Purpose: Alpha-1 antitrypsin deficiency (AATD) affects approximately 1 in 1500 people of European descent and is characterized by predominate basal lung emphysema which manifests early in life. This study builds upon previous studies in AATD which examine apparent diffusion coefficients (ADC) using a single diffusion weight. We extend the traditional single diffusion weighted ADC approach into the MRI morphometry approach which employs multiple diffusion weights to probe mean airspace lengths across an imaging voxel. We hypothesize that patients with AATD would show significantly elevated mean linear intercept ($L_m$) values as compared to COPD ex-smokers and healthy never-smokers.

Materials and Methods: Seven subjects with a diagnosis of AATD, eight COPD ex-smokers with radiographic evidence of emphysema and 5 never-smokers provided written informed consent to a study protocol approved by a local research ethics board and Health Canada. Subjects were evaluated using spirometry, plethysmography, thoracic imaging, the St. George’s Respiratory Questionnaire (SGRQ) and 6-minute walk test. MRI was performed on a whole body 3T system and $^1$H anatomical, $^3$He static ventilation and $^3$He diffusion images were acquired for all subjects. A custom built IDL algorithm was used to fit the diffusion weighted images to a known signal decay equation and obtain MRI measurements of an $L_m$. Regional measurements were computed using custom built MATLAB software after exporting the results outputted by IDL. Differences between subgroups were evaluated using ANOVA performed in Graphpad Prism V6.02. Post-hoc multiple comparison tests were performed using a post-hoc Tukey test. Results were considered significant when the probability of making a Type 1 error was less than 5% ($p<.05$).

Results: There were significant differences between all three subgroups across spirometry, plethysmography, CT evidence of emphysema, and $^3$He MRI diffusion measurements. Post-Hoc multiple comparisons show no difference in spirometry or CT measurements between COPD ex-smokers and AATD subjects ($p>.05$). However, AATD subjects show elevated $L_m$ values as compared to COPD ex-smokers ($p<.001$), this is accompanied by worse perceived patient quality of life as measured by SGRQ ($p=.02$). There was qualitative visual evidence of elevated $L_m$ values in the basal portion of the lung consistent with disease pathology but this apical/basal distribution was not significant ($p>.05$).

Conclusion: MRI derived mean linear intercept provides a sensitive measurement of airspace enlargement even in the case where spirometry and CT show no difference in disease severity.

References: