Optimistaion of b-value distribution in biexponential modelling

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Introduction Traditionally, ADC determination involves mono-exponential fitting of diffusion weighted imaging (DWI) data, thus potentially ignoring microperfusion contributions to the signal decay at low *b*-values. Recent work has demonstrated that it is technically possible to acquire DWI data of the brain [1] and other organs [2-6] with low *b*-values in an attempt to quantify this perfusive fraction of the ADC decay curve via bi-exponential modelling. However, large uncertainties in the fitted parameters have prevented the widespread adoption of this technique. Efforts to optimise the acquisition protocol have been made [7] and it appears evident that increased sampling at low *b*-values to adequately define the rapidly decaying perfusive weighted component is necessary. Adapting the work of Shrager *et al* [8], which investigated optimal time spacing for T_2 measurements in mono- and bi-exponential systems, this study aims to assess the optimal *b*-value spacing in bi-exponential modelling of various tissue organs.

Methods Synthetic data simulating the MR signal decay of a bi-exponential system was created in Matlab (The MathWorks Inc) using the following equation

$$S_b = S_0\left([1-f]e^{-bD'} + fe^{-bD^*}\right)$$

where *f* is the perfusion fraction, *D′* is the pure diffusion coefficient, *D** is the pseudo diffusion coefficient, *b* is the *b*-value, and S_0 (S_b) is the signal at a *b*-value of 0 (*b*) s/mm^2. Data was created for 4 tissue types using literature obtained parameter values (brain: f=5%, D*=10μm^2/ms, D′=1μm^2/ms [1]; breast: f=10%, D*=15μm^2/ms, D′=1.15μm^2/ms [2]; kidney: f=30%, D*=15μm^2/ms, D′=1.5μm^2/ms [3]; liver: f=30%, D*=60μm^2/ms, D′=1μm^2/ms [4]). Gaussian noise was added to produce data ranging from SNR=10:1 to SNR=1000:1. The simulated data was calculated using 10 *b*-values determined from the Power Law formula where the i^{th} *b*-value is given by

$$b_i = b_{min} + (b_{max} - b_{min})\left(\frac{i-1}{n-1}\right)^r$$

where b_{min}=0, b_{max}=1000 s/mm^2, *n*=10, and *r* varied from 1 (linear spacing) to 5. For each combination of *b*-value distribution, organ parameters and SNR level 1000 cases were generated. Bi-exponential fitting was performed using simplex minimisation. Initial *D′* estimates were determined by a mono-exponential fit to *b*>500 s/mm^2 data points with initial *D** and *f* estimates based on extrapolation of this mono-exponential curve to *b*=0 s/mm^2. Data was also fitted to a mono-exponential model for comparison.

Results For the brain data bi-exponential fitting consistently overestimated the perfusion fraction *f* in all but the highest SNR regimes with estimates of ~9.5% at SNR < 20 compared with the nominal value of 5%. Mono-exponential analysis also provided a better fit (lower RMSE) in the low SNR regime. Similar results were obtained for breast synthetic data. For tissues with a high perfusion fraction (liver and kidney) bi-exponential fitting consistently outperformed mono-exponental fitting for all SNR values. Because of the rapid loss in signal from the perfusive component the optimal sampling strategy occurred when r=3.0 (corresponding to *b* = 0, 1.4, 11, 37, 87, 171, 296, 471, 702 and 1000 s/mm^2) and above.

Discussion This work has demonstrated that bi-exponential fitting of synthetic DWI data is feasible using 10 *b*-values. When a relatively small perfusive component fraction is present (≤10%) a relatively high SNR in the DW images appears to be necessary, otherwise a mono-exponential model provides a better fit. For tissues with a rapid (≥15μm^2/ms) and large perfusive component (≥30%) adequate sampling of low b-values using a non-linear spacing strategy is paramount for accurate fitting. However, the use of very low *b*-values in imaging is often difficult, wherein imaging gradients may contribute significantly to the 'true' *b*-value as compared to the inputted desired *b*-value. Future work will attempt to assess the effect of imaging gradient contributions on the fitting methods developed.

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