Positive End Expiratory Pressure (PEEP) and Surfactant Administration Decrease Airspace Dilatation in Ventilated Rats after Pulmonary Saline Lavage

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INTRODUCTION: Surfactant depletion causes atelectasis and predisposes subjects to ventilator associated lung injury (VALI). This phenomenon seems to be due to abnormalities in alveolar geometry and mechanics, including dilatation of residual ventilated airspaces. Alveolar recruitment attenuates VALI but the mechanisms of this effect are not entirely clear, which is partly due to the lack of adequate instruments to assess airspace geometry. We hypothesized that alveolar recruitment by surfactant administration (SA) and positive end expiratory pressure (PEEP) reduces airspace dilatation in ventilated rats with surfactant depletion caused by pulmonary saline lavage (SL). Airspace size was quantified as apparent diffusion coefficient (ADC) of ^{3}He, using hyperpolarized (HP) gas diffusion MRI.

METHODS: Healthy (n=6) male Sprague-Dawley rats were anesthetized, intubated, paralyzed and ventilated with constant tidal volume (V_T) of 10 ml/kg and respiratory rate of 60 BPM and underwent SL (30 ml/kg) three times, approximately 10 minutes apart. All animals then received SA (bovine lipid extract surfactant, 50 mg/kg). Imaging was performed at PEEP of 0 and 9 cmH_2O: a) at healthy baseline; b) after SL; c) after SA. ADC MRI was performed using a diffusion-weighted gradient echo pulse sequence in a 4.7-T MRI scanner equipped with a 12-cm, 25-G/cm gradients and a 2-3/4"-ID quadrature 8-leg birdcage body coil (Stark Contrast). Eight diffusion-weighted images were acquired with centric phase-encoding, and interleaved acquisition through b-values = 0, 6, 5, 4, 3, 2, 1, 0 s/cm^2. FOV=6×6cm^2, ST=6mm, MS=64×64, TR=4.5ms, and TE=3.3. Diffusion sensitizing gradient was applied along the phase-encoding (L–R) direction with the following timing parameters: Δ=1ms, δ=200μs, and τ=180μs. Spin density maps were acquired using a gradient echo pulse sequence with TR=3.2ms, TE=1.6ms, and MS=128×128 (other parameters as above). Each image was obtained during an inspiratory hold at the end of each PEEP period and after ventilation with 1:4 O_2 in ^{3}He. Mean ADC values were obtained from maps of coronal slices. Three additional animals underwent computed tomography (CT) scans (ImTek MicroCAT II) under a ventilation maneuver similar to HP ^{3}He MRI protocol described above. Density images were obtained for comparison to the corresponding HP ^{3}He ADC images, with the following imaging parameters: 500 µA, 80 kVp, exposure time = 400 ms, 360 projections around the animal, transverse FOV=4×4 cm^2, MS=512×512, NS=768. To avoid blurring due to respiratory motion, only one view per breath was acquired during each mechanically-gated breath-hold. This resulted in a whole lung acquisition time of approximately 11 minutes per PEEP level.

RESULTS: ADC values (mean±SD) for each condition are shown in **Table 1**. CT scans and ADC maps from two representative animals are shown in **Figures 1** and **2**, respectively. SL caused atelectasis, documented by widespread increase in CT densities, and airspace dilatation, detected by an increase in ADC (+37.8%). As shown in **Figure 2**, the overall lower SNR of the post-SL HP ^{3}He MR spin density images indicates a lower airspace fraction per lung tissue volume unit. At pre-SL baseline, PEEP caused lung inflation (**Figure 1**) and a significant increase in ADC value (**Figure 2**) due to volume expansion of ventilated airspaces. After SL, PEEP no longer increased ADC (–3.8%). SA caused a statistically significant but small decrease in ADC (–6.5%) at PEEP 0 cmH_2O. However, adding PEEP 9 cmH_2O after SA further decreased ADC (–9.0% vs. SA PEEP 0 cmH_2O), which reached healthy baseline values measured at the same PEEP. CT scans obtained in the same conditions detected markedly decreased CT opacities, suggesting alveolar recruitment, only when SA and PEEP were applied at the same time.

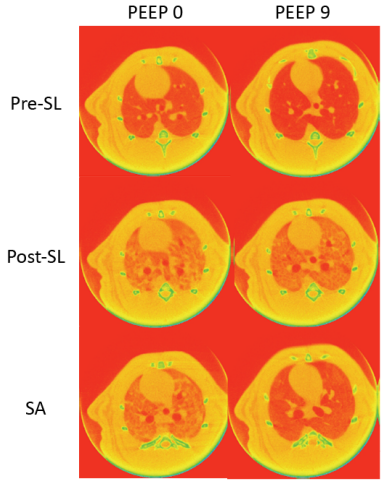

Figure 1. Representative CT images at PEEP 0 and 9 cmH_2O in three experimental stages

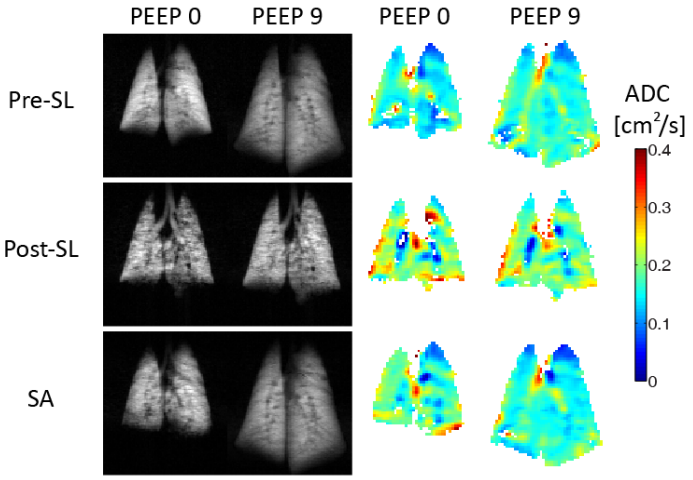

Figure 2. Representative spin density maps and ADC images at PEEP 0 and 9 cmH_2O in three experimental stages

	Mean ± SD ADC values (cm^2/s)	
	PEEP 0 cmH_2O	PEEP 9 cmH_2O
Healthy Baseline	0.156 ± 0.010	0.186 ± 0.014 *
Saline Lavage	0.215 ± 0.013 #	0.207 ± 0.010
Surfactant Administration	0.201 ± 0.019 #	0.183 ± 0.015 *

* p<0.001 vs. PEEP 0; # p < 0.001 vs. Healthy Baseline

Table 1. ADC values of low and high PEEP in three stages

CONCLUSION: The presented results confirm that surfactant depletion by SL causes widespread atelectasis and simultaneous dilatation of residual ventilated airspaces. This effect is likely conductive to VALI, as shown in animal studies, and is difficult to identify using conventional radiological and physiological instruments. HP MRI enables to detect pathological airspace dilatation caused by atelectasis and to assess the effects of therapeutic strategies. In fact, PEEP and SA synergistically recruited atelectatic lung and decreased ADC, documenting a reduction of airspace dilatation. This effect is likely beneficial, as shown by animal studies. HP MRI could have a role in the identification of optimal ventilatory strategies, with the aim of protecting the lungs from VALI.