Application for QIBA Project Funding

Title of Proposal: Quantifying variability in measurement of pulmonary nodule (solid, part-solid and ground glass) volume, longest diameter and CT attenuation resulting from differences in reconstruction thickness, reconstruction plane, and reconstruction algorithm.		
QIBA Committee/Subgroup: qCT		
NIBIB Task Number(s) which this project addresses: 5-7		
Project Coordinator or Lead Investigator Information:		
Last Name: Garg	First Name: Kavita	Degree(s): MD
Institution/Company: University of Colorado Denver, Department of Radiology		

Please check the primary category for this proposal from among the following:

- [x] 1. Identification of Technical Characteristics and Standards
  - [x] a. Creation and refinement of protocols for image acquisition, analysis, quality control, etc., for specific clinical utility
  - [x] b. Phantom development and testing
  - [x] c. Identification and assessment of intra-reader bias (1) and variance across scanners and centers
  - [x] d. Identification and assessment of inter-reader bias and variance across scanners and centers
  - [ ] e. Other
- [x] 2. Clinical Performance Groundwork
  - [x] a. Assessment of intra-reader sensitivity and specificity
  - [x] b. Assessment of inter-reader sensitivity and specificity
  - [x] c. Other
- [x] 3. Clinical Efficacy Groundwork
  - [x] a. Assessment of correlation between new biomarker and 'accepted-as-standard' method
  - [x] b. Characterization of value in clinical trials
  - [x] c. Characterization of value in clinical practice
  - [ ] d. Development/merger of databases from trials in support of qualification
  - [ ] e. Other
- [x] 4. Resources (money and/or people) committeed from other sources.

Clinical CT data will be from standard of care imaging of existing patients.
Vital Images / Vitrea software

Project Description:
Recently released initial results of the National Lung Screening Trial (NLST) show mortality reduction by 20% in the CT arm compared with CXR. If screening becomes widely adopted in those at high risk, follow-up investigation of positive scans will impose a major burden on the health care system. In patients with positive scans, a risk stratification strategy or quantitative analysis of lung nodules could reduce this burden by reducing the rate of follow-up in those who are determined to be at lower risk. Quantitative CT analysis for solid nodules has been attempted previously, however there is no significant data available for subsolid nodules. Adenocarcinoma is the most common histologic type of lung cancer which presents as a spectrum of nodules of varying attenuation including subsolid types. With better understanding of histopathology, it is now recommended that thin-section CT technique should be used for part solid lesions to record the size of a) the solid component and b) total tumor size including both solid and ground-glass components. Changes in shape, size and attenuation help determine follow-up and when intervention is appropriate. However, there are technique- and patient -related factors which potentially result in measurement variation of subsolid nodules. We have also observed significant nonlinearity in CT attenuation values (0-100HU), varying between models and devices.

This project attempts to find the causes and degree of variance in the measurement of part solid nodules. Two readers will measure nodule attenuation (HU and density histograms), volume and diameter per RECIST independently in random fashion. Lung phantom scans on a wide selection of CT scanners will be performed to assess inherent variability in nodule density between systems.

Hypothesis: There will be greater variability in measurement of subsolid nodules and solid component of part-solid nodules compared to solid nodules on thin-section CT. The measurement planes and algorithms will affect lesion diameters. Nonlinearities in CT density across systems may have an impact on classification of subsolid nodules.

Primary Objective: Define the variability in measurement of pulmonary nodule (solid, part-solid and ground glass nodules) volume, longest diameter and CT attenuation resulting from differences in reconstruction thickness, reconstruction plane, and reconstruction algorithm.

CT Technique: Helical CT imaging (using $\geq$ 16-slice MDCT) of the chest without intravenous contrast during inspiration (using routine chest CT protocol for lung nodules with following parameters). All clinical imaging performed on 16- or 64-slice scanner. Clinical and phantom data acquired using technique below.

Scan range: Lung apices through lung bases, Topogram (low-dose): 10 mA, 80 kVp, **kVp:**120, **mA:**80 to 100, scan time:0.5 sec, **mAs:**40 (BMI < 25kg/$m^{2)}$ or 50 for BMI > 25kg/m^2, Detector collimation:0.75 mm (16-channel or greater), Table increment:18 mm/rotation (16-channel), Pitch:< 1, Reconstructed slice thickness: 2.0 mm**,** Slice reconstruction interval:2.0 mm (contiguous). Images will be reconstructed at soft tissue (B30) and lung algorithms (B60) in axial, sagittal and coronal planes. Raw data will be saved to reconstruct images at different slice collimation (1 mm and 3 mm).

Analysis Technique: RECIST and nodule density measures performed via McKesson PACS, with automated volume segmentation using the Vital Images Lung Nodule Analysis toolkit.

Deliverables: Inter-and intra-observer variation in nodule diameter and volumes in 10 cases with subsolid nodules. Degree of variation in these measurements with different collimations, soft tissue and lung algorithms, during inspiration and expiration (when available) in 3 imaging planes. Degree of nonlinearity in phantom nodule density.

Timeline: -Within first 4 months (after project funding)

- Expedited IRB, phantom purchase, phantom nodule development
- Start clinical scans and nodule measurements

Next 4 months: nodule measurements and interim data analysis
Last 4 months: Final data analysis (intra- and inter-observer variation), compare RECIST with volumes, degree of variance of measurements with collimation, algorithms, during inspiration and expiration in different imaging planes and thicknesses. Evaluation of phantom data.