# Lung Morphometry using Hyperpolarized Xenon-129: Preliminary Experience

Kai Ruppert[1], James D. Quirk[2], John P. Mugler III[1], Talissa A. Altes[1], Chengbo Wang[1], G. Wilson Miller[1], Iulian C. Ruset[3,4], Jaime F. Mata[1], F. William Hersman[3,4], and Dmitriy A. Yablonskiy[2]

*[1]University of Virginia, Charlottesville, VA, United States, [2]Washington University, St. Louis, MO, United States, [3]Xemed LLC, Durham, NH, United States, [4]University of New Hampshire, Durham, NH, United States*

**Introduction:** Techniques sensitive to lung structure at the alveolar level are valuable for assessing lung function in health and disease. MR imaging using hyperpolarized gases offers such sensitivity. While early studies of hyperpolarized-gas diffusion in lung airspaces [1-3] demonstrated substantial changes in gas diffusivity in emphysematous lungs as compared to healthy lungs, these changes in diffusivity were not linked to specific alterations in lung microstructure. The recently described helium-3 (He3) lung-morphometry technique [4], which is also based on in-vivo MR measurements of the diffusivity of hyperpolarized He3 gas in the lung, provides information on the lung microstructure in terms of mean airspace chord length (Lm), lung parenchyma surface-to-volume ratio (S/V) and the number of alveoli per unit lung volume (Na) – parameters most commonly used by lung physiologists to characterize lung morphometry. However, due to the high cost and limited supply of He3, lung morphometry with hyperpolarized xenon-129 (Xe129) might become an attractive alternative for widespread application. Herein, we report first results of lung morphometry based on Xe129.

**Methods:** Our method is based on the theoretical background developed previously [5], where MR imaging parameters and the theory of Xe129 gas diffusion in acinar airways were adjusted (as compared to He3) to account for the substantially different free diffusion coefficients $D_0$ (0.14 $cm^2/s$ for dilute Xe129 in air vs. 0.88 $cm^2/s$ for He3 in air) and gyromagnetic ratios ($\gamma$ = 11.8 MHz/T for Xe129 vs. 32.4 MHz/T for He3). Imaging was performed at 3 T (Trio, Siemens Medical Solutions, Malvern, PA) using a custom-built 32-channel receive array with integrated asymmetric birdcage transmit coil. A diffusion-weighted gradient-echo-based sequence with either three (0 $s/cm^2$, 12.5 $s/cm^2$, 50 $s/cm^2$) or five (0 $s/cm^2$, 12.5 $s/cm^2$, 25 $s/cm^2$, 37.5 $s/cm^2$, 50 $s/cm^2$) *b* values was used to acquire 5 or 4 30-mm slices, respectively. Other imaging parameters included: TR/TE 19.7/14.0 ms; flip angle 9°; and in-plane resolution 6.5×6.5 mm. The bipolar diffusion-sensitization gradient was applied in the slice-select direction with ramp times of 300 μs, flat-top times of 4500 μs, and no delay between positive and negative lobes. Enriched xenon gas (87% Xe129) was polarized by collisional spin exchange with an optically-pumped rubidium vapor using a prototype commercial system (XeBox-E10, Xemed LLC, Durham NH). One healthy subject and one subject with cystic fibrosis (CF) inhaled, from residual volume, a gas mixture having a total oxygen concentration of 21% and containing 0.7-L of hyperpolarized Xe129 polarized to 30-50%, room air and oxygen. All experiments were performed under a Physician's IND for imaging with hyperpolarized Xe129 using a protocol approved by our institutional review board. Informed consent was obtained in all cases.

For each image voxel, the data from all channels in the receiver array were jointly analyzed using Bayesian probability theory [6] and a mathematical model of Xe129 gas diffusion in lung acinar airways [5]. In this approach, the lung acini are treated as networks of cylindrical airways covered with alveoli [7,8] and Xe129 diffusion measurements are used to determine the mean values of acinar-duct radii (R), airway-lumen radii (r), and the depth of the alveolar sleeve (h = R – r). From these measurements, standard morphometric parameters such as the alveolar density Na, mean chord length Lm, and S/V can be calculated [4].

**Results and Discussion:** The average values of h, Lm and R were 90 ± 60 μm, 220 ± 70 μm, and 270 ± 100 μm, respectively, for the healthy volunteer, and 90 ± 60 μm, 240 ± 40 μm, and 280 ± 80 μm, respectively, for the subject with CF. Figure 1 depicts representative axial maps of h, Lm and R from the healthy human volunteer. These findings are in good agreement with those from He3 lung morphometry studies in healthy subjects and histological measurements. In the future, we will perform He3 and Xe129 morphometry studies in the same subjects for a direct comparison.

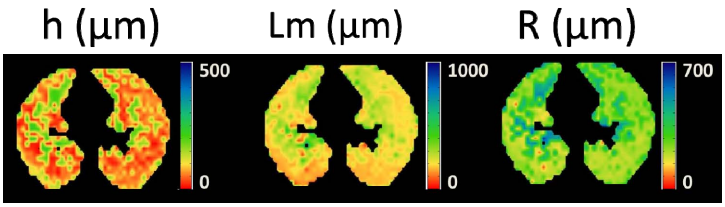


**Figure 1.** Representative axial maps of sleeve depth h, mean chord length Lm and acinar-duct radii R obtained with Xe129 lung morphometry in a healthy human volunteer at 3 T.

While the underlying theory was initially developed for diffusion of dilute Xe129 in air ($D_0$ = 0.14 $cm^2/s$), $D_0$=0.10 $cm^2/s$ may be a more realistic value for the gas mixture encountered in the lung, which might lead to a systematic error. Further, for some of the images acquired with larger *b*-values, we noticed motion artifacts in the vicinity of the heart that could also affect the calculated parameter values.

**Conclusion:** Our initial findings for Xe129-based lung morphometry indicate that this technique is technically feasible and might become a viable alternative to He3-based lung morphometry for the time when He3 becomes either unavailable or at least uneconomical. Future studies are required for additional optimization of this promising method.

**References:** **[1]** Saam BT et al. Magn Reson Med 2000;44:174-9. **[2]** Chen XJ et al. Proc Natl Acad Sci USA 2000; 97:11478-81. **[3]** Salerno M et al. Radiology 2002;222:252-60. **[4]** Yablonskiy DA et al. J Appl Physiol 2009;107:1258-65. **[5]** Sukstanskii AL, Yablonskiy DA. Magn Reson Med 2011. **[6]** Quirk JD et al. J Magn Reson 2009;198:49-56. **[7]** Haefeli-Bleuer B, Weibel ER. The Anatomical Record 1988;220:401-414. **[8]** Rodriguez M et al. Am J Anat 1987;180:143-55.

**Acknowledgements:** Supported by NIH grants R01-HL070037, R01-HL105586 and R44-HL087550, and Siemens Medical Solutions.