Longitudinal Study of Pulmonary Ventilation with ^{3}He MRI in Asthma Patients

Robert V Cadman[1], David G Mummy[2], Scott K Nagle[1,3], Nizar N Jarjour[4], Mark L Schiebler[3], Ronald L Sorkness[5], and Sean B Fain[1,3]

[1]*Medical Physics, University of Wisconsin-Madison, Madison, WI, United States,* [2]*Biomedical Engineering, University of Wisconsin-Madison, Madison, WI, United States,* [3]*Radiology, University of Wisconsin-Madison, WI, United States,* [4]*Department of Medicine, University of Wisconsin-Madison, Madison, WI, United States,* [5]*School of Pharmacy, University of Wisconsin-Madison, Madison, WI, United States*

Purpose: The evolution of ventilation defects in obstructive lung diseases such as asthma is of interest in understanding disease progression, regional variation of disease, and response to treatment. The purpose of this work was to evaluate the reproducibility of ventilation defects in asthma patients over a period of up to five years.

Methods: These studies were approved by our IRB, and all research subjects gave informed consent for MR imaging with ^{3}He. Subjects were initially recruited and enrolled in an asthma study at our institution (hereafter the "baseline study"). The baseline studies, performed between 2008 and 2011, were cross-sectional in design and included CT imaging, plethysmography, and spirometry in addition to MRI. In 2012, four of these subjects returned to participate in a pilot study of novel pulmonary MRI techniques (hereafter the "pilot study"), in which the ^{3}He MRI functioned primarily as a reference image. Other subjects from the baseline study volunteered to participate in an ongoing expansion of the baseline study which is longitudinal in design (hereafter the "follow-up study"), and were imaged in 2013. The baseline and pilot studies did not involve drug interventions coincident with the MRI exams. In the follow-up study ventilation series were acquired both before and after administration of a sufficient number of puffs of albuterol to reach maximum bronchodilation, with a total of approximately 30 minutes between the two series to allow the albuterol to take effect.

MRI was performed on a clinical 1.5 T scanner (Signa HDx, GE Healthcare, Waukesha, WI) with the broadband imaging option installed. The coil was either a single-channel elliptical birdcage-style coil (Rapid Biomedical GmbH, Rimpar, Germany) or a flexible quadrature coil (Medical Advances, Milwaukee, WI) tuned to the ^{3}He Larmor frequency of 48.64 MHz. In either case, the body coil in the scanner was used for proton imaging while the ^{3}He coil was in place.^{3}He was prepared in a prototype commercial polarizer (HeliSpin, Polarean, Durham, NC) and dispensed into a fluoropolymer bag for delivery to the subject. The dose volume was ~1 L. The subject inhaled the dose from functional residual capacity and then held his/her breath for the duration of image acquisition. The imaging sequence was multi-slice fast gradient-echo with acquisition matrix 128×128 zero-padded to 256×256, FOV 40×40 cm^2, and phase FOV 60%. In the baseline study, TR = 7.8 ms and TE = 4 ms, while for the later studies, TR = 6.5 ms and TE = 2.9 ms. In the first two studies ("baseline" and "pilot"), the slice thickness was 15 mm, but slice thickness was reduced to 10 mm in the follow-up study.

Longitudinal ^{3}He ventilation images were assembled from the three studies and evaluated by a radiologist who was blinded to the subject and time point. The location of ventilation defects were identified in each slice. The baseline exam and the subsequent time point from the pilot or follow-up study were compared to classify defects based on regional character into three categories: persistent (co-incident at both times), emergent (appearing at second time point), or reversed (resolving at second time point). A defect which could be traced across multiple slices was only counted once. Only exams prior to bronchodilator administration were used for this classification with qualitative assessment post-bronchodilator when available.

Results: Longitudinal data were available for 7 subjects (mean ± std. dev. age 44.2±11.6 years, 6 male and 1 female, 5 severe and 2 non-severe asthmatics, 2.9±1.1 years between time points). In these subjects, a total of 92 persistent defects, 120 emergent defects, and 62 reversed defects were counted (**Figure 1**). **Figure 2** shows the axial slice located immediately below the carina of the same lung from the baseline study (**Fig. 2A**), and follow-up study before and after bronchodilator (**B vs. C**). A large emergent ventilation defect that incompletely resolves after bronchodilator is seen in the follow-up study (**arrowheads Fig. 2B,C**). The size of the defect suggests central airway involvement that is relatively refractory to bronchodilator treatment. Examples of persistent (**asterisks Fig. 2A–C**) and reversed (**long arrow Fig. 2A**) defects are also illustrated.

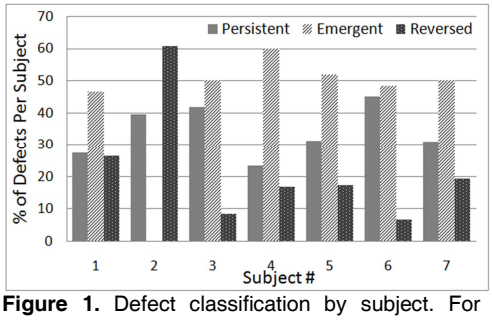

Figure 1. Defect classification by subject. For each of the seven subjects who participated in two of the studies described in the text, the percentage of defects falling into each of the three categories is shown.

Discussion: Although ventilation defects are often a prominent feature in ^{3}He MRI of a diseased lung, the persistence of defects over time is not well understood. One study observed that ~40% of defects were persistent but that many defects which appeared after methacholine challenge on repeated visits were resolved following subsequent bronchodilator treatment.[1] Another study observed defects at baseline, following exercise challenge, and after recovery[2] and showed ~20% of defects recurred at the same or similar locations. Investigators have also noted the gravity dependence of ventilation patterns may affect recurrence in the supine position. Here we demonstrate the feasibility of categorizing defects based on their longitudinal presentation. In the ongoing follow-up study new baseline images have been acquired in 46 subjects to date. We hypothesize that emergent ventilation defects after asthma exacerbation correspond to sites of new airway injury and are using ^{3}He MRI to guide bronchoscopic assessment[3] of inflammatory cells and vascular markers of injury[4] compared to well-ventilated control regions.

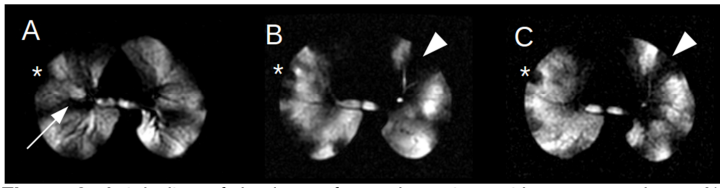

Figure 2. Axial slice of the lung of a male patient with severe asthma. A) Baseline image from February 2011. B) Follow-up image acquired in October 2013 pre-bronchodilator and C) post-bronchodilator treatment. Markers indicate emergent (arrowheads), persistent (asterisks), and reversed defects (long arrow).

Conclusions: Although ventilation defects are a significant feature of ^{3}He MRI images of asthmatic lungs, the relationship of those defects to clinical symptoms of asthma is not well understood. The large fraction of emergent defects observed suggests the disease process may recruit new airways over time. Image guided bronchoscopy of these regions may yield important insights into the factors driving asthma severity and progression.

References: [1]de Lange et al., Radiology. 2009 Feb;250(2):567-75. [2]Niles et al., Radiology. 2013 Feb;266(2):618-25. [3]Fain et al., Acad Radiol. 2008 Jun;15(6):753-62. [4]Johansson et al., Am J Respir Crit Care Med. 2013 Jul 15;188(2):167-78.