Probing Lung Geometry: Measurement of time-dependent diffusion of hyperpolarized ^{129}Xe in healthy mice

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Introduction: Most of the recent hyperpolarized (HP) gas diffusion studies have focused on the changes in apparent diffusion coefficient (ADC) of the gas in diseased lungs with a single diffusion time [1], although it is well-known that ADC in restricted space changes depending on its diffusion time. So far, it has been demonstrated in the porous material studies that the time-dependent ^{129}Xe diffusion allows geometric evaluation of the sample [2]. But to our knowledge, in vivo measurement of the significant geometric parameters such as surface-to-volume ratio and tortuosity of lungs has not been reported. In the present study we applied the time-dependent diffusion measurement to the healthy mouse lung using HP ^{129}Xe MR spectroscopy and tried to estimate surface-to-volume ratio and tortuosity.

Methods: The 3% xenon gas mixture, which consists of 3% Xe, 12% N_2 and 85% He, was polarized on the home-built hyperpolarizing system using 90 W laser diode arrays (Coherent Japan). Three male ddY mice (35-40g) were used in the present study. The mouse was anesthetized by an intraperitoneal injection of pentobarbital (40mg/kg) and masked for spontaneous inhalation of the 3% xenon gas mixture and oxygen gas. All the measurements were performed on Varian unity-INOVA NMR spectrometer equipped with a 9.4T magnet and ^{129}Xe-^{1}H tunable imaging probe (Doty Scientific Inc.). Diffusion weighted spectra of HP ^{129}Xe gas in the lung were acquired by pulsed gradient echo sequence [3] modified to add slice selection gradients. The acquisition parameters were: predelay = 1sec; RF pulse = 1000μs Gaussian-shaped gas-phase selective pulse; flip angle = 30°; spectral width = 30kHz; data point = 20k; axial slice thickness = 5mm; NEX = 8. In order to change diffusion time, the duration between a pair of bipolar diffusion gradients (Δ) was changed from 0.6 to 3 ms. The diffusion gradient width (δ) was set to be $\delta = \Delta - 0.05$ms when $\Delta \le 1.0$ms and fixed to 1.0ms when $\Delta > 1.0$ms. In the measurement of ADC at each diffusion time, the strength of diffusion gradient was changed as 0, 10, 15, 20 gauss/cm for diffusion weighting. The time-dependent ADC in the pulmonary airspace was obtained from the diffusion weighted spectra, and surface-to-volume ratio (S/V) and tortuosity (α) of the lung was estimated from the following equations [2]:

$$\frac{D(t)}{D_0} \rightarrow 1 - \frac{4}{9\sqrt{\pi}}\frac{S}{V}(D_0 t)^{1/2} \quad \text{(short time asymptote)}, \qquad \frac{D(t)}{D_0} \rightarrow \frac{1}{\alpha} \quad \text{(long time tortuosity asymptote)},$$

where D_0 is the effective unrestricted diffusion coefficient of xenon in the inhaled gas and calculated to be $D_0 = 33.0\text{mm}^2/\text{s}$ from Chapman and Enskog Theory and Wilke's law.

Results and Discussion: Figure 1 shows diffusion weighted HP ^{129}Xe spectra acquired from the mouse lung at diffusion time (Δ) = 1.5ms. Figure 2 shows the plot of $D(t)/D_0$ against normalized diffusion length of $(D_0t)^{1/2}$. It was observed commonly in three healthy mice that $D(t)/D_0$ decreases with increasing $(D_0t)^{1/2}$ within the range up to $(D_0t)^{1/2} \sim 0.2$mm and approaches a nonzero finite value of ~0.1 in the range $(D_0t)^{1/2} \ge 0.2$mm. By using the equation described above, the surface-to-volume ratio and tortuosity of the mouse lung were estimated to be $23 \pm 2\text{mm}^{-1}$ and 12 ± 2, respectively. These geometric parameters would be sensitive to the microstractural changes in alveoli and intra-acinar pathway and useful to differentiate between bronchiolar and alveolar changes in emphysematous lungs.

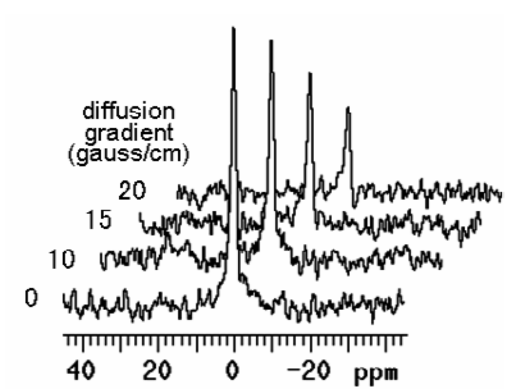

Figure 1 Diffusion weighted ^{129}Xe spectra acquired from the healthy mouse lung with a diffusion time Δ=1.5ms.

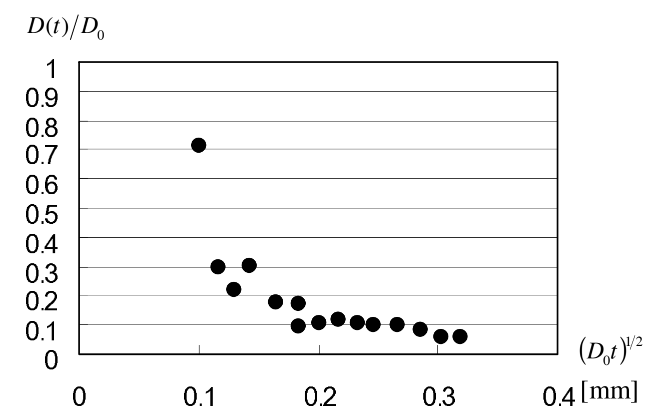

Figure 2 Plot of $D(t)/D_0$ against normalized diffusion length $(D_0t)^{1/2}$.

References: [1] Saam BT et al. Magn Reson Med 2000;44:174-179. [2] Mair RW et al. Phys Rev Lett 1999 83 3324-3327. [3] Mair RW et al. J Magn Reson 1998;135:478-486.