Ventilation strategy to minimize the effect of residual gas volume on ADC in rat lungs

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Introduction: Diffusion is directly related to molecular mobility and it is described by diffusion coefficients. If a mixture contains gases with very different molecular weights and diffusion coefficients, the intra-diffusion coefficient [1, 2] measured for the NMR-resonant species will be quite sensitive to the concentration of all the components [3]. This makes the ADCs measured with hyperpolarized gases dependent on the gases in the lung and their concentrations.
To study the effect of the residual gas volume on the ADC, a positive end expiratory pressure (PEEP) is introduced. In the present work we propose a ventilation strategy which minimizes the dependency of ADC on the residual volume.

Ventilation and image protocols: Wistar rats (~250g) were anaesthetized with thiopental sodium and intubated. Animals were connected to a mechanical respirator-applicator and placed in the supine position into the magnet. The breathing rate was set to 60 breaths per minute. Animals breathed in and out at tidal volume during the ventilation phase. In the data acquisition phase, three pre-washes and a full-inspiration breath-hold (~23 mbar) were applied with HP-gas. Animals were ventilated either with no PEEP (PEEP0) or PEEP of 5mbar (PEEP5). Two different ventilation schemes, regarding the utilized gases in the ventilation and the acquisition phase, were used, Air (A) and Mixture (M). In A (n=13), the ventilation was performed with room air and a bolus of pure HP^3He was used in the acquisition period. In M (n=10), animals were ventilated with a mixture of 21% O_2 and 79% ^4He and the imaging data was acquired with a bolus of 23% of N_2 and 77% of HP^3He. The calculated free diffusion coefficient of these two mixtures was very similar, 1.5836 and 1.5805cm^2/s, respectively.
Three animals were used to obtain an ADC-PEEP curve. They were ventilated using strategy A and with a breath-hold of ~12 mbar of pressure and PEEP in the range 0 – 8 mbar.
Two extra animals were measured using both ventilation strategies and at both PEEPs (0 and 5 mbar).
Images were acquired with a radial ComSpiRa sequence on a Bruker Biospec 70/20 spectrometer operating at 0.5T. Four diffusion images of 200 radii were acquired in an interleaved order. Diffusion time was 1.5ms and the b-values were 0.05, 0.707, 2.11 and 4.26 $s{\cdot}cm^{-2}$.

Results: Figure 1 shows the behaviour of three animals measured with strategy A. A decrease in ADC by increasing the PEEP can be seen. The mean decrease of ADC is 15% between 0 and 8 mbar of PEEP. Figure 2 shows a significant decrease of ADC ($P<0.001$) when PEEP was increased from 0 to 5 mbar in strategy A. However, an ANOVA revealed no significant differences between PEEP groups in strategy M. The differences in ADC between PEEP0 and PEEP5 for two control animals were calculated for each strategy. Figure 3 shows a high ADC difference when ventilating with strategy A whereas this difference was reduced when measuring with strategy M.

Discussion and conclusions: Inspiration of 21% O_2 was necessary while ventilating animals to provide them with good ventilation conditions. The addition of N_2 in the imaging gas mixture in strategy M was based on its similar molecular weight compared to O_2 and on the fact that it does not affect the ^3He polarization level. The precise concentration of HP^3He and N_2 (77% - 23%, respectively) was chosen such that the resulting free diffusion coefficient was similar to the one obtained for the ventilation gas mixture. Thus, by breathing 79% of ^4He and 21% of O_2 and by imaging with HP^3He/N_2 we could guarantee the same free diffusion coefficient in the final mixture in the lung, independent of the ratio between both mixtures. The application of a PEEP was used to increase the volume of the residual gas in the lung thus decreasing the volume of the incoming gas. In strategy M, the application of a PEEP did not show any significant difference in ADC values compared to the measurements at PEEP 0. A strong ADC dependence on PEEP was observed when ventilating the animals with strategy A. This must be due to the fact that room air has a lower diffusion coefficient than ^3He. By increasing PEEP the amount of air remaining in the lung increases, making the subsequent mixture with HP-gas less diffusive. However, in M the diffusion coefficient of the final mixture was the same regardless the PEEP applied, in other words, regardless of the ratio between incoming and residual gas volumes. In combination, these results suggest that the manoeuvre of washing with HP-gas was not sufficient with respect to the removal of all residual air.
We conclude that the use of gas mixtures can be advantageous in all ADC measurements comprising a single breath hold (in both human and animal experiments). We finally note that a characteristic of emphysema is an increase of residual volume. Without these considerations, ADC values may mainly reflect differences in gas concentration and not in alveolar size, as expected, making the differentiation between healthy and disease conditions more difficult.

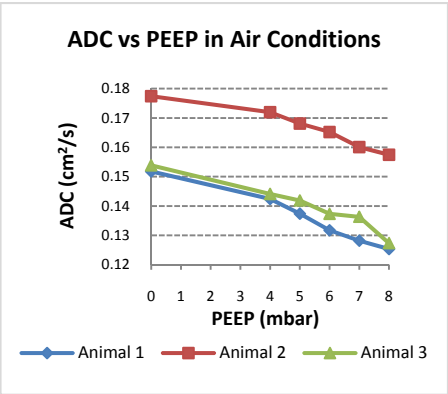

Figure 1. ADC-PEEP curve of three animals ventilated with room air and imaged with a bolus of pure HP^3He. Breath-hold pressure of ~12mbar.

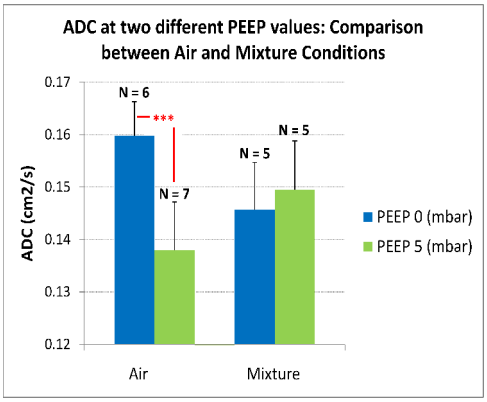

Figure 2. Mean and standard deviation of ADC of animal groups measured at different PEEPs and strategies (A and M). Number of animals contained in each group is shown above the corresponding column. The significant difference between PEEP0 and PEEP5 in strategy A is shown. No significant differences were found when measuring with strategy M.

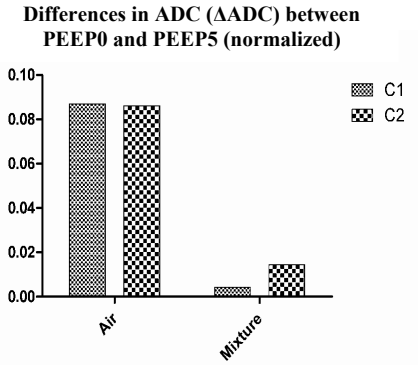

Figure 3. Two control animals measured at PEEP0 and PEEP5 under both strategies. The ADC differences between both PEEPs in both strategies are shown. ADC proved to be different when measuring with strategy A whereas these differences vanished when using strategy M. They were normalized to the value at PEEP0.

References: **[1]** Hirschfelder JO *et al*. Molecular theory of gases and liquids. New York: Wiley; 1954. **[2]** Hirschfelder JO *et al.* Chemical Reviews, 1949;44:205-231. **[3]** Bidinosti CP *et al*. Journal of Magnetic Resonance, 2003;162:122-132.
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