EFFECT OF PULMONARY HYSTERESIS ON AIRSPACE DIMENSIONS DURING POSITIVE END EXPIRATORY PRESSURE TRIALS IN MECHANICALLY VENTILATED RATS USING HYPERPOLARIZED GAS DIFFUSION MRI

Maurizio Cereda[1], Yi Xin[2], Kiarash Emami[2], Jessie Huang[2], Jennia Rajaei[2], Harrilla Profka[2], Biao Han[2], Puttisarn Mongkolwisetwara[2], Stephen Kadlececk[2], Nicholas Kuzma[2], Stephen Pickup[2], Brian Kavanagh[3], Clifford Deutschman[1], and Rahim Rizi[2]

[1]Department of Anesthesiology and Critical Care, University of Pennsylvania, Philadelphia, Pennsylvania, United States, [2]Department of Radiology, University of Pennsylvania, Philadelphia, PA, United States, [3]Departments of Critical Care Medicine and Anesthesia, Hospital for Sick Children, University of Toronto, Toronto, Ontario, Canada

INTRODUCTION: Pulmonary hysteresis is an energy dissipation mechanism characterized by higher lung volumes and lower transpulmonary pressures during deflation, as compared to inflation. This phenomenon may explain why positive end expiratory pressure (PEEP) has better physiological effects when applied along a deflation ramp and could be advantageously used to minimize airspace stress. However, the contribution of the peripheral airspaces to overall lung hysteresis is poorly understood. Previous studies provided conflicting evidence regarding changes in airspace dimensions and the role of alveolar recruitment vs. inflation during hysteresis. We explored changes in airspace dimensions due to hysteresis using hyperpolarized gas magnetic resonance imaging (HP-MRI) during mechanical ventilation.

METHODS: Healthy, male Sprague-Dawley rats (n = 15, 400±50 g) were anesthetized, transorally intubated, and ventilated in the supine position with room air and the following initial ventilator settings: V_T=10 mL/kg, PEEP 0 cmH_2O, rate 53 min^{-1}. To standardize lung recruitment history, an alveolar recruitment maneuver was performed prior to the first image acquisition. This maneuver was necessary to attenuate the confounding effect of atelectasis on MRI measurements, as shown in a previous study [1]. Ten animals underwent HP-MRI, and the apparent diffusion coefficient (ADC) values of ^{3}He were measured during ascending and descending PEEP trials (Figure 1A). After performing the baseline measurements, PEEP was increased from 0 to 9 cmH_2O in 3 cmH_2O increments and returned to baseline in a similar fashion. ADC was obtained using a 4.7-T MRI scanner (Varian Inc., Palo Alto, CA) during inspiratory holds at the end of each PEEP period and after ventilation with a 1:4 oxygen in ^{3}He mixture. A diffusion-weighted gradient echo pulse sequence was applied along the phase-encoding (L–R) direction with the following timing parameters: Δ=1ms, δ=200μs, and τ=180μs. Images were acquired in a transverse slice right below the heart with the following imaging parameters: FOV=6×6cm^2, ST=10mm, MS=64×64, α=4~5°, TR=6.6ms, and TE=4ms. For each image, mean ADC values were obtained. In a separate group of five rats undergoing a similar protocol, we used computed tomography (CT) to quantify end-inspiratory lung gas volume (EILV) from three-dimensional whole-lung reconstructions (Figure 1B) using a density analysis of gas content. CT analysis was also used to confirm the absence of atelectasis in this model, due to the successful performance of recruitment maneuvers prior to imaging procedures. In all animals, peak inspiratory pressure (PIP) and dynamic compliance (C_{dyn}) were measured.

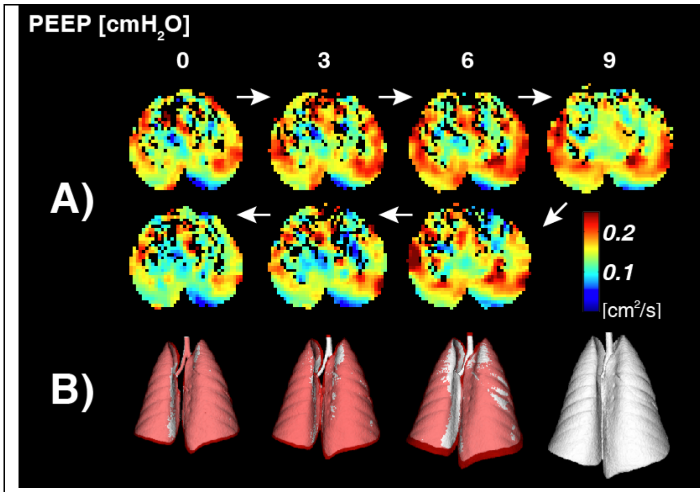

Figure 1. Representative MRI and CT images obtained during trials of ascending and descending PEEP: (A) ADC maps; (B) three-dimensional CT reconstructions (white: ascending PEEP, red: descending PEEP).

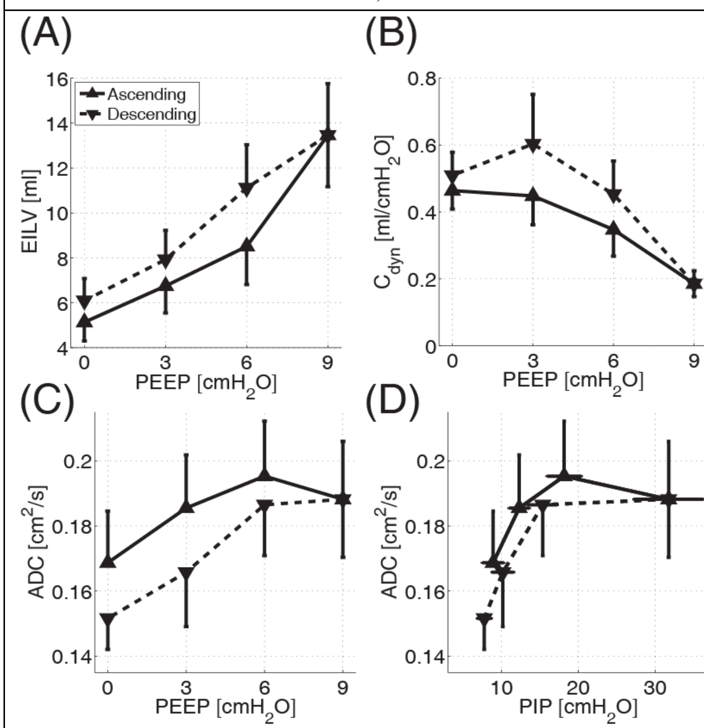

Figure 2. Group averages and SD for: (A) EILV vs. PEEP, (B) C_{dyn} vs. PEEP, C) ADC vs. PEEP, D) ADC vs. PIP.

RESULTS: Hysteresis was confirmed by the presence of larger lung volumes during descending vs. ascending ramps, as shown by the three-dimensional CT reconstructions in Figure 1 B. Quantitative analysis of lung CT density confirmed the increase in EILV ($p < 0.01$; Figure 2A) during descending vs. ascending PEEP ramps. These increases in lung volume were also associated with an improvement in lung mechanics, as documented by the larger C_{dyn} observed in the descending ramp ($p < 0.01$; Figure 2B). Hysteresis was associated with a smaller ADC value at given values of PEEP ($p < 0.01$; Figures 1A, 2C) and PIP (Figure 2D) during the descending vs. ascending ramps. This finding suggests that, despite larger lung volumes, hysteresis was associated with an increased number of ventilated airspaces and an overall decrease in their size. ADC showed a biphasic response to ascending PEEP, with a larger (15.8%) increase during initial inflation (PEEP 0-6 cmH_2O) followed by a smaller (3.6%; $p < 0.01$) decrease between PEEP 6-9 cmH_2O. This result is likely due to the reopening of newly recruited smaller airspaces, which is also suggested by others' results [2]. Both ADC and EILV values decreased monotonically during descending PEEP, suggesting homogenous airspace deflation in the absence of derecruitment.

CONCLUSIONS: The mechanisms of lung inflation, deflation, and hysteresis continue to be unclear despite decades of anatomical and physiological research. Our study provides insight on the mechanisms of lung volume changes during hysteresis in healthy subjects. We provide *in vivo* radiological evidence that, in the absence of atelectasis, pulmonary hysteresis in ventilated healthy rats is likely due to the recruitment of smaller airspaces during lung inflation. These airspaces remained open during descending PEEP. Thus, setting PEEP along a descending ramp may decrease airspace dimensions and, in doing so, may also attenuate the propensity to lung injury.

REFERENCES: [1] Cereda et al., *J. Appl. Physiol.* 110, 499-511 (2011); [2] Namati et al. *Am J Respir Cell Mol Biol,* 38, 572-8 (2008).