

MONDAY, SEPTEMBER 26TH 2011

## 247. Advances in lung function testing from infancy to adulthood

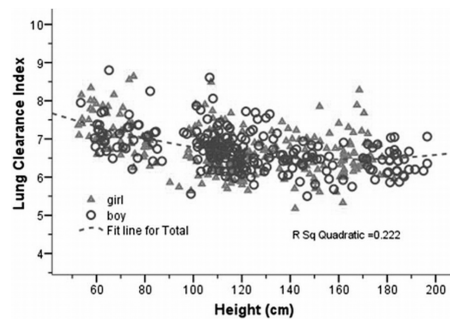
### P2010

#### Lung growth and ventilation inhomogeneity in health

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Lung clearance index (LCI), a measure of ventilation inhomogeneity derived from multiple breath washout is more sensitive in detecting early lung disease than spirometry in preschool (PS) and school age (SA) children. In health, LCI appears to be stable in PS and SA children, but has been reported to be slightly higher during infancy. We aimed to develop a reference range for LCI from birth to 19y. **Methods:** LCI data from two centres using a respiratory mass spectrometer (Amis 2000) & the inert gas SF<sub>6</sub>, measured using either a mask (0-5y) or mouthpiece (>5y), while supine (infant) or seated, were collated. 485 datasets from 359 healthy subjects (44%boys; 257 from London; 102 from Goteborg; Range: age (0.1-18.7y); height (52-196cm)) were analysed.

**Results:** Height & age were significant predictors of LCI on univariable & multivariable analyses. Mean (SD) LCI was 7.2 (0.5) in infants (0.1-2y); 6.7 (0.6) in PS (3-5y); 6.5 (0.5) in SA (6-12y) and 6.5 (0.5) in those >13y. The inverse relationships between LCI & height or age were not linear, being most marked in the younger years & no longer significant by SA.



LCI was not significantly different between centres, after adjusting for height & age.

**Conclusions:** Although LCI is fairly constant from PS years into adolescence, it is significantly higher during early life. Reference ranges to take developmental changes and measurement conditions into account should be developed for better interpretation in children with lung disease.

### P2011

#### Specific airway resistance is overestimated during tidal breathing vs panting in healthy children

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**Rationale:** Modern plethysmographic equipments allow the measurement of specific airway resistance (sRaw) during tidal breathing (tb), a potentially useful technique in children unable to perform the panting maneuver (p), a reference technique to minimize the thermal artifact. Equipment softwares are implemented with algorithms to correct for this artifact when computing sRaw. It is not known how well this correction performs with reference to sRaw in children. The hypothesis tested here is that both techniques provide similar estimates of sRaw.

**Objective:** To compare sRaw<sub>tb</sub> and sRaw<sub>p</sub> in children.

**Methods:** sRaw<sub>tb</sub> and sRaw<sub>p</sub> were measured in 6 healthy children aged 7-10 years, using a commercially available pressure plethysmograph.

**Results:** sRaw<sub>tb</sub> (mean ± sd = 10.4±2.0 hPa-sec; breathing rate = 0.5±0.1 Hz) was significantly larger (p=0.006) than sRaw<sub>p</sub> (5.8±2.2 hPa-sec, breathing rate = 3.1±0.5 Hz). The finding hold true for Raw computed from the associated measurement of thoracic gas volume (Raw<sub>tb</sub> = 6.3±1.2 hPa-sec/L; Raw<sub>p</sub> = 2.9±1.0 hPa-sec/L, p=0.005).

**Conclusion:** sRaw is significantly overestimated by tb as compared with p. This is possibly explained by non instantaneous changes of gas temperature and humidity in the airways, a fact that may not be taken into account in the correction algorithm. The impact of overestimating sRaw<sub>tb</sub>'s - and hence Raw<sub>tb</sub> - on routine airway function testing in patients has to be identified.

### P2012

#### Impaired lung function in children born preterm is related to severity of neonatal lung disease

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Advances in neonatal care have led to a shift in the pathophysiology of bronchopulmonary dysplasia (BPD). The impact of contemporaneous preterm birth and BPD on long term respiratory health remains unclear. This study aims to relate mid-childhood respiratory function with neonatal variables in children born ≤32 w gestational age (GA).

**Methods:** Children aged 9 to 11 y (≥ 37 w GA controls, n=37; 84 born ≤32 w gestation including 53 with BPD) performed 4 lung function tests (forced oscillation, static lung volumes, spirometry and gas transfer (DLCO)). Associations between lung function (expressed as Z scores) and neonatal variables (GA, birth weight Z-score and durations of mechanical ventilation (MV) and O<sub>2</sub>) were explored using multiple linear regression.

**Results:** Children with BPD had increased respiratory resistance (R<sub>rs</sub>) and reactance (X<sub>rs</sub>), reduced FEV<sub>1</sub> and FEF<sub>25-75</sub> compared to children born preterm without BPD and controls (one-way ANOVA; post-hoc comparisons p<0.04). DLCO was reduced in the BPD group compared to preterm but not healthy children (p<0.05). Static lung volumes were not different between groups. Duration of supplemental O<sub>2</sub> was associated with increased R<sub>rs</sub> (p<0.005) and reduced DLCO (p=0.01). Duration of MV was associated with increased X<sub>rs</sub> (p=0.001) and together with birth weight Z-score (p=0.02), was predictive of reduced FEV<sub>1</sub> (p=0.005).

**Conclusions:** Children born ≤32w GA with BPD have worse lung function compared to preterm children without BPD. Impaired lung function in mid-childhood is associated with severity of neonatal lung disease as reflected by duration of MV and supplemental O<sub>2</sub>, further reinforcing the long-term impacts of preterm birth on lung health.

### P2013

#### Interpretation of passive respiratory mechanics in infants: Should we normalise by body weight?

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**Introduction:** Tidal volume (V<sub>T</sub>) and respiratory compliance (C<sub>rs</sub>) are commonly normalised for body weight; whether this is appropriate beyond the neonatal period or in weight restricted children remains unclear.

**Aim:** To examine the relationship between V<sub>T</sub>, C<sub>rs</sub> and growth in healthy infants.

**Methods:** The Jaeger BabyBody (v4.6) was used to assess lung function (LF) in healthy, sedated term Caucasian infants.

**Results:** Technically satisfactory V<sub>T</sub> and C<sub>rs</sub> from 140 infants [median (range) age: 38 (3-105) w] were available on 192 & 84 occasions respectively (Table). The average relationship between V<sub>T</sub> or C<sub>rs</sub> and weight was constant over time

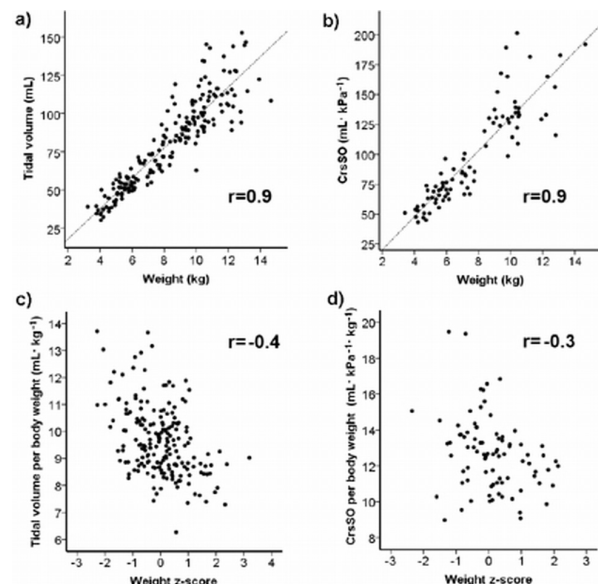


Figure 1

Table 1

	n	Mean (SD)	Range
$V_T$ (mL kg <sup>-1</sup> )	192	9.6 (1.3)	6.3–13.7
Crs (mL kPa <sup>-1</sup> kg <sup>-1</sup> )	84	12.7 (2.0)	9.0–19.5

but between-subject variability increased with growth (Fig. 1a&b). 95% Limits based on  $V_T$ /kg or Crs/kg would over-estimate predicted range in the youngest and under-estimate it in older infants, leading to potential misdiagnosis.  $V_T$ /kg or Crs/kg were inversely related to weight z-score (Fig. 1c&d); light-for-age babies had higher values than those who were heavier. This again may lead to misdiagnosis especially in those with impaired growth (eg, CF).

**Conclusions:** Reporting infant LF/kg body weight is inappropriate. Equipment-specific regression equations are needed to avoid misinterpretation; for this a larger dataset is required. We would welcome contributions of similar data from other centres.

#### P2014

##### Tracking of lung function obtained by whole-body plethysmography in infants and children with cystic fibrosis (CF)

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**Rationale:** The assessment of lung function tracking, (data stability over time and predictability based on early measurements) could provide a better understanding how genetic and environmental factors as well as treatment regimens influence lung function decline in CF.

**Objectives:** (i) Impact of lung function assessment during infancy on follow-up and lung function decline during childhood. (ii) Determination of physiological mechanisms influencing progression in CF in relation to the genotype.

**Methods:** Lung function was assessed in 70 infants (35 males, 35 females) with CF at ages 2.8 to 26.7 months as well as during childhood (4.3–18.4 years) by serial (infant)-whole-body plethysmography pertaining to functional residual capacity (FRCpleth) and effective airway resistance (sReff). Using predicted values obtained by LMS statistics (see abstract 854139), z-scores of FRCpleth and sReff were computed by Box-Cox transformation using the age-varying parameters L (skewness), M (median) and S (coefficient of variation).

**Results:** During infancy only 7.6% of CF patients presented with normal lung function; 33.3% showed either pulmonary hyperinflation or bronchial obstruction, but 59.1% presented with both. There was a significant association with later outcome represented by the LCI and the FEF50. If genotypes are stratified according to the presence or absence of F508del and subgrouped according to the nature of mutations, FRCpleth and sReff can achieve discrimination.

**Conclusions:** Evaluation of lung function by plethysmography is an important diagnostic and predictive tool, featuring good outcome parameters, and worth to be established early in life.

#### P2015

##### Pressure oscillations after airway interruption pre- and post-bronchodilator in wheezy preschool children

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Changes in mouth pressure during flow interruption (Pmo transients) can be used to assess airway resistance (Rint). Initial pressure oscillations can cause difficulties in estimating Rint but are themselves a marker of airway status as their amplitude increases [1] with bronchodilator (BD) and decreases with methacholine [2].

To investigate this measurement, we analysed Pmo transients pre- and post-bronchodilator in 13 preschool children with recurrent wheeze on 2 separate visits 4 weeks apart. The median (range) age of the children at the first visit was 52 months (38 to 64 months). The amplitude of the first upward oscillation as a proportion of end-interruption pressure was calculated and compared with Rint calculated by linear back extrapolation. The median value of at least 5 acceptable transients was assessed for amplitude (Posc) and Rint by linear back extrapolation (LBE30/70). Posc increased significantly (paired t-test) with BD both at visit 1, with mean (SD) pre 1.38 (0.25), post 1.63 (0.32) and visit 2, with pre 1.39 (0.29), post 1.61 (0.37). LBE30/70 decreased significantly with BD both at visit 1, mean (SD) pre 1.08 (0.27), post 0.88 (0.21) and at visit 2, pre 1.08 (0.26), post 0.92 (0.22). However there was no significant relation between Posc change and LBE30/70 change in response to BD (Pearson's correlation coefficient).

These results suggest that Pmo oscillation amplitude after flow interruption may provide an alternative measure of airway mechanics which merits further study.

##### References:

- Bridge PD et al. *Pediatr Pulmonol* 2005; 40:420–425.
- Kivastik J et al. *Clin Physiol Funct Imaging* 2000; 29:45–52.

#### P2016

##### Cough flow volume profile in ataxia telangiectasia

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**Introduction:** Weak coughing is perceived as the cause for recurrent respiratory system infection leading to lung function deterioration in Ataxia telangiectasia (A-T) disease. The cough profile of these patients has not been studied.

**Aim:** To explore the feasibility of the cough-flow-volume profile for detecting cough performance in A-T patients.

**Methods:** Thirty five A-T patients (age 12.7±4.9yrs) were studied. Patients performed forced expiratory flow volume (FVC) and maximal voluntary cough (FVC-cough) maneuvers. Analysis of data included: Inspiratory volume (IC) prior to cough; FVC-cough, Peak cough flow and number of spikes per maneuver. Values were related to publish data of healthy population of similar ages and are presented as actual and as%predicted.

**Results:** We found that IC prior to cough was 0.85±0.47 (l) (36.1±15.0%); FVC-cough was 1.00±0.51 (l) (43.6±15.4%); Peak cough flow was 3.27±1.53 (l/s) (45.5±15.0%); Peak cough flow to Peak expiratory flow ratio was 1.06±0.24 vs. 1.48±0.22 in healthy and the number of spikes/maneuver were 2.0±0.8 vs. 6–12 in healthy population. All parameters were significantly lower than healthy (P<0.001). Additionally, Peak cough flow increased with age but the yearly increase rate was significantly lower than normal, (0.157 vs. 0.423 l/s/year; respectively, P<0.005).

**Conclusions:** Our findings indicate that A-T patients have a weak cough compared to healthy of similar ages and that cough ability worsens with age. Cough flow volume curve, as well as forced vital capacity maneuvers, should be considered a mainstay in the clinical assessment of A-T patients.

The study was funded by the J. Baum foundation of the Israeli Lung Association, Tel Aviv, Israel.

#### P2017

##### The maximum oxygen consumption in children with asthma and/or obese children: A multi purpose assessment

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Asthma and obesity have had an increasing trend in recent decades, constituting one of the major priorities in the health of children.

**The aim** of this study was to compare the respiratory function and oxygen consumption in four groups of children: obese, asthmatics, obese-asthmatic and controls, in order to assess their metabolic pattern and respiratory values.

**Methods:** 152 children, 8 to 16 y.o., divided as follows: 31 asthmatics, 42 controls, 56 obese and 23 obese-asthmatics children were tested. Every child performed spirometry, respiratory muscles (endurance) and oxygen consumption (VO<sub>2</sub>) evaluation, obtained on a cycloergometer according to a protocol of increasing effort. **Results:** Spirometric values were comparable between obese and controls (average FEV<sub>1</sub> 105 and 107% pred, respectively), whereas there was a s.s. difference (p < 0.05) between asthmatics and obese-asthmatics. Endurance was lower in obese (26.97 J) and obese-asthmatics (24.06 J) than in asthmatics alone (31.52 J) and controls (31.98 J), but without any s.s. difference (p=0.60). The maximal VO<sub>2</sub>/kg was lower in obese (30.63 ml/kg/min) and obese-asthmatics (31.95 ml/kg/min) than in controls (37.19 ml/kg/min) or asthmatics (41.72 ml/kg/min) (p=0.0001 for each one).

**Conclusion:** The increase in body weight does not seem to affect spirometric values but obese children have a lower value of endurance, probably due to a respiratory muscle weakness and VO<sub>2</sub>/kg max was lower in obese than asthmatics, probably due to alterations in the cardio respiratory system.

#### P2018

##### Exercise induced bronchoconstriction and dyspnoea in asthmatic children

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**Introduction:** Dyspnoea is thought to signal the mismatch between afferent information arising from the respiratory system and metabolic needs. Dyspnoea is induced by airway obstruction but is variably expressed. A poor perception of dyspnoea has been hypothesized to be a determinant factor to life threatening asthma. Little data on the relationship between obstruction and dyspnoea are available in children.

**Aim of the study:** To establish the relation between exercise-induced bronchoconstriction (EIB) and dyspnoea in asthmatic children.

**Methods:** 53 asthmatic children (6 - 16 years old) were studied at baseline and 5 min after exercise. Dyspnoea was rated qualitatively—and quantitatively by the

pediatric scale "Pictorial-CERT" ( $\Delta Sc = 0$  to 10). EIB was assessed by the relative change in FEV1 ( $\Delta FEV1$ ) and the child classified as responder (R) or nonresponder (NR) based on a threshold decrease in FEV1 = 8%.

**Results:** Anthropometric characteristics and baseline FEV1 were similar in R's and NR's. The qualitative items "Pictorial-CERT", "Pictorial-CERT" and "Pictorial-CERT" were more frequently quoted by R's than NR's ( $p < 0.05$ ). There was a significant but loose correlation between  $\Delta FEV1$  and  $\Delta Sc$  ( $R^2 = 0.12$ ;  $p < 0.001$ ). Eight subjects were identified as poor perceivers because of significant bronchoconstriction contrasting with  $\Delta Sc \leq 2$ . These subgroup characteristics were similar to other children.

**Conclusion:** Bronchoconstriction and perception of dyspnoea are significantly but weakly associated in asthmatic children. Some children exhibit a poor perception of EIB. A systematic evaluation of dyspnoea during exercise challenge may help in the screening of subjects at risk of life-threatening asthma.

**P2019**

**Agreement between interrupter resistance and spirometry in a large population of asthmatic children**

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**Background:** Interrupter resistance (Rint) is routinely used to assess airway patency in children, but its relationship with spirometry has never been assessed in a large population of children.

**Objectives:** A retrospective study to compare baseline values and post-bronchodilator (post-BD) changes in Rint and spirometry in asthmatic children.

**Methods:** Rint measures (SpiroDyn'R, Dyn'R, France) were performed before spirometry (Masterscreen, Jaeger, Germany). Statistics: correlations between baseline Rint and FEV1 or FEF2575%, and ROC study for the Rint cutoff to distinguish between children with and without reversibility in FEV1 (>12% baseline).

**Results:** Data from 645 children (408 boys, median (range) age 7.9 (4.2-18.3) y) showed significant correlations between Rint and FEV1 or FEF2575% ( $r=0.69$  and  $0.71$ , respectively for raw data, and  $r=0.49$  and  $0.54$ , respectively for % of predicted; all  $p < 0.0001$ ).

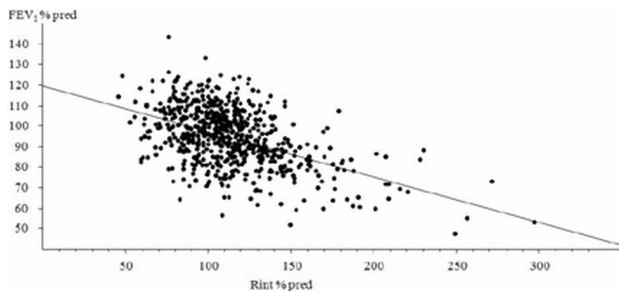


Figure 1

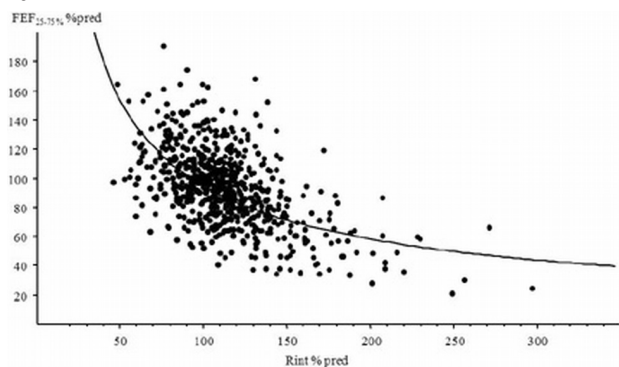


Figure 2

Reversibility in FEV1 (270 children) was best detected by a -35% of predicted Rint decrease (AUC=0.79, 0.70 sensitivity and specificity).

**Abstract P2021 - Table 1**

	M	S	L
FRCpleth			
Boys	127.77 + 162.52*age	0.1213 + 0.0046*age - 0.00031*age <sup>2</sup> + 0.000025*age <sup>3</sup>	0.48
Girls	128.42 + 167.91*age	0.0685 + 0.03835*age - 0.00423*age <sup>2</sup> + 0.000147*age <sup>3</sup>	0.48
sReff			
Boys	0.39 + (age/(130.24 + 21.51*age - 94.6*SQRT(age)))	0.12 + (age/(247.9 + 33.88*age - 149.5*SQRT(age)))	0.86
Girls	0.39 + (age/(59.88 + 14.38*age - 47.7*SQRT(age)))	0.17 + 0.00034*age <sup>2</sup>	0.37

**Conclusion:** We found a good agreement between Rint and spirometry to assess airway caliber and study BDeffect.

**P2020**

**Bench test of an O<sub>2</sub>/CO<sub>2</sub> sensor based MBW system using a lung model**

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Lung volume assessment using tracer gas multiple breath washout (MBW) systems needs validation under realistic conditions. We used a lung model allowing for different tidal volumes (TVs), functional residual capacities (FRCs), and respiratory rates (RRs) under BTPS conditions. We tested a nitrogen (N<sub>2</sub>) MBW prototype (Exhalyzer D; Eco Medics) based on an ultrasonic flowmeter, a main-stream CO<sub>2</sub>, and a side-stream O<sub>2</sub> sensor.

Linearity of O<sub>2</sub> and CO<sub>2</sub> sensors was assessed after two point calibration using a mass spectrometer (AMIS 2000; Innovision). For FRC measurements, a double chamber plexiglas lung model was filled with water, heated, and mechanically ventilated at various ranges of FRCs (900 to 4000 mL), TVs (250 to 850 mL), and RRs (30 to 15/min). N<sub>2</sub> MBW tests (n = 71) using 100% O<sub>2</sub> were done on three days. Using custom designed software (TestPoint) we synchronized gas to flow signals to preset and manually optimized settings, and calculated FRC as cumulative expired N<sub>2</sub> volume divided by the difference of MBW start minus end N<sub>2</sub> concentration.

O<sub>2</sub> and CO<sub>2</sub> sensors were linear (linear regression r<sup>2</sup> was 0.99 for both). Using preset synchronization settings, mean difference of lung model minus measured FRCs was -7.4 mL (-0.04% of mean FRC), limits of agreement ranged from 160.4 mL to -175.2 mL (5.8% to -5.9% of mean FRC). After optimized synchronization, mean difference of FRCs was -7.7 mL (-0.25% of mean FRC), limits of agreement ranged from 50.8 mL to -66.2 mL (1.8% to -2.3% of mean FRC).

This lung model seems suitable for validation of MBW systems. The new N<sub>2</sub> MBW system precisely measures in vitro FRCs under realistic conditions. Careful synchronization of signals is crucial for accurate FRC measurements.

**P2021**

**Reference data transition of whole-body plethysmography from infancy to childhood**

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**Rationale:** Advances in plethysmographic measurement techniques have made it possible to obtain lung function data in infants [1] and children. However, application remains limited by the lack of appropriate transitional normative data from infancy to childhood, especially for effective specific airway resistance (sReff).

**Objectives:** On previously collected lung function data, updated prediction equations were modeled spanning from infant's years to childhood, using the LMS method.

**Methods:** Normative lung function data from 67 healthy young infants aged 2.3 to 28.2 (10.8±6.3) months and children aged 5.1 to 16.8 (10.4±2.9) years were evaluated, and prediction equations for functional residual capacity (FRCpleth), and sReff were computed. Applying the LMS method in R environment using GAMLSS package [2] the changing distribution of the measurements is summarized by three curves representing the median (M), coefficient of variation (S) and skewness (L) in relation to age.

**Results:** The present prediction equations feature the first attempt to provide continuous normative data of infants with a smooth transition into childhood (Table 1).

**Conclusions:** Updated prediction equations of plethysmographic data for infants and children applying LMS statistics provide a new basis for longitudinal evaluation of lung function in children with lung disease.

**References:**

- [1] Respiration 1993, 60:1-8.
- [2] Statistics in Medicine 2004, 23:3053-3076.

MONDAY, SEPTEMBER 26TH 2011

**P2022****Comparison of a new nitrogen multiple breath washout method to mass spectrometer SF6 washout in cystic fibrosis subjects**

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**Background:** The lung clearance index (LCI) obtained from SF6 multiple breath washout (MBW) is a sensitive index of peripheral airway dysfunction in cystic fibrosis (CF) [1]. SF6 LCI values are lower and show stronger agreement between laboratories than historical N2 LCI using conventional N2 analyzers [1]. Formal comparison between the two types of MBW systems has not been performed to date. This study compared FRC and LCI obtained using both methods: mass spectrometer SF6 MBW and a new indirect N2 MBW system (Exhalysor D, EcoMedics, Duernten, Switzerland) in CF subjects.

**Methods:** 10 CF subjects, median (range) 17 (15-40) yrs performed MBW in triplicate using an SF6-based mass spectrometer MBW system and an Exhalysor D indirect N2-based MBW system (main stream infrared CO2 sensor, side stream laser O2 sensor). FRC and LCI were calculated using similar software algorithms. Results expressed as mean (SD) and between-test comparisons made using students t-tests.

**Results:** There was no significant difference between FRC values (N2 FRC 2.82 (0.71) vs. SF6 FRC 2.53 (0.70), p=0.37), however N2 LCI, 12.52 (3.14), was significantly higher than SF6 LCI, 9.77 (2.46) (p=0.043). Within-session repeatability (coefficient of variation, CV%) did not differ between the groups: N2 FRC 6.8 (2.9)% vs. SF6 FRC 5.5 (3.1)%, and N2 LCI CV 5.0 (3.6)% vs. SF6 LCI CV 4.7 (2.8)%.

**Conclusions:** LCI values obtained with the new indirect N2 MBW system were greater than those obtained with the current gold standard SF6 mass spectrometer based system. FRC values and within-session repeatability were similar.

**References:**

[1] Robinson PD et al. European Respiratory Monograph; 2010. p. 87-104.

**P2023****Excluding extreme breaths from analysis can change conductive airway ventilatory inhomogeneity by over 25% in cystic fibrosis**

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Gas washout tests assess ventilatory inhomogeneity. Analysis of normalised phase 3 slopes (SnIII) allows differentiation of inhomogeneity of conducting and acinar airways (S<sub>cond</sub> and S<sub>acin</sub>). Standardising data collection and analysis in subjects with a wide range of tidal volumes remains problematic, though multiplying each SnIII by the expired tidal volume (Vt) of the breath has been used as a correction. Our

Aim was to examine the effect of excluding breaths with extreme Vt on S<sub>cond</sub>.

**Methods:** We performed multi-breath nitrogen washout in 16 children with CF aged 6-17 yr. An auditory signal indicated when the child has inspired a pre-set Vt. Measurements were performed in triplicate in all except 2 and analysed with a custom-built programme. SnIII from every breath was plotted against lung turnover (TO), separately for each run and for all runs combined. The slope of SnIII against TO was calculated for all data between 1.5 and 6 TO to determine S<sub>cond</sub>. Analysis was repeated after excluding breaths that differed from the mean expired Vt by >10%. Results were compared with paired t-tests and Bland-Altman plots.

**Results:** The number of breaths between 1.5 and 6 TO ranged from 7-26. 15 children had 1-10 extreme breaths excluded, which had no effect on S<sub>cond</sub> for the group as a whole (mean, 95%CI=-0.0015, -0.0076 to 0.0046, p= 0.61). In 5/16 cases S<sub>cond</sub> altered by >25%. Biggest changes were seen in those with lowest values of S<sub>cond</sub>. Size and direction of the change was unrelated to the number of breaths excluded.

**Conclusion:** Retaining or excluding individual breaths can make a significant difference to S<sub>cond</sub>, which may be relevant in longitudinal studies.

**P2024****Double tracer gas single breath washout – Comparison with conventional lung function tests in children with and without cystic fibrosis**

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A tidal single breath washout (SBW) has been shown to have potential as new lung function test. We calculated indices describing the shape of the SBW curve,

and investigated their variability and association with conventional lung function tests in cystic fibrosis (CF) and healthy children.

70 CF children, mean (SD) age 11.7 (3.5) years, and 42 healthy children aged 11.5 (3.9) years performed nitrogen multiple breath washout (MBW) and helium and sulfur hexafluoride SBW using a side-stream ultrasonic flowmeter (Eco Medics AG). 8 CF children and 10 controls performed MBW and SBW on a second day. Molar mass (MM) SBW curves were plotted vs. expired volume. MM-slopes of tidal phase II and III (MM\_SII; MM\_SIII), and area under the MM curve (AUC) were calculated. Mean (SD) between-test coefficient of variation (CV%) for MM\_SIII, MM\_SII, and AUC was 15.5 (13.3)%, 15.3 (11.4)%, and 8.7 (6.5)%, respectively. All three CV% were similar between CF and healthy children. MM\_SIII was associated with expired tidal volume (TV) and mean tidal flow (MTEF), and MM\_SII with TV. MM\_SIII and MM\_SII differed significantly between CF and healthy children. MM\_SIII and MM\_SII were associated with the lung clearance index (p<0.001 for both) but not with spirometry indices. AUC was not associated with lung function test parameters.

We identified double tracer gas SBW indices reliably characterizing ventilation inhomogeneity (VI) and separating healthy from CF children despite considerable overlap. More detailed analyses are needed to better understand underlying pathophysiological phenomena and to obtain additional yet unknown information on VI from this test.

**P2025****Quality control of spirometry in children: Can ERS/ATS criteria replace visual inspection?**

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Expert's visual rating is an integral part of quality control for spirometry but is not always done. In our multi-centre reference study (LuNoKiD) we investigated whether quality criteria based on back-extrapolated-volume (BeV), reproducibility and forced-expiratory-time (FET) are feasible and can replace visual inspection.

Caucasian children 4 to 18 years old were recruited. Spirometry was carried out according to international standards under field conditions. Experts rated visual acceptability of each curve (9 per individual). We tested feasibility, sensitivity and specificity of the currently recommended quality control criteria, and determined optimal cut-offs and combinations of the three computer-based quality measures using visual acceptability as gold standard.

A total of 3133 of 5104 investigated subjects were healthy and included. 72% of these had visually acceptable flow-volume curves. In this group, 95% met ATS/ERS recommendations for BeV, 90% for reproducibility and 47% for FET. Best correspondence with visual acceptability was reached when choosing the cut-offs 4.6% for BeV (in percent FVC) and 1.8 sec for FET. The best combination of the three measures showed good overall concordance with visual acceptability but still a specificity of 56% only.

Our study supports the hypothesis that - in contrast to BeV and reproducibility - ATS/ERS-recommended cut-offs for FET are not feasible under field conditions. The low specificity of the optimal combination of the three quality measures further demonstrates that these cannot replace visual control.

**P2026****Relationship between lung function using forced oscillation technique (FOT) with recent symptoms in young children with asthma**

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**Background:** Use of FOT to assess lung function in young children is increasingly reported in the clinical setting. However, associations between bronchodilator responsiveness (BDR) as assessed by FOT and recent symptoms in young children with asthma have not been reported. We aimed to investigate the relationships between recent respiratory symptoms and BDR using FOT in young children with asthma.

**Methods:** 70 children (aged 3 to 6y) with mild asthma were studied twice 5 months apart. FOT (resistance and reactance at 8 Hz: Rrs8 and Xrs8, respectively) was measured prior to- and 15 mins following Salbutamol (600 µg) inhalation. The BDR was assessed using absolute and relative changes in Rrs8 and Xrs8. Respiratory symptoms in the month prior to each visit were obtained using daily diary card. We performed regression analyses assessing the impact of respiratory symptoms on the transformed absolute and relative BDR in Rrs8 and Xrs8.

**Results:** Pre- and post BD Rrs8 and Xrs8 data were obtained from 70 children at visit 1, and 56 children at visit 2. There were no differences in BDR for Rrs8 with any reported symptoms. In contrast, Xrs8 BDR was significantly larger (p<0.05)

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in children reporting wheeze that required relievers in the month prior to FOT testing.

**Conclusions:** In children with mild asthma increasing symptom incidence requiring reliever use is associated with an increased BDR in Xrs8. These data suggest that symptoms in early childhood asthma result in alterations in peripheral airways function. Alternatively, it may indicate that the FOT is poorly sensitive to asthma related lung disease in young children. Further research addressing this question is required.

**P2027****In vitro validation of nitrogen multiple breath washout using ultrasonic equipment**

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Over the last years, ultrasonic equipment for Multiple Breath Washout (MBW) including measurement of functional residual capacity (FRC) and assessment of ventilation inhomogeneity has been developed (EasyOne Pro, nnd Medizintechnik AG, Switzerland). Accuracy of the ultrasonic flow sensor has been demonstrated against mass spectrometry. Validity and feasibility have been demonstrated in single and in multi-centre studies using SF<sub>6</sub> as the tracer gas. Recently, the washout procedure has been changed to nitrogen washout. All analysis steps, including delay correction between flow and side-stream molar mass signals were automated to facilitate clinical use.

However, calculation of both, FRC and parameters of ventilation homogeneity depend on accuracy of the underlying algorithms. The aim of the present study was to assess the accuracy of the EasyOnePro software for calculating FRC from nitrogen MBW using a novel lung model.

The lung model consists of an inner and an outer water-filled Plexiglas chamber (Soloplex AB, Sweden) and is driven by a mechanical ventilator (Evita, Dräger, Germany); the water level of the inner chamber, which is partially separated by a wall to allow ventilation, determines the target FRC. 60 measurements were performed using FRC target volumes between 350 and 4000 ml. Respiratory rates were set between 10 and 20 min<sup>-1</sup> and tidal volumes between 300 and 800 ml.

Within-test repeatability of three measurements was below 0.76% for all settings. Mean difference between target FRC and measured FRC was 3.28% (95% CI -45 ml; +31 ml). We conclude that the Easy One Pro Software accurately calculates FRC.