Human Pulmonary pO2 at 0.2T with Hyperpolarized 129Xe

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Introduction

Variable flip angle techniques may be used to enhance measurements of pO2 and pO2 depletion in the lung utilizing hyperpolarized gasses. The new sequences potentially provide a more sensitive indicator of intrapulmonary pO2 and in particular temporal pO2 depletion due to oxygen uptake. Previous methods with hyperpolarized He employed imaging sequences which varied the time between images and utilized either one or two flip angles [1,2].

Theory

During a hard rf pulse, it is quite reasonable to neglect the effects of relaxation. This allows us to treat the pulse as a delta function. It is also assumed that the transverse magnetization has decayed to zero before the pulse. Under these conditions, the Bloch equation for the longitudinal magnetization can be shown to be:

$$dM_z/dt = -\frac{M_z}{T_1} - kM_z - M_z\frac{(1-\cos\alpha)\delta(t)}{(1-(1-\cos\alpha)S(t))} \qquad [1]$$

where the flip angle of the rf pulse is given by α at time t=0, $\delta(t)$ is the Dirac delta function, and $S(t)$ is a step function. Relaxation is given by T_1 and k represents the loss of magnetization due to exchange and/or outflow of magnetization. This factor would be zero for hyperpolarized He and nonzero for hyperpolarized Xe. Eq. [1] may be considered to provide a Bloch equation model for hyperpolarized MRS. Since $1/T_1$ is proportional to pO_2 (0.000373/mbar-s), it may written as $1/T_1=a*pO_2+bt\ dpO_2/dt$. For a train of rf pulses which can occur at various times (t_n) with various flip angles(α_n), solution of Eq. [1] gives:

$$M_z = M_z(0)\exp(-(k+a*pO_2)t - \frac{b}{2}\frac{\partial pO_2}{\partial t}t^2)\prod_{n=1}^{N}(1-(1-\cos\alpha_n)S(t-t_n)) \qquad [2]$$

The measured signal at a given time, t_n, is then given by $M_z(\sin(\alpha_n))$.

Methods

A logical first approach is to maintain a nearly constant SNR for each signal measurement. Thus the flip angle for each pulse is iteratively calculated to compensate for loss of magnetization due to relaxation (based on the initial estimated pO2 level) and rf demagnetization. If the initial actual pO_2 level is close to the estimated value used for the sequence design, then the observed signal will vary linearly with time. If there is additional pO_2 depletion due to oxygen consumption then the signal will be observed to vary quadratically with time.

A GE Profile IV MRI scanner (0.2T) was interfaced with a broadband console (Tecmag Apollo) at Brigham and Women's Hospital, Boston, MA. ^{129}Xe was polarized on site using a polarizer developed and built at University of New Hampshire[3]. All human subject experiments followed FDA IND and IRB approved protocols. The signal was measured from the entire lung during a single breathhold. As most of the long volume consists of alveolar volume, then measurements taken from the whole lung should reflect the alveolar oxygen concentration. Flip angle calibration was performed separately by employing the same sequence of flip angles on a sample cell with hyperpolarized Xe without O_2. Typically a single constant scale factor for all flip angles provided a good fit to the data (see Fig. 1). The variable flip angle sequence typically employs different TR spacings to minimize rf demagnetization and to increase time resolution at later times.

Analysis and Results

For comparison, a constant flip angle experiment was run on a human volunteer. After correcting the data for rf demagnetization, the data suggested a slight departure from an exponential to give the values in Fig.2. Fig. 3 shows a typical run from a human volunteer at rest and Fig.4 shows the same volunteer performing a mild steady state exercise (alternately kicking his/her legs prior and during the breathhold).

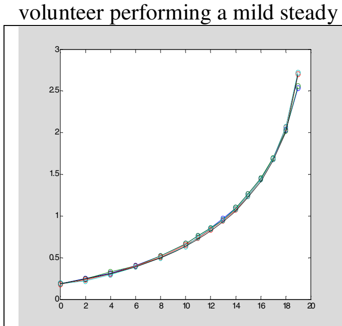

Fig.1 Typical flip angle calibration on a cell with hypXe. Fitting required a single scaling factor of 0.77 for all flip angles.

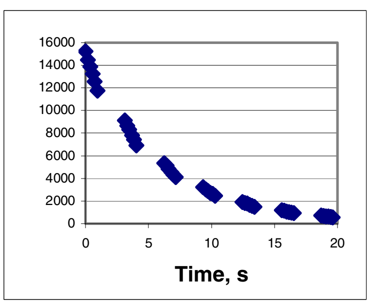

Fig 2. Signal decay from a sequence of 42 constant flip angle pulses with 2 TR values in one normal healthy volunteer. pO_2=281mbar, dpO_2/dt= -1.1mbar/s.

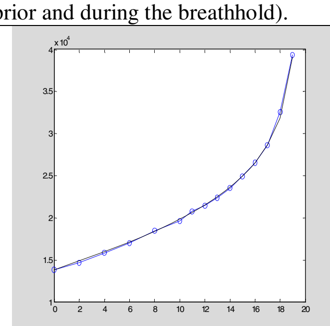

Fig. 3. Data and fit on a human volunteer at rest. Fit gives: pO_2=226mbar, dpO_2/dt= 0 mbar/s.

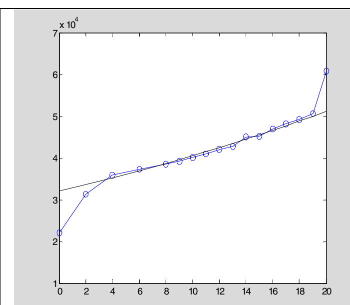

Fig. 4. Data and fit on a human volunteer exercising. Fit gives: pO_2=173mbar, dpO_2/dt= 0 mbar/s.

Discussion

Both constant and variable flip angle experiments with Xe indicate higher rest values of alveolar pO_2 than expected. Possibly this discrepancy is caused by the exchange term. Based upon estimated values of alveolar pO_2, this exchange term is estimated to have a time constant (1/k) of 36 sec. A drop in pO_2 levels from rest was measured upon exercising, though temporal oxygen consumption during a breathhold was not observed. Thus it seems that pO_2 measurements with hyperpolarized Xe is more complicated to understand than with hyperpolarized He.

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