Repeatability of Mono- and Bi-Exponentially Modelled Diffusion at 3 Tesla

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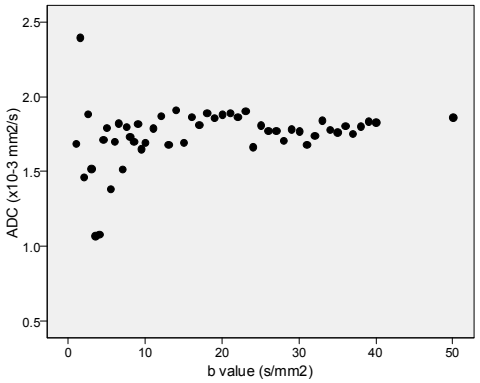
Introduction Whilst the reduction in ADC of cancerous tissues generally provides insufficient discrimination to be used as a stand-alone diagnostic tool it has been suggested that ADC may be useful in monitoring tumour response to treatments such as radiotherapy and/or neoadjuvant chemotherapy [1-3]. Traditionally, ADC determination involves mono-exponential fitting of the 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 prostate and other organs with low *b*-values to quantify this 'perfusive' fraction of the ADC decay curve via bi-exponential modelling [4,5]. However, no attempt has been made to assess the repeatability of such work which, amongst other factors, is clearly dependent on accurate *b*-value implementation by system manufacturers. This can be problematic, especially at very low *b*-values, where imaging gradients may contribute significantly to the 'true' *b*-value as compared to the inputted desired *b*-value. Assessment of these effects and repeatability determination are therefore important prior to the acquisition of clinical data.

Methods All DW images were acquired on a 3 Tesla (MR750) GE Scanner using a spin-echo EPI based sequence (TE/TR 86/12000 ms, flip angle 90°, field of view 24 cm, matrix size 128×128, slice thickness 5 mm, number of averages 1). Diffusion gradients were applied along all 3 axes simultaneously for all experiments. A cylindrical water phantom was imaged at 60 *b*-values ranging from 0 to 1000 s/mm^2, with a higher concentration of measurements at lower values, to assess the efficacy of bi-exponential fitting. After image acquisition data was analysed using an ROI approach with in-house developed software. For the phantom data, using b=0 s/mm^2 and b=(0<x≤1000) s/mm^2 a plot of ADC versus *b*-value was produced. To assess the repeatability of bi-exponential fitting 6 volunteers were scanned twice on consecutive days using 20 *b*-values. ROIs were drawn in white matter and the data fitted to both a bi-exponential and mono-exponential diffusion model. Finally, the repeatability was determined via the methodology previously described by Bland and Altman [6] and utilised in assessing the reproducibility of pharmacokinetic modelling [7].

Results The relationship between calculated ADC and nominal *b*-value is shown for *b*-values ≤ 50 s/mm^2 in the graph alongside. For b-values > 50 s/mm^2 calculated ADC values demonstrated less than 1% difference. As is evident there is a marked variability in ADC as the *b*-value is decreased below 10 s/mm^2 suggesting that reliance on these measurements is problematic. The results of the volunteer repeatability analysis are shown in the table below. The mono-exponentially calculated D appears to be the most repeatable parameter with a 21% change in value required, on an individual patient basis, to be confidently attributed to a treatment effect. The least repeatable parameter is D* which entails a 74% treatment induced change.



	Mean ± SD	Repeatability	% Change Required
f (%)	9.37 ± 1.47	2.87	30.6
D′ (×10^{-3} mm^2/s)	0.62 ± 0.10	0.19	31.6
D* (×10^{-3} mm^2/s	10.71 ± 4.04	7.92	74.0
D (×10^{-3} mm^2/s)	0.76 ± 0.08	0.16	21.4

f – Perfusion fraction, D' – Diffusive coeff. (bi-exp), D* - Perfusive coeff. (bi-exp), D – Diffusion coeff. (mono-exp)

Discussion This work has demonstrated that mono-exponential fitting of DWI brain data appears to be reasonably repeatable and thus has the potential to monitor relatively small treatment induced changes. Bi-exponential fitting of this data is less repeatable especially with regard to calculation of the 'perfusive' component. The variation in calculated ADC for low *b*-values must be taken into consideration and may lead to a more judicious selection of b-values when acquiring data for bi-exponential fitting.

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