QIBA Lung Density Biomarker Committee

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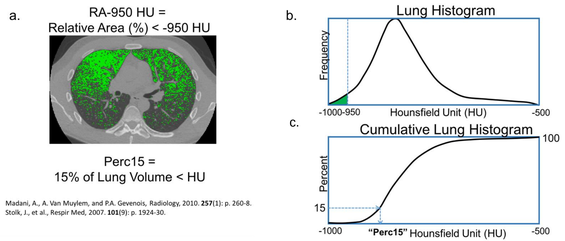
Quantitative Imaging Biomarkers Alliance — RSNA

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**)

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.

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.

Biomarker Committee Activities

QIBA-SRM Phantom Development and Testing

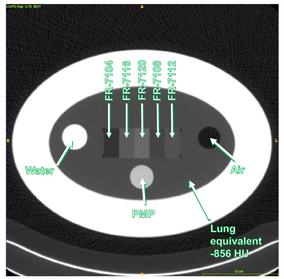


Fig. 2 - NIST Standard Reference Material SRM-2088 for scanner qualification. Foam inserts, machined from commercially available sheet stock (General Plastics, FR-7104, 7108, 7112, 7116 and 7120 – last two digits represent nominal density in lb/ft^3), have been certified for the physical density value in kg/m^3

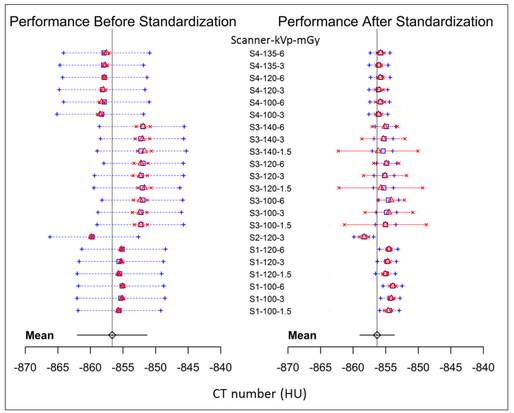


Fig. 3 - CT lung density measures vary with scanner calibration, x-ray spectrum and filtration. Harmonization with Linear Mixed Effects model shows improved accuracy and reduction in variability due to scanner and protocol. Data were obtained from a phantom study on CT scanners from 4 manufacturers with 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.

Other Recent and Ongoing Activities

Lung Density Software Reproducibility Study

- CT images from 50 participants from the COPDGene™ cohort study were selected for analysis; n=10 participants across each GOLD grade (GOLD 0-IV) in which both standard dose and low dose CT images were acquired.
- Eight vendors participated anonymously in the study; n=4 were research/open source and n=4 were commercial.
- The Radiological Society of North America (RSNA) acted as a neutral broker between vendors and the QIBA Lung Density Biomarker Committee to ensure the committee was blinded to vendor identity.

Objective 1: To evaluate the reproducibility of CT total lung volume (TLV), LAA-950 and Perc15 measurements using segmentation and software analysis tools from different vendors.

The reproducibility coefficient (RDC) measures the reproducibility across different vendors, and is defined as: $RDC = 1.96\sqrt{2\sigma^2}$, where σ^2 is the mean of the variances of repeated measurements on the same participant. Low RDC values indicate high reproducibility between vendors.

Table 1 – The RDC for TLV, LAA-950 and Perc15 for 8 different software vendors with and without quality assurance (QA) using manual correction of lung volume segmentation.

Parameter	Inter-software RDC without QA	Inter-software RDC with QA
TLV (L)		
Total	0.35	0.35
Vendor 1	0.38	0.38
Vendor 2	0.26	0.26
Vendor 3	0.26	0.26
Vendor 4	0.48	0.48
Vendor 5	0.25	0.25
Vendor 6	0.46	0.46
Vendor 7	0.31	0.31
Vendor 9	0.26	0.26
LAA-950 (%)		
Total	1.2	1.2
Vendor 1	1.2	1.2
Vendor 2	1.1	1.1
Vendor 3	1.1	1.1
Vendor 4	1.2	1.2
Vendor 5	1.2	1.2
Vendor 6	1.5	1.5
Vendor 7	0.9	0.9
Vendor 9	1.2	1.2
Perc15 (HU)		
Total	1.8	1.8
Vendor 1	1.6	1.7
Vendor 2	1.5	1.6
Vendor 3	1.5	1.5
Vendor 4	2.3	2.3
Vendor 5	2.1	2.1
Vendor 6	2.0	2.0
Vendor 7	1.4	1.4
Vendor 9	1.7	1.7

Overall, inter-software RDC was low at 0.35L, 1.2% and 1.8HU for TLV, LAA-950 and Perc15, respectively. For all vendors, inter-software RDC remained following QA: 0.35L, 1.2% and 1.8HU for TLV, LAA-950 and Perc15, respectively. Intra-software RDC was also generated by having the vendors perform repeated measurements without QA; all vendors had an intra-software RDC of 0.

Table 2 – The RDC for TLV, LAA-950 and Perc15 by vendor type (research or commercial) with and without QA with manual correction.

Parameter	Inter-software RDC without QA	Inter-software RDC with QA
TLV (L)		
Research	0.39	0.39
Commercial	0.32	0.32
LAA_{950} (%)		
Research	1.2	1.2
Commercial	1.2	1.1
Perc15 (HU)		
Research	1.7	1.7
Commercial	1.6	1.6

Research and commercial vendors RDC was comparable for TLV, LAA-950 and Perc15 measurements with and without QA.

Objective 2: To compare CT TLV, LAA-950 and Perc15 measurements from standard dose (SD) and low dose (LD) images.

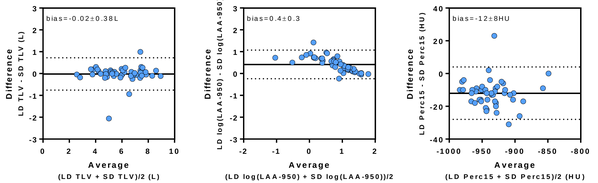


Fig. 4 – Bland-Altman plots for TLV, LAA-950 and Perc15 measurements for a representative vendor for SD and LD images. Bland-Altman plots indicate negligible bias for SD and LD TLV measurements. However, a bias for higher LAA-950 and lower Perc15 measurements was reported for LD compared to SD images.

Conclusion: High reproducibility was reported across eight different software vendors for TLV, LAA-950 and Perc15 measurements. Reproducibility was comparable for research/open source and commercial vendors, and QA had minimal impact on measurement variability between vendors. The bias between SD and LD LAA-950 and Perc15 measurements is a concern for longitudinal studies and methods to mitigate bias should be investigated.

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: Canon, 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 COPDGene™ imaging centers

For more information →

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