What can multiple b-value ^{3}He MRI tell us about lung micro-structure in healthy elderly never-smokers?

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Target Audience: Scientists interested in multiple b-value diffusion-weighted imaging for pulmonary applications.

Purpose: Diffusion-weighted noble gas pulmonary MRI provides *in vivo* images with a contrast uniquely sensitive to molecular displacement at cellular and sub-cellular length scales. Using hyperpolarized gas diffusion MRI, local *in vivo* measurements of lung morphological and architectural parameters can be estimated. Previous studies have optimized the theoretical models for translating anisotropic diffusion measurements and evaluated the short and long-term reproducibility of this approach. We estimated the external airway radius (R) and internal airway radius (r) of the alveolar dimensions[1] to evaluate potential differences in acinar duct morphometries in healthy older never-smokers.

Methods: ***Subjects:*** Participants provided written informed consent to the study protocol approved by the local research ethics board and Health Canada. Healthy subjects (60-90 years of age) with ≤ 0.5 pack year smoking history and without acute or chronic respiratory disease were evaluated using hyperpolarized ^{3}He MRI, spirometry and plethysmography during a single visit.

Image Acquisition and Analysis: MRI was performed on a whole body 3T MRI system (MR750 Discovery, GEHC, Milwaukee, WI) with broadband imaging capability. All ^{3}He MRI employed a whole body gradient set with maximum gradient amplitude of 4.8 G/cm and a single-channel, rigid elliptical transmit/receive chest coil (RAPID Biomedical GmbH, Wuerzburg, Germany). The basis frequency of the coil was 97.3 MHz and excitation power was 2 kW using an AMT 3T90 RF power amplifier (GEHC). Subjects were positioned supine in the scanner and for both ^{1}H and ^{3}He MRI, subjects were instructed by a pulmonary function technologist to inhale a gas mixture from functional residual capacity (FRC), and image acquisition was performed under breath-hold conditions. The data for *in vivo* lung morphometry were acquired using a multi-slice 2D gradient echo diffusion weighted sequence with a matrix size of 128x128, across seven 30mm coronal slices (flip angle θ = 4°, TE = 1.2 ms, TR=4.7 ms, b = 0, 1.6, 3.2, 4.8, 6.4 s/cm^2); the diffusion-sensitization gradient pulse ramp up/down time = 500 μs with a diffusion time = 1460 μs and no gap between lobes. All 5 interleaved sets of images were acquired during a single breath-hold. As previously described[1], external (R) and internal (r) airway radii were computed from diffusion-weighted data on a pixel-by-pixel basis using a custom-built IDL 6.4 algorithm which searched for the global minimum to determine longitudinal (D_L) and transverse (D_T) diffusion coefficients. The free diffusion coefficient of ^{3}He gas in lung airspaces (D_0) was determined to be concentration-independent and assumed to be 0.84 cm^2/s.

Results: Table 1 shows demographic, pulmonary function, ADC and lung morphometry measurements for 40 older never-smokers. The acinar duct morphometry results were within the physiologically-valid range of parameters characteristic for healthy lungs[2]. MRI estimates of alveolar density (Na), mean linear intercept (Lm), R and alveolar sleeve depth (h) were not significantly correlated with diffusing capacity of the lung for carbon monoxide (DL_{CO}) which was normal for all subjects. Estimated values of R, r, Lm and Na for individual subjects were similar with low variance. Figure 1 shows relationships between airway morphometry with spirometry and ADC measurements. Both internal airway radii and mean linear intercept were significantly related to FEV_1/FVC (r^2=0.11, r^2=0.10 respectively) and ADC (r^2=0.31, r^2=0.32). External airway radii (r^2=0.12, p=.03) and Na (r^2=0.12, p=.03) were both significantly related to height.

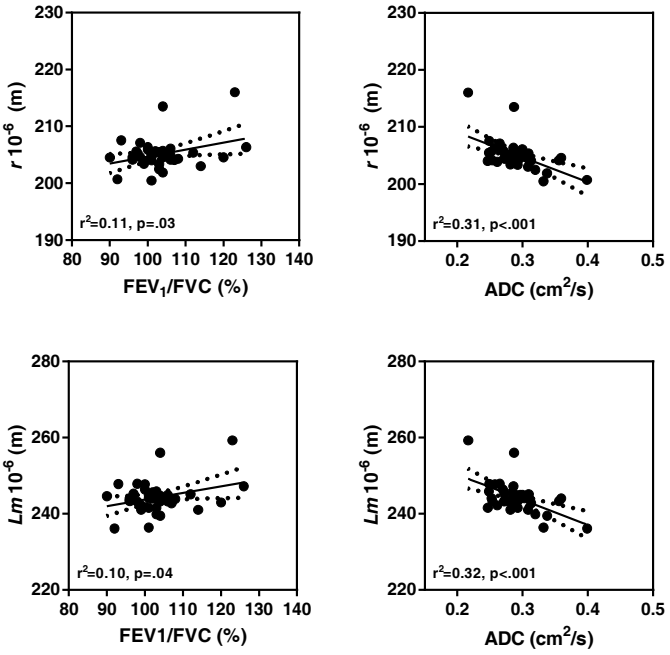

Figure 1. Relationship between airway morphometry (*r* and *Lm*), spirometry (FEV_1/FVC) and MRI (ADC) measurements

Table 1. Healthy Older never-smoker Measurements

Older Never-smokers (n=40)	
Parameter	Mean (SD)
Age (yrs)	73.2 (6)
Height (m)	1.7 (0.1)
FEV_1/FVC (%)	103.5 (7.3)
RV/TLC (%)	39.5 (7.1)
V_A (L)	5.5 (1.2)
D_{LCO} ($\%_{pred}$)	90.1 (15.8)
ADC (cm^2/s)	0.289 (0.03)
R 10^{-6} (m)	326.7 (3.5)
r 10^{-6} (m)	205.1 (2.7)
h 10^{-6} (m)	121.6 (4.3)
Lm 10^{-6} (m)	244.3 (4.0)
Na (m^{-3})	1.29E+10 (4.2E+8)
D_L (cm^2/s)	0.808 (0.16)
D_T (cm^2/s)	0.320 (0.07)

Discussion and Conclusions: Preliminary results show that MRI measurements of lung morphometry in healthy older never-smokers were elevated compared to previous results reported in younger never-smokers[3]. Such results are compatible with senile emphysematous changes to healthy parenchyma that accompanies aging.

References:

1 Sukstanskii, A. L. & Yablonskiy, D. A. In vivo lung morphometry with hyperpolarized 3He diffusion MRI: theoretical background. *J. Magn. Reson.* **190**, 200-210, doi:10.1016/j.jmr.2007.10.015 (2008).

2 Sukstanskii, A. L., Quirk, J. D. & Yablonskiy, D. A. Probing lung microstructure with hyperpolarized He gradient echo MRI. *NMR Biomed.*, doi:10.1002/nbm.3150 (2014).

3 Quirk, J. D., Chang, Y. V. & Yablonskiy, D. A. In vivo lung morphometry with hyperpolarized He diffusion MRI: Reproducibility and the role of diffusion-sensitizing gradient direction. *Magn. Reson. Med.*, doi:10.1002/mrm.25241 (2014).