Assessing the Persistence of Ventilation Defects in Asthmatics at Baseline and Following Methacholine Challenge Using Hyperpolarized ^{3}He MRI

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Introduction

Is asthma a disease that manifests itself by decreasing ventilation diffusely, throughout the lungs, or are there particular, localized regions of the lungs that are chronically poorly ventilated? This is an important question, because asthma affects about 20 million adults and seven million children in the U.S. Recent hyperpolarized (HP) ^{3}He MR imaging studies demonstrate that asthma gives rise to a heterogeneous distribution of signal defects in the lungs (1). ^{3}He MRI has also revealed that ventilation defects seen in asthma are not exclusively short-lived, transient defects observed over hours or days as many might have predicted—some defects can persist for weeks and even months (2, 3). Here, we used HP ^{3}He MRI to determine the total number of defects that remained in the same location, and how they changed in size, over a time period of about 45 days, at baseline and during provoked periods of bronchoconstriction induced by administration of the bronchoconstrictor, methacholine (Mch).

Methods

The HIPAA-compliant research protocol in this study was approved by the local Institutional Review Board. Informed consent was obtained from all recruited subjects. Data were obtained from two mild-to-moderate and three severe asthmatic subjects. The subjects were scanned at baseline and after Mch challenge during one scanning session (day 1), and then were scanned at baseline and after Mch challenge during a second scanning session approximately 45 days later (day 2). HP ^{3}He static ventilation MRI scans were performed using a flexible ^{3}He lung coil (Clinical MR Solutions) with a Fast Gradient Echo pulse sequence acquiring coronal multi-slice images with the following parameters: 46 cm FOV, 0.75 PhaseFOV, 128×256 matrix, 13 mm slice thickness, TE/TR 1.2 ms/5 ms, and interleaved data acquisition. For each scan, 1 liter of an approximately 33% HP ^{3}He- 67% N_2 mixture that was polarized to about 20% was administered for the subject to inhale. Two readers evaluated the images from the two separate days, and determined the total number of defects in each slice that remained the same on the two days, the number of defects that became resolved on the second day, the number of new defects that appeared on the second day, according to the method employed in (2). In addition, for those defects that remained the same on the second day, the readers scored whether they became smaller, larger, or remained the same size (2). Ventilation volumes were calculated from the images using a semiautomatic algorithm.

Results and Discussion

HP ^{3}He MR ventilation baseline and Mch images from a representative severe asthmatic subject are shown in Figure 1. The top row shows the image at baseline (left) and after Mch (right) on day 1; the bottom row shows this data from day 2. The average number of defects across all subjects indicates that at baseline, 75% ± 40 remained in the same location between the two imaging sessions. The data at baseline had a high degree of variability from subject to subject, as indicated by the standard deviations. Not surprisingly, after a Mch challenge, the total number of defects increased by 170% ± 47 on day 1 and 173% ± 32 on day 2 (mean = 172%), and total ventilation volume decreased by a mean of 20%. Comparing the post-Mch challenge images for each subject, the total number of ventilation defects that occurred in the same location averaged 96% ± 4. At baseline, 30% ± 50 of defects were new on day 2, whereas post-Mch, only 5% ± 5 of defects were new on day 2. Overall, the post-Mch images exhibited a small degree of variability. Thus, we observed that, for individual asthmatics, Mch challenges predictably increased the number of ventilation defects from baseline as expected, but that, from one bronchial provocation to the next, almost all the defects occurred in the same anatomic regions of the lungs. Also, some transience in defects was seen comparing baseline images, but much less was evident comparing post-Mch images.

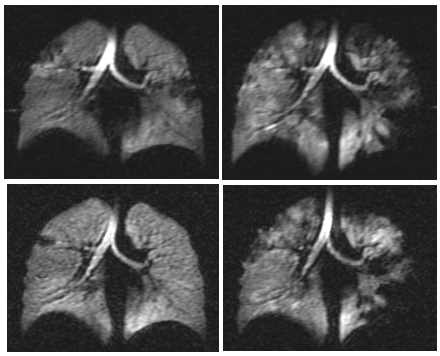

Figure 1. ^{3}He MRI images at baseline (left column) and after Mch challenge (right column), at day 1 (top row) and day 2, 45 days later (bottom row).

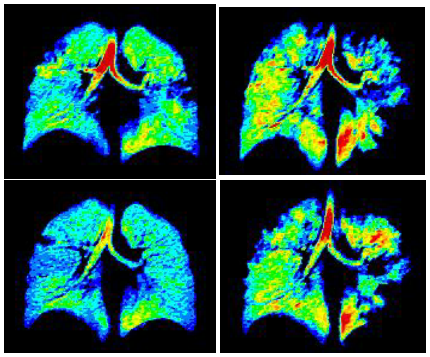

Figure 2. ^{3}He MRI fractional ventilation maps at baseline (left column) and after Mch challenge (right column), at day 1 (top row) and day 2, 45 days later (bottom row).

Conclusions

Our results suggest that Mch provocations in asthmatics increase the number of ventilation defects from baseline, but that defects tend to remain in the same location from one provocation to another. Also, some transience in defects tends to occur at baseline, but much less occurred between the provocations. Our results suggest that respiratory dysfunction in asthma has an important localized component.

References: 1. Tzeng et al., J Appl Physiol. 2009;106:813. 2. EE de Lange, et al., Radiology. 2009;250:567. 3.EE de Lange, et al., J Allergy Clin Immunol. 2007;119:1072.