Using Hyperpolarized ^{129}Xe MRI to Quantify Differences in Regional Ventilation in Older Versus Younger Asthmatics

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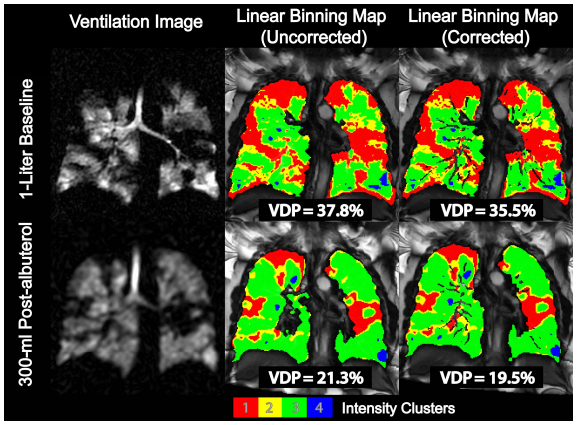
Target Audience: Hyperpolarized Gas MRI, Clinical MRI Lung Imaging, Asthma

Purpose: The treatment of asthma is often less effective in elderly asthmatics than in younger asthmatics. Yet most published studies focus on younger asthmatics and often exclude subjects aged over 65 to avoid the confounding effects from other obstructive lung disorders such as COPD. In this study, using hyperpolarized (HP) ^{129}Xe MR imaging of ventilation, we evaluate functional differences between younger (18-35 yrs) and older (55-75 yrs) asthmatics, as well as age-matched healthy controls. A secondary goal was to evaluate short-term image reproducibility, and in a select group of asthmatics, to evaluate bronchodilator response. In order to quantify the ^{129}Xe ventilation images, we further refined our previously introduced [1] semi-automated extension of the methods of Kirby et al [2] to calculate ventilation defect percentage (VDP). Specifically, we further correct the VDP to account for B_1 in-homogeneity [3,4], and the effects of pulmonary vasculature [3,5].

Methods: A total of 29 volunteers (10 younger asthmatics, 10 older asthmatics, 5 younger controls, and 4 older controls) underwent two ^{129}Xe MR baseline-scans, 5 min apart, after inhaling 1-liter of HP ^{129}Xe (85% enriched, polarized to 7-10%). A subset of asthmatics also underwent two HP ^{129}Xe scans 10 min and 15 min after taking 4 puffs of albuterol. Post-albuterol scans used 300 mL of Xe (polarized to 10-15%) diluted with 700 mL of N_2. ^{129}Xe MRI was acquired with a multi-slice GRE: FOV=40/36 cm (1 L/300 mL), 12.5 mm slice, matrix=128/64×128/64, BW=8.3 kHz, α=7-10°, TR/TE=8.1/1.9 ms. To enable semi-automated quantification, the thoracic cavity was delineated using a breath-hold ^{1}H FIESTA (SSFP) image: FOV=40 cm, 12.5 mm slice, matrix=256×256, α=45°, TR/TE=2.8/1.2 ms, BW=125 kHz. These scans were registered to the ^{129}Xe MRI using the Image Registration Toolkit [6]. The registered ^{1}H image was then segmented by seed-based region growing to create a thoracic cavity mask within which the ^{129}Xe intensities were analyzed. The mask was then morphologically closed to fill small gaps caused by vascular structures. In a second step, those vascular structures that fully excluded ^{129}Xe signal were removed using the vessel-enhancing algorithm introduced by Frangi[5]. ^{129}Xe MRI was then corrected for B_1 in-homogeneity using the N4ITK algorithm in Advanced Normalization Tools (ANTs) [7]. Finally, the ^{129}Xe intensity within the thoracic cavity mask was rescaled by the top percentile to a range of 0-1. The resulting intensities were classified by linear binning [1] into 4 clusters consisting of <0.15 (defects), 0.15–0.30 (hypointense), 0.30–0.85 (normal), and >0.85 (hyperintense). The lowest of these clusters, labeled as ventilation defects, was used to calculate the VDP.

Results: ^{129}Xe MRI was successfully acquired in all subjects with sufficient quality to undergo semi-automated segmentation. The figure shows ^{129}Xe MRI and binning maps obtained from an older asthmatic (age = 69 yrs) pre- and post-albuterol. The correction methods reduced baseline VDP from 37.8% to 35.5%. After albuterol administration, corrected VDP was reduced to 19.5%. Among all subjects, VDP readily separated the younger and older asthmatic groups (7.4 ±4.4% vs. 12.6 ±9.0%, p<0.05). Similarly, baseline VDP was significantly different for younger versus older controls (4.4 ±2.3% vs. 11.8 ± 8.5%, p<0.05). ^{129}Xe MRI was highly reproducible for the two scans taken both at baseline (p<0.0001)) and post-albuterol (p<0.0001). Moreover, albuterol significantly reduced VDP in the (n=11) asthmatics who received it (from 12.0±8.3% to 8.2±4.9%, p=0.0029). Albuterol caused smaller ventilation improvements in younger asthmatics (from 7.3±2.9% to 5.2±2.5%, p=0.005) than in older asthmatics (from 16.2±9.2% to 10.6±5.4%, p=0.01).



Ventilation images and associated linear binning maps pre- and post-corrections for a 69-yr-old asthmatic before and after albuterol administration.

Discussion and Conclusion: This study demonstrated the feasibility and reproducibility of ^{129}Xe MRI with corrected linear binning to observe and quantify regional ventilation obstruction and bronchodilator response in asthma [8]. The method reliably differentiates the baseline ventilation patterns of older vs. younger subjects, consistent with prior observations. This study also shows that older asthmatics exhibit a significantly greater baseline VDP than younger asthmatics. Moreover, the semi-automated modified linear binning method provides a promising means to not only accelerate objective image analysis, but can be readily extended to provide other measures of regional function such as regional distribution and heterogeneity.

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References: (1) He et al., ISMRM 2013: p 1451. (2) Kirby et al., Acad Radiol 2012;19(2):141-152. (3) Tustison et al., J Magn Reson Imaging 2011;34(4):831-841. (4) Tustison et al., IEEE Trans Med Imaging 2010;29(6):1310-1320. (5) Frangi et al., IEEE Trans Med Imaging 1999;18(10):946-956. (6) Rueckert et al., IEEE Trans Med Imaging 1999;18(8):712-721. (7) Avants et al., Neuroimage 2011;54(3):2033-2044. (8) Kirby et al., Radiology 2011;261(1):283-292.