Quantitative CT of Obstructive Lung Disease: Standardized Protocols with Reduced CT Dose

Quantitative Lung CT Measures

The primary mission of the QIBA development strategy for the COPD/Asthma technical subcommittee is to identify best practices for quantitative CT measures of lung parenchymal density. This includes:

- Development and publication of standard protocols based on current best practices.
- Claims of test object reproducibility and limits for detecting reduction (increase) in parenchymal density (i.e. progression (regression) of emphysema or air trapping) with qCT.
- Research and testing of emerging and future methods to reduce radiation dose and improve quantitative accuracy.

Proposed Image Bio-Markers

The most established measures of lung parenchymal density are RA950 and Perc15 (Figure 1):

- The RA950 is defined as the relative lung area (or lung voxels) at total lung capacity (TLC) with CT attenuation below -950 Hounsfield units (HU).
- The Perc15 is defined as the HU value at which 15 percent of all voxels have a lower density.

These measures are the most common, based on studies comparing to tissue histology in resected lung [1] and established in longitudinal studies of emphysema progression [2].

RA950 and Perc15 in COPD

COPDGene 2 “Test Object”

Forest plots of the results of meta-analysis: (a) for Perc15 and RA950 before VA.

Claims

Mean repeatability coefficients were calculated from the meta-analysis using the random effects model [8], shown in a summary Forest plot (Figure 3), for before and after volume adjustment (VA). Each study reported limits of agreement (LOA), defined as 1.96SD from the mean, from which the repeatability coefficient (RC) can be calculated. The RC is deemed the Smallest Real Difference (SRD), to be used in the claims.

- Perc15 before VA and (c) RA950 before VA.
- For RA950, only two studies performed VA, and the effect of VA on the bias and precision were statistically insignificant.

Technical Improvements: Reducing Radiation Dose

Automatic Exposure Control (AEC): an important limitation of AEC for qCT methods is that different vendors use significantly different approaches to adjust X-ray tube current as a function of patient size. We propose a common phantom setup designed to test AEC protocols across different scanner platforms including GE Healthcare, Toshiba Medical, Philips and Siemens Healthcare systems (Figure 5).

Phantoms used are COPD Gene with:

- A: 25.9 cm sphere attenuation ring that is near-water electron density standard.
- B: 20.3 cm sphere attenuation ring (eFALSTA).
- C: 18.3 cm sphere attenuation ring (NIST).
- Standard Lung protocol for: Severe Asthma Research Program.
- Median target dose (~105 mAs).

Figure 6: Improvements in airway wall resolution with increased sampling, higher frequency kernel and adaptive statistical IR. These improvements are maintained with a reduction of CT dose by a factor of 2-4.

Conclusions and Next Steps

- Meta-analysis showed negligible bias with upper bound repeatability coefficients of 5.1% for RA950 and 18.3 HU for Perc15 after volume adjustment (Figures 3 and 4).
- IR reconstruction methods can preserve median parenchymal density and enhance airway wall thickness measures to help reduce CT dose.
- Studies to standardize AEC and IR approaches across vendors and develop an inventory of future development priorities for future development.

References:


Author Information

Table 1: Examples of profile specifications

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Inclusion Criteria</th>
<th>Study Duration</th>
<th>Scan Type</th>
<th>Minimum Density</th>
<th>Mean Density</th>
<th>Median Density</th>
<th>RA950</th>
<th>Perc15</th>
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<td>Lai et al.</td>
<td>2012</td>
<td>4166 subjects with stage B COPD</td>
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<td>Park et al.</td>
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<td>1.15</td>
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</table>

Figure 2: Using the COPDGene test object, calibration across sites and vendors over time becomes feasible. Foams of different density (QLFP-1, 2, 3), acrylic, water and air standards are included.

Figure 3: Meta-analysis of the bias (mean of the difference between scan 1 and scan 2 for each subject) was also performed for (a) Perc15 after VA, (b) Perc15 after VA, and (c) RA950 after VA.

Figure 4: Technical Improvements: Reducing Radiation Dose

Automatic Exposure Control (AEC): an important limitation of AEC for qCT methods is that different vendors use significantly different approaches to adjust X-ray tube current as a function of patient size. We propose a common phantom setup designed to test AEC protocols across different scanner platforms including GE Healthcare, Toshiba Medical, Philips and Siemens Healthcare systems (Figure 5).

Figure 5: Phantom configuration used for preliminary tests of AEC across GE and Siemens platforms. A modified Allerson phantom [10] is also being considered.

Iterative Reconstruction (IR) methods generally impact the standard deviation of lung density measures but not their median values [11]. Model-based IR methods such as ASIR, VEO, SAFIRE and ADMIRE are promising methods to reduce CT dose for qCT measures of both parenchymal density [11] and airway dimensions (Figure 6) [12].

Figure 6: Improvements in airway wall resolution with increased sampling, higher frequency kernel and adaptive statistical IR. These improvements are maintained with a reduction of CT dose by a factor of 2-4.

Conclusions and Next Steps

- Meta-analysis showed negligible bias with upper bound repeatability coefficients of 5.1% for RA950 and 18.3 HU for Perc15 after volume adjustment (Figures 3 and 4).
- IR reconstruction methods can preserve median parenchymal density and enhance airway wall thickness measures to help reduce CT dose.
- Studies to standardize AEC and IR approaches across vendors and develop an inventory of future development priorities for future development.

Figure 7: COPD/Asthma Biomarker Committee will specify CT protocol requirements to obtain repeatable and robust measures of RA950 or Perc15 through a published Profile.

- Minimum noise and spatial resolution thresholds will be set.
- Specifications require a noise standard deviation(s) of ≤ ±20 HU, an isotropic voxel size of ≤ 0.9 mm, a scan time of 8-10s, and a low dose threshold (≤ 4 months separating the two time points to mitigate the degree of disease progression.
- Perc15 and/or RA950 HU measurement methods were used to assess lung involvement and involvement in longitudinal studies of emphysema progression [2].

Figure 8: Forest plots of the results of meta-analysis: (a) for Perc15 and RA950 before VA.