

A quantitative technique for assessing the temporal dynamics of regional specific ventilation in response to methacholine challenge in asthma using oxygen enhanced proton MRI

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Purpose: Asthma is a spatially heterogeneous, temporally dynamic disease. During asthma exacerbations, bronchial smooth muscle contraction, inflammation and/or mucus secretion provoke airway narrowing, which in turn alters regional ventilation within the lung. These constrictions are variable in both space and time. The goal of this abstract is to present an improved post-processing algorithm that increases the temporal resolution of Specific Ventilation Imaging (SVI), a quantitative, oxygen-enhanced MRI technique that produces maps of regional specific ventilation (SV, the ratio of fresh gas to end-expiratory volume of a given lung region) within the lung.

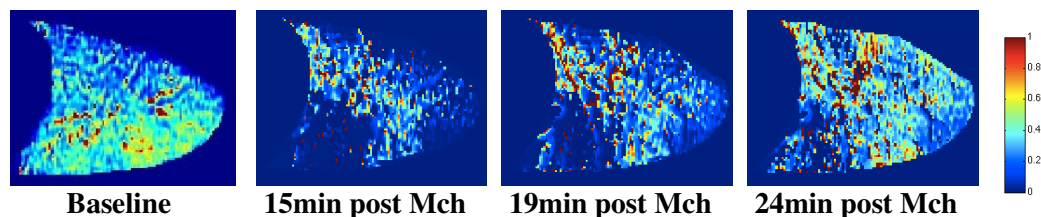
Methods: SVI¹ consists of acquiring consecutive T₁ weighted images at the end of each breath (every ~5s) while a subject voluntarily gates their respiration in time with audible cues. As the oxygen delivered to and dissolved into lung tissues shortens T₁, the rate of change of signal intensity following a sudden change in inspired oxygen concentration is a surrogate for the regional oxygen wash-in/wash-out time constant. This time constant is determined by the local SV. The current protocol consists of 5 wash-in/wash-out cycles alternating between room air and 100% O₂ (40 breaths/cycle, 200 breaths total). The time course of signal intensity (on a per voxel basis) is correlated to the expected dynamics of 50 simulated lung units of varying SV (ranging from 0.01-10, equally spaced on a log₁₀ scale), and the most representative (maximally correlated) SV is determined.

In order to capture the temporal dynamics of recovery from a methacholine (Mch, a bronchoconstrictor) induced asthmatic event, we implemented a sliding window approach, 120 breaths long (600s), shifted by 40 breaths (200s, 67% overlap). This provided SV maps for 5 minute overlapping periods, centered 3min20s apart, with each window containing 3 air-oxygen cycles.

A mild intermittent asthmatic (female, 23 years old) was imaged at baseline, and after exposure to inhaled 1mg/ml dose of Mch (PC₂₀ dose). Post-bronchoconstriction imaging started 12min after exposure. A 15mm thick sagittal slice in the right lung was imaged (FOV 40x40cm, 256x128 resolution) using an inversion recovery fast spin echo (echo spacing 5ms, 1100ms inversion time) HASTE sequence, in a GE 1.5T Signa HDx 14.0 TwinSpin system.

Results: The figure displays the baseline SV map, as well as consecutive SV maps, documenting recovery from Mch-induced bronchoconstriction. In this subject, the posterior dependent and apical regions of the lung had very low specific ventilation following bronchoconstriction.

Specific ventilation in these regions recovered post-Mch challenge, yet remained below baseline levels 24 minutes post bronchoconstriction.



Time course of recovery following methacholine(Mch)-induced bronchoconstriction in a mild intermittent asthmatic (Mch dose 1mg/ml). A sliding window SVI analysis (window length, 120 breaths, 600s, overlap 67%) was applied with 3 maps presented above centered at 15 min, 19 min and 24 min post Mch inhalation. The recovery of ventilation to previously bronchoconstricted regions can be clearly seen from left to right in the figure

Conclusion: With novel post-processing, SVI can be used to

quantitatively track temporal changes in the regional distribution of specific ventilation on the order of < 5 minutes. This permits study of the temporal nature of bronchoconstriction and bronchodilation, as well as the impact of therapeutic inhaled agents in a manner not previously possible. The technique has the potential to uncover mechanistic information on the regional differences in asthma and to be used as a biomarker in clinical trials.

Target Audience: MR imagers and clinicians interested in lung imaging, drug companies interested in quantitative measurements of the outcome of inhaled therapies.

References: 1. Sá, R. C. *et al.* Vertical distribution of specific ventilation in normal supine humans measured by oxygen-enhanced proton MRI. *J Appl Physiol* **109**, 1950–1959 (2010).