Measurement of nonlinear decay of alveolar partial pressure of oxygen in mice using 3He-MRI

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INTRODUCTION:Partial pressure of oxygen (pO_2) and its depletion rate characterising oxygen consumption are important parameters in lung function assesment. pO_2 is known to decrease exponentially in the lungs during apnea (1). All previous pO_2 measurements both in animals as well as in human subjects (2) were restricted to short breath-hold periods when linear decrease of pO_2 can be assumed. Among laboratory animals mice are very useful due to the wide range of available transgenic mouse models. However, high metabolic rate of these animals results in very fast pO_2 decrease making it necessary to study the oxygen decay dynamics without using the simplified model of linear decrease of pO_2. In this work we present the first results of pO_2 measurements in mice using this novel approach. To be able to follow rapid changes of pO_2, fast spiral single-breath method with sliding window technique used for RF correction was exploited.

THEORY: During breath-hold oxygen removal from the lungs is exponential with time: $pO_2(t) = p0\exp(-t/r)$, where p0 is the initial partial pressure of oxygen and r is the oxygen depletion time constant. The ^{3}He signal decay in presence of paramagnetic oxygen can be described by: $S(t) = S_0\exp(-\int(pO_2(t)/\zeta)dt)$, where ζ is the oxygen induced decay constant (2.6 [bar.s] @ 37°C) (3). The integral of pO_2 can be obtain from: $\int pO_2(t)dt = -\zeta.\ln(S(t)/S_0)$. Fitting the plot of $\int pO_2(t)dt$ versus time with $p0.r.(1-\exp(-t/r))$ allows to derive both parameters of interest: p0 characterising ventilation and r – related to oxygen uptake and perfusion.

SUBJECTS AND METHODS: The experiments were performed on a 2 T magnet. ^{3}He was polarized using a home-built spin-exchange polariser. Male mice from strain c57BL/6 were anaesthetised by intraperitoneal injection of sodium pentobarbital and tracheotomised. Pure ^{3}He or mixtures of ^{3}He and air (total volume of 0.8 ml) were administered through the endotracheal tube and imaging followed immediately. Spiral sequence with 12 interleaved spirals per image and 1024 samples/spiral was used (flip angle = 5 deg, TE = 2 ms, TR = 27.3 ms, FOV = 40mm). Series of 12 coronal or transverse projections were obtained with delay time of 527 ms between consecutive images. The first two images in each series were acquired without any delay between them and served to estimate the depolarisation effect due to RF excitation.

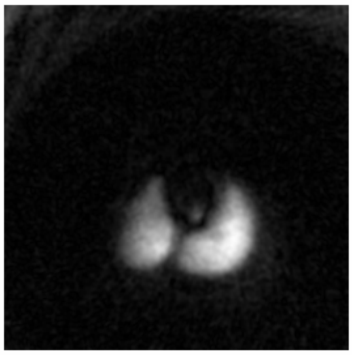

Fig.1. Transverse projection of mouse lungs.

RESULTS: Fig 1 presents transverse projection of the lungs filled with mixture of ^{3}He and air resulting in estimated final oxygen concentration of about 11 %. The SNR of all the images was ranging between 30 and 100 permitting to perform accurate fitting of p0 and r. Exemplary plot of the time course of the integral of pO_2 for ROI = 8 mm^2 is shown in figure 2. Initial partial pressure of oxygen and oxygen depletion time constant were derived from the fit with χ^2 per degree of freedom of 1.72. The values of p0 were measured to be in good agreement with the estimated O_2 concentration whereas the r values were found to poorly depend on the O_2 concentration.

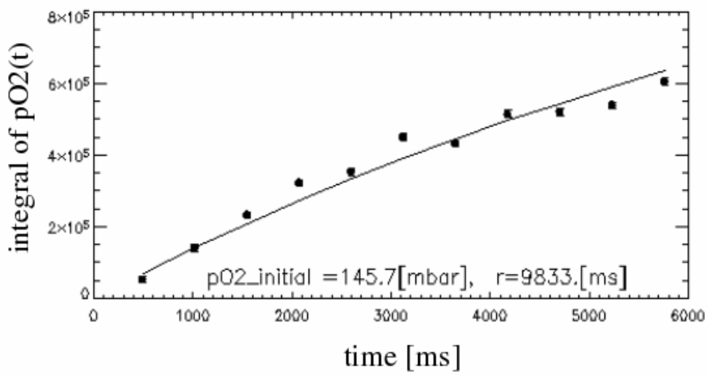

Fig.2. Time evolution of pO_2 integral for ROI of 8mm^2.

CONCUSIONS: This study demonstrates the possibility of assessing alveolar pO_2 values in mouse models using HP ^{3}He. It also demonstrates the relevance of using a nonlinear O_2 concentration decay model when imaging time and O_2 depletion time constant are in the same range.

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