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Copd 2018: The international debate on A new COPD phenotype characterized by hyperpolarized Xenon-129 MRI - Kun Qing- University of Virginia

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Purpose: Airway-predominant Chronic Bronchitis (CB) and alveolar-predominant Emphysema (EM) were regarded as major phenotypes of smoke-induced COPD. Routine clinical tools, including Pulmonary Function Tests (PFTs) and Computed Tomography (CT), have their limitations to characterize COPD. This study will characterize COPD phenotypes using a new imaging tool - hyperpolarized Xenon-129 (Xe129) MRI. Methods: 13 healthy and 33 COPD subjects were recruited and underwent PFT, CT. COPD patients were phenotyped into three groups by PFT percent diffusion capacity (%DLCO) and CT percent of EM lung tissue (%EM): 1) EM: low %DLCO and high %EM, 2) CB: high %DLCO and low %EM and 3) mixed indeterminate (IND) phenotype: low %DLCO but low %EM. Xe129 MRI was subsequently administered to determine airflow limitation by measuring percent of ventilation dead space (%VD) and alveolar gas uptake by measuring Xe129 diffused into interstitial tissue (tissue/gas ratio, reflecting lung tissue integrity) or into red blood cells (RBCs) (RBC/tissue ratio, reflecting gas exchange and pulmonary perfusion). Results & Discussion: Using the criteria described above, 18% of patients (6/33) were EM predominant; 21% (7/33) were CB phenotype and surprisingly, 61% (20/33) were IND phenotype. The IND group had %FEV1 substantially overlapped the CB group ($p>0.05$) and did not show significantly higher %VD than the control group ($p>0.05$). Also, no statistical differences were found in Xe129 tissue/gas ratios among the control, CB and the IND groups ($p>0.05$). However, the RBC/tissue ratios, measuring gas transfer from the interstitium further to the blood stream, were much lower in the mixed group as compared to all other groups ($p<0.05$). Conclusion: There seemed to be a new mixed phenotype of COPD identified in a majority of COPD patients, which had minimal emphysematous tissue destruction, but impaired gas exchange to the blood as indicated by Xe129 MRI.

The pulmonary function test (PFT) is used to diagnose chronic obstructive pulmonary disease (COPD). PFT is widely used to determine the extent of COPD and its therapeutic reaction. Complex mixing of COPD phenotypes, however, requires a diagnostic tool with the ability to assess roader aspects of lung pathophysiology, and this is the primary reason why PFTs do not provide sufficient correlation with disease status and progression to serve as a reliable surrogate endpoint. What's required is a validated and robust collection of COPD biomarkers that can provide COPD phenotyping and staging, quick response assessment to a wide range of therapies, and monitor disease progression.The expectation is that the hyperpolarized xenon magnetic resonance imaging (HXe MRI) would be able to diagnose and influence patients in the early stages of COPD, direct the selection of effective therapies and prolong life. Two assessments of the HXe MRI will be carried out in this proposal. A single sequence combining a high-resolution image of inhaled HXe with a proton image acquired

at the same breath-hold will result in compromised airflow for the fraction of the lung volume. A new imaging protocol that exploits the chemical shift sensitivity of xenon to the lung 's separate tissue compartments allows detailed mapping of exchanges of gas through the lung tissue and into red blood cells. We assume that these HXe MRI signatures will access physiological information

previously inaccessible through the conventional chest PFT and multimodality CT, (MDCT).We also believe that these picture signatures would boost our ability to determine phenotypes of COPD and the status of the disease better than the PFT and MDCT. Higher resolution of the HXe MRI based on the lung anatomy will further increase the diagnostic sensitivity and specificity. Chronic Obstructive Pulmonary Disease (COPD) is a complex condition whose development includes underlying physiological

and functional changes, many of which are not well established with the diagnostic studies currently available.We propose to develop comprehensive signatures of hyperpolarized xenon129 imaging and

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confirm that they can quantify the multifactorial components of the phenotype and severity of COPD disease and enable monitoring of patients with COPD diagnosis for meaningful changes in lung functions.Research and development of pulmonary xray computed tomographic (CT) and magnetic resonance imaging (MRI) was motivated, in part, by the quest for subphenotyping common chronic lung diseases such as chronic obstructive pulmonary disease (COPD).Disease biomarkers that go beyond anatomy and structure to include pulmonary functional measurements such as regional ventilation, perfusion, and inflammation are being validated for thoracic CT and MRI, the main COPD research instruments. Furthermore, there was also a push to enhance spatial and contrast resolution while at the same time reducing or eliminating exposure to radiation.This review therefore focuses on our evolving understanding of patient relevant and clinically important COPD endpoints, and how current and emerging MRI and CT tools and measurements can be used to identify , quantify and utilize them.Because reviews of pulmonary CT and MRI imaging physics and reviews of other COPD imaging approaches have been previously pu blished and well outlined, we are concentrating on the existing clinical issues in COPD and the potential for newly developed applications of MR and CT imaging to solve these. Here we summarize the methods of MRI and CT imaging and their clinical translation for generating

reproducible and sensitive COPD measurements related to pulmonary ventilation and perfusion as well as morphology of parenchyma. COPD 's main clinical issues provide an essential context within which pulmonary imaging needs to move quickly to tackle the staggering burden, costs, as well as COPD related mortality and morbidity.

Despite decades of research, there is a lack of therapies that modify progression or mortality from chronic obstructive pulmonary disease (COPD). Despite considerable efforts to discover and develop new COPD interventions, progress has been slow. In addition, while COPD is still diagnosed and categorized on the basis of symptoms

associated with chronic airflow limitations, these measures are weakly correlated with important clinical outcomes.A wide range of imaging methods can be used to research the pulmonary system, including those that rely on tissue absorption of x-ray radiation (chest x-ray and CT), radiofrequency stimulation (magnetic resonance imaging: MRI) or signals produced from radioactive particles injected or inhaled (simple gamma emission projection imaging, single photon emission tomography (SPECT) and positron emission).