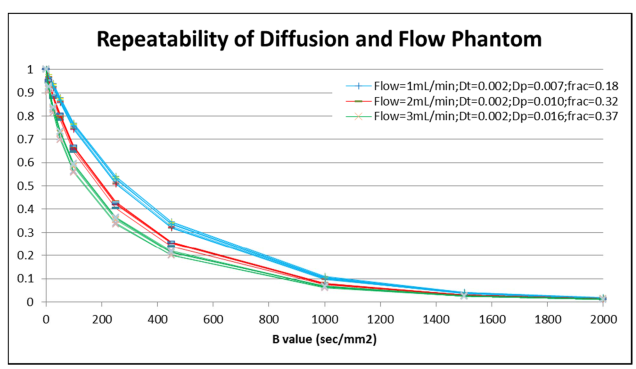

Figure 2

References: Cho, G. Y., Kim, S., Jensen, J. H., Storey, P., Sodickson, D. K., & Sigmund, E. E. (2012). A versatile flow phantom for intravoxel incoherent motion MRI. *Magnetic Resonance in Medicine, 67*(6), 1710-1720.