INTER-OBSERVER REPRODUCIBILITY OF LONGITUDINAL HYPERPOLARIZED HELIUM-3 MAGNETIC RESONANCE IMAGING OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Purpose

There is an increasing need for the characterization of disease through longitudinal imaging studies and in particular in Chronic Obstructive Pulmonary Disease (COPD), as pulmonary imaging is playing an important role in clinical trials and disease progression studies. However, imaging measurements are known to be biased under conditions of low signal-to-noise ratio (SNR) and because of observer or measurement error. To better understand the limitations of hyperpolarized Helium-3 Magnetic Resonance Imaging (^{3}He MRI) in longitudinal COPD studies, the objective of this work was to determine the associations between longitudinal ^{3}He MRI measurement changes, with image SNR and inter-observer variability.

Materials and Methods

Subjects: Fifteen COPD subjects were enrolled from the local tertiary health care center and from COPD clinics at three local teaching hospitals. COPD subjects were enrolled who were current non-smokers, categorized according to GOLD criteria, required a disease diagnosis of at least one year, and a smoking history of at least 10-pack-years.

Imaging: Hyperpolarized ^{3}He gas was provided by a turn-key, spin-exchange polarizer system. Doses (5 mL/kg) were administered in 1 L plastic bags diluted with ultrahigh purity, medical grade nitrogen. Magnetic resonance imaging was performed on a whole body 3.0 Tesla Excite 12.0 MRI system with broadband imaging capability. For ventilation or T1-unweighted imaging, multi-slice coronal images were obtained using the fast gradient-echo method with centric k-space sampling (14s total data acquisition, TR/TE/flip angle = 4.3 ms/1.4 ms/7°, BW = 31.25, FOV = 40 x 40 cm, matrix 128 x 128, 14 slices, 15 mm slice thickness, 0 cm gap) for the simultaneous acquisition of a ventilation image (no T_1-weighted sensitization) and a T_1-weighted image.

Image Analysis: Two observers blinded to subject identity, disease status and timepoint, analyzed images in an image visualization environment (digital copy) with room lighting levels equivalently established for all image analysis sessions. T1-unweighted images were examined for manual segmentation of the defects using custom-designed image visualization software. Ventilation defect volume (VDV) was determined by manual segmentation of regions of signal void, known as ventilation defects, in all slices following two-dimensional rigid single point image registration of the ^{1}H and ^{3}He slices based on the carina. Observer reproducibility was evaluated for two different observers using the interclass correlation coefficient (ICC), coefficient of variation (COV) and linear regression (r^2). SNR was determined by calculating the mean pixel value inside a 10 by 10 voxel region of interest (ROI) for four representative regions inside the lung parenchyma, and dividing by the standard deviation of the mean pixel values inside a ROI of the same size at the four corners. SNR was determined for each slice and then averaged to obtain a single SNR value for each subject at each time point.

Results

Significant increases in ^{3}He MRI VDV were detected at follow-up for both Observer 1 (p=.007) and Observer 2 (p=.005). There was no significant relationship between the changes in SNR and the changes in VDV for Observer 1 (r=-.17, p=.55) or for Observer 2 (r=.15, p=.59). As shown in Figure 1A, inter-observer reproducibility was determined for two observers for VDV; ICC= .93, COV= 26% and r^2= .78 (p<.0001). Additionally, there was no significant relationship between image SNR and inter-observer variability for VDV (r=-.06, p=.75) (Figure 1B, Figure 2).

Conclusions

Inter-observer reproducibility was determined to be high, and there was no association between inter-observer variability and SNR. Therefore we can conclude that the variability in observer's measurements were not affected by image SNR and increases in VDV measurements at follow-up may reflect functional changes within the airways of the COPD ex-smokers, suggestive of disease progression.

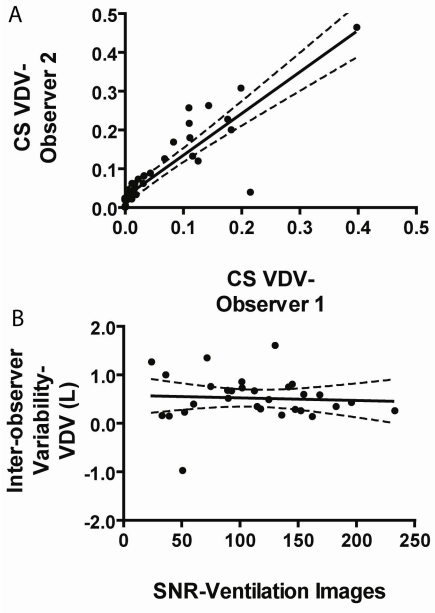

Figure 1. Relationship between center slice ventilation defect volume (CS VDV) for two observers (A), and the relationship between inter-observer variability and SNR (B)

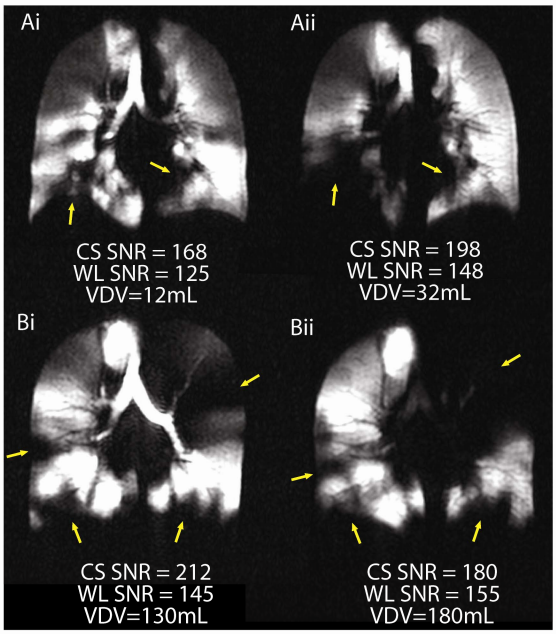

Figure 2. Comparison of SNR and VDV measurements for two representative subjects at BL (i) and FU(ii)