

Measurement of pulmonary partial pressure of oxygen and oxygen depletion rate with hyperpolarized helium-3 MRI: a preliminary reproducibility study on pig model

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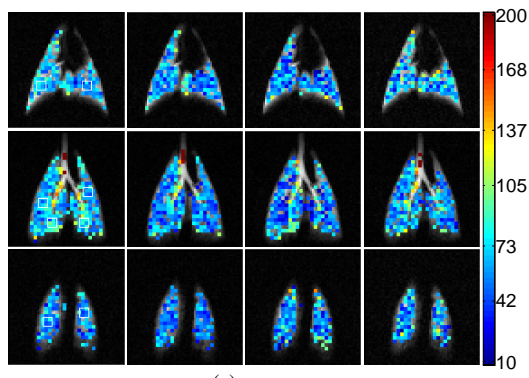
Introduction: Pulmonary partial pressure of oxygen (pO_2) and oxygen depletion rate (R) are two important parameters of lung function. The dependence of hyperpolarized ^3He ($\text{HP } ^3\text{He}$) T_1 on local oxygen concentration provides the basis for high-resolution mapping of the regional distributions of pO_2 and R in the lung. Although the oxygen-sensitive $\text{HP } ^3\text{He}$ MRI technique has been applied in human subjects and several animal species, reproducibility studies are rarely reported in the literature. This work presents a preliminary reproducibility study on a pig model. In this study, important scan parameters, such as measurement timing and flip angle, are optimized to minimize the noise-induced measurement uncertainty.

Method: The *in-vivo* animal experiments were conducted under a protocol approved by the Animal Use Committee at the University of Pennsylvania. Four normal Yorkshire pigs (~20kg) were scanned with a 1.5T Siemens Sonata MRI system. In each experiment, the pig was placed supine in a commercial birdcage RF coil (RAPID Biomedical, Würzburg, Germany) tuned to the ^3He resonance frequency 48.48MHz. During a pulmonary oxygen measurement, a tidal volume of 500 mL, consisting of 100 mL O_2 , 200 mL ^3He , and 200 mL N_2 gas, was administered to the animal by a commercial-prototype ventilator. Three coronal slices in the supine direction were acquired by a small flip angle gradient echo pulse sequence with the following imaging parameters: FOV=260 mm, slice thickness=30 mm, slice spacing=6 mm, TR/TE=6.4ms/2.9ms, matrix size=64x64, and flip angle ≈ 4.5 degrees. Six images were acquired for each slice at the following timings: [0.0000, 1.1125, 8.6275, 15.4400, 20.2550, and 23.0700] seconds. The measurement timing and flip angle were optimized by minimizing the measurement uncertainty expressions derived from the multiple regression fitting method [2]. Depending on the available ^3He gas volume, the pulmonary oxygen measurement was repeated 2-4 times in each pig. The parametric maps were generated using a bin-based data processing procedure, which applied the multiple regression fitting method to extract the pO_2 and R .

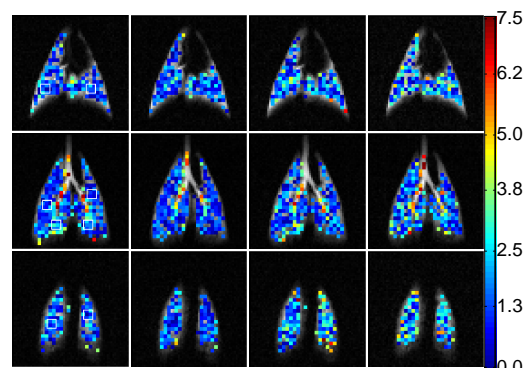
Result and Discussion: Variations of global mean, percentiles, and regions-of-interest were calculated from the maps to analyze reproducibility. The variation of a parameter (global mean, percentile, or ROI mean) in repeated measurements is calculated according to:

$$\delta = \frac{\text{max} - \text{min}}{\text{mean}}$$

Here max, min, and mean respectively stand for the maximum, minimum, and mean values of the repeated measurements. In Fig.1 (a) and (b), we show the fitted parametric maps of p_0 and R obtained from the $\text{HP } ^3\text{He}$ MRI pulmonary oxygen reproducibility study. This experiment corresponds to pig experiment #3 in Table 1,



(a) p_0 maps



(b) R maps

Fig.1. Parametric maps of a normal pig (#3) experiment for a pulmonary pO_2 reproducibility study with $\text{HP } ^3\text{He}$ MRI. a) maps of initial oxygen partial pressure p_0 . b) maps of oxygen depletion rate R . In a) and b), the columns, from left to right, correspond to the first through fourth measurements. The white square boxes in the first column represent ROIs for reproducibility analysis. The unit of the color bar is Torr for p_0 and Torr/s for R .

Table 1. Global p_0 values for repeated measurements in the $\text{HP } ^3\text{He}$ pulmonary oxygen reproducibility study on the pig model. Values are listed as [mean \pm standard deviation] (Torr). The last column is the variation of the global mean.

Pig #	Slice #	Measurement #				Variation of mean (%)
		1 st	2 nd	3 rd	4 th	
1	1	127 \pm 21	125 \pm 19	-	-	1.6
	2	127 \pm 18	125 \pm 28	-	-	1.6
	3	114 \pm 18	105 \pm 23	-	-	8.2
2	1	109 \pm 14	105 \pm 15	-	-	3.7
	2	94 \pm 16	95 \pm 17	-	-	1.1
	3	85 \pm 15	87 \pm 13	-	-	2.3
3	1	67 \pm 16	62 \pm 18	59 \pm 21	69 \pm 23	15.6
	2	76 \pm 27	64 \pm 28	60 \pm 24	69 \pm 30	23.8
	3	59 \pm 16	54 \pm 13	62 \pm 25	62 \pm 23	13.5
4	1	90 \pm 11	94 \pm 16	114 \pm 12	-	24.2
	2	89 \pm 12	87 \pm 14	103 \pm 20	-	17.2
	3	78 \pm 7	81 \pm 11	79 \pm 14	-	3.8

Table 2. Global R values for repeated measurements in the $\text{HP } ^3\text{He}$ pulmonary oxygen reproducibility study in the pig model. Values are listed in [mean \pm standard deviation] (Torr/s) form. The last column is the variation of the global mean.

Pig #	Slice #	Measurement #				Variation of mean (%)
		1 st	2 nd	3 rd	4 th	
1	1	1.50 \pm 1.00	2.22 \pm 1.16	-	-	38.7
	2	2.19 \pm 1.00	2.68 \pm 1.44	-	-	20.1
	3	2.27 \pm 0.98	3.26 \pm 1.46	-	-	35.8
2	1	1.64 \pm 1.13	1.32 \pm 0.90	-	-	21.6
	2	2.58 \pm 1.03	2.43 \pm 0.99	-	-	6.0
	3	2.38 \pm 0.91	2.51 \pm 0.94	-	-	5.3
3	1	1.43 \pm 0.94	1.45 \pm 0.90	1.75 \pm 1.19	1.99 \pm 1.21	33.8
	2	1.84 \pm 1.51	1.54 \pm 1.25	1.77 \pm 1.31	2.07 \pm 1.53	29.4
	3	1.53 \pm 0.93	1.41 \pm 0.90	2.24 \pm 1.47	2.31 \pm 1.31	48.1
4	1	0.72 \pm 0.42	0.49 \pm 0.41	0.89 \pm 0.45	-	57.1
	2	1.56 \pm 0.55	1.08 \pm 0.53	1.59 \pm 0.77	-	36.2
	3	1.61 \pm 0.39	1.39 \pm 0.55	1.39 \pm 0.52	-	15.0

in which three slices were scanned and four repeated measurements were performed. In Tables 1 and 2, we list all the global statistical values (mean \pm standard deviation) of p_0 and R obtained in the reproducibility study on the pig model. The last column of each table shows the variation of mean of the repeated measurements. The global statistical analyses show that average variation of global mean is 9.7% for pO_2 and 28.9% for R , and that the average variation of percentiles (10th, 25th, 50th, 75th and 90th) and inter-quartile range is 15.0% for pO_2 and 34.9% for R . The region-of-interest analysis on the manually-selected regions shows that the average variation of mean is 11.3% for pO_2 and 23.4% for R .

Conclusion: In this work, we present the preliminary results of a reproducibility study of pO_2 and R performed on pig model with $\text{HP } ^3\text{He}$ MRI.

References: 1.) Deninger, A. J. *et al.*, *J Mag Res* **141**, 207 (1999). 2.) J. Yu *et al.*, *Mag Res Med* **2007** (accepted).