Performance Evaluation of Various Numerical Algorithms for a Multi-Compartmental IVIM-Model

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Introduction: Diffusion-weighted MRI (DWI) is a non-invasive imaging technique that detects thermally driven, random motion of water molecules in living tissue and is able to characterize its interaction with cell membranes, macromolecules and potential diffusion barriers in terms of an apparent diffusion coefficient ADC with or without restriction. Le-Bihan proposed a bi-exponential model to separate intra- and extracellular diffusion from incoherent motion of water molecules within randomly oriented capillaries – IVIM [1-3]. Several studies have utilized IVIM for various clinical applications in the abdomen (tumors, liver cirrhosis) and animal experiments [4] although the interpretation of data in the context of classical perfusion remains disputable [5].
The presence of noise and patient motion in DWI, which cannot be sufficiently eliminated through postprocessing or special acquisition techniques, may substantially affect IVIM parameter estimation reliability [6]. Especially low number of b-value DWI suffers from the intrinsic inability to differentiate bulk or peripheral motion (whole body movement, bowel motion, breathing, pulsation due to cardiac cycle) from the incoherent molecular motion (diffusion and perfusion). The quantitative assessment of IVIM-parameters in the brain is even more complicated due to the fact of its anisotropic diffusion. The deconvolution of multi-exponential processes like water diffusion in living tissue is a strongly ill-posed problem and the necessity for a large number of signal points and SNR is imminent for a reliable separation of more than one exponential time constant [7-10]. The evaluation of current fitting modalities for IVIM data and investigating their limitations in relation to SNR and number of b-values is therefore prudent.

Methods: In the frame-work of Monte Carlo simulations a numerical toolbox was developed in a high level programming language (IGOR-Pro 6.1, Wavemetrics Inc. OR, USA) to test the ability and SNR-thresholds of various numerical exponential, multi-exponential fitting and analysis algorithms for the purpose of IVIM data analysis: i) Levenberg-Marquardt LS, ii) maximum likelihood estimates (MLE), iii) genetic algorithm for multi-exponential fitting, iv) non-negative least-squares (NNLS), and v) regularized NNLS.
Data were generated according to a bi- and tri-exponential pulsed field gradient (PFG) diffusion model (generalized Stejskal-Tanner equation [11]) with multiple b's (3 to 64), b-values and spacing of b-values, diffusion coefficients, and SNR: $S = S_0 \cdot \sum_{i=1}^{3} DF_i \cdot \exp(-bD_i)$ were DF are the individual diffusion fractions for each diffusion coefficient D. Noise was generated with either Gaussian or Rician distribution for SNR between 10 and 1000. Regularized NNLS with corresponding diffusion signal kernel was performed with 121 log-spaced diffusion coefficients between 0.1 and 1000 $\mu m^2/ms$ (Fig.1, top). Each analyzed signal decay curve results in a diffusion distribution (spectrum) displaying the diffusion fraction for each apparent diffusion coefficient ADC (in the following denoted as D) (Fig.1, top right corner). The novelty of this hereby introduced approach lies in its semi-continuous nature and therefore its ability to derive quantitative diffusion fraction maps from any arbitrary D or range of D-values. For example, the vascular perfusion fraction vPF can be determined from the inverse solution of the signal decay function by taking the ratio of the integral D between 10-100$\mu m^2/ms$ and the total integral.

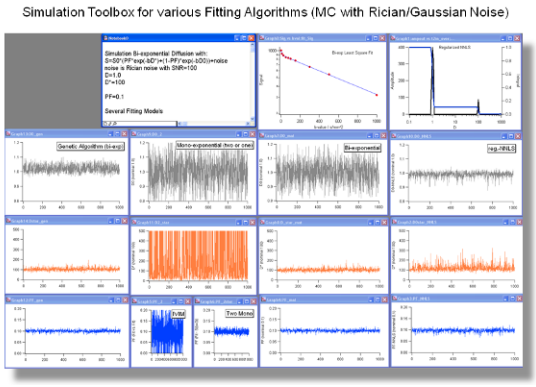

Fig.1: Screen safe of the Monte Carlo performance fitting simulation toolbox in IGOR-Pro 6.1 with Levenberg-Marquardt LS fitting, regularized NNLS and genetic multi-exponential algorithm at various noise realizations.

Results: Fig.2 lists a few results in comparison for the extraction of IVIM-model parameters D, D* and vPF (vacular perfusion fraction) from a bi-exponential model with the various numerical algorithms. Although mean values for 1000 noise realisations are very robust and comparable between the fitting methods the variance of the simulated data shows large deviations. Even at hypothetically very high SNR=1000 the conventional IVIM-approach (Mono-exp/S0) with fitting a mono-exponential to b-values>100 and estimating the perfusion fraction from the difference of the interception of this fit with the y-axis and the b0-signal falls strongly behind the slightly more advanced method like bi-exponential routines. For moderate to low SNR>100 the most critical part in obtaining reliable and reproducible parameter estimations with conventional LS-fit is the proper determination of adequate start values which have to be obtained from the signal curve (e.g. S0, baseline offset etc.) or must be guessed. That is why generic algorithms and reg.-NNLS routines result in much more robust fitting results with lower overall standard deviation even at very low SNR.

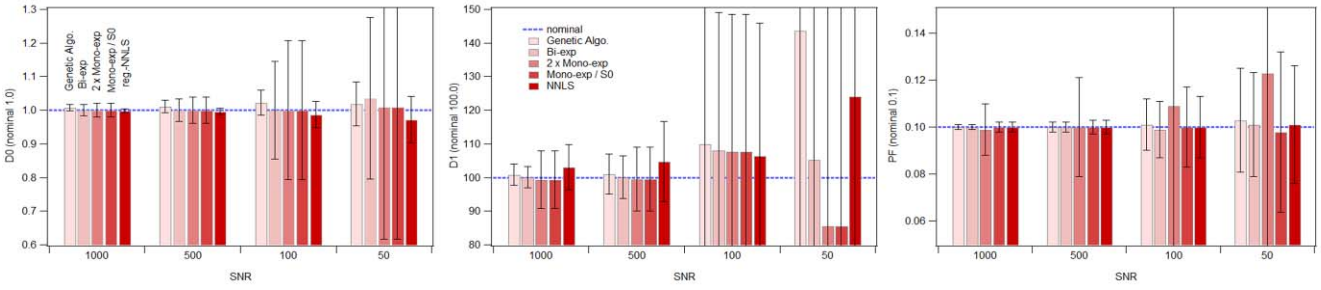

Fig.2: Comparison of three parameter estimates for an IVIM bi-exponential model for various fitting routines showing the mean and standard variation for D (denoted as D0), D* (denoted as D1) and the perfusion fraction PF after 1000 noise realisations. The best reliability is achieved with genetic algorithms and regularized NNLS.

Conclusion: Advanced numerical fitting routines like genetic algorithms or regularized NNLS show superior performance in terms of robustness and reliability in extracting multi-compartmental parameters from DWI. We hypothesize that their application for the analysis of current IVIM-protocols with generally low SNR is advantages.

References: [1] Le Bihan D, Radiology 161 (1986):401; [2] Le Bihan D, J Comput Assist Tomogr. 15 (1991),19; [3] Le Bihan, D. et al. *Radiology,* 168 (1988),497; [4] Henkelman, R.M. et al., MRM 32 (1994), 464; [5] Henkelman, R.M., MRM 16 (1991), 470; [6] ; Schneider, M. et al. ISMRM 2012, #2029; [7] Whittall, K. et al. MRM 41 (1999), 1255; [8] Whittall, K., MacKay, A., JMR 84 (1989), 134; [9] Whittall, K. in "Signal treatment and signal analysis in NMR", p. 44, Elsevier, Amsterdam, 1996; [10] Bennett, KM et al. MRM 50 (2003), 727; [11] Stejskal, E. O.; Tanner, J. E.; J Chem.Phys. 42 (1965), 288