Le Lung Clearance Index est-il supérieur à la pléthysmographie (pour détecter une atteinte débutante des voies aériennes périphériques) ?

Peut-on utiliser d'autres mesures aux EFR ?

Christophe Delclaux
Service de Physiologie – Explorations Fonctionnelles
Centre du Sommeil

Université Paris Cité

Hôpital Robert Debré

Atteinte des voies aériennes périphériques (obstruction débutante), quelles mesures ?

- Lung Clearance Index ou LCI
- Pléthysmographie
    - Résistance spécifique des voies aériennes: sRaw
    - Distension thoracique: mesure des volumes statiques
- Oscillations forcées

Développement d'un test diagnostic *(Lijmer JG, Empirical evidence of design-related bias in studies of diagnostic tests. JAMA. 1999;282:1061-1066)*

Problème du « gold standard » : quelle mesure de référence ?

- Scanner thoracique
- *Spirométrie car mesure « habituelle »*
- *Valeurs normales: sujets sains*

An Official American Thoracic Society Workshop Report: Optimal Lung Function Tests for Monitoring Cystic Fibrosis, Bronchopulmonary Dysplasia, and Recurrent Wheezing in Children Less Than 6 Years of Age

Margaret Rosenfeld, Julian Allen, Bert H. G. M. Arets, Paul Aurora, Nicole Beydon, Claudia Calogero, Robert G. Castile, Stephanie D. Davis, Susanne Fuchs, Monika Gappa, Per M. Gustaffson, Graham L. Hall, Marcus H. Jones, Jane C. Kirkby, Richard Kraemer, Enrico Lombardi, Sooky Lum, Oscar H. Mayer, Peter Merkus, Kim G. Nielsen, Cara Oliver, Ellie Oostveen, Sarath Ranganathan, Clement L. Ren, Paul D. Robinson, Paul C. Seddon, Peter D. Sly, Marianna M. Sockrider, Samatha Sonnappa, Janet Stocks, Padmaja Subbarao, Robert S. Tepper, Daphna Vilozni; on behalf of the American Thoracic Society Assembly on Pediatrics Working Group on Infant and Preschool Lung Function Testing

AnnalsATS Volume 10 Number 2 | April 2013

As sRaw is the product of airway resistance (Raw) and FRC, both of which may increase in the presence of airway obstruction and hyperinflation, it is a potentially useful method for identifying obstructive lung disease in young children.

	In RV				reschool Rint	Preschool FOT	MBW
Commercial equipment	Yes					Yes	Yes
Standard operating procedure	Yes					Yes	Yes
Safe	Yes*					Yes	Yes
Feasible	Yes*					Yes	Yes
Adequate population-based reference data	No†	No†	Yes‡	No	Yes‡	Yes‡	Yes‡
Within-test intrasubject variability measured	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Discriminates disease population from healthy control subjects							
CF	Yes	Yes	Yes§	Yes	No	Conflicting	Yes
BPD	Yes	Yes	Unknown	Unknown	Unknown	Unknown	Probably not
Recurrent wheeze	Yes	No	Yes¶	Unknown	Yes¶	Unknown	Probably
Evidence for clinical utility	Not assessed	Not assessed	Not assessed	Not assessed	Not assessed	Not assessed	Not assessed

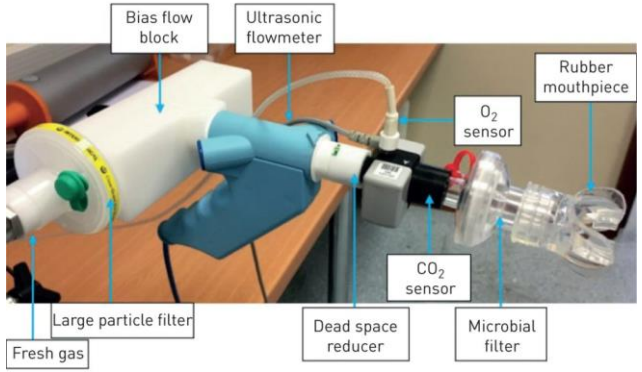
Le Lung Clearance Index (LCI) : Index de clairance pulmonaire

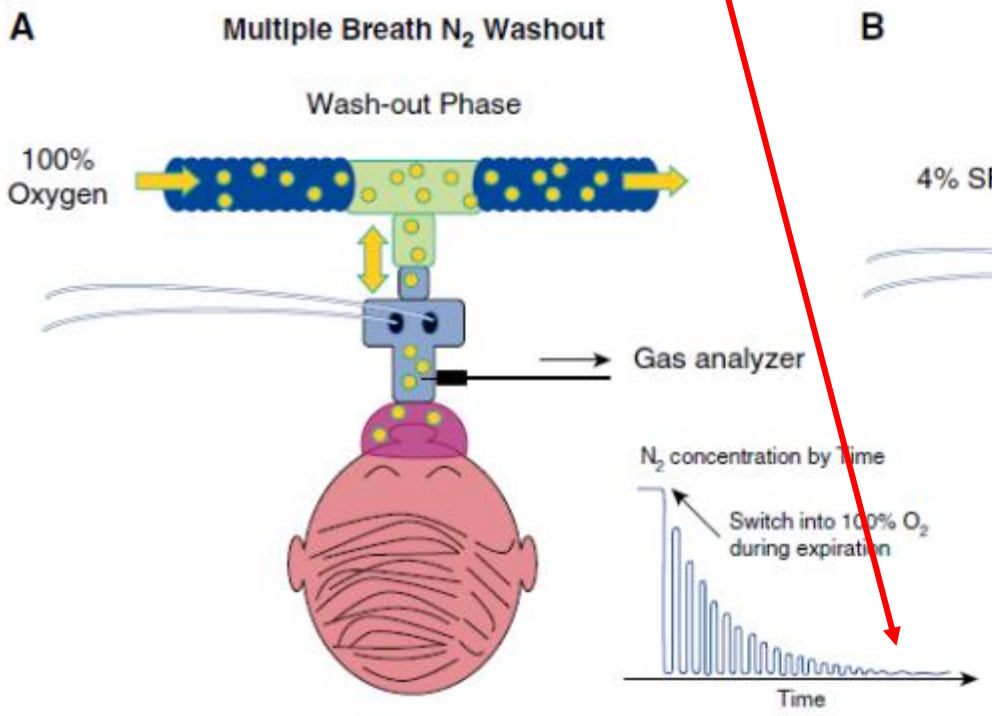
Mesure en ventilation spontanée
Inhalation d'oxygène à FIO2 100%
Clairance de l'azote (N_2)
Norme établie

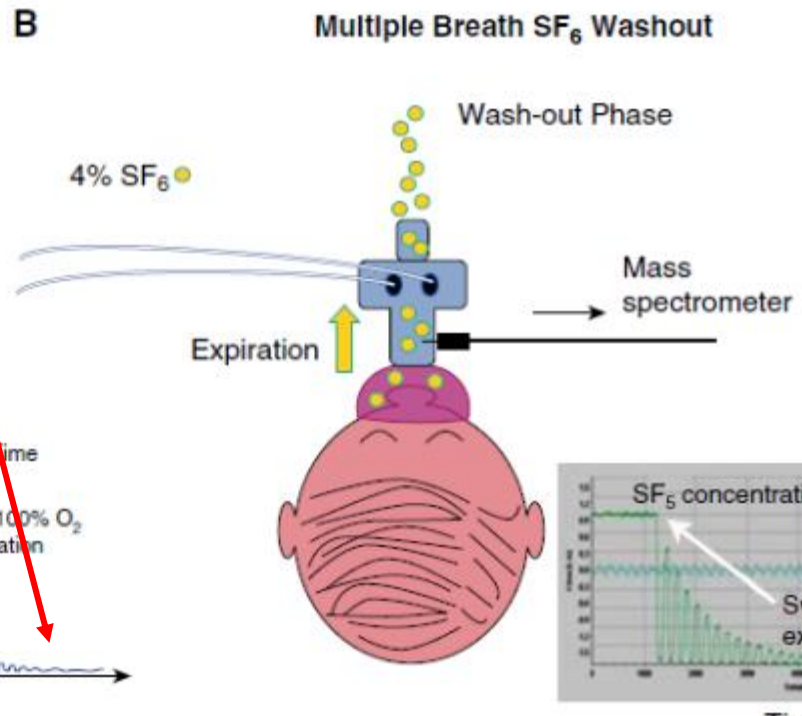
LCI = CEV/FRC

In other words, LCI represents a measure of the number of times the volume of gas in the lung at the start of the washout (the FRC) must be turned over in order to wash out the tracer to the pre-defined endpoint. With increasing disease severity, LCI increases.

Elimination « complète » quand la [N_2] diminue à 1/40ème de la concentration initiale: $LCI_{2,5\%}$







Thorax (1952), 7, 111.

A NEW INDEX OF THE INTRAPULMONARY MIXTURE OF INSPIRED AIR

BY

MARGARET R. BECKLAKE

From the Department of Medicine, Postgraduate Medical School of London, and the Cardio-Pulmonary Unit, C.S.I.R. Department of Medicine, University of the Witwatersrand

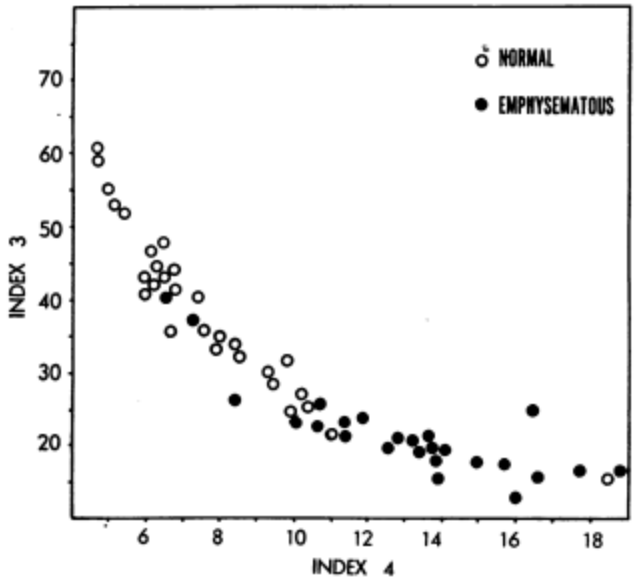


FIG. 2.—Comparison of index 3 (after Bates and Christie) with index 4 (lung clearance index).

THE "LUNG CLEARANCE INDEX"

It seemed that a simpler index might be provided by an estimate of the litres of ventilation required to wash each litre of the functional residual air (F.R.A.) free of nitrogen while the subject breathes pure oxygen. This has been named the "lung clearance index" and is calculated as follows :

$$\frac{\text{Litres ventilation required to wash 90\% F.R.A. free of } N_2}{\text{90\% F.R.A.}}$$

On the other hand, the close grouping of the normals as calculated by index 4 gave a standard deviation of ± 1.68 about the mean of 7.02. For this index, figures greater than 10.38 are likely to indicate impaired intrapulmonary mixing with a significant difference from the normal.

Multiple-breath inert gas washout and spirometry versus structural lung disease in cystic fibrosis

P M Gustafsson,[1] P A De Jong,[2,3,4] H A W M Tiddens,[2] A Lindblad[1]

Thorax 2008;**63**:129–134.

LCI: cercles noirs
VEMS: cercles blancs
FEF75: cercles gris

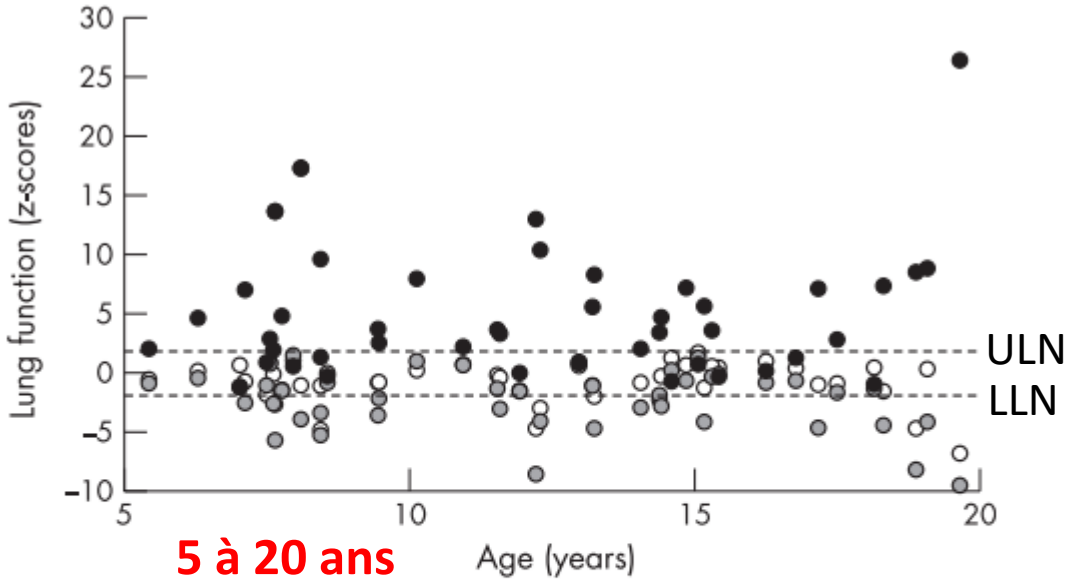


Figure 1 Lung function (lung clearance index (LCI), forced expiratory volume in 1 s (FEV_1) and maximal expiratory flow when 75% of forced vital capacity was expired (FEF_{75})) expressed as z-scores plotted against age in 44 children and teenagers with CF. Black filled circles denote LCI, open circles FEV_1 and grey circles FEF_{75}. The horizontal hatched lines denote the upper and lower limits of normality (LLN) for the lung function variables.

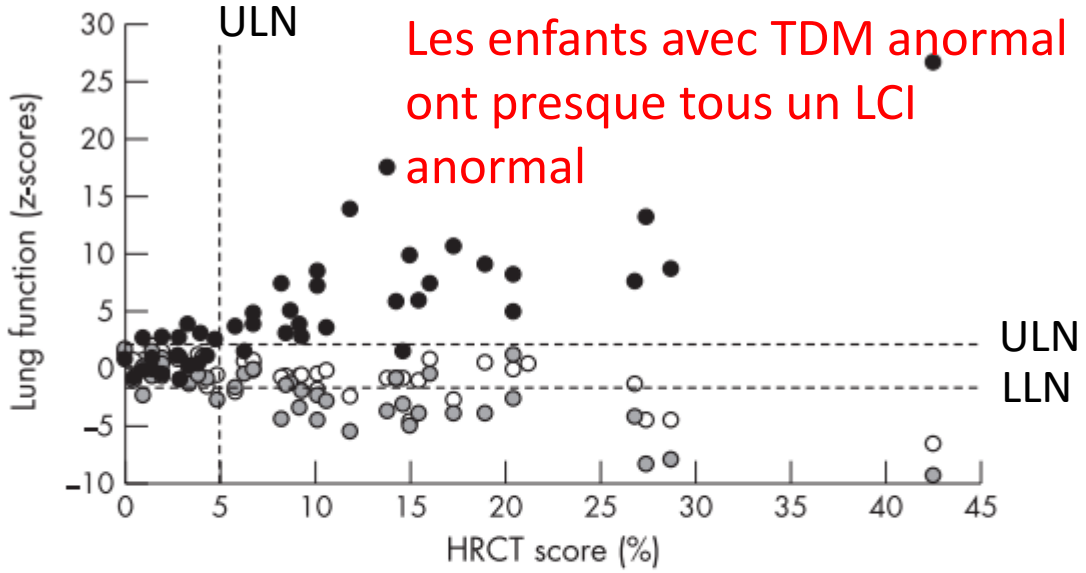


Figure 2 Lung function (lung clearance index (LCI), forced expiratory volume in 1 s (FEV_1) and maximal expiratory flow when 75% of forced vital capacity was expired (FEF_{75})) expressed as z-scores plotted against HRCT (composite scores) in 44 children and teenagers with CF. Black filled circles denote LCI, open circles FEV_1 and grey circles FEF_{75}. Vertical hatched line denotes upper limit of normality (ULN) for HRCT score and horizontal hatched lines denote upper and lower limits of normality (LLN) for the lung function variables.

Table 1 Agreement between LCI, FEV_1 and FEF_{75} and structural lung changes classified as abnormal or normal

	Bronchiectasis		HRCT score		Air trapping	
	Yes	No	>5%	⩽5%	>30%	⩽30%
LCI						
Abnormal	22	9	25	6	15	16
Normal	4	9	2	11	1	12
	p = 0.033		p<0.001		p = 0.027	
FEV_1						
Abnormal	5	2	7	0	4	3
Normal	21	16	20	17	12	25
	p = 0.761		p = 0.062		p = 0.413	
FEF_{75}						
Abnormal	16	3	17	2	12	7
Normal	10	15	10	15	4	21
	p = 0.008		p = 0.003		p = 0.004	

LCI, lung clearance index; FEV_1, forced expiratory volume in 1 s; FEF_{75}, maximal expiratory flow when 75% of forced vital capacity was expired; HRCT, high-resolution CT.
HRCT score >5% is defined as abnormal and >30% air trapping is defined as abnormal.
p Values refer to the Yates corrected χ^2 test.

Conclusions: LCI is a more sensitive indicator than FEV_1 or FEF_{75} for detecting structural lung disease in CF, and a normal LCI almost excludes HRCT abnormalities. The finding of an abnormal LCI in some patients with normal HRCT scans suggests that LCI may be even more sensitive than HRCT scanning for detecting lung involvement in CF.

Quel gold standard ?

Table 2 Sensitivity and specificity (expressed as percentage with 95% confidence intervals in parentheses) for LCI, FEV_1 and FEF_{75} with respect to HRCT-defined structural lung abnormalities

	Bronchiectasis	HRCT score	Air trapping
LCI			
Sensitivity	85 (71 to 98)	93 (83 to 100)	94 (82 to 100)
Specificity	50 (27 to 73)	65 (42 to 87)	43 (25 to 61)
FEV_1			
Sensitivity	19 (4 to 34)	26 (9 to 42)	25 (4 to 46)
Specificity	89 (74 to 100)	100 (100 to 100)	89 (78 to 100)
FEF_{75}			
Sensitivity	62 (43 to 80)	63 (45 to 81)	75 (54 to 96)
Specificity	83 (66 to 100)	88 (73 to 100)	75 (59 to 91)

LCI, lung clearance index; FEV_1, forced expiratory volume in 1 s; FEF_{75}, maximal expiratory flow when 75% of forced vital capacity was expired; HRCT, high-resolution CT.

Lung Clearance Index and Structural Lung Disease on Computed Tomography in Early Cystic Fibrosis

Kathryn A. Ramsey[1,2*], Tim Rosenow[1,3*], Lidija Turkovic[1], Billy Skoric[4,5], Georgia Banton[1], Anne-Marie Adams[4,5], Shannon J. Simpson[1], Conor Murray[6], Sarath C. Ranganathan[4,5,7], Stephen M. Stick[1,8†], and Graham L. Hall[1†]; on behalf of AREST CF[‡]

American Journal of Respiratory and Critical Care Medicine Volume 193 Number 1 | January 1 2016

Table 1. Demographics of Study Population

Characteristics	Infants	Preschool	School Age
Number of children	42	39	38
Number of visits	49	52	48
Age, yr	0.94 (0.57)	5.42 (1.05)	9.77 (2.48)
Sex, n (males/females)	16/26	16/23	21/17
Height, *z*-score (95% CI)	0.03 (−0.20 to 0.28)	0.08 (−0.20 to 0.34)	−0.20 (−0.44 to 0.04)
Weight, *z*-score (95% CI)	−0.12 (−0.33 to 0.53)	0.19 (−0.13 to 0.51)	0.26 (−0.04 to 0.55)
FEV_1, L (95% CI)			1.80 (1.65 to 1.95)
FEV_1, *z*-score (95% CI)			−0.13 (−0.51 to 0.26)
FVC, L (95% CI)			2.19 (2.03 to 2.34)
FVC, *z*-score (95% CI)			0.23 (−0.12 to 0.57)
Phe508del/Phe508del	58% (25/42)	62% (25/39)	54% (21/38)
Phe508del/other	36% (16/42)	30% (12/39)	35% (14/38)
Severe genotype	88% (38/42)	91% (35/39)	88% (34/38)
Multiple breath washout			
FRC	0.19 (0.08)	0.91 (0.19)	1.51 (0.77)
Lung clearance index	7.81 (0.80)	8.17 (1.22)	8.35 (1.78)
First moment ratio	2.30 (0.28)	1.78 (0.24)	1.95 (0.91)
Second moment ratio	11.02 (4.16)	8.80 (2.05)	7.19 (3.41)
PRAGMA-CF scores			
Bronchiectasis present	20% (10/49)	69% (36/52)	69% (33/48)
Air trapping present	58% (29/49)	85% (44/52)	94% (45/48)
Bronchiectasis extent, %	0.18 (0.34)	1.88 (3.38)	2.05 (3.21)
Air trapping extent, %	1.35 (2.73)	6.37 (12.02)	20.8 (21.34)
Disease extent, %	1.35 (1.05)	4.26 (4.29)	4.86 (5.13)

+ 72 enfants témoins

Spirométrie normale

Air trapping très précoce et très prévalent: associé à une distension aux EFR ?

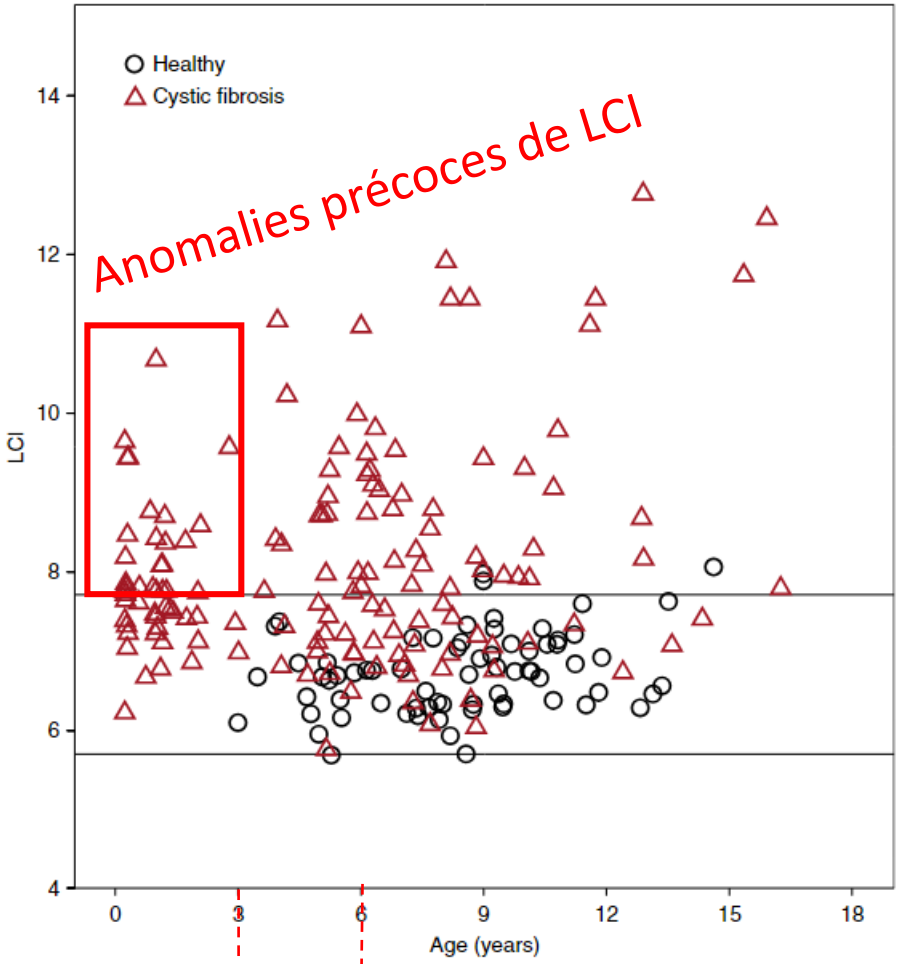


Figure 1. Lung clearance index (LCI) plotted against age for healthy control children (*circles*) and children with cystic fibrosis (*triangles*). *Horizontal lines* indicate the upper (7.7) and lower (5.7) limits of normal for LCI.

Age de la spirométrie

Age de début des EFR préscolaires

- sRaw
- IOS ou FOT

Table 2. Agreement between LCI and Presence of Bronchiectasis on the Basis of Chest CT Using PRAGMA-CF Scores

	Infants	Preschool	School Age
LCI ULN	Derived from Lum *et al.*, 2013 (26)	7.7	7.7
Abnormal LCI	22% (11/49)	58% (30/52)	58% (28/48)
Bronchiectasis present	20% (10/49)	69% (36/52)	69% (33/48)
Concordance	65% (32/49)	69% (36/52)	73% (35/48)
κ-Coefficient	−0.03 (−0.05 to 0.16)	**0.35 (0.10 to 0.60)***	**0.42 (0.20 to 0.64)***
Sensitivity, %	20 (2.5 to 56)	69 (52 to 84)	73 (55 to 87)
Specificity, %	77 (61 to 89)	69 (41 to 89)	73 (45 to 92)
Positive predictive value, %	18 (2.3 to 52)	83 (65 to 94)	86 (67 to 96)
Negative predictive value, %	79 (63 to 90)	50 (28 to 72)	55 (32 to 77)

Table 3. Agreement between LCI and Presence of Air Trapping on the Basis of Chest CT Using PRAGMA-CF Scores

	Infants	Preschool	School Age
LCI ULN	Derived from Lum *et al.*, 2013 (26)	7.7	7.7
Abnormal LCI	22% (11/49)	58% (30/52)	58% (28/48)
Air trapping present	58% (29/49)	85% (44/52)	94% (45/48)
Concordance	65% (32/49)	60% (31/52)	56% (27/48)
κ-Coefficient	**0.30 (0.06 to 0.54)***	0.15 (−0.13 to 0.43)	−0.02 (−0.16 to 0.14)
Sensitivity, %	38 (19 to 59)	63 (45 to 79)	58 (42 to 72)
Specificity, %	92 (74 to 99)	53 (28 to 77)	33 (0.84 to 91)
Positive predictive value, %	82 (48 to 98)	73 (54 to 88)	93 (77 to 99)
Negative predictive value, %	61 (43 to 76)	41 (21 to 64)	5 (0.13 to 25)

Early follow-up of lung disease in infants with cystic fibrosis using the raised volume rapid thoracic compression technique and computed tomography during quiet breathing

Pediatric Pulmonology. 2017;52:1283–1290.

Rémi Gauthier[1] | Yann Cabon[2] | Marie Agnes Giroux-Metges[3] | Cecile Du Boisbaudry[3] | Phillipe Reix[4] | Muriel Le Bourgeois[5] | Raphael Chiron[6] | Nicolas Molinari[2] | Magali Saguintaah[7] | Francis Amsallem[8] | Stefan Matecki[8]

Scanner thoracique en ventilation spontanée

CTqb score: In a normal population, CTqb Z-scores higher than three correspond to a quantile higher than 97.5% (and thus indicate abnormal presence of air trapping in lungs).[30] At V1, 66% of infants had a CTqb score >3 and 50% at V2.

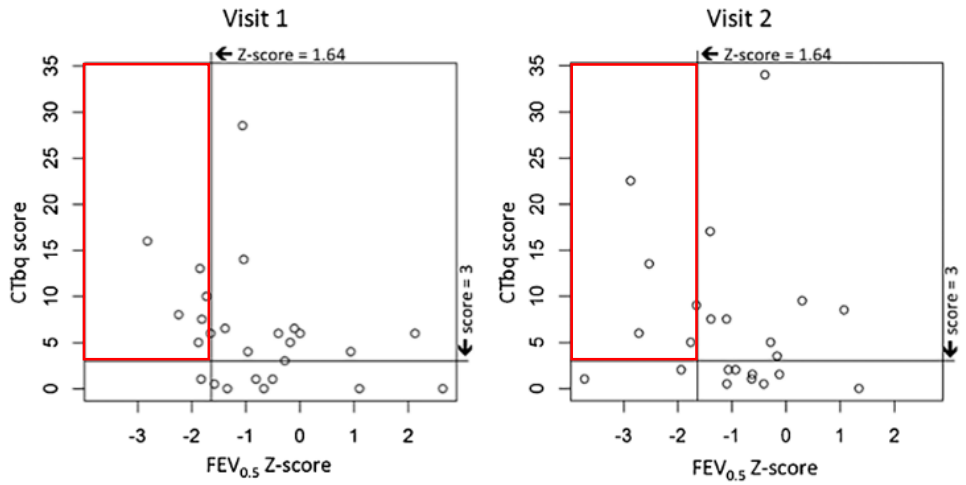


FIGURE 2 Relationship between pulmonary function at 10 weeks (visit 1) and 13 months (visit 2) of age in infants with cystic fibrosis detected by newborn screening. The upper limits (95th percentiles) of the "normal range" for the $FEV_{0.5}$ z-score (−1.64) and CTqb score (3) are represented by a vertical and horizontal line, respectively. At both visits, infants with normal $FEV_{0.5}$ z-score and CTqb score are in the lower right quadrant. Infants with abnormal CTqb score and normal $FEV_{0.5}$ z-score are in the higher right quadrant, while those with abnormal $FEV_{0.5}$ z-score and normal CTqb are in the left lower quadrant.

30% des nourrissons à V1 ont un z-score de FEV0.5 <-1,64, 28% à V2

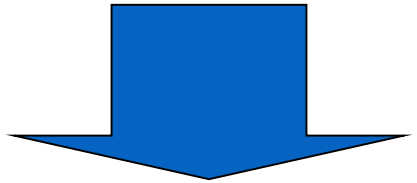
66% des nourrissons à V1 ont un CTqb score 3, 50% à V2

TABLE 1 Age, anthropometric characteristics, lung function parameters, and CTqb score of children with cystic fibrosis at the first (V1; 10 weeks of age) and second visit (V2; 13 months of age)

	V1	V2
N	30	28
Age weeks	11 [9.9, 11.9]	56.29 [54.9, 60.3]*
Weight (kg)	4.7 [4.3, 5.4]	9.4 [8.7, 10.0]*
Height (cm)	56 [54.0, 58.1]	75 [72, 77]*
BMI	15.2 [14.4, 16.1]	17.1 [16.1, 17.5]*
Weight z-score	−0.62 [−1.3, 0.1]	0.0 [−0.6, 0.8]*
Height z-score	−0.7 [−1.5, 0.3]	−0.4 [−1.0, 0.5]
BMI z-score	−0.5 [−1.1, 0.3]	0.2 [−0.2, 0.6]*
Bf (cpm)	41 [37, 46]	32 [29, 36]*
Vt (mL/kg)	9 [8.3, 9.6]	9.7 [9.0, 10.5]*
FRC (mL/kg)	20 [18.6, 22.9]	23.2 [19.2, 25.8]
Bf z-score	0.22 [−0.6, 1.1]	0.7 [0.3, 1.7]
Vt z-score	−0.4 [−1.1, 0.2]	−0.3 [−0.7, 0.4]
FRC z-score	0.6 [0.2, 1.5]	1.1 [0.5, 2.1]
$FEV_{0.5}$ (mL)	132.0 [121.1, 143.5]	275.0 [254.0, 303.8]*
FVC (mL)	153.0 [138.0, 182.7]	361.5 [309.7, 408.7]*
FEF_{25-75} (mL/s)	250.0 [196.4, 288.0]	464.0 [395.5, 503.7]*
$FEV_{0.5}$ z-score	−1.1 [−1.7, −0.3]	−1.0 [−1.7, −0.2]
FVC z-score	−1.1 [−1.9, 0.2]	−0.9 [−1.5, −0.1]
FEF_{25-75} z-score	−1.72 [−2.76, −0.49]	−1.74 [−2.24, −1.08]
CTqb z-score	5.0 [1.0, 6.5]	3.7 [1.4, 8.6]

Comparaison des EFR versus scanner thoracique (gold standard ?)

- anomalies précoces (nourrisson) de LCI
- LCI méthode plus sensible que spécifique
- Bonne valeur prédictive positive d'anomalies scannographiques
  (bronchectasies et piégeage gazeux)



Evaluation des EFR versus valeurs normales (5% d'erreurs assumées)

The Evolution of Airway Function in Early Childhood Following Clinical Diagnosis of Cystic Fibrosis

Sarath C. Ranganathan, Janet Stocks, Carol Dezateux, Andrew Bush, Angie Wade, Siobhán Carr, Rosemary Castle, Robert Dinwiddie, Ah-Fong Hoo, Sooky Lum, John Price, John Stroobant, Colin Wallis, and The London Collaborative Cystic Fibrosis Group

AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE VOL 169 2004

37 nourrissons avec CF

33 témoins sains

Technique de compression: RVTRC

TABLE 2. MEASUREMENTS OF ANTHROPOMETRY AND AIRWAY FUNCTION ON EACH TEST OCCASION

	Test 1			Test 2		
	CF Mean (*SD*)	Healthy Mean (*SD*)	Difference: CF − Healthy (*95% CI*)	CF Mean (*SD*)	Healthy Mean (*SD*)	Difference: CF − Healthy (*95% CI*)
Age, wk*	28.4 (16.6–43.0)	7.4 (5.7–8.9)	13.3, 25.6§	59.0 (48.3–69.0)	33.7 (28.1–50.1)	13.1, 27.6§
Weight, kg*	6.66 (4.90–8.12)	4.82 (4.45–5.61)	0.67, 2.45§	8.90 (8.11–10.7)	8.72 (8.18–9.13)	−0.40, 1.05
Weight z score‖‖	−1.78 (1.42)	−0.11 (1.1)	−2.2, −1.2§	−0.97 (1.4)	0.44 (1.0)	−1.8, −1.0§
Length, cm*	66.3 (60.1–71.9)	57.5 (55.3–60.1)	4.8, 11.4§	75.1 (72.5–80.1)	71.4 (70.0–76.1)	0.9, 4.9‡
Length z score‖‖	−0.73 (1.6)	0.37 (1.0)	−1.7, −0.5§	−0.18 (1.5)	1.1 (1.0)	−1.9, −0.7§
FVC, mL	215 (81)	162 (60)	−22† (−44, −0.4)¶	365 (93)††	367 (84)††	−37* (−71, −1)¶
$FEV_{0.5}$, mL	178 (65)	144 (51)	−30‡ (−50, −9)¶	267 (64)**	299 (56)††	−51§ (−77, −25)¶
FEF_{75}, ml · s^{-1}	217 (100)	210 (87)	−53† (−97, −8)¶	305 (126)††	389 (109)‡‡	−89‡ (−147, −31)¶
$FEV_{0.5}$/FVC%	83 (10)	91 (5)	−4 (−8, 0)‖	74 (13)	83 (7)	−8† (−13, −3)‖
FVC z score¶¶	−1.9 (1.4)	−0.33 (1.3)	−1.57§ (−2.2, −0.9)	−1.5 (1.3)	−0.37 (1.3)	−1.1§ (−1.8, −0.5)
$FEV_{0.5}$ z score¶¶	−2.1 (1.8)	−0.18 (1.5)	−1.6§ (−2.7, −1.1)	−2.0 (1.6)	−0.13 (1.3)	−1.9§ (−2.5, −1.1)
FEF_{75} z score¶¶	−1.0 (1.7)	0.04 (1.3)	−1.42‡ (−1.7, −0.28)	−1.0 (1.7)	0.23 (1.0)	−1.2‡ (−1.9, −0.56)
$FEV_{0.5}$/FVC z score¶¶	−0.01 (1.2)	0.25 (0.53)	−0.26 (−0.70, 0.20)	−0.49 (1.8)	0.51 (0.74)	−1.0‡ (−1.7, −0.31)

Z-scores de fonction des VA diminués dès 28 mois

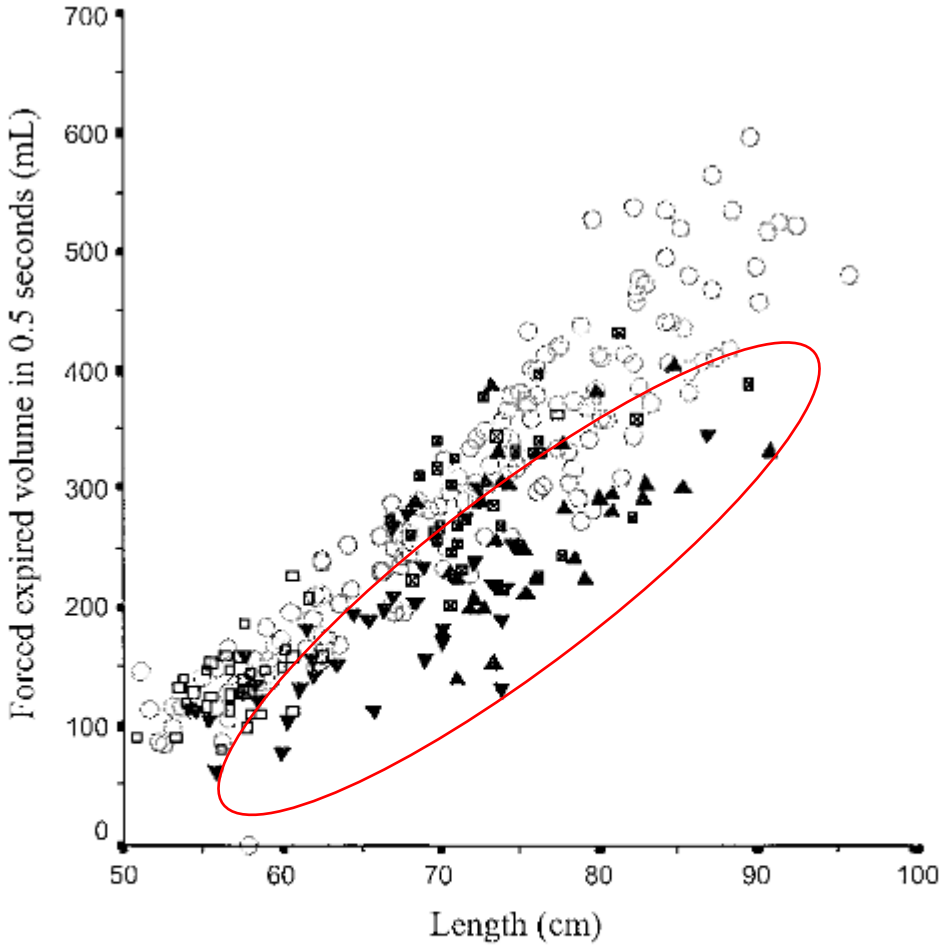


Figure 2. Association of $FEV_{0.5}$ with length for healthy subjects (*open square*, occasion one; *closed square*, occasion two) and infants with CF (*closed inverted triangles*, occasion one; *closed triangles*, occasion two) in this study and that of the cross-sectional reference population of Jones and colleagues (9) (*open circles*).

Multicenter Evaluation of Infant Lung Function Tests as Cystic Fibrosis Clinical Trial Endpoints

Stephanie D. Davis[1*], Margaret Rosenfeld[2*], Gwendolyn S. Kerby[3], Lyndia Brumback[4], Margaret H. Kloster[5], James D. Acton[6], Andrew A. Colin[7‡], Carol K. Conrad[8], Meeghan A. Hart[9], Peter W. Hiatt[10], Peter J. Mogayzel[11], Robin C. Johnson[1], Stephanie L. Wilcox[3], and Robert G. Castile[12]

AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE VOL 182 2010

100 nourrissons, 10 centres américains

TABLE 1. CHARACTERISTICS OF PARTICIPANTS WITH CYSTIC FIBROSIS AT THE ENROLLMENT VISIT (N = 100)

Characteristic	Mean (SD) or %
Age, mo	14.0 (6.2)
Length	
cm	74.1 (7.2)
Percentile	32.7 (26.4)
Weight	
kg	9.2 (2.0)
Percentile	27.7 (26.3)
Male, %	55
Race, %	
White	87
Hispanic	9
African American	2
Asian or Pacific Islander	1
Other	1
Genotype, %	
ΔF508 homozygous	55
ΔF508 compound heterozygous	37
Other	5
Unknown/not done	3
Diagnosis suggested by newborn or prenatal screening, %*	21
Exposed to cigarette smoke, %†	11
Family history of asthma, %‡	30
Pseudomonas isolated from respiratory culture, %§	12
Shwachman score (41)	69.9 (6.3)

Faisabilité tout à fait acceptable

Surtout pour la plethysmographie (CRF)

RVRTC: Raised Volume Rapid Thoracoabdominal Compression

TABLE 2. FEASIBILITY OF PERFORMING PULMONARY FUNCTION TEST PROCEDURES

	Enrollment *n (%)*	6-Mo Visit *n (%)*	12-Mo Visit *n (%)*	1-Mo Reproducibility *n (%)*	Total *n (%)*
No. of PFTs attempted*	100 (—)	91 (—)	77 (—)	74 (—)	342 (—)
Plethysmography†					
Acceptable	91 (91)	78 (86)	67 (87)*	67 (91)	303 (89)
Not acceptable	8 (8)	10 (11)	3 (4)	3 (4)	24 (7)
Data not obtained‡	1 (1)	3 (3)	7 (9)	4 (5)	15 (4)
RVRTC measures§					
Acceptable	76 (76)	64 (70)	55 (71)	51 (69)	246 (72)
Not acceptable	19 (19)	11 (12)	15 (19)	9 (12)	54 (16)
Data not obtained‡	5 (5)	16 (18)	7 (9)	14 (19)	42 (12)
Fractional lung volumes‖					
Acceptable	72 (72)	60 (66)	50 (65)‡	50 (68)	232 (68)
Not acceptable	24 (24)	20 (22)	17 (22)	11 (15)	72 (21)
Data not obtained‡	4 (4)	11 (12)	10 (13)	13 (18)	38 (11)

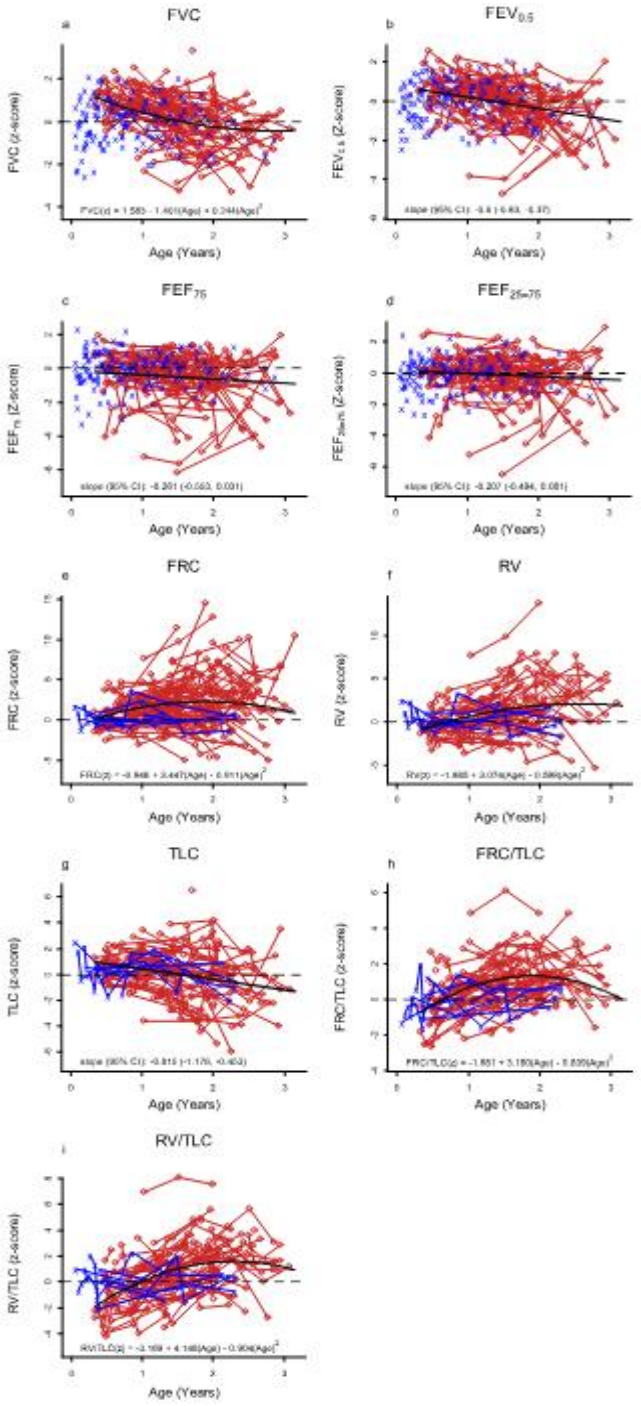


Figure 2. Plots of infant pulmonary function test Z scores versus age for the cystic fibrosis (CF) participants and the historical control subjects, with the average trend in Z scores by age among the participants with CF superimposed (*thick, solid lines*). Measurements for historical control data are in *blue*. The measurements for the infants with CF are in *red*, and repeated measures are connected by the *red segments*. *Dashed lines* indicate a z score of zero. FEF_{25-75} = 25–75% of forced expiratory flow; FEF_{75}, 75% of FEF; RV = residual volume; TLC = total lung capacity.

TABLE 5. AVERAGE Z SCORES AMONG CYSTIC FIBROSIS PARTICIPANTS, OVERALL AND BY AGE CATEGORY

	N (*n*)*	Mean (95% *CI*)
FRC	303 (96)	1.92 (1.39 to 2.45)
0–1 yr	71 (41)	0.99 (0.44 to 1.55)
1–2 yr	156 (88)	2.17 (1.56 to 2.78)
2–3 yr	76 (45)	2.16 (1.18 to 3.14)

TABLE 6. PERCENTAGE OF CYSTIC FIBROSIS PARTICIPANTS WITH AT LEAST ONE ABNORMAL LUNG FUNCTION MEASUREMENT

Parameter	N*	Percentage
$FEV_{0.5}$	90	(17.8)
FEF_{25-75}	90	(21.1)
FEF_{75}	90	(25.6)
FVC	90	(14.4)
FRC	96	(67.7)
FRC:TLC	88	(36.4)
RV:TLC	88	(44.3)
TLC	88	(31.8)
RV	88	(54.5)

Definition of abbreviations: FEF_{25-75} = 25–75% of forced expiratory flow; FEF_{75}, 75% of FEF; RV = residual volume; TLC = total lung capacity.

Abnormal lung function measurement defined as a Z score of less than −1.64 for $FEV_{0.5}$, FEF_{25-75}, FEF_{75}, and FVC, and a Z score greater than 1.64 for FRC, FRC:TLC, and RV:TLC (5% of the reference population would be expected to have a Z score < -1.64 and 5% > 1.64).

* N = number of cystic fibrosis participants with at least one acceptable measure.

Distension thoracique précoce (à partir de 1 an)

Lung function is abnormal in 3-month-old infants with cystic fibrosis diagnosed by newborn screening

Thorax 2012;**67**:874–881.

Ah-Fong Hoo,[1] Lena P Thia,[2] The Thanh Diem Nguyen,[2] Andrew Bush,[3] Jane Chudleigh,[1] Sooky Lum,[2] Deeba Ahmed,[2] Ian Balfour-Lynn,[3] Siobhan B Carr,[4] Richard J Chavasse,[5] Kate L Costeloe,[6] John Price,[7] Anu Shankar,[8] Colin Wallis,[1] Hilary A Wyatt,[7] Angela Wade,[9] Janet Stocks,[2] on behalf of the London Cystic Fibrosis Collaboration (LCFC)

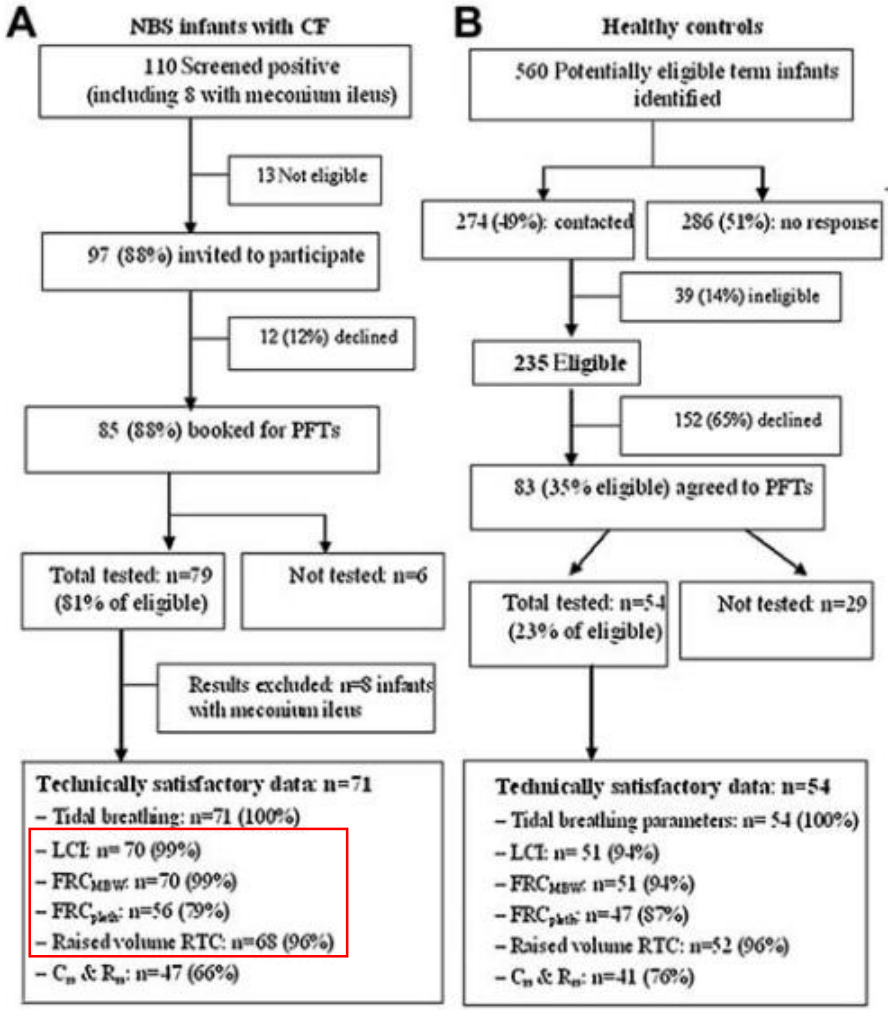


Table 2 Infant details at time of lung function test

	Infants with CF (n=71)	Healthy controls (n=54)
Age at test*, weeks	11.4 (2.3)	12.2 (2.0)

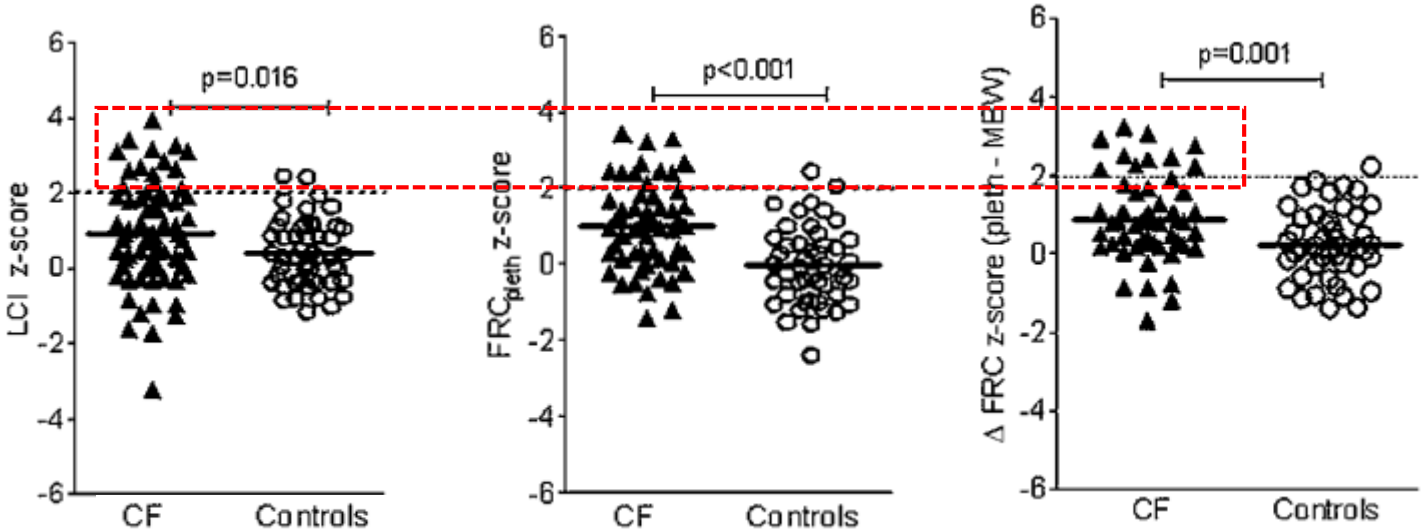


Table 3 Comparison of lung function in 71 infants with cystic fibrosis and 54 healthy controls

Variables according to test order	n	Infants with CF	n	Healthy controls	Δ (95% CI) CF − controls	p Values
Multiple breath washout						
LCI, z-score*	70	0.90 (1.38)	51	0.39 (0.88)	0.51 (0.10 to 0.91)	0.016
FRC_{MBW}, z-score*	70	0.15 (0.95)	51	−0.23 (0.86)	0.38 (0.05 to 0.71)	0.023
Plethysmography						
FRC_{pleth}, z-score†	56	0.77 (1.15)	47	−0.08 (1.03)	0.85 (0.43 to 1.28)	<0.001
ΔFRC z-scores (pleth − MBW)	55	0.68 (1.10)	45	0.19 (0.92)	0.48 (0.08 to 0.88)	0.018

Hyperinflation (FRC_{pleth} >1.96 z-scores) was identified in 18% (10/56) of infants with CF and was significantly correlated with diminished FEF_{25-75} ($r=-0.43$, $p<0.001$) but not with LCI or $FEV_{0.5}$. 21% avec une augmentation de LCI

A trois mois: pourcentage équivalent de mesures anormales pour LCI et FRC, sans corrélation

Lung function deterioration in school children with cystic fibrosis

Pediatric Pulmonology. 2020;1–9.

Katarzyna Walicka-Serzysko[1,2] | Magdalena Postek[1,2] | Justyna Milczewska[1,2]
Dorota Sands[1,2]

- LCI: lung clearance index as a measure of VI,
- FRC_{pleth}: plethysmographic functional residual capacity measured by whole-body plethysmography,
- FRC_{MBNW}: functional residual capacity measured by MBNW technique,
- V_{TG}: an index of the volume of trapped gas was calculated as the difference between FRC_{pleth} and FRC_{MBNW} ($V_{TG} = FRC_{pleth} - FRC_{MBNW}$),[18]
- R_{tot}: total airway resistance,
- R_{eff}: specific airway resistance,
- sR_{eff}: effective specific airway resistance as a measure of airway narrowing.

From maximal expiratory flow (MEF)-volume curves were calculated:

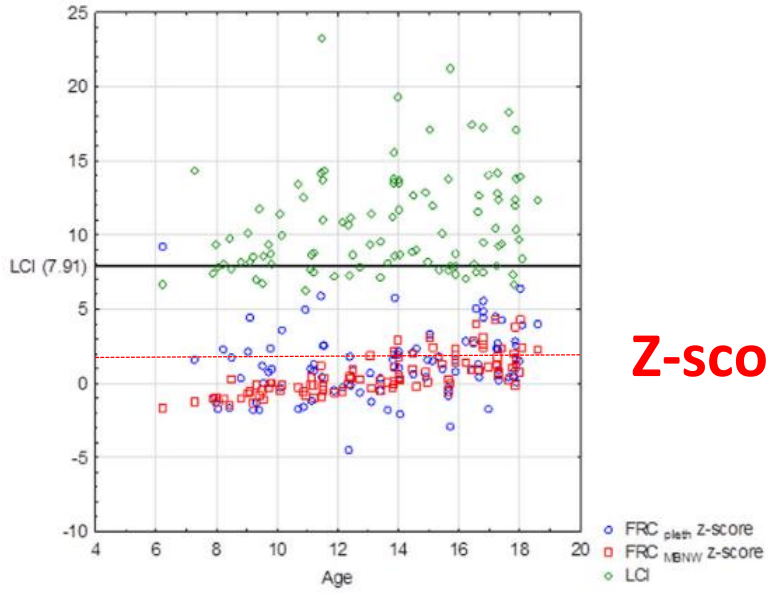
- FVC,
- FEV_1,
- MEF_{50} of FVC.

sRaw = Raw x CRF

TABLE 1 Characteristics of the study population and microbiological status

	n (Aged 7-18)	%	n (Aged 7-12)	%	n (Aged 13-18)	%
Patients	100		40	40	60	60
Males	44	44.00	13	32.50	31	51.67
Females	56	56.00	27	67.50	29	48.33
CFTR genotype						
F508del/F508del	47		18		29	
F508del/other	36		15		21	
Other/other	17		7		10	

FIGURE 1 Correlation of lung function parameters with cystic fibrosis (CF) patients' age: plethysmographic functional residual capacity (FRC_{pleth}) z-score, FRC_{MBNW} z-score and lung clearance index (LCI) ($R_{Spearman} = 0.28$ $P < .05$; $R_{Spearman} = 0.77$ $P < .05$; $R_{Spearman} = 0.24$ $P < .05$). For LCI the upper limit of 7.91 was presented according to normative data for healthy children 20 [Color figure can be viewed at wileyonlinelibrary.com]



Z-score FRC: +1,645

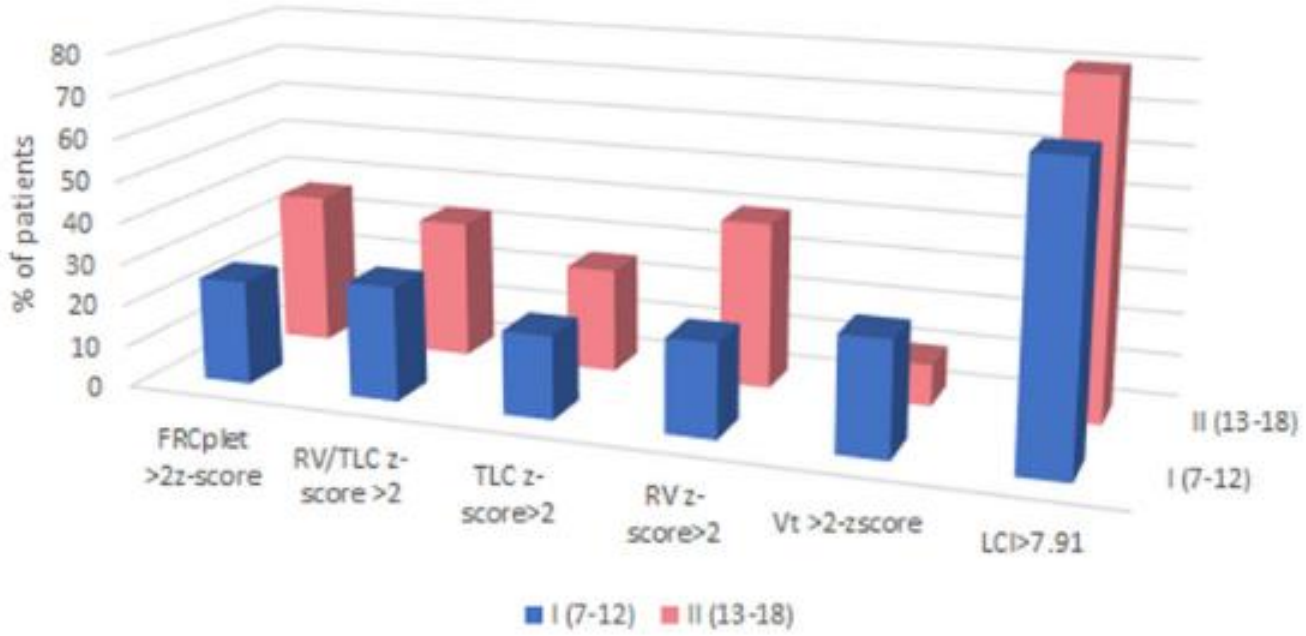


FIGURE 2 Comparison of parameters of lung function in two age study groups (7-12 and 13-18) of patients with CF. FRC_{pleth} measured by whole-body plethysmography; VTG: an index of the volume of trapped gas was calculated as the difference between FRC_{pleth} and FRC_{MBNW} (VTG = FRC_{pleth} − FRC_{MBNW}); LCI as a measure of ventilation inhomogeneity (value 7.91 was fixed as the upper limit of normal (ULN) for healthy Caucasian school-aged children 20) 135 × 102 mm (120 × 120 DPI). CF, cystic fibrosis; DPI, dots per inch; FRC_{pleth}, plethysmographic functional residual capacity; LCI, lung clearance index; RV, residual volume; TLC, total lung capacity [Color figure can be viewed at wileyonlinelibrary.com]

ULN = z-score +1,96

LCI mesure la plus sensible: anormale chez 60% des enfants

RV/TLC: anormal chez ~25% des enfants

Serial Lung Function and Responsiveness in Cystic Fibrosis during Early Childhood

Kim G. Nielsen, Tacjana Pressler, Bent Klug, Christian Koch,† and Hans Bisgaard

AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE VOL 169 2004

39 enfants mucoviscidosiques

2 à 7 ans

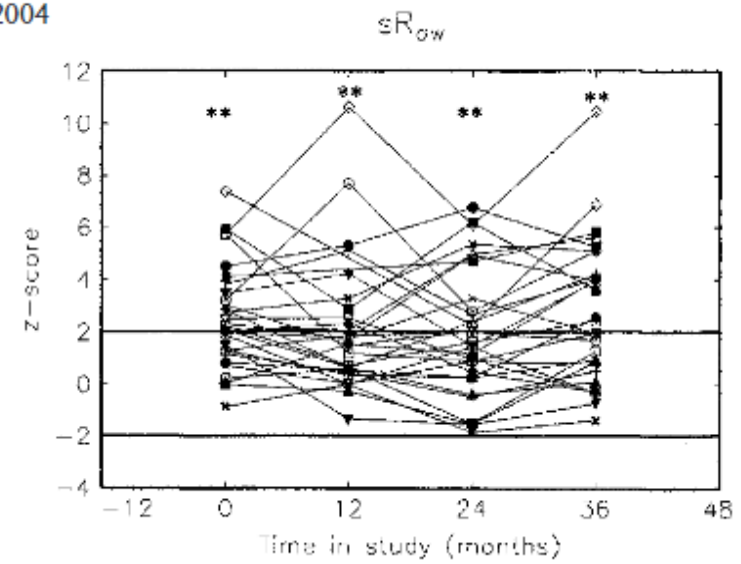
Suivi fonction de 36 mois

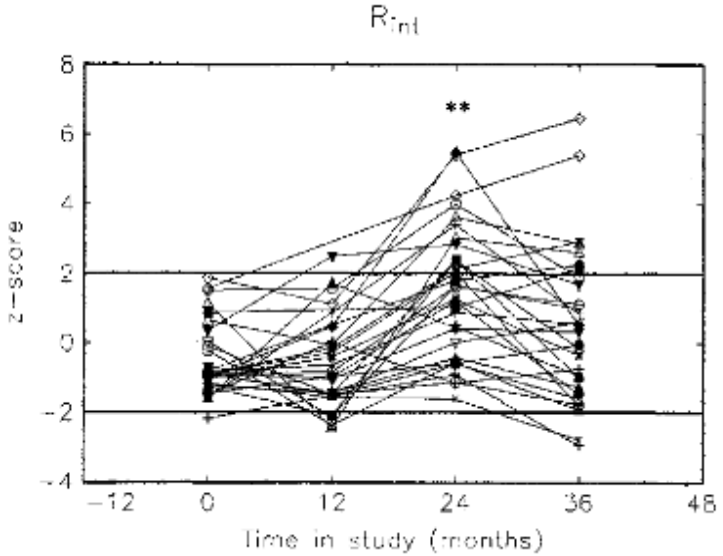
- sRaw
- Rint
- R5Hz et X5Hz
- Spirométrie

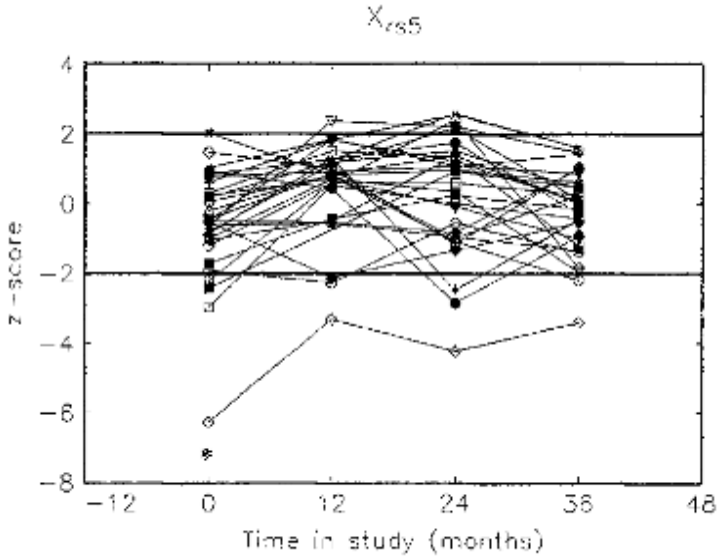
Message:

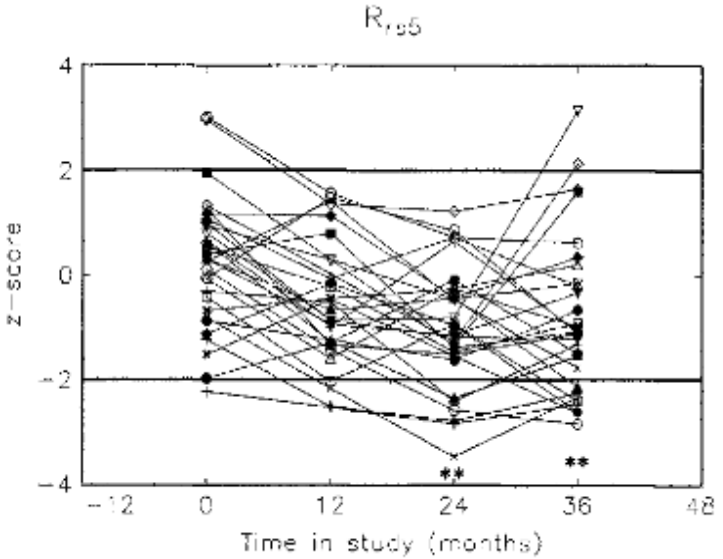
sRaw mesure la plus sensible

(avant l'ère du LCI)









Multiple-Breath Washout as a Marker of Lung Disease in Preschool Children with Cystic Fibrosis

Paul Aurora, Andrew Bush, Per Gustafsson, Cara Oliver, Colin Wallis, John Price, John Stroobant, Siobhan Carr, and Janet Stocks on behalf of the London Cystic Fibrosis Collaboration

AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE VOL 171 2005

40 enfants mucoviscidosiques de 2 à 5 ans

37 témoins sains

TABLE 2. N
COMPLETI
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MEASUREM
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Multiple-brea
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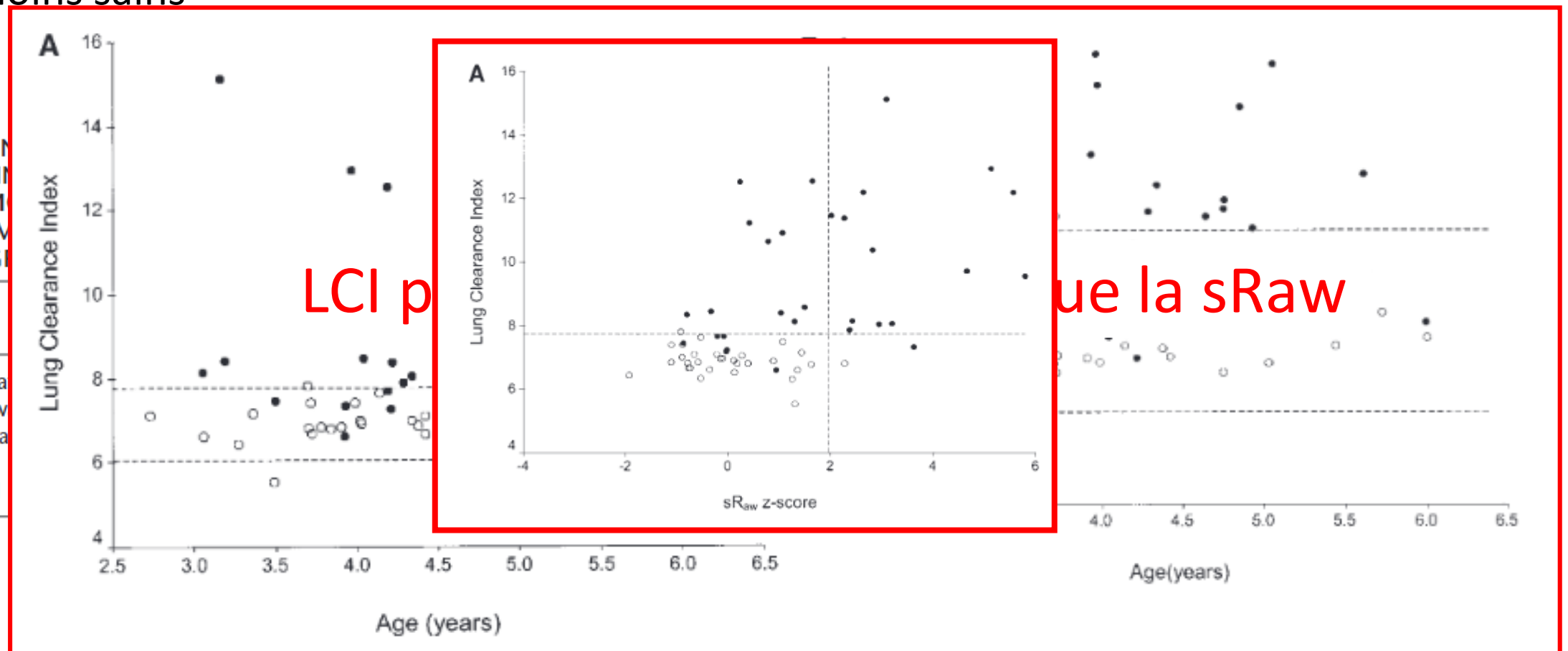
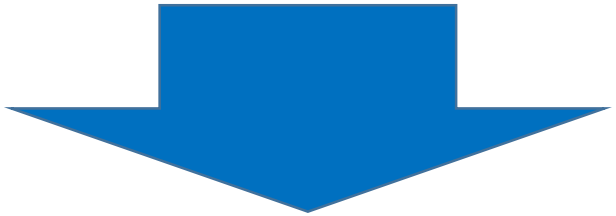
Plethysmogra
Spirometry
Full protocol



Chez le nourrisson:

- Distension thoracique précoce (mesure de CRF)
- Anomalies précoces des voies aériennes: TVO ?

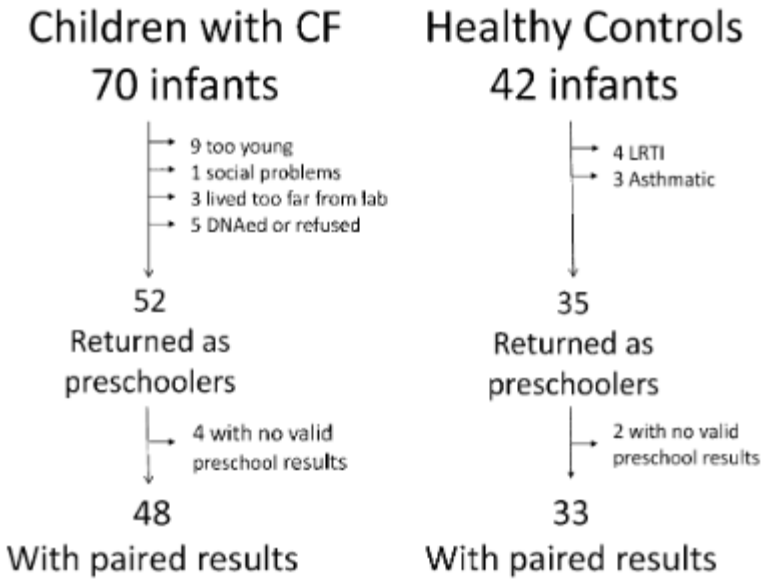


Pourquoi la spirométrie à l'âge scolaire est généralement normale ?

Lung Function from Infancy to the Preschool Years after Clinical Diagnosis of Cystic Fibrosis

Wanda J. Kozlowska[1], Andrew Bush[2], Angela Wade[3], Paul Aurora[1,4], Siobhán B. Carr[5], Rosie A. Castle[1†], Ah-Fong Hoo[1], Sooky Lum[1], John Price[6], Sarath Ranganathan[7], Clare Saunders[1], Sanja Stanojevic[1,3], John Stroobant[8], Colin Wallis[4], and Janet Stocks[1], for the London Cystic Fibrosis Collaboration*

AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE VOL 178 2008



Methods: The raised volume technique was used during infancy and incentive spirometry during the preschool years

After adjustment for height, a diagnosis of CF per se accounted for a significant mean reduction of 7.5% in $FEV_{0.75}$ and 15.1% in $FEF_{25–75}$, but not in FVC, $FEV_{0.5}$, or FEV_1 when compared with healthy control subjects studied over the 6 years

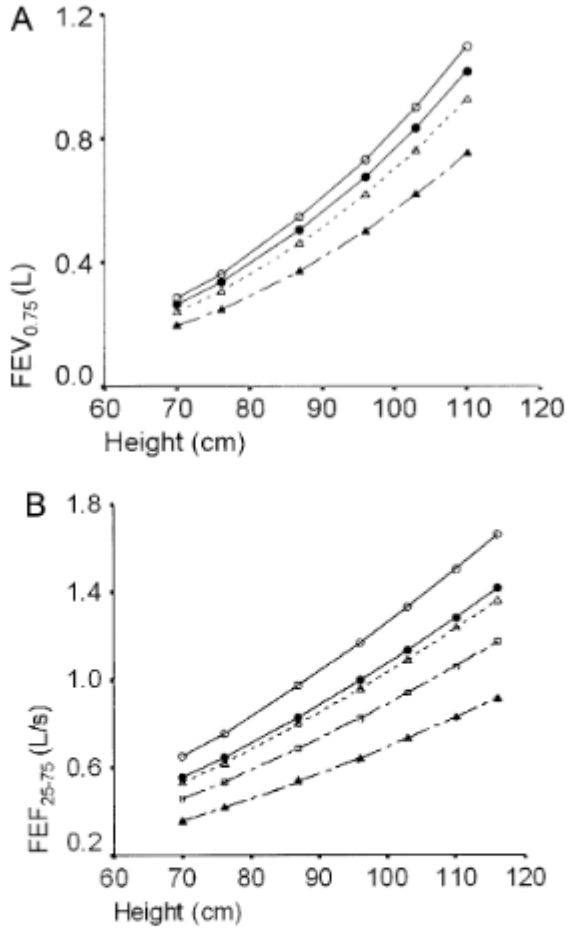


Figure 2. Association of (*A*) $FEV_{0.75}$ and (*B*) $FEF_{25–75}$ with height based on the model in Table E3 in the online supplement. The figure illustrates the differences in predicted values for a child who is a healthy control (*open circles*), has CF (cystic fibrosis) (*solid circles*), has CF and first grew *Pseudomonas aeruginosa* (PsA) before their first lung function test (*open triangles*), has CF and PsA with wheeze on auscultation at every visit (*solid triangles*), and has CF and PsA with cough at every visit (*open squares*) (for $FEF_{25–75}$ only). No prediction line is shown for $FEV_{0.75}$ for a child with CF, PsA, and cough at every visit because cough was not a significant predictor variable for $FEV_{0.75}$ (Table E3).

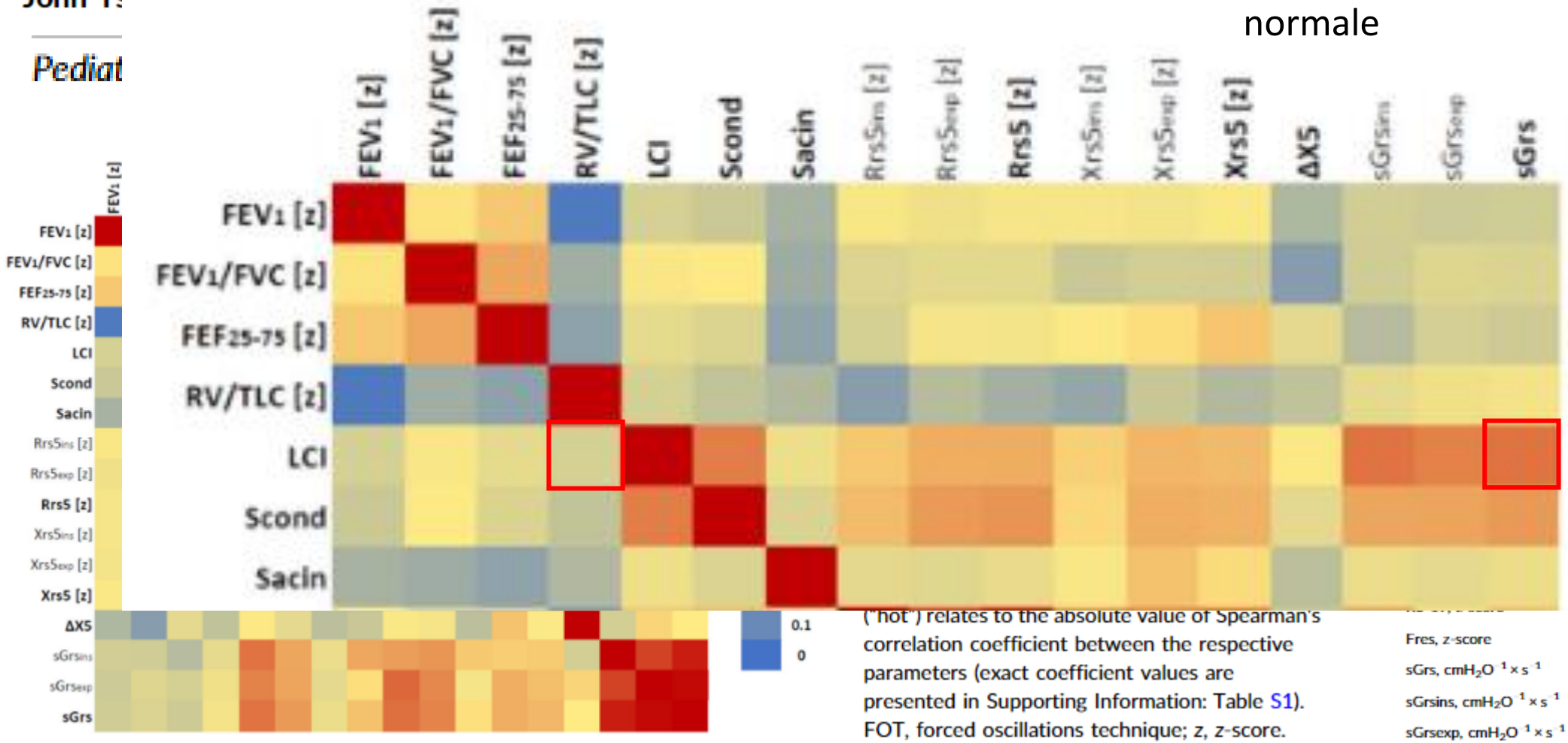
FEFV were obtained using the RVT, according to international guidelines, in sleeping, young children less than 2 years of age
FEFV measures: FVC, $FEV_{0.5}$,$FEV_{0.75}$, FEV_1, and $FEF_{25–75}$

Low-frequency oscillometry indices to assess ventilation inhomogeneity in CF patients

Sotirios Fouzas MD, PhD[1] | Christos Kogias MSc, MD[2] |
Maria Gioulvanidou MSc, MD[2] | Aris Bertzouanis MD[1] |
Elisavet-Anna Chrysochoou MD, PhD[2] | Michael B. Anthracopoulos MD[1] |
John Ts

Pediat

Spirométrie normale



("hot") relates to the absolute value of Spearman's correlation coefficient between the respective parameters (exact coefficient values are presented in Supporting Information: Table S1). FOT, forced oscillations technique; z, z-score.

TABLE 1 Characteristics of the study cohort ($N = 45$).

Demographics	
Sex, male (N, %)	18 (40)
Age, years	15.9 ± 5.6 (6.9–27)
Weight, kg	50 ± 15 (22–79)
Height, cm	155 ± 16.3 (118–183)
BMI, kg/m^2	20.3 ± 3.3 (12.6–28.4)
Spirometry	
FEV1, z-score	−0.19 ± 0.93 (−2.18 to 1.22)
	to 1.35)
	to 1.23)
	to 1.09)
	to 1.80)
	to 2.20)
	to 2.47)
	to 2.88)
	8.8)
	−0.116)
	−0.525)
	to 3.59)
	to 4.00)
	to 4.26)
	to 2.08)
	to 1.42)
	to 2.29)
	to 1.77)
	to 3.42)
Fres, z-score	0.46 ± 1.6 (−2.06 to 4.79)
sGrs, cmH$_2$O $^{-1}$ × s $^{-1}$	0.088 ± 0.024 (0.038–0.137)
sGrsins, cmH$_2$O $^{-1}$ × s $^{-1}$	0.092 ± 0.022 (0.044–0.143)
sGrsexp, cmH$_2$O $^{-1}$ × s $^{-1}$	0.086 ± 0.026 (0.034–0.133)

Conclusions

Le LCI est aussi sensible voire plus que la CRF_{pleth} chez le nourrisson

ANSM: PUBLIÉ LE 07/09/2001 - MIS À JOUR LE 15/03/2021
L'utilisation de l'hydrate de chloral est restreinte aux enfants entre 2 mois et 5 ans, en cas de nécessité d'immobilisation totale et prolongée (au moins une demi-heure) indispensable à la réalisation des investigations diagnostiques suivantes : Explorations Fonctionnelles Respiratoires (EFR)

Le LCI est-il supérieur à la pléthysmographie: réponse OUI

Utilisation des IOS pour sélectionner les candidats au LCI ?

Mais en pratique la détection par EFR des anomalies précoces de fonction est-elle encore un enjeu (en dehors des essais thérapeutiques) ?