Respiratory-Gated 3D Hybrid PR for Hyperpolarized He-3 Ventilation Imaging in Asthma-like Small Animal Model

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Intro

Asthma presents a major burden on the health system as incidences continue to increase globally [1]. Respiratory-gated small animal hyperpolarized He-3 MRI has been demonstrated for excellent depiction of relative ventilation in small animals [2,3]. The use of fusion imaging for study of the lungs has previously been demonstrated in small animals [4,5]. A BN (Brown Norway) rat model has been developed showing reduced lung function, increased airway resistance, spontaneous airway closure, gas trapping, and airway remodeling features consistent with chronic asthma in humans [6]. We demonstrate the use of fusion imaging for detection of regional variations in ventilation and correlation to lung structure.

Methods

MR imaging was performed on a standard 1.5 T whole body scanner with broadband capability (GE Health Care, Milwaukee WI). Animals were sedated, intubated, and ventilated during He-3 and T1-weighted MRI. A custom ventilation system was used to allow proper oxygenation of the animal He-3 MRI. Hyperpolarized He-3 MRI was performed using a respiratory-gated 3D Hybrid PR sequence with projection acquisition in the coronal plane and centric filling in Z. He-3 imaging parameters included TR/TE = 12.5/2.9 msec, ~7 deg flip angle, 14 cm FOV, 160 readout points, 8.93 KHz BW, 24 x 4mm slices in Z, and total imaging time of 11 min. The He-3 MR ventilation data was reconstructed into 12 x 150 msec phases to allow detection of dynamic ventilation changes and to better resolve the lung structure. Anatomical information was found using T1-weighted FGRE MRI with TR/TE = 100 / 1.9 ms, 12 cm FOV, 256 readout points, and 0.5 mm slice thickness. Images were then manually coregistered using fiducial markers. Six animals (3 asthma-like and 3 controls) were studied and all animal procedures were approved by the Animal Use and Care Committee. Asthma-like rats were inoculated with Sendai virus (parainfluenza type 1) at 3-4 weeks of age leading to chronic airway dysfunction by 11 weeks. Following *in vivo* imaging, animals were sacrificed, lungs extracted and fixed in formalin. Lungs were then imaged using a T1 weighted FSE sequence that was co-registered to the ventilation image to aid in guided histology to ascertain the mechanisms of regional variations in ventilation. Also microCT was performed on the excised lungs to determine airway structure.

Results

Results for a typical asthma-like animal and control are shown in Figure 1. Ventilation defects that match the uniformly scattered defects found in recent work on human asthma [7] are found in the asthma models (Figure a-c, arrows). No such defects were found in control animals (Figure 1 d-f). The regions of high and low ventilation are being explored with histological sections.

Conclusions

In vivo fusion imaging or He-3 ventilation and T1-weighted MR has been demonstrated for detection and locating of the regional variations in a small animal model for human asthma. Use of the 3D He-3 image acquisition allowed detection of regional ventilation defects in asthma-like animals with no such defects found in controls. The use of noninvasive imaging and proper ventilation allow the opportunity for longitudinal studies in the same animals to examine regional changes over time or therapy. In addition, ex vivo T1-weighted imaging of the excised lungs fused to the in vivo ventilation data can enable guided histological sampling to determine mechanisms for regional ventilation variations. Future work will include comparisons of imaging results to histological samples comparing ventilated to non-ventilated regions.

References

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Figure 1. Co-registered asthma-like He-3 ventilation (hot metal) and T1-weighted coronal posterior a), coronal anterior b) and axial images c) showing ventilation defects (arrows). d)-f) Corresponding image slices of control animal with no ventilation defects present in the lungs.

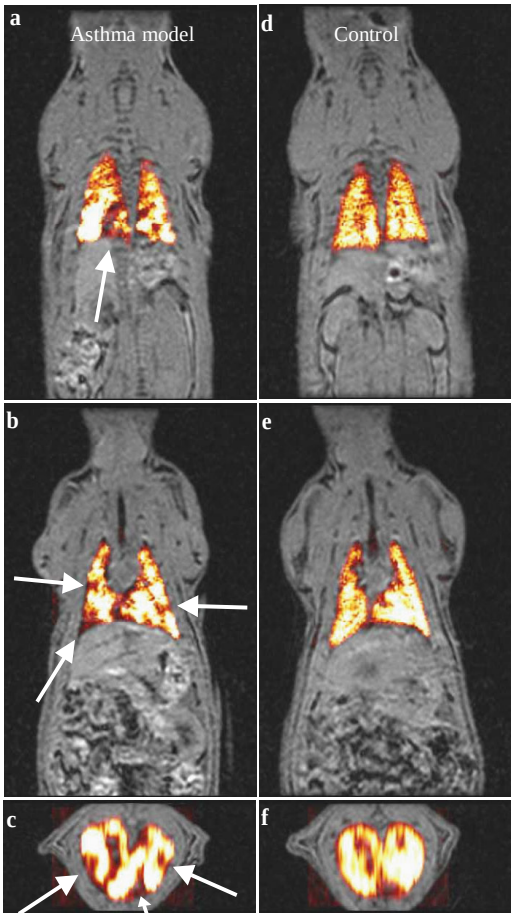

Figure 2. Dynamic ventilation images over time a)-c) asthma model and d)-f) control animal.