How to optimize *b*-values for *in vivo* lung morphometry with ^{3}He diffusion MR

A. L. Sukstanskii[1], Y. V. Chang[2], G. L. Bretthorst[1], M. S. Conradi[2], D. A. Yablonskiy[1]
[1]Radiology, Washington University, St. Louis, Missouri, United States, [2]Physics, Washington University, St. Louis, Missouri, United States

Introduction: A previously reported method for *in vivo* lung morphometry is based on evaluation of anisotropic diffusion of ^{3}He gas in acinar lung airways [1]. However, the accuracy of this method has not been analyzed yet. Herein we present a theoretical analysis of estimated experimental errors inherent to this approach. We derive expressions representing a dependence of these errors on experimental conditions and diffusion pulse sequence *b*-values.

Theory: We use an approach developed by Bretthorst [2, 3] to analyze how the estimated diffusion coefficients depend on the "true" diffusion coefficients, signal-to-noise ratio, data sampling and total number of data values. The basic quantity in Bayesian analysis is a joint posterior probability $P(\{p_j\}|D\,\sigma I)$ for model parameters $\{p_j\}$ given all of the data *D*, the standard deviation σ and the prior information *I*. For the model, in which ^{3}He gas diffusion in lung acinar airways approximated by cylinders [1], the signal *S* as a function of the *b*-value depends on three parameters: the signal amplitude S_0 and diffusion coefficients along the cylinder axis, D_L, and perpendicular to it, D_T:

$$S(b) = S_0 \exp(-bD_T)(\pi/4bD_{an})^{1/2} \cdot \mathrm{erf}\left[(bD_{an})^{1/2}\right], \text{ where } D_{an} = D_L - D_T . \quad (1)$$

The standard deviation σ coincides with a Gaussian prior probability that is assigned to represent what is known about noise. In the high signal-to-noise approximation $P(\{p_j\}|D\sigma I) \propto \exp(-Q/2\sigma^2)$, where $Q = \sum\left[\hat{S}(b_i) - S(b_i)\right]^2$ [2, 3]. Here $S(b_i)$ depends on the model's parameters to be estimated $\{S_0, D_L, D_T\}$ according to Eq.(1); $\hat{S}(b_i)$ is determined by the same Eq.(1) with substitution $\{S_0, D_L, D_T\} \to \{\hat{S}_0, \hat{D}_L, \hat{D}_T\}$, where $\hat{S}_0, \hat{D}_L, \hat{D}_T$ are "true" values of these parameters. The sum in *Q* is over the *b*-values, $b_i = i\cdot\Delta b, \quad i = 0,1,...,N-1$. To estimate any parameter in the model, a posterior probability for the parameter should be calculated. This reduces to integrating $P(\{p_j\}|D\,\sigma I)$ over the two other parameters. The integrations result in the posterior probabilities for the parameters $\{p_j\}$ in the Gaussian form, $P(p_j|D\sigma I) \propto \exp(-(p_j - \hat{p}_j)^2/2\sigma_j^2)$, where σ_j is the standard deviation of the parameter p_j.

Results: The estimated values of the parameters $\{p_j\}$ can be written as

$$(p_j)_{est} = \hat{p}_j \pm \sigma_j = \hat{p}_j(1 \pm \varepsilon_j), \quad \varepsilon_j = \frac{1}{SNR\cdot\sqrt{N}}\cdot U_j(B_L, B_T), \quad (2)$$

where ε_j are the expected relative errors of the estimated parameters, *SNR* is the signal-to-noise ratio. Explicit expressions of the functions U_j of parameters $B_L = \Delta b\cdot N\cdot\hat{D}_L$ and $B_T = \Delta b\cdot N\cdot\hat{D}_T$ are not displayed here due to their complicated structure.

The analytical predictions given by Eq. (2) were verified by computer simulations. For this, Gaussian noise was added to ideal data (from Eq.(1) with known D_L and D_T) and then analyzed according to Eq.(1) to get the apparent values of D_L and D_T. This was repeated for each case 100 times to calculate the rms uncertainties in the reported D_L and D_T and corresponding relative errors ε_L and ε_T. Results are in a good agreement with Eq. (2).

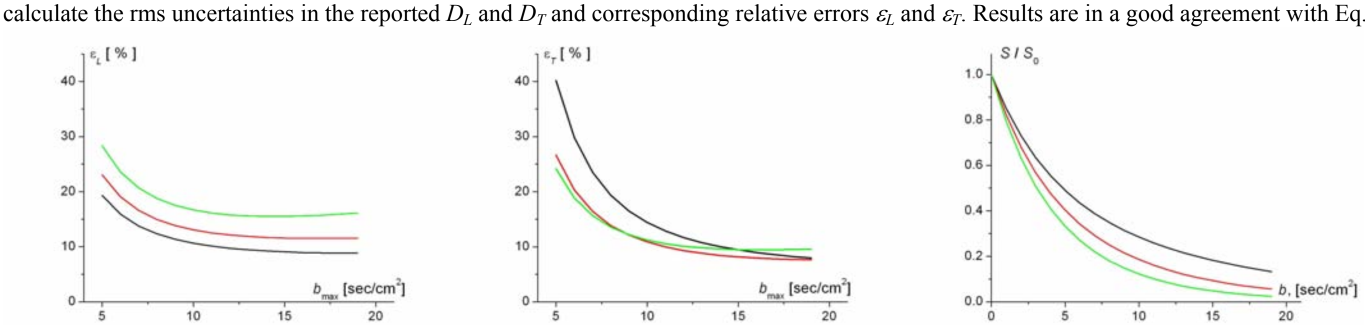

Figure 1 illustrates the dependence of the relative errors ε_L and ε_T of the estimated diffusion coefficients D_L and D_T as functions of the maximal *b*-value, $b_{\max} = \Delta b\cdot(N-1)$, for $SNR = 100$, $\hat{D}_L = 0.4\,\mathrm{cm}^2/\mathrm{sec}$, $N = 9$. Black, red and green lines correspond to $\hat{D}_T$ = 0.05, 0.1 and 0.15 cm^2/sec, respectively. The *b*-value dependence of the signal (1) for the same values of $\hat{D}_L$ and $\hat{D}_T$ is shown in Fig.1c.

Discussion: An analysis shows that for a fixed *N* the errors ε_L and ε_T as functions of $b_{\max}$ have minima at some values of $b_{\max}$ depending on $\hat{D}_L$ and $\hat{D}_T$. Although these minima are achieved at rather high *b*-values, the signal, due to the slower than exponential dependence on *b* (1) may still remain above a noise level (e.g., minima at the green line in Fig. 1a,b are achieved when the signal is about 0.1). The minima are rather shallow and are barely visible on the plots. Such a dependence is rather advantageous because accurate results can be achieved even at substantially smaller *b*-values as compared to the minima.

Acknowledgement: Supported by NIH grant R01 HL 70037.

1. D. A. Yablonskiy, A. L. Sukstanskii, J. C. Leawoods, D. S. Gierada, G. L. Bretthorst, S. S. Lefrak, J. D. Cooper, and M. S. Conradi, Proc. Nat. Acad. Sci. **99**, 3111 (2002). **2**. G. L. Bretthorst, *Bayesian Spectrum Analysis and Parameters Estimation* (Springer-Verlag, New York, 1988).. **3**. G. L. Bretthorst, Concepts Magn. Reson. **27A**, 73 (2005).