Measurement of the exponential decay of alveolar partial pressure of oxygen using hyperpolarized ^{3}He MRI in animals and human subjects

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Purpose: Respiratory diseases are one of the main causes of death worldwide [1] and a lot of effort is undertaken to develop new techniques to assess lung function. Using hyperpolarized (HP) ^{3}He-MRI it is possible to locally measure the alveolar partial pressure of oxygen (pO_2) and its temporal evolution during apnea [2]. Most of the pO_2 measurement approaches currently used in humans and animals are based on a linear model of pO_2 decay, $pO_2(t) = p_0 - Rt$, where p_0 denotes the initial partial pressure of oxygen and R – the oxygen depletion rate. However, partial pressure of oxygen is known to decrease exponentially during apnea [3] and the linear approximation is only valid for short periods of breath-hold. The aim of this work was to demonstrate the feasibility of using the physiologically more appropriate exponential model of pO_2 decay both in animals and in humans. The proposed model is given by: $pO_2(t) = p_0\exp(-t/r)$ [4] where p_0 is the initial partial pressure of oxygen and the oxygen depletion time constant r depends on the metabolic rate of the animal.

Theory: The signal decay of HP ^{3}He related to the presence of oxygen can be described by: $S(t) = S_0\exp(-\int(pO_2(t)/\xi)dt$, where ξ denotes the oxygen induced decay constant [2]. Thus, the integral of $pO_2(t)$ can be expressed as: $\int pO_2(t)dt = -\xi\ln(S(t)/S_0)$. Finally, the parameters of interest (p_0, r) can be obtained by fitting the plot of $\int pO_2(t)dt$ versus time with the following function: $p_0 r\exp(1-\exp(-t/r))$.

Methods: *Data acquisition*: *In vivo* pO_2 measurements were performed in 6 mice, 6 rats, 3 rabbits and 7 human subjects. Small animal studies were performed on a 2T magnet, while the experiments involving rabbits and human subjects were performed on a 1.5T clinical scanner. For animal studies, ^{3}He was polarized using a spin exchange polarizer. With local ethics committee approval, mice, rats and rabbits were anaesthetised and tracheotomised. Before each acquisition, their lungs were insufflated with HP ^{3}He. For human subjects, clinically certified HP ^{3}He was used. The subjects were asked to inspire a mixture nitrogen and HP ^{3}He from a plastic bag (Tedlar) and to hold their breath during the acquisition. A single acquisition spiral pO_2-sensitive sequence was used [5] with the sequence parameters summarized in Table 1. The images were reconstructed using a gridding algorithm (ref). *Image analysis*: The exponential model of pO_2 decay during apnea was used for data analysis. Parametric maps of p_0 and r were computed. The mean values of both parameters as well as their distribution across the lungs were assessed. *Simulation*: Numerical simulations were performed to evaluate when the use of the nonlinear pO_2 decay model is necessary to obtain satisfying accuracy of the measured parameters. Exponential decay of pO_2 was simulated assuming different inter-image delays, corresponding to typical experimental conditions in different species. Gaussian noise was added to match experimental SNR and both models were used to compute pO_2 decay parameters.

Table 1. Sequence parameters for the studied species.

	mice	rats	rabbits	humans
single image acquisition time [s]	0.3	0.3	0.2	0.2
number of images	12	12	9	9
inter-image delay time [s]	0.5	2.3	4.0	4.0
total acquisition time [s]	8.6	26.0	25.8	25.8
FOV [mm]	40	60	219	400

Results: Parametric maps of p_0 and r were calculated (Fig. 1.) and the mean values were computed (Table 2.). The mean p_0 values were in agreement with the values expected in case of an anoxic gas mixture inhalation. The mean values of r show gradual increase with subjects decreasing metabolic rate per unit mass (BMR/unit mass), in accordance with physiology. Simulation results showed no significant differences in the mean p_0 obtained with both models. However, the estimation accuracy of the oxygen depletion related parameters (R and r) was significantly affected by the acquisition duration. If the total acquisition time is comparable to the oxygen depletion time constant (r), the use of the linear model leads to underestimation of R. On the contrary, the value of r can be accurately assessed only when the acquisition duration is of the order of the oxygen depletion time constant or longer.

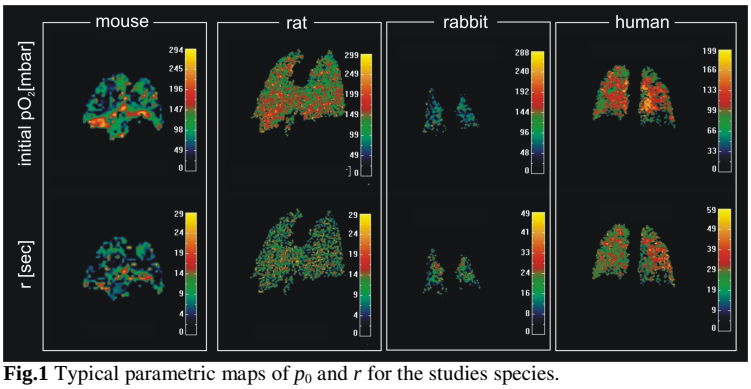

Fig.1 Typical parametric maps of p_0 and r for the studies species.

Table 2. Mean p_0 and r values for the studies species.

	mice	rats	rabbits	humans
p_0 [mbar]	76.8 ± 18.0	83.8 ± 20.3	91.0 ± 31.2	95.7 ± 8.2
r [s]	6.47 ±1.82	11.6 ± 4.2	17.8 ± 6.9	31.2 ± 4.0
BMR/unit mass [ml O_2/h/g]	1.49	0.67	0.28	0.10

Conclusions: The exponential model of pO_2 decay was successfully applied to measure initial pO_2 and oxygen depletion time constant r in mice, rats, rabbits and humans. The results of the simulations suggest that the use of the linear model is well justified when the total acquisition time is shorter than the oxygen depletion time constant, r. In case of longer acquisition duration, the exponential model should be applied. Therefore, care must be taken when establishing the sequence timing in order to assure satisfying level of measurement accuracy.

References: 1. Anderson R, Smith B, Natl Vital Stat Rep 53:1 (2005), 2. Deninger A et al., J Magn Reson 141:207 (1999), 3. Lai Y-L, Hildebrandt J, J Appl Physiol 42: 255 (1978), 4. Cieslar et al., NMR in Biomed 20:383 (2007), 5. Cieslar et al., Magn Reson Med 57:423 (2007)