# Multiple regression method for optimizing scan parameters in pulmonary partial pressure oxygen measurement by hyperpolarized 3He MRI

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**Introduction:** Hyperpolarized $^3$He magnetic resonance imaging (MRI) is capable of measuring the partial pressure oxygen ($P_AO_2$) and oxygen depletion rate (ODR) of the lung. In the current techniques, some important scan parameters, such as measurement timing and flip angle, are not optimized [1,2,3]. This work presents a single acquisition technique based on the multiple regression method. The method allows us to obtain an analytical expression for the measurement uncertainties and thus provides a way to optimize the scan parameters.

**Method :** During the hyperpolarized $^3$He MRI $P_AO_2$ measurements, the normalized signal decay in a series of images can be expressed as $E_n = ln(S_n/S_0) = \varepsilon \cdot n - 1/\xi \cdot p_0 \, t(n) + 1/(2\xi) \cdot R \cdot t^2(n)$, where $p_0$ is the initial oxygen pressure, $R$ is the oxygen decay rate, $n$ is the image number , $t(n)$ is the acquisition end time of the $n^{th}$ image, $\varepsilon = N \cdot ln(cos(\alpha))$ is the flip angle factor, $N$ is the image resolution, $\alpha$ is the flip angle and $\xi$ is the relaxation constant. We notice that $E_n$ is a linear combination of the three unknowns $\varepsilon$, $p_0$ and $R$ multiplied by the associated functions $n$, $t(n)$ and $t^2(n)$ . Thus a multiple regression method can be applied to retrieve the most likely values of $\varepsilon$, $p_0$ and $R$ from a series measured signal $y_n$. The problem is equivalent to the minimization of $\chi^2 = \sum_{n=1}^{M} \frac{1}{\sigma_n^2}(y_n - E_n)^2 = \sum_{n=1}^{M} \frac{1}{\sigma_n^2}\left[ y_n - \left( \varepsilon \cdot n - \frac{1}{\xi} p_0 \cdot t(n) + \frac{1}{2\xi} R \cdot t^2(n) \right) \right]^2$. By setting the partial derivatives of $\chi^2$ to zero, with respect to $\varepsilon$, $p_0$ and $R$, a set of three linear equations can be obtained. Solving this set of linear equations will yield the solutions for $\varepsilon$, $p_0$ and $R$. The measurement uncertainties in the presence of noise can be analytically derived from the solutions by applying the error propagation theorem. In the solutions we notice there exists a flexibility in choosing the measurement timing $t(n)$, as long as it is not linear function of $n$. We can also observe that different $t(n)$ will give different measurement uncertainties on $p_0$ and $R$. Based on the analytical uncertainty expression we can compare different timing schemes and find an optimal one. In table 1, we compare four different single acquisition timing schemes with the double acquisition scheme. The main difference between the schemes is the variation pattern of interscan time between two consecutive images. We calculated the $p_0$ and $R$ uncertainties under the following simulation condition: initial polarization level resulting SNR=80 of the first image at $\alpha$ =2.5 degree, resolution 64x64, image number 6, breath hold time 20s, $p_0$ =140 mbar and $R$ =2.5mbar/s. The uncertainty vs. flip angle curves are plotted in fig.1. We notice the hybrid scheme gives optimal noise performance on both $p_0$ and $R$ at the optimal flip angle 4.5 degrees.

| | Timing (s) | Optimal α for PO2 | Optimal α for R |
|---|---|---|---|
| **hybrid** | 0.0, 1.2, 8.0, 14.0, 18.0, 20.0 | [5.0; 16 ] | [4.2; 1.2] |
| **decrease** | 0.0, 8.0, 13.0, 16.0, 18.0, 20.0 | [4.2; 10] | [5.0; 4.4] |
| **increase** | 0.0, 1.2, 4.0, 6.0, 16.0, 20.0 | [4.4; 43] | [4.0; 3.0] |
| **even** | 0.0, 1.2, 5.0, 10.0, 15.0, 20.0 | [5.2; 26] | [4.2; 1.7] |
| **double** | τ1=1, τ 2=4 | [5.2; 7] | [4.4; 0.6] |

**Table 1.** The timing of the four single acquisition schemes and double acquisition technique, with their corresponding optimal flip angle α listed in [α, uncertainty] form

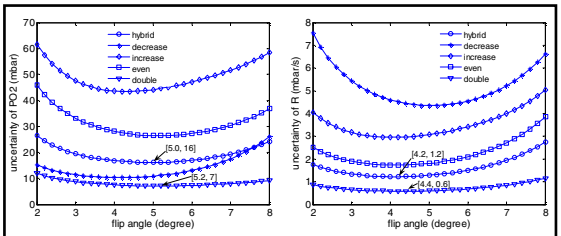


**Fig.1.** Measurement uncertainty vs. flip angle curves of the four single acquisition schemes and the double acquisition technique. The optimal flip angle and its related measurement uncertainty of hybrid scheme and double acquisition are marked in the corresponding curves.

**Result and Discussion:** The animal experiment was conducted under an IACUC approved protocol. A New Zealand rabbit was sedated with ketamine and placed supine in a solenoidal coil inside a 1.5T scanner (Siemens Sonata). Hyperpolarized (HP) $^3$He gas was prepared in a prototype polarizer (Amersham Health, Durham, NC). The animal was ventilated with a home-built ventilator. A tidal volume of 25ml consisting of 5ml O2 and 20ml HP 3He gas was administered to the rabbit after two $^3$He pre-washes. A 2D Gradient Echo sequence was used for imaging with the key parameters: FOV: 140mm; slice thickness: 15mm; TR/TE:7.1s/2.8s; basic resolution: 64x64. The measurement timing was the hybrid scheme in table.1. We repeated the measurement 4 times with 30-second separations. In table 2, we list the measured values of $p_0$, $R$ and $\varepsilon$ for three slices. The measurements show a high reproducibility in a statistical sense. Figure 2 shows the $p_0$, $R$ and $\varepsilon$ maps and histograms of middle slice for the first and fourth measurement.

| | | Po2 (Torr) | ODR (Torr/s) | α (degree) |
|---|---|---|---|---|
| Slice1 | 1 | 120±16 | 1.6±0.9 | 4.8±0.3 |
| | 2 | 110±14 | 1.7±1.0 | 5.0±0.5 |
| | 3 | 114±14 | 1.4±0.6 | 4.9±0.4 |
| | 4 | 111±15 | 1.5±0.7 | 4.9±0.4 |
| Slice2 | 1 | 116±16 | 2.1±0.8 | 5.0±0.4 |
| | 2 | 111±14 | 2.3±1.0 | 5.1±0.4 |
| | 3 | 118±16 | 2.3±0.9 | 5.0±0.5 |
| | 4 | 113±16 | 2.1±0.9 | 5.0±0.4 |
| Slice3 | 1 | 109±15 | 2.6±0.9 | 5.1±0.4 |
| | 2 | 106±15 | 2.5±0.9 | 5.1±0.4 |
| | 3 | 110±13 | 2.7±1.0 | 5.1±0.4 |
| | 4 | 106±13 | 2.7±0.9 | 5.1±0.3 |

**Table 2.** Statistical values of PO2,ODR and α of the four measurements for three slices in the rabbit experiment. Numbers are listed in [average ± standard deviation] form.

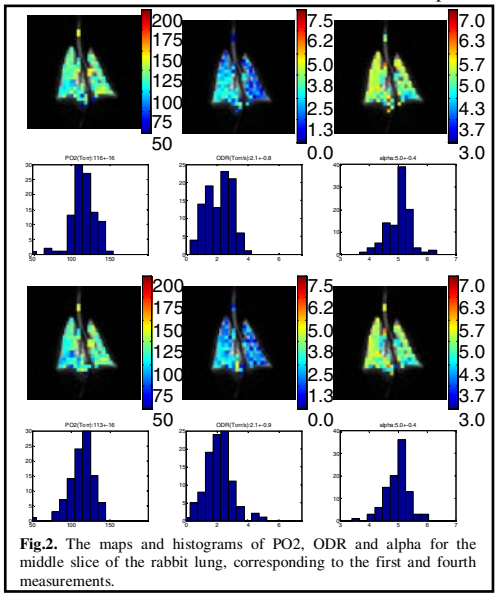

**Fig.2.** The maps and histograms of PO2, ODR and alpha for the middle slice of the rabbit lung, corresponding to the first and fourth measurements.

**Conclusion:** In this work we present the multiple regression method for optimizing the scan parameters in Hyperpolarized $^3$He MRI pulmonary $P_AO_2$ and ODR measurements. When applying this technique, the repeated measurements in the animal experiment show a good statistical reproducibility.

**References:** 1.) Deninger, A. J. *et al.*, *J Mag Res* **141**, 207 (1999). 2.) Deninger, A. J. *et al.*, *Mag Res Med* **47**, 105 (2002). 3.) Fischer, M.C. *et al.*, *Mag Res Med* **52**, 766 (2004).

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