

Quantitative Assessment of Alveolar Recruitment with Hyperpolarized Gas MRI

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INTRODUCTION: Acute Respiratory Distress Syndrome (ARDS) is a critical lung disorder characterized by the impairment of respiratory mechanics and gas exchange. ARDS can lead to inflammation in the alveoli, and eventually to atelectasis (alveolar collapse) and gas exchange deficiency. Techniques have been devised by various researchers to recruit collapsed alveoli and keep them open with the aid of mechanical ventilation. However, the optimal strategy for alveolar recruitment is still uncertain. Various combinations of high/low tidal volume (TV) and higher-than-normal positive end-expiratory pressure (PEEP) maneuvers have been proposed with different and sometimes contradictory results in terms of survival rate. These recruitment maneuvers are similar in that they all attempt to increase the proportion of aerated alveoli at end-expiration while preventing over-inflation of well ventilated lung regions, but the best strategy is still debated. In this project, we attempt to assess the sensitivity of hyperpolarized (HP) gas diffusion MRI as a noninvasive and regional metric of alveolar recruitment and dynamics. The long-term objective is to develop the measurement of regional apparent diffusion coefficients (ADCs) as a probe to longitudinally assess alveolar collapse, recruitment and inflation and to compare the outcome of different recruitment maneuvers. The motivation for this approach hinges on the simple but effective fact that, once recruited with an elevated PEEP and exposed to a fixed tidal volume, the groups of alveoli will expand to an averaged volume (Figure 1), whereas in the case of the partially collapsed alveoli, the recruited alveoli may be subject to an over-extension, which can be manifested in a larger ADC value.

METHODS: Healthy male Sprague Dawley rats were intubated and connected to a custom-designed small animal ventilator (SAV). The SAV is capable of delivering the breathing gas with an accuracy of $\pm 100\mu\text{L}$ /breath and real-time monitoring of peak inspiration pressure (PIP). The rats breathed a mixture of $^4\text{He}:\text{O}_2$ (4:1) at 60 BPM with I:E=1:2 at a $\text{TV}=\frac{3}{4}\text{FRC}$ as measured with a rodent plethysmography spirometry system. The PEEP was applied by immersing the SAV exhale line in a graduated water column. For imaging, rats were ventilated with five identical breaths of HP $^3\text{He}:\text{O}_2$ (4:1) followed by a 3-s breath-hold (Figure 2) during which ADC ^3He images were acquired using a double acquisition diffusion-weighted gradient echo imaging pulse sequence in a 50-cm bore 4.7-T MRI scanner (Varian, Inc.) equipped with 12-cm, 25-G/cm gradients and a 2-3/4"-ID quadrature 8-leg birdcage body coil (Stark Contrast). Imaging parameters were as follows: diffusion time $\Delta=1\text{ms}$ along phase encoding direction; b -values = 0.00, 3.73, 2.18, 1.00 and 0.00 s/cm^2 ; FOV=6cm; ST=6mm; MS=64x64; $\alpha=5^\circ$. The PEEP value was varied between 0 (black) and 9 cm H_2O (red) with a timing sequence as shown in Figure 3 for three different studies.

RESULTS: Typical ADC maps and respective histograms before and after applying the PEEP maneuver are shown in Figure 3. Study I was performed after keeping the rat ventilated in supine position for more than two hours before acquiring the first image. The ADC value observed at the beginning of the session (0.20 cm^2/s) was large compared to the post-maneuver ADC value (0.15 cm^2/s). Study II, on the other hand, commenced after less than an hour of supine ventilation and shows a relatively lower ADC at the beginning of the session (0.17 cm^2/s). In Study I, the ADC-PEEP dependency after the recruitment maneuver was reproducible over multiple cycles; this reflects the volume-dependency of ADC as a result of alveolar enlargement. In Study II, after an initial recruitment maneuver at steady PEEP=9 cm H_2O , the rat remained ventilated at zero PEEP for more than 90 minutes, and intermittent acquisitions were performed which depicted a slow and steady increase of ADC up to a value close to the initial ADC value in Study I (0.19 cm^2/s). Further application of high PEEP subsequently resulted in a decline in ADC value approaching the post-recruitment value from the beginning of the experiment. This behavior was also partially observed in Study I with shorter time delay between each repeated cycle.

DISCUSSION AND CONCLUSION: Preliminary results show the potential of HP gas diffusion MRI as a non-invasive technique for quantitative assessment of alveolar recruitment and expansion. Studies in healthy rats show an apparently larger pre-PEEP ADC value compared to the post-PEEP value under ventilation with the same tidal volume. This can be interpreted as the slow accumulation of collapsed alveoli due to maintaining the supine posture for long periods of time. Further studies will be necessary to assess the effect of different recruitment maneuvers and postures on ADC values. Application should be focused on animal models of alveolar collapse (e.g. ARDS models). More accurate analysis of alveolar dynamics will require study of ADC regional heterogeneity, preferably over the entire lung with the aid of a 3D imaging sequence. Furthermore, the coupled expansion (i.e. variable volume) and collapse (i.e. binary closure) of alveoli will require more specific experimental design to isolate or minimize the effect of either factor on the other. Finally, the observations must be cross-validated with other techniques, such as high resolution CT as currently utilized in clinical studies.

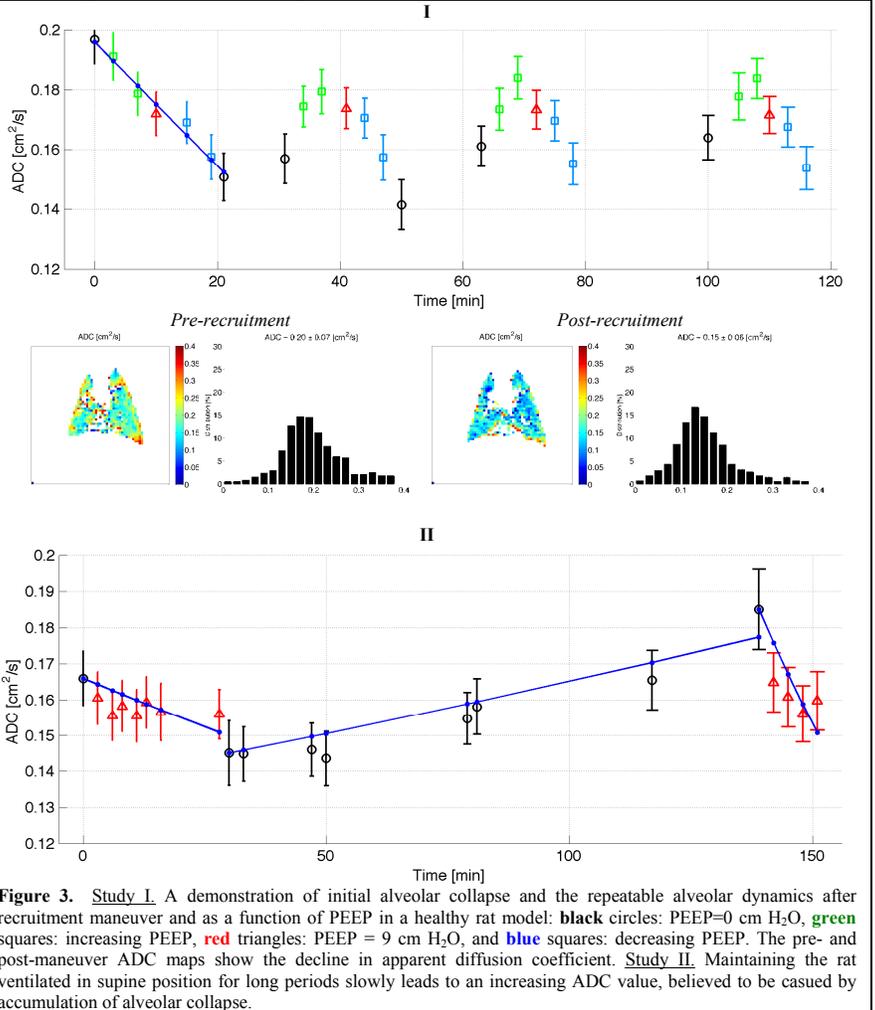
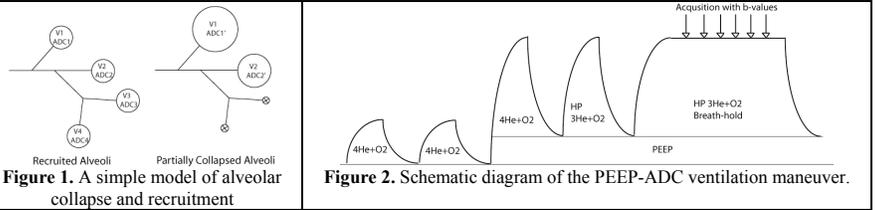


Figure 3. Study I. A demonstration of initial alveolar collapse and the repeatable alveolar dynamics after recruitment maneuver and as a function of PEEP in a healthy rat model: black circles: PEEP=0 cm H_2O , green squares: increasing PEEP, red triangles: PEEP = 9 cm H_2O , and blue squares: decreasing PEEP. The pre- and post-maneuver ADC maps show the decline in apparent diffusion coefficient. Study II. Maintaining the rat ventilated in supine position for long periods slowly leads to an increasing ADC value, believed to be caused by accumulation of alveolar collapse.