Association between spirometry controlled chest CT scores using computer-animated biofeedback and clinical markers of lung disease in children with cystic fibrosis

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Computed tomography:

All scans were performed by volumetric spiral CT imaging on a Toshiba Aquillion 64 CT scanner (Toshiba Corporation, Tokyo, Japan; 100 kVp, mAs-modulation; SD = 19 in inspiratory and SD = 27 in expiratory sequences, rotation 0.4 s). The average effective dose for both inspiratory and expiratory CT was 1.56 mSv (range 0.76– 4.05) and calculated using age-specific conversion factors (E1).

CF-CT scoring:

Good inter-observer agreement with a reference observer was secured prior to scoring the study cohort, using training CT’s that were scored by an experienced reference scorer.

Inter-observer agreement on training CF-CT scores was calculated using intra-class correlation coefficients for calculated total and subdomain scores, supplemented by weighted kappa statistics on individual observations for subdomains (coefficients ≥ 0.8 indicate excellent agreement, 0.6-0.8 good agreement, 0.4 – 0.6 moderate agreement, 0.2 – 0.4 fair agreement, and <0.2 poor agreement), and Bland-Altman plots to display signs of systematic bias in subdomains.

Inter-observer agreement on training CT scoring using intra-class correlation coefficients ranged from good (AT and airway wall thickening: 0.77) to excellent (CF-CT total score: 0.88).

The weighted kappa statistics on every individual observation ranged from moderate (0.43 (AWT), 0.48 (parenchyma), 0.53 (AT)) to good (0.71 (BE), 0.61 (mucus plugging), 0.67 (all scores combined)). Bland-Altman plots showed no sign of systematic bias in any of the sub-scores (Fig. E1).

Fig. E1 Bland-Altman plots for total score and subdomains assessing systematic bias between scorers in the training CTs done prior to scoring the study cohort.

| Score Type                      | Correlation Coefficient |
|--------------------------------|-------------------------|
| Total score                    | \( \kappa = 0.67 \)    |
| Bronchiectasis score           | \( \kappa = 0.71 \)    |
| Airway wall score              | \( \kappa = 0.43 \)    |
| Mucus plugging score           | \( \kappa = 0.61 \)    |
| Parenchymal change score       |                         |
| Air trapping score             | \( \kappa = 0.53 \)    |
Results:
Comparisons of the study cohort with the non-included subjects:

The included cohort was compared to the non-included subjects and exhibited no significant differences, though no patients in the non-included group had ABPA or chronic *P. aeruginosa* infection (Table E1).

Table E1 Comparison between study cohort and excluded subjects.

| Subjects                              | Study cohort    | Non-Included    | Test |
|---------------------------------------|-----------------|-----------------|------|
|                                       | n=64            | n=14            |      |
|                                       | Numbers         | Numbers         |      |
|                                       | %               | %               | p    |
| **Males**                             |                 |                 |      |
|                                       | 34              | 7               | 0.2  |
| **Homozygote del-508**                | 33              | 8               | 0.2  |
|                                       | 5               | 0               | 0.4  |
| **Chronic *P. aeruginosa***           | 21              | 6               | 0.2  |
| **ABPA**                              | 7               | 0               | 0.2  |
| **FEV$_1$<80%**                       | 13              | 3               | 0.3  |
| **FVC<80%**                           | 5               | 2               | 0.3  |
| Other outcomes (means)                |                 |                 |      |
| **Age**                               | 12.3            | 13.3            | 0.3  |
| **BMI-z scores**                      | -0.1            | -0.5            | 0.1  |
| **P. aeruginosa IgG**                 | 2.0             | 3.0             | 0.5  |
| **Aspergillus IgG**                   | 48.7            | 55.3            | 0.8  |
| **S. aureus %**                       | 33.9            | 34.0            | 1.0  |

ABPA: Allergic bronchopulmonary aspergillosis. BMI: Body mass index.
References

E1. Deak PD1, Smal Y, Kalender WA. Multisection CT protocols: sex- and age-specific conversion factors used to determine effective dose from dose-length product. Radiology. 2010; 257:158-66. doi: 10.1148/radiol.10100047.