Hyperpolarized 3He MRI Heterogeneity and Ventilation Defect Volume Correlates with Asthma Severity

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Introduction

Asthma has drawn more public attention recently because of its rapidly increasing prevalence, affecting up to one in four urban children. Constriction and inflammation in asthmatics respiratory system narrow the airways, which cause heterogeneous ventilation in the lungs. To assess the chronic respiratory impairment in asthmatics, we performed hyperpolarized (HP) ^{3}He MRI to image the change in ventilation distribution in asthmatic (2 severe, 2 mild-to-moderate) and healthy (n=2) subjects at baseline, after methacholine (Mch) challenge, after deep inspirations (DI) following Mch challenge, and after Albuterol administration.

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 4 asthmatic (2 severe, 2 mild-to-moderate) and 2 healthy subjects. HP ^{3}He static ventilation MRI scans were performed with a Fast Gradient Echo pulse sequence acquiring coronal multislice 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 was administered for the subject to inhale. HP ^{3}He MRI was performed before Mch challenge (preMch), after Mch challenge (postMch), after deep inspirations (postDI), and after Albuterol administration (postAlb). Regions of ventilatory defects were measured from a representative middle slice of each image series using a manual segmentation method to obtain relative measures of preMch (D_b), postMch (D_m), post-Alb (D_{Alb}) and postDI (D_{DI}) defect volumes for each patient. A reference maximum possible lung slice volume (V_w) was derived for the same image slice using the same method. Results are presented as proportions of defect volumes D over the maximum slice volume V i.e. D_b/V_w, Dm/V_w, D_{Alb}/V_w, and D_{DI}/V_w. The acquired images were rigidly coregistered, then processed to yield local fractional volume occupied by HP ^{3}He and local ventilation heterogeneity. The local heterogeneity for each pixel of the lung images was computed by calculating the pixel intensity coefficient-of-variation for a region of interest around each pixel.

Results and Discussion

Representative preMch, postMch, postDI, and postAlb images and the corresponding defect-segmented images from each of the 3 subject groups are presented in Figure 1.

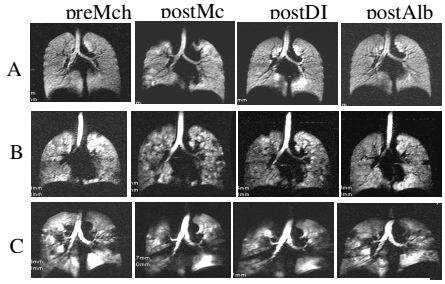
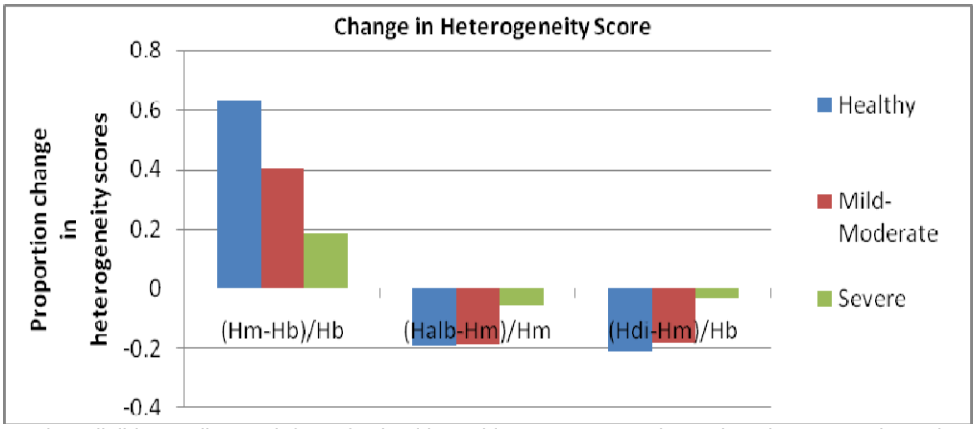


Figure 1. ventilation HP 3He images for preMch, postMch, postDI, and postAlb



At baseline, the HP ^{3}He MR ventilation images showed negligible ventilatory defects for healthy subjects. However, the asthmatic groups showed significantly higher defect volumes at baseline with 10.3±9.7%, for mild to moderates and 30.0±12.2% for severe asthmatics. After Mch challenge, ventilation defects clearly increased for all groups with 15.6±12% defect volumes for healthy subjects, 26.3±9% for mild-to-moderates and 38.0±22% for severe asthmatics. After taking DI's, 7.01±5.2% of defect volumes remain in healthy subjects, compared to 11.2% and 38.7±13% for mild-to-moderate and severe asthmatics respectively. Unlike in healthy subjects, DIs appeared to have little impact on diminishing defect volumes in the asthmatic lung. Further, DIs had more of an effect on mild-to-moderates than severe asthmatics, suggesting that DIs have a muted bonchodilatory effect in severe asthmatics. After Albuterol administration, the defect volume decreased dramatically to near baseline values for healthy subjects 0.893±0.67%, and to smaller than baseline values in mild-to-moderate and severe asthmatics, 6.67±0.89 and 15.4±7.7% respectively. For each condition, we also calculated the heterogeneity score for the entire set of images. Mch challenge produced a ventilation heterogeneity score percentage change from baseline that was largest in the healthy subjects, 63%, smaller in the mild-to-moderate asthmatics, 40%, and least in the severe asthmatics, 18%. The healthy subjects and mild-to-moderate asthmatics showed recovery of heterogeneity score following DIs of 21% and 18% respectively, suggesting a bronchodilation effect, while the severe asthmatics had impaired bronchodilation ,3%. Albuterol was shown to reverse the induced heterogeneity from Mch challenge in healthy,19%, mild-to-moderate ,18%, and severe, 5%, subjects. The lack of efficacy of albuterol in reversing airway heterogeneity in severe asthmatics suggests that it might not be completely effective during an acute asthma exacerbation.

Conclusion

This study shows that HP ^{3}He MRI is effective in monitoring changes in airway function and lung ventilation after different respiratory challenges and maneuvers as detailed above. More importantly, HP ^{3}He MRI is capable of identifying characteristic differences in lung ventilation between asthmatics of different disease severity and control subjects. Further, as depicted by the heterogeneity score, in an airway constricted by methacholine, bronchodilators, are less effective in patients with severe asthma.