Dr. R Graham Barr

COPD is the third leading cause of death globally and in the United States. The increase in COPD prevalence and mortality is unexplained, particularly among women and minorities. Medical therapies for COPD, however, exclusively target the airways and none affects emphysema or reduces mortality in COPD.

The Multi-Ethnic Study of Atherosclerosis (MESA) COPD Study tested the endothelial hypothesis of emphysema in humans and found that 1) pulmonary microvascular blood flow (PMBF) on magnetic resonance imaging (MRI) is reduced in mild, moderate and severe COPD and emphysema; 2) endothelial microparticles (EMPs) are increased and endothelial progenitor cells (EPCs) are reduced and 3) gene expression in the peripheral blood was strongly linked to PMBF. These findings support the endothelial hypothesis of emphysema and suggest the PMBF may be a fundamental and targetable imaging biomarker in emphysema and COPD.

The proposed study is a longitudinal continuation of the MESA COPD Study in which we aim to perform cardiopulmonary MRI and lung computed tomography (CT), assess regional oxygen tension and regional airflow using hyperpolarized helium (3He) and perform an interventional study to test the following hypotheses: 1) reduced PMBF in emphysematous COPD compared to controls is independent of local oxygen tension and regional ventilation assessed on 3He MRI and persists during the administration of supplemental oxygen to eliminate HPV; 2) cor pulmonale parvus has pulmonary vascular and systemic causes in emphysematous COPD: RV-EDV is associated with regional hypoxic pulmonary vasoconstriction assessed on 3He MRI and reduced systemic venous return to the RV assessed by IVC flow on MRI; RV-EDV will increase during administration of supplemental oxygen therapy; RV-EDV will increase with the use of tiotropium bromide; 3) 3-D registration of MR pulmonary perfusion and CT lung parenchymal images will demonstrate that regions of the lung that are hypoperfused develop emphysema.

Confirmation of these aims would provide clinical biomarkers of volume status in COPD, mechanisms to approach RV dysfunction, surrogate endpoints for clinical trials and provide a paradigm shift in COPD pathogenesis that justify testing of existing and novel therapies targeted to vascular function in COPD.