Hyperpolarized 3He MRI Apparent Diffusion Coefficients to derive Non-invasive Lung Pressure-volume Curves

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Introduction: Pressure-volume curves (PV-curves) of the lung reflect the global static mechanical properties of the respiratory system and yield information such as lung compliance, total lung capacity, and lung elasticity. Typically, PV-curves are generated experimentally in vivo by measuring transpulmonary pressure at various lung volumes while the patient is sedated and a volume of gas is administered to inflate the lung; transpulmonary pressure is measured by taking the difference between the esophageal pressure (as a surrogate of pleural pressure) and airway pressure, with the esophageal pressure itself measured using a balloon or water-filled catheter inserted into the mid-esophagus. The procedure is somewhat invasive and uncomfortable, and as such, it is generally only performed on patients already mechanically ventilated which limits the use of PV-curves in other patients. A non-invasive method of generating the same information in a wider variety of patients would be of great value. Accordingly, we propose to noninvasively generate PV-curves in patients using experimentally-derived hyperpolarized ^{3}He magnetic resonance imaging (MRI) apparent diffusion coefficients (ADC). Experimental ADC values are used to derive alveolar/acinar size (1) and using established mathematical models of the lung (2) transpulmonary pressure at various volumes is derived and PV-curves can be generated.

Methods and Theory: An established mathematical model of the lung (2) is based on parameters such as alveolar expansion, lung volume, lung compliance, surface tension and alveolar size is described in equation 1 where γ is the surface tension of the alveoli, S is the surface area of the alveoli, V is the volume of the alveoli, n is the number of duct fibers surrounding the duct, F(l) is the force-length function of the duct fibers in the duct, N is the number of alveolar fibers, L is the length of the fibers surrounding the alveoli, and F(L) is the force-length function of the fibers in the alveoli.

$$P_{tp} = \underbrace{\frac{2}{3}\gamma(S_{alveoli})\frac{S_{alveoli}}{V_{alveoli}}}_{SurfaceTension} + \underbrace{\frac{1}{3V_{lung}}nF(l)l + \frac{1}{3V_{lung}}NF(L)L}_{TissueForces} \quad (1)$$

To derive the alveolar volume from experimentally obtained ^{3}He ADC values, we take advantage of the fact that the diffusion coefficient (D) of a gas undergoing Brownian motion can be expressed in terms of the distance traversed (D) during the diffusion time (t_d) by the Einstein-Smoluchoski equation (2) and the ADC can be described using the same relationship.

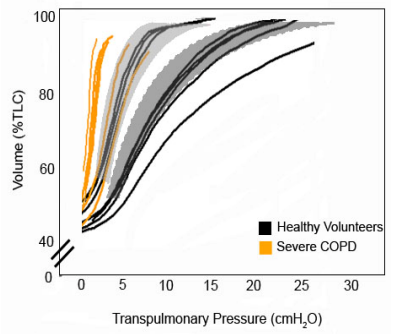
$$D = \frac{l^2}{2t_d} \quad (2)$$

$$\overline{D} = \frac{1}{3}D_L + \frac{2}{3}D_T \quad (3)$$

$$\frac{D_L}{D_T} = 3.0 \quad (4)$$

$$\gamma = 0.25V + 40 \quad (5)$$

$$F(L) = (\frac{L}{L_0} - 1)e^{\alpha(\frac{L}{L_0}-1)} \quad (6)$$



The diffusion of ^{3}He in the lungs is not unidirectional, but anisotropic and therefore the ADC acquired is an average diffusion average diffusion coefficient ($\overline{D}$) that is described in terms of two components of diffusion, the transverse (DT) and longitudinal (DL) diffusion coefficient (equation 3). The distribution and orientation of these airways and alveoli can be approximated by a single averaged distribution function with all alveolar structures assumed to have the same geometric parameters, and therefore the same transverse and longitudinal diffusion coefficients. Yablonskiy et al (1) have computed the DT and DL previously and showed that the relation between these two parameters as shown in equation 4. Combining Equations 2 and 3, and recognizing that $\overline{D}$ is equivalent to the ADC, we obtain can obtain an estimate of alveolar radius. Surface tension is a function of the surface area of the alveoli and also related to surface tissue surfactant. In this model we assume that surface tension is not altered in COPD and hence the same parameter is used for subjects with COPD and healthy volunteers. The relationship between surface tension in alveoli and the surface area of the alveoli has been modeled extensively in literature where a relationship between surface tension and lung volume was approximated (3) where γ is in dynes/cm, and V is lung volume as a percent of TLC. Normal values of surface tension range from 5-15 dynes/cm (4). In our model, the lung volume of each subject was calculated as the bottom of tidal volume plus 1 L of inhaled ^{3}He gas. The force-length relationship of fibers in the alveoli or the alveolar duct, (the two types of fibers contributing to the tissue forces) is described in equation 6. The length of the tension of the fibers is as shown in equation 6 where α is 4.65 dyne fits the force-length relationship data. L is the length of the fiber (in either the duct, or the alveoli), and LO is the un-stretched length of the fiber, which was approximated as the length of the fiber at RV. Using Weibel's model (5) of the microstructure in the lung, the $\frac{L}{L_0}$ can be approximated as $\frac{r}{r_0}$, where r is the radius of the alveoli. In this model, r_0 was approximated as the radius of the alveoli at RV, and RV was experimentally derived using plethysmography Equations 1, 5 and 6 provide a complete description of the model, where the dependent variables are the alveolar radius (derived from ADC measurements), total lung capacity and residual volume (plethysmography).

Results: Subject PV-curves are generated and shown with shaded light grey indicating experimental PV-curves previously measured in severe COPD, and shaded dark grey region for healthy volunteers, with our generated data in black (HV and orange (severe COPD). **Conclusions:** Transpulmonary pressure gradients can be modeled in subjects with COPD and healthy volunteers using alveolar size approximated by experimental ^{3}He ADC measurements.

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