Comparison of regional ventilation defect distribution between oxygen-enhanced and hyperpolarized He-3 MRI

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TARGET AUDIENCE: Radiologists, clinicians, and image scientists interested in the clinical evaluation of ventilation in obstructive lung disease.

PURPOSE: Oxygen Enhanced MRI with 3D radial ultrashort echo time (OE-MRI) is an emerging technique for the evaluation of lung ventilation[1]. Contrast corresponding to ventilation may be achieved in patients due to the paramagnetic T1 shortening effect of breathing different concentrations of O_2. OE-MRI holds potential for rapid clinical translation due to the cost effectiveness and simple imaging protocols required, however, the accuracy of OE-MRI compared to other MRI methods such as hyperpolarized noble gas MRI (HP-MRI)[2] has yet to be demonstrated. The purpose of this work is to directly compare the heterogeneity of ventilation as characterized with OE-MRI against HP-MRI in a cohort of cystic fibrosis (CF) patients.

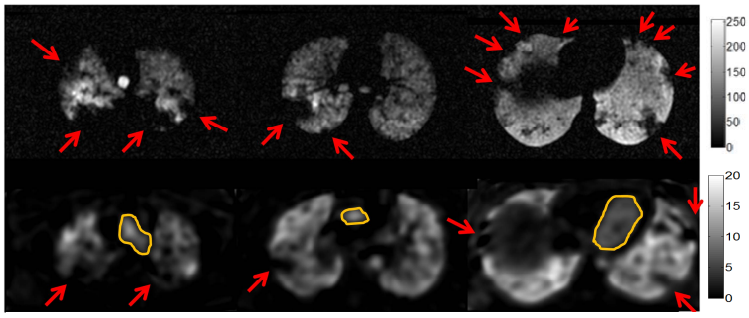

Figure 1: HP-MRI (top) and corresponding OE-MRI (bottom) images of ventilation for a subject with identifiable defects. Ventilation defects identified are highlighted with red arrows. The oxygenated blood pool in OE-MRI is highlighted in orange. The scale in HP-MRI is signal intensity, while for OE-MRI the scale is Percent Signal Enhancement.

METHODS:

HP-MRI: Five subjects with CF were recruited for this HIPAA compliant and IRB approved human study. 2D He-3 HP-MRI images (V_{He}) were acquired in a stack of contiguous slices under the following scan parameters: 1.56 x 1.56 x 10 mm, FOV = 40 cm, TR = 6.5 ms, TE = 2.9 ms, flip angle = 9°, with a dedicated He-3 rigid body coil (Rapid Biomedical GmbH, Rimpar, Germany). Images were acquired in a single 15 s breath hold. For structural reference, a stack of 2D slices (V_{struct}) on the proton channel was acquired with the same resolution and field of view.

OE-MRI: subjects also underwent back to back OE-MRI scans with the following scan parameters: 3.2 mm isotropic resolution, FOV = 32 cm^3, TR = 2.9 ms, TE = 0.080 ms, flip angle = 8°, with an 8-channel cardiac surface coil (GE Healthcare, Waukesha, WI). OE-MRI required 9 minutes (3.5 minutes at 21% O_2 to acquire V_{021}, a two minute wash-in period, followed by 3.5 minutes at 100% O_2 to acquire V_{100}) while subjects breathed freely under prospective respiratory gating to end-expiration with a 50% acceptance window. V_{021} and V_{100} images were reconstructed offline and Fermi filtered to 1 cm isotropic resolution. V_{021} was then registered to V_{100} using the ANTs deformable registration toolkit[3]. The OE-MRI volume (V_{OE}) was calculated as the percent change between V_{021} and V_{100}[4].

Analysis: The axial slices from V_{100} and V_{OE} that had the best structural agreement with V_{struct} on visual inspection were selected for further analysis. These slices were then deformably co-registered using ANTs to ensure matching spatial coordinates of the OE-MRI and HP-MRI images. A radiologist with 6 years experience blindly and independently identified ventilation defects **(fig. 1)** on both V_{OE} and V_{He}. In addition, voxelwise comparison of V_{He} and V_{OE} signal intensities was made utilizing masked lung volumes generated using a fully automated 3D region growing algorithm written in Matlab[5]. A Spearman's rank sum correlation coefficient was calculated to compare observed signal of ventilation.

RESULTS: Of the 158 total ventilation defects identified, 52 (33%) occurred in both imaging techniques, while 70 (44%) appeared in HP-MRI only, and 36 (23%) appeared with OE-MRI only. The voxel-wise correlation coefficient, R, between HP-MRI and OE-MRI was statistically significant for all subjects but with a low to moderate degree of correlation (mean R = 0.36 ± 0.10; **table 1**).

Subject ID	R	P
1	0.29	$< 10e^{-5}$
2	0.26	$< 10e^{-5}$
3	0.39	$< 10e^{-5}$
4	0.51	$< 10e^{-5}$
5	0.38	$< 10e^{-5}$

Table 1: voxelwise Spearman's correlation coefficient (R) and associated P values between OE-MRI and HP-MRI.

DISCUSSION: The high number of defects present on OE-MRI that also appeared on HP-MRI demonstrates the potential of this technique as an alternative to HP-MRI. However, given that the largest portion of ventilation defects identified were present on HP-MRI alone, a comparatively greater sensitivity of the HP-MRI technique compared to OE-MRI may be concluded. This might be explained by the higher SNR and in-plane spatial resolution of HP-MRI. The OE-MRI method required low-pass filtering which could blur many of the smaller defects that are readily identified on HP-MRI. In addition, the physiology of the two scans is likely to differ, given the very different time scales of the two MRI acquisitions. OE-MRI may allow for oxygen to wash-in to partially obstructed ventilation defects over the 3 minute scan, better reflecting steady-state gas ventilation with diminished contrast between V_{021} and V_{100}. Alternatively, the short 15 s breath-hold of HP-MRI captures only a snap-shot of ventilation prior to late-filling of partially obstructed defects. It is likely that the degree of perfusion weighting in OE-MRI influences the contrast between normal and defected regions on OE-MRI. In any case, the modest correlation coefficient between regional images of ventilation suggests an oxygen enhanced model where a mechanism outside pure ventilation has a nontrivial contribution to the OE-MRI signal.

CONCLUSIONS: To our knowledge, this is the first study comparing HP-MRI and OE-MRI to evaluate regional ventilation defects. The whole-lung coverage provided by 3D radial OE-MRI could be readily compared to HP-MRI as a reference standard. OE-MRI shows promise as an inexpensive alternative for depicting regions of ventilation defect. Although correlation coefficients were low to moderate, it is anticipated that further advancements in data acquisition will improve the capability of OE-MRI in the evaluation of regional defects in lung disease.

REFERENCES: [1] Kruger SJ, *MRM;* submitted for publication. **[2]** Fain SB, *JMRI* 2010. **[3]** Avants BB, *Neuroimage* 2011; **[4]** Edelman RR, *Nat Med* 1996. **[5]** Matlab v7.9.0, the MathWorks Inc. 2010