A simple model of gas exchange in the lung for hyperpolarized Xe129

Y. V. Chang[1]
[1]Mechanical Engineering, Washington University, St. Louis, MO, United States

Introduction Hyperpolarized ^{129}Xe is a unique contrast agent for pulmonary MRI because of its solubility in lung tissue and blood. Driven by diffusion, like other blood gases (O_2, CO_2) in the lung, the dissolved xenon (DX) is under rapid exchange with the free xenon gas in the alveolar space. Quantification of xenon exchange in the lung can therefore not only measure the microstructure, but the *function* of the lung. With the large chemical shifts of DX—197 ppm for xenon in tissue and blood plasma (TP) and 217 ppm for xenon in the human red blood cells (RBC) (Fig. 1)—one can saturate DX without disturbing the xenon gas and observe the uptake (1), or replenishment (2), of DX due to exchange using chemical shift saturation recovery (CSSR, (3)). We present here a simple model of gas exchange that interprets both TP- and RBC-xenon signals as functions of gas-exchange time, which allows simultaneously quantification of lung density, microstructure, function, and physiology.

Methods In order to study xenon exchange in different lung compartments we must separate the TP and RBC xenon peaks in the DX signal. While the TP xenon resonates consistently at 197 ppm, the frequency of the RBC xenon is species dependent: for rabbits (4) and mice (5) it is close to the TP xenon and is between 197 and 203 ppm. In this case the entire dissolved xenon signal in the real/imaginary channel can be fitted to a double-Lorentzian in the frequency domain after phase correction: $F(f)=\sum_{l=1,2}\frac{a_l}{(f-f_l)^2+w_l^2}$ [1], where f_l are the peak positions and a_l and w_l (l=1,2) are fitting parameters (4); for many other species the RBC xenon (rats – 211 ppm (2), dogs – 212 ppm (1), humans – 217 ppm (6)) is farther apart from the TP xenon and they cannot be fitted with a common phase factor due to the dephasing between them; instead, they can be fitted using the double-Lorentzian with individual phase factors (θ_l): $F(f)=\sum_{l=1,2}\frac{a_l\exp(-i\theta_l)}{w_l+i(f-f_l)}$ [2], from which $\mathrm{Re}[F(f)]=\sum_{l=1,2}a_l\frac{w_l\cos\theta_l-(f-f_l)\sin\theta_l}{(f-f_l)^2+w_l^2}$ [3] and $\mathrm{Im}[F(f)]=\sum_{l=1,2}-a_l\frac{w_l\sin\theta_l+(f-f_l)\cos\theta_l}{(f-f_l)^2+w_l^2}$ [4] are the real and imaginary parts, respectively. The signal intensity of each peak can be obtained by numerically integrating the corresponding Lorentzian.

Theory The calculation is based on the solution of the 1D diffusion equation for DX in a simplified model of lung septum as shown in Fig. 1, where we assumed the total septal thickness and the air-blood barrier thickness to be d and δ, respectively. As results, the normalized TP xenon signal $S_{TP}(t)$ and the RBC xenon signal $S_{RBC}(t)$ by the corresponding gas signal amplitudes as functions of the gas exchange time t are, respectively (7),

$$S_{TP}(t)=b\left[\frac{2\delta}{d}-\frac{8}{\pi^2}\sum_{n=\mathrm{odd}}\frac{1}{n^2}\left(1-\cos\frac{n\pi\delta}{d}\right)e^{-n^2t/T}\right]+b(1-\eta)\left\{2\left[\left(1-\frac{2\delta}{d}\right)\frac{t}{t_X}-\frac{8T}{\pi^2t_X}\sum_{n=\mathrm{odd}}\frac{1}{n^4}\cos\left(\frac{n\pi\delta}{d}\right)\left(1-e^{-n^2t/T}\right)\right]+\left(1-\frac{t}{t_X}\right)\left[\left(1-\frac{2\delta}{d}\right)-\frac{8}{\pi^2}\sum_{n=\mathrm{odd}}\frac{1}{n^2}\cos\left(\frac{n\pi\delta}{d}\right)e^{-n^2t/T}\right]\right\}, \quad [5]$$

$$S_{RBC}(t)=b\eta\left\{2\left[\left(1-\frac{2\delta}{d}\right)\frac{t}{t_X}-\frac{8T}{\pi^2t_X}\sum_{n=\mathrm{odd}}\frac{1}{n^4}\cos\left(\frac{n\pi\delta}{d}\right)\left(1-e^{-n^2t/T}\right)\right]+\left(1-\frac{t}{t_X}\right)\left[\left(1-\frac{2\delta}{d}\right)-\frac{8}{\pi^2}\sum_{n=\mathrm{odd}}\frac{1}{n^2}\cos\left(\frac{n\pi\delta}{d}\right)e^{-n^2t/T}\right]\right\}. \quad [6]$$

There are 5 shared parameters between $S_{TP}(t)$ and $S_{RBC}(t)$: b, δ/d, T, η and t_X, where $b=\lambda dS_A/V_g$ is the normalization constant and $T=d^2/(\pi^2D)$ is the gas-exchange time constant for xenon in the lung. The other parameters are: λ — average Ostwald solubility of xenon in tissue and blood; S_A/V_g — surface-area-to-volume ratio (SVR); D — average diffusion coefficient of xenon dissolved in tissue and blood; η — fraction of RBC xenon in the blood; t_X — capillary transit time. t_X is introduced to take into account the effect of blood flow, which is illustrated in Fig. 2. From η the hematocrit (Hct) can be estimated using $\mathrm{Hct}=\frac{\eta/\lambda_{RBC}}{\eta/\lambda_{RBC}+(1-\eta)/\lambda_P}$, where λ_{RBC} and λ_P are the xenon solubilities in RBC and plasma, respectively.

Results Using the nominal parameter values for human (S_A/V_g=250 cm^{-1}, λ≈0.12, d≈10 μm, δ≈2 μm, T≈30 ms, η≈0.5, t_X=1.5 s (8-12)) $S_{TP}(t)$ and $S_{RBC}(t)$ in Eqs. [5] and [6], respectively, are plotted in Fig. 3. These curves in Fig. 3 qualitatively interpret the plots of data available in the literature (2,13-15).

Discussion and Conclusions The validity of the proposed model of exchange can also be verified by examining its approximations. Specifically, adding $S_{TP}(t)$ and $S_{RBC}(t)$, and setting δ=0, we recover the expression for the entire DX signal ($F(t)$) when the barrier is ignored, which was first derived by Patz et al. (16); further, by setting $1/t_X$=0 we arrive at the simple result assuming no flow ([5] in (17)). In summary, we have presented a simple model of gas exchange which expresses the DX signals in terms of important pulmonary parameters. By fitting the xenon uptake data using the proposed model one can simultaneously measure lung microstructure, physiology, and function. It can potentially be used to detect a variety of pulmonary diseases.

References (1) Ruppert K et al. NMR Biomed 2000;13:220 (2) Driehuys B et al. PNAS 2006;103:18278 (3) Patz S et al. Euro J Radiol 2007;64:335 (4) Chang YV et al. ISMRM 2010;4602 (5) Imai H et al. MRM 2010;64:929 (6) Chang YV et al. ISMRM 2009;4384 (7) Chang YV arXiv:1008.3961 (2010) (8) Coxson HO et al. Am J Respir Crit Care Med 1999;159:851 (9) Ladefoged J et al. Physiol Med Biol 1967;12:353 (10) Gil J et al. Lab Invest 1988;58:466 (11) Gehr P et al. Respir Physiol 1978;32:121 (12) Hogg JC et al. J Appl Physiol 1994;77:1795 (13) Mansson S et al. MRM 2003;50:1170 (14) Abdeen N et al. MRM 2006:56:255 (15) Chang YV et al. ISMRM 2008;201 (16) Patz S et al. ISMRM 2008;2678 (17) Ruppert K et al. MRM 2004;51:676

Acknowledgements The author was supported by NIH grant R21EB005834.

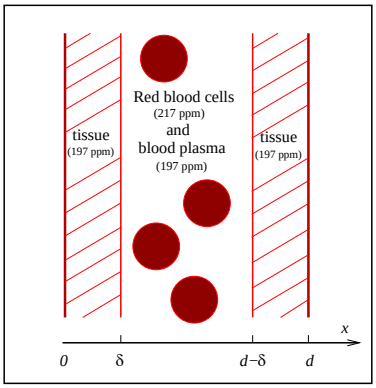

Figure 1 A simplified model of lung septum. Septal thickness = d, barrier thickness = δ. Xenon in tissue and blood plasma resonates at 197 ppm, xenon in the red blood cells resonates at 217 ppm.

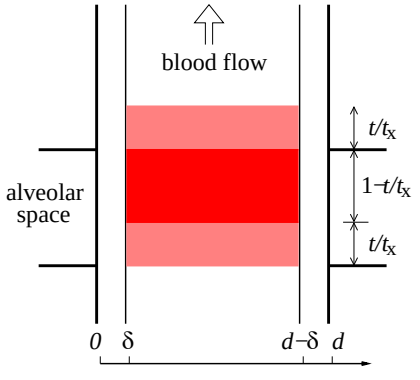

Figure 2 Effect of blood flow on gas exchange in the calculation of $S_{RBC}(t)$. The pink areas are partial volumes of exchange due to blood flow.

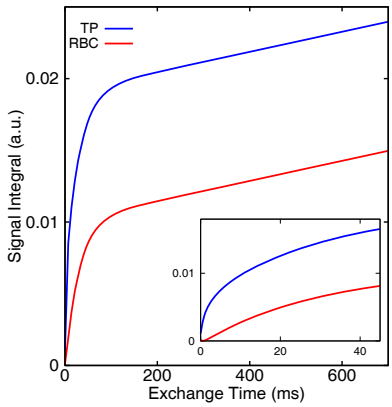

Figure 3 Plots of $S_{TP}(t)$ (blue) and $S_{RBC}(t)$ (red) in Eqs. [5] and [6], respectively.