Hyperpolarzied 129Xe Human Gas Exchange at 0.2T with XTC

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Introduction

Xenon Transfer Contrast (XTC), developed by Ruppert et al [1], measures gas exchange, i.e. ^{129}Xe diffusion from alveolar gas space to lung parenchymal tissue. Ruppert et al demonstrated XTC in rabbit and dog lungs. XTC gives an indirect measure of gas exchange from alveoli to tissue by looking at the modulation on the gas phase signal after applying multiple 180's to the dissolved phase. Here we modify this method to allow all data to be acquired in a single breath-hold and also report the first human pulmonary gas exchange results with XTC. Xenon dissolves in tissue with a partition coefficient of 20% and during an exchange time of 50ms, ~1% of the gaseous xenon diffuses into tissue with an equal amount diffusing back from tissue to gas phase. By inversion of the tissue phase spins, the effect on the gas phase is doubled. In addition, the XTC method repeats the inversion-exchange sequence many times to build up a large modulation in the gas state signal in those areas of the lung where exchange exists. For short exchange times such that xenon only diffuses into the thin (~2um) parenchymal layer separating air sac from vasculature, the signal from dissolved state is diffusive, increasing as sqrt(time) [2]. Thus XTC is an elegant method to produce large modulations of the gas phase signal from a very small gas exchange fraction.

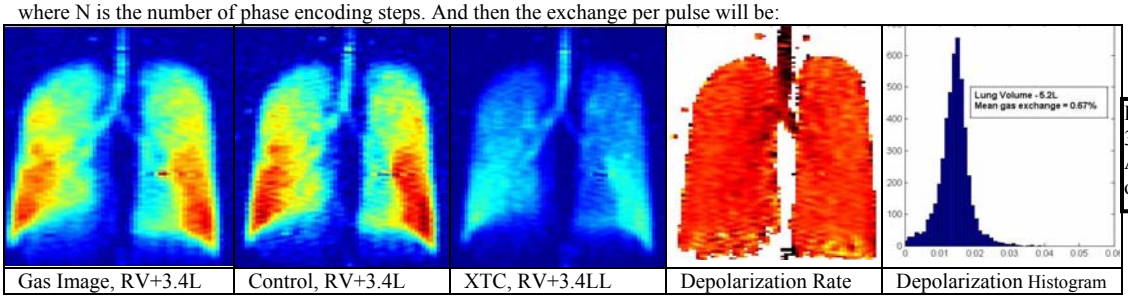
Methods

A GE Profile IV MRI scanner (0.2T) was interfaced with a broadband console (Tecmag Apollo) at Brigham and Women's Hospital, Boston, MA. A Mirtech, Inc. whole body RF coil (Q~300) operating at ^{129}Xe frequency (2.361MHz) was used for all human studies. ^{129}Xe was polarized on site using a polarizer developed and built at University of New Hampshire [3] with typical polarization of 45% at a production rate of 1.2L/h. Polarized xenon was frozen to separate from the buffer gases and then thawed into a tedlar bag with T_1=20min. Experiments were performed in <3min after thawing. All human subject experiments followed FDA IND and IRB approved protocols. Three gradient echo projection images were acquired in a single breath-hold: S_{Gas}, $S_{Control}$, S_{XTC}, where the flip angles were 4°, 4°, and 12° respectively. The gas phase was set on resonance and the dissolved phase is then at +485Hz (205ppm). Between the first 2 images, there are 44 repeats of the "180° – exchange" sequence component at -205ppm and between the last two images there are 44 repeats at +205ppm. Ruppert et al used two separate breath-holds in animal experiments for each image pair. The first image pair is used to correct for T_1 relaxation and RF depletion between images. Then the ratio of the control image to the corrected XTC image represents the depolarization due to gas exchange during 44 exchange cycles. Exchange time = 50ms. For selective excitation, we used a RF pulse that was constructed from the FT of a trapezoidal waveform whose FWHH was 490Hz. This resulted in less than a 1° flip angle 205ppm away from the center frequency. XTC was performed on 5 subjects at 2 different lung volumes.

Analysis and Results

If S_{Gas} and $S_{Control}$ are the first 2 images then decay due to T_1 relaxation and RF depletion is $R_{RF,T_1} = S_{Control}/S_{Gas}$, and $S_{XTC} = S_{Control} \cdot R_{RF,T_1} \cdot R_{Exchange}$. To calculate gas exchange values, the difference in the flip angles must be taken into account, i.e. $R_{exchange} = \left(S_{XTC}/S_{Control} R_{RF,T_1}\right) \cdot \left(\sin(\alpha_{Control})/\sin(\alpha_{XTC})\right) \cdot \left(\cos(\alpha_{XTC})/\cos(\alpha_{Control})\right)^{N/2}$, where N is the number of phase encoding steps. And then the exchange per pulse will be:

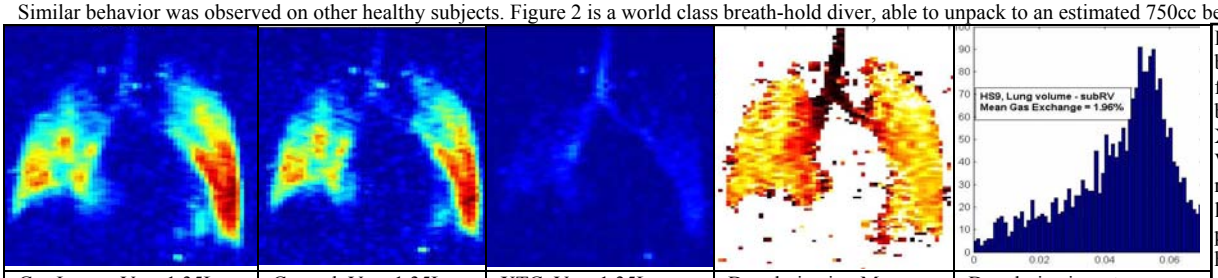
$$R_{Exchange,1} = 1 - \sqrt[44]{R_{Exchange}}$$



Gas Image, RV+3.4L | Control, RV+3.4L | XTC, RV+3.4LL | Depolarization Rate | Depolarization Histogram

Figure 1. Normal healthy adult: 3.4L above residual volume (RV) Average exchange = 0.67%. 1.8L of ^{129}Xe was inhaled.

Experiment on subject in Fig. 1 was conducted at lower lung volume (V_L) as well. Average exchange rate increased from 0.67% at V_L=5.2L to 1.3% at V_L=3.5L. Similar behavior was observed on other healthy subjects. Figure 2 is a world class breath-hold diver, able to unpack to an estimated 750cc below RV before inhalation.



Gas Image, V_L ~ 1.35L | Control, V_L ~ 1.35L | XTC, V_L ~ 1.35L | Depolarization Map | Depolarization Histogram

Figure 2. World class breath-hold diver starting from $\mathbf{V_L}$~750cc (est.) below RV. Inhaled Xe/O2 of 440cc. Ventilation defects may reflect airway closure at low or negative trans-pulmonary pressure. Note high avg exchange of 2%.

In this experiment after unpacking, 350cc of Xe was inhaled with an additional 21% oxygen. Mean exchange was 1.96%. In a second experiment at lung volume of ~1.6L, mean exchange was 2.04%.

Discussion

As expected gas exchange increases with decreasing V_L, proportional to S/V_L in the simplest lung models. However, the dependence is much stronger than that extrapolated from S/V measurements in animal lungs fixed by vascular perfusion [4]. The world class breath-hold diver, at lung volumes below RV, shows markedly heterogeneous ventilation and exchange. The ventilation defects are likely the result of airway closure at low or negative transpulmonary pressures from the unpacking maneuver. The extremely large gas exchange heterogeneity may similarly reflect large variations in regional ventilation and S/V.

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References

[1] Kai Ruppert et al., MRM 51: 676-687 (2004)
[2] Butler et al., *J Physics: Condensed Matter*, 14, L297-L304 (2002).
[3] I.C. Ruset et al, 13th Annual ISMRM, Miami Beach, p1839 (2005).
[4] J. Gil et al., 1979.
[5] Patz et al, 14th Annual ISMRM, Seattle (2006).