Separate Determination of Factors affecting the Hyperpolarized ^{129}Xe Washout Curve observed in Mouse Lungs under Spontaneous Respiration

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INTRODUCTION

Hyperpolarized (HP) ^{129}Xe MRI/MRS have been expected to be an important tool in the functional analysis of lung and brain, and several studies have been made to realize utility of such a new modality. In the present study, we focused on the analysis of ^{129}Xe washout curve observed in the chest of mouse under spontaneous respiration so that diagnostics can be performed in a noninvasive manner. Factors affecting the slope of the washout curve are derived based on the Kety's model and investigated spectroscopically to propose a method of separate determination.

^{129}Xe washout model

Starting from the basic model of ^{129}Xe uptake and washout in lungs (1) intensity of the gas signal S_n in the nth excitation is given as the function of washout time t for the washout process of spontaneous respiration,

$$\ln(S_n) = [\{\ln(\cos\alpha)/TR-(R_f/V_a) + (1/T_{1a}) + (\lambda Q /V_a)\}]t + \ln(S_1) \qquad [1]$$

where α, TR, T_{1a}, R_f, V_a, λ, and Q are rf flip angle, repetition time, relaxation time in alveolar gas space, second ventilation volume, total volume of functional residual capacity and tidal volume, gas/blood partition coefficient, and pulmonary capillary blood flow, respectively.

METHODS

The HP ^{129}Xe gas was produced in a homebuilt flow-type optical pumping system previously described (2) and the polarization level attained was 3-5 %. The HP Xe gas was supplied to ddY male mice (35 - 40 g) under pentobarbital (50 mg/kg) anesthesia through a mask attached to the head of mice after mixing with oxygen. MRS/MRI experiments were performed on Varian Unity INOVA 400WB equipped with 9.4 T vertical magnet and ^{129}Xe, ^{1}H and ^{19}F switchable Litz coil. ^{129}Xe spectrum was acquired in every 1.4 sec under presaturating rf pulses centered at the dissolved phase signals near 200 ppm when observing the washout process. The washout curve was obtained by measuring the ^{129}Xe signal after changing the Xe gas from the HP one to the normal one at thermal equilibrium.

RELUTS and DISCUSSION

The gas and dissolved phase ^{129}Xe peaks were observed at 0 and 190-200 ppm, respectively, from the chest of mouse. At the steady state after the HP gas inhalation, the gas signal was observed to oscillate with a rate of about 2.5 cycles/sec, which was considered to reflect the rate of respiration. Separate determination of the factors determining the slope of semilogarithmic plots of Eq.[1] was achieved as follows. The rf flip angle α was determined through the dual flip angle method (3) where the washout curve was measured using α and 2α pulses and the slope was compared. The ratio of R_f/V_a was determined from the slope of washout curve with SF_6 as well as from the changes in signal intensity measured every 0.1 seconds at the steady state in the experiment using SF_6 gas instead of the HP gas. Because SF_6 has very short T_1 of the order of msec and very low solubility in tissue, its slope in the washout curve is determined only by the R_f/V_a term. The residual term $(1/T_{1a})+(\lambda Q/V_a)$, which can be regarded as the apparent relaxation rate $1/T_{1a}^*$, was derived by subtracting the above determined factors including α and R_f from the experimentally observed slope (Table.1). Thus, apparent relaxation time in alveoli T_{1a}^* was determined to be 14 sec.

Table.1 Parameters determined in the washout curve analysis [sec^{-1}]

Slope of the washout curve	$\frac{\ln(\cos\alpha)}{TR}$	$\frac{R_f}{V_a}$	$\frac{1}{T_{1a}^*} = \frac{1}{T_{1a}} + \frac{\lambda Q}{V_a}$
0.353	0.024	0.261	0.068

CONCLUSION

The washout process of ^{129}Xe gas under spontaneous respiration was successfully analyzed by a mono-exponential decay. The slope of the semilogarithmic plot in the wasout curve was affected by the three factors including flip angle, second ventilation, and apparent relaxation time, which can be estimated separately by means of the NMR observation using hyperpolarized as well as the thermal equilibrium gases. Such quantitative analysis would be useful for the evaluation of malfunctions in lungs such as insufficient ventilation or diffusion.

REFERENCE

(1) S. Peled et al. MRM 36:340 (1996), (2) J Fukutomi et al. J Magn. Reson. 160:26 (2003), (3) H Fujiwara et al. J Magn. Reson. 150:156 (2001)