Is Chest Computed Tomography Useful in Newborn Screened Infants with Cystic Fibrosis at One Year of Age?

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Data Supplement

Background

As part of a multicentre longitudinal research study of lung function and structure in infants with cystic fibrosis (CF) diagnosed by newborn screening (NBS),[E1,2] thin section CT scans under general anaesthesia (GA) were performed at 1 year of age in centres participating in the London Cystic Fibrosis Collaboration (LCFC) using similar GA and imaging protocols. With the same GA, infants underwent bronchoscopy with broncho-alveolar lavage after the performance of chest CT.

In this study we evaluated procedures required for a multi-institutional evaluation of lung disease in infants with CF. Specifically, we evaluated the use of a standardised protocol for CT scanning in infants under GA as well as the use of the Brody-II scoring system for quantifying lung disease in NBS CF infants at a year of age. We hypothesised that significant changes will be detected by 1 year of age but that inter-observer agreement using Brody-II scores will be lower in NBS CF infants than in older children, due to the greater proportion of subjects with no, or only subtle, abnormalities.[E3,4]

This online supplement (OLS) provides additional details regarding standardised GA protocol, CT scanning parameters, protocol for different image acquisition, verification of adherence to protocol through objective measures, radiation exposures, CT scores and other issues which could not be included in the main article due to space constraints.

1. Recruitment and Informed consent

The screening, recruitment, follow-up and parental attitudes to participating in this research study have been described in detail in previous publications.[E1,5] Families of eligible infants were provided separate written informed consent for each part of this observational study. With respect to the CT scan under GA, they were provided with written information augmented by verbal explanations about the potential risk associated with the small additional radiation exposure with having the CT scan at a year of age. They were advised that:

- All radiation (including the background environmental radiation to which we are all exposed) carries a small risk of damage to cells, which may lead to cancer after many years or decades.
- The extra radiation from having one CT scan using the proposed protocol for this study would be equivalent to about half that which their child would receive each year from background sources.

Of the 70 CF NBS infants who underwent lung function assessments at 3 months and 1 year of age,[E1,2] 65 infants agreed to chest CT scans. Remaining families declined due to concerns about GA and CT scanning.

2. General Anaesthesia protocol

- *Ventilate the child to maintain an appropriate end tidal CO_2 (4.5-5 kPa or 33.8-37.6 mmHg) with the addition of positive end expiratory pressure (PEEP=5 cmH_20), using a handheld pressure gauge/manometer.*
- *During initial mask bagging prior to intubation, there is a tendency for air to enter the stomach which could elevate the diaphragm and decrease lung volume. Pass a nasogastric tube and apply suction to reduce any gastric distension PRIOR to initial topogram/ scout.*
- *Maintain baseline ventilatory pattern prior to scan via anaesthetic machine using pressure controlled intermittent positive pressure ventilation (IPPV),*
    - *Respiratory rate 20 breaths per minute*
    - *Inspiratory: Expiratory (I:E) ratio 1:2*
    - *Tidal Volume (VT) 8-10ml/kg*
    - *PEEP: 5 cmH_2O*

- *To minimise the development of atelectasis, administer slow inflations with prolonged inspiratory phase, peak inspiratory pressure (PIP) of 25-35cmH_2O and PEEP of 5-6 cmH_2O using manual ventilation (recruitment maneuvers) prior to the scan.*

3. Scanning protocol and parameters

The following written protocol was given to all anaesthetists and radiologists after detailed explanations of the procedure and the importance of adhering to protocol in order to minimise anaesthesia-related atelectasis and obtain the CT scans at standardised volumes. Table E1 and E2 provide details of the different scanners used in the three centres and the scanning parameters used.

- *Radiographer to select and load the CF scan protocol and, once ready for topogram, to say 'READY FOR TOPOGRAM'.*
- *Anaesthetist to switch the child from being ventilated on the anaesthetic machine to using manual ventilation. The anaesthetist to ensure that patient breath-hold occurs on full inspiration at 25 cmH_2O and to say 'GO FOR TOPOGRAM' (while Topogram/scout was performed) until instructed to release by radiographer who will then say 'FINISHED'. This is essential to facilitate appropriate coverage of the entire lung fields when planning the inspiratory acquisition.*
- *Radiographer to set up both the inspiratory and expiratory acquisitions with coverage from lung apices to bases. Reduce coverage by 30mm at the lung bases for the expiratory acquisition to reduce over-irradiation in the abdomen. Include a 6sec delay prior to scan initiation to ensure lungs are at maximum expiration. Once ready, radiographer to say 'START INFLATIONS for INSPIRATORY SCAN'.*

- *Anaesthetist to perform:*
    - *6 deep slow inflations to 35- 40cmH_2O with a PEEP of 6 cmH_2O to reverse any anaesthetic-related atelectasis, followed by*
    - *4 deep slow inflations to 25cmH_2O with a PEEP of 5 cmH_2O to provide standard lung volume history.*
    - *During the inspiratory scan, the child's lungs are held in inspiration for 6s at 25 cmH_2O, until radiographer instructs 'FINISHED INSPIRATORY SCAN'.*
- *Anaesthetist to cease ventilation and decrease PEEP to zero to allow passive expiration to relaxed end expiratory volume.*
- *Once lung deflation completed (ZERO PEEP); anaesthetist to instruct radiographer by saying 'GO FOR EXPIRATION' (by which time the scanner will have moved into place ready to commence the expiratory acquisition). The aim of the subsequent 6 second delay before scan commencement is to ensure completely stable end expiratory level attained with no subsequent volume drift.*
- *Radiographer to inform anaesthetist when scan complete and that normal ventilatory support can be resumed.*

Table E1: Details of CT scanners used across the three centres

Centre	Multidetector CT scanner model
A	Somatom Definition Dual-Source (64 slice)*
B	Somatom Definition Flash (128 slice)*
C	Somatom Sensation (64 slice)*

Footnote: * Siemens Healthcare, Forchheim, Germany

Table E2: Details of scanning parameters used

	Topogram	**Inspiratory Spiral**	**Expiratory Spiral**
Tube voltage (kVp)	80	100	100
Tube current (mAs)	20	17	20
CTDIvol (mGy)		0.57	0.67
Detector collimation		64 x 0.6mm	
Tube rotation time		0.5 seconds	
Scan Pitch		1	1
Coverage	~ 256 mm	~140 mm	~ 30mm less than inspiratory range
Scan slice width		1mm	
Reconstructed slice thickness		1mm	
Reconstruction algorithm		• 1st reconstruction- B60 sharp kernel • 2nd reconstruction- B30 medium-soft kernel	• B60 sharp kernel
Reconstruction Window Setting		• 1st reconstruction - lung parenchyma setting (1200WW, -600WL) • 2nd reconstruction - mediastinum setting (400WW, 50WL)	• lung parenchyma setting
Post processing		2mm coronal reconstruction on B60 lung setting	

Using the CT parameters described in methods (main MS) and Table E2 in the OLS, the estimated target radiation dose is ~1.5 mSv for the combined volumetric inspiratory and expiratory scans, with an estimated dose range up to 2mSv.

4. CT scoring methodology

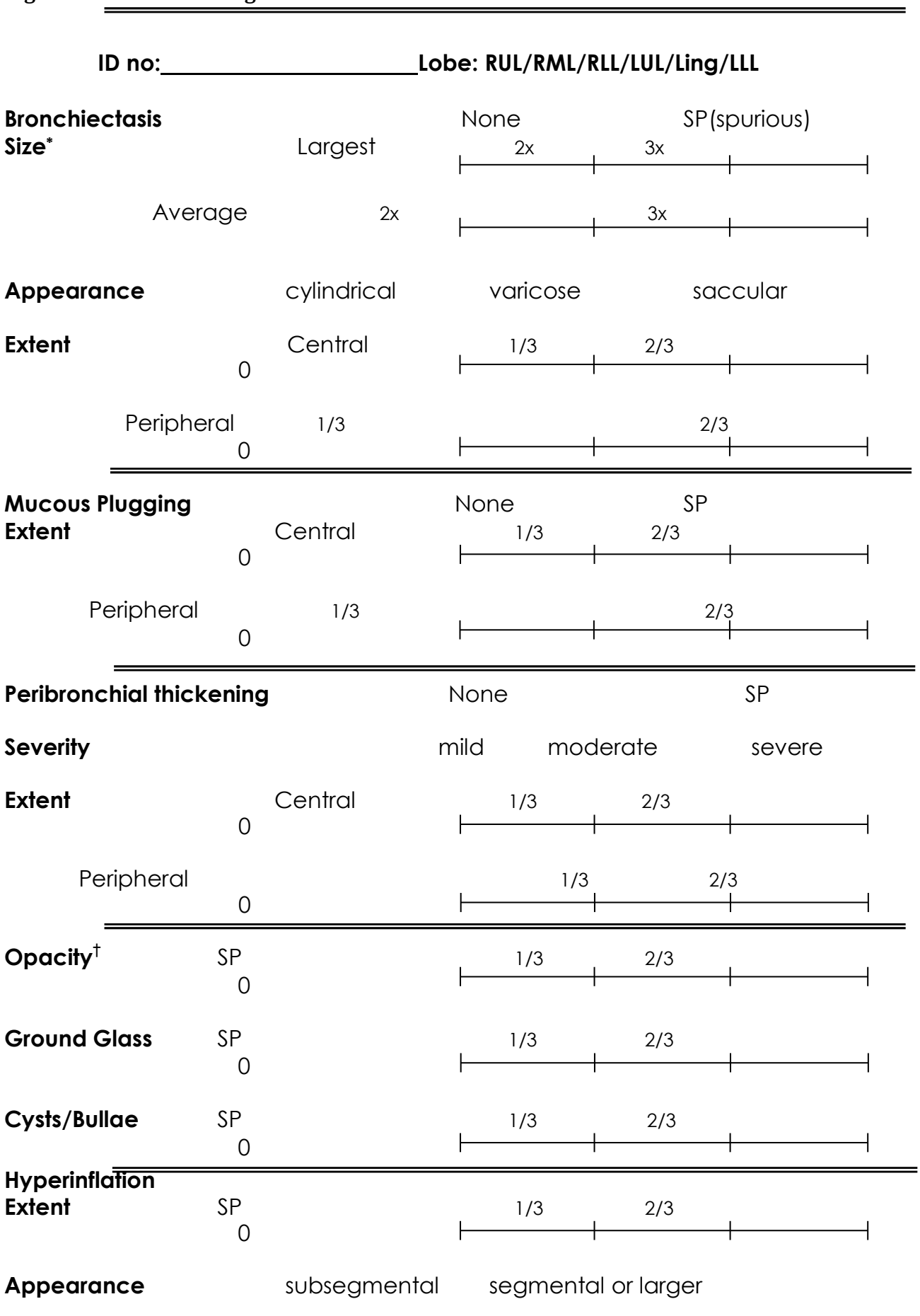
The Brody-II scoring system [6] assesses the severity and extent of bronchial dilatation and bronchial wall thickening, the extent of parenchymal changes of consolidation, ground glass opacification and cysts, extent of mucous plugging and finally the extent and location of air-trapping (based on expiratory scans), referred in Figure E1 as hyperinflation score, in each lobe. Distribution of each abnormality was described according to its central or peripheral location within each lobe. Peripheral lung was defined as the portion of lung within 2 cm of the costal or diaphragmatic pleura whilst central portion accounted for the rest of the lung. Each subject's lungs were divided into 6 lobes, three on each side. A score sheet was filled out for each lobe of the lung, including the lingula as a separate lobe. Therefore for an individual, there were 6 score sheets filled in. The sum of the sub-scores of each abnormality was calculated which, together with the total scores, form the basis of the results. (Figures E1 and E2).

Bronchial dilatation was assessed both in the central and peripheral lung, and rated from 0-3 for both severity and extent.[6] A broncho-arterial ratio (BAR) >1 specified in Brody II was used to define bronchial dilation in this study, as also used in CF-AREST. A critical nuance of this is whether bronchial diameter is evaluated from outer wall to outer wall, or as luminal diameter. While rarely specified in reports, when it is, it is the luminal, rather than external diameter that should be recorded, as was used in the present study.

Mucous plugging was similarly assessed in both central and peripheral lung, and scored from 0-3 for extent. Peribronchial thickening was assessed centrally and peripherally, rated from 0-3 for extent and rated mild, moderate or severe. Parenchymal changes not assessed elsewhere in the scoring system were also given a score from 0-3 for each of: ground glass, dense opacity and cysts or bulla. Finally, air-trapping was rated from 0-3 for extent, and classified as either segmental or sub-segmental. The overall severity score had a theoretical range from 0(normal) to

243(severe abnormality in all categories present throughout each lobe). The maximum ranges of bronchial dilatation and air trapping were 0 to 72 and 0 to 27 per scan respectively.

Figure E1: CFCT Scoring Sheet



Legend: Each score sheet was completed for each lobe i.e. six score sheets were completed for each infant.

*In this Brody-II scoring sheet, the term 'bronchiectasis', previously used in older children has been replaced by bronchial dilatation throughout this manuscript. Many of the bronchial luminal changes observed were mild and borderline and if the term bronchiectasis was used, it might suggest irreversible damage which in this age group with mild severity this may not be the case.

†The category of parenchyma changes consist of the sum of opacity seen, ground glass appearance and evidence of cysts or bullae.

Figure E2: HRCT scoring system

Bronchiectasis score (range 0 to 12)	= (	Extent of bronchiectasis in central lung 0 = none 1 = 1/3 of lobe 2 = 1/3 to 2/3 of lobe 3 = >2/3 of lobe	+	Extent of bronchiectasis in peripheral lung 0 = none 1 = 1/3 of lobe 2 = 1/3 to 2/3 of lobe 3 = >2/3 of lobe	) x	Average bronchiectasis size multiplier 0.5 = 0 1 = 1 1.5 = 1.25 2.0 = 1.5 2.5 =1.75 3 = 2
where						
Average bronchiectasis size	= (	Size of largest dilated bronchus 1 = <2x 2 = 2x-3x 3 = >3x	+	Average size of dilated bronchi 1 = <2x 2 = 2x-3x 3 = >3x	) /	2
Mucous plugging score (range 0 to 6)	=	Extent of mucous plugging in central lung 0 = none 1 = 1/3 of lobe 2 = 1/3 to 2/3 of lobe 3 = >2/3 of lobe	+	Extent of mucous plugging in peripheral lung 0 = none 1 = 1/3 of lobe 2 = 1/3 to 2/3 of lobe 3 = >2/3 of lobe		
Peribronchial thickening score (range 0 to 9)	= (	Extent of peribronchial thickening in central lung 0 = none 1 = 1/3 of lobe 2 = 1/3 to 2/3 of lobe 3 = >2/3 of lobe	+	Extent of peribronchial thickening in peripheral lung 0 = none 1 = 1/3 of lobe 2 = 1/3 to 2/3 of lobe 3 = >2/3 of lobe	) x	Severity of peribronchial thickening 1 = mild 1.25 = moderate 1.5 = severe
Parenchyma score (range 0 to 9)	=	Extent of dense parechymal opacity 0 = none 1 = 1/3 of lobe 2 = 1/3 to 2/3 of lobe 3 = >2/3 of lobe	+	Extent of ground glass opacity 0 = none 1 = 1/3 of lobe 2 = 1/3 to 2/3 of lobe 3 = >2/3 of lobe	+	Extent of cysts or bullae 0 = none 1 = 1/3 of lobe 2 = 1/3 to 2/3 of lobe 3 = >2/3 of lobe
Air Trapping score (range 0 to 4.5)		Extent of air trapping 0 = none 1 = 1/3 of lobe 2 = 1/3 to 2/3 of lobe 3 = >2/3 of lobe	X	Appearance of air trapping 1 = subsegmental 1.5 = segmental or larger		

5. Verification of adherence to protocol for manual ventilation during the procedure

In an attempt to standardise image acquisition across three different sites, training sessions were provided for the relevant anaesthetists and radiographers. Initial images displayed some dependent atelectasis and there were concerns that these may be related to the variation in ventilatory pressures or patterns used by different anaesthetists. To monitor adherence, inflation pressures and volumes were objectively measured through a respiratory monitor, $NICO_2$® [E7] during the procedure (Table E3). Screenshots of measurements recorded using $NICO_2$® during the different image acquisitions can be seen in Figure E3.

Table E3: The number (percentage) of scans performed, attendance of research team and objective monitoring in each centre.

	Total	Centre A	Centre B	Centre C
Number (%) scans performed/centre	65	10/65 (15%)	38/65 (58%)	17/65 (26%)
Number (%) attended by research team	50/65 (77%)	7/10 (70%)	28/38 (74%)	15/17 (88%)
Number (%) with objective monitoring	37/65 (57%)	5/10 (50%)	19/38 (50%)	13/17 (76%)

The research fellow (LT) attended 50 (77%) of the CT procedures in all three centres and objectively measured ventilation in 37 (57%) cases using the $NICO_2$® respiratory monitor. Of the 65 scans, 15% were performed at centre A, 58% at centre B and 26% at centre C.

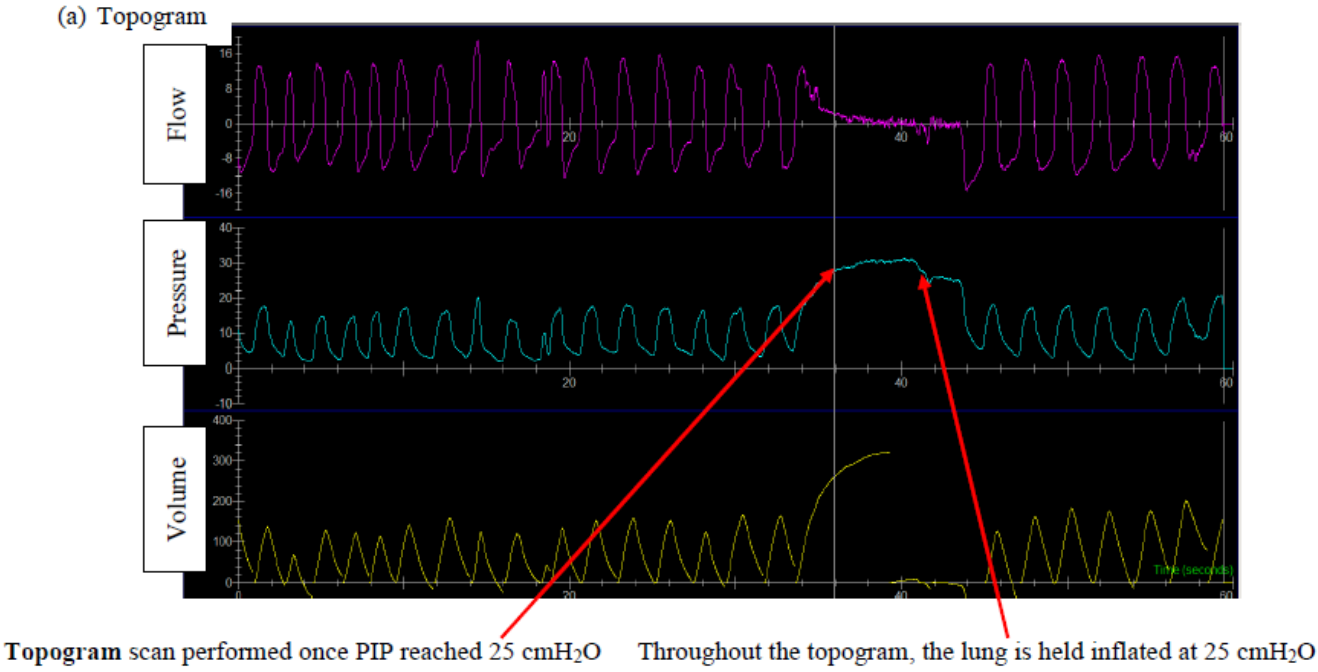
By using the respiratory monitor, ventilatory pattern was found to be similar across the three centres (Table E4). Figure E4 illustrates examples of when ventilatory protocol was not closely adhered to during the GA process for CT scanning.

Table E4: Ventilatory pressures monitored across the three centres using the $NICO_2^{®}$ respiratory monitor

	Centre A	Centre B	Centre C	Overall
PIP during recruitment	32.8(30.4;34.2)	32.6(30.1;35.5)	33.0(30.7;35.5)	32.9(30.6;35.1)
PEEP during recruitment	7.4(6.1;9.8)	8.0(6.5;9.1)*	5.2(2.9;7.6)*	7.2(5.4;8.8)
PIP during breath-hold	26.0(16.3;28.8)	27.6(25.5;29.0)	25.1(23.7;26.2)	26.2(24.5;27.9)

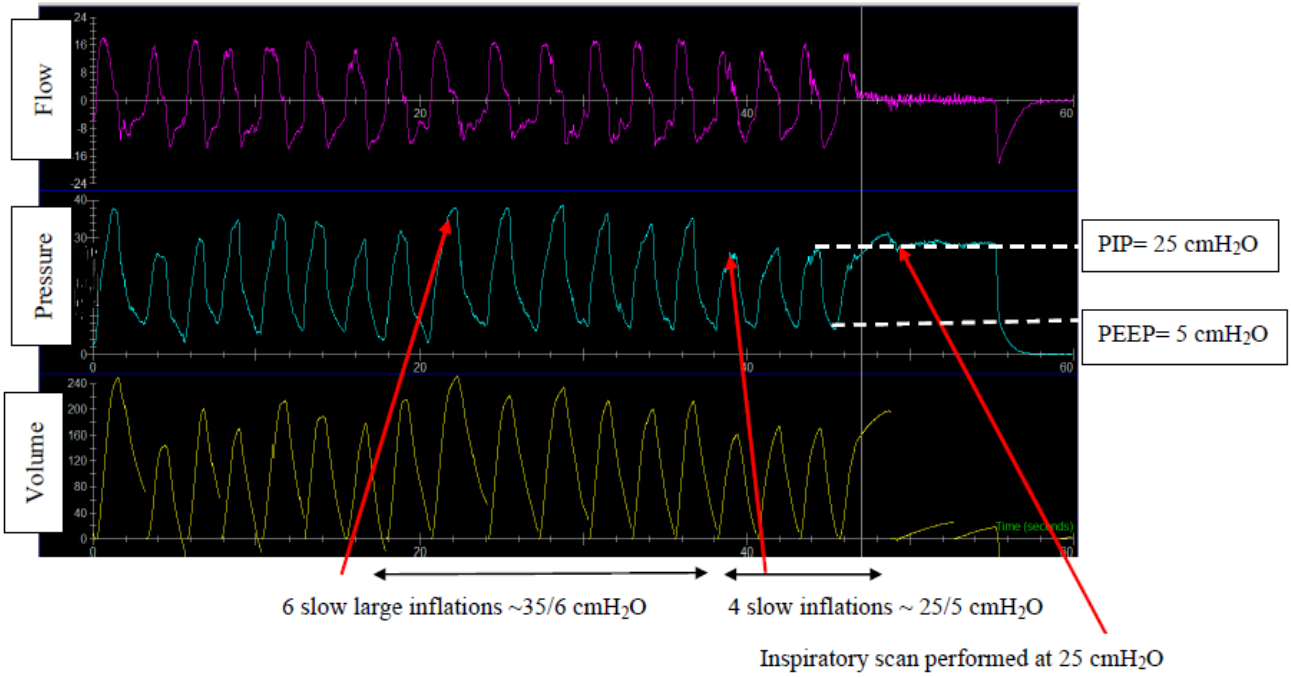
Footnote: Results expressed as median (inter-quartile ranges) cm H_2O. *significant diff $p<0.05$

Figure E3: Screenshot of $NICO_2$® measurements during GA for chest CT scan

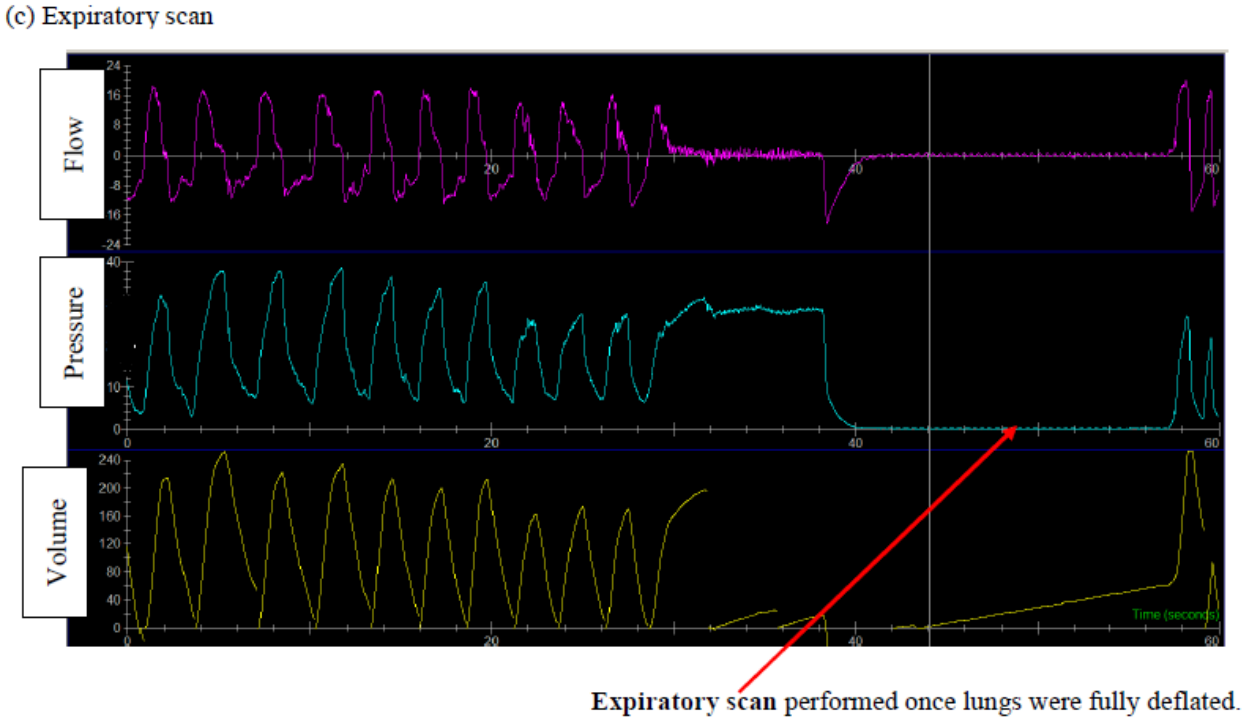


Legend: The top trace (purple) records the flow, the middle trace (turquoise) records the pressure and the bottom trace (yellow) records the volume of each inflated breath during GA. Prior to performing the topogram, baseline ventilation provided initially via the anaesthetic machine using tidal volume of 8-10 ml/kg and PEEP 5 cmH_2O. Once ready for topogram, ventilation was switched to manual ventilation. During topogram, the infant's lungs were inflated to a PIP of ~25 cm H_2O and when this pressure was attained, topogram was acquired during the breath hold at PIP 25 cmH_2O.

(b) During recruitment maneuvers and inspiratory scan

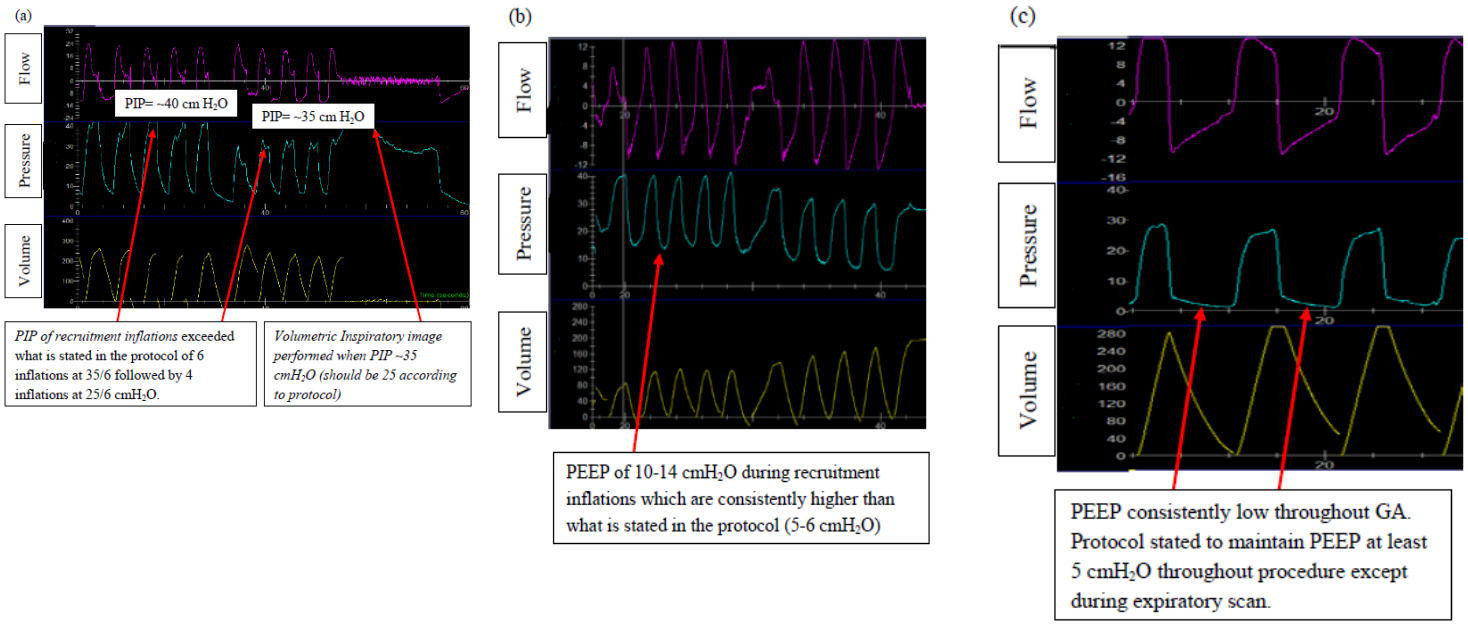


Legend: Prior to the inspiratory scan being acquired, 6 larger and slower inflations of PIP 35-40 cmH_2O were administered to reverse any GA-related atelactasis followed by 4 smaller and slow inflations of 25/5 cmH_2O. During the last of the 4 smaller inflations, the inflation was held at 25 cmH_2O and once attained, the inspiratory image was acquired.



Legend: Immediately following the acquisitionof the inspiratory scan, the inflation was released and the infant's lungs were allowed to deflate down to their elastic equilibrium volume, FRC (zero PEEP), before the expiratory scan was performed.

Figure E4: Examples of $NICO_2$® measurement screenshots, showing examples of when GA did not closely adhered to protocol.



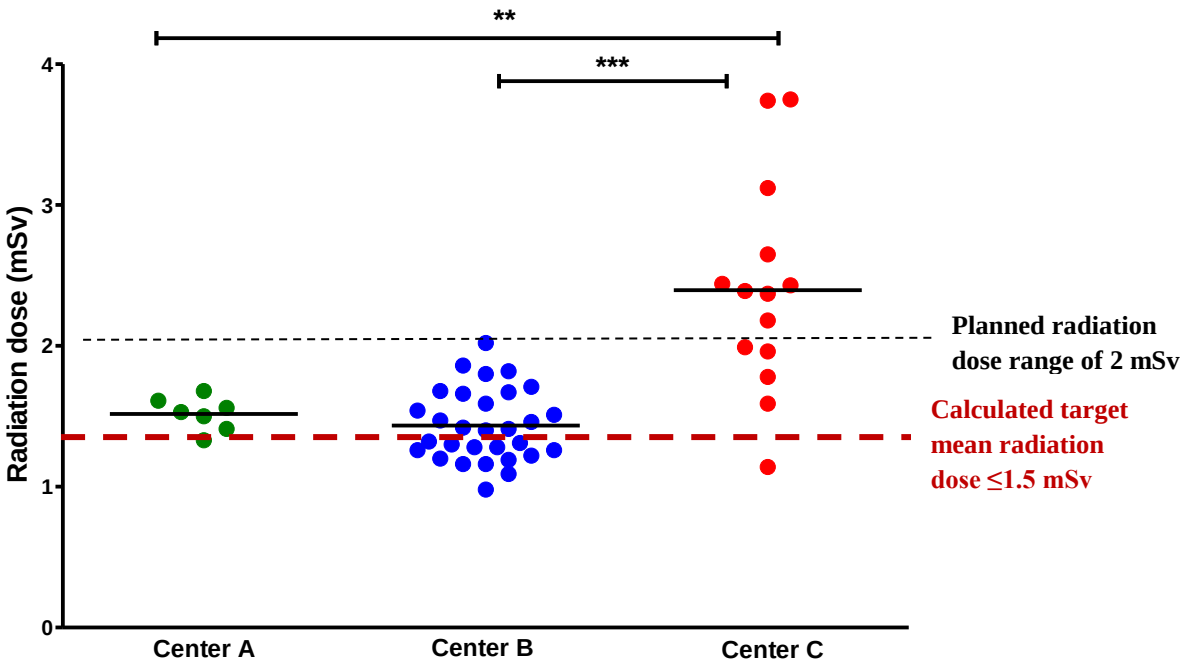
6. Radiation doses

Radiation exposure was minimised using automated dose modulation which performs a real time assessment of body thickness and adjusts tube current to provide consistent image quality. Patient dose information including CT dose index (CTDIvol, unit mGy) and dose-length product (DLP, unit mGy·cm) was recorded for each examination. The effective dose (E) was estimated from taking the DLP and applying a pediatric age specific conversion coefficient that is 0.026 for a child between 4 months and 1 year, and a correction factor of 2 to correct for the use of a 32 cm rather than 16 cm phantom. The formula used was: DLP x 2 x 0.026 = estimated effective dose milliSievert (EmSv).[E8,9]

Results of radiation doses across centres

The highest median radiation exposure was measured at centre C with a lower dose at centre A and the lowest dose at centre B (Table E5 and Figure E3). The greater variability in radiation doses observed in centre C may be due to the slightly different type of scanner (Table E1) and/or the fact that it was not possible to organise a dedicated radiographer to perform procedures within that hospital.

Figure E5: Radiation doses from chest CT across three centres



Legend: Solid horizontal line demonstrates the median radiation doses from each centre. mSv: milliSievert; a unit of measure for effective radiation exposure.**p<0.01; ***p<0.001

Table E5: Effective radiation doses from volumetric inspiratory and expiratory chest CT scans across three centres (n=53)*

	Centre A (n=7)	Centre B (n=31)	Centre C (n=15)	Overall dose
Median (mSv)	1.53	1.31	2.38	1.50
Inter- quartile range, IQR (mSv)	1.37- 1.65	0.86- 2.02	1.14- 3.75	1.24-1.84

Footnote: n= number of scans performed in each centre. mSv= milliSievert, unit of measuring ionising radiation. *The first eight scans performed were limited to 3-slices expiratory scans so have been excluded from these calculations. With these limited expiratory scans (n=8), median (IQR) radiation dose was 1.07(0.92;1.34) mSv. Of the remaining 57 full

volumetric scans, radiation dose for 4 of the later scans could not be calculated due to the lack of available qualified staff.

7. Scoring results

Training scans and scoring

Prior to the two observers commencing their scoring of study scans, they underwent two training sessions. Training scans were provided by the AREST-CF team from children with CF aged 1- 4 years in whom data had been acquired using a similar full volumetric inspiratory and expiratory imaging protocol standardised at an inspiratory lung volume of 25 cmH_2O as in this LCFC study; although in the early published reports of the AREST study, only 3 image slices were acquired at end expiration. Both observers independently evaluated the first 6 training scans (training batch 1) using the Brody-II scoring system.[E6] Scores were then compared and the cases with different scores were discussed by video-conference, with particular attention to differences in the identification of bronchial dilatation.

A second batch of six training studies was then independently evaluated and scores compared (training batch 2). The level of agreement for bronchial dilatation with this second training batch improved when compared to the first batch and was deemed acceptable by both observers (Table E6), who then progressed to the scoring of CT scans obtained for the definitive LCFC study of NBS infants with CF. Agreement for mucous plugging and parenchymal change sub-scores were lower with the second training batch leading to an overall lower Kappa agreement with the total scores of the second training batch. Figure E6 shows the range of sub-scores allocated by the two scorers during the two training batches.

Table E6: Inter-observer agreement of scores according to Brody-II scoring system during the two training batches

	Training batch 1 (n=6)	Training batch 2 (n=6)
Age of infants (years)*	2.0 (1.2; 2.6)	2.3 (1.4; 3.0)
Bronchial dilatation[#]	0.27 (0.08; 0.46)	0.45 (0.17; 0.72)
Air trapping[#]	0.82 (0.68; 0.95)	0.79 (0.67; 0.92)
Total CT scores[#]	0.75 (0.61; 0.90)	0.43 (0.10; 0.75)

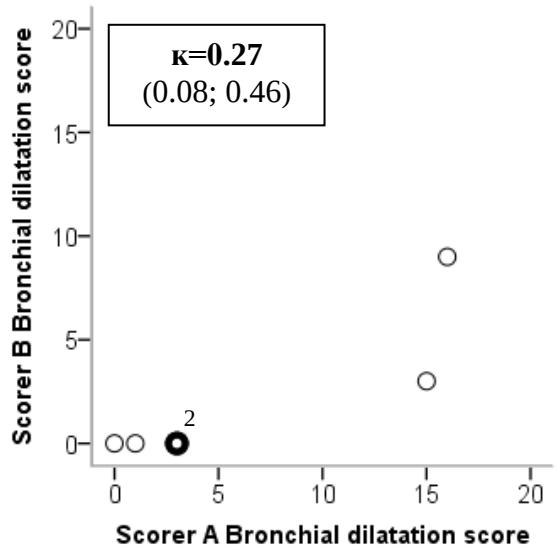
Footnote: * Age expressed as median (interquartile range) in years. [#] Agreement expressed as mean Kappa coefficient (95% confidence interval) using linear weighted Kappa statistics.

Figure E6: Scores allocated by scorers A and B for the two batches of training scans (n=12)

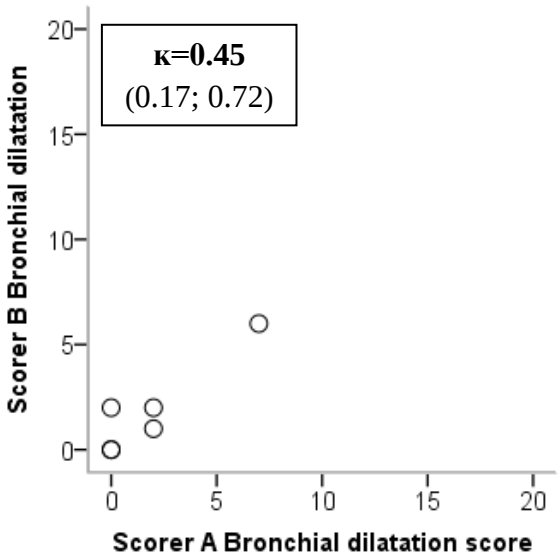
1st training batch (n=6)

2nd training batch (n=6)

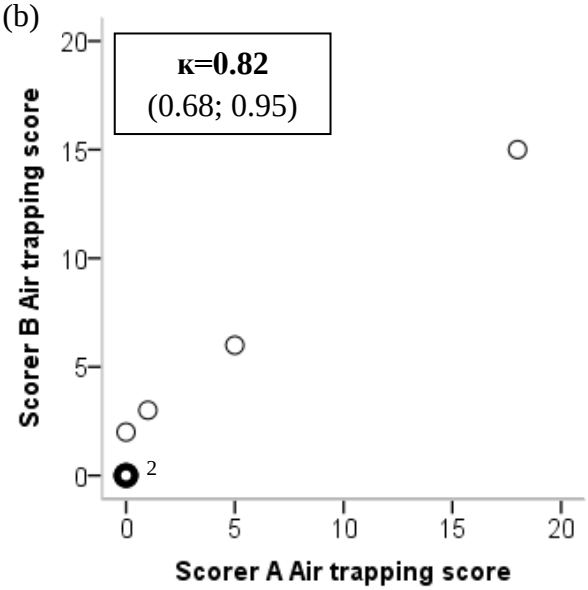
(a)



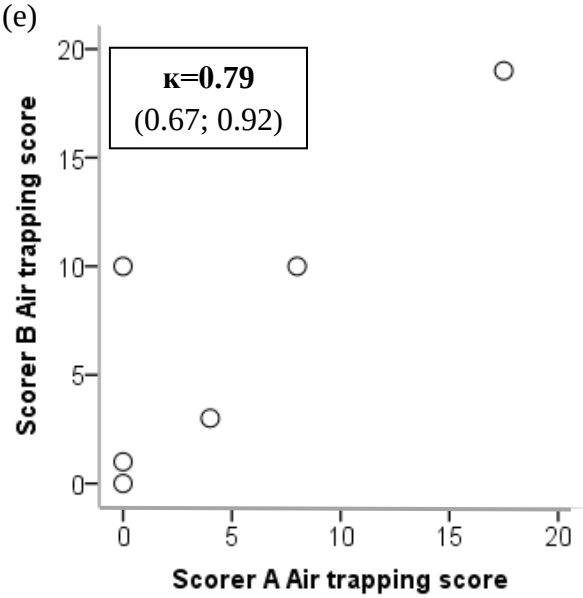
(d)



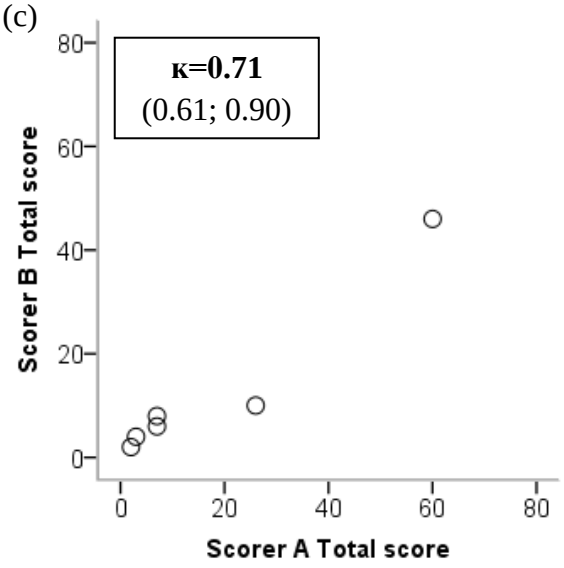
(b)



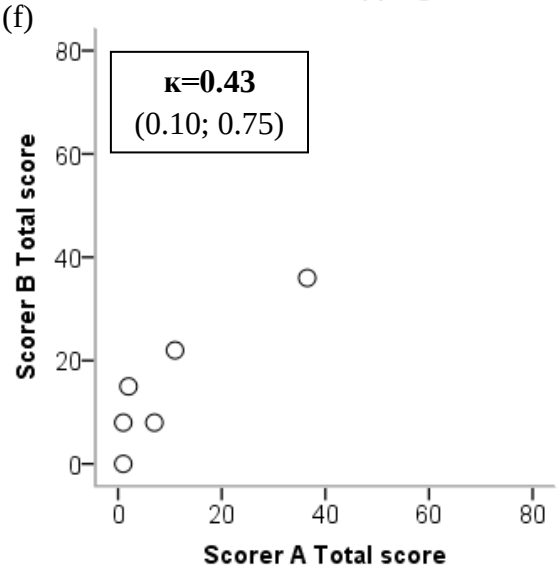
(e)



(c)



(f)



Legend: Scores allocated by scorers A and B for the two training batches with first batch scores represented by plots a to c and second batch scores represented by plots d to f. Bolder circles represent overlapping results with the number of overlapping data next to it. κ= Kappa coefficient (95% CI)

Panels (a-f) shows paired scores allocated by scorer A and B for each training scan in terms of bronchial dilatation and air trapping sub-scores and total CT scores during each of the two training batches. In (a & c): scorer A gave higher bronchial dilatation score and total score compared to scorer B at first training batch but subsequently allocated more similar scores during the second training batch (d & f). With air trapping (b & e), both observers were consistent with their scores at first and second training batches. Scans from both batches were similar in terms of severity for air trapping (median, range) [Batch 1: scorer A: 0.5(0-18) and scorer B: 2.5(0-15); Batch 2: scorer A: 2 (0-18) and scorer B: 6.5 (0-19)]. There appeared to be higher scores during the 1st than 2nd batch for both bronchial dilatation [Batch 1: scorer A (median, range): 3(0-16) and scorer B: 0(0-9) vs. Batch 2: scorer A: 1(0-7) and scorer B: 1.5(0-6)], and for total CT scores [Batch 1: scorer A 7 (2-60) and scorer B 7 (2-46) vs. Batch 2: scorer A: 4.5 (1-37) and scorer B 11.5 (0-36)].

Re-assessment of discrepant sub-scores following initial scoring of the LCFC scans

Of the 65 LCFC scans analysed, discrepancies were found in 50. A record of these was collated by LT. Following a short general discussion about the scoring system, both scorers independently re-scored these discrepant observations, blinded to their own and their counterpart's initial scores. Analysis of the discrepant cases showed that 90% of observed differences were between a score of 0 (normal), and 1 (minimal to mild disease). Following this rescoring of discrepant sub-scores, good agreement was observed for bronchial dilatation [Mean Kappa coefficient=0.62 (95% CI: 0.39; 0.86)] and excellent agreement for air-trapping [Mean Kappa coefficient=0.88 (95% CI: 0.81; 0.96)]. These Kappa coefficients for agreement were higher than those obtained during the initial scoring of the LCFC scans when the mean (95% CI) Kappa coefficient was 0.21 (0.05; 0.37) for bronchial dilatation and 0.66 (0.49; 0.83) for air trapping (see Table 3, main paper).

This reassured both scorers that improved inter-observer agreement could be achieved before undertaking complete rescoring of a selected sub-set of 22 LCFC scans 8 months after initial scoring, although subsequently this did not prove to be the case. The subset of 22 scans that underwent rescoring was selected by LT, who was not involved in the scoring process, and who selected every third scan from the list of study participants that had had CT scans, without any reference to scores previously allocated."

Intra-observer agreement of sub-scores during initial and re-scoring of LCFC scans

Both scorers only achieved fair intra-observer agreement for bronchial dilatation sub-score (Figure E7, panels a&b) but strong agreement for air trapping (Figure E7, panels c&d) after an interval of ~8m. Scorer A detected an identical proportion of changes when re-scoring as

did scorer B, with the exception of one less child with bronchial dilatation on re-score (Table E7).

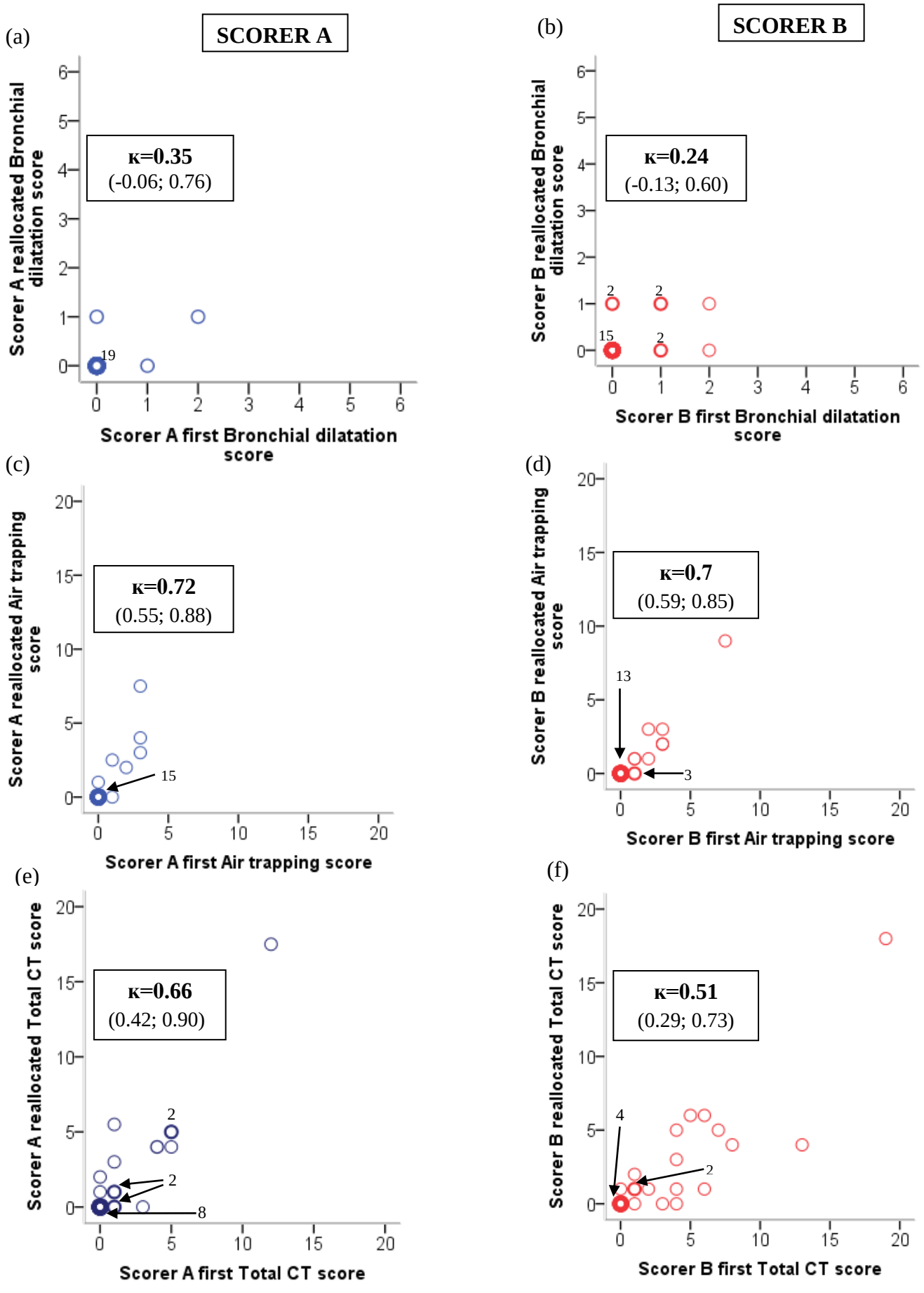
Although Kappa agreement between scorers was only fair for bronchial dilatation initially with minimal improvement during rescoring, agreement as to the presence or absence of bronchial dilatation or air trapping rather than the actual scores allocated was consistently achieved in >80% of the scans on initial and rescoring rounds. (Table E7).

Table E7: Inter-observer agreement with respect to presence or absence of bronchial dilatation and air trapping during initial and re-scoring rounds

	Bronchial Dilatation			**Air trapping**		
	Present	Absent	Total % agreed	Present	Absent	Total % agreed
initial scoring of all 65 scans	5 (8%)	48 (74%)	82%	16 (25%)	37 (57%)	82%
initial scoring of subset (n=22)	2 (9%)	17 (77%)	86%	5 (23%)	14 (67%)	90%
repeat scoring of subset (n=22)	1 (4.5%)	17 (77%)	81.5%	5 (23%)	14 (64%)	87%

The challenges faced, even by those with considerable expertise in the field, in discriminating very mild changes that could be attributed to bronchial dilation or air trapping from normal are illustrated in Figure 2 of the main paper in which discrepancies were observed both between and within observers with respect to scores allocated on two different occasions.

Figure E7: Intra-observer agreement for scorers A and B when rescoring bronchial dilatation, air trapping and total score after an interval of 8 months (n=22)



Legend: Scores allocated by scorer A represented as blue circles and by scorer B represented as red circles. Bolder circles represent overlapping results with the number of overlapping data next to it.

κ= Kappa coefficient (95% CI): fair intra-observer agreement for bronchial dilatation and total scores (panels a & b and e & f) and strong intra-observer agreement for air trapping (panels c & d). Although similar percentages of changes were detected on both occasions, the observers did not necessarily detect changes in the same infants during the two separate rounds.

Table E8: Comparison of measures of within- and between-observer variability used in the current and selected previous studies

Study	Current study		Brody et al[*][E6]		Owens et al[†][E4]	Brody et al* [E3]	De Jong et al [E10]	Stick et al [E11]
Population studied	NBS CF		NBS and clinically diagnosed CF		Clinically diagnosed CF	Clinically diagnosed CF	Clinically diagnosed CF	NBS CF
Age: years [‡]	1.0 (0.1)		10.5 (0.7)		7.8 (1.3)	6-10 [§]	5-52 [§]	1.1(0.3-3.3)[‖]
Scoring system	Brody-II		Brody-II		Brody-II	Brody-II	Brody-II	Specific[**]
Measure of variability	Between Obs kappa	Within Obs kappa	Between Obs variability	Within Obs variability	Between Obs Kendall's tau	Within Obs kappa	Between Obs ICC	Within Obs kappa
Bronchial dilatation	0.21	0.24/0.35	0.04	0.06	0.77	0.64	0.88	0.64
Air-trapping	0.66	0.72/0.72	0.07	0.04	0.59	0.55	0.27	0.55

Footnote: [*]Studies included scorer A as an observer. [†]Studies including scorer B as an observer. Obs = Observer; ICC = Intraclass correlation

[‡]Age at time of CT scan, expressed as mean (SD) unless otherwise stated. [§] Age expressed as range. [‖]Age as median (inter-quartile range) [**]

AREST-CF CT scoring system

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