Detection of Interstitial Lung Disease in Humans with Hyperpolarized ^{129}Xe

S. Patz[1], J. P. Butler[2], I. Muradyan[1], M. I. Hrovat[3], H. Hatabu[1], P. F. Dellaripa[4], I. M. Dregely[5], I. Ruset[5], and F. W. Hersman[5]

[1]Radiology, Brigham and Women's Hospital, Boston, MA, United States, [2]Harvard School of Public Health, Boston, MA, United States, [3]Mirtech, Inc, Brockton, MA, United States, [4]Rheumatology, Brigham and Women's Hospital, Boston, MA, [5]Physics, University of New Hampshire, Durham, NH, United States

Introduction

An important feature of ^{129}Xe is its solubility in tissue and the fact that the dissolved phase of ^{129}Xe has a chemical shift of ~200ppm from the gas phase. This allows separate and direct measurement of both phases. After saturation of the dissolved phase ^{129}Xe magnetization, observation of subsequent replenishment of ^{129}Xe magnetization by diffusion from the alveolar gas spaces to septal tissue can provide functional physiological information about the lung [1-5]. The initial, short-time, behavior of the ^{129}Xe diffusion curve behaves as $\sqrt{t}$ and allows one to determine alveolar surface area per unit gas volume S_A/V_{gas} [2]. Examination of the longer time behavior provides information about septal thickness and pulmonary blood flow [1,3,4]. Using a chemical shift saturation recovery (CSSR) method, we demonstrate the ability to detect increased septal thickness in human subjects with interstitial lung disease (ILD).

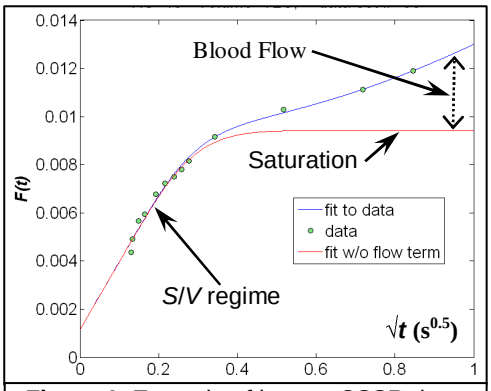

Figure 1. Example of human CSSR data.

Methods

Four healthy subjects and two subjects with mild to moderate ILD were studied following protocols approved both by our local IRB and by a FDA IND. Experiments were performed at 0.2T using a Tecmag Apollo research spectrometer interfaced to a GE Profile IV 0.2T magnet. Whole lung CSSR data were obtained using the CSSR method of Butler et al [2] where a selective RF pulse is used to destroy the ^{129}Xe magnetization in the dissolved phase (time t=0) followed by a diffusion time t and interrogation of the dissolved phase magnetization to determine the diffusion of ^{129}Xe atoms into the dissolved phases from the alveolar gas spaces during time t. At 0.2T one cannot easily distinguish the different dissolved phase spectral peaks and therefore the dissolved phase peaks were all grouped together in our analysis. Similar to methods of Ruppert et al. [1], Mansson et al. [3] and Driehuys et al. [4], we solved the 1D septal diffusion equation. In our case, we used a rectilinear geometry and included a separate term for blood flow. The ratio F of the dissolved state magnetization at time t relative to that in the gas phase at t=0 was found to be:

$$F(t) = F_0 + \frac{\lambda\tau}{2}\frac{S_A}{V_{gas}}\left(\frac{t_{cap}-t}{t_{cap}}\right) f(Dt/\tau^2) + (2)\frac{\lambda\tau}{2}\frac{S_A}{V_{gas}}\left[\frac{t}{t_{cap}} - \frac{8\tau^2}{D\pi^4}\frac{1}{t_{cap}} g(Dt/\tau^2)\right],$$

where

$$f(x) = 1 - \sum_{n,odd}\frac{8}{\pi n^2}\exp\left[-x\pi^2 n^2\right], \quad g(x) = 1 - \sum_{n,odd}\frac{1}{n^4}\exp\left[-x\pi^2 n^2\right],$$

λ is the Ostwald solubility coefficient, D_{diss} is the diffusivity of ^{129}Xe in the dissolved phase, τ is the septal thickness, and t_{cap} is the transit time of blood through the gas exchange region. Before breathing xenon, a subject is instructed to perform 2 cycles of a deep breath to TLC followed by exhalation to close to RV. This ensures there is an identical breathing history before the experiment for each subject. During a single breath-hold experiment, multiple diffusion times were measured ranging from 17 to 750ms. Nonlinear least squares fits were performed to the analytical form for $F(t)$ to obtain estimates of S_A/V_{gas}, τ, and t_{cap}. Experiments were performed at three different lung volumes (LV) for healthy subjects and at TLC for the ILD subjects. At least two repeats of each breath-hold experiment were performed. Standard pulmonary function tests were performed to obtain RV and TLC for each subject. Our protocol allowed for a maximum breath-hold time of 40s for healthy subjects and 20s for those with ILD. For each experiment, 1-2 liters of ^{129}Xe with 50-60% polarization were prepared with an on site University of New Hampshire polarizer [6]. Literature values of D_{diss} and λ were used to calculate S_A/V_{gas} from the early time slope of F vs. $\sqrt{t}$.

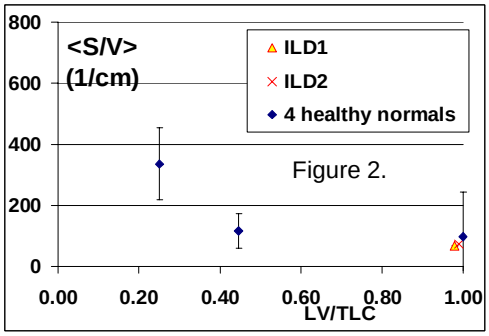

Figure 2.

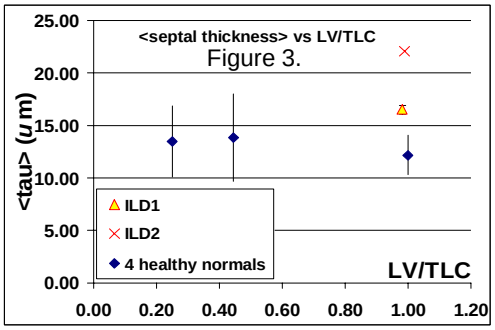

Figure 3.

Results

Figure 1 shows a typical CSSR data set. As expected, the data is linear with respect to $\sqrt{t}$ at early times. Excellent fits to the data were obtained. After the fit parameters were obtained, the fit was also plotted with $t_{cap}\rightarrow\infty$ to illustrate the effect of blood flow; the red curve of Fig. 1 shows what is expected for septal saturation without blood flow. Figures 2 and 3 show S_A/V_{gas} and τ respectively vs. lung volume normalized to TLC. As expected, S_A/V_{gas} decreases with increasing LV and there is no significant difference between healthy subjects and the two ILD subjects at TLC. For healthy subjects, Figure 3 shows a relatively flat dependence of τ with LV and a significant difference between the two ILD subjects and the 4 normal subjects at TLC.

Discussion and Conclusions

We have obtained initial evidence that ^{129}Xe diffusion CSSR can identify subjects with mild to moderate ILD as having increased septal thickness compared to normal healthy subjects.

Acknowledgement This work was supported by NIH RO1 HL073632.

References

1. Ruppert et al, *MRM*, 51:676-687(2004). 2. Butler et al, *J Phys: Cond Matter*, 14, L297-L304 (2002). 3. Mansson et al, *MRM* 50:1170-1179 (2003). 4.Driehuys et al, *PNAS* 103:18278-18283 (2006). 5. Patz et al, *Eur J Rad*, 2007. 6. Ruset et al, *Phys Rev Lett* 96, (2006).