Optimization of Regional Measurements of Lung Ventilation in Presence of Uncertain Model Parameters

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INTRODUCTION: The accuracy of measurements of regional lung ventilation using a sequential series of hyperpolarized ^{3}He breaths [1] highly depends on the applied RF pulse flip angle, which in turn has a profound effect on the signal buildup dynamics. A too small flip angle results in loss of sensitivity due to small generated MR signal and a too large flip angle can compromise signal buildup information from one breath to another due to excessive depolarizing of the residual ^{3}He signal in the parenchyma and airways. Selecting an optimum flip angle to maximize an index of performance is therefore of interest. However fractional ventilation can vary in different regions of the lung, as well as different subjects, making it fundamentally a challenge to define a global performance index to meet global optimality. Moreover, variation in other model parameters such as oxygen concentration and number of images can alter the optimality conditions.

METHODS: The magnetization buildup in an airway can be recursively expressed as: $M_A(j) = r\cdot M_T(j-1) + (1-r)\cdot M_A(j-1)\cdot \exp\left[D_{RF} + D_{O_2}\right]$ for a sequence of breaths, where r is the *apparent fractional ventilation*, including the rebreathing effect of conductive airways, where $D_{RF} = N_{PE}\ln(\cos\alpha)$ and $D_{O2} = -\tau/T_{1,O2}$, with $T_{1,O2}$, $= \xi/PO_2$. The magnetization and signal build-up history in airways were simulated using: $M_S = 1$ [a.u.], $N = 30$, $\tau = 1$ s, $N_{PE} = 64$, $P_S = 140$ mbar, $V_T = 2$ ml, and $V_R = 6$ ml. The relationship between r and the model parameters are in general governed by the nonlinear set of recursive equations. Using $\alpha = 5°$ the magnetization buildup was simulated using $r \in [0.15, 0.55]$. Each parameter was then allowed to vary over a finite range, serving as the *a priori* value in lieu of its *true* value and solved for r. The relative error $\Delta r = \delta r/r$ was calculated as a measure of sensitivity to the respective model parameter, using $\alpha \in [3.0, 7.0]°$ and $P_AO_2 \in [0, 200]$ mbar. In addition the accuracy of r measurements were assessed on the ^{3}He polarization (and therefore the SNR). The A Monte-Carlo simulation was performed over a range of 5<SNR<60 in the second image of the sequence (1000 iterations at each noise level). Finally the effect of including a limited number of ventilation images in the fitting process was used to assess the robustness of the model in the range of $3<N<10$. A simple performance index of the form $PI_\alpha = \max[S_A(p) - S_A(I)]$ is proposed as a guideline to select an optimal flip angle value, where $S_A(p)$ represents the signal corresponding to 80% of steady signal in a given ROI, and p is the (nearest) breath number that this 80% signal is achieved at. The choice of this index leads to an α value which is a conservative balance between the achievable SNR and the signal buildup information.

RESULTS: As shown in Figure 1.c over/under-estimating α values results in a monotonic over/under-estimation of r. Small fractional values are affected to a larger extent by misestimation of α. Overestimating α by one degree results in more than 80% overestimation of r=0.15, whereas it only affects r=0.45 by 20%. The effect of misestimation of P_AO_2 is illustrated in Figure 1.d; it demonstrates a much smaller effect on relative error than is the case for α. For the same example, overestimating P_AO_2 at 200 mbar, results in about 4% underestimation of r=0.15, whereas the effect on r=0.45 is almost negligible. Figure 1.a shows the evolution of Δr as a function of the SNR for different r_A values and 20 breaths. An SNR>20 limits the relative error to 10%. However in general smaller r_A values show better robustness against added noise. Inclusion of a larger number of images (and therefore a larger quantity of gas) can offset the SNR impact. Figure 1.b shows the variation of Δr with respect to the number of images in the fit procedure, showing that relative error in r_A drops exponentially with increasing number of images, e.g. the same level of Δr is retained as SNR=20 with 5 images, while requiring 8 images at an SNR=10. With the objective of minimizing the breath number p at which 80% of steady state signal is reached ($S_A(p)=S_{80}=0.80S_\infty$), flip angle and fractional ventilation were varied over their feasible ranges. Figure 2 summarizes the range of optimal flip angle values for each r value as a function p. The largest flip angle in each r range can be selected as the candidate α_{opt}, to maximize the achievable SNR. Note that optimization is inclusive, i.e. for any given r, the α_{opt} meets the optimality requirement for any smaller r as well.

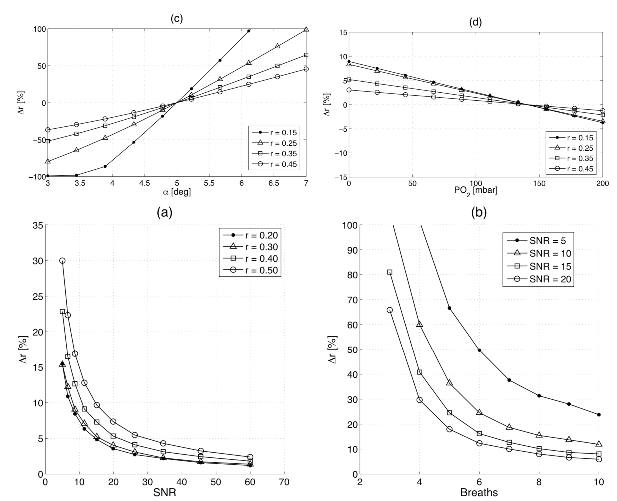

Figure 1. The sensitivity of the serial ventilation sequence in predicting airway fractional ventilation value (r_A) to **(a)** SNR in the first image, and **(b)** number of images included in the analysis. The sensitivity of the serial ventilation sequence in predicting airway fractional ventilation value (r_A) to model parameters, including **(c)** incorrect assumption of flip angle value; and **(d)** incorrect assumption of oxygen tension.

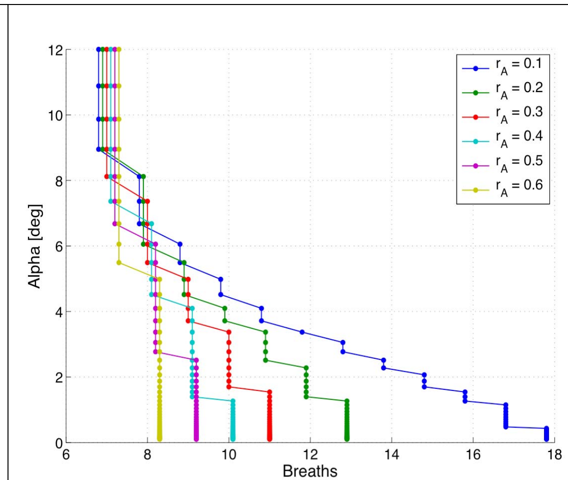

Figure 2. Sensitivity of the ventilation measurements (r_A) to **(a)** incorrect assumption of static dead space value; **(b)** ignoring static dead space.

DISCUSSION:

The determining factor in the number of images acquirable in one session is the HP ^{3}He production capacity. The commercial ^{3}He polarizer utilized in this study had a capacity of 1 liter per run. This volume can provide several tens to hundreds of HP ^{3}He breaths in rodents and small animals, but capacity can be a limiting factor in large animals and humans. For large species, however, the gas mixture can be diluted with ultra-high-purity N_2 gas to achieve larger quantities of imaging gas, provided that the polarization level of ^{3}He is adequate to meet the final magnetization necessary to perform the study, as determined by the SNR requirements. The optimality of the flip angle value is a multivariable problem that ultimately depends on the requirements of the study. Several factors including the available amount of HP ^{3}He for imaging, sensitivity within a desired range of r values, and the available ^{3}He polarization level can affect this decision. Ultimately, a suitable performance index has to be devised by the researchers to incorporate the critical factors to be met by measurements. In this manuscript the criterion was defined as the maximum flip angle which yields 80% of steady state signal at a desired number of breaths. This PI is based on the idea that reaching S_{80} allows for a reasonably accurate estimation of r. As shown in Figure 2, this choice can widely vary depending on the r value. As a general rule a larger number of breaths provides better accuracy in measurements and therefore it should be the determining factor in selecting an optimal flip angle. As a secondary consideration, the range of r values of interest can serve as a guideline.

REFERENCES: [1] Emami K, *et al.* A Novel Approach to Measure Regional Lung Ventilation Using Hyperpolarized 3He MRI – Potential in Clinical Studies; ISMRM 16th Scientific Meeting, Berlin, Germany: May 2007.