Regional Mapping of Gas Uptake by Lung Tissue and Blood in Subjects with Asthma using Hyperpolarized Xenon-129 MRI

Kun Qing[1], Kai Ruppert[1,2], Tally A. Altes[1], Yun Jiang[3], Jaime F. Mata[1], G. Wilson Miller[1], Yang Yang[1], Yun M. Shim[1], Steven Guan[1], Iulian C. Ruset[4,5], F. William Hersman[4,5], and John P. Mugler[1]

[1]*University of Virginia, Charlottesville, VA, United States,* [2]*Cincinnati Children's Hospital, Cincinnati, OH, United States,* [3]*Case Western Reserve University, Cleveland, OH, United States,* [4]*Xemed LLC, Durham, NH, United States,* [5]*University of New Hampshire, Durham, NH, United States*

Target audience: Physicians and scientists interested in functional lung imaging or obstructive lung diseases such as asthma.

Introduction: Asthma is characterized by reversible bronchial obstruction. Ventilation perfusion mismatch is common in patients with asthma suggesting that there is a vascular component to the disease, a component that is not evaluated with spirometry-the standard clinical test in asthma. Three-dimensional Xe-129 dissolved-phase imaging[1] provides a non-invasive method to directly map gas uptake by tissue and blood in the human lung. For this study, we used this technique to investigate functional changes in the lungs of subjects with asthma, and compared the results to those from healthy subjects.

Methods: The study group included 12 healthy subjects (age 19-59 yrs, FEV_1 %pred 104%±13%, FEV_1/FVC 0.81±0.05) and 10 asthmatics (age 22-56 yrs, FEV_1 %pred 77%±18%, FEV_1/FVC 0.65±0.10). A multi-echo 3D radial pulse sequence[1] was used for acquiring dissolved- and gas-phase Xe129 images. Sequence parameters were: TR 19 ms, $TE_1/TE_2/TE_3$ 0.74/2.36/3.98 ms (dissolved) and TE_1/TE_2 0.74/2.36 ms (gas), flip angle 23° (dissolved) and 0.4° (gas), acquisition time ~10 s, and voxel volume 7.6 x 7.6 x 17 mm^3. The Hierarchical IDEAL method[2] was used to separate the tissue and RBC components from the multi-echo dissolved-phase images. For quantitatively analyzing lung function, four ratios were generated: total dissolved-phase-to-gas, tissue-to-gas, RBC-to-gas and RBC-to-tissue (the latter three shown as maps). In a subset of the subjects (two healthy, eight asthmatics), coronal Xe129 diffusion-weighting images were also acquired for calculation of apparent diffusion coefficient (ADC) values using the following pulse-sequence parameters: TR/TE 13.8/9.4 msec, flip angle 8.5°, voxel volume 6 x 6 x 25 mm^3, *b* values 0 and 10 s/cm^2. MR studies were performed at 1.5T (Avanto; Siemens) using a flexible Xe129 chest RF coil (Clinical MR Solutions), under a physician's IND for hyperpolarized Xe129 MRI. Informed consent was obtained in all cases and a physician supervised each study. Enriched xenon gas (87% Xe129) was polarized using a prototype commercial system (XeBox-E10, Xemed).

Results & Discussion: Healthy subjects showed generally homogeneous signal distribution in all images (Fig.1). All ratios were relatively consistent among subjects: total dissolved-phase-to-gas: 1.37%±0.15% (mean ± standard deviation), tissue-to-gas: 1.18%±0.14% , RBC-to-gas: 0.33%±0.06%, and RBC-to-tissue: 0.28±0.05. For diffusion-weighted imaging, the whole-lung ADC values measured in the two healthy subjects were 0.033 cm^2/s (21 yrs) and 0.045 cm^2/s (54 yrs), which were consistent with other measurements[3].

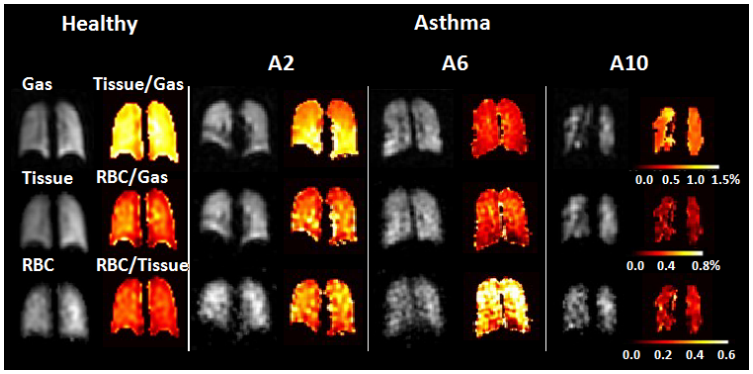

Figure 1. Representative Xe129 ventilation images (gas), images of Xe129 dissolved in lung tissue and RBCs, and corresponding ratio maps from one healthy volunteer and three asthmatics. Low tissue-to-gas ratios and elevated RBC-to-tissue ratios were seen in the left upper lung of A2 and throughout the lungs of A6. Subject A10 had all ratios lower than normal.

The overall gas uptake (represented by total dissolved-phase-to-gas ratios, Fig.2) for asthmatics (mean=1.04%) was lower than that for the healthy group (p=0.004).

Seven asthmatics (blue in Fig.2) had RBC-to-gas ratios (mean=0.28%) similar to healthy subjects[1], but unlike healthy subjects they showed lower tissue-to-gas ratios and higher RBC-to-tissue ratios, either regionally (A2, Fig.1) or throughout the lung (A6, Fig.1). Their mean tissue-to-gas ratio was 0.80%, lower than that for healthy (p<0.001). In six asthmatics who underwent diffusion-weighted imaging, the whole-lung ADC values were in the normal range (0.035±0.004cm^2/s). Hyperexpansion of the lung, which is known to occur in asthma, may contribute to low tissue-to-gas ratios, but may not account for all of the difference between asthmatic and healthy subjects. The mean RBC-to-tissue ratio for these seven asthmatics was 0.39, much higher than that for the healthy group (p<0.001), and was possibly due to increased pulmonary blood flow[4] or enhanced tissue-to-RBC exchange brought by angiogenesis, which has been reported in histological specimens from asthmatics.

All ratios were relatively low in the two asthmatics older than 50 (age 53 and 56, red in Fig. 2, A10 shown in Fig. 1). Specifically, the tissue-to-gas ratios were 0.94% and 0.91%, and the RBC-to-tissue ratios were 0.21 and 0.20, which corresponded to RBC-to-gas ratios of 0.20% and 0.18%. Also, the whole-lung ADC values measured in these two subjects were higher than normal (0.049 cm^2/s and 0.053 cm^2/s). All of these findings are similar to those seen in COPD[1].

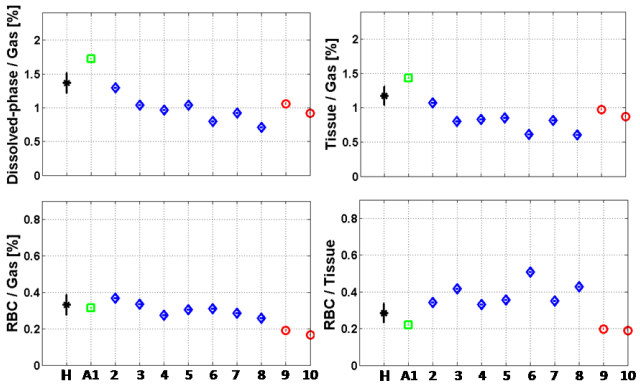

Figure 2. Whole lung ratio values for the healthy subject group (mean and standard deviation plotted on the left in black) and the individual 10 asthmatics.

One female subject (A1, 22 yrs, green in Fig. 2), whose results were generally different than those for the asthmatics, had relatively high gas uptake, showed very few ventilation defects, and had a low mean ADC value (0.028 cm^2/s).

Conclusion: The relatively high RBC-to-tissue ratios, low tissue-to-gas ratios, and normal ADC values found in seven of the ten asthmatics in this study represent a unique combination that has not been seen in healthy or COPD subjects. These values may be associated with airway inflammation and remodeling of both the airways and vasculature, while longterm disease progression could cause irreversibly impaired lung function from tissue destruction, as seen in the two older asthmatics that had results similar to those seen in COPD.

References: [1] Qing K, et al. J. Magn. Reson. Imaging. doi: 10.1002/jmri.24181. [2] Tsao J, et al. Magn.Reson. Med., 70: 155-159. doi: 10.1002/mrm.24441. [3] Kaushik SS, Magn Reson Med 2011;65(4):1154-1165. [4] Kumar SD, et al. Am J Respir. Crit. Care Med. 1998 Jul; 158(1): 153-6.

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