Quantitative Analysis of MCh Induced Ventilation Changes in Mouse Lungs in a Time Series

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INTRODUCTION: Recent high-resolution ^{3}He MRI in mouse models of asthma [1] provide opportunities to understand airway biology by showing regional ventilation changes. ^{3}He images of ovalbumin-sensitized mice [2] taken before and after challenge with methacholine (MCh) showed significant regional airway narrowing and closure [1]. To maximize the value of ^{3}He MRI, it is important to quantify the regional ventilation changes depicted in the images. For this, we had originally proposed using a simple thresholding technique to distinguish unventilated from ventilated lung. Although this method can visualize and quantify dramatic changes such as constriction of an entire lobe, simple thresholding is not sensitive to subtle changes in airway caliber or to diffuse ventilation changes. To improve sensitivity to these subtle changes in ventilation, we describe a post-processing scheme to quantify regional ventilation changes before and after MCh challenge and show that it is sensitive to both changes in airway caliber and subtle regional alterations in ventilation.

METHODS: Image Acquisition: The time series images are acquired using a 2D radial encoding sequence with a hardpulse excitation at a spatial resolution of 187x187 μm^2 in-plane. All animal procedures were approved by the Duke Institutional Animal Care and Use Committee. The first image in the time series is always a baseline ventilation image, following by 25 to 200 μg/kg of MCh injected in a rapid bolus (~3 s). In total, six ovalbumin-sensitized mice were scanned with MCh administration. The same protocol was used in a control C57BL/6 mouse without MCh injection to show that the image analysis technique only picks up changes in ventilation and compensates for signal decay due to non-physiological factors.

Image Analysis: A critical component of the MCh challenge image analysis is to account for changes in signal intensity resulting from loss of polarization and T_1 decay. To achieve this, we normalize all images by the signal intensity in the trachea where we know that 100% of the ^{3}He is replenished on each breath [3]. Normalization to the trachea signal is valid because we use radial imaging and thereby avoid the diffusion attenuation of signal in the large airways that would be inherent in Cartesian sampling. The normalized images now contain information regarding ^{3}He volume distribution, which is exact for 3D images and approximate for 2D images. Once the images are normalized, they can be subtracted from the baseline image to create difference maps that readily show the regions of hypoventilation (<0 on difference map) and hyperventilation (>0 on difference map). An additional benefit is that regions of airway narrowing are also revealed.

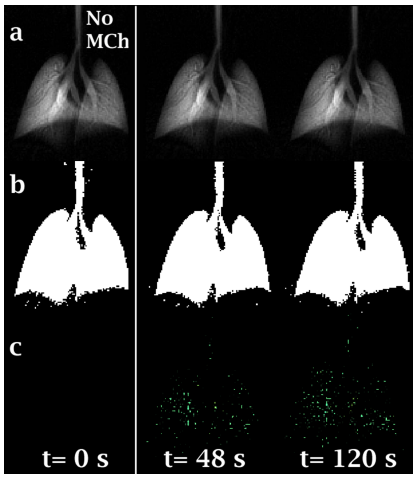

Figure 1: a) Baseline time-series data acquired from a C57BL/6 mouse at three different time points; b) thresholded ventilation images showing no change in ventilation; c) difference maps created from percent ^{3}He volume showing close to 0% change in all regions of the lung.

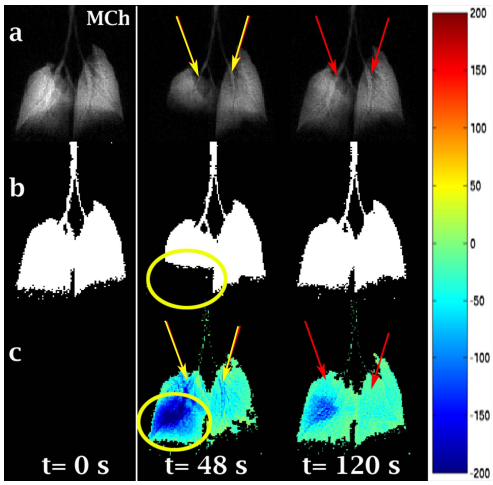

Figure 2: a) Baseline time-series data acquired from an ovalbumin-sensitized mouse showing airway narrowing (yellow arrows) and focal ventilation change; b) thresholded ventilation images pick up focal change (oval); c) difference maps shows airway narrowing (yellow arrows), airway recovery (red arrows) focal change (oval), and diffuse changes in the whole lung.

RESULTS AND DISCUSSION: Fig. 1 shows a) time series, b) thresholded images, and c) difference map created from ^{3}He volume images; in a C57BL/6 mouse with no injection. As expected, neither the threshold images nor the ^{3}He volume difference maps show any changes. Fig. 2 shows the technique applied in to an ovalbumin-sensitized mouse. Fig. 2a shows the time series images that displays airway narrowing (yellow arrows in left and right lung) and the subsequent recovery at t=120 s (red arrows in left and right lung). The time series also shows a focal loss of ventilation in the lower right lobe. While the thresholded images (Fig. 2b) pick up the focal change (shown by oval), it fails to pick up the airway caliber change or residual hypoventilation at t=120s. By contrast, the ^{3}He volume difference maps pick up airway narrowing (yellow arrows), airway recovery (red arrows), and focal (oval) and diffuse changes in ventilation as shown in Fig. 2c. A plot of normalized thresholded pixel count, and change in ^{3}He volume shows an increased sensitivity with the technique proposed in this work. Similar regional plots can also be created to show the effect of MCh in different regions of the lung.

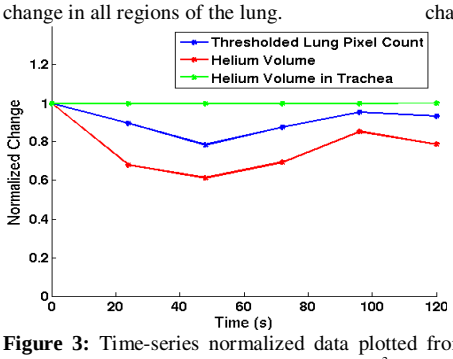

Figure 3: Time-series normalized data plotted from whole lung showing the increased sensitivity with the ^{3}He volume technique (red) compared to thresholded lung image (blue). The green plot shows uniform volume distribution in the trachea.

CONCLUSION: We have demonstrated a straightforward image analysis method to quantify regional changes in ventilation resulting from MCh challenge. This technique will allow pulmonary scientists to study asthma models on a global, as well regional level, in a quantitative manner.

REFERENCES:

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Work was performed at the Duke Center for In Vivo Microscopy, an NCRR/NCI National Resource (P41 RR005959/U24 CA092656), and funding from Merck Frosst Canada Ltd.