Comparison of Different Fitting Algorithms for Analysis of High b-value Prostate Diffusion Imaging

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Introduction: In biological tissues, microscopic motion detected by diffusion-weighted MRI (DW-MRI) includes both diffusion of water molecules (influenced by the structural components of the tissue) and complex underlying cellular components and structures that hinder and restrict the diffusion of water molecules (as well as microcirculation of blood in the capillary network (perfusion)). To date, most clinical DW-MRI studies have employed a so-called "monoexponential" model for data analysis, which produces a single parameter – the apparent diffusion coefficient (ADC) – for assessing diffusion characteristics. While studies have shown that ADC values correlate with Gleason scores in prostate cancer (1), specific ADC values vary substantially between studies in which different b-values, or diffusion settings, are used.

DW-MRI using a wider range of b-values permits derivation of non-monoexponential diffusion models allows interrogation of both low-mobility (intra-cellular or bound water molecules) and high-mobility (extra-cellular) water populations. Several models have been proposed in recent studies, including bi-exponential (BE) model (2), stretched exponential (SE) model (3), and non-Gaussian (NG) – Kurtosis model (4).

To fit parameters to the measured MR signal intensities as a function of b-value, a non-linear least squares (NLLS) algorithm is usually used. LSQ assumes that the noise is normally distributed. Since at high b-values the noise follows a Rice distribution, this assumption is typically not valid and the diffusion parameter estimation might be inaccurate if the Rice distribution of magnitude DW data is not taken into account. To account for the Rician noise at low signal-to-noise ratio (SNR) images at high b-values, the maximum likelihood (ML) algorithm has been applied to provide unbiased diffusion parameter estimates (5)(6).

BE	$\frac{S(b)}{S_0} = (1-f)\cdot\exp(-b\cdot D_1) + f \cdot \exp(-b\cdot D_2)$	f, D_1, D_2
SE	$\frac{S(b)}{S_0} = \exp(-b\cdot DDC)^{\alpha}$	α, DDC
NG	$\frac{S(b)}{S_0} = \exp\left(-b\cdot D_{\text{app}} + \frac{1}{6}b^2\cdot D_{\text{app}}^2\cdot K\right)$	D_{app}, K

Methods: *Simulations*: Monte Carlo simulation was carried out to assess the properties of the two fitting algorithms at a range of SNRs and for three different models. Data were simulated by adding Gaussian noise to complex signal (real and imaginary components) for an eight-channel phased-array coil assuming uncorrelated noise to simulate a Rician distribution of the magnitude signal. The resultant signal was fitted to all three models. The percentage noise is expressed as a percentage of the signal intensity at b=0. For each set of b-value, and each noise level, 1024 simulations were performed. For each combination of b-values, the data was fitted to the model using the Levenberg-Marquardt method for NLLS curve-fitting and the ML algorithm with a Rician noise distribution. Accuracy was assessed by the relative bias, defined as the percentage difference between the fitted and ideal parameter values.

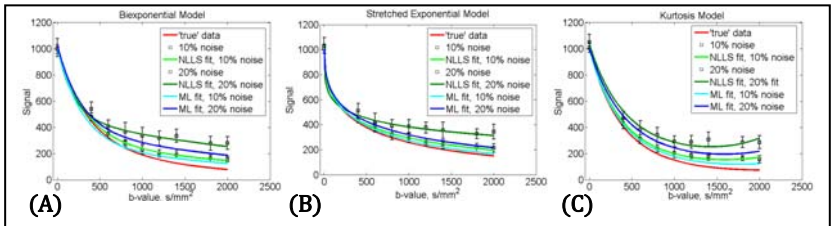

Fig. 1: Fit (simulations) results from ML and NLLS estimates for (**A**) BE, (**B**) SE and (**C**) NG – Kurtosis models. The blue curves are the ML fits and the green curves are the NNLS fits. %noise = 10% and 20%.

MR Data: The institutional review board issued a waiver of informed consent for this HIPAA-compliant retrospective study. Twenty-two patients with biopsy-proven prostate cancer underwent standard 3-Tesla MRI. DW-MRI at nine b-values (0, 400, 600, 800, 1000, 1200, 1400, 1800, and 2000 s/mm²) were acquired. On b=0 images, noise was measured as the standard deviation from the mean signal in an artifact-free ROI in the rectum.

Results & Discussion: Fig. 1 shows results from the Monte Carlo experiment. The decays of normalized DW signal typically observed in the normal peripheral zone tissue with the multiple b-value acquisitions and all three models. As compared to 'true' data (no noise), the NLLS fit, NLLS overestimates D_1 (24% and 62% at 10% and 20% respectively) compared to 5% and 34% for ML method. For SE model, *DDC* is underestimated by 10.5% and 37% with NLLS fit, compared to ML fit which underestimates by 10.1% and 5.2%. For NG model, *D*app is underestimated by 4.4% and 24% with NLLS fit, compared to ML fit which underestimates by 1.3% and 8.4%. Similar pattern of results were obtained from *in vivo* prostate data from a benign and tumor ROIs (Fig 2). It must be noted that ML estimate of diffusion parameters is significantly limited if the noise level is not accurately known *a priori*.

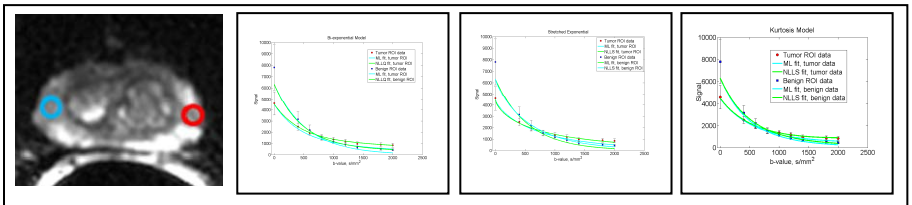

Fig. 2: Comparison of fit results with the ML and NLLS algorithms with the BE, SE, and NG – Kurtosis model from a benign (blue) and tumor (red) region-of-interest.

Conclusions: By accounting for the distribution of noise, the ML analysis yields accurate estimates of f, D_1, and D_2 (BE model), α and *DDC* (SE model), and D_{app} and K (NG model), while the NLLS method, which does not incorporate noise, might introduce bias in estimating these parameters.

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