Quantification of Human Lung Function and Structure Using Dissolved-phase Hyperpolarized ^{129}Xe

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Introduction Hyperpolarized gas (HPG) MRI is a powerful tool to probe lung function and structure. Between the two readily polarizable noble gases, ^{129}Xe and ^{3}He, ^{129}Xe is naturally abundant and dissolves into lung tissue and blood. In particular, its solubility makes xenon an ideal tool to observe gas exchange — the essential function of the lung. We have proposed a method to measure a series of critical parameters for lung function and structure (septal wall thickness, surface-area-to-volume ratio (SVR), hematocrit, etc.) using the dynamics of the dissolved xenon in the lung[1]. We present in this study our initial experience of applying this method in healthy human lungs.

Theory We consider S_{TP}, the signal of xenon in tissue and blood plasma at ~197 ppm, and S_{RBC}, the signal of xenon in the red blood cells at ~218 ppm, as functions of the gas exchange time t. $S_{TP}(t)$ and $S_{RBC}(t)$ are expressed in terms of the following pulmonary parameters: SVR, air-blood barrier thickness (δ), septal wall thickness (d), saturation time constant (T), hematocrit (Hct), and pulmonary capillary transit time (t_X). $S_{TP}(t)$ and $S_{RBC}(t)$ therefore contain important information about lung function. We refer to the set of $S_{TP}(t)$ and $S_{RBC}(t)$ as the model of xenon exchange, or MOXE[1].

Methods Measurements were performed in 6 healthy volunteers using Siemens whole body scanner at 1.5 T or 3T and a quadrature coil or a custom-built 32 channel coil (approved by our Institutional Review Board). Enriched ^{129}Xe (86%) was polarized to ~50% using a prototype xenon polarizer from Xemed LLC. One liter of pure xenon or xenon mixture (50% xenon + 50% N_2 or 50% xenon + 33% air + 17% O_2) was inhaled from functional residual capacity (FRC) before each measurement at breath-hold. Transmitter efficiency was calibrated using segments of repeated RF pulses. Delays were inserted between segments to allow for T_1 relaxation in the absence of RF consumption. Both flip angle and T_1 can be measured by fitting signal magnitudes to a function of both RF pulse number and time. A modified version of a previously described sequence[2] was used for xenon uptake (or exchange) measurement. Modifications include shifted (208 ppm) and longer (1600 μs) RF pulses for human lung, optional RF shape (Gaussian or rectangular), variable number of saturation pulses (3 to 8) to ensure complete saturation of dissolved xenon, and a 1˚ excitation pulses for xenon gas at 0 ppm for signal calibration. The real and imaginary parts of the dissolved xenon signals were fitted to a double Lorentzian shape[3] to extract the widths and amplitudes of the TP and RBC xenon. To compute $S_{TP}(t)$ and $S_{RBC}(t)$, the respective phase-corrected peaks are numerically integrated, normalized by the corresponding gas-peak amplitude, corrected for flip angle difference between xenon gas and dissolved xenon, and compensated for T_2* decays and RF bandwidth coverage. $S_{TP}(t)$ and $S_{RBC}(t)$ are then fitted to MOXE in order to measure the pulmonary parameters listed in Theory[1].

Field (T)	gas frq (Hz)	gas T_1 (ms)	gas T_2* (ms)	TP pos (ppm)	RBC pos (ppm)	TP T_2* (ms)	RBC T_2* (ms)
1.5	17.603025	27.3 ± 3.8	17.1 ± 3.7	197.1 ± 0.5	216.6 ± 2.4	2.08 ± 0.15	1.58 ± 0.08
3	34.09125	14.4 ± 1.1	6.5 ± 2.2	196.8 ± 0.9	218.6 ± 1.2	1.08 ± 0.12	0.78 ± 0.16

Table 1 Fitting parameters from RF calibration and dissolved xenon signals. "Xenon" ignored in all names (e.g., TP pos = TP xenon position). All values were measured in whole lung.

ID	field (T)	SVR (cm^{-1})	δ/d	T (ms)	Hct	t_X (s)
1	3	170	0.106	35.5	0.15	1.46
2	3	209	0.18	11.2	0.212	0.86
3	3	272	0.06	29.5	0.25	1.25
4	1.5	153	0.156	32.7	0.32	0.97
5	1.5	229	0.128	55.7	0.21	1.88
6	1.5	357	0.62	32.8	0.32	1.53
average		232 ± 75	0.12 ± 0.05	33 ± 14	0.24 ± 0.06	1.33 ± 0.38
literature		250	0.2	--	0.4	1.6

Table 2 Pulmonary parameters obtained by fitting xenon uptake to MOXE. The fitting details and auxiliary parameters can be found in Ref. (1).

Results The average resonance frequencies and the fitting results from transmitter calibration and the whole-lung dissolved xenon signals at both fields (N=3 for each) are listed in Table 1, and some typical results are plotted in Figs. 1-3. The pulmonary parameters measured using MOXE and the corresponding literature values[4-7] are listed in Table 2. Detailed fitting procedure and the auxiliary parameters used for human lung can be found in Ref. (1). A typical data set is plotted in Fig. 4.

Discussion The measured whole-lung T_2* of TP and RBC xenon and the trend of T2* changes at the two field strengths agree with previous measurements[3,8]. The pulmonary parameters measured using MOXE are all reasonable compared to the literature values[4-7]. We note that the discrepancy in hematocrit (Hct) could shed light on the solubilities of xenon in blood[9]. We also note that incomplete saturation of dissolved xenon, likely due to inaccurate RF calibration or B_1 inhomogeneity, could cause errors in the measurements, especially for δ/d.

Conclusions Our initial experience of applying the model of xenon exchange, MOXE, in healthy humans at both 1.5 and 3 T indicates this is a highly promising method for measurement of lung function and structure. The sensitivity of this method for detecting pathological changes will be assessed for various pulmonary abnormalities.

References (1) Chang YV MRM (DOI:10.1002/mrm.24304) (2) Chang YV et al. ISMRM 2008:201 (3) Chang YV et al. ISMRM 2010:4602 (4) Ladefoged J et al. Physiol Med Biol 1967;12:353 (5) Gil J et al. Lab Invest 1988;58:466 (6) Coxson HO et al. Am J Respir Crit Care Med 1999;159:851 (7) Gehr P et al. Respir Physiol 1978;32:121 (8) Mugler III JP et al. ISMRM 2009:2207 (9) Goto T et al. Brit J Anaesth 1998;80:255.

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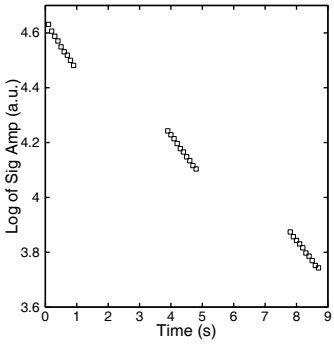

Figure 1 Flip angle calibration was performed by applying segments of repeated RF pulses with delays between segments to allow for T1 relaxation in the absence of RF consumption.

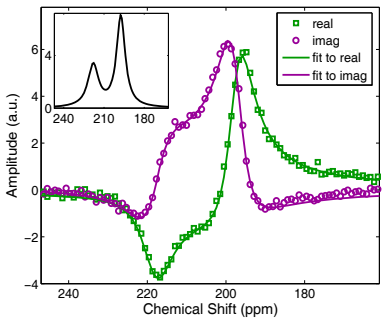

Figure 2 The real and imaginary parts of the dissolved-xenon signal were fitted to a double-Lorentzian line shape simultaneously. The inset shows the lineshape with both peaks at 0 phases.

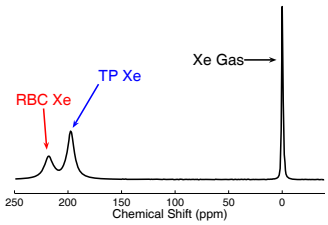

Figure 3 Xenon spectrum in human lung with all three peaks corrected in phase. This spectrum was used to calculate the relative intensity of dissolved xenon at a given exchange time.

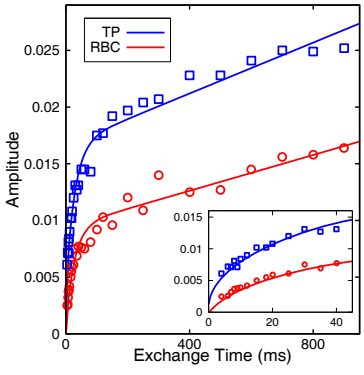

Figure 4 A typical xenon uptake data set fitted to MOXE. The inset demonstrates good agreement between data and theory at short exchange times.