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Title: CT scan derived emphysema scores correlate with spirometry and gas exchange but not acute exacerbation rates (AER) or COPD assessment test (CAT) in COPD subjects with and without alpha-1-antitrypsin (AAT) deficiency

Dr. Ronald 3220 Dandurand rdandurand@videotron.ca MD [1], Dr. Tomás 3221 Carroll tcarroll@rcsi.ie [2], Dr. Raúl San José 3222 Estépar rjosest@bwh.harvard.edu [3], Dr. Jean 3223 Bourbeau jean.bourbeau@mcgill.ca MD [1] and Dr. David 3224 Eidelman david.h.eidelman@mcgill.ca MD [1]. [1] Montreal Chest Instiute and McGill University Health Centre, McGill University, Montreal, QC, Canada, H2X 2P4 ; [2] Department of Medicine, Royal College of Surgeons in Ireland, Dublin, Ireland and [3] Brigham and Woman's Hospital, Havard Medical School, Boston, MA, United States .

Body: We previously reported 24 patients with AAT deficiency (AATD) and found them not different from non-AATD subject in terms of lung function, AER and CAT scores. We aimed to expand our observations to include emphysema scores derived from thoracic CT scans. 23 genotyped subjects with serum AAT levels <1.15g/L (2 MS, 3 MZ, 2 SS, 1 ZZ, 15 MM) and 23 ≥1.15g/L had thoracic CT scans available. MM subjects were subdivided into serum AAT levels ≥ and < 0.91g/L as the $MM_{<0.91}$ group may have null or rare alleles and require SERPINA1 gene sequencing. Lung emphysema was determined using a threshold of -950 HU to define the low attenuation area percentage (LAA% (-950 HU)) and measured with Airway Inspector (www.airwayinspector.org). Demographics, physiology, AERs, CAT scores and LAA% (-950 HU) did not differ between groups. LAA% correlated with FEV_1 ($r=-0.42$, $p<0.01$), D_{Lco} ($r=-0.50$, $p<0.01$) and FEV_1/FVC ($r=-0.73$, $p<10^{-8}$, Figure 1) but not AER ($r=0.08$, $p=0.61$) or CAT scores ($r=-0.02$, $p=0.89$).

In this small group of COPD patients emphysema scores did not differ between those with and without AATD and correlated with the FEV_1, FEV_1/FVC and D_{Lco}. These results support the notion that airway-parenchymal interdependence is an important determinant of airflow obstruction in both AATD and non-AATD COPD patients.