QIBA Lung Density Biomarker Committee:

Harmonization Across Platforms

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Background and Profile Progress

The CT Lung Density Biomarker Committee is working to harmonize and define Quantitative CT (QCT) protocol requirements to obtain repeatable, robust measures [1,2] of the relative area below -950 HU (RA-950 HU) and the HU threshold at which the lower 15 percent of a lung histogram falls (Perc15) through a published profile (**Figure 1**). Previously published data has shown vendor inconsistences using these QCT measures [3]. Therefore, more advanced image quality specifications are favored over preset parameter settings to allow flexibility in developing and supporting quantitative density measures [4].

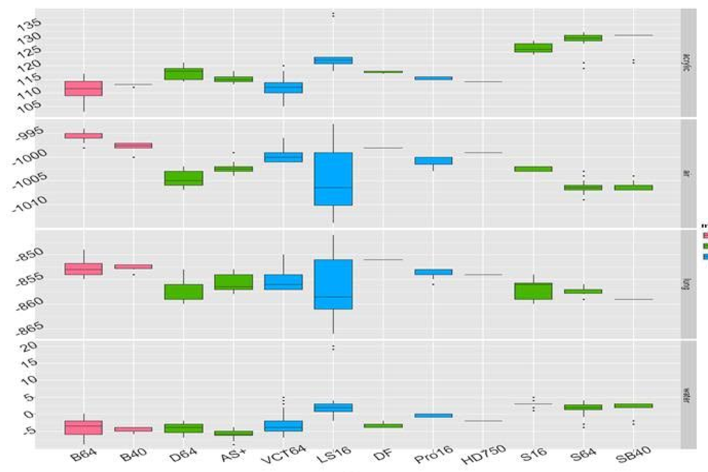

Figure1: Demonstrates the scanner variation across vendors in the COPDGenetics study. Studies like COPDGene rely heavily on density scale (HU) accuracy to correctly phenotype the lung

QCT Image quality specifications include:

•Acquire a 3D volume encompassing the lungs in a single breath-hold of less than or equal to 10 seconds.
•Acquire isotropic voxel size of < 0.9 mm
•Maintain a noise standard deviation ≤ ±20 HU for a matched kernel reconstruction (estimated lung equivalent foams by subtracting repeated helical scans).

Spatial resolution and noise thresholds were identified using the COPDGene2 test object scanned with conventional dose (~7.5 mGy CTDIvol) protocol and using the edge response function and NIST qualified foams with lung equivalent densities [5,6].

This approach enables vendors to ***adapt*** their architectures and reconstruction algorithms to meet desired quantitative measurement standards thus ***fostering creativity***, better vendor ***involvement*** and ***compliance***, and ***flexibility*** as CT systems continue to evolve.

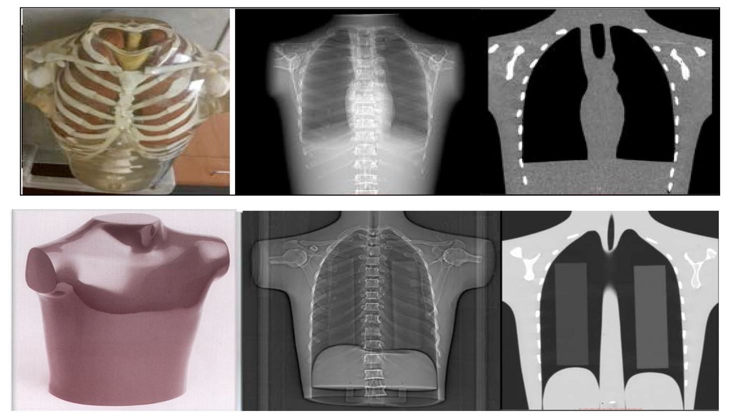

Figure 2: Top Row: Alderson 1 Phantom, Model RS-111T with photograph, radiograph and coronal CT slice image. The phantom was used for estimating noise for AEC parameters under conditions approximating a medium sized patient. **Bottom Row:** Alderson 2 phantom with embedded NIST foams**.**

References:

1. Madani, A., et al., *Pulmonary Emphysema: Radiation Dose and Section Thickness at Multidetector CT Quantification—Comparison with Macroscopic and Microscopic Morphometry.* Radiology, 2007. **243**(1): p. 250-257.
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4. Newell, J.D., et al, Development of quantitative computed tomography lung protocols. J Thorac Imaging, 2013. 28(5): p. 266-71.
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Baseline Performance Standard for AEC

To establish a "target" or baseline performance standard for automatic exposure control (AEC), an anthropomorphic phantom with a low density foam (**Figure 2:Top**) was scanned using a current conventional dose CT protocol used in a multi-center clinical research study of severe asthma (SARP)[7].

In this approach, constant tube currents are adjusted up or down to one of 3 settings based on patient body mass index (BMI) with associated constant tube current $CTDI_{vol}$ estimates (small BMI = 2.8 mGy, medium BMI = 7.6 mGy, large BMI = 11.4 mGy).

Noise performance was estimated by subtracting repeated helical scans to obtain two noise realizations with the measurement derived from the standard deviation (SD) within a spherical volume of interest (VOI) of radius 13.5 mm scanned using phantoms of various "equivalent body sizes" under varying AEC parameter settings (**Figure 3** and **Table 1**).

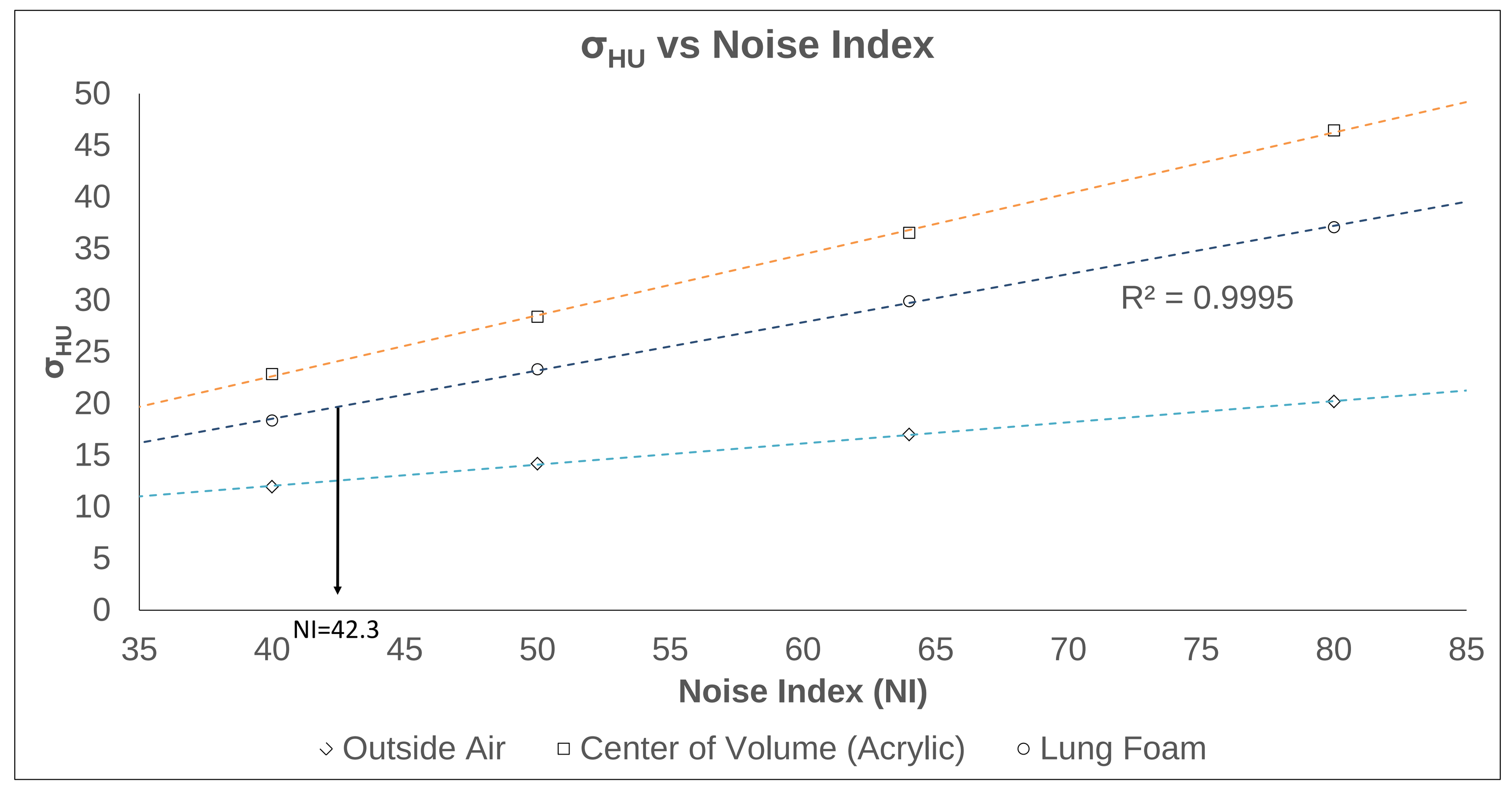


Figure 3: Determination of the noise performance in "lung equivalent" foam of the Alderson 1 phantom for noise index (NI) values ranging from 20-80 on the GE CT750HD. The threshold for noise was determined in the foam to be $|\sigma_{HU}| < 20$ units, which corresponds to that obtained for a dose equivalent protocol (NI ≅ 42, see arrow) defined as the **"**Conventional Dose" protocol.

Scanner	Phantom (diameter)	AEC Parameters Tested
GE CT750 HD	**16 cm CTDI (Small Body Size)** 20 cm Water **32 cm CTDI with 16 cm core removed (Medium Body Size)** **32 cm CTDI (Large Body Size)** 35 cm Polyethylene 48 cm Polyethylene Alderson Alderson 2	Noise Index (NI) = 20, 28.28, 40, 42.3, 56.56, 66.5, 80
Siemens SOMATOM Definition AS	**16 cm CTDI (Small Body Size)** 20 cm Water **32 cm CTDI with 16 cm core removed (Medium Body Size)** **32 cm CTDI (Large Body Size)** 35 cm Polyethylene 48 cm Polyethylene Alderson	Quality Reference mAs (QR mAS= 150, 300, 600)
Siemens SOMATOM Force	**16 cm CTDI (Small Body Size)** 20 cm Water **32 cm CTDI with 16 cm core removed (Medium Body Size)** **32 cm CTDI (Large Body Size)** 35 cm Polyethylene 48 cm Polyethylene Alderson Alderson 2	Quality Reference mAs (QR mAS= 150, 300, 600)
Siemens SOMATOM Definition Edge	**16 cm CTDI (Small Body Size)** **32 cm CTDI with 16 cm core removed (Medium Body Size)** **32 cm CTDI (Large Body Size)** Alderson Alderson 2	QR mAs= 29, 54, 70, 72, 94, 150, 162, 300, 60
Toshiba Aquilion One	Anthropomorphic 3D Printed	Standard Deviation (SD)= 5, 8, 12, 20, 30

Table 1: Summary of experiments performed on 5 different CT scanners using various phantoms. Equivalent body size phantoms were designated as the 32 cm CTDI phantom (large body), the 32 cm CTDI phantom with the 16 cm core removed (medium body), and the 16 cm CTDI (small body).

AEC Harmonization

Harmonization was implemented by matching dose ($CTDI_{vol}$) across manufacturers and/or models by using a common reference scanner at the lead center for a given multi-center trial. In our harmonization scheme, the common reference scanner was the GE 750 HD. Participating centers would then scan the small, medium, and large equivalent phantoms for a range of AEC parameter settings and these reference curves (**Figure 4**) would be used to match performance to a given noise or dose threshold.

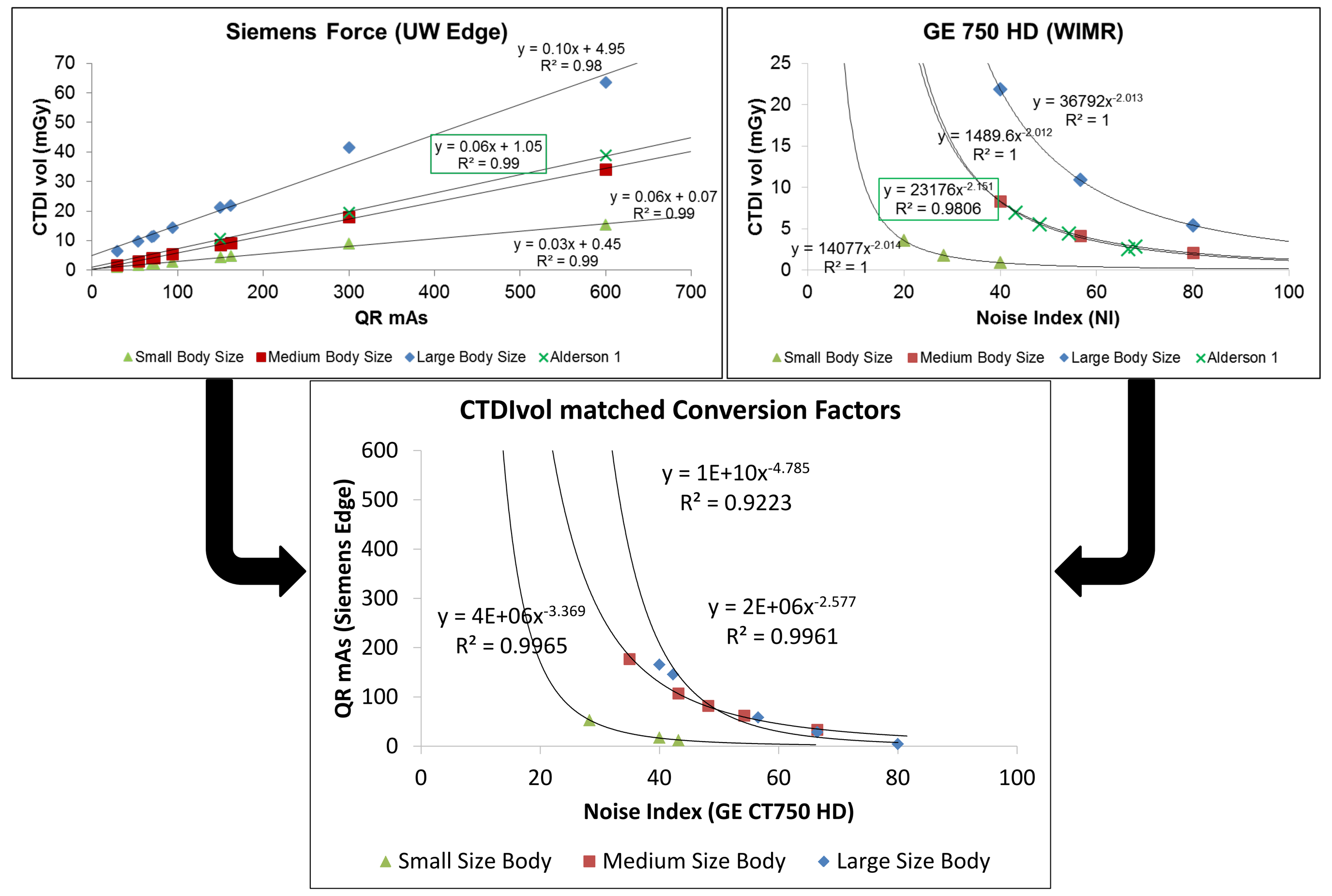


Figure 4: A. Measurements of $CTDI_{vol}$ versus Siemens' AEC parameter, quality reference mAs (QR mAs), on the Somatom Edge. **B.** Measurements of $CTDI_{vol}$ versus GE's AEC parameter, noise index (NI), on the Discovery CT750 HD. **C.** Matching $CTDI_{vol}$ from both experiments, empirically determined conversion factors for each body size can be used to translate protocols between platforms.

Scanner Calibration

To achieve higher precision of CT lung density as a biomarker than currently available, it is essential to harmonize scanner calibrations using the same phantom object to arrive at a consistent CT HU value for lung density assessments. The Committee coordinated scanning of the COPDGene2 phantom by vendors to assess scanner variations, which facilitated the following scheme for recalibration: The HU value for each foam (averaged over the bulk of the foam volume, obtained using common software) is plotted against the known physical density and fitted by linear regression The slope (k_i) and intercept (b_i) of the fit are used to describe the calibration of scanner *i*., which are scanner dependent but material independent. The intercept b_i captures the air value that can deviate from -1000. The goal is to remove this scanner dependence by imposing a common slope and intercept, and the recalibration transforms each scanner's HU value to HU':

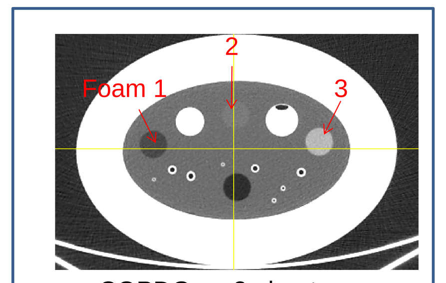
$$\boldsymbol{HU' = \frac{k_0}{k_i}(HU - b_i) + b_0} \qquad (1)$$

Let k_0 = 0.95 [HU/(kg/m³)] and b_0 =-1000 HU, **HU'** is thus recalibrated and better harmonized across scanners.

Vendor Harmonization R1 – COPDGene2 Phantom

The results from the first round of vendor scanning using the COPDGene2 phantom at 4 different scanners (Siemens, GE, Philips, and Toshiba) revealed discrepancies of 4 to 5 HU (standard deviations from 1.86 to 2.90 HU) for the 3 embedded reference foams (designated as nominal weight 4, 12, and 20 lb) from scanner to scanner. The recalibration was performed using the 3 embedded foams by plotting the measured HU values vs. the nominal density values (corresponding to SI units of 64.07, 192.22, and 320.37 kg/m³, respectively).

While these densities were not verified and could deviate from the nominal values based on production specifics, for demonstration purposes it was adequate. The recalibration was performed using equation (1). The results before and after recalibration are shown in **Fig. 5**.



COPDGene2 phantom

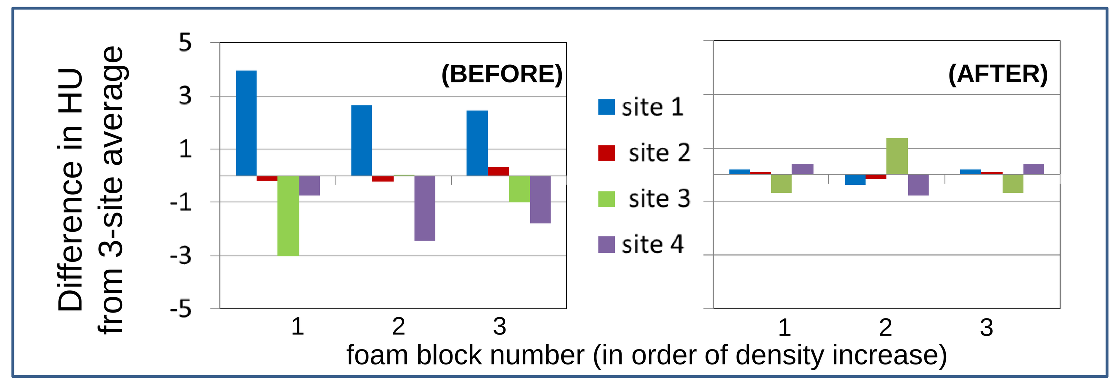
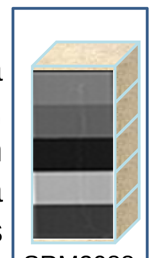


Figure 5: The differences of the HU values for each of the 3 foam density between each site and the 5-site average before and after recalibration.

Vendor Harmonization R2 - NIST SRM Foams

The NIST Standard Reference Material (SRM) 2088 consists of a suite of foams with 5 densities from 60 kg/m³ to 325 kg/m³, developed from the same foam stocks as the 3 reference foams in the COPDGene2 phantom, but with each foam block assigned a unique density using the formal SI-traceable certification process [8].



SRM2088

The SRM is used in round 2 of the vendor scanning in air alongside the COPDGene2 phantom to provide a more precise calibration. Round 2 scanning has been completed on scanners at 3 sites: **A**.Toshiba Aquilion One at NIH, **B**. Philips Brilliance 16 at NIST **C.** Siemens SOMATOM Force at U of Iowa. The HU value differences before and after recalibration shown in **Figure 6**. The improvements are comparable to the initial results of using the embedded foams for the COPDGene2 phantom study, but precision and accuracy must be further assessed.

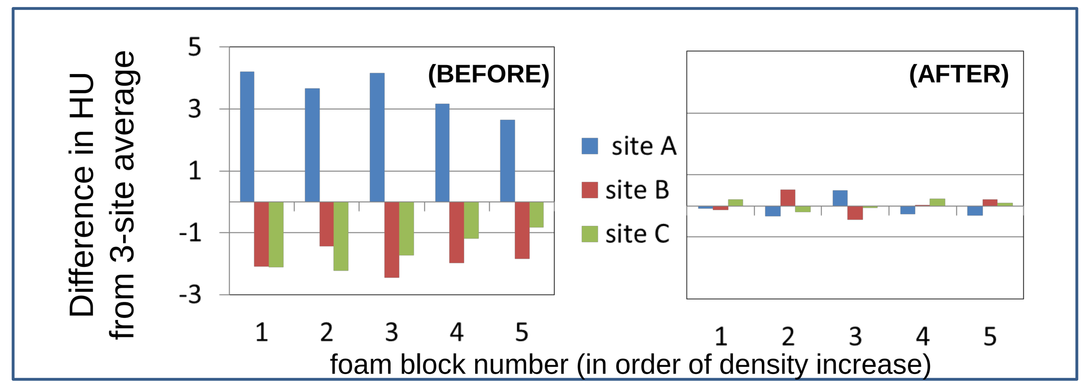


Figure 6: The differences of the HU values for each foam density between each site and the 3-site average before and after recalibration.

Conclusions and Next Steps

- Protocol harmonization has been successfully applied cross-platform between Siemens and GE automatic exposure control systems (**Figure 3 and 4**)
- Extension of protocol harmonization, with proper calibration, between other manufacturers such as Philips and Toshiba will continue.
- The detailed scanner calibration harmonization will be verified for all manufacturers.

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