# Age-Dependent Changes in Alveolar Microstructure of Healthy Adults by in vivo Lung Morphometry with Hyperpolarized 3He Diffusion MRI

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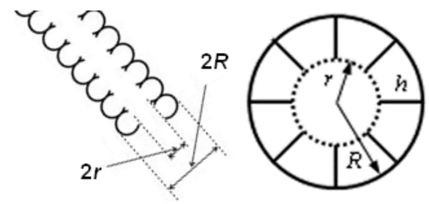
TARGET AUDIENCE: Researchers and clinicians interested in lung physiology and the effects of aging on pulmonary structure.

PURPOSE: Lung morphometry with hyperpolarized helium-3 MRI is a highly sensitive technique for the non-invasive measurement of alveolar microstructural parameters (1); including mean chord length (*Lm*), alveolar depth (*h*), acinar duct radius (*R*), alveolar density ($N_v$), and acinar lumen radius (*r*). It is based upon the Weibel model of the acinar duct geometry (2) (illustrated in the figure to the right). Pulmonary function in adults is known to decline with age (3), however the physical changes associated with this decline are poorly understood as conventional techniques are unable to non-invasively resolve acinar structure. Here we show that helium-3 lung morphometry overcomes these limitations, establishing a non-invasive age-dependent baseline of lung structural parameters in healthy subjects. As these same parameters are known to change with early emphysema (4), this baseline is also essential for detecting pathological changes.




METHODS: All subjects provided informed consent and procedures were performed with approval from the FDA and local IRB. 36 healthy never-smokers were recruited (age = 38±17, 17F/19M, 26 Caucasian/9 African American/1 Hispanic) for helium-3 MRI. Helium-3 gas was hyperpolarized using a Nycomed Amersham Imaging IGI.9600.He polarizer and axial diffusion $^3$He MRI images were acquired on a Siemens 1.5T Avanto or Sonata scanner with 7x7 mm$^2$ resolution over three 30-mm axial slices (flip angle θ=5.5°, TR/TE=13/8.3 ms, b=0-10 s/cm$^2$, diffusion time Δ=1.8 ms). Subjects inhaled 1 liter of a 40/60 mixture of hyperpolarized $^3$He gas in nitrogen from functional residual capacity and held their breath for nine seconds.

RESULTS: All helium lung morphometry parameters were found to depend significantly upon the age of the subject, but not upon race, sex, or MRI scanner used (ANOVA, α=0.05). The table below gives the average values and age dependence for each of the lung morphometry parameters. The figure below plots the age dependence for these parameters, including the 95% confidence intervals for the linear response model.

DISCUSSION: With increased age, there is a significant decrease in alveolar density ($N_v$, -5%/decade), driven by both an increase in acinar duct lumen (*r*, 8%/decade) and a decrease in the alveolar depth (*h*, -7%/decade). These changes are in the same direction but smaller in magnitude than those associated with the onset of early emphysema (4). The annual change in ADC measured here (calculated from all 6 b-values) is identical to previously published results (5).

CONCLUSION: This cross-sectional study provides insight into the changes in acinar structure as a result of aging in a healthy adult population and illustrates the importance of including an age-matched control population for observational studies. It also establishes a baseline of age-dependent lung parameters for use in future studies to detect pathologic changes.

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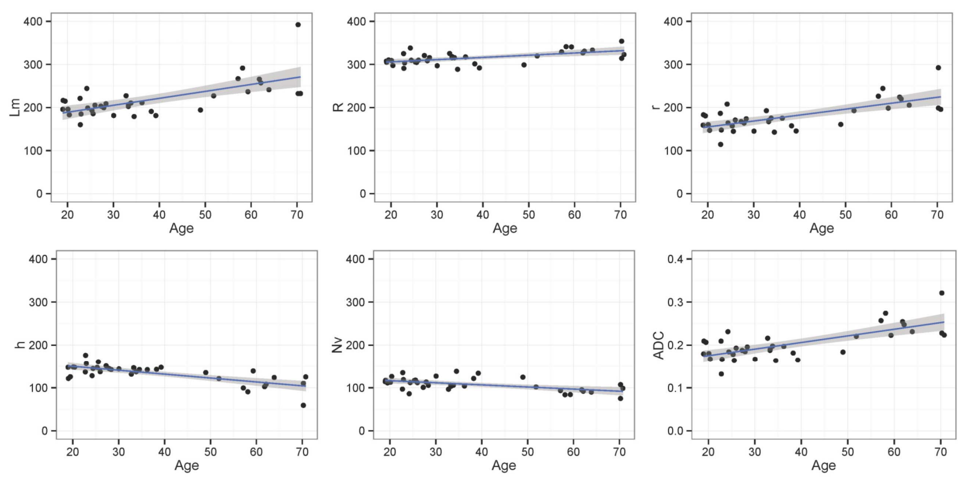
| Parameter | Mean | Annual Change |
|---|---|---|
| Lm (µm) | 218 | 1.6 |
| R (µm) | 316 | 0.5 |
| h (µm) | 135 | -0.9 |
| r (µm) | 179 | 1.4 |
| $N_v$ (cm$^{-3}$) | 107 | -0.5 |
| ADC (cm$^2$/sec) | 0.202 | 0.0015 |

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