Gas Diffusion Image Reduction Metric with Improved Sensitivity to Heterogeneous Lung Disease

A. Samiee[1], S. J. Kadlecek[2], K. Emami[2], Y. Xu[2], H. Hamedani[3], Y. Xin[2], P. Mongkolwisetwara[2], N. N. Kuzma[2], P. Magnusson[4], L. V. Søgaard[4], S. Diaz[5], W. Miller[6], M. D. Rossman[7], M. Ishii[8], and R. R. Rizi[2]

[1]Mechanical and Aerospace Engineering, University of California, San Diego, San Diego, CA, United States, [2]Radiology, University of Pennsylvania, Philadelphia, PA, United States, [3]Radiology, University of Pennsylvania, Philadelphia, Philadelphia, United States, [4]Danish Research Centre for Magnetic Resonance, Copenhagen University Hospital Hvidovre, Hvidovre, Denmark, [5]Department of Clinical Sciences, Malmö University Hospital, Malmö, Sweden, [6]Department of Radiology, University of Virginia, Charlottesville, Virginia, United States, [7]Pulmonary, Allergy & Critical Care Division, University of Pennsylvania, Philadelphia, PA, United States, [8]Otolaryngology–Head & Neck Surgery, Johns Hopkins University, Baltimore, MD, United States

INTRODUCTION: Early diagnosis of emphysema, characterized by breakdown of the alveolar walls, is implausible by conventional standard clinical tests. MRI-based imaging techniques based on hyperpolarized (HP) gas technology, e.g. ^{3}He, have been developed capable of quantitatively assessing the free-motion of respiratory gas molecules in the lung. A robust and sensitive algorithm however is required to reduce these measurements to scalar metrics that can differentiate between the healthy and potentially at-risk populations. HP gas MR images sensitive to Apparent Diffusion Coefficient (ADC) of gas species indicate the extent to which atoms can diffuse freely in the lung. In an emphysematous lung, destruction of alveolar walls results in relatively larger air spaces and higher ADC values. The most commonly used metric obtained from ^{3}He MRI is the mean of the ADC distribution. Two small-scale studies suggest more sensitivity of this metric to early emphysematous changes than any other modality. Despite being universal and straightforward, this approach can undesirably mask regional distributions of abnormalities, especially when they are dominated by surrounding normal regions. This work presents a sensitive scalar metric from ADC distribution of the lungs to effectively distinguish subjects with abnormal pulmonary function from healthy subjects.

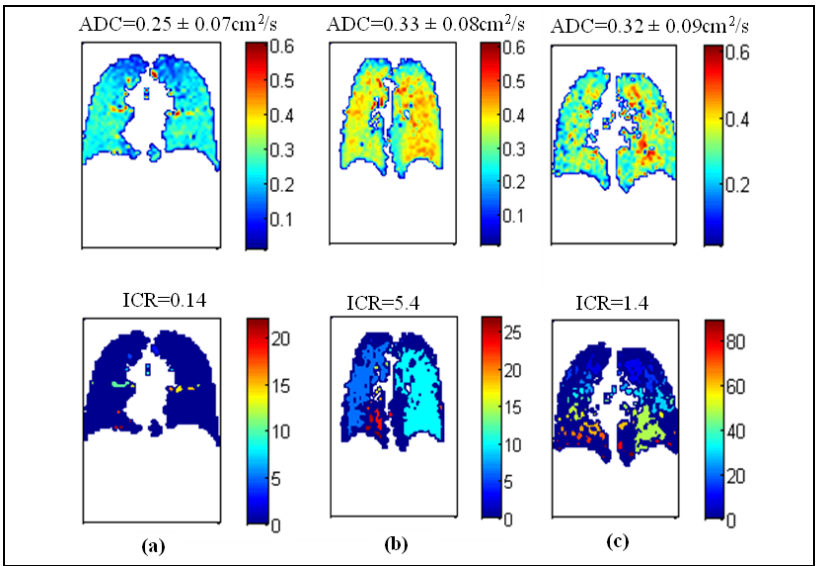

Figure 1. Apparent diffusion coefficient map (ADC, top) and connected regions map (ICR, bottom) for a representative (a) healthy subject, (b) smoker, and (c) COPD patient.

METHODS: A scalar number is derived from the ADC distribution in the lungs, termed the *Index of Connected Regions* (ICR). Voxels are selected from the ADC map exceeding a cutoff value, as determined from images of healthy control subjects. Connected clusters of above-threshold voxels in each slice of the lung are identified, and the volume of each region normalized to the total lung volume is calculated. We define the ICR index as: $ICR = (V_1^k + V_2^k + \ldots + V_n^k)^{1/k} / V$, where V_i is the volume of the i^{th} connected region, V is the total lung volume on the corresponding slice, and k is the adjustment order of the relative weight of the small and large regions. **Figure 1** shows ADC maps and connected region maps of a representative healthy, smoker and COPD subjects. A cutoff threshold of 0.35 cm^2/s was employed to generate these plots. For $k > 1$, the small-volume regions, which are more likely to arise from low SNR and thresholding noise, have insignificant weight on the value of ICR. This results in an ICR value dominated by large connected regions. For $k = 1$, the metric is simply reduced to thresholding approaches common to CT evaluation of emphysema. Preliminary analysis suggests that k=2 is a more effective choice, as it properly distinguishes common forms of disease while maintaining a reasonable insensitivity to noise.

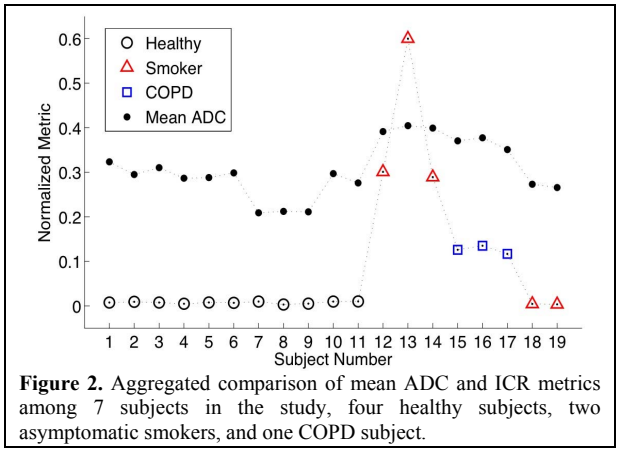

Figure 2. Aggregated comparison of mean ADC and ICR metrics among 7 subjects in the study, four healthy subjects, two asymptomatic smokers, and one COPD subject.

RESULTS: Shown in **Figure 2** are the normalized values of mean ADC and ICR for 19 aggregated studies (consisting of both separate and repeat measurements on subjects from each of the listed three groups). Results suggest that, unlike the mean ADC, ICR metric can effectively differentiate normal lungs from the abnormal ones. In other words, lung ADC map is reduced to a scalar metric in such a way that large regions of apparent abnormal behavior are weighted more heavily than a set of smaller regions comprising the same volume. This has the effect of reducing the effect of single- or few-voxel areas, which are more likely biased by noise or normal anatomical features (e.g., airways). We propose that this technique greatly increases the dynamic range between normal and diseased subjects with more heterogeneous distribution of lung disease, as shown in **Figure 2**. Note the rapid increase in ICR in the disease population as compared to the subtler change in mean ADC due to utilization of imaging information in the detection of emphysematous regions. Measurements 18 and 19 belong to one athlete asymptomatic smoker who showed a very similar response to healthy subjects. **Figure 3** demonstrates that the ICR value of the healthy group is more significantly different from that of the unhealthy group, when compared to mean ADC values, even though the asymptomatic smoker is pooled with the other two unhealthy individuals.

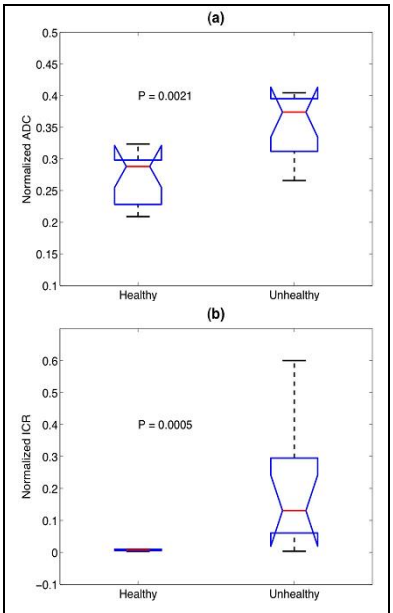

Figure 3. Comparison of group statistics for the normalized mean ADC and ICR Emphysema Index between the healthy and unhealthy groups.

CONCLUSION: We have introduced a metric to reliably identify unhealthy lungs based on the emphysema-induced heterogeneity of respiratory gas ADC distribution. This methods can be potentially applied to other HP gas MRI measurements (e.g. ventilation or oxygen tension images) as well as other modalities such as CT. Since apical dominance and other regional patterns are known to be an important and reproducible characteristic of emphysema, we hypothesize that the methods, which are specifically sensitive to localized parameter elevation can be more indicative of early progression of disease and can help distinguish disease phenotypes.