Quantitative CT of Obstructive Lung Disease:

Towards More Robust and Accurate Measures

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Quantitative Lung CT Measures

Quantitative lung CT measures in obstructive lung disease emphasize measures of low density lung parenchyma and central airway structures. These measures, especially their regional extent and distribution, are potential surrogate measurements of *emphysema, air trapping, and airway remodeling in* chronic obstructive pulmonary disease (COPD) and asthma.

Density Threshold Measures

One of the more established measures is the "low attenuation area" or "emphysema index" defined as the percentage of lung voxels at total lung capacity (TLC) with CT attenuation below a given threshold. The standard thresholds used for severity of emphysema include -950 Hounsfield units (HU) and -910 HU. The -950 HU threshold has been validated with histology, while the -910 HU threshold is thought to be less sensitive to image noise for detecting mild to moderate disease.

Air trapping is also evaluated using a density threshold, but the CT exam is obtained at a lung inflation volume corresponding to functional residual capacity (FRC) and the threshold for the mask is -850 HU. The rationale for this choice is based on empirical measures of air vs. tissue density that have been translated to quantitative studies in asthma (Figure 1).

Density Threshold for Air Trapping in Asthma (-850 HU at FRC)

Figure 1: Yellow voxels have attenuation below -850 HU Indicating regions of air trapping.

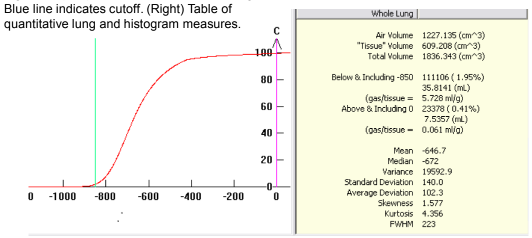
One-Day Course Announcement:

Quantitative CT Imaging of the Lung
Union South, Madison, WI
University of Wisconsin-Madison
Co-sponsored by the International Workshop for Pulmonary Functional Imaging (IWPFI) and the Quantitative Imaging Biomarkers Alliance (QIBA).
Online registration for the conference at:
https://www.radiology.wisc.edu/education/conferences/iwpfi/index.php

A third alternative method, the 15th percentile method [cites] (sometimes termed "Perc 15"), is defined as the threshold at which 15 percent of all voxels have a lower density. Longitudinal studies of emphysema have emphasized the 15th percentile.

Cumulative Histogram of Attenuation Values for Expiratory Lung (-850 HU at FRC)

Figure 2: (Left) Red line is cumulative histogram; Blue line indicates cutoff. (Right) Table of quantitative lung and histogram measures.



Each of these methods is evaluated using a single-point cutoff value of the cumulative histogram (Figure 2) and thus are closely correlated. There is measurement bias due to scanner calibration, reconstruction kernel, radiation dose, and slice thickness. At present multi-center studies must carefully control CT scan protocol to achieve reliable measures of emphysema and air trapping using CT.

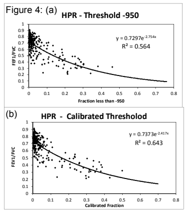
Density Correction Using Improved Test Object Design

The current design of the COPDGene Reference Test object contains foams with CT numbers similar to lung CT numbers (Figure 3). The Test Object consists of an outer ring and insert. The size and shape is similar to the adult human chest. So it will have beam hardening, x-ray scatter and dose equivalent to the adult human:

- **Outer ring (35cm×25cm 5cm thick, CT number 15HU at 120kV)**
- **Insert (foam with a CT number of -850HU to -860HU)**
- **Acrylic rod (113 HU), water tube, and hole (air) are large 3 cm details.**
- **8 polycarbonate tubes simulate airways**
- **3 additional foams bracketing different ranges of lung parenchymal densities (Table 1).**

Table 1: Specific Attributes of QIBA Lung Reference Foams (QLRF)

Foam Number (see Fig. 3)	Foam Type	Nominal Density (g/cm³)	Mean Attenuation (HU)
QLRF-1	FR-7120	0.321	-706
QLRF-2	FR-7112	0.193	-831
QLRF-3	FR-7104	0.064	-938



Using the COPDGene test object, calibration across sites or time (e.g. during longitudinal studies) becomes feasible. The consequences of shifts in CT number on the severity of emphysema and degree of air trapping metrics is under investigation. However one potential approach is to use attenuation of air in the trachea to linearly correct the scale of measures (Figure 4).

Figure 4. Improved correlation with whole lung function (FEV1/FVC) measures before (a) and after (b) correcting for differences in air density within the trachea.

COPDGene** Reference Test Object with NIST Investigated Foams

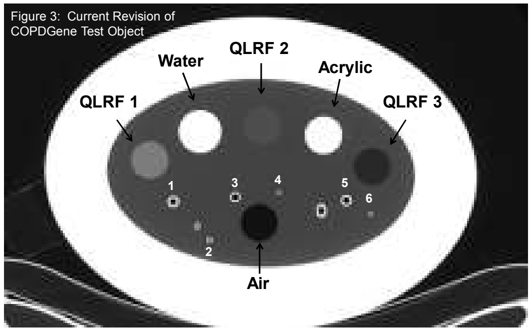


Figure 3: Current Revision of COPDGene Test Object

NIST traceable lung CT reference standard

National Institute of Standards and Technology (NIST) of the US Department of Commerce is charged with developing measurement standards for US industries, whose recent effort includes a lung density reference material for CT measurements. NIST personnel became involved with the QIBA COPD/Asthma Technical Committee in identifying and charactering the foam samples as a candidate for a standard reference imbedded in the insert of improved design. A Standard Reference Material based on these foams will be issued separately.

The ongoing qualification of the foam standards includes repeated measures of attenuation for different arrangements of the phantom and its surroundings. CT measurements were performed with the COPDGene test object with lung reference foams in the standard arrangement and placed flat on patient table. The CT scans were acquired using the Philips Brilliance16 scanner at NIST. Consequently, reconstructed images from 4 arrangements of the test objects were acquired as in Figure 4. Relevant parameters were 120 kV, Pitch = 0.563, 0.795 sec rotation speed, CTDIvol = 5.4 mGy, collimation = 500 mm, Slice Thickness = 1 mm, Increment = 0.5 mm, DFOV = 365 mm, Pixel size = 0.7 mm. Images were acquired at 70 and 140 mAs and with a low and high frequency modulation transfer function (MTF) reconstruction kernel.

Figure 4:
Reconstructed Images of the 4 phantom arrangements

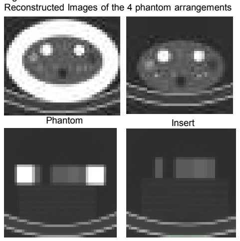


Table 2: Repeated measures of COPDGene Test Object

Scale HU Rec B; stdm = stdev from 3 scans

Ref Foams	Standard	stdm	Insert	stdm
QLRF-1	-942.41	0.28	-944.53	0.15
QLRF-2	-832.38	0.31	-833.04	0.20
QLRF-3	-708.12	0.26	-710.90	0.13
	Standard Flat		Insert Flat	
QLRF-1	-938.33	0.07	-942.21	0.13
QLRF-2	-831.23	0.10	-833.36	0.14
QLRF-3	-704.76	0.13	-708.97	0.10

Measurements demonstrate no effects of reconstruction kernel or tube current (Table 2). Effort is underway to investigate a spectrally independent description of the material's HU value using the dual-energy method.

*Any mention of commercial products is for information only; it does not imply recommendation or endorsement by NIST.

Quantitative CT for Airway Morphology Assessment

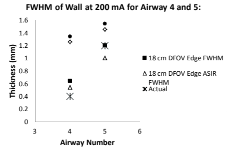
Air morphology is the measurement of the airway lumen areas and airway wall thicknesses. Typically more distal airways (3rd to 6th airway generations) correlate better with pulmonary lung function measures suggestive that distal segments are most relevant for depicting regional disease.

The COPDGene test object was scanned at 6.6 mGy CTDIvol. The wall thickness and lumen diameter of the 6 axial oriented tubes using 0.5 mm slice images of the Test Object (labeled 1-6 in Fig. 3) were measured over 30 mm axially using the FWHM method. The significant over-estimation of wall thickness and underestimation of smaller airway lumen diameters (2, 4 and 6) suggests spatial resolution is limiting (Table 3).

Table 3: Quantitative measures of axial oriented simulated airways (tubes 1-6 in Figure 3). Measures with greater than 30% error are highlighted in bold font.

Tube	True Value	Wall Thickness		True Value	Lumen Diameter	
	Wall Thickness	Mean	Standard Deviation	Lumen Diameter	Mean	Standard Deviation
1	**1.5**	**1.70**	**0.04**	6.0	5.73	0.08
2	**0.6**	**1.44**	**0.06**	**3.0**	**1.98**	**0.06**
3	**0.9**	**1.40**	**0.05**	6.0	5.45	0.14
4	**0.4**	**1.34**	**0.06**	**2.5**	**1.42**	**0.30**
5	**1.2**	**1.55**	**0.04**	6.0	5.59	0.17
6	**0.4**	**1.39**	**0.07**	**2.5**	**1.40**	**0.18**

Figure 5:



Reducing display field of view with a higher resolution modulation transfer function (MTF) improves accuracy of wall thickness (Figure 5) and lumen measures (not shown). Adaptive statistical iterative reconstruction (ASIR) yields comparable results.

Next steps for the COPD/Asthma Technical Committee

- **Determine the consequence of CT scanner inconsistencies identified on COPDGene Study scanners on the severity of emphysema, degree of air trapping metrics of COPDGene cases in order to develop methods obtain consistent measurements.**
- **Use the COPDGene Reference Test object to identify best parameters for improving accuracy of quantitative CT while mitigating radiation dose.**
- **Apply these improvements to development of a QIBA COPD/Asthma Profile**
- **Work with manufacturers to standardize CT attenuation measurements at lower end of the Hounsfield scale using the COPDGene Test Object as a standard.**

** The Genetic Epidemiology of COPD Study (www.COPDGene.org) is a study to identify genes that increase an individual's risk of developing COPD. The Study evaluated 10,000 subjects using 44 CT scanners. The COPDGene Study supported the development, evaluation and uses the COPDGene Reference Test