Hyperpolarized Helium-3 MR Imaging of Methacholine Challenge Testing in Asthmatics

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Introduction

The methacholine challenge test is a commonly used clinical test for the diagnosis of asthma. It involves inhaling methacholine, a direct cholinergic agonist, that causes a brief constriction of the bronchial airways, and then measuring changes in spirometry. The reaction to methacholine is far more intense in asthmatics than in non-asthmatics.

Hyperpolarized helium-3 (H3He) is a new MR contrast agent which allows MR imaging of airspaces and has been used to obtain images of lung ventilation in subjects with a variety of lung diseases (1-7). Preliminary data in asthma suggests there may be a correlation between the size and number of H3He ventilation defects and the severity of asthma (7). The hypothesis of this study was that H3He ventilation defects appear following exposure to a bronchoconstrictor and reverse following treatment with a bronchodilator in asthmatics.

Methods

Three subjects, 2 asthmatics (age 21 and 24 years) and 1 normal subject (age 25 years), underwent a standard clinical methacholine challenge test. Both of the asthmatics had a greater than 20% drop in forced expiratory volume in 1 second (FEV1) at an inhaled methacholine dose of 2.5 mg, consistent with the diagnosis of asthma. The normal subject had a less than 5% drop in FEV1 even with the maximum dose of methacholine, 25 mg. Subsequently, a repeat methacholine challenge test was performed in the MR scanner room. Subjects underwent H3He MRI three times: immediately before methacholine, 2-3 minutes following methacholine inhalation and 30-50 minutes following an albuterol nebulizer treatment. The ^{3}He gas was polarized using a laser polarizer (Nycomed-Amersham Imaging, Princeton, NJ, USA). Polarizations of 30-45% were typically attained. Imaging was performed on a broadband 1.5 T MR scanner (Vision, Siemens Medical Systems, Iselin, NJ, USA). Flexible quadrature 48MHz transmit-receive RF coils are used for the helium imaging (IGC-Medical Advances, Milwaukee, WI). These consist of a prototype rectangular wrap coil, 30 x 108 cm, and an improved version with arm cutouts for patient comfort and 30% more coverage in the superior-inferior direction, while maintaining comparable SNR. Subjects inhaled a mixture of approximately 300 cc of H3He and 700 cc of N_2 from a plastic bag and held their breath. Coronal H3He lung images were obtained using a FLASH sequence with typical parameters: TR 7.6 ms, TE 2.7 ms, FA 9°, FOV 420 cm2, slice thickness 1 cm, matrix 112x128 and slice acquisition time 0.79 s.

Results

The two asthmatics had a few small H3He ventilation defects on the baseline scans (Figure 1A), a common finding in asthmatics (7). Following methacholine inhalation, the asthmatics developed numerous H3He ventilation defects and a heterogeneous ventilation pattern with multiple areas of increased and decreased signal intensity (Figure 1B). These ventilation defects partially resolved following treatment with inhaled albuterol (Figure 1C). This correlated with measured changes in spirometry. Following methacholine, the asthmatic shown in Figure 1 had a drop in FEV1 from 118% to 73% of predicted (a greater than 20% decrease), and following albuterol treatment the FEV1 returned to near baseline (FEV1 110% of predicted). The normal subject had no H3He ventilation defects on the baseline scan and developed only a few small areas of decreased or absent H3He ventilation following methacholine.

Discussion

This study demonstrates that H3He MR ventilation defects can be induced in asthmatics by the inhalation of methacholine (a medically induced asthma exacerbation) and these defects improve following treatment with albuterol. The ventilation changes paralleled those of the spirometry. In addition, the rapid appearance of ventilation defects following administration of a bronchoconstrictor suggests that bronchoconstriction alone can cause H3He MR ventilation defects. These results suggest that H3He MR findings correlate with asthma severity and demonstrate the potential of H3He MR for evaluating asthma activity and response to treatment.

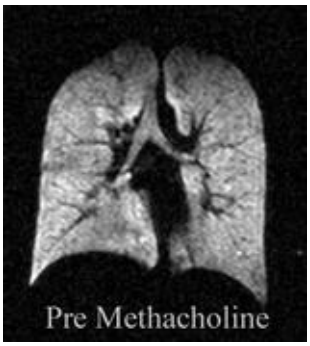

Figure 1A: Coronal H3He MR image of an asthmatic pre methacholine demonstrates no ventilation defects.

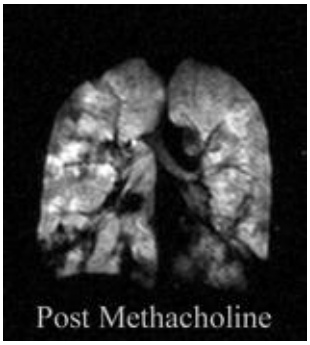

Figure 1B: Asthmatic (same as above) 2 minutes after inhaling methacholine devloped numerous H3He MR ventilation defects.

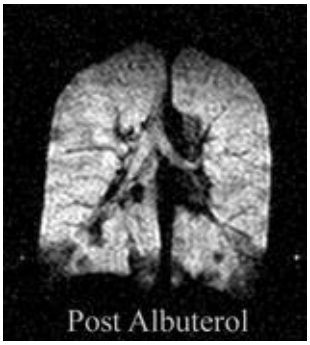

Figure 1C: Asthmatic (same as above) 30 minutes following albuterol treatment demonstrates partial resolution of the H3He MR ventilation defects.

References

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