Imaging of Lung Micromechanics with Hyperpolarized Gas Diffusion MRI: Regional Compliance

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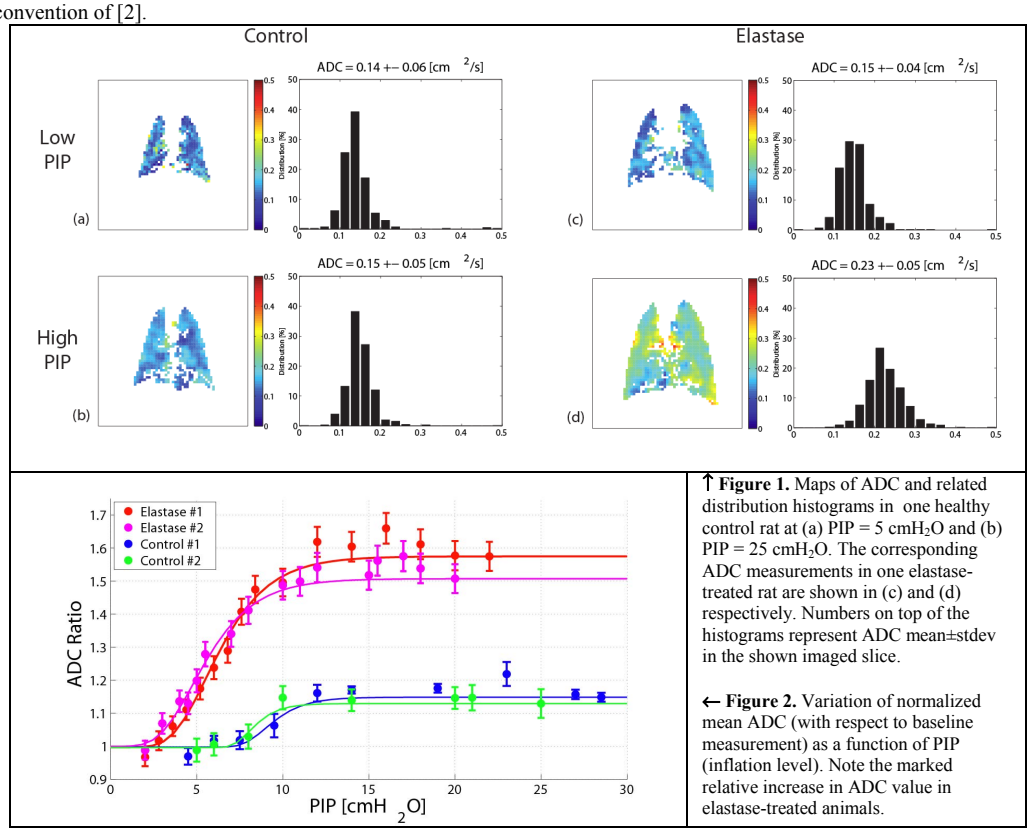
INTRODUCTION: Emphysema is characterized by abnormal enlargement of lung components distal to the terminal bronchioles and is accompanied by alveolar wall destruction and tissue density loss. Changes in micromechanical properties of lung tissue lead to an increase in regional compliance and a decrease in elastic recoil. This regional information can assist in studying formation and progression of emphysema. However, at this point there is no technique that is non-invasive and sensitive enough to acquire regional lung compliance information either in clinic or in research. In this study we assess the sensitivity of hyperpolarized (HP) gas diffusion MRI as a noninvasive and regional metric of alveolar expansion. The long-term objective of this project is to use regional apparent diffusion coefficient (ADC) of HP gas for longitudinal assessment of regional changes in compliance and pulmonary microstructure.

METHODS: Healthy and elastase-induced Sprague-Dawley rats (n=2 in each cohort, body weight (BW)=250±50g) were utilized in this study. Emphysema was induced through a single intratracheal instillation of 22U/100g of porcine pancreatic elastase, and animals were studied approximately 3 months after the model induction. For imaging, the rats were anesthetized, intubated, temporarily paralyzed, and mechanically ventilated by a custom small-animal MR-compatible ventilator with a delivery accuracy of ±100μL/breath. Rats were breathing a mixture of $^4He:O_2$ (4:1) at 60 BPM and I:E=1:2, at a nominal V_T=¾FRC as measured with a rodent plethysmography system. The animal's peak inspiratory pressure (PIP) was continuously monitored and recorded by a high-precision MR-compatible optical pressure transducer (Samba Sensors AB). Before starting the imaging, the rats underwent an alveolar recruitment maneuver using a stepwise sequence of positive end-expiratory pressure (PEEP) levels (as discussed in Cereda, M. *et al.* in this conference) to minimize the effect of atelectasis on ADC measurements. For ADC imaging, the lung inflation level was controlled by varying the inhalation time at a fixed inspiratory flow rate, corresponding to PIP levels ranging from 3 to 30 cmH_2O. Rats were ventilated with five identical breaths of HP $^3He:O_2$ (4:1) gas mixture at the designated inflation level followed by a 3-sec breath-hold during which five diffusion-weighted images were acquired corresponding to b-values = 0.00, 3.73, 2.18, 1.00 and 0.00 s/cm^2. This procedure was repeated immediately with identical but reversed polarity diffusion gradient b-values. These 10 diffusion-weighted images were then combined to yield the ADC map of the imaged slice according to a double-acquisition diffusion imaging scheme described earlier [1]. Images were acquired using a diffusion-weighted gradient echo imaging pulse sequence with centric phase-encoding in a 50-cm bore 4.7-T MRI scanner (Varian Inc) equipped with a 12-cm, 25-G/cm gradients and a 2.75"-ID quadrature 8-leg birdcage body coil (Stark Contrast). Images were acquired in the middle coronal slice of the rat lung with the following imaging parameters: FOV=6×6cm^2, ST=6mm, MS=64×64, α=4~5°, TR=6.6ms, and TE=4ms. Diffusion sensitizing gradient was applied along the phase-encoding (L–R) direction with the following timing parameters: Δ=1ms, δ=200μs, and τ=180μs according to the naming convention of [2].

RESULTS: ADC maps and frequency distribution histograms for one rat from each group are shown in **Figure 1** corresponding to a representative low and high PIP value. Apart from the apparent enlargement of lung size at the higher inflation level, a systematic difference between elastase-induced and healthy animals was observed. In addition to exhibiting a somewhat higher ADC value at baseline (0.13± 0.06 cm^2/s vs. 0.15±0.04 cm^2/s, corresponding to elastase-induced lung tissue damage [3]), emphysematous lungs show a much larger relative increase in ADC value for the same change in inflation level. In addition, the ADC distribution in the imaged slice became much broader for higher inflation levels. **Figure 2** summarizes the results for all four animals by showing the relative change in the mean ADC value as a function of PIP. The ADC values were normalized with respect to the baseline ADC measurement for intersubject comparison. The larger relative change in normalized ADC in elastase-treated lungs is likely an indication of the elevated compliance of lung tissue in these animals compared to healthy controls. Notably, in all animals the normalized ADC values reach a plateau at or around PIP=12 cmH_2O. The effect of elastase treatment is minimally apparent in the ADC values at low PIP levels (with values ranging between 0.14 and 0.15 cm^2/s), but it is clearly manifested at higher inflation levels (plateau ADC values are more than 50% above the baseline values in elastase-treated animals, compared to healthy controls at less than 20% above their baseline values).



↑ **Figure 1.** Maps of ADC and related distribution histograms in one healthy control rat at (a) PIP = 5 cmH_2O and (b) PIP = 25 cmH_2O. The corresponding ADC measurements in one elastase-treated rat are shown in (c) and (d) respectively. Numbers on top of the histograms represent ADC mean±stdev in the shown imaged slice.

← **Figure 2.** Variation of normalized mean ADC (with respect to baseline measurement) as a function of PIP (inflation level). Note the marked relative increase in ADC value in elastase-treated animals.

CONCLUSION: Preliminary results of ^3He ADC measurements as a function of inflation level in healthy and elastase-treated rats show that differential ADC measurements are a more sensitive marker to alterations in lung tissue mechanics and can be potentially used to derive regional information about lung tissue compliance. Modifications of HP gas diffusion MRI protocols of this type can potentially provide more information about airway size and mechanics compared to static single-point ADC measurements, and should motivate wider adoption of these methods for non-invasive investigational and diagnostic applications. Further investigations of these phenomena in larger samples and correlating them with well-established global lung measurements are required and are subject of the ongoing research.

REFERENCES: [1] Emami, K, *et al.* Proc Intl Soc Mag Reson Med 2007; [2] Yu, J, *et al.* J Magn Res Imag2007; [3] Emami, K, *et al.* J Appl Physiol 2010.