MRI and PET Imaging of Asthma-Like Reaction to a Segmental Ragweed Challenge in a Small Animal Model

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Introduction

The ability to non-invasively visualize the spatial distribution and severity of physiological changes associated with asthmatic reactions can facilitate understanding of the cause and aid in the treatment of asthma. The goal of this work is to use multimodality imaging to non-invasively observe the ventilation, inflammation, and metabolic components of the physiological response to asthma-like reactions in a small animal model. MRI imaging of lung ventilation using hyperpolarized Helium-3 and gated projection acquisition (PR) has been demonstrated for small animal imaging[1,2]. Furthermore, increased signal in the lungs on proton density weighted MRI has been correlated to edema in the lungs following challenge[3]. Finally, enhanced FDG uptake by immune cells, particularly neutrophils has been demonstrated in asthma-like response[4]. Together, these methods provide a more comprehensive characterization of the asthma-like response to facilitate research on the mechanisms and treatment of asthma during longitudinal studies in this small animal model.

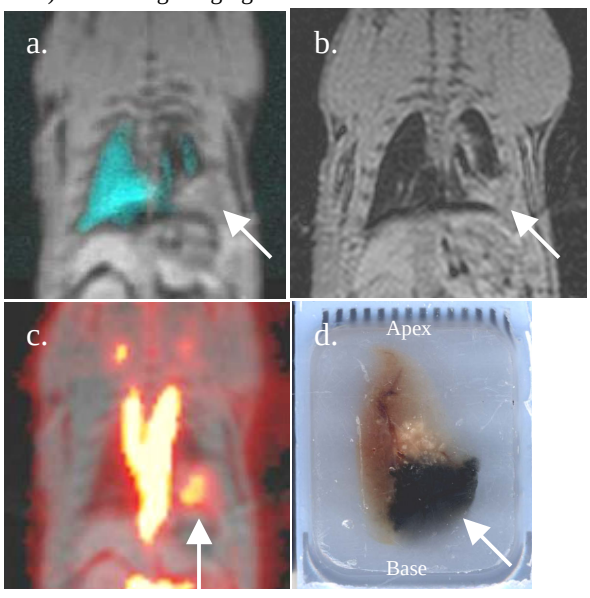
Materials

A custom ventilation system was used to deliver three air breaths to every Helium-3 breath to properly oxygenate the animal. A gated 2-d PR acquisition with full azimuthal sampling and 128 radial samples was used to acquire images over an 8cm field of view using a 1.5 T whole body MRI scanner with echospeed gradients and broadband capability (Signa LX, GE Medical Systems, Milwaukee, WI). Gating of the sequence was employed to average over several helium breaths to provide cine images over an effective time resolution of 75 msec of the breath cycle with an in-plane voxel size of 0.6 x 0.6 mm^2. A dual coil system was used to co-register He-3 ventilation images with T1-weighted images. Cartesian T1 weighted scans of TR/TE = 100 ms / 1.9 ms at 256 sampling density were acquired over a 12 cm FOV and at 0.5 mm slice thickness. This provided a nearly isotropic 0.5 mm voxel size for the detection of fluid buildup in the lungs. PET images were acquired on the UW Micropet P4 (Concorde Microsystems, Knoxville TN). A 90 minute dynamic [F-18]FDG imaging session was performed with a 2-3mCi/kg dose of the metabolic tracer. PET images were reconstructed with OSEM to a pixel size of 0.5 x 0.5 x 1.2 mm^3 with final image resolution of ~ 2mm FWHM. Animals were sensitized to ragweed pollen 3 weeks prior to imaging. Imaging was performed prior to a segmental challenge of the allergen to determine a normal state. Post challenge imaging was conducted 20hrs after the challenge to allow development of an allergic reaction simulating an asthmatic reaction. Following imaging, animals were sacrificed and the lungs excised and evaluated for inflammation.

Results

All images prior to allergen challenge showed no inflammation reactions or anomalous ventilation. However, the post-challenge He-3 ventilation image (Fig. 1a) shows a defect in the mid-left lobe of the lung. Corresponding fluid buildup in the mid-left lung is visible in the T1-weighted image of the same animal (Fig. 1b). A PET image of [F-18]FDG uptake indicates enhanced glucose metabolism in the corresponding region of the left lung (Fig. 1c). Tissue evaluations and the India Ink stained region confirm the location of the ragweed allergen insufflation and inflammatory reaction corresponds to the site of the anomalous ventilation and inflammation shown through imaging (Fig. 1d).

Figure 1: Images of the same animal following allergen challenge showing a) a defect in the He-3 MR ventilation image (blue) co-registered to T1-weighted proton density b) increased fluid build-up in the T1-weighted MR image and c) increased glucose metabolism in the [F18]-FDG PET image (hot metal) co-registered to T1-weighted MR, all in the same region of the left lung. d) Left lateral lung tissue sample showing location of challenge insufflation (black India Ink stain) confirming imaging results.



Discussion and Conclusions

We have successfully visualized and correlated the ventilation, inflammation, and glucose metabolism for a segmental asthma-like response in a small animal model. These methods allow for disease characterization and treatment in longitudinal studies. Future work will quantify measured MRI response to tissue histology and [F-18]FDG-PET.

References

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