Application for Round-6 QIBA Project Funding

Title of Proposal: CT Lung Density Biomarker: Translating Phantom Harmonization to Clinical Practice		
QIBA Biomarker Committee/Task Force: Lung Density Biomarker Committee		
NIBIB Contract Objective(s) which this project addresses: Objectives 4, 5		
PI (Project Coordinator or Lead Investigator Information)		
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Total Amount Requested:		

Project Description

COPD is the third most common cause of death in the US, and the death rate is projected to increase over the next 20 years. CT density metrics, such as RA-950 and Perc15, have been widely studied as quantitative image biomarkers (QIB) for the diagnosis and monitoring of lung density changes due to emphysema (COPD). Scanner make and model remains a substantial source of variation in clinical CT densitometry of the lung. The QIBA Lung Density Committee is developing a Profile to provide specifications for CT lung densitometry, and has taken steps to address this challenge. The Committee has organized two rounds of phantom studies, using a custom-designed phantom (COPDGene 2) that incorporates a calibrated set of foams. Data were acquired from 4 scanner models, using 1 to 9 combinations of kVp and mAs protocols per scanner. Preliminary results have shown promising utility of a calibrated lung density phantom with calibrated foams in reducing the scanner variation to the 1 HU level. Because the densities of the reference foams in the COPDGene 2 phantom were uncalibrated, this phantom was retrospectively calibrated against a suite of 5 NIST traceable reference standard lung density foams (SRM-2088), covering the nominal range of -950 HU to -695 HU, incorporated into a new phantom (QIBA-SRM, Phantom Lab) with the same composition as the COPDGene 2 phantom. We request support to translate this phantom-based calibration to COPDGene, a multi-site, multi-vendor longitudinal clinical research trial.

COPDGene is designed to identify the genetic associations of COPD and characterize chest CT phenotypes in COPD subjects. In the first phase of COPDGene, 9,529 cigarette smokers with and without COPD underwent CT, and currently, in Phase 2, subjects are undergoing follow-up CT at 5 years. Differences in CT density measurements among CT models have been a significant source of variation in COPDGene, and harmonization of the measured values would be very helpful. The current CT protocol for COPDGene requires the use of a fixed dose of 200 mAs (average CTDIvol 7.6 mGy), but the study is transitioning to a reduced dose protocol (developed with the QIBA lung density committee) that uses automatic exposure control (AEC) and iterative reconstruction (IR) (CTDIvol 3.0 mGy). During this transition phase, subjects are being scanned with both protocols during the same visit, offering an opportunity to compare the harmonized measurements at conventional dose and reduced dose. To date we have scanned 170 COPDGene subjects with both reduced and conventional dose scans. Our phantom study showed that harmonization reduced standard deviation of multi-vendor phantom attenuation measurements by approximately 50%. However, we believe that use of human subject scans will increase scanner-related variation because of increased scatter from body habitus, and we estimate that in human subjects, harmonization will reduce the standard deviation of attenuation measurements by 5-20%.