Hyperpolarized ^{3}He Magnetic Resonance Imaging of Ventilation Defect Volume Variability in COPD

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INTRODUCTION: The use of hyperpolarized helium-3 magnetic resonance imaging (^{3}He MRI) to measure whole lung ventilation and regional ventilation defects in COPD has been undertaken by a number of research groups and recently at our center in an assessment of 25 age-matched subjects stratified by disease (1). It has been previously established in a wide range of respiratory diseases that whole lung and regional ventilation defects can be visualized using ^{3}He MRI and a number of attempts have been made to quantify regional ventilation defects by objective scoring (2) and image processing techniques (3). In this work, we present ^{3}He MRI measures and same-day and 7-day scan-rescan variability of whole lung ventilation and center-slice ventilation defects in patients with COPD and age-matched healthy volunteers. The results indicate that regional ventilation measurements obtained by helium MR have high reproducibility when evaluated from scans acquired on the same day. For repeated scans acquired 7 days later, ventilation defect volumes are highly reproducible in most patients and healthy subjects but overall reproducibility is lower. Correlations between ventilation defect volumes and measurements of baseline FEV_1 are also assessed. We suggest that this is due to differences in ventilation defect volume within 7 days in a few specific patients and that these differences are physiological in nature and not due to image analysis or image acquisition changes. This finding has implications for the use of ventilation defects and whole lung volume in longitudinal studies of COPD and suggests that even in stable patients with COPD, regional ventilation volumes and defect volumes may change over short periods of time.

METHODS: Imaging was performed at 3.0 Tesla (General Electric Health Care GEHC) using pure hyperpolarized helium (35%) provided by a turn-key spin-exchange polarizing system (Helispin®, GEHC). The gas was administered mixed 1/3 with medical nitrogen as previously described (1). Single-slice images from a diffusion-weighted series were obtained in the coronal plane using a fast gradient-echo method (TE=1.2 ms, TR=4 ms, 128 x 128). All subjects performed same-day reproducibility scanning and twenty three subjects returned within 7+/-2 days for a final scanning session. Spirometry was performed pre- and post-MRI. For whole lung ventilation volume analysis, MRI volumes were imported into 3DQuantify and for all image slices the ^{3}He signal was manually outlined as previously described (1). For ventilation defect analysis, the centre slice ^{3}He image was directly compared to the centre slice ^{1}H image and individual ventilation defects were scored as areas with no ^{3}He signal that resided within the thoracic cavity and manually outlined as previously described (1). Total centre slice ventilation defect volume was calculated as the sum of all defect volumes in the centre slice. Reproducibility was assessed for same-day and 7-day repeated scans using the Intraclass Correlation Coefficient and Lin's Concordance Coefficient. Linear regression was used to assess the association between centre slice defect volume and pulmonary function measurements.

RESULTS: Overall same-day and 7-day reproducibility of ventilation defect volumes provided in Table 1 using the ICC and LCCC show that same-day reproducibility is high, and 7-day scan reproducibility is lower than same-day results. Upon review of all individual subject measurements it is clear that for some subjects, 7-day rescan images do indeed differ from baseline scan and rescan images, and this resulted in different ventilation defect volumes calculated. The association between baseline ventilation defect volume with pulmonary function measurements evaluated for individual subject groups are provided in Table 2 and indicate that ventilation defect volume is highly associated with pulmonary function measures.

DISCUSSION: The longitudinal assessment of COPD patients using spirometry suggests that global lung function measurements vary little in stable patients, with progressive declining function over time. ^{3}He MRI offers another indirect but regional measure of ventilation volume and ventilation defects. In this study we show same-day reproducibility for centre slice defect volumes that is high and lower 7-day reproducibility. Upon analysis of individual patient images we find that most subjects have highly reproducible same-day and 7-day results and a few subjects (n=6) show greater variability. We suggest that the image differences are due to physiological changes that have occurred in these specific subjects and although global pulmonary function measurements are not different, regional ventilation changes have occurred. This may have implications for the use of ^{3}He MRI in longitudinal studies and suggests that even in stable patients with COPD, regional ventilation volumes and defect volumes change over short periods of time, that are not reflected by standard spirometry measures of global pulmonary function.

REFERENCES:1)Parraga et al *Invest Radiology* 2006 Sub. 2) S. Samee et al. *J.Allergy Clin.Immunol.* 2003;111:1205-1211.3) N. Woodhouse et al *J.Magn Reson.Imaging 2005;* 21:365-369. **ACKNOWLEDGEMENTS:** Supported by the Ontario Research and Development Challenge Fund, the Canadian Institutes of Health Research, Robarts Research Institute, Merck Research Laboratories and Merck Frosst Canada Limited. The helium polarizer was made available to Robarts by Merck Research Laboratories through an agreement between Merck and General Electric Health Care. We thank Wilfred Lam, Cyndi Harper-Little, Liz Lorusso and Alexei Ouriadov for assistance with MRI data acquisition and Sandra Halko and Christine Piechowicz for clinical coordination and subject recruitment.

	Same Day Scan-Rescan		7-Day Scan-Rescan	
	ICC	LCCC	ICC	LCCC
Ventilation Defect Volume				
Mild-Moderate COPD (n=9)	.94	.94	.59	.62
Severe COPD (n=8)	.96	.96	.63	.58
ALL (n=25)	.97	.98	.74	.75

Table 1. Same Day and 7-Day scan-rescan variability o centre slice ventilation defect volume for mild-moderate severe COPD subjects

	Pearson Correlations Pulmonary Function Measurements				
Ventilation Defect Volume	FEV_1	FVC	Day Peak Flow	Night Peak Flow	FEV1/FVC
Healthy Volunteers (n=8)	-.63	-.56			-.23
Mild-Moderate COPD (n=9)	-.12	0	-.37	-.37	-.1
Severe COPD (n=8)	-.72	-.3	-.61	-.32	-.76
ALL (n=25)	-.61	-.3	-.62	-.52	-.71

Table 2. Ventilation Defect Volume Associations with Pulmonary Function Measurements