Volume Localized Measurement of Oxygen Partial Pressure (pO2) in the Human Lung with 3D Hyperpolarized 3He MRI

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Introduction A method of volume-localized quantification of pO_2 in the lungs is presented which uses repetitive frame 3D gradient echo imaging of ^{3}He. The method is demonstrated with experiments on phantoms containing ^{3}He and known concentrations of O_2 and also *in-vivo* at breath-hold. The method was compared with the results from an equivalent 2D thin slice methodology and 2D whole lung projections.

Theory There are three factors that affect the time course of the ^{3}He longitudinal polarization whilst imaging during breath-hold:

i) RF depolarization. **ii)***T1* depolarization, dominated *in vivo* by O_2 ($T1_{O2} \approx 20$ s) this changes during breath-hold due to gas exchange in the alveolar-capillary bed. **iii)** Mixing of gas polarization between different regions of the lung due to Brownian diffusion and flow –this is an issue in 2D imaging with diffusion of gas out of slice in the inter-image delay.

A 3D sequence excites the whole of the lungs per view, therefore RF depolarization effects can be deconvolved from the pO_2 contribution to *T1*. If a time series of *n* images is acquired during the same breath-hold, then the n^{th} image has an intensity given by Eq.[1] where α is the flip angle, *N* is the number of RF pulses applied per image acquisition ($N=N_Y N_Z$) and $\xi = 2.61$ bar × s at 310 K [3].

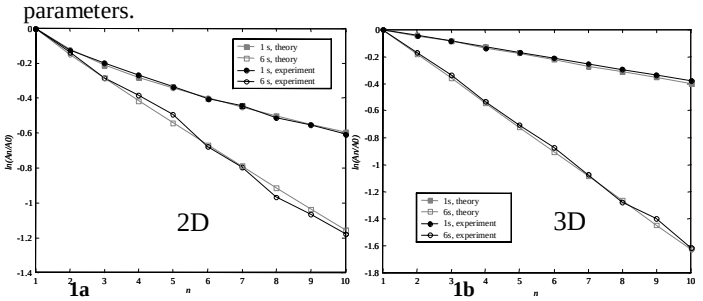
$$A_n = A_0(\cos\alpha)^{nN} \exp\left(-\frac{1}{\xi}\int_0^{t_n} pO_2(t)dt\right) \quad [1] \qquad pO_2(\bar{t}_n) = \xi\frac{\left[\ln(A_n(\tau_1)/A_0) - \ln(A_n(\tau_2)/A_0)\right]}{n(\tau_2-\tau_1)} \quad [2]$$

Eq. [1] assumes that the whole of the sample experiences the same RF history, with a uniform flip angle α, being delivered across the sample- a condition that is met in 3D imaging assuming a uniform B1 coil homogeneity. Eq. [1] also assumes diffusion is negligible. If two sets of experiments are performed with different inter-image delay times, τ_1 and τ_2 , with the same α, then elimination of α from [1] gives the pO_2 as a function of the mean inter-image time-see Eq.[2]. This can then be approximated by a linear relation with a constant rate of decrease (*R*) in-vivo during breath-hold [1]; $pO_2(t)=p_0 - Rt$.

Simulations Numerical simulations of the signal decay were performed, these accounted for the *T1* factors described above but also included the effects of *diffusion* and the effects of depolarization due to a non-ideal slice profile. See [4] for further details of the methods of simulation.

Materials All work was performed on a 1.5T whole body MRI system (Philips, Eclipse). The ^{3}He gas was polarized to 30% with rubidium spin exchange apparatus. Phantom studies were performed using Tedlar bags containing known volumes of N_2, ^{3}He and O_2 at 1 bar –see Table 1. *In-vivo* studies were also conducted on three healthy volunteers in two separate breath-holds following inhalation from a Tedlar bag filled with 300 ml ^{3}He and 700 ml N_2.

Methods An optimised 3D gradient echo sequence was used N_x =128 samples, BW 31.25 kHz, TR 6.4 ms, TE 3.4 ms –see [4] for more details of sequence. Two successive time series of *n* images were then collected with inter-image delays given by τ_1 and τ_2 –see Table for 3D & 2D imaging parameters.



1a **1b**

Phantom	pO2 (bar)	α_1°	α_2°	τ_1 (s)	τ_2 (s)	N_z	N_y	*n*
3D	0.068	0.8	0.8	1.5	8.0	8.0	28.0	7.0
2D thin slice	0.048	3.1	3.1	1.0	6.0	1.0	128.0	10.0
2D thick slice	0.064	0.9	0.9	1.0	6.0	1.0	128.0	10.0
In-vivo								
3D study 1(n=3)		1.0	1.0	1.7	6.0	8.0	28.0	7.0
3D study 2 (n=1)		0.8	0.8	3.7	8.0	12.0	48.0	5.0
3D study 3 (n=1)		0.8	1.6	5.0	5.0	12.0	48.0	5.0
2D projection		2.0	2.0	1.0	6.0	1.0	80.0	6.0
2D thin slice		2.0	2.0	1.0	6.0	1.0	128.0	6.0

Table 1

Results and Discussion The black circles in Fig 1a and 1b are the results from the phantom experiments. Both sets of simulations (gray squares) show a good fit with the experimental results (black). The thin slice **2D** results (Fig. 1a) show a departure from a mono-exponential predicted by Eq [2] alone for the τ_1=1 s time series. The volume **3D** results (Fig. 1b) show a mono-exponential from for both time series indicating accurate pO_2 estimation. Fitting Eq.[2] for the thin **2D** slice data gave a 4-fold underestimate in pO_2=0.011 bar (c.f. 0.048 actual pO_2) and a positive rate of decay R= +8.1 ×10^{-4} bar s^{-1} which should be negligible considering the fixed pO_2. The volume (**3D**) results (Fig. 1b) show a mono-exponential form for both time series, and gave pO_2=0.065 bar (c.f. 0.064 actual pO_2) and R= 0 bar s^{-1} which is in good agreement.

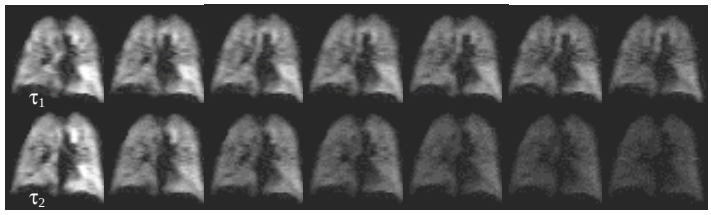


Fig. 2 shows the two time series of images from in-vivo study 1 (*n*=7). ROI measurements from the in-vivo data give a p_0 in the range 0.11 –0.17 bar which is consistent with values we have measured with a non-slice selective 2D acquisition [1] (results not shown for space).

Conclusion The 3D volume localized estimates of pO_2 (0.09 - 0.18 bar) are consistent with those published previously from images acquired from 2D whole lung projections [1,2]. The volume coverage allows accurate mapping of pO_2 in 3D. We have shown with experiments and simulations of the diffusion equation that the equivalent 2D thin slice technique gives a systematic *underestimate* of pO_2 when the localized gas diffusion is significant (factor of 4 under estimate for D=0.9 cm^{2}s^{-1} representative of free ^{3}He in air). Care should be exercised when using 2D slice selective methods in disease where high ADC is expected such as in bullous emphysema.

References: [1] Deninger AJ et al, J Magn Reson. 1999; 141:207-2161] **[2]** Deninger AJ et al, Magn Reson Med. 2002 47(1):105-14. **[3]** Saam B et al Phys. Rev. A. 1995 52(1):862-865. **[4]** Wild JM et al Magn Reson Med. 2004;52(3):673-8..