Optimal strategy for b-values selection for lung morphometry with hyperpolarized 3He diffusion MRI

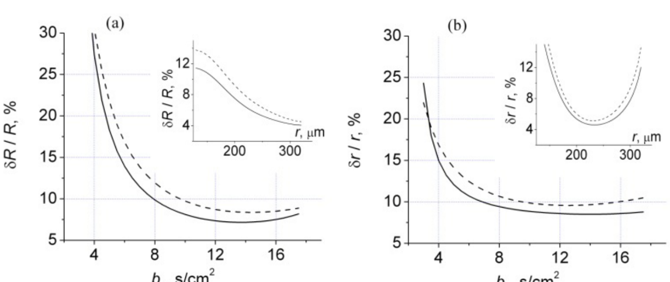
A. L. Sukstanskii[1], J. D. Quirk[1], M. S. Conradi[2], and D. A. Yablonskiy[1,2]

[1]Mallinckrodt Institute of Radiology, Washington University, St. Louis, Missouri, United States, [2]Physics, Washington University, St. Louis, Missouri, United States

Introduction: The lung morphometry technique [1] allows the evaluation of lung microstructure based on an MRI measurement of hyperpolarized ^{3}He gas diffusion. In this approach, acinar lung airways are considered as cylinders covered by alveolar sleeves [2]. Diffusion of ^{3}He gas in each airway is anisotropic and described by distinct longitudinal and transverse diffusion coefficients, D_L and D_T. An analytical expression for the diffusion MR signal as a function of *b*-value was derived taking into account the fact that airways with a flat distribution across all orientations are present in each imaging voxel. In [3], the relationships between D_L and D_T and geometrical parameters of alveolar airways – external, *R*, and internal, *r*, radii - were found. This approach allows estimation of *R* and *r* from multi *b*-value MR experiments [1,3]. An important practical question is how to optimize experimental sequence parameters for a given restricted imaging time (usually about 10-second breathhold). Herein we provide estimates of the values of the optimal *b*-values that allow evaluation of lung geometrical parameters with minimal errors.

Theory: Previously we have developed a theory of parameters optimization assuming an equidistant data sampling [4]. Here we generalize this theory for non-equidistant sampling. We use Bayesian analysis [4-6] to analyze how the estimated geometrical parameters *R* and *r* depend on their "true values", signal-to-noise ratio, data sampling and total number of data values *N*. The basic quantity in Bayesian analysis is a joint posterior probability $P\left(\{p_j\}\middle|Data,\sigma,I\right)$ for model parameters $\{p_j\}$ given all of the data *Data*, the noise standard deviation σ, and the prior information *I*. In the high signal-to-noise approximation $P\left(\{p_j\}\middle|Data,\sigma,I\right)\propto\exp\left(-Q/2\sigma^2\right)$, where $Q=\sum_{n=0}^{N-1}\left[\hat{S}(b_n)-S(b_n)\right]^2$. Here $S(b_n)$ depends on the model's parameters to be estimated: $S(b_n)=S_0\exp(-bD_T)\operatorname{erf}(\sqrt{b(D_L-D_T)})/\sqrt{4b(D_L-D_T)/\pi}$, where D_L and D_T are functions of airways geometrical parameters *R* and *r* and *b*-value [3]. Function $\hat{S}(b_i)$ is determined from $S(b_i)$ by substitution of the parameters $p_i=\{r,R,S_0\}$ with their "true" values $\hat{p}_i$. To estimate any parameter in the model, a posterior probability for the parameter should be calculated, from which the estimated values of the parameters can be found in the form: $\left(p_j\right)_{est}=\hat{p}_j\pm\delta p_j$, $\delta p_j=SNR^{-1}\cdot\left(\Delta_j/\Delta\right)^{1/2}$, where δp_j are the expected uncertainties of the estimated parameters, $SNR=\sigma/S_0$ is the signal-to-noise ratio; Δ and Δ_j are the determinant and the j^{th} minor of the matrix $\mathbf{A}$ with the rank *M* equal to the number of the model parameters. Matrix elements are: $A_{ij}=\sum_{n=0}^{N-1}S_i(b_n)S_j(b_n)$, where $S_i=\partial S/\partial p_i$ calculated at $p_i=\hat{p}_i$. For the model of ^{3}He gas diffusion in lung acinar airways, developed in [1,3], the signal *S* as a function of the *b*-value depends on three parameters: the signal amplitude S_0 and two geometrical parameters of the airways - *R* and *r*. Hence, the minimum number of *b*-values is three. As expected, the optimal $b_0=0$; the two other b-values will be denoted as b_1 and b_2.

Results and Discussion: The optimal set of *b*-values, resulting in the best parameter estimates, corresponds to the minimum of δp_j with respect to b_1 and b_2. Our analysis demonstrates that for typical values of *R* and *r* characteristic to human lungs, the optimal b_1 lays in a narrow interval 1.5 – 2.5 s/cm^2, whereas the optimal b_2 is rather high and lays in the interval 12 – 20 s/cm^2. Such high *b*-values require strong diffusion-sensitizing gradients which are not always available and assumes a sufficiently high SNR to accurately measure the strongly-attenuated signal at these b-values. Fortunately, the minima of b_2-dependence are rather shallow and, therefore, practically the same quality of the parameter estimates can be achieved with smaller than optimal b_2 values. This statement is illustrated in the Figure below where the relative errors of the radii estimates, $\delta R/R$ (a) and $\delta r/r$ (b), are shown (solid lines) for the airway parameters characteristic to the healthy lungs ($R=335\ \mu\text{m}$, $r=150\ \mu\text{m}$, and $SNR=100$, $b_1=2\ \text{s/cm}^2$). The relative errors in the parameter estimates corresponding to $b_2>8\ \text{s/cm}^2$ do not exceed 10%. For comparison, similar relative errors are shown (dashed lines) for experiments with 6 equidistant *b*-values (from 0 to b_2) and $SNR=100/\sqrt{2}$ (decrease in *SNR* by the factor $\sqrt{2}$ is due to the decreased flip angle necessary to acquire the additional *b*-values). As we see, for the same maximal gradient, the 3*b*-value pulse sequence with non-equidistant optimized *b*-values result in smaller uncertainties of the estimated parameters than 6*b*-value pulse sequence. The results shown in Figure correspond to the airways' geometrical parameters characteristic to the healthy lungs. In mild emphysema the external airway radius *R* slightly increases whereas the internal radius *r* increases substantially. The insets in Figure illustrate the dependence of the relative errors on the internal radius *r* for a fixed $R=350\ \mu\text{m}$, and $b_1=2\ \text{s/cm}^2$, $b_2=8\ \text{s/cm}^2$. The relative error of the external radius *R* monotonically decreases, whereas that of the internal radius *r* has a minimum at $r=230\ \mu\text{m}$. The 3*b*-value pulse sequence provides more precise parameter estimates over the range of parameter values tested.



Conclusion: In the range of the airway geometrical parameters corresponding to healthy lungs and lungs with initial stages of emphysema, the optimized 3*b*-value pulse sequence results in the relative errors in the parameter estimate 10% smaller than that can be achieved by means of a substantially longer 6*b*-value pulse sequence with equidistant sampling [4]. This reduced imaging time can be harnessed to decrease the duration of breath-hold or to increase the number of acquired slices.

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