Optimization 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

$$S_b = S_0 [1 - f] e^{-b D'} + f e^{-b D^*}$$

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: $f=5\%$, $D^*=10\mu m^2/\mu s$, $D'=1\mu m^2/\mu s$ [1]; breast: $f=10\%$, $D^*=15\mu m^2/\mu s$, $D'=1.15\mu m^2/\mu s$ [2]; kidney: $f=30\%$, $D^*=15\mu m^2/\mu s$, $D'=1.5\mu m^2/\mu s$ [3]; liver: $f=30\%$, $D^*=60\mu m^2/\mu s$, $D'=1\mu m^2/\mu s$ [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 $\sim9.5\%$ 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-exponential 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 ($\leq10\%$) 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 ($\geq15\mu m^2/\mu s$) and large perfusive component ($\geq30\%$) 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.