Reproducibility and Diffusion Direction Dependence of Helium-3 Lung Morphometry

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TARGET AUDIENCE: Researchers interested in lung physiology and the sensitivity of clinical trials to detect pulmonary disease.

PURPOSE: Lung morphometry with hyperpolarized helium-3 MRI (1) is a highly sensitive technique for the non-invasive measurement of alveolar microstructural parameters including mean chord length (*Lm*), alveolar depth (*h*) and acinar duct radius (*R*). To use this technique in longitudinal studies and therapeutic trials, it is important to further establish its reproducibility.

METHODS: All subjects provided informed consent and procedures were performed with approval from the FDA and local IRB. Five healthy never-smokers were recruited (age = 31±19). Helium-3 gas was hyperpolarized using a Nycomed Amersham Imaging IGI.9600.He polarizer and axial gradient echo diffusion ^{3}He MRI images were acquired on a Siemens 1.5T Avanto 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.

Four subjects repeated helium imaging during the same imaging session with the diffusion gradient oriented along the readout (R-L) and slice selection (S-I) directions. In one subject, an additional diffusion measurement was acquired along the phase encoding direction (A-P). Two subjects repeated diffusion imaging along the readout direction twice in a single session and these subjects returned for longitudinal scanning at four months. An additional subject was rescanned after a 27 month delay.

RESULTS: No statistically significant effects from repeated measures (short or long term) or diffusion direction were detected for any of the measurements studied (ANOVA, all $p > 0.05$). The values of all lung morphometry parameters demonstrate a high degree of reproducibility both during different inhalations on the same day and four months apart. The figure below demonstrates the reproducibility of parameter maps over the short term (same day) and long term (four months), and for different diffusion gradient orientations (RO vs. SS). The average % coefficient of variation (%CV) for the diffusion direction and reproducibility scans over all subjects are given in the Table.

DISCUSSION: The mean lung morphometry measurements are highly reproducible across repeated scans. While there are subtle differences in the parameter maps, these effects are small, especially compared to early emphysematous changes (2), and most likely result from movement or variations in inflation levels between scans. Techniques to dynamically monitor breathing patterns during imaging could improve the reproducibility of the inflation level and therefore the parameter maps obtained. Slight differences in slice positioning are also to be expected for scans conducted in different months. Similarly, the consistency of the parameter estimates across different orientations of the diffusion gradient suggests that with our voxel size there is a minimal effect from possible anisotropic distribution of acinar duct directions and the presence of large conducting airways occupying approximately 5-10% of lung. The %CV of our helium lung morphometry measurements are consistent with prior studies of helium ADC reproducibility over the short term (3-5) and with different diffusion gradient orientations (6,7), suggesting similar reliability between methods.

CONCLUSION: This study demonstrates the reproducibility of helium-3 lung morphometry measurements and its independence on the diffusion gradient orientation. The latter is significant as it allows for a substantial reduction of imaging time – a measurement with only one gradient orientation direction is necessary and sufficient. Together, this provides confidence for the use of helium-3 lung morphometry for longitudinal studies and clinical trials.

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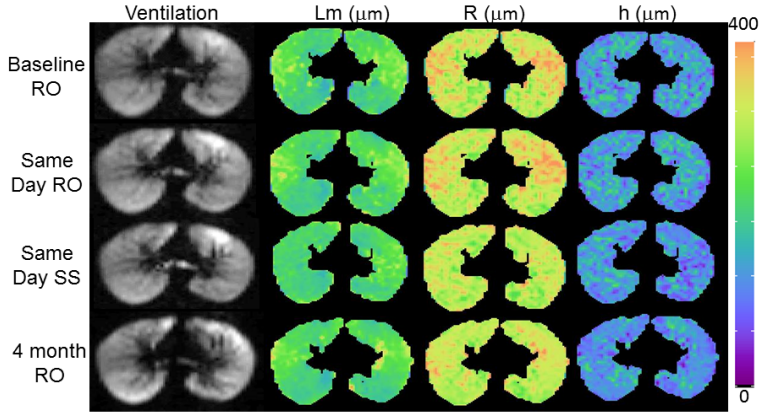
Average %CV	***h***	***Lm***	***R***
Diffusion Direction	1.7%	2.6%	1.7%
Same Day Reproducibility	2.0%	2.1%	0.8%
Long Term Reproducibility	3.1%	2.9%	1.6%



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