

**3º Jornadas Nacionales de Medicina Interna
Pediátrica**

Tipo Actividad: *Conferencia*

Día: *Jueves 9 de agosto*

Horario: *13:30 a 14:30*

**Título: *Evaluación funcional pulmonar: cuándo,
cómo, por qué***

Nombre y Apellido: Marcus JONES

Evaluación funcional pulmonar en niños: cuándo, cómo, por qué

Marcus H Jones, MD PhD

Laboratorio de Fisiologia Respiratória / Centro Infant

Instituto de Investigaciones Biomédicas

Pontificia Universidade Catolica do Rio Grande do Sul

Brasil

Outline

Review lung function tests used in infants and young children (<6 years) in clinical practice and in research settings.

Discuss **briefly** infant pulmonary function test, Rint, MBW, and spirometry in preschoolers with clinical examples

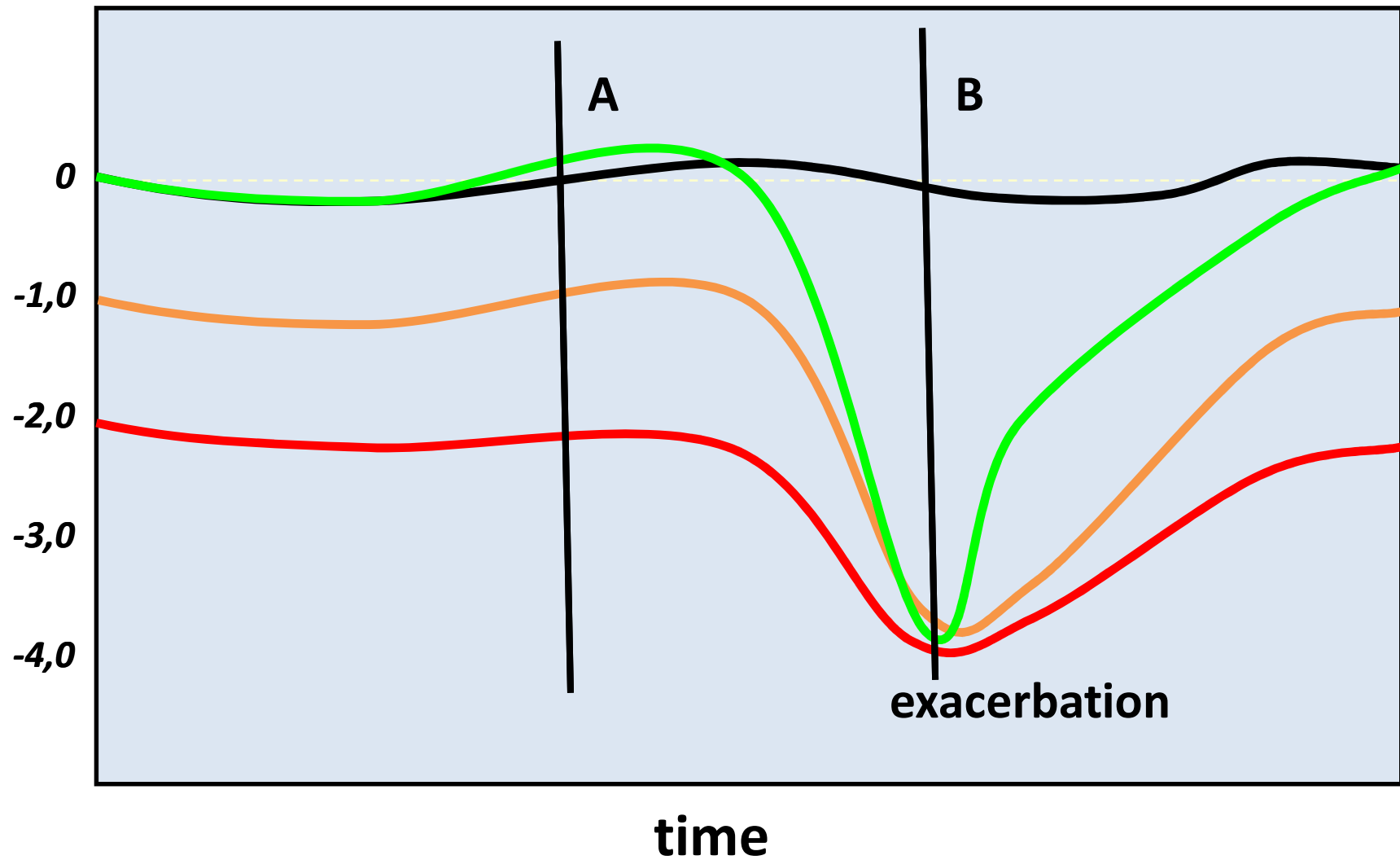
Discuss their **utility** on Cystic Fibrosis, bronchopulmonary dysplasia and recurrent wheeze.

Clinical Role of Lung Function Tests

- monitor disease severity over time
- evaluate response to treatments
- serve as objective outcome measures in clinical research studies.
- not a diagnostic tool !!

Lung Function: When?

FEV₁ Z-score



Lung Function Tests

1. Infant Pulmonary Function Testing (Raised Volume Rapid Thoracic Compression)

Infants

2. Multiple Breath Washout Technique

Infants and Preschoolers

3. The Interrupter Technique

Preschoolers

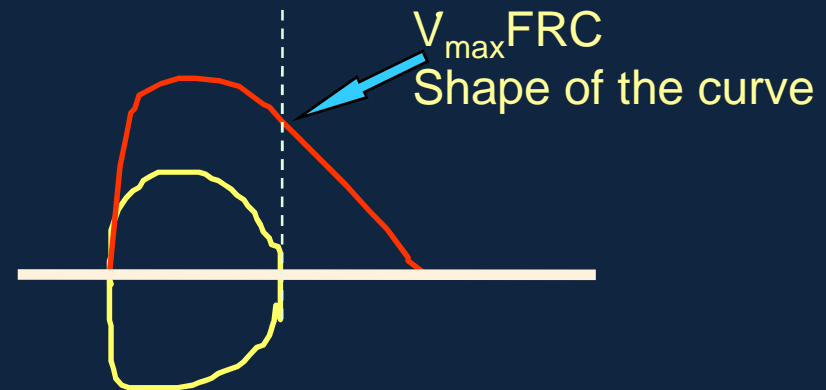
4. Preschool Spirometry

Preschoolers

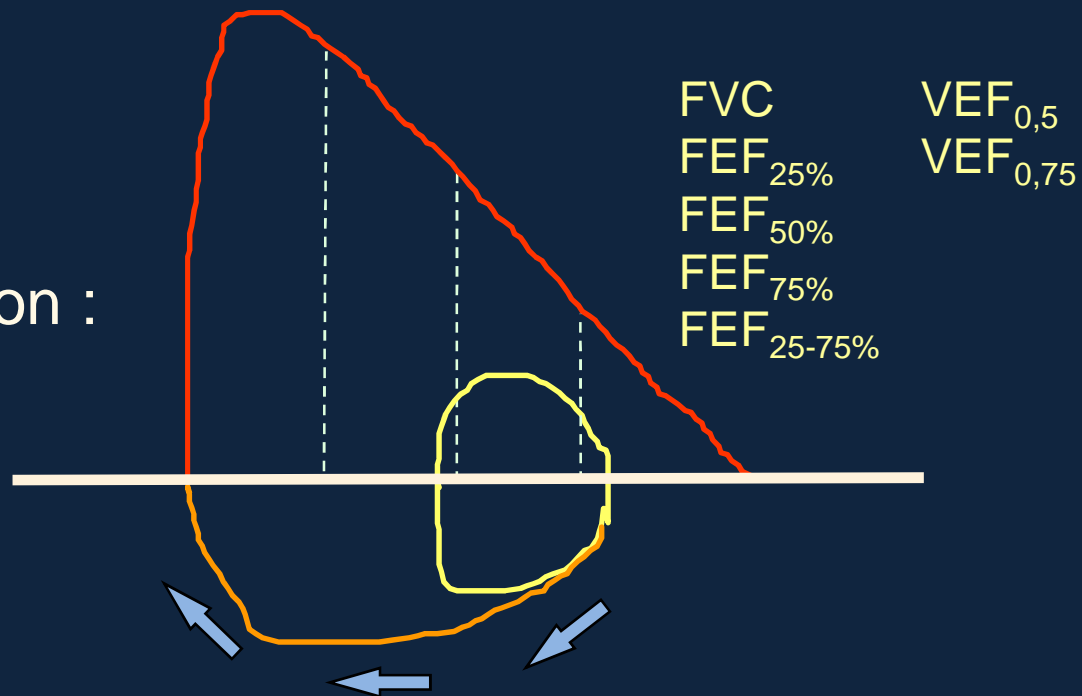
Infant Pulmonary Function Testing

Infants: $V_{max}FRC$ and RV-RTC

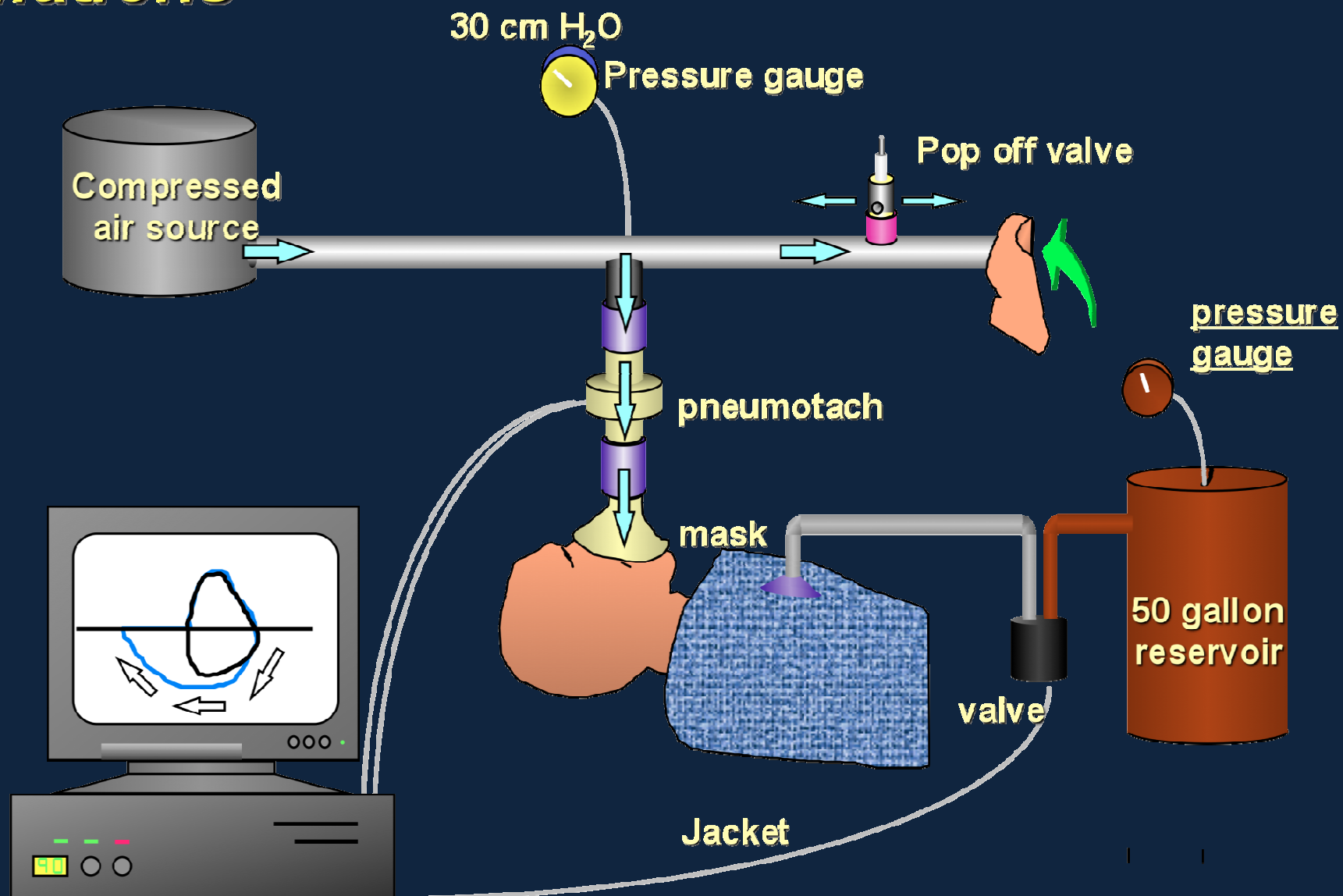
Forced expiration:
Tidal Volume



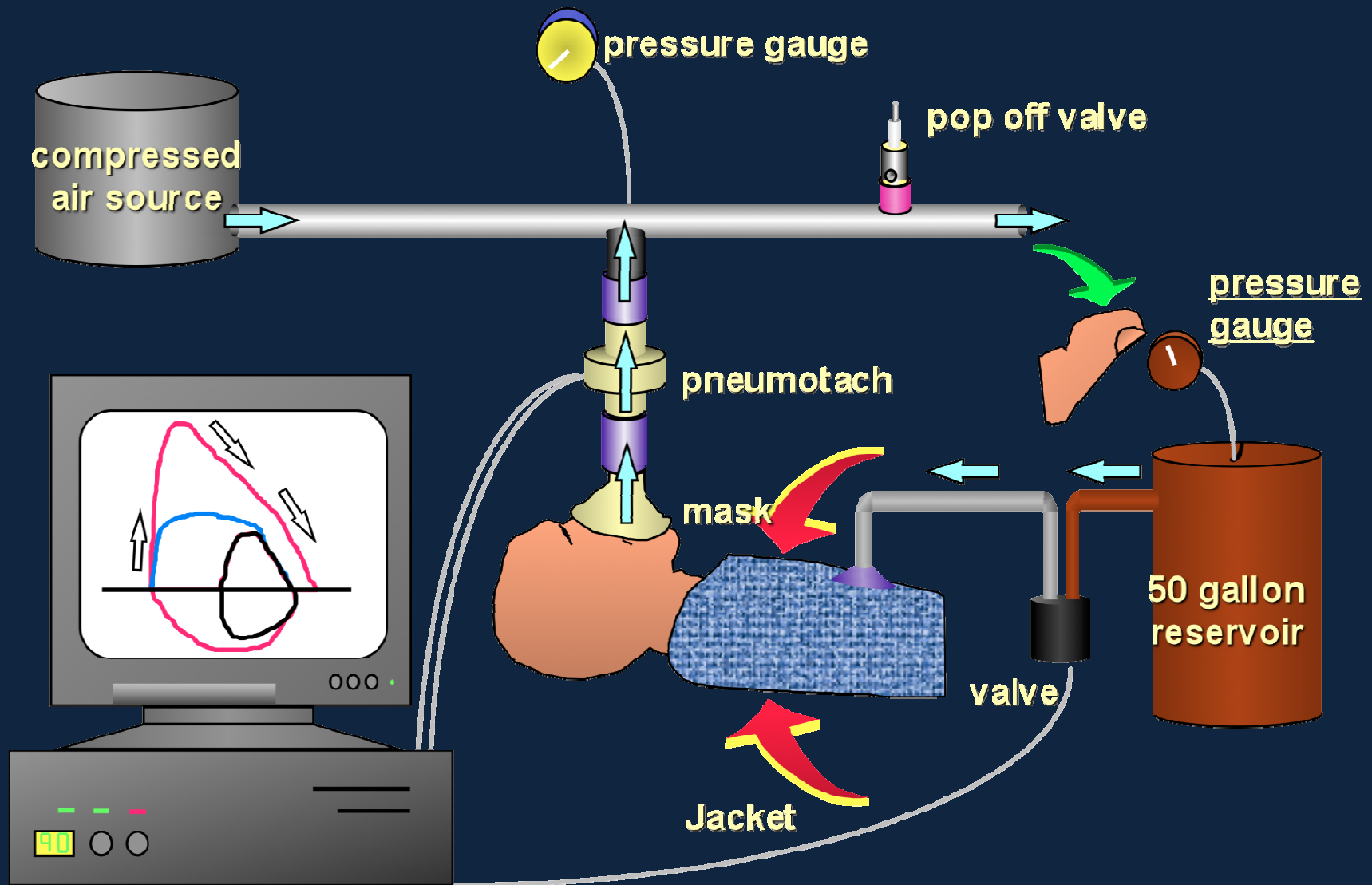
Forced expiration :
Raised Volume



Inflations



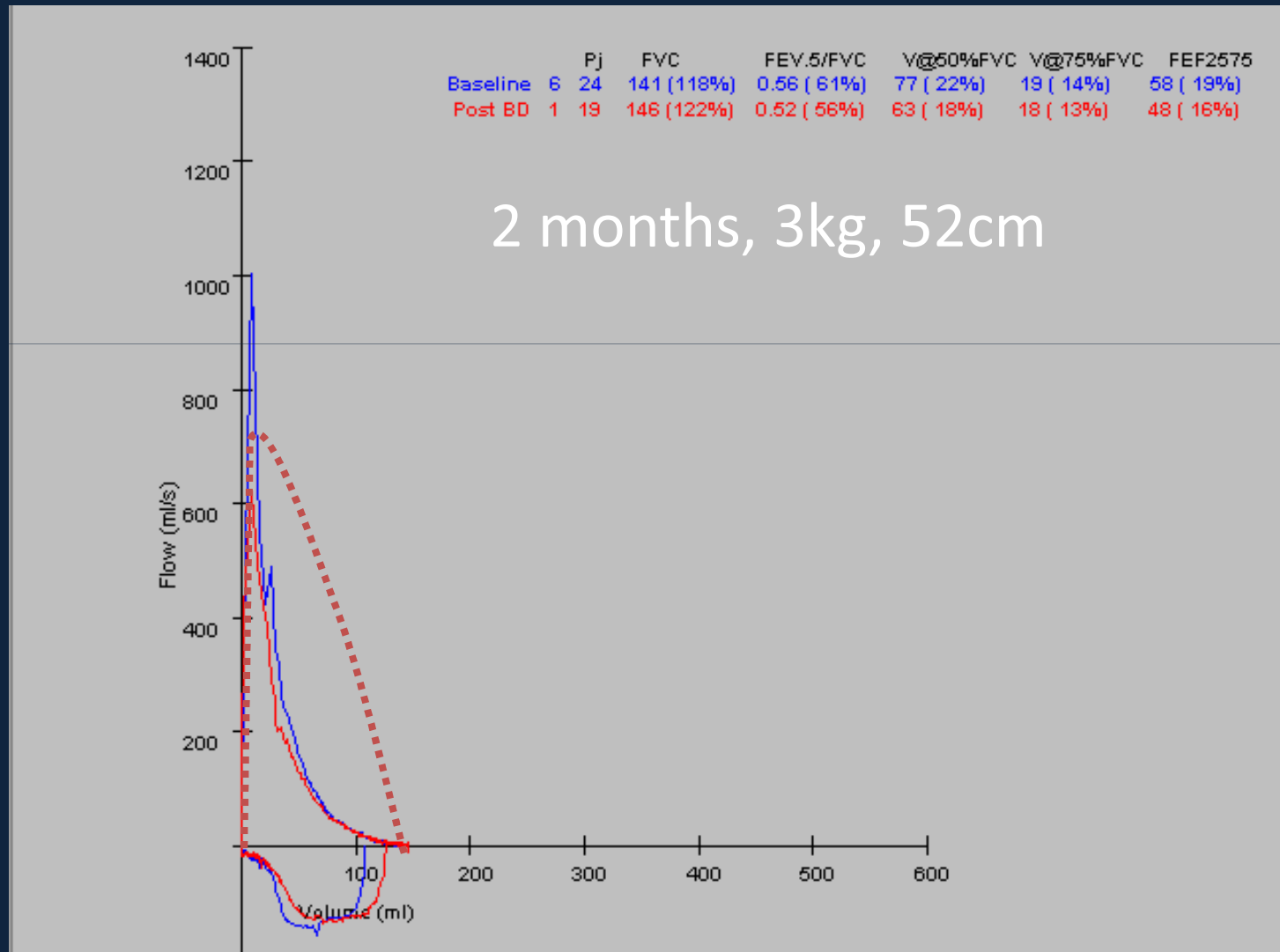
Forced expiration



Cystic Fibrosis - RVRTC

- RVRTC measurements can detect diminished lung function in CF infants, though the degree of abnormality reported varies by cohort and measurement device/technique.
- Diminished RVRTC measurements in early infancy appear to track into later infancy, through the pre-school years and into school age.

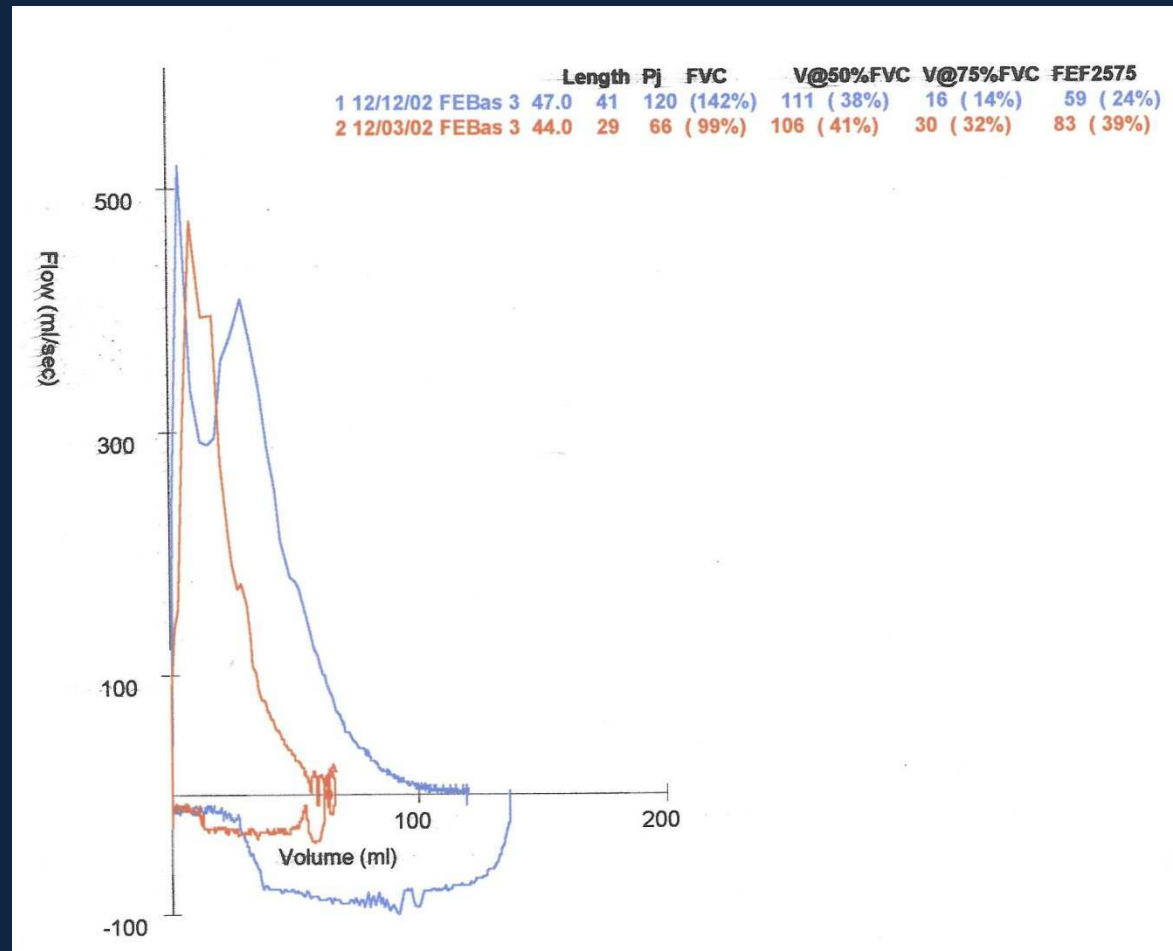
Cystic fibrosis, respiratory symptoms since birth



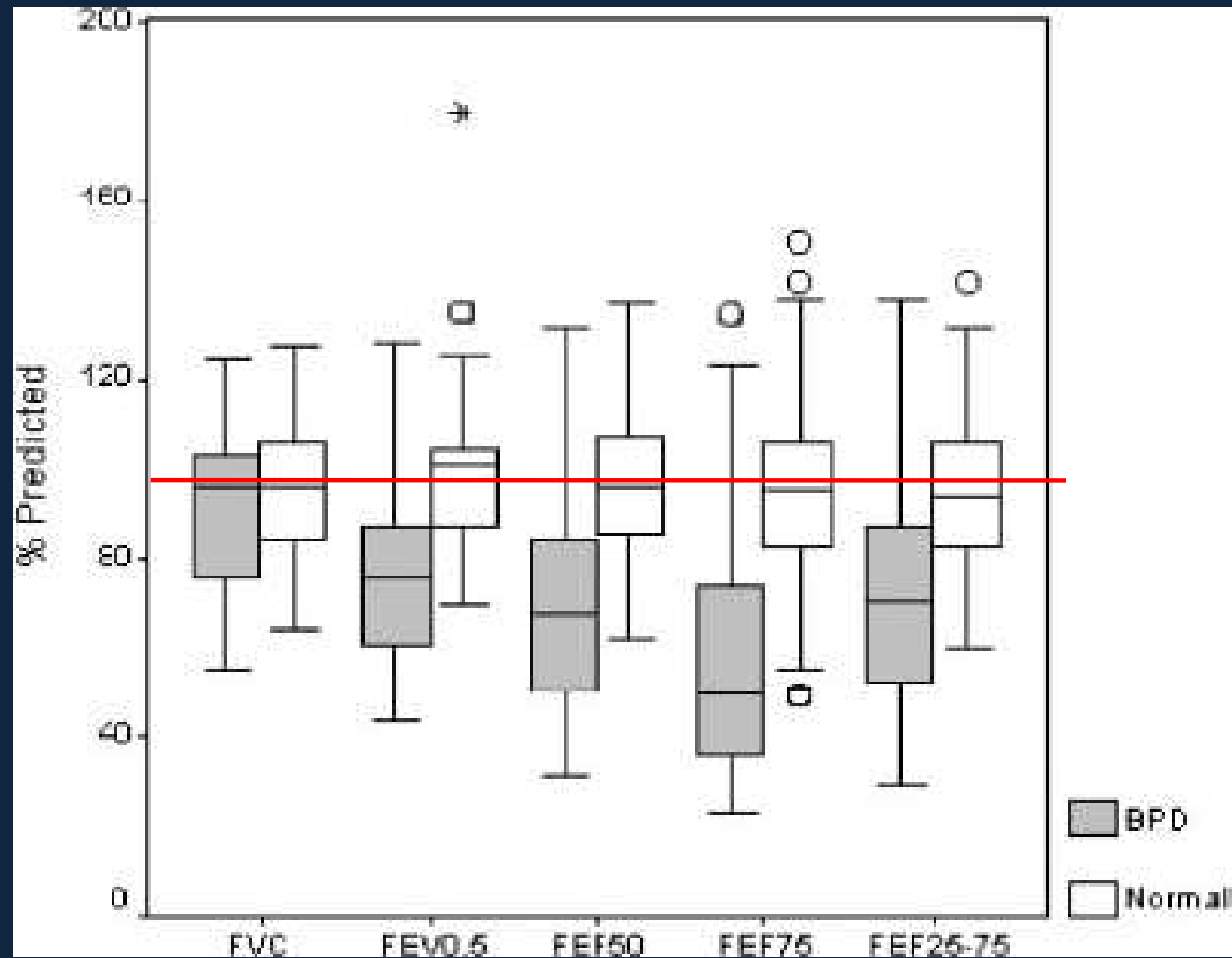
BPD / Prematurity -RVRTC

- Reduced expiratory flows when BPD infants were compared to controls
- Interestingly, RVRTC detected reduced flows even in healthy preterm without BPD

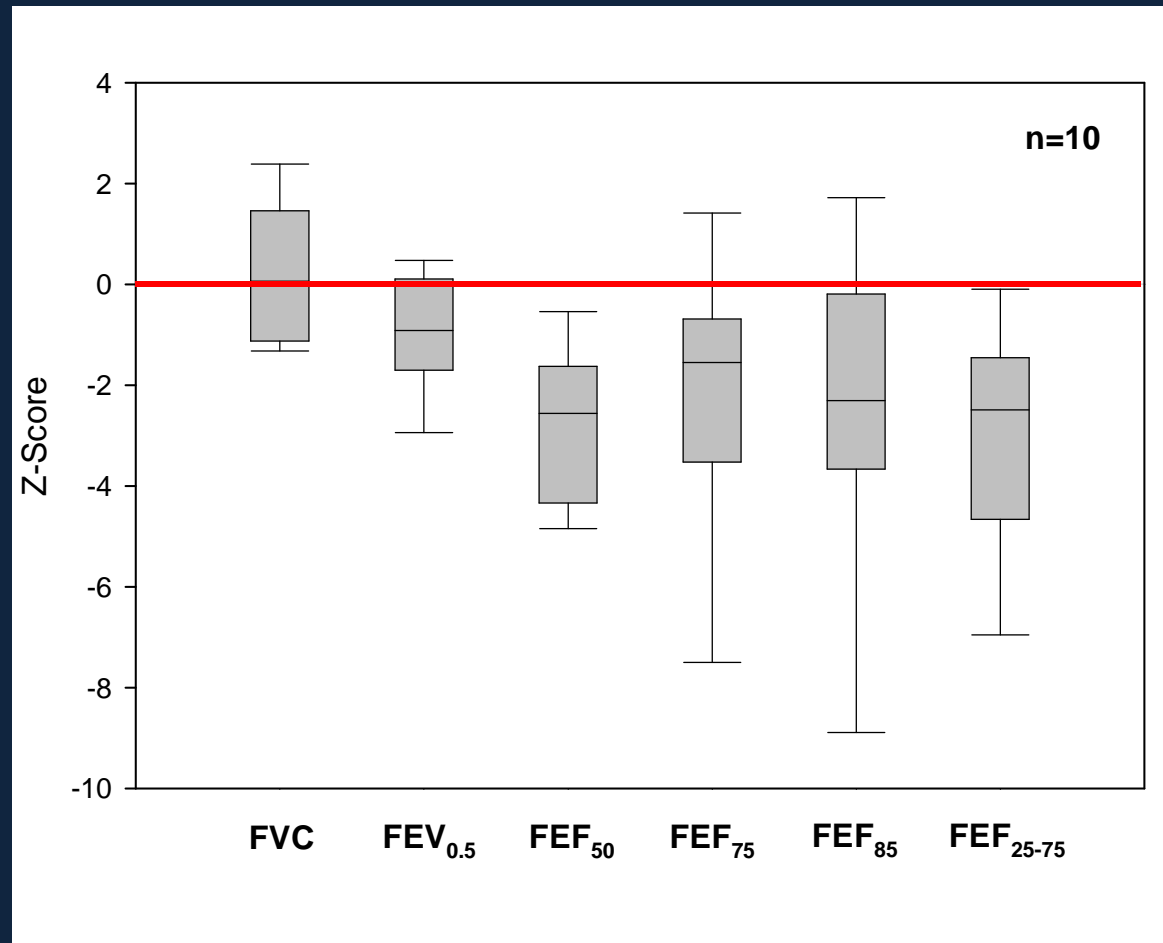
BPD infant, before and after furosemide



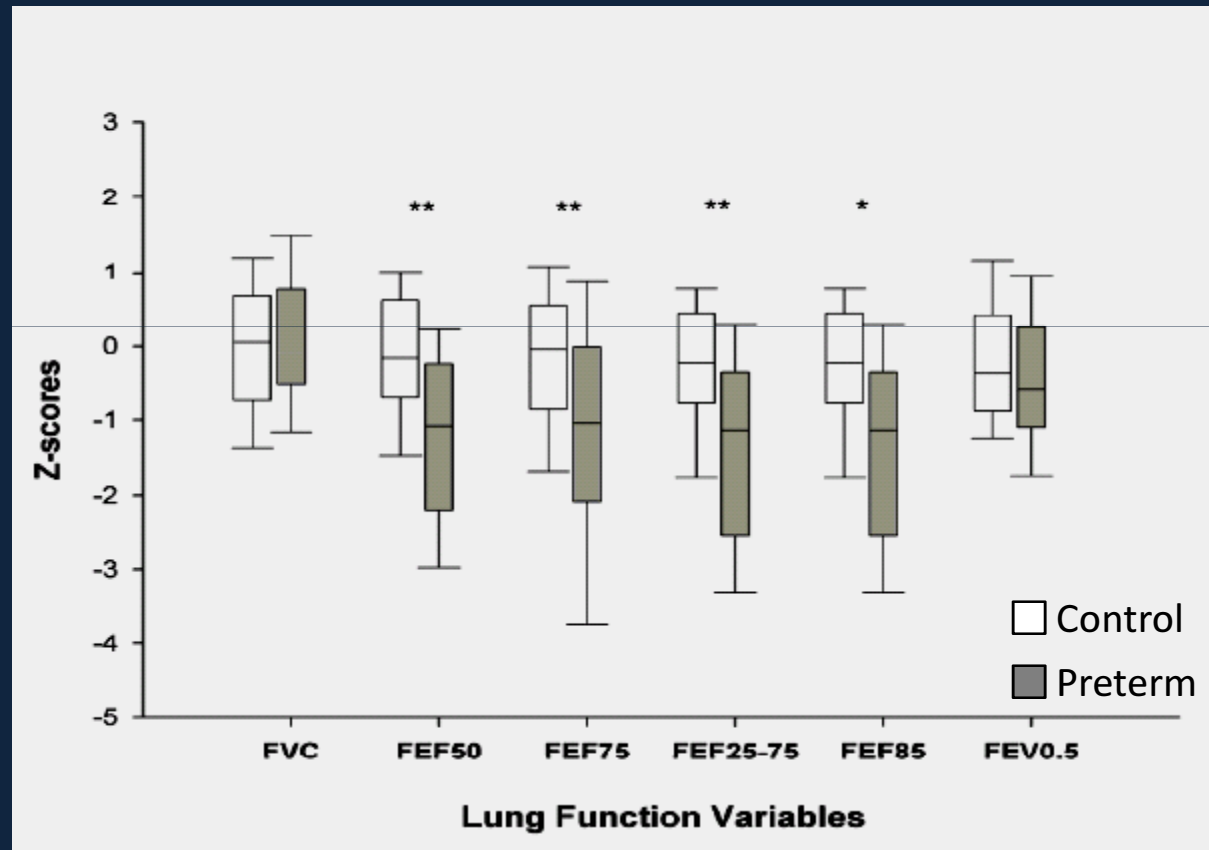
Lung function in infants with BPD



Preterm infants 26-29w GA



Healthy preterm infants

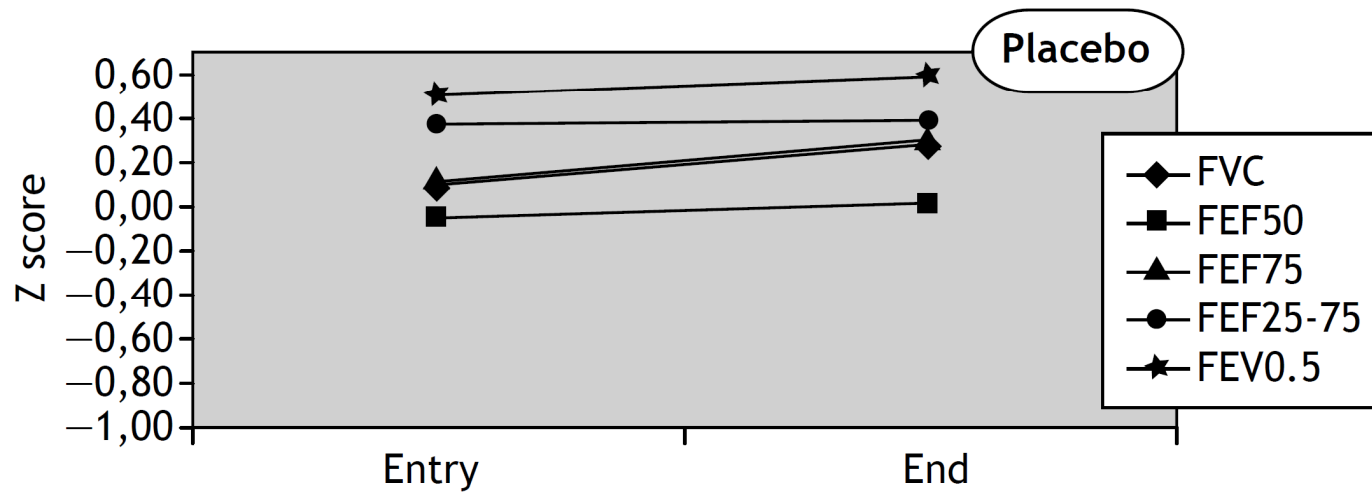
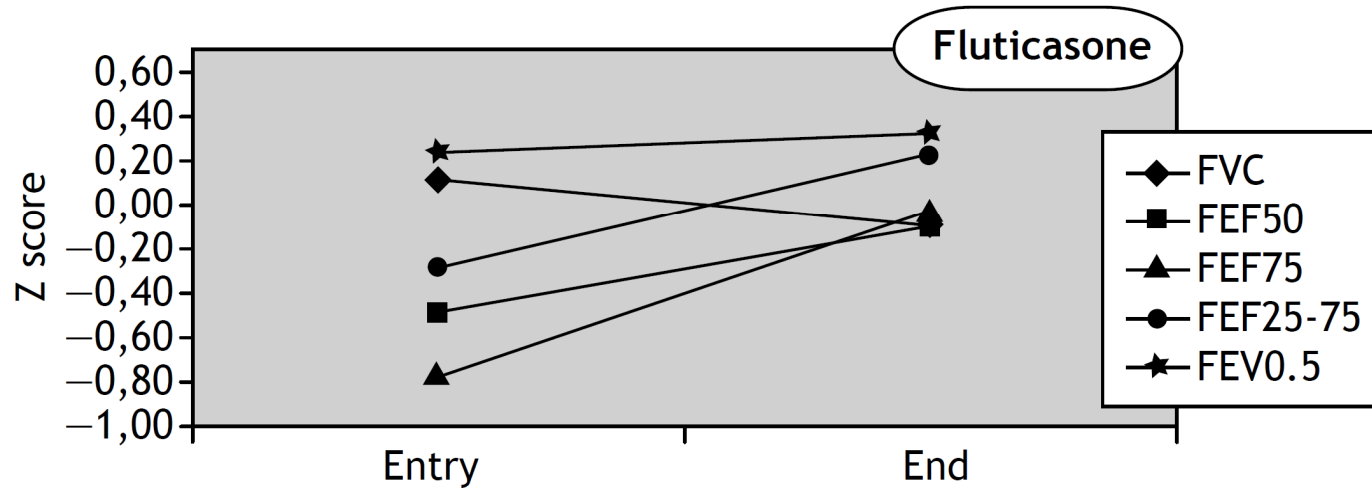


Reduced Lung Function in Healthy Preterm Infants in the First Months of Life
Am. J. Respir. Crit. Care Med. 173: 442-447

Recurrent wheeze

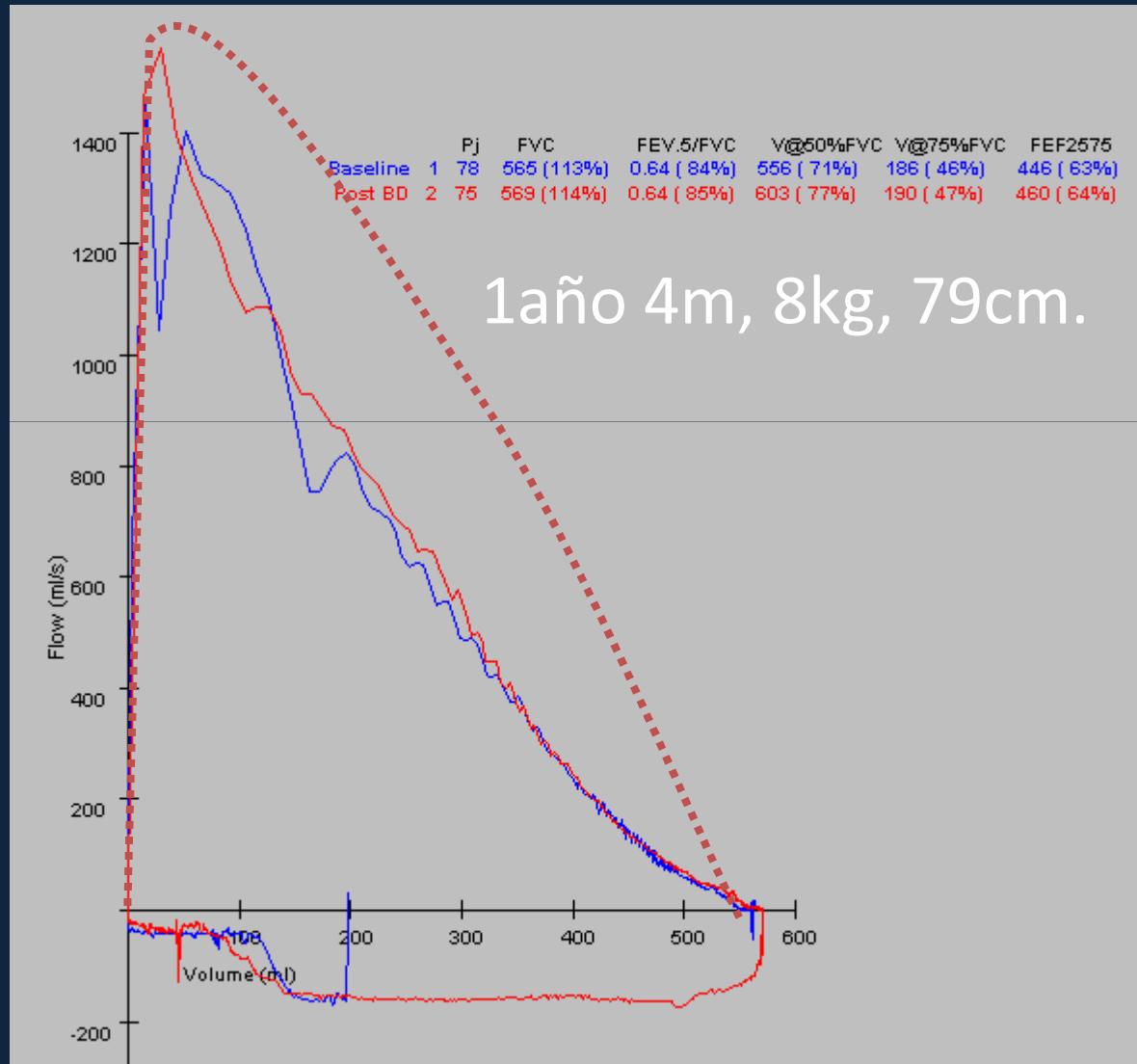
- Diminished forced expiratory flows and $FEV_{0.5}$ have been reported in infants with recurrent wheeze
- Interestingly, minimal bronchodilator responsiveness has been reported

Lung function changes in infants with RW after 3 months treatment with inhaled fluticasone or placebo.



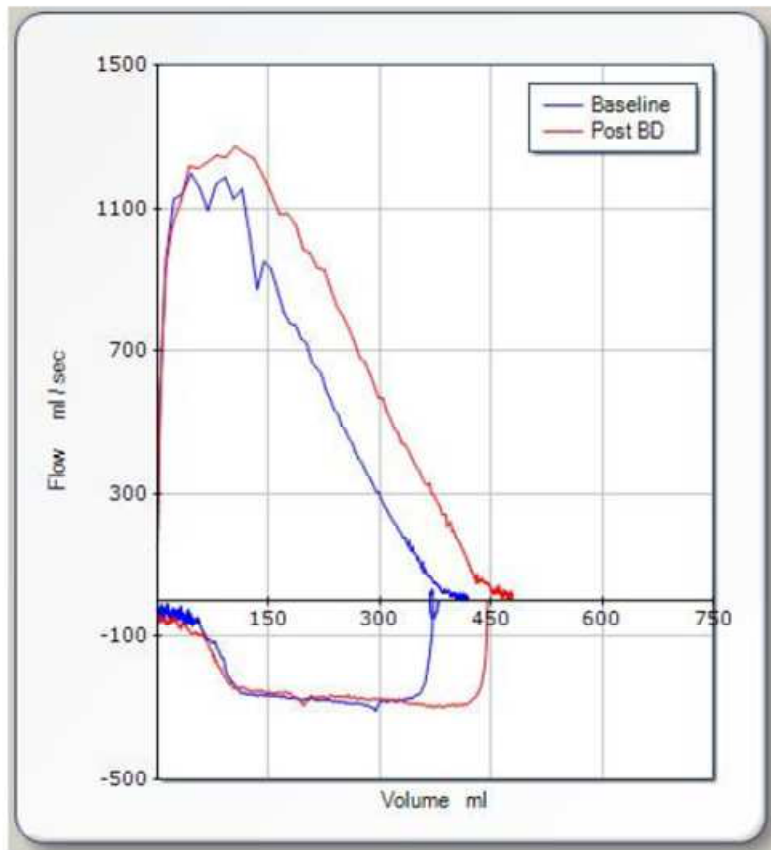
Recurrent wheeze

Investigating lung hypoplasia



Recurrent wheeze, PIBO?

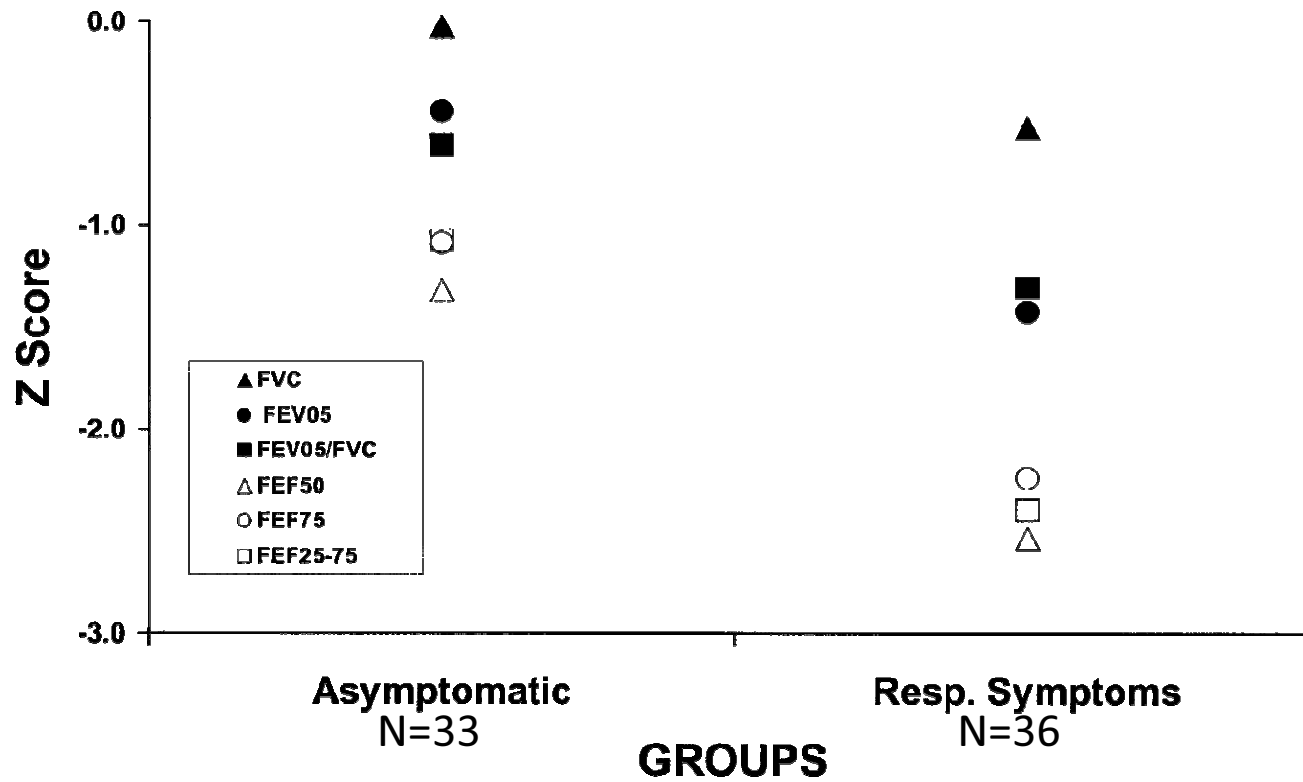
Laboratorio de Funcao Pulmonar de Lactentes
Hospital Sao Lucas - PUCRS
Fone (51) 3384-5104



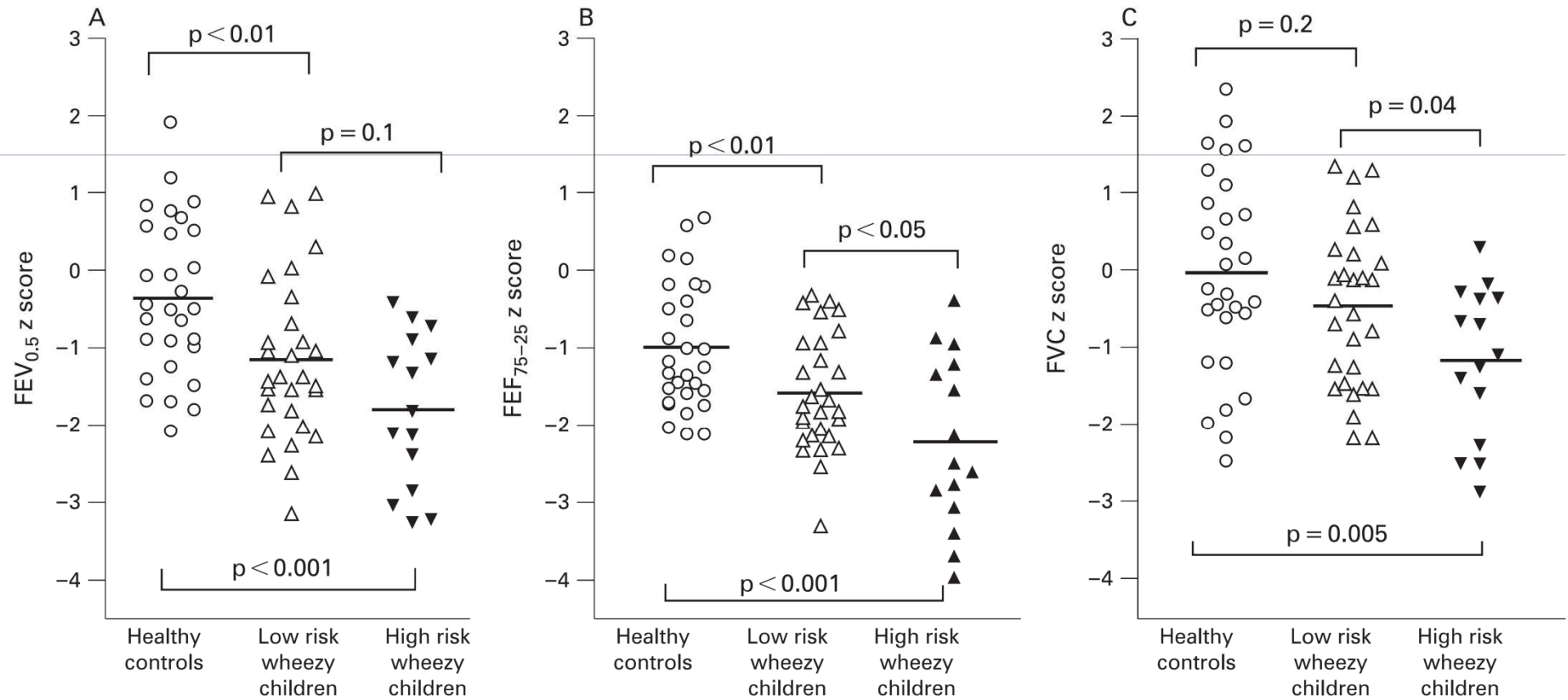
Baseline			
Frame	6		
Pj	29		
	Actual	% Predicted	Z score
FVC	418	73.3%	-1.94
FEV 0.5	318	75.7%	-1.86
FEV.5/FVC	0.759	103%	.37
FEF50	669	79.9%	-1.07
FEF75	239	53.4%	-2.16
FEF2575	565.3	73.4%	-1.48

Post BD			
Frame	7		
Pj	54		
	Actual	% Predicted	Z score
FVC	479	84%	-1.09
FEV 0.5	373	89%	-.78
FEV.5/FVC	0.78	105.7%	.7
FEF50	842	100.6%	.03
FEF75	336	75.1%	-.99
FEF2575	726.07	94.2%	-.28

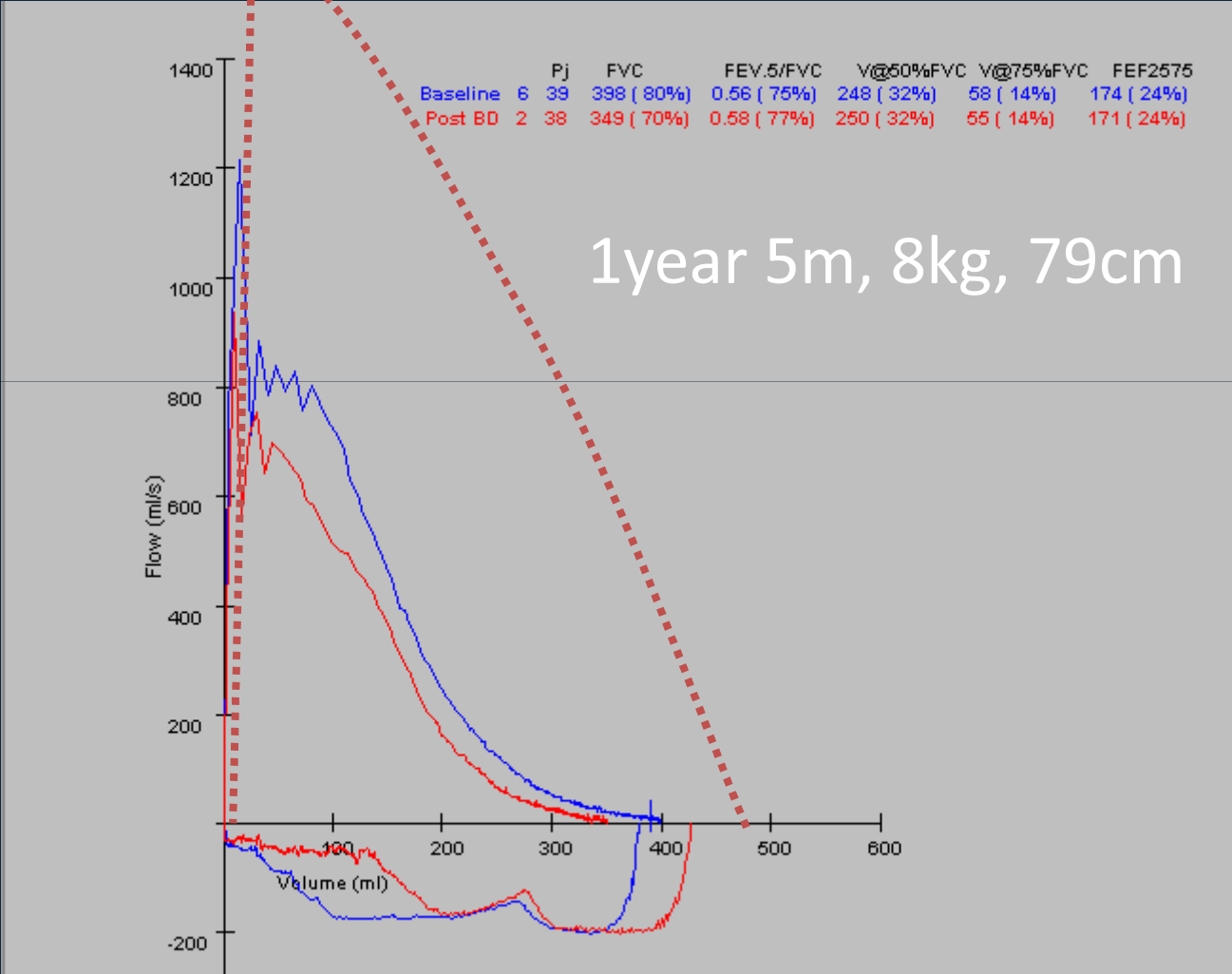
Sensitivity of IPFT



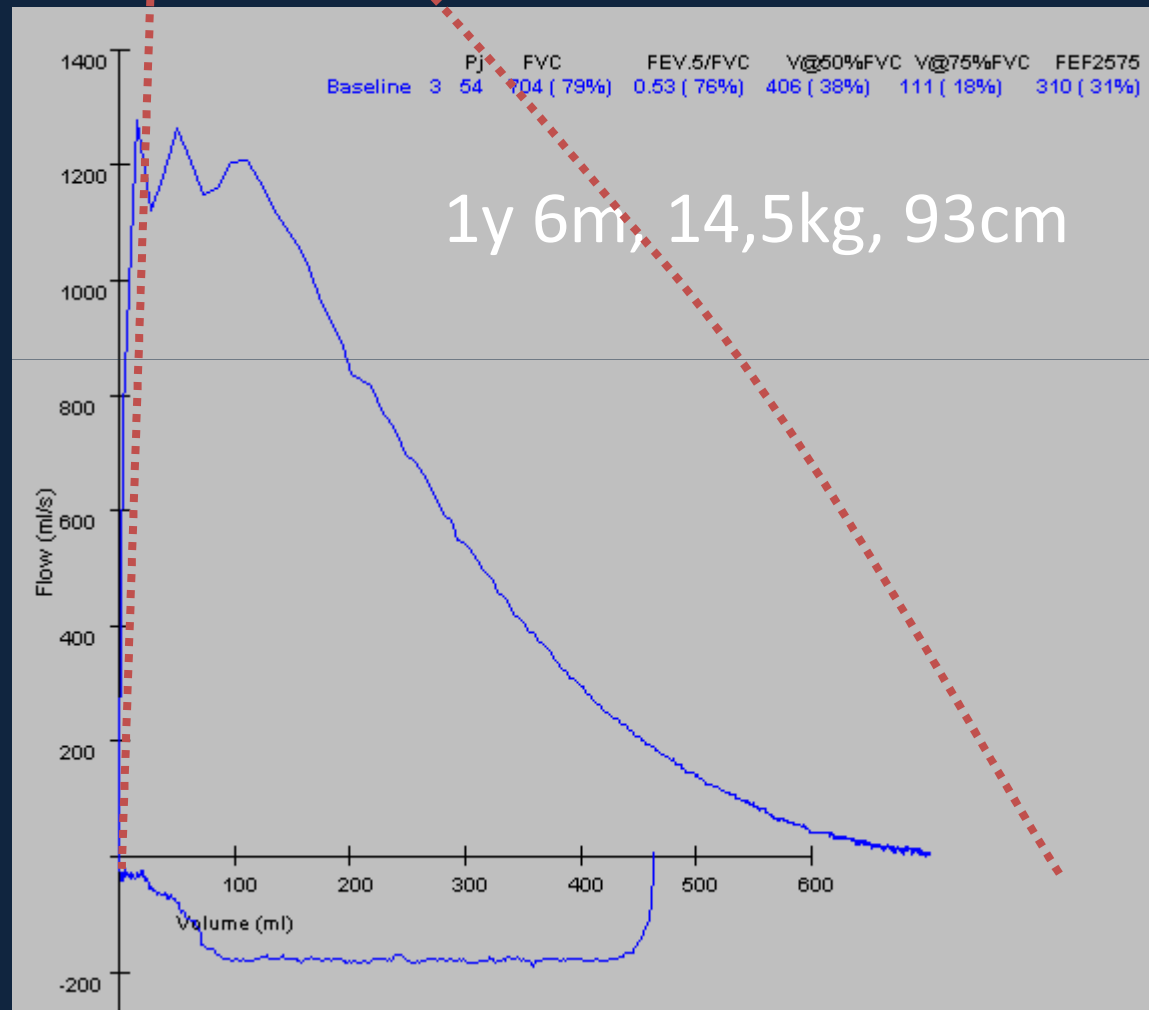
Recurrent wheeze



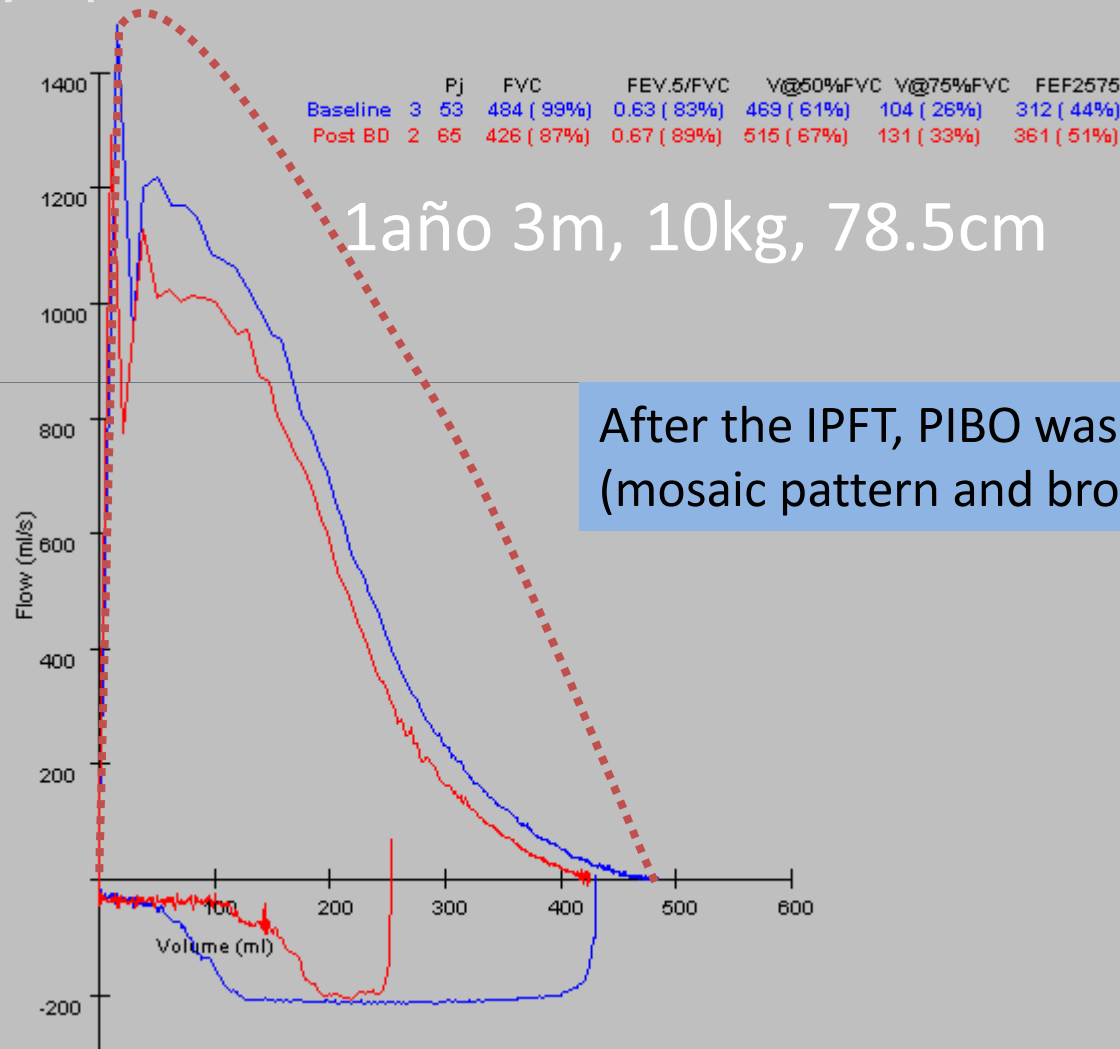
Bronchiolitis obliterans



Bronquiolitis obliterante.

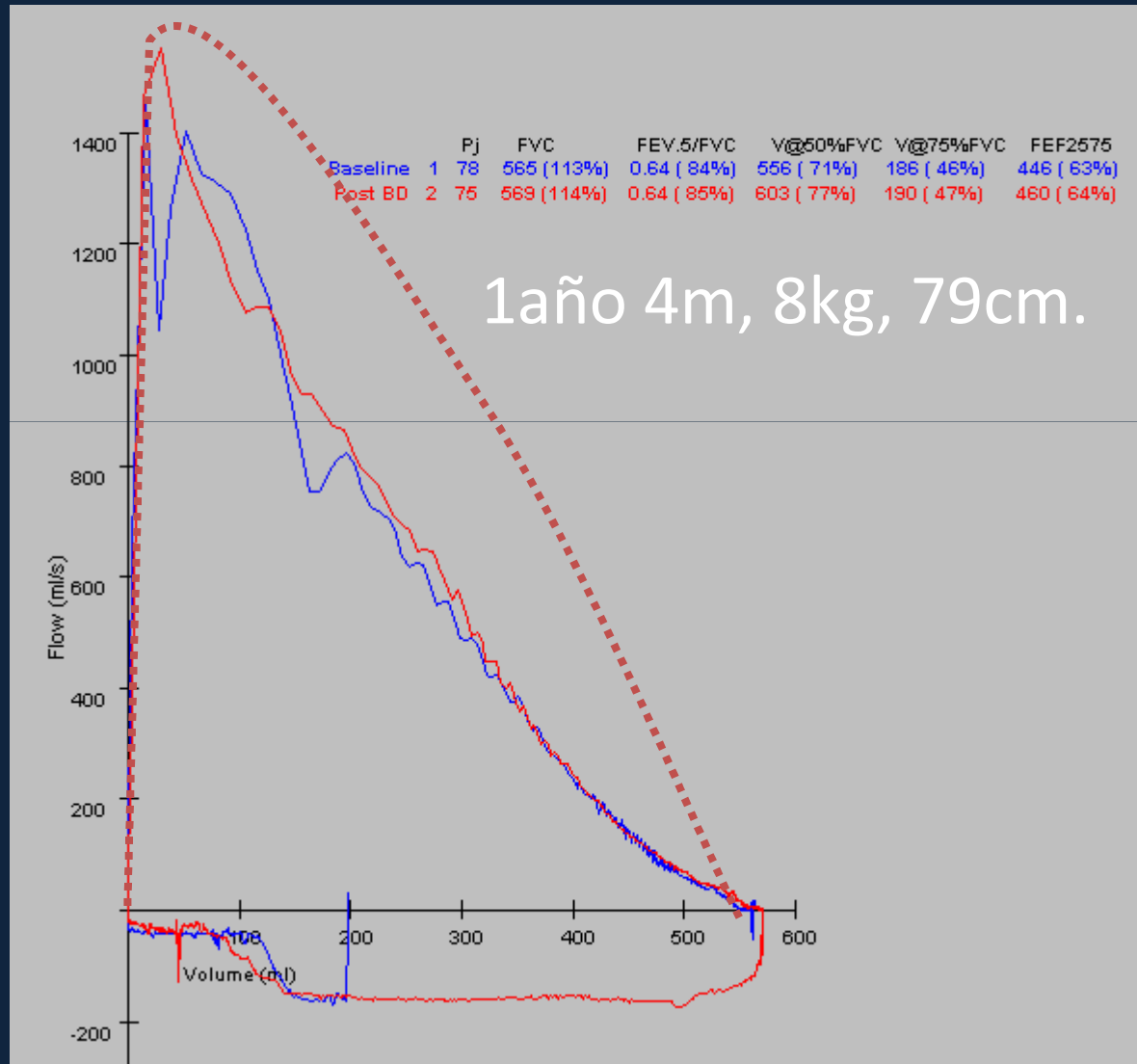


Recurrent wheeze,
3 admissions to ICU, MV 4 days
No symptoms in the last 2 months

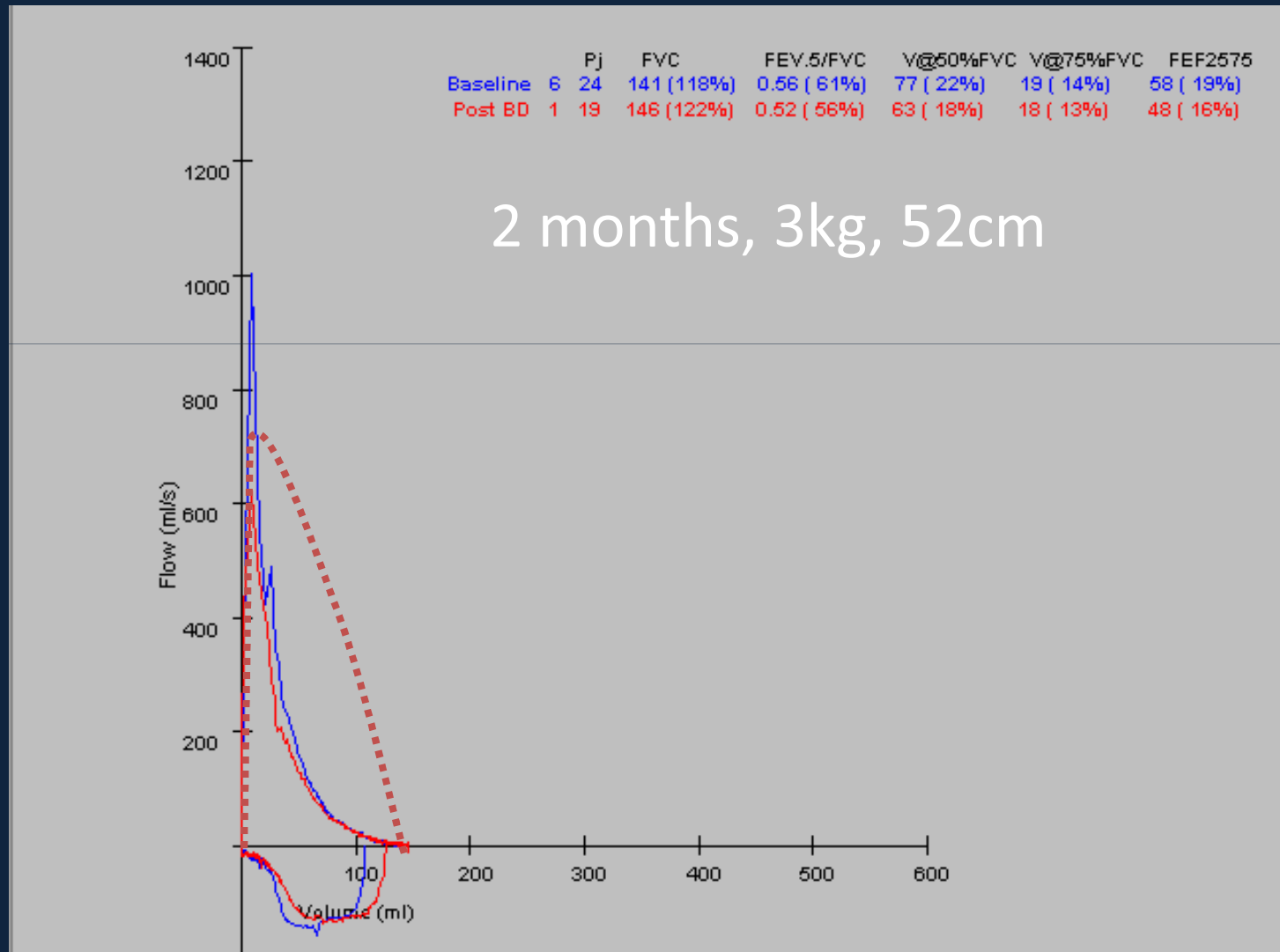


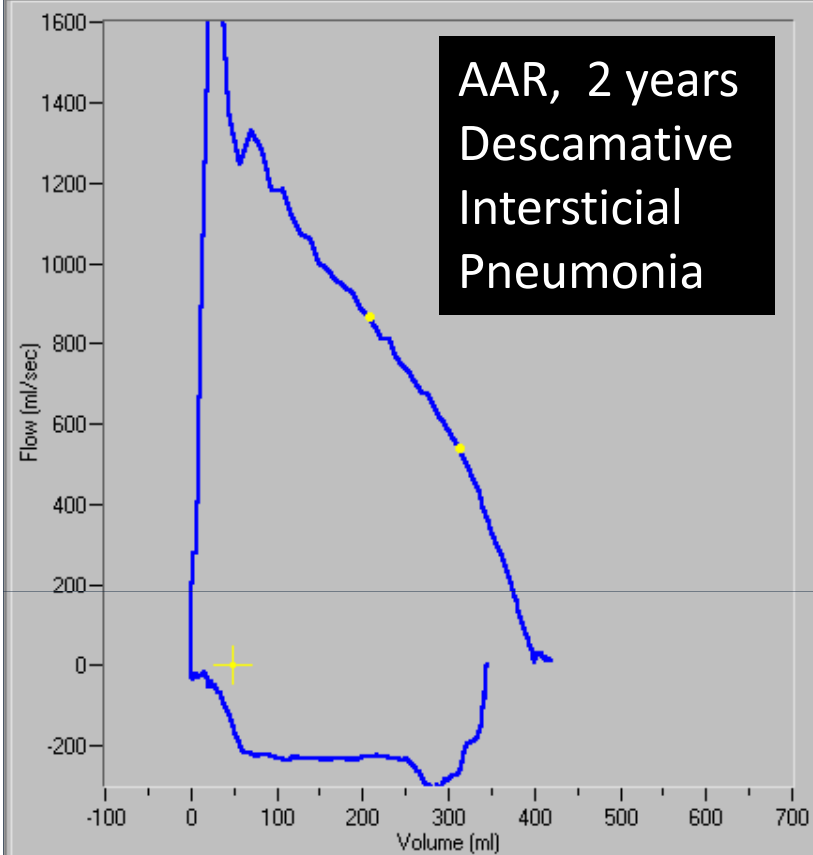
Recurrent wheeze

Investigating lung hypoplasia



Cystic fibrosis, respiratory symptoms since birth





#	Test	Fr#	Pj	FVC	V50	V75	2575	FVC	V50	V
				%o	%o	%o	%o			
0	Baseline	4	57	58	91	102	91	418	865	5
1	Baseline	*4	57	58	91	102	91	418	865	5

Sample Inflate
 Forced Jacket
 Room
 Mouth
 Bias Flow
 Auto Vent
 Inflate/PEFV

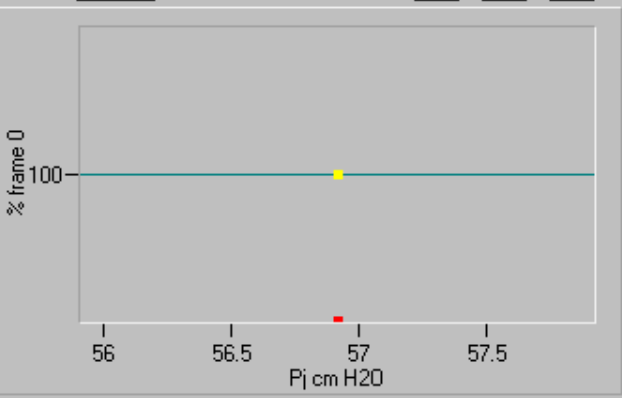
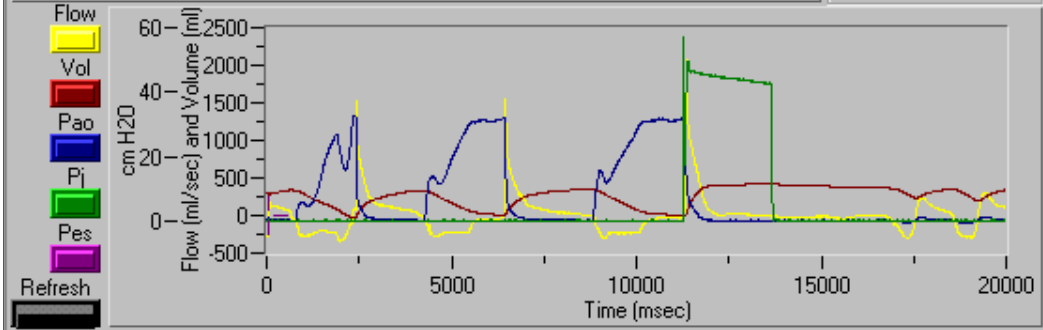
Save + Overlay Save Best
 Save Delete
 Clear

Graph Auto Scale Smooth flow Save Results Clear Results

End Points Plot delay 5 Refresh product Area50 FVC V50 V75 2575

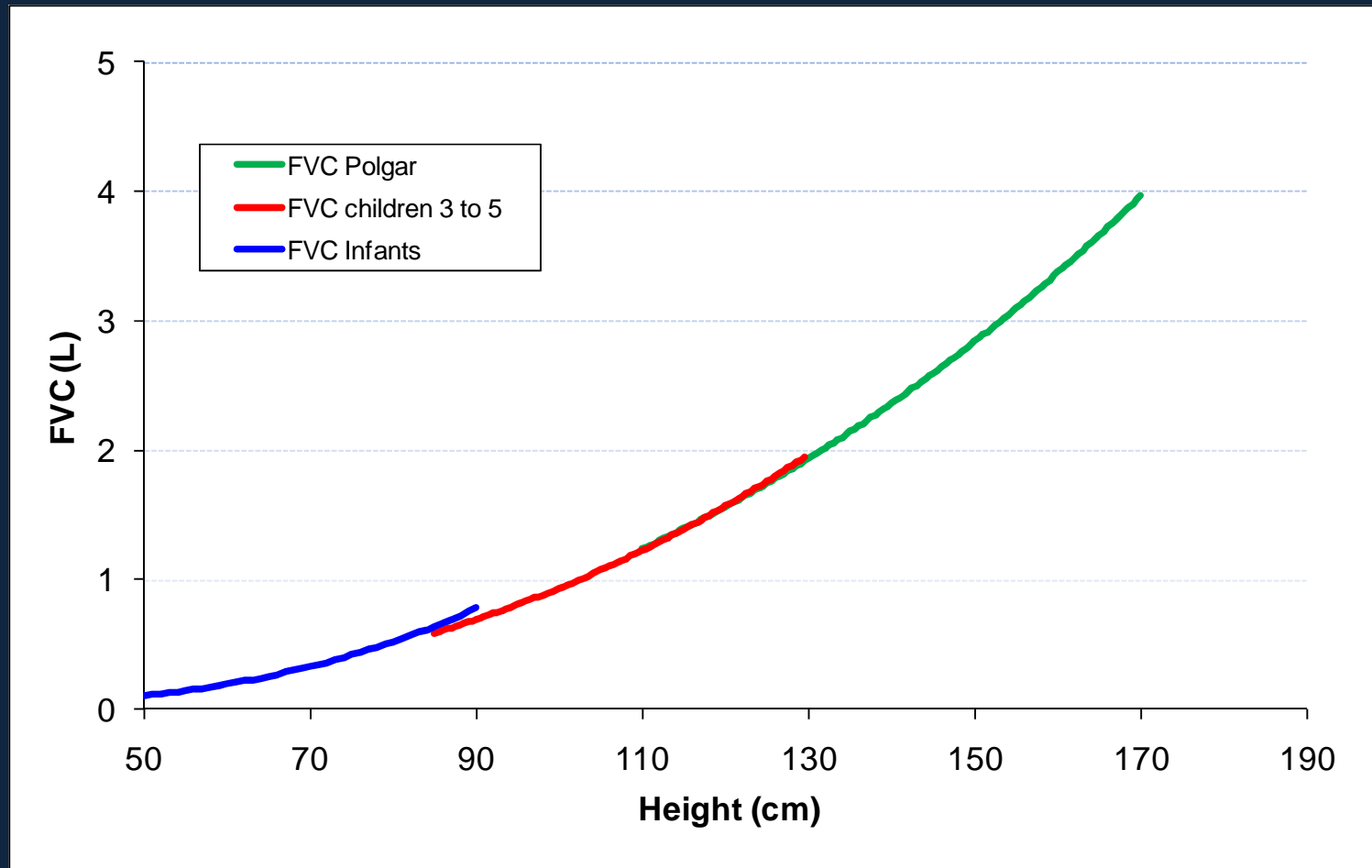
Alignment
 TLC FRC
 Inflate RV

Retrieve
 Date 12/15/ < > << >>
 Get Best
 Curve 0

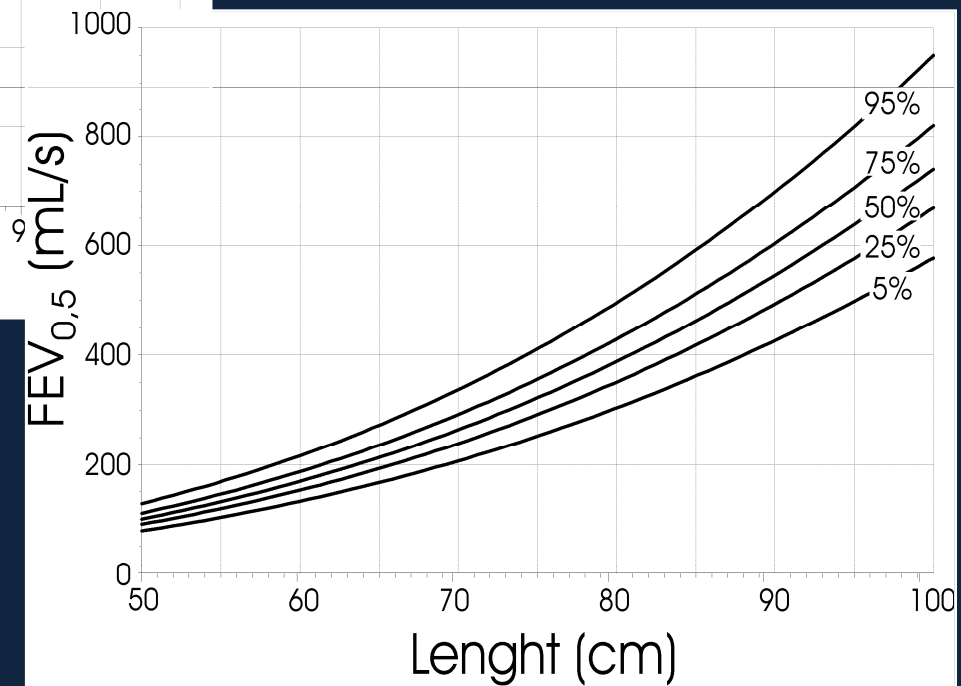
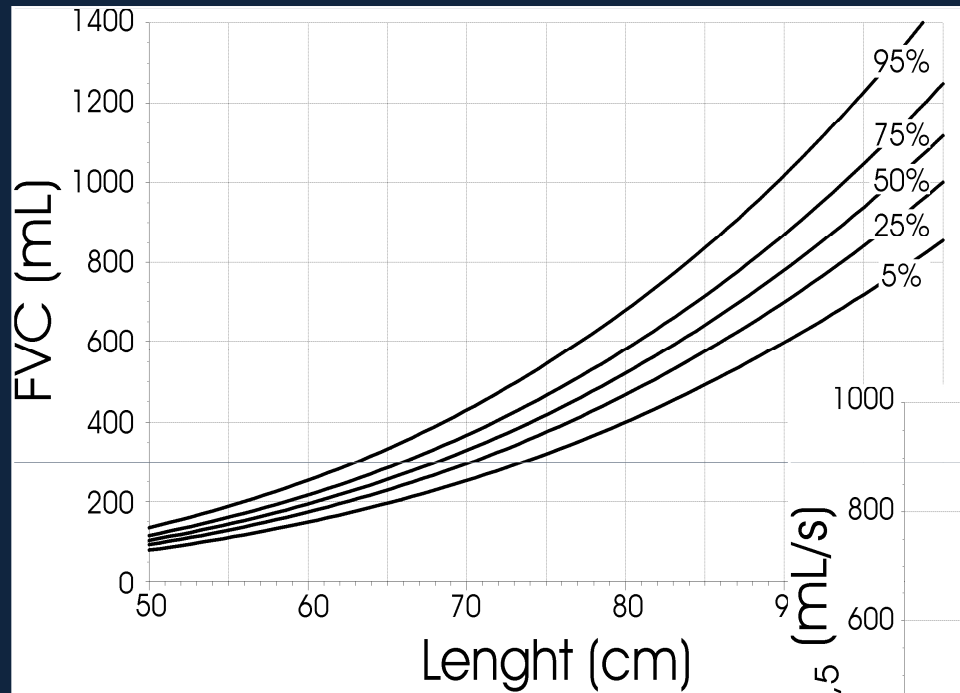


Test Type
 Comment
 Time
 40 50 60
 30 70
 20 80
 10 90

IPFT - Reference values

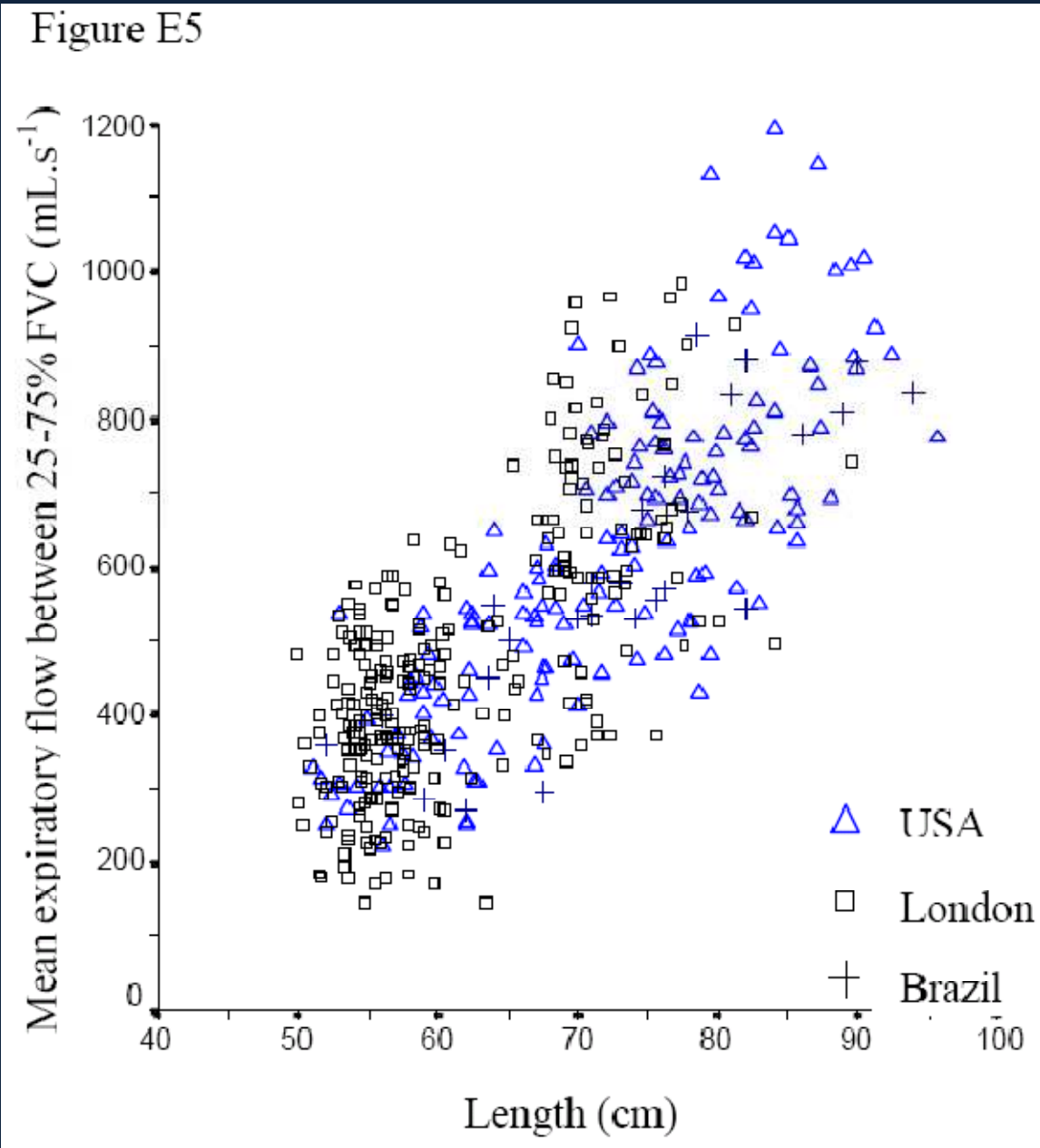


CVF and VEF_{0.5}

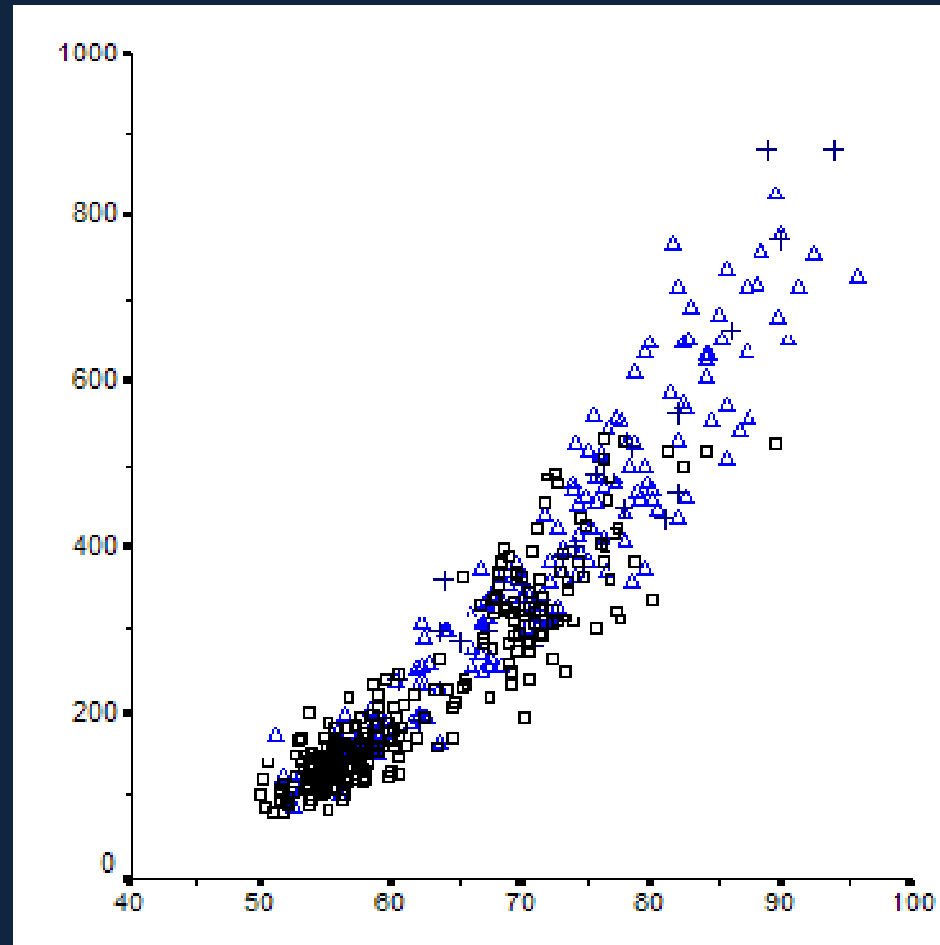


Jones et al, American Journal of Critical Care & Respiratory Medicine, 2000

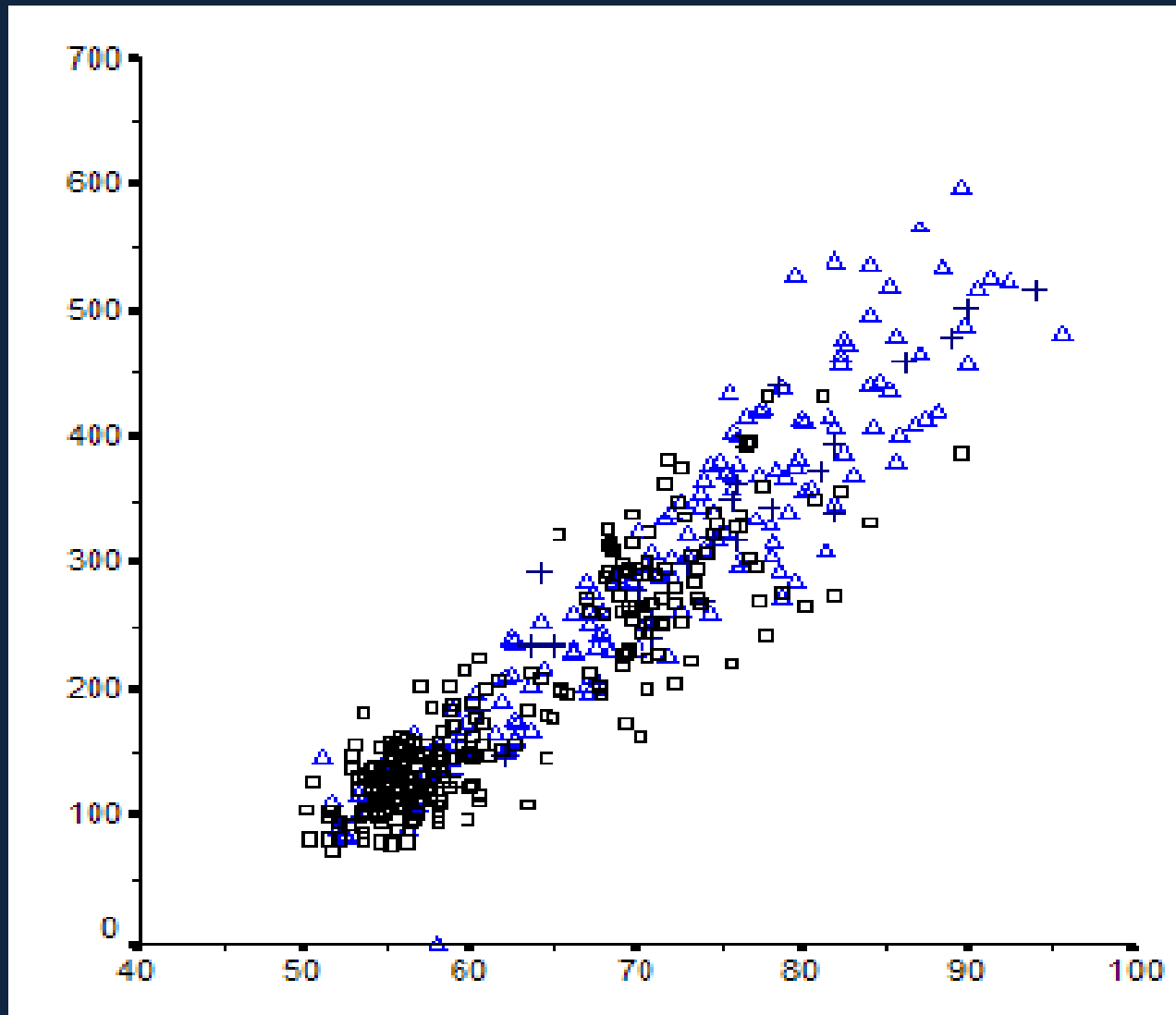
Data from USA, UK and Brazil



FVC Indianapolis, Londres, Porto Alegre



FEV_{0.5} Indianapolis, Londres, Porto Alegre



FUTURE DIRECTIONS

- Many factors, including need for sedation, lack of appropriate reference data (multicenter and other devices) and time and resource intensity, have limited the clinical role for the RVRTC.

Multiple Breath Washout Technique

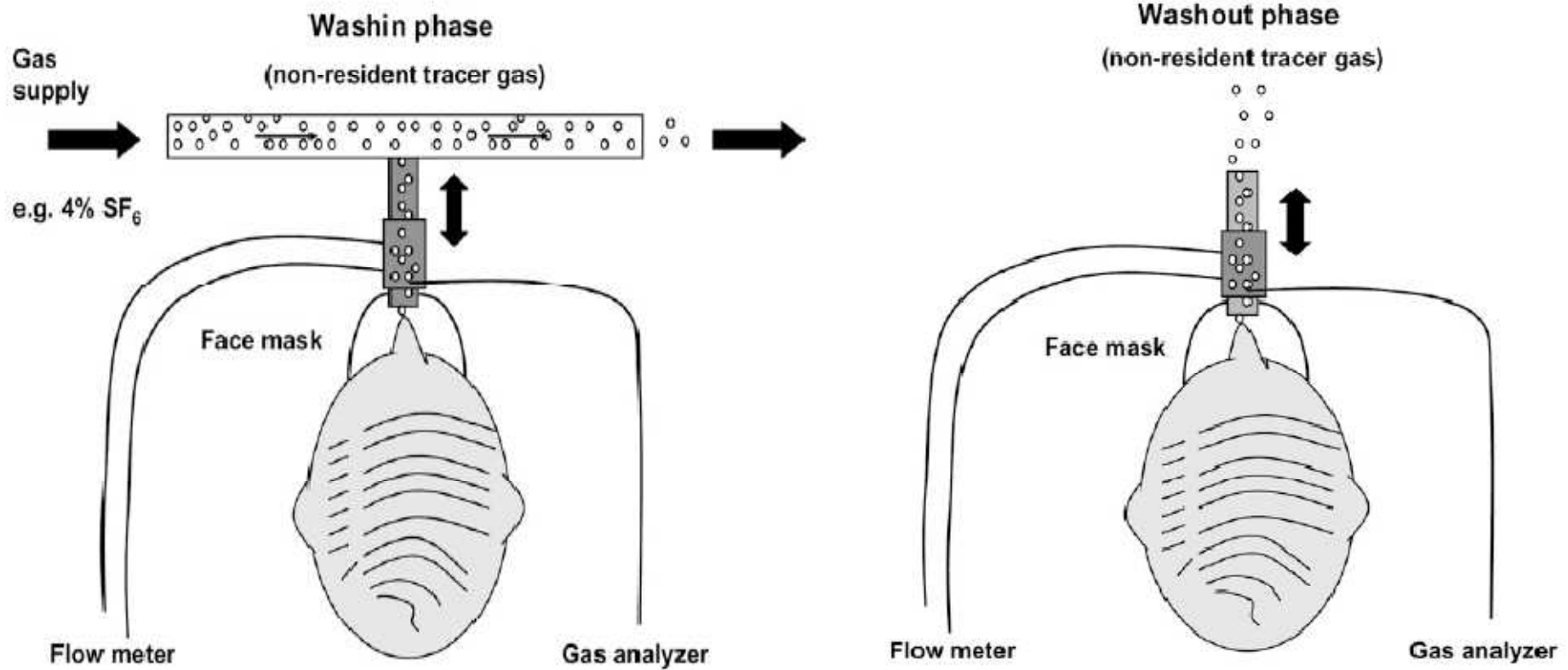
Multiple-Breath Washout Lung Clearance Index

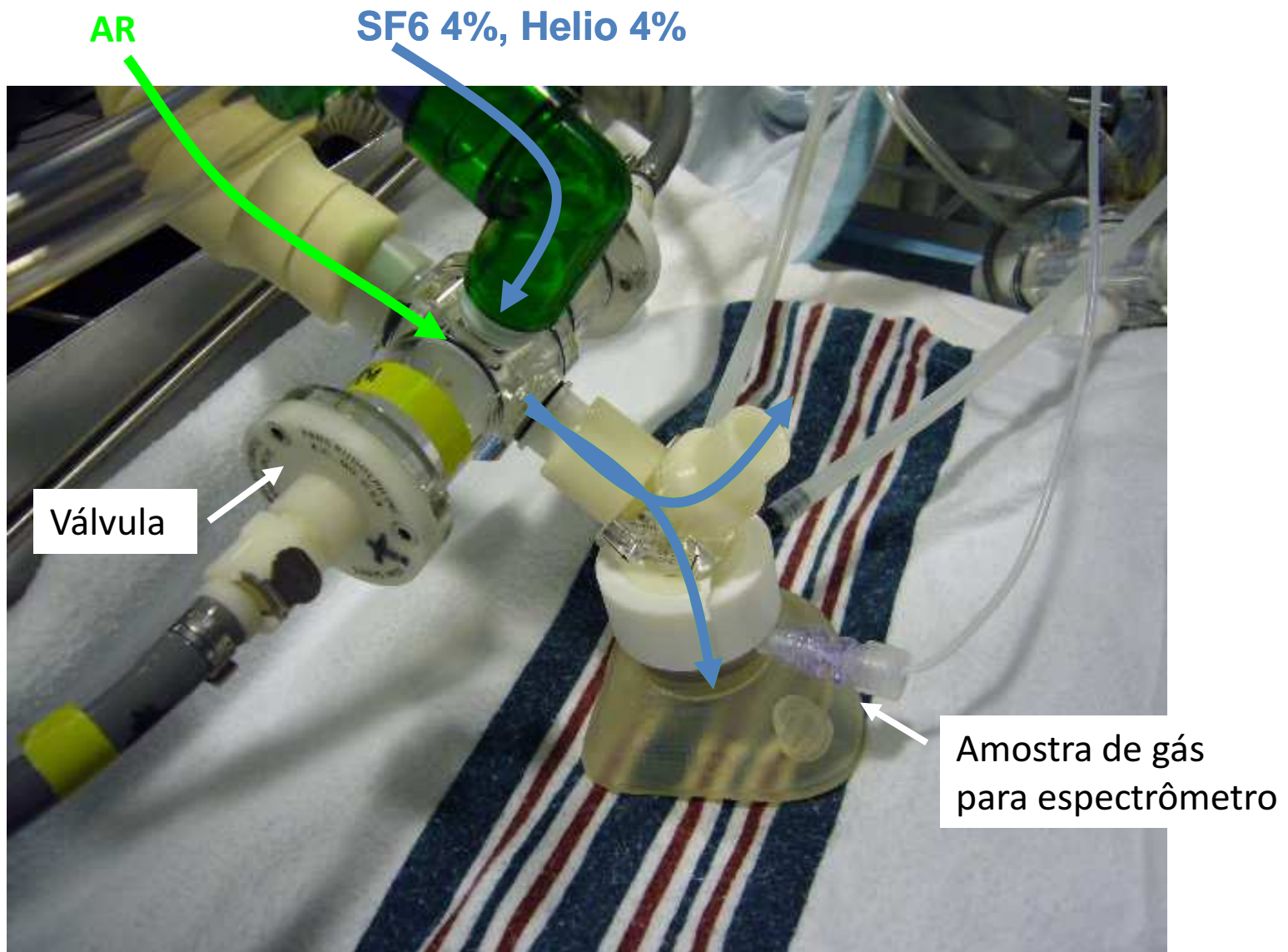
- The multiple breath inert gas washout (MBW) test assesses the efficiency of gas distribution and mixing within the lungs.
- MBW provides a measure of lung volume (FRC) and of ventilation inhomogeneity (VI) due to the heterogeneous distribution of disease processes.

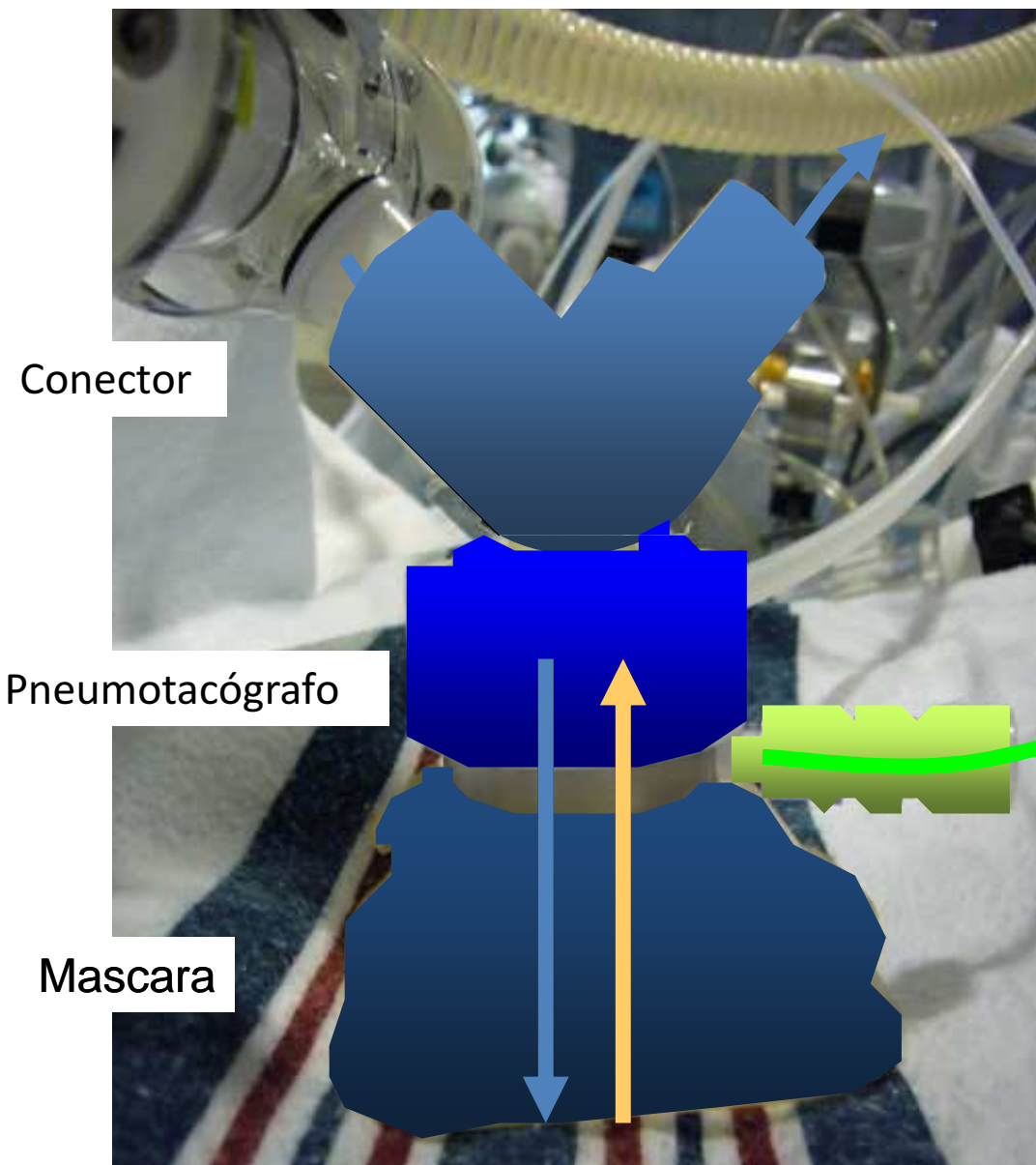
Multiple-Breath Washout Lung Clearance Index

- Measurement of ventilation distribution
- Nitrogen, SF₆, Helium can be used
- Child seated, breathing through a mouthpiece
- Small external deadspace (<2mL/kg)
- Washin until equilibrium is reached
- Washout should continue until the gas has fallen below 1/40th of the initial concentration

Washin and washout



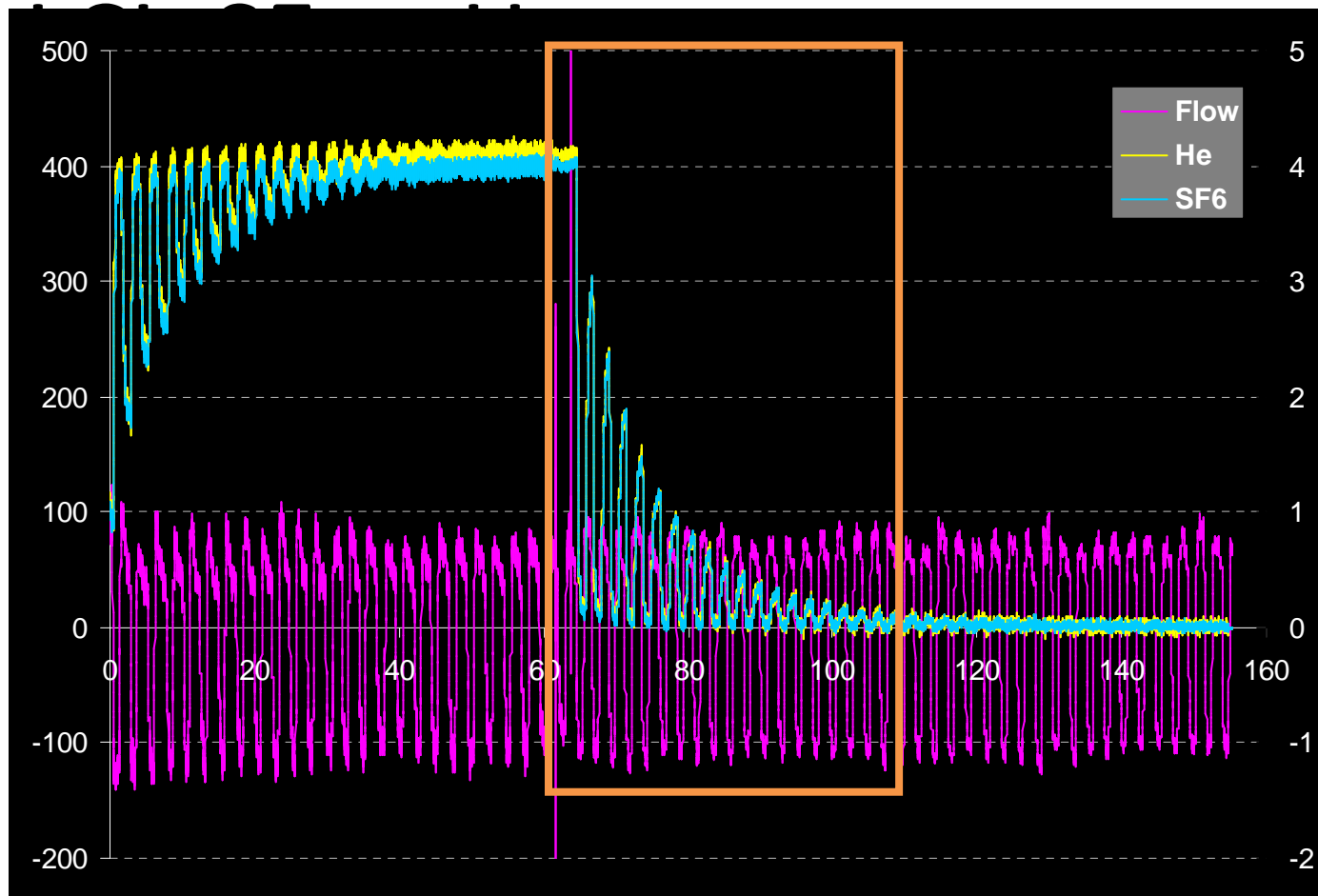




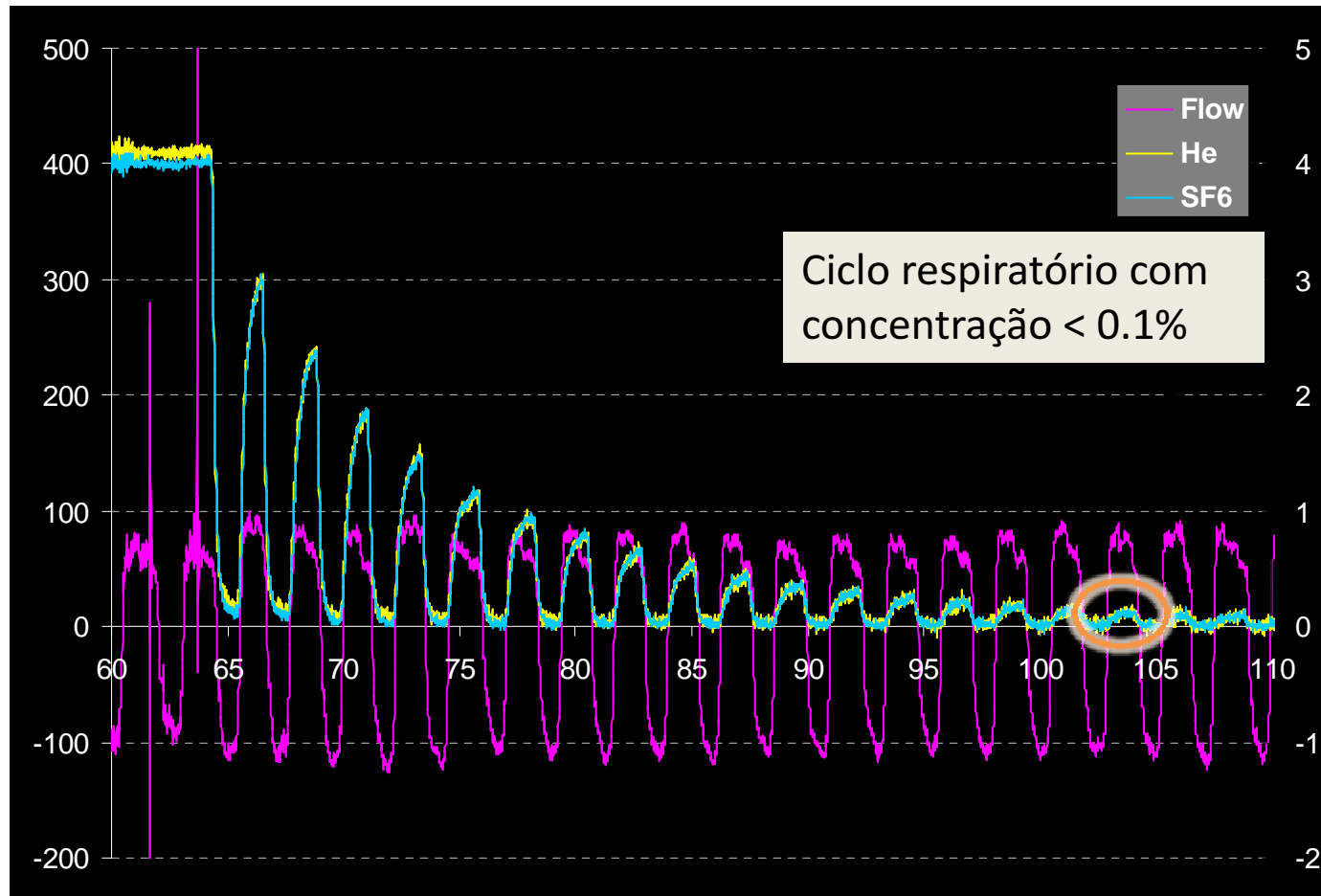
Ar, SF6 ou Helio

Amostra para
Espectrômetro de massa

← Washin → Washout →

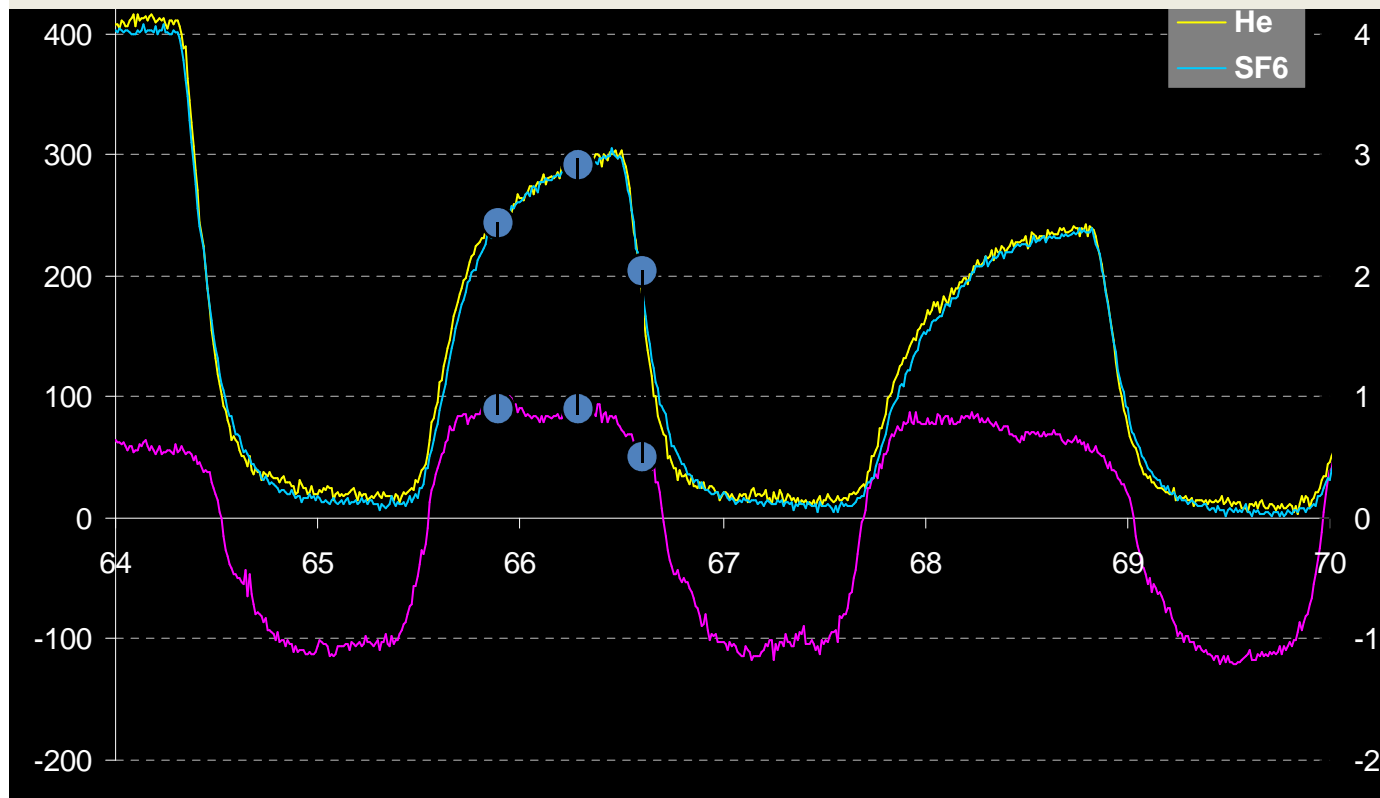


LCI in Infant with Cystic Fibrosis



Lung volume Measurements

Pela integração de Fluxo (pneumotacografo) e concentração (espectrômetro de massa) podemos calcular a massa do gás exalado e consequentemente o volume pulmonar (CRF ou CPT)



MBW: summary

- Useful to assess ventilation distribution and measure FRC
- Minimum cooperation
- Equipment range from expensive to very expensive
- Data reporting: mean values from a minimum of 2 washouts that differ less than 10% for FRC

LCI reference values

TABLE 13. REFERENCE VALUES FOR THE LUNG CLEARANCE INDEX OBTAINED IN CHILDREN USING AN SF₆ MULTIPLE-BREATH WASHOUT METHOD

Authors	Population		Predicted LCI, Mean (SD)
	n	Age (yr)*	
Aurora and colleagues (31)	30	4.3 (0.8)	6.89 (0.44)
Aurora and colleagues (30)	33	11.3 (3.1)	6.45 (0.49)
Gustafsson and colleagues (66)	28	11.4 (range, 3–18)	6.33 (0.43)

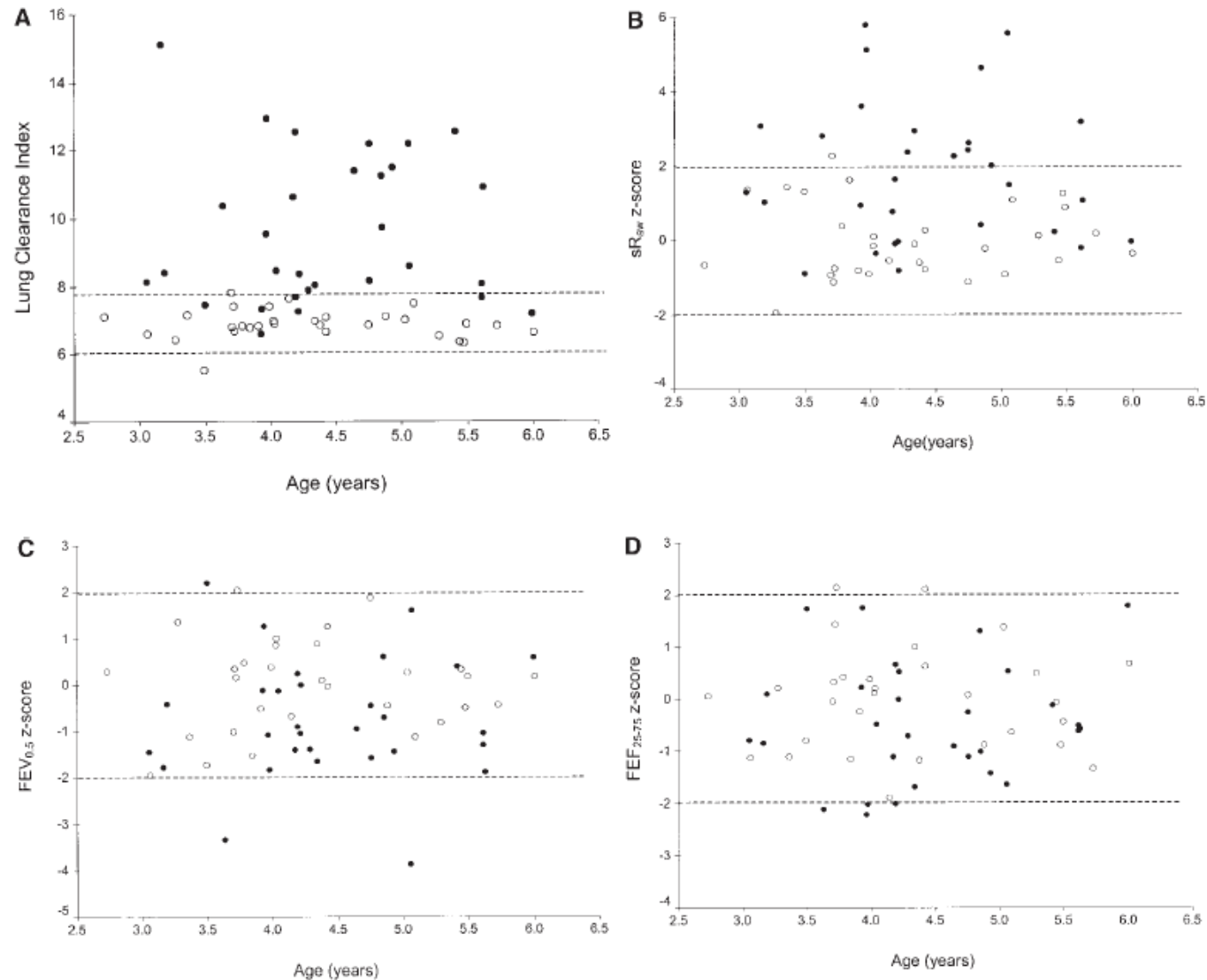
* Values for age are mean (SD).

Cystic Fibrosis - MBW

- Increased LCI values are a consistent finding in CF cohorts, detectable from infancy
- Abnormal LCI values in the preschool age range are stronger predictors than preschool FEV₁ of subsequent abnormal school age FEV₁, suggesting potential utility as a clinical outcome in early CF. In infants, a combination of MBW and RVRTC appears most useful.

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



BPD - MBW

- Studies have demonstrated only small effects of gestational age and intubation duration on FRC, but not LCI, in later infancy.
- These recent results suggest limited utility of MBW in the management and follow up of “new” BPD.

Recurrent wheeze - MBW

- Increased LCI and S_{cond} values in multiple-trigger wheeze compared to episodic (viral) wheeze and healthy controls have been reported, consistent with the pattern of VI abnormality described in older children and adults with established asthma.

FUTURE DIRECTIONS

- The clinical utility of MBW is promising in CF, asthma and preschool wheeze, but a number of challenges remain before the technique can be established in routine clinical care.
- Feasibility in routine clinical care of CF infants and preschoolers, using mass spectrometry- based equipment, has been demonstrated in specialized centres, however, successful transition into *widespread* clinical practice will require well validated, more affordable commercial equipment, which is not currently available.

The Interrupter Technique

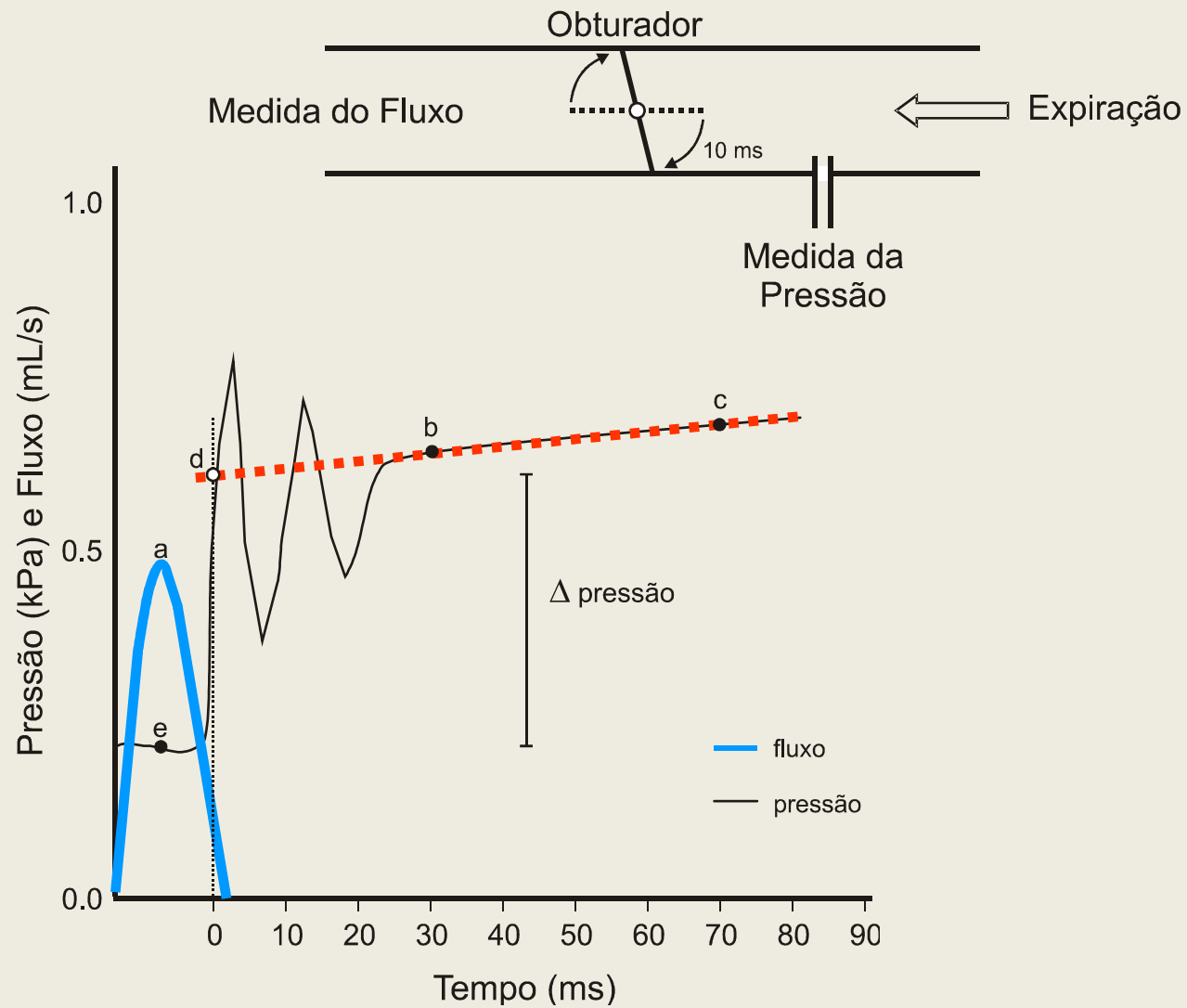
Rint

- Principle: during a sudden airway occlusion at the mouth, alveolar and mouth pressure equilibrate rapidly. Rint is this pressure divided by the flow.
- Child seated, breathing through a bacterial filter, noseclip and cheeks supported
- Occlusion in less than 10ms, for 100ms, set to coincide with peak flow, during expiration
- 10 occlusions should be recorded, report the median of acceptable measurements

Resistência pelo método do Interruptor - Rint



Rint – Data Acquisition





Posicionamento



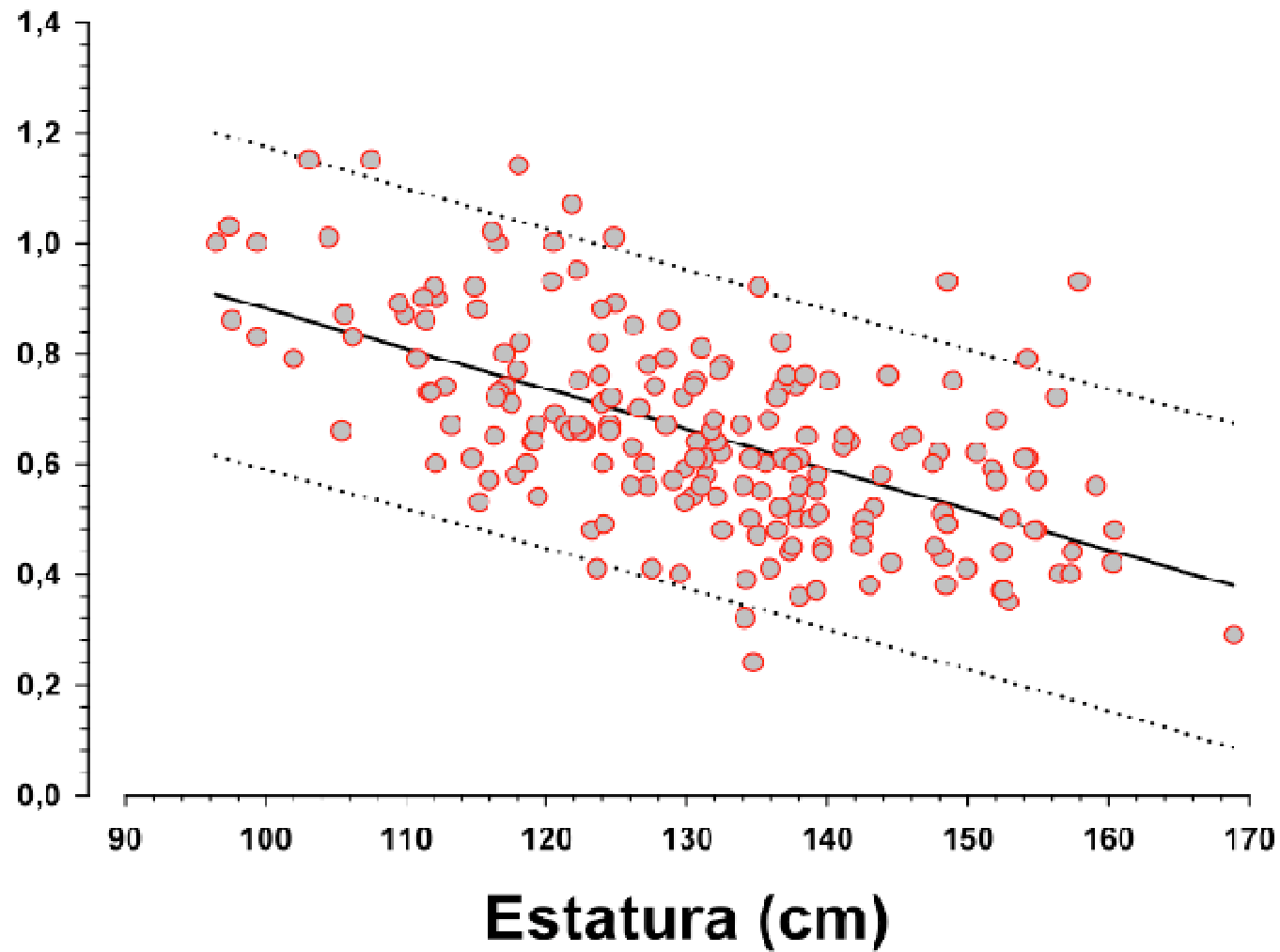
Mensuração

Reference values: Rint

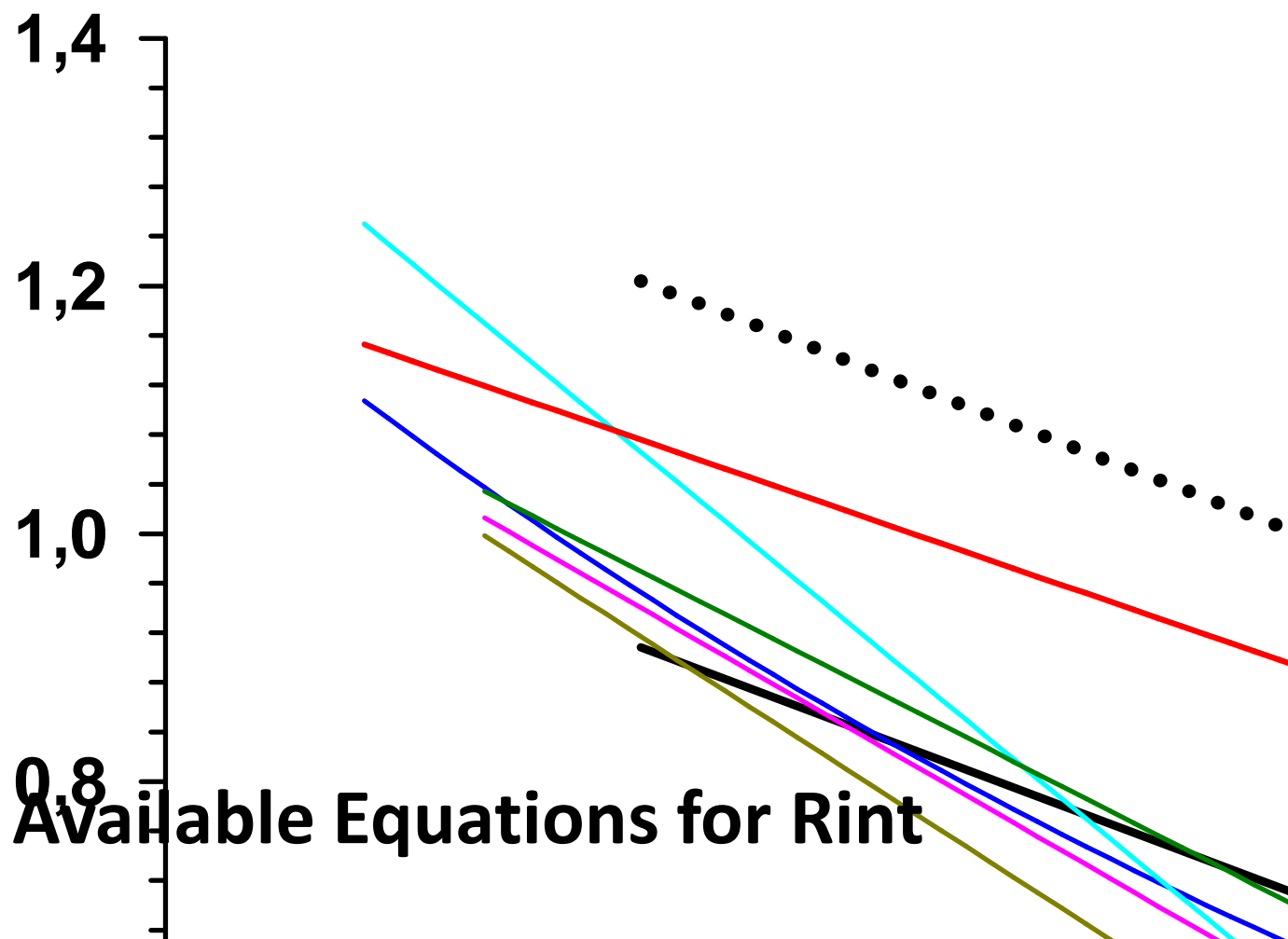
TABLE 7. INTERRUPTER TECHNIQUE: REFERENCE VALUES IN CHILDREN

Authors	Interruption Trigger	No. of Subjects, Ethnicity	Age (yr)	Rint ($kPa \cdot L^{-1} \cdot s$)
Oswald-Mammosser and colleagues (23)	Mid-V _T	36 White	4–16	Rint _I mean (SD), 0.43 (0.14) Rint _E mean (SD), 0.52 (0.19)
Merkus and colleagues (22)	Peak tidal flow	54 White	2–7	Rint _I = 2.59 – 0.017 H (RSD = 0.12) Rint _E = 2.61 – 0.016 H (RSD = 0.13)
Lombardi and colleagues (21)	Peak tidal flow	284 White	3–6	Rint _I = 2.276287 – 0.013710 H (RSD = 0.1908) Rint _E = 2.126878 – 0.012538 H (RSD = 0.2038)
McKenzie and colleagues (53)	Peak tidal flow	236 White, Afro-Caribbean, Bangladeshi	2–10	log ₁₀ Rint _E = 0.116 – 0.0396 A (RSD = 0.101) log ₁₀ Rint _E = 0.528 – 0.00569 H (RSD = 0.104)
Merkus and colleagues (56)	Peak tidal flow	208 White	3–13	log ₁₀ Rint _E = 0.645 – 0.00668 H (RSD = 0.093)
Beydon and colleagues (25)	20–80% of V _T	91 White	3–7	Rint _I = 2.289 – 0.0137 H (RSD = 0.17) Rint _E = 2.021 – 0.0112 H (RSD = 0.18)

Data from Healthy Children in Porto Alegre



(Pa/L/s)



Cystic Fibrosis - Rint

- most studies have shown that Rint measurements do not distinguish health from disease
- two longitudinal studies in 21 and 30 preschool children with CF and have shown no changes in Rint despite radiographic worsening
- These studies suggest that Rint will have limited clinical utility in the preschool CF population.

BPD - Rint

- The application of Rint in neonates and infants is limited by their low peak expiratory flows

Recurrent wheeze - Rint

- baseline Rint does not discriminate well between healthy children and those with recurrent wheeze
- BDR has been found to be a better tool for distinguishing recurrent wheezers from healthy children.

FUTURE DIRECTIONS - Rint

- Rint is able to detect changes in airway caliber.
- the use of Rint as an endpoint in clinical studies, and its sensitivity to detect peripheral airways obstruction and structural damage are unknown.

Preschool Spirometry

Spirometry Preschoolers

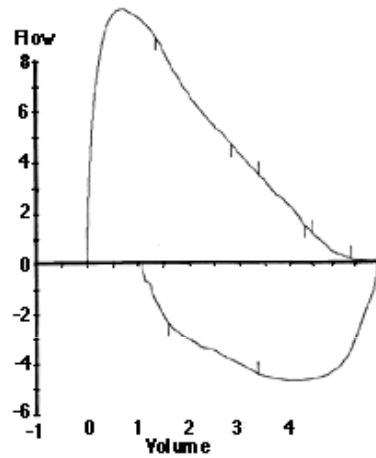
ATS/ERS 2007

- modifications to the ATS/ERS adult criteria are necessary for this young age group
- For the start of the test, the classic adult criteria is not appropriate and a VBE of less than or equal to 80 mL or less than 12.5% of the FVC may be applicable to the preschoolers.
- a 3 second exhalation time would be acceptable
- early or premature termination should be considered if flow ceases at greater than 10% of the peak flow

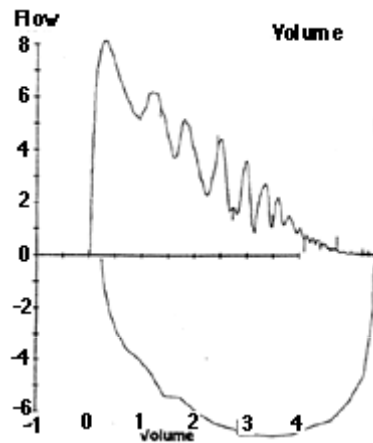
Spirometry Preschoolers

- When assessing repeatability, two reproducible flow-volume curves is desirable; however, one curve, if deemed technically acceptable, should not be excluded.
- the second highest FVC and FEVt should be within 0.1 L or 10% of the highest

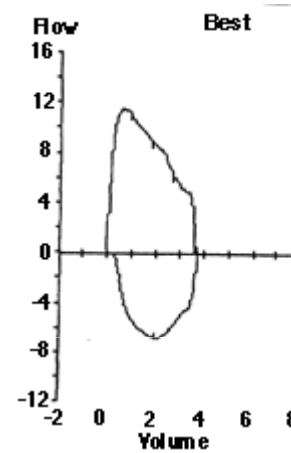
Visual inspection of the flow volume curve



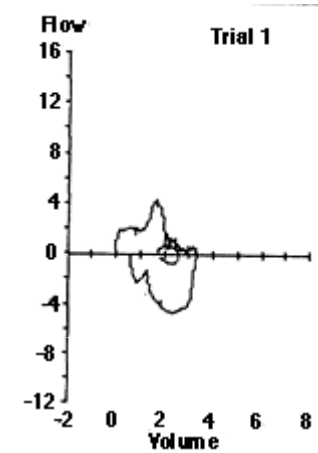
Normal



Tosse

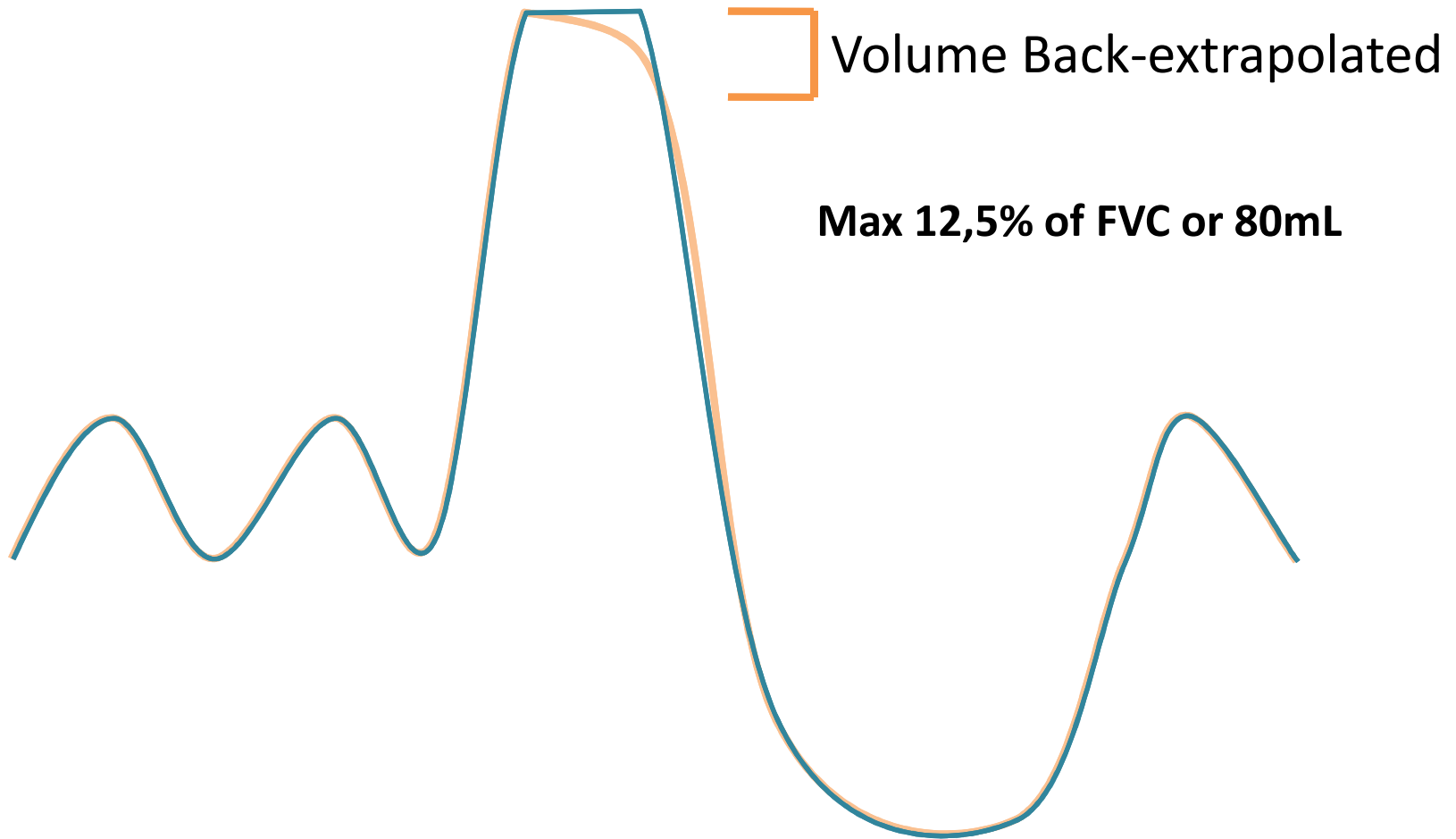


Terminação precoce

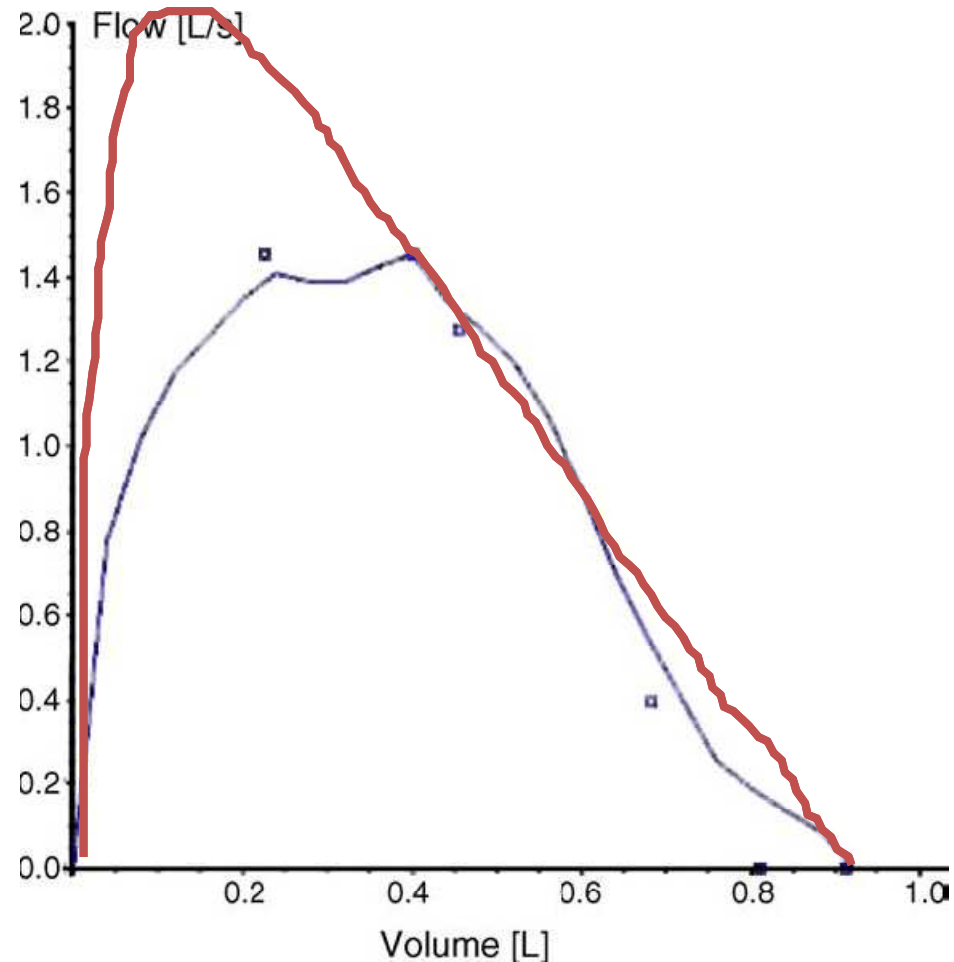


Esforço variável

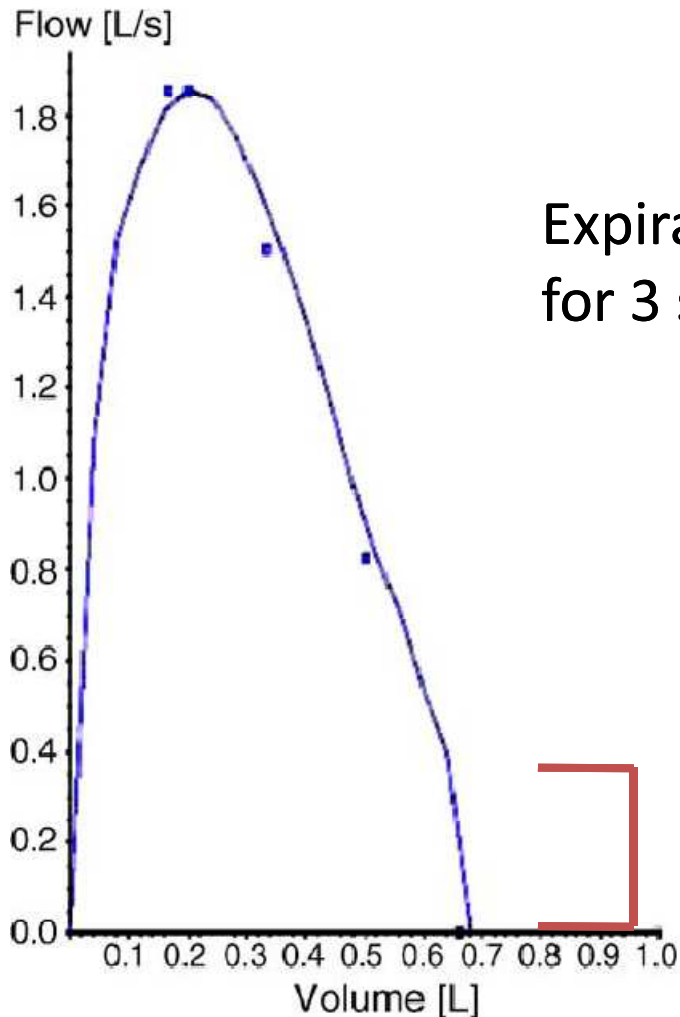
Volume Back-extrapolated



Exemplo de Início Lento da Manobra Expiratória Forçada



Early Termination



Expiration should be maintained for 3 seconds. (Adults 6s)

Max 10% of Peak Flow

CF - Spirometry

- abnormalities in lung function are already present at this age.
- Deficits noted in infancy persist into the preschool years.
- Longitudinal evaluations demonstrate that lung function declines with age, but the rate of decline is highly variable.

BPD - Spirometry

- Spirometry could potentially provide a useful longitudinal measurement for young children with BPD, in whom both lung growth and airway obstruction may be significantly abnormal in early life.
- Unfortunately there is a paucity of data on preschool spirometry in children with BPD, and no data to show that spirometry is clinically useful in this population.

Recurrent wheeze - Spirometry

- spirometry can be performed to establish baseline lung function and document bronchodilator responsiveness
- a post-bronchodilator increase between 12-15% in $FEV_{0.5}$, $FEV_{0.75}$ or FEV_1 is more commonly observed in preschool children with a clinical diagnosis of asthma

FUTURE DIRECTIONS

- Spirometry can be successfully applied to the preschool population in the clinical setting to identify disease states and track lung function over time.
- Reference values are available at European Respiratory Journal
- MULTI-ETHNIC REFERENCE VALUES FOR SPIROMETRY FOR THE 3-95 YEAR AGE RANGE: THE GLOBAL LUNG FUNCTION 2012 EQUATIONS
- www.growinglungs.org

Take Home Messages

INFANTS

- RVRTC = obstructive diseases
- MBW = more sensitive than RVRTC for CF

PRESCHOOLERS

- Rint = BD response may be useful for asthma
- Spirometry = easy to perform, good for follow-up and BD response
- The “**best test**” depends on the clinical questions

Thank you
Questions are welcome