Matching Experimental Data to a 1D ^{129}Xe Gas Exchange Model

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Introduction

Upon inhalation hyperpolarized ^{129}Xe readily dissolves in lung tissue and rapidly establishes a dynamic equilibrium between the alveolar volume (gas phase) and lung parenchyma (dissolved phase). The associated large chemical-shift difference of about 200 ppm between these two compartments permits the magnetization in the dissolved phase to be selectively manipulated, for example by applying a series of 180°/-180° frequency-selective RF-pulse pairs centered on the dissolved-phase frequency. Due to the ongoing xenon exchange between the gas and dissolved-phase compartments, the gas-phase signal decreases as a function of the delay time between the 180° and -180° pulses of each pair. As shown previously (1), this signal loss (depolarization) per RF-pulse pair increases toward an asymptotic value as the delay time increases (see Fig. 1). Presumably, the depolarization versus delay-time behavior reflects underlying characteristics of the lung parenchyma. The purpose of this study was to apply a diffusion model to previously reported experimental data (1) as a means to potentially extract parameters of physiological significance.

Methods

By extending the half-space calculations employed by Butler et al in (2), a simple 1D model of gas diffusion across the alveolar membrane can be used to predict the time course of the xenon magnetization following magnetic labeling of the dissolved-phase atoms by 180°/-180° frequency-selective RF-pulse pairs. The following assumptions were made: a) the xenon diffusion constant D_m inside the membrane is homogeneous; b) concentration gradients in the alveolar volume equilibrate instantaneously due to the high diffusion constant of the gas; c) the gas-phase concentration C_a remains constant during gas exchange since the dissolved-phase compartment is much smaller; d) negligible T1 relaxation occurs on the time scale of the experiment (< 60ms). Under these conditions the xenon concentration C_m inside the alveolar membrane as a function of position x, and delay time τ separating the inversion pulses of a 180°/-180° RF pulse pair, can be estimated as:

$$C_m(x,\tau) = \lambda C_a - \sum_{n=1}^{\infty} \frac{8\lambda C_a}{(2n-1)\pi} \cdot \sin\frac{(2n-1)\pi x}{L} \cdot \exp\left(-D_m\left(\frac{(2n-1)\pi}{L}\right)^2 \tau\right), \qquad [1]$$

where λ is the Ostwald solubility coefficient for xenon in lung tissue and L is the membrane thickness. The signal S_m from the ^{129}Xe atoms in the dissolved phase is then:

$$S_m(\tau) \propto \int_0^L C_m(x,\tau)\,dx\,. \qquad [2]$$

Since T1 relaxation mechanisms have been neglected in the model, the only way that signal from the ^{129}Xe atoms in the alveolar volume, S_a, can change is due to the influx of inverted spins from the dissolved-phase. For a sufficiently long time τ' after the -180° pulse, the experimentally determined relative gas-phase depolarization $f_D = S_a(\tau') / S_a(0)$ is given by:

$$f_D(\tau) \to -\frac{2(S_m(0) - S_m(\tau))}{S_a(0)} \quad \text{for} \quad \tau' >> \frac{L^2}{D_m\pi^2}\,. \qquad [3]$$

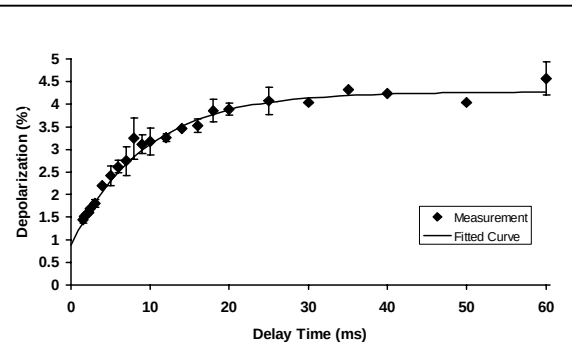

Figure 1: Gas-phase depolarization in the lung of a 3-kg adult New Zealand rabbit as a function of the delay time τ between the 180° and -180° RF pulses centered at the ^{129}Xe dissolved-phase frequency.

Results

An exponential function of type $f_D(\tau) = A_0 + A_1(1 - \exp(-\tau / A_2))$ was fit to the experimental data from reference 1 (see Fig. 1); the best fit (in a least-squares sense) was: $f_D(\tau) = 0.87(\pm0.04) + 3.4(\pm0.04)(1-\exp(-\tau/9.3(\pm0.02)\text{ms}))$. By combining Eqs. 2 and 3, and in the limit of a long τ ($\tau >> L^2 / (9D_m\pi^2)$), one obtains $f_D(\tau) \propto 1 - \exp(-D_m(\pi/L)^2\tau)$. A comparison of this result to the fit of the experimental data, assuming an average membrane thickness in rabbits of 5.5µm (3), yields an effective xenon diffusion constant of $D_m = 3.3\cdot10^{-6}\text{cm}^2/\text{s}$ for the lung parenchyma, which compares favorably to literature values for other tissue types (4). Also, from Eq. 3 in the limit of a long τ with $\lambda = 0.094$ for saline and the asymptotic value of $f_D(\tau\to\infty) = 4.27\%$, it follows that about 1.1% of all ^{129}Xe atoms reside in the dissolved phase and that the dissolved-phase compartment volume is about 11% of the gas-phase volume. Using these parameters in conjunction with Eq. 1, it is feasible to predict the xenon penetration depth in tissue as a function of τ. It was found that after an initial rapid exchange of ^{129}Xe atoms near the surface, the exchange front moves gradually towards the interior and reaches the center of the membrane after approximately 8 ms. Finally, assuming roughly spherical alveoli, the tissue volume fraction and the membrane thickness can be used to compute an average alveolar diameter of 75 µm, again in good agreement with the literature (3).

Discussion

By employing a relatively simple model of gas exchange, it was possible to extract the effective xenon tissue-diffusion constant, the membrane penetration depth as a function of time, the average lung tissue fraction and the average alveolar diameter from experimental measurements of the gas depolarization. Since the associated experimental studies were performed in healthy rabbits, our analysis provides baseline values that will serve as a reference for the detection of pathological changes in disease models. Although this work was restricted to global spectroscopy studies, we foresee no major obstacles to obtaining high-resolution spatial maps of these quantities in the future.

References

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