QIBA Lung Density Biomarker Committee

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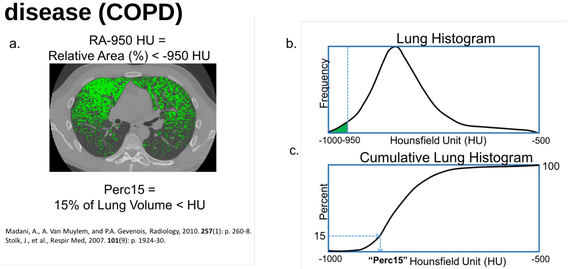
Quantitative Imaging Biomarkers Alliance — RSNA

Quantitation – Why and How

CT remains the gold standard for imaging-based phenotyping of chronic obstructive pulmonary disease (COPD)



Madani, A., A. Van Muylem, and P.A. Gevenois, Radiology, 2010. **257**(1): p. 260-8. Stolk, J., et al., Respir Med, 2007. **101**(9): p. 1924-30.

Fig. 1 - Lung density biomarkers of emphysema include:

a. The relative area of the lung with attenuation values lower than -950 Hounsfield Units (HU) at full inspiration (RA -950; **a,b**). Also referred to as low attenuation areas or LAA-950.

b. The 15th percentile point of the lung histogram, i.e. the cut off value in HU below which 15% of all voxels are distributed (Perc15; **c**)

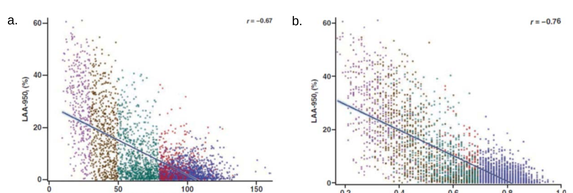


Fig. 2 – Correlation of LAA-950 with physiologic measurements from spirometry grouped by disease severity as measured by Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD) staging system for 4062 subjects.
a., Scatterplot shows LAA-950 on inspiratory CT, and forced expiratory volume in 1s (FEV1).
b., Scatterplot shows LAA-950 and ratio of FEV1 to forced vital capacity (FVC). Line shows best-fit linear correlation.

Blue = control subjects (smokers w/o COPD), red = subjects w/ GOLD stage 1, green = subjects w/ GOLD stage 2, brown = subjects w/ GOLD stage 3, purple = subjects w/ GOLD stage 4.

Schroeder, Joyce D., et al. "Relationships between airflow obstruction and quantitative CT measurements of emphysema, air trapping, and airways in subjects with and without chronic obstructive pulmonary disease." American Journal of Roentgenology 201.3 (2013): W460-W470.

Biomarker Committee Activities

Profile Development Status

Stage	Description
Biomarker Committee (BC) Drafting and Review	The Profile specifies requirements and guidance on best practices to achieve the performance stated in the claims.
Public Comment and Review	Stakeholders in the public domain offer constructive comment that is formally address by the BC.
Field Testing and Technical Confirmation	Profile is made available for testing at more than one facility, systems, and persons and is understood and shown to meet the specifications.
Claim Confirmed	Overall performance was determined and claim was achieved.

We are now releasing the Profile for public comment

CT Lung Density Profile Claims:

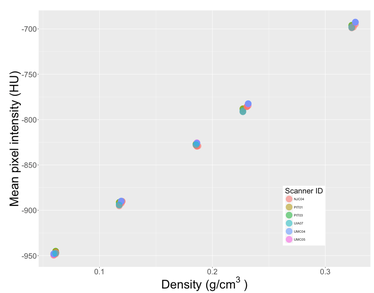
For detection of an increase in extent of emphysema with 95% confidence:

1. An increase in RA-950 of at least 3.7% is required without lung volume adjustment (VA),
2. A decrease in Perc15 of at least 18 HU is required without lung VA, and 11 HU with VA.

Initial Field Testing

QIBA-SRM phantoms (Fig.4) distributed to 5 COPDGene imaging sites → Phantoms scanned using COPDGene study protocol → Scanner and CT protocol specific calibrations computed based on NIST-certified reference materials → RA -950 and VA Perc15 values for COPDGene subjects scanned at these sites will be adjusted by phantom-based correction factor → Corrected results to be compared with lung function and other clinical parameters

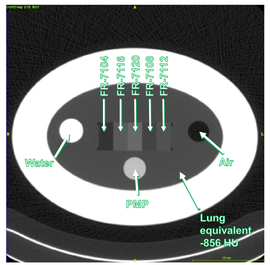
Fig. 3 – Scatterplot of known physical densities versus mean HU value in scans obtained at several COPD Gene imaging sites. Mean pixel intensities within NIST-certified foam materials in QIBA-SRM phantoms provide data for calculation of scanner-specific correction factors.



Other Recent and Current Groundwork Projects

QIBA-SRM Phantom Development and Testing

Fig. 4 - NIST Standard Reference Material SRM-2088 for scanner qualification. Foam inserts, machined from commercially available sheet stock (General Plastics, FR-7104, 7108, 7112, 7116 and 7120 – last two digits represent nominal density in lb/ft^3), have been certified for the physical density value in kg/m^3



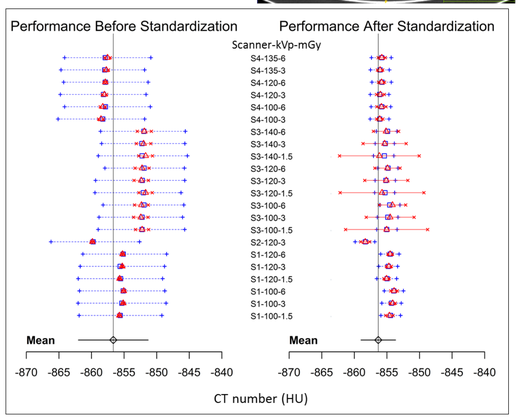
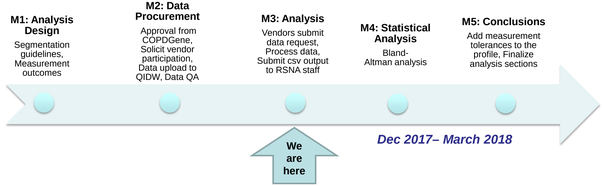


Fig. 5 - CT lung density measures vary with scanner calibration, x-ray spectrum and filtration. Harmonization with Linear Mixed Effects model shows improved accuracy and reduction in variability due to scanner and protocol. Data were obtained from a phantom study on CT scanners from 4 manufacturers with several protocols at various kVp and exposure settings. Red symbols and lines are the measured data points, and the blue ones are the predicted values using the Linear Mixed Effects model. The 95 % confidence intervals of the mean CT number is [-862.0 HU, -851.3 HU] before standardization, and [-859.0 HU, -853.7 HU] after standardization, shown as the error bars for the overall mean at the bottom.

Chen-Mayer, HH, et al. "Standardizing CT lung density measure across scanner manufacturers." Medical physics 44.3 (2017): 974-985.

Lung Density Software Reproducibility Study



Data Breakdown

- ✓ 100 COPDGene scans (50 subjects each w/ original protocol and reduced dose series)
- ✓ Uniform Gold Distribution across subjects (10 of each, 0-4 Gold)

Segmentation Criteria/Data Analysis

- ✓ Segmentation of the whole lung cavity, with right and left lung separation
- ✓ Segmentation removal of blood vessels and airways
- ✓ Generation of the image histogram for the remaining lung parenchymal tissues
- ✓ Calculation of the percentage of lung volume below the -950 HU threshold (RA -950 HU), HU value below which 15% (Perc15) of the total parenchymal tissue voxels fall, and the total lung volume.

Key Points/Assumptions

- ✓ 5-6 month timeline for remaining work
- ✓ QIDW used for CT data housing
- ✓ Participation from 14 vendors
  - ✓ RSNA shall remove identification
  - ✓ Sites shall specify commercial or open source academic and if data processing is fully- or semi-automatic

What We're Doing and How YOU Can Participate!

Specific Accomplishment and Plan	Organization Standing Activities
• Repeatability meta-analysis to define claims	• Bi-monthly QIBA Meetings and updates at RSNA
• Development of lung foam density standards for vendor testing and scanner qualification (QIBA-SRM phantom)	• CT scanner manufacturer updates: Toshiba, Siemens, Philips and GE representatives
• Groundwork and recommendations on lung inflation density corrections	• Software vendor updates: VIDA Diagnostics, Imbio LLC
• Development of statistical and physical harmonization methods	• Supplementary Funding Proposals
• Development of low CT dose protocols for chest using AEC and iterative reconstruction	• Updates to CT coordinating committee
• Drafting of biomarker profile	• Field testing at select COPD Gene imaging centers

For more information, please visit: http://qibawiki.rsna.org

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