Optimizing b-value distribution for IVIM imaging using adjusted weighting factors

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Purpose: Intra-voxel incoherent motion (IVIM) imaging differentiates between true molecular diffusion (*D*), diffusion due to perfusion (*D**), and quantifies perfusion fraction (*f*). IVIM imaging has been applied to e.g. characterize and stage, in a non-invasive way, several pathological changes of the liver [1, 2]. However, results from its clinical application have been ambiguous and this can be, at least in part, explained by the dependence of IVIM parameter estimation on the choice of b-value combination that is used to sample the data [3, 4]. In [3] the optimal b-value combination is chosen through the minimization of an error propagation factor, assuming equal relative contributions of each parameter to the total estimation error. It was shown in [4] that the performance of the method depends on the perfusion regime and on T2 relaxation effects. In this paper we hypothesize that the performance of the method described in [3] is influenced by the relative contribution of *D*, *D** and *f* to the total error. In order to investigate this, we quantify the relative contributions of each parameter to the total error and we compare the performance of [3] considering equal and different error weights for *D*, *D** and *f*.

Methods: The IVIM signal follows a bi-exponential model combining the effects of D and D*:

$$S = S_0\left((1-f)e^{-bD} + fe^{-b(D+D^*)}\right). \qquad (1)$$

where S_0 is the nominal signal intensity for b=0. In order to estimate the error of IVIM parameters, the error propagation factor as defined in [3] was calculated as:

$$\zeta(n) = \frac{S_0}{x(n)}\sqrt{\sum_{m=1}^{4}\sum_{p=1}^{4}\left[A^{-1}(n,m).A^{-1}(n,p).\sum_{i=1}^{N_b}\left(\frac{\partial S(b_i,x)}{\partial x(m)}.\frac{\partial S(b_i,x)}{\partial x(p)}\right)\right]}. \qquad (2)$$

where *n* varies from 1 to 4, *x(n)* refers to each of the IVIM parameters (*D*, *D**, *S0* and *f*), $A=J^TJ$, and *J* is the Jacobian matrix of *S(x)*. The total error that is propagated into IVIM parameters is calculated as:

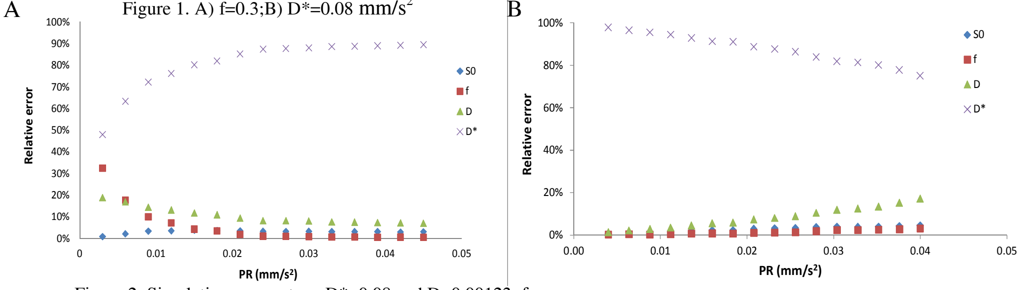
$$\zeta_{total} = \int_{D^*_{min}}^{D^*_{max}}\int_{D_{min}}^{D_{max}}\int_{f_{min}}^{f_{max}}\left(W_f\zeta_f + W_D\zeta_D + W_{D*}\zeta_{D*} + W_{S_0}\zeta_{S_0}\right)df\,dD\,dD^*. \qquad (3)$$

The quantification of the relative contribution of S_0, *D*, *D** and *f* to the total error were computed using (2) and considering different values for the perfusion rate (*PR*), here defined as *PR=D*×f*. Furthermore, *PR* was varied either by fixing *D** and varying *f* or vice-versa. The performance of different b-value distributions (with N_b=10 [4]) in estimating IVIM-DWI parameters were tested in the presence of (Rician) noise using Monte Carlo simulations with 1000 noise realizations. Noise effects on estimated parameters were quantified with Relative Error (*RE*) and Bias (*B*) defined as: $RE=\sigma_{X_E}/X$ (4) and $B=(\overline{X_E}-X)/X$ (5), where σ_{X_E} is the standard deviation associated the estimation of parameter X over 1000 noise realizations and $\overline{X_E}$ is the average of X estimations over all noise realizations.

Three b-value distributions were considered in these set of simulations: 1) *Conventional(C)*: b-values are chosen more or less heuristically as in clinical applications (e.g. 0, 5, 15, 30, 40, 80, 100, 200, 400, 800); 2) *Optimum with equal weights (OEW)*: Obtained from the minimization of (3) with $W_f=W_D=W_{D*}=W_{S0}=0.25$; 3) *Optimum with different weights (ODW)*: Obtained from the minimization of (3) but with $W_f \neq W_D \neq W_{D*} \neq W_{S0}$. In *ODW*, weights were taken from the results of the first set of simulation studies.

Results: The quantification of the relative contribution of S_0, *D*, *D** and *f* to the total error as a function of PR is shown in figure 1. In fig. 1A, where f is kept fixed at 0.3 and D* is varied, results show that the relative contribution of each parameter to the total error varies considerably, especially for lower values of PR. Furthermore, D* shows the highest contribution to the total error, varying between 50% for lower PR values, and approximately 90% for higher values of PR. Results in fig. 1B, where D*=0.08 mm/s^2 and f varies confirms that D* explains most of the error associated with IVIM parameter estimation, with a relative error that varies between 80%, for higher values of PR, to approximately 100% for very low PRs. However, for the same variation range of PR, it is not indifferent whether the latter is changed by varying f or D*. The relative error of D*, D and f appears to be more sensitive to variations in PR when f is kept fixed. Finally, figure 2 shows that in the presence of noise, the performance of the optimum b-value distribution in estimating D* when compared to that of the conventional distribution, improves when considering different rather than equal weights. However, for very low SNR values, the conventional b-value distribution outperforms both OEW and ODW distributions.

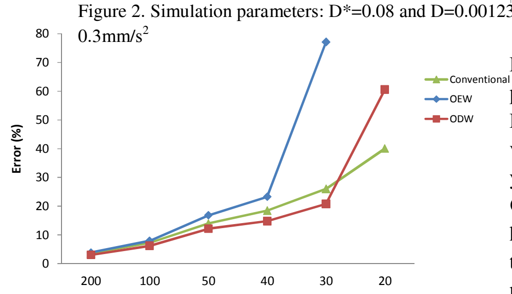
A Figure 1. A) f=0.3;B) D*=0.08 mm/s^2 B



Similar results (not shown) were obtained for *B*. For D and f (results not shown) differences are smaller.

Discussion: IVIM parameter estimation is highly dependent on which b-values are used to sample the data [4]. The optimization of b-value distribution by means of minimizing an error propagation factor has been recently proposed [3] to increase the accuracy of IVIM parameter estimation. In this paper we show that D* has the major contribution to the total propagated error. Furthermore, the relative contribution of each parameter to the total propagated error depends on the perfusion rate, especially in the case where the perfusion rate changes due to the variation of D*. Finally, it is shown that in the presence of noise, the *ODW* b-value distribution outperforms the *OEW* b-value distribution for all ranges of SNR. Striking is the fact that the conventional distribution appears to yield lower D* error than those yielded by *OEW* and *ODW* distributions for very low SNRs.

Figure 2. Simulation parameters: D*=0.08 and D=0.00123, f = 0.3mm/s^2



Conclusion: The performance of optimized b-value combinations [5] for IVIM parameter estimation is highly dependent on the perfusion regime that underlies the tissue under study. For best performance, the weight of each parameter in the total propagated error should be adjusted to match expected perfusion regime of the tissues.

References: [1] Luciani et al., Radiology, 249(3), 891-899, 2008 [2] Guiu et al., Radiology, 265, 96-103, 2012 [3] Zhang et al., Magn Res Med, 67, 89-97, 2012 [4] Gonçalves et al., ISMRM 2013, Abstract #4159