Estimation of Rat Lung Surface to Volume Ratio and Xenon Diffusing Capacity Using Hyperpolarized ^{3}He and ^{129}Xe Gases

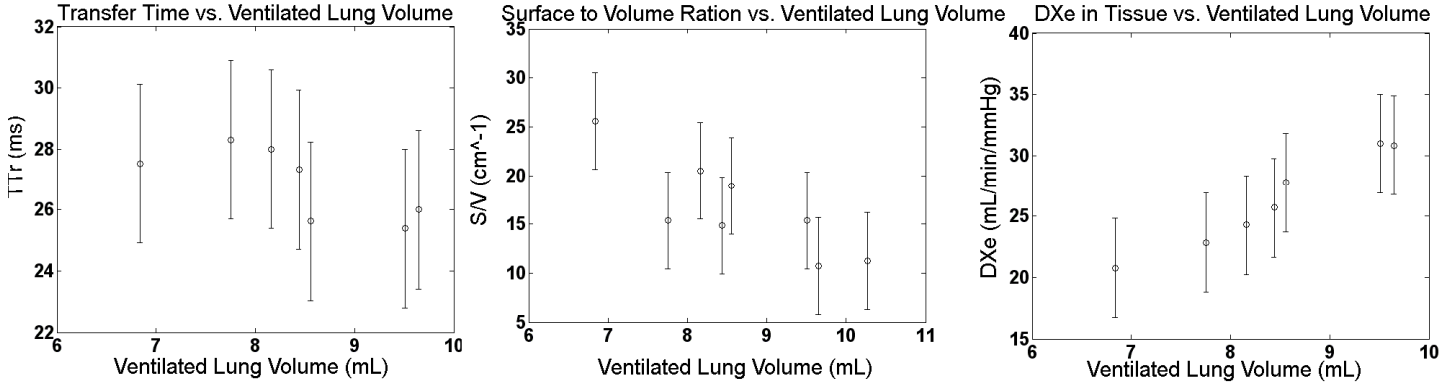
M. S. Fox[1,2], A. Ouriadov[1], W. Dominguez-Viqueira[1,3], M. Couch[1,2], and G. E. Santyr[1,3]

[1]Imaging, Robarts Research Institute, London, Ontario, Canada, [2]Physics and Astronomy Dept, University of Western Ontario, London, Ontario, Canada, [3]Medical Biophysics, University of Western Ontario, London, Ontario, Canada

Introduction: Hyperpolarized ^{129}Xe is a novel gaseous contrast agent which also dissolves in the lung parenchyma and blood compartments, offering an interesting palette of potential biomarkers of pulmonary disease. ^{129}Xe signals from the dissolved compartments have different chemical shifts and can be selectively saturated and allowed to recovery as a function of delay time as in the chemically selective saturation recovery (CSSR) technique [1,2] . CSSR has previously been used to study surface-to-volume ratio (S/V) as well as the diffusing capacity of xenon (D_{Xe}) in the lung which is analogous to diffusing capacity of carbon monoxide [3]. For S/V measurement, CSSR data are modeled at short delay times (< 1 s) whereas diffusing capacity is measured by modeling the CSSR data over the entire range of delay times. In this work, both S/V and D_{Xe} are measured in healthy rat lungs using ^{129}Xe CSSR over a complete range of delay times. The behavior of S/V and D_{Xe} is investigated as a function of ventilated lung volume in the rat lung by varying the lung pressure. Ventilated lung volumes (|VLV|) were measured using 3-D ^{3}He MR imaging under pressure-matched conditions.

Methods: Healthy male Sprague Dawley rats (418 ±14 g) were anesthetized, intubated orally, suture-sealed and ventilated using a custom ventilator (GEHC). Normal ventilation consisted of room air at a rate of 60 bpm, tracheal pressure ranging between 12-18cmH_2O and tidal volumes of 8mL/kg. Imaging was performed at 3 T (MR750, GEHC) using an insertable gradient coil having a maximum gradient strength of 50mT/m and two bird-cage RF coils tuned to the appropriate ^{129}Xe and ^{3}He frequencies (35.33MHz and 97.31MHz). Hyperpolarized ^{3}He was polarized to levels in excess of 40% using a turn-key polarizer (Helispin, GEHC). Hyperpolarized ^{129}Xe was polarized to levels of ~10% using a home-built continuous flow xenon polarizer incorporating a cryo-freeze bag collection method. ^{3}He imaging was performed using a 3DFGRE sequence with variable flip angles (VFA) for measurement of |VLV| [4]. Imaging parameters included: FOV of 5cm^2, 128x128x32 matrix size with a slice thickness of 1mm. Images were thresholded and segmented using seeded region growing (Microview, GEHC) and absolute ventilated volumes (|VLV|) were calculated using a partial-volume correction algorithm previously described [1]. Following ^{3}He imaging, ^{129}Xe CSSR was performed by changing RF coil and gas type in the ventilator reservoir. The CSSR technique used 14 delay times corresponding to 0.76, 6, 12, 21, 27, 36, 42, 51, 75, 201, 501, 1001, 2001, 3001 ms. |VLV| and CSSR data were both obtained in a single breath-hold interval at the same tracheal pressures (P_{tr}) ranging between 7 cmH_2O and 17 cmH_2O by adjusting the gas reservoir pressure. CSSR signals from the lung parenchyma were normalized to respective gas signals in each spectrum and the appropriate theoretical model was fitted to the data using a non-linear least squares algorithm to extract S/V [1] or D_{Xe} [3] respectively.

Results: We have measured |VLV|, DXe and S/V in three animals (n=3) between a range of ventilated volumes of 7 to 12mL.



Discussion: In Fig. 1 (left), the transfer time for xenon to diffuse into tissue remains approximately constant as is expected because the transfer time is related to the thickness as well as the solubility of xenon at the gas-tissue interface, both of which are not expected to depend on volume. Figs. 2 (middle) and 3 (right), indciate that both S/V and D_{Xe} exhibit a dependence on |VLV|. This is as expected for S/V, confirming an inverse relationship with increasing volume comparable to human findings [1].. D_{Xe} exhibited an increase with |VLV| perhaps not surprising since this measure is normalized by the ratio of alveolar volume to barometric pressure [1], the former not changing significantly since the changes in actual lung pressure are small. All of these trends were derived from data acquired using the CSSR technique at different delay times. This work underlies the importance of applying the desired theoretical model to the appropriate range of data at known lung pressure and volume to reveal different physiological parameters. For example, S/V may be useful for diseases that effect the alveolar surface area (e.g. emphysema), whereas D_{Xe} is affected by changes in the gas-tissue interface (e.g. barrier thickness) and is useful for characterizing inflammation and fibrosis [3]. In summary, surface area to volume ratio and xenon diffusing capacity both show a dependence on lung volume that must be considered when measuring and interpreting ^{129}Xe chemically selective saturation recovery data in vivo.

References: 1. Patz S. et al. Acad Radiol 2008; 15:713-727. 2. Mansson S. et al. Magnetic Resonance in Medicine 50:1170-1179 (2003). 3. Abdeen N. et al. Magnetic Resonance in Medicine 56:255-264 (2006). 4.Akhavan Sharif M.R. et al. NMR Biomed. 2009; 22: 1-9

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