Quantitative Measurement of Regional Lung Compliance in Rat Model Using Polarized Gas MRI

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Introduction: Static compliance is a measure of lung elasticity and is defined as the change in volume of the lung per unit change in pressure. Various pathologies are known to produce changes in the static lung compliance. For example, emphysema, which is characterized by the loss of connective tissue components in the lung, produces an increase in the static lung compliance; pulmonary fibrosis with its increased interstitial connective tissue causes a decrease in lung compliance. Some surgeons believe that regional maps of lung compliance will be the most sensitive predictor of response to lung volume reduction surgery. A technique capable of measuring static lung compliance in small rodents is of particular value because of our increasing dependence on molecular and genetic methods, many of which are applicable only to small rodent systems, for studying pulmonary disease. Our method is based on calculating the airspace lung volume at the end of inspiration by measuring the build-up of magnetization after successive HP ^{3}He breaths. These measurements can be used to normalize regional measures of fractional ventilation and thus determine regional changes in lung volume induced by inspiration. Combining these results with pressure measurements gives the desired regional compliance. The accuracy of this technique can be determined by comparing summed local airspace volumes with those determined by pulmonary function testing.

Method: Experiments were conducted in accordance to an IACAC approved protocol. 450 g ± 75 g, male Sprague-Dawley rats were intubated and maintained on interperitoneal xylazine, pancuronium, and ketamine anesthesia; the rats were ventilated using a MRI compatible ventilator (Amersham Health, Durham, NC). Imaging was performed on a small-bore 4.7 T animal magnet (Varian Inc.) using a birdcage coil. The hyperpolarized ^{3}He was generated via the spin-exchange optical pumping method with the use of a commercial polarizer (Amersham Health, Durham, NC). Fractional ventilation was determined using the method introduced by Deninger [1]. The number of Helium breaths ranged from one to twenty-five with a tidal volume between 2.5 and 3.6 ml. The helium images were obtained using the following imaging parameters: T_E: 3.3 ms, T_R: 10 ms, FOV: 6 cm, Slice thickness: 4 mm, Flip angle 10°, Matrix size: 128x128. Flip angle calibrations were performed using a double pulse technique with minimal interscan times. Pulmonary function testing was performed prior to each imaging experiment to assist with image normalization. Airspace volume maps were created by comparing the regional, corrected, saturation value of the ^{3}He signal in the limit of a large number of breaths to a reference volume in the trachea. These maps were combined algebraically with the fractional ventilation maps and measured airway pressure to yield the compliance maps of figure 1.

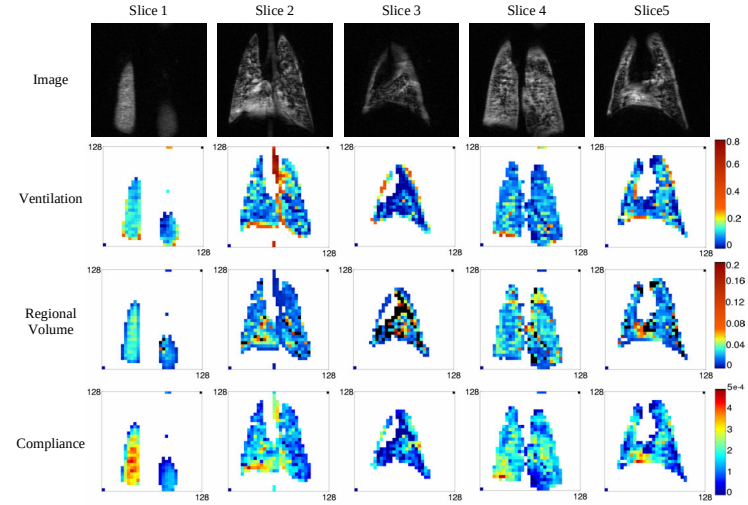

Figure 1. The first, second, third, and fourth rows represent, HP ^{3}He MR images, fractional ventilation, regional airway volume, and regional compliance maps respectively. The columns denote different lung slices. Back pixels represent regions where insufficient signal to noise was present to analyze data. Note that fractional ventilation, regional lung volumes, and compliance maps are relatively uniform, since this is a normal lung. Their distributions are different; however, since each is dependent on different physiologic parameters; these differences illustrate uniqueness of the different contrast mechanisms for studying lung disease. Regional volumes in units of ml. Compliance in units of ml per cm of H_2O.

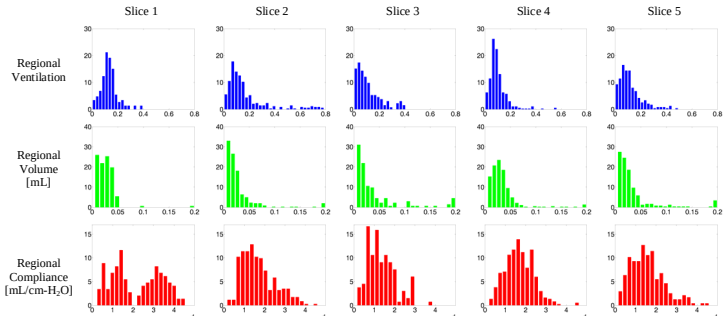

Figure 2. Histograms of fractional ventilation (first row), regional lung volumes (second row), and regional compliance (third row). The columns as in Figure 1. Changes in lung volumes are presented in units of ml. Compliance is in units of ml/cm of water. Again note how the distribution differ due to the unique contrast mechanism of each measurement.

Results and Discussion: Sample results are depicted in figures 1 and 2. Note that the ^{3}He images and fractional ventilation maps are relatively homogenous through the lung fields. Maps of expiratory airspace lung volumes are shown in row 3 of figure 1. Compliance maps, while also appearing relatively homogenous, demonstrate a position dependent distribution unique from fractional ventilation. We note that maps of regional changes in lung volume induced by respiration, which are intimately related to regional ventilation, are linearly related to compliance maps and are therefore not shown. Histograms of the data are show in figure 2. In all cases, the measured changes in lung volume due to respiration sum to within 10% of tidal volume: suggesting that compliance measures are highly accurate.

Conclusion: It is possible to accurately measure regional changes in lung volume induced by ventilation. These values can be used to calculate regional static compliance maps in small rodents. These maps are qualitatively different from fractional ventilation maps, suggesting that they provide a new contrast mechanism for studying, monitoring, and detecting diseases that affect pulmonary mechanics such as emphysema.

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References: 1) Deninger, A.J., et.al., Magn Reson Med. 2002 Aug;48(2):223-32.