Alveolar Gas Diffusion MRI as a Function of Pulmonary Pressure

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INTRODUCTION: Acute Respiratory Distress Syndrome (ARDS) is a critical lung disorder characterized by 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. Alveolar recruitment maneuvers with varying and fixed positive end-expiratory pressure (PEEP) values have been devised to recruit collapsed alveoli and keep them open with the aid of mechanical ventilation. However the optimal strategy for the alveolar recruitment strategy is still uncertain. Various combinations of high/low tidal volume (TV) and higher-than-normal PEEP maneuvers have been proposed with different and sometimes contradictory results in terms of survival rate. Hyperpolarized (HP) gas MRI has the potential to noninvasively and quantitatively measure the dynamics of alveolar expansion and recruitment and assess the efficacy of the PEEP maneuvers to gain better understanding in this area of lung research.

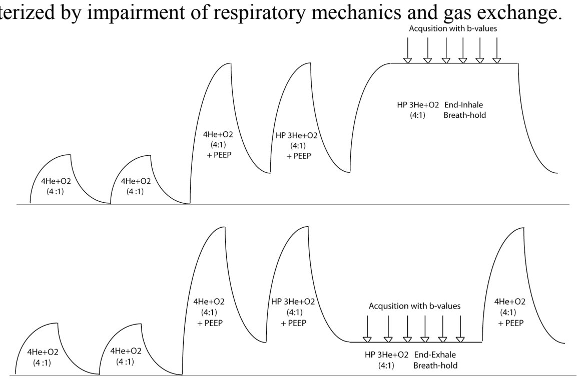

Figure 1. Schematic diagram of the PEEP-ADC ventilation maneuver with (TOP) end-inhale and (BOTTOM) end-exhale breath-hold.

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 ±100µL/breath and real-time monitoring of peak inspiration pressure (PIP). The rats breathed a mixture of ^{4}He:O_2 (4:1) at 60 BPM with I:E=1:2 at a TV=¾FRC as measured with a rodent plethysmography spirometry system. The PEEP was applied by submerging the SAV exhale line in a graduated water column. For imaging, rats were ventilated with five identical breaths of HP ^{3}He:O_2 (4:1) followed by a 3-s breath-hold – either at end-inhale (EI) or end-exhale (EE) – during which ADC ^{3}He images (**Figure 2**) 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 following: diffusion time Δ=1ms 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=64×64 and α=5°. The PEEP value was varied between 0 (black) and 12 cm H_2O (red) as shown in **Figure 3**.

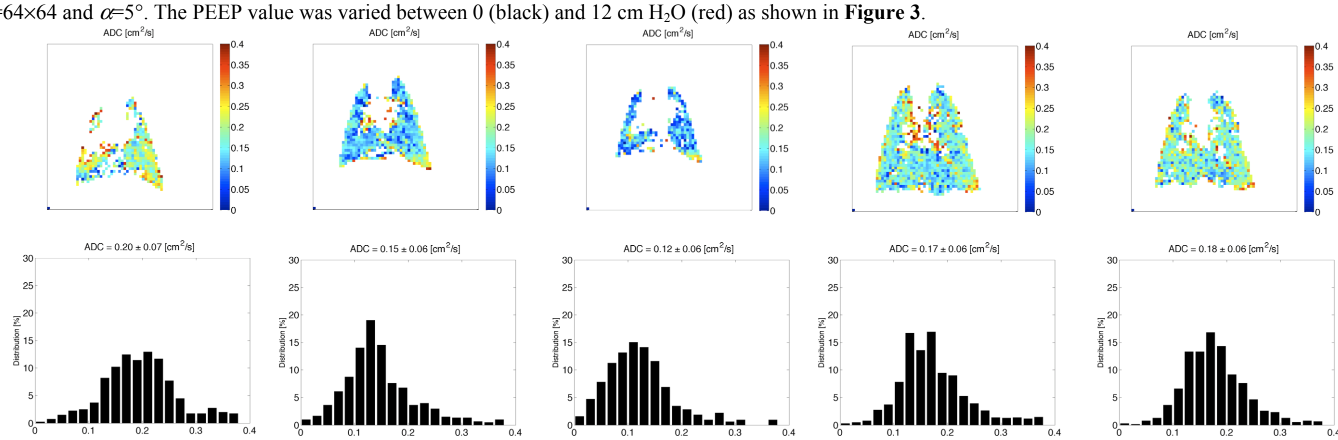

Figure 2. ADC maps and histograms for **(a)** pre-PEEP-maenuver, **(b)** EI no PEEP, **(c)** EE no PEEP, **(d)** EI PEEP=12cmH_2O, and **(e)** EE PEEP=12cmH_2O. The apparent difference in lung size for EI and EE, as well as no PEEP and large PEEP visible.

RESULTS: Representative ADC maps and respective histograms at EI and EE for zero PEEP and maximum PEEP (12 cm H_2O) are shown in **Figure 2**. Also shown is the initial ADC map prior to performing the recruitment maneuver. The high ADC value (0.20 cm^2/s) is believed to be due to groups of initially collapsed alveoli accumulated during the long duration that the rat was in the supine position (over 2 hours) prior to imaging (this is discussed in more detail in a separately submitted abstract). Beyond this initial phase, the EI and EE ADC values behave in a similar fashion with higher DC corresponding to higher PEEP as shown in **Figure 3**. However, for any given PEEP value the corresponding EI ADC is larger than EE ADC which confirms the over-inflation (in addition to the already expanded lung) associated with tidal volume.

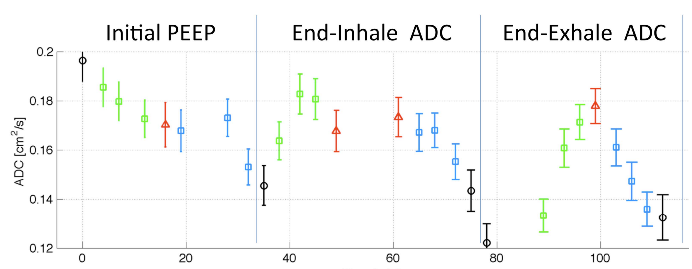

Figure 3. Summary of ADC measurements as a function of PEEP value for the initial recruitment maneuver followed by end-inahle and end-exhale PEEP maneuvers in a healthy rat model: **black** circles: PEEP=0cmH_2O, **green** squares: increasing PEEP, **red** triangles: PEEP=12cmH_2O, and **blue** squares: decreasing PEEP.

DISCUSSION AND CONCLUSION: Earlier work by our group demonstrated that at no PEEP, the ADC value increases proportionally to the breath size, depicting the mere over-inflation of alveoli. In this study the tidal volume was held constant to isolate the effect of PEEP on alveolar expansion. Initially the studies were performed using air as the normal ventilation gas between each imaging breath-hold. This proved to introduce a systematic artifact in the ADC measurements due to the varying quantity of residual volume for each PEEP value, which in turn resulted in a substantially different gas concentration after mixing ^{3}He with air in residual capacity. Therefore ^{4}He:O_2 mixture was used for normal ventilation of rats instead of air to eliminate this problem. Current results show the potential of HP gas diffusion MRI as a non-invasive technique for quantitative assessment of alveolar inflation as a function of residual volume. Further studies will be necessary to assess the effect of different recruitment maneuvers and animal posture. More accurate analysis of alveolar dynamics will require study of ADC regional heterogeneity (instead of only mean values), and preferably over the entire lung using a 3D imaging sequence. Furthermore, the challenge associated with the coupled dynamics of alveolar expansion (i.e. variable volume) and alveolar collapse (i.e. binary closure) is a major task that requiring dedicated research.