The use of forced oscillation technique in children with restrictive physiology

Andre Gie [1], Ruan Swanepoel [2], Marieke M. van der Zalm [1] and Pierre Goussard [1]

[1]Department of Paediatrics and Child Health, Faculty of Medicine, Stellenbosch University, Cape Town, South Africa. [2]Division of Pulmonology, Department of Medicine, Tygerberg Hospital, Cape Town, South Africa.

Corresponding author: Andre Gie (agie@sun.ac.za)

Shareable abstract (@ERSpublications)
The forced oscillation technique (FOT) may not identify lung function abnormalities in children with restrictive physiology. FOT findings correlate poorly with spirometry and plethysmography testing in children with diffuse parenchymal lung disease. https://bit.ly/4h4lilh

Cite this article as: Gie A, Swanepoel R, van der Zalm MM, *et al*. The use of forced oscillation technique in children with restrictive physiology. *Breathe* 2025; 21: 240106 [DOI: 10.1183/20734735.0106-2024].

Received: 28 May 2024
Accepted: 16 Jan 2025

Monitoring pulmonary function is essential to diagnose pulmonary function deficits, evaluate progression of lung disease, monitor treatment response and track pulmonary function. The forced oscillation technique (FOT) is increasingly used to evaluate pulmonary mechanics in children. It is postulated to detect small airway disease and its use has been investigated in cystic fibrosis, asthma, recurrent wheeze and lung disease of prematurity [1–3]. However, FOT and spirometry can have discordant findings, suggesting that the two techniques may evaluate different pathology and are not interchangeable [4, 5].

FOT is performed during tidal breathing, this allows younger children, acutely ill children and those with severe lung disease to perform the test [6]. Spirometry, the most used pulmonary function test (PFT), requires increased patient cooperation to perform the forced vital capacity (FVC) manoeuvre. Often cited as a limitation, this allows for the identification of abnormal FVC which may result from diverse lung diseases including severe airway disease with air trapping, diffuse parenchymal disease, intrathoracic masses, thoracic cage abnormalities and neuromuscular disease. It is unclear whether FOT identifies abnormal lung physiology associated with diminished lung volume.

Here we describe the FOT and PFT findings in children with diffuse lung disease (DLD) and restrictive physiology.

Patients and methods

We identified children receiving respiratory care for DLD with restrictive physiology (FVC less than the lower limit of normal (LLN)) at a tertiary hospital in Cape Town, South Africa between June and December 2023. Clinical and laboratory data were collected from electronic medical records. Chest radiography and chest computed tomography (CT) scans were collected through the electronic picture archiving and communication systems and reported on by paediatric pulmonologists (A. Gie and P. Goussard).

PFTs were performed according to American Thoracic Society and European Respiratory Society (ERS) standards and guidelines [7, 8]. FOT was performed using the Tremoflo C–100 system (Thorasys Thoracic Medical Systems Inc.), which superimposes "pseudo–random noise" on to tidal breathing (frequencies from 5 to 37 Hz), following the procedures proposed by the ERS [9].

Spirometry (forced expiratory volume in 1 s (FEV_1), FVC, FEV_1/FVC) and plethysmography (total lung capacity (TLC), residual volume (RV)) measurement Z-scores were calculated using the Global Lung Function Initiative race neutral reference equations [10]. FOT Z-scores (resistance at 5 Hz (R_5) measured in $kPa \cdot s \cdot L^{-1}$, resistance change from 5 to 20 Hz ($R_{5–20}$), and area under the reactance curve (A_X) measured in

kPa·L^{-1}) were calculated in the Tremoflo software, using established reference equations [11, 12]. The FOT results are presented with the device generated "oscillogram" which displays the resistance (upper) and reactance (lower) curves across the range of frequencies as well as the FOT outcome results with Z-score and coefficient of variance underneath. The study was approved by Stellenbosch University's Health Research Ethics Committee (C24/02/004) with informed consent/assent of the participants and parents.

Case 1

This case concerns a 4-year-old girl with autoimmune-mediated microscopic polyangiitis and diffuse alveolar haemorrhage. She presented in her second year of life in high-output cardiac failure secondary to anaemia (haemoglobin level of 4.6 g·dL^{-1}). Despite pulsed high-dose corticosteroids and hydroxychloroquine therapy she had multiple relapses and required prolonged mechanical ventilation due to hypoxaemia. Open lung biopsy confirmed acute-on-chronic alveolar haemorrhage. She was weaned from ventilation but remained oxygen-dependent and tachypnoeic with diffuse crackles on auscultation. Chest imaging demonstrated diffuse opacity on chest radiography and ground-glass appearance on CT chest (figure 1).

She could not perform spirometry or plethysmography, however, she could perform FOT. Despite the DLD, FOT did not demonstrate abnormal lung mechanics. FOT resistance and reactance curves were normal and A_X was low (1.62 kPa·L^{-1}, Z-score of −1.7).

Case 2

The patient was an 8-year-old girl with constrictive pericarditis, left-sided chylothorax, pulmonary lymphatic congestion and undefined DLD due to presumed tuberculosis. She presented with tachypnoea, hypoxia and increased respiratory effort. However, despite extensive investigations, including pericardial biopsy, no definitive diagnosis was made.

The chylothorax did not respond to medical therapy or dietary manipulation, and required a surgical pericardial window and ligation of the thoracic duct. Following 6 months of anti-tuberculosis therapy and ligation of the lymphatic duct, she had no respiratory symptoms at rest, although her exercise capacity was diminished.

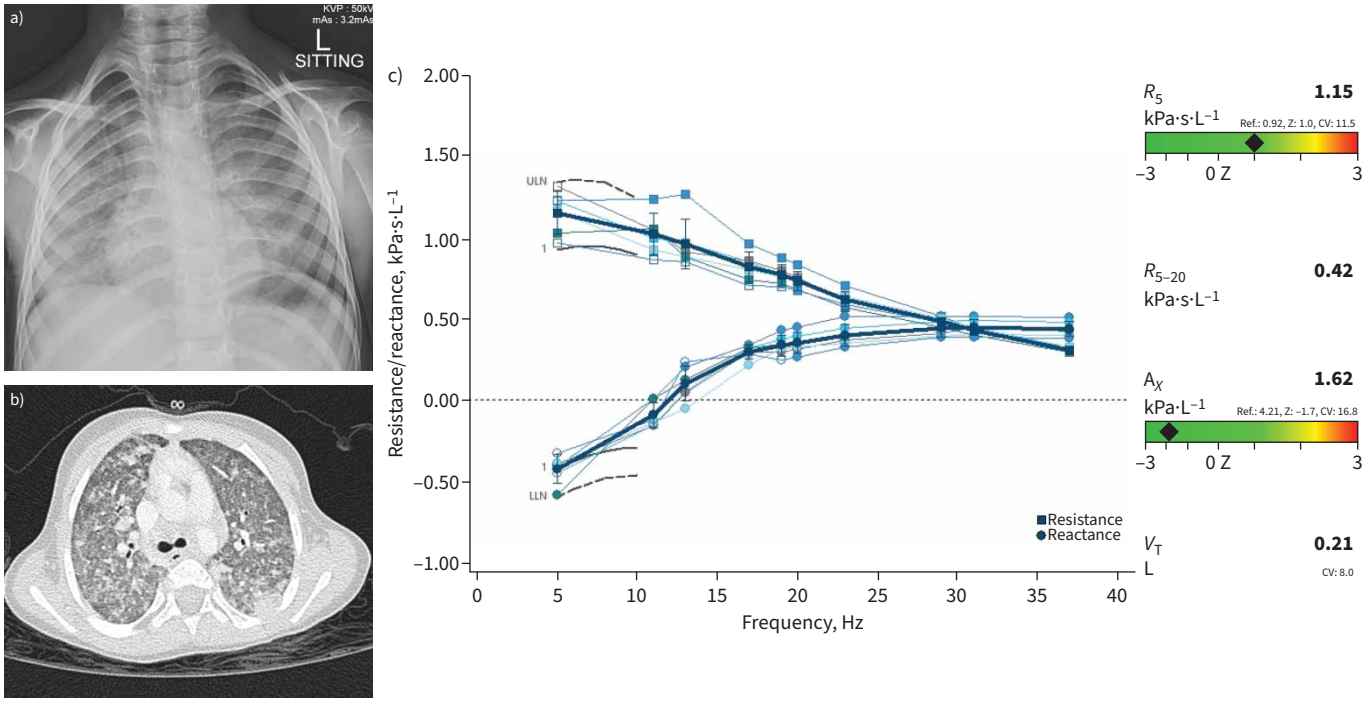

FIGURE 1 Chest imaging and forced oscillation respiratory resistance and reactance curves for the patient described in case 1. a) Chest radiograph demonstrating diffuse alveolar opacification of both lung fields. b) Axial contrast-enhanced computed tomography chest image in the lung window confirms diffuse bilateral ground-glass opacification at the level of the carina. c) Forced oscillation test results showing normal respiratory resistance and reactance curves from 5 Hz to 30 Hz. The line labelled "1" indicates the Z+1 line for resistance and reactance. R_5: respiratory resistance at 5 Hz; $R_{5–20}$: resistance change from 5 to 20 Hz; A_X: area under the reactance curve; CV: coefficient of variation (%); V_T: tidal volume; ULN: upper limit of normal; LLN: lower limit of normal.

Spirometry (after completion of tuberculosis therapy) demonstrated restrictive physiology: forced vital capacity (FVC) 1.0 L (Z-score of −3.586), forced expiratory volume in 1 s (FEV_1) 0.89 L (Z-score of −3.518) and FEV_1/FVC 87% (Z-score of −0.574). Plethysmography confirmed restrictive lung disease: total lung capacity (TLC) 1.59 L (Z-score of −3.121) and residual volume (RV) 0.60 L (Z-score of −0.045). FOT did not demonstrate abnormal respiratory resistance (R_5 0.58 kPa·s·L^{-1}, Z-score of −0.3) or reactance at any frequency (A_X 0.68 kPa·L^{-1}, Z-score of −1.3) (figure 2).

Case 3

The patient in this case was a 17-year-old adolescent with idiopathic pulmonary haemorrhage who initially presented at 9 years of age with diffuse alveolar haemorrhage. She was on maintenance oral corticosteroid therapy and azithromycin (10 mg·kg^{-1}) three times per week. She attends school and performs activities of daily living without becoming hypoxic. However, she has limited exercise tolerance. On respiratory examination she is tachypnoeic at rest with diffuse bilateral crackles on auscultation. A CT chest showed diffuse bilateral ground-glass opacification (figure 3).

Spirometry reveals restrictive physiology with minimal airflow limitation: FVC 1.52 L (Z-score of −2.94), FEV_1 1.21 L (Z-score of −3.38) and FEV_1/FVC 79% (Z-score of −1.69). Plethysmography confirmed the restrictive lung disease: TLC 2.11 L (Z-score of −3.72) and RV 0.63 L (Z-score of −0.51). Despite the

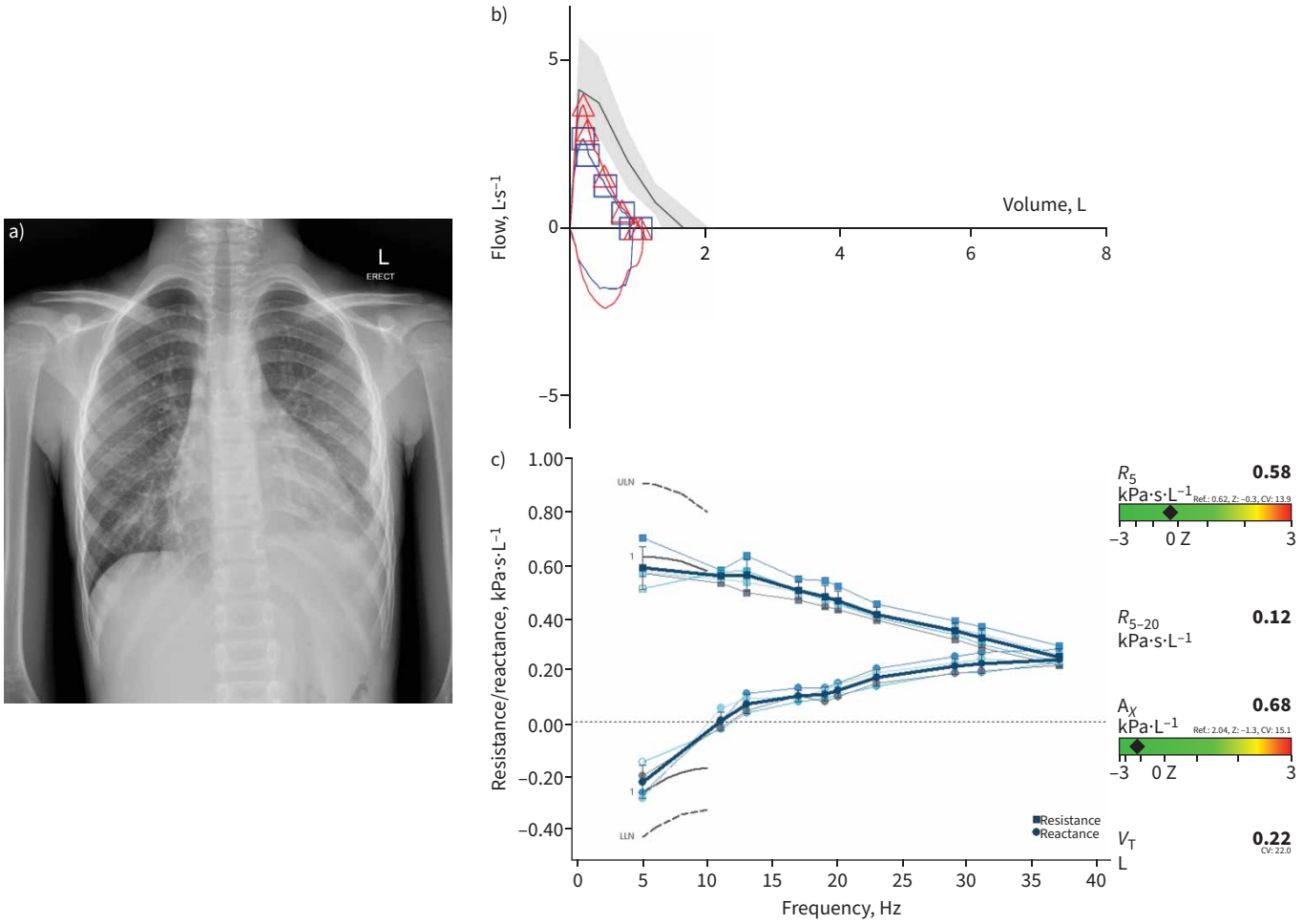

FIGURE 2 Chest radiograph, spirometry flow–volume loops and forced oscillation curves for the patient described in case 2. a) Anteroposterior chest radiograph exhibiting left pleural thickening with small pleural fluid collection along with a diffuse interstitial pattern of the lung fields and a bulky cardiac shadow. b) Spirometry flow–volume loops with diminished forced vital capacity with maintained peak expiratory flow (grey shading signifies the normal range). c) Forced oscillation test results demonstrating normal respiratory resistance and reactance curves with upper (ULN) and lower limits of normal (LLN). The line labelled "1" indicates the Z+1 line for resistance and reactance. R_5: respiratory resistance at 5 Hz; $R_{5–20}$: resistance change from 5 to 20 Hz; A_X: area under the reactance curve; CV: coefficient of variation (%); V_T: tidal volume.

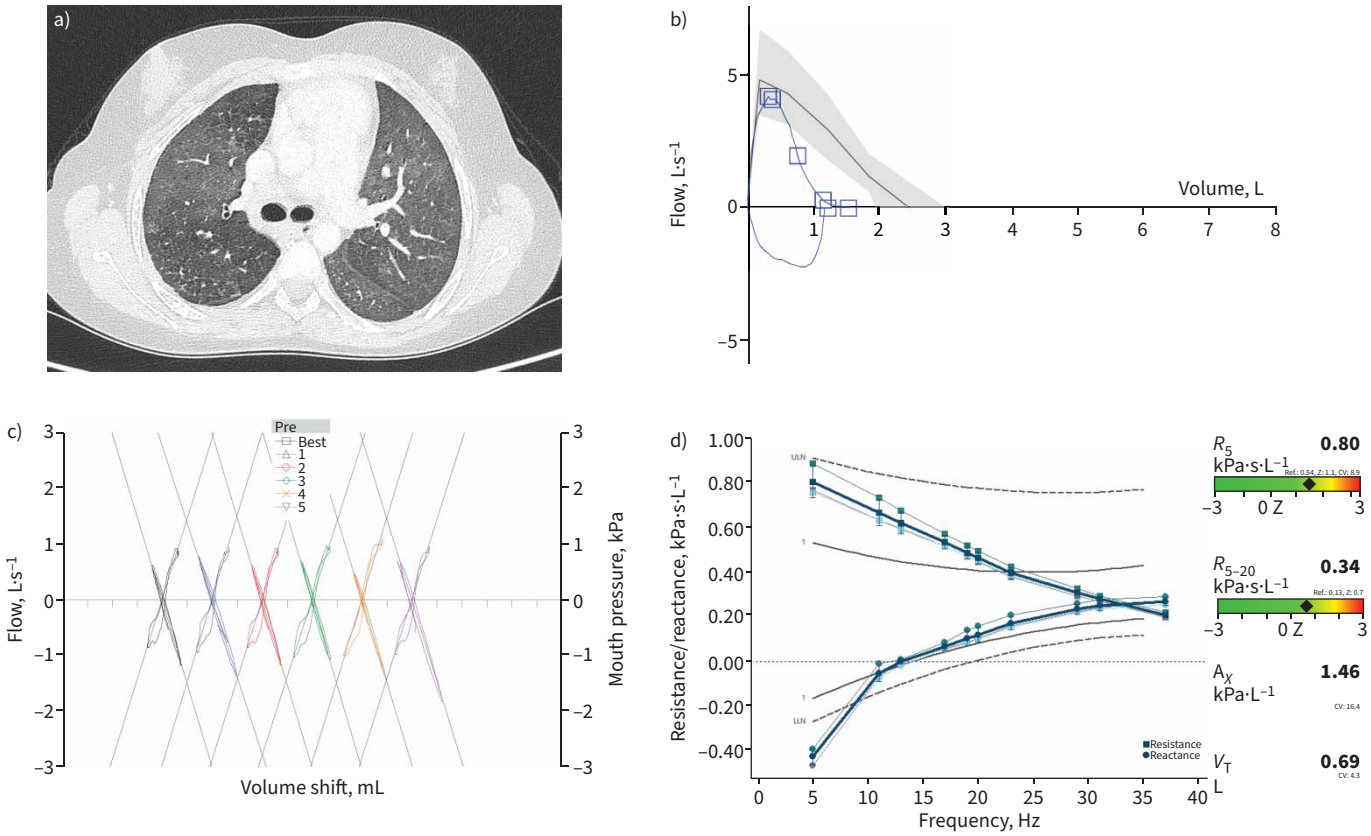

FIGURE 3 Chest computed tomography (CT) scan and pulmonary function tests for the patient described in case 3. a) Axial contrast-enhanced CT-chest image at the level of the carina demonstrates diffuse bilateral ground-glass opacity with mild mosaic attenuation suggesting a degree of small airway disease. b) Spirometry flow–volume loops with decreased forced vital capacity and minimal airflow limitation. c) Plethysmography pressure–volume shift loops demonstrate little airway obstruction and decreased lung compliance. d) Forced oscillation test resistance curve remains below the upper limit of normal (ULN) from 5 Hz to 35 Hz. Reactance is below the lower limit of normal (LLN) only at 5 Hz and normal from 10 Hz to 35 Hz indicating the most significant disruption to lung mechanics is in the periphery of the lung. The line labelled "1" indicates the Z+1 line for resistance and reactance. R_5: respiratory resistance at 5 Hz; $R_{5–20}$: resistance change from 5 to 20 Hz; A_X: area under the reactance curve; CV: coefficient of variation (%); V_T: tidal volume.

restrictive physiology and DLD on chest imaging, FOT was largely normal. Respiratory resistance was normal (R_5 Z-score of 1.143, $R_{5–20}$ Z-score of 0.6589) and on the reactance curve only respiratory system reactance at 5 Hz (X_5) was below LLN.

Case 4

This case concerns a 16-year-old girl with fibrotic lung disease due to idiopathic alveolar haemorrhage complicated by pulmonary hypertension, requiring dual-agent medical therapy and home oxygen. She suffered diminished exercise tolerance and was tachypnoeic at rest. Respiratory examination demonstrated digital clubbing, limited chest expansion, and diffuse bilateral crackles. Chest imaging established diffuse fibrotic lung disease with widespread ground-glass opacity on CT-chest (figure 4).

Spirometry demonstrated mixed respiratory physiology with airflow limitation (FEV_1 0.65 L, Z-score of −4.604, FEV_1/FVC Z-score of −3.266) and diminished FVC (1.05 L, Z-score of −3.711). Plethysmography was not performed. Inconsistent with the airflow limitation exhibited by spirometry, FOT resistance was normal (R_5 1.00 kPa·s·L^{-1}, Z-score of 1.6 and $R_{5–20}$ 0.44 kPa·s·L^{-1}, Z-score of 0.44). However, reactance was abnormal with $X_{5–20}$ below LLN.

Case 5

The patient in this case was a 14-year-old boy with metastatic thyroid carcinoma having completed chemotherapy and radioactive iodine [13]. His medical history included, premature birth at 27 weeks gestational age with prolonged ventilation and oxygen dependence. Following the neonatal period he was

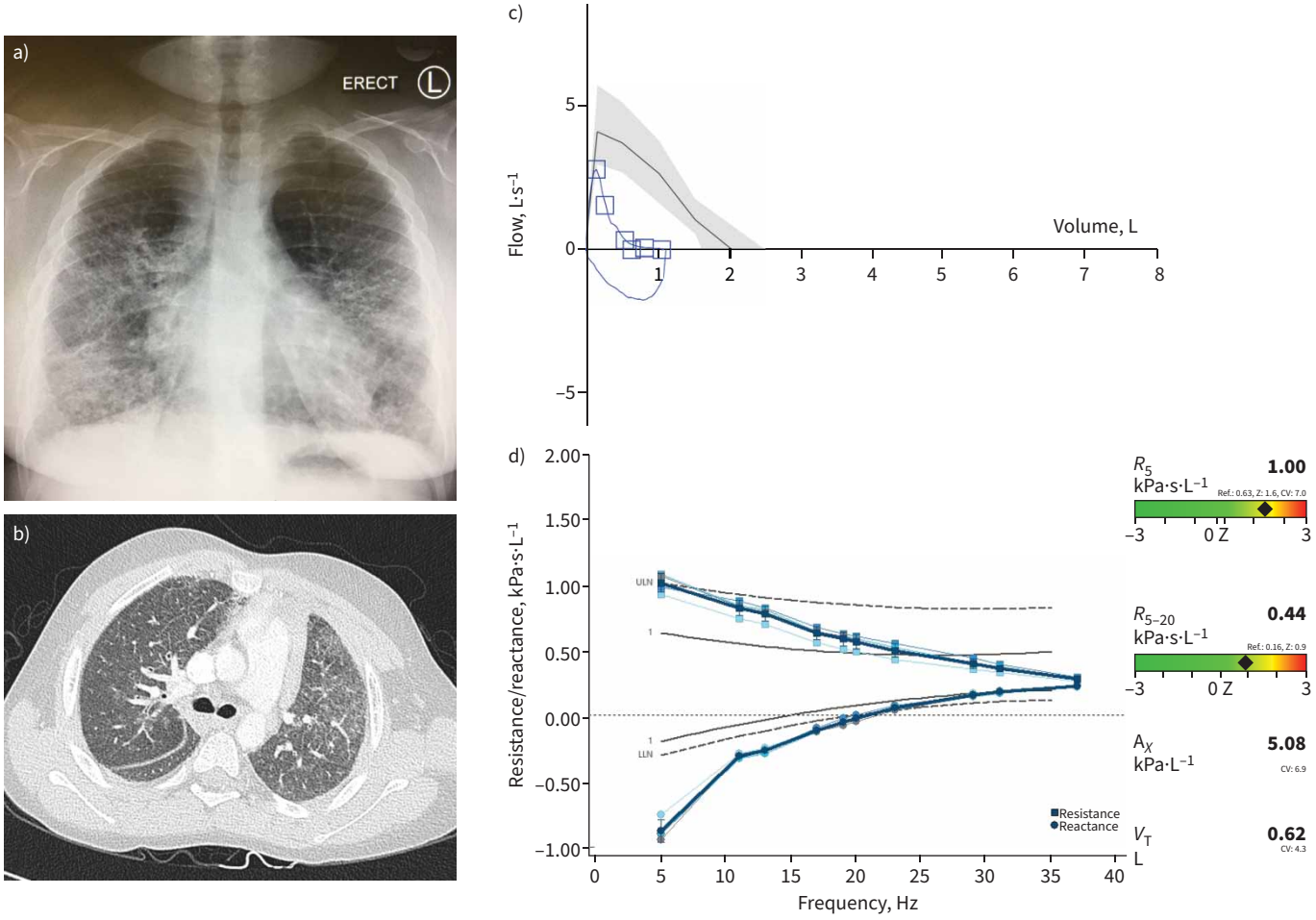

FIGURE 4 Chest imaging and lung function test results for the patient described in case 4. a) Anterior–posterior chest radiograph demonstrating diffuse interstitial lung disease suggestive of fibrosis with apical-caudal gradient and the worst disease in the lower lung zones. b) Axial contrast-enhanced computed tomography chest image in the lung window at the level of the carina confirms widespread fibrotic changes in the lung parenchyma with ground-glass opacity, additionally the main pulmonary trunk is larger than the descending aorta in keeping with pulmonary hypertension. c) Spirometry flow–volume loop (the expected range is shaded grey) demonstrating mixed obstructive and restrictive physiology and abnormally low forced vital capacity with a concave expiratory limb after peak flow is reached. d) Forced oscillation test demonstrating normal resistance curve with abnormal reactance through the majority of the frequency range. The line labelled "1" indicates the Z+1 line for resistance and reactance. R_5: respiratory resistance at 5 Hz; $R_{5–20}$: resistance change from 5 to 20 Hz; A_X: area under the reactance curve; CV: coefficient of variation (%); V_T: tidal volume; ULN: upper limit of normal; LLN: lower limit of normal.

well prior to the diagnosis of thyroid carcinoma. He was tachypnoeic at rest, with reduced chest expansion and no adventitious sounds on auscultation. He suffered limited exercise tolerance and required home oxygen. Chest imaging showed diffuse bilateral micronodular metastases (figure 5).

Spirometry demonstrated severely diminished airflow and volume (FEV_1 0.65 L, Z-score of −4.62, FVC 0.83 L, Z-score of −4.84), and FEV_1/FVC 78%, Z-score of −1.75). Plethysmography confirmed restrictive lung disease (TLC 1.51 L, Z-score of −4.09 and RV 0.87 L, Z-score of 0.32). FOT resistance was normal across all frequencies. Reactance tracked just below LLN (A_X Z= 2.53) and was most abnormal at X_5.

Discussion

In this case series we demonstrate that in children and adolescents with diffuse parenchymal lung disease and restrictive physiology, FOT may not identify significantly disrupted pulmonary physiology (table 1). Children able to perform PFTs had abnormal pulmonary function with diminished airflow and TLC, which correlated well with disease severity on chest imaging and clinical examination. FOT did not demonstrate these abnormalities to the same degree and was either normal or when abnormal was not disrupted to the same degree as other PFTs.

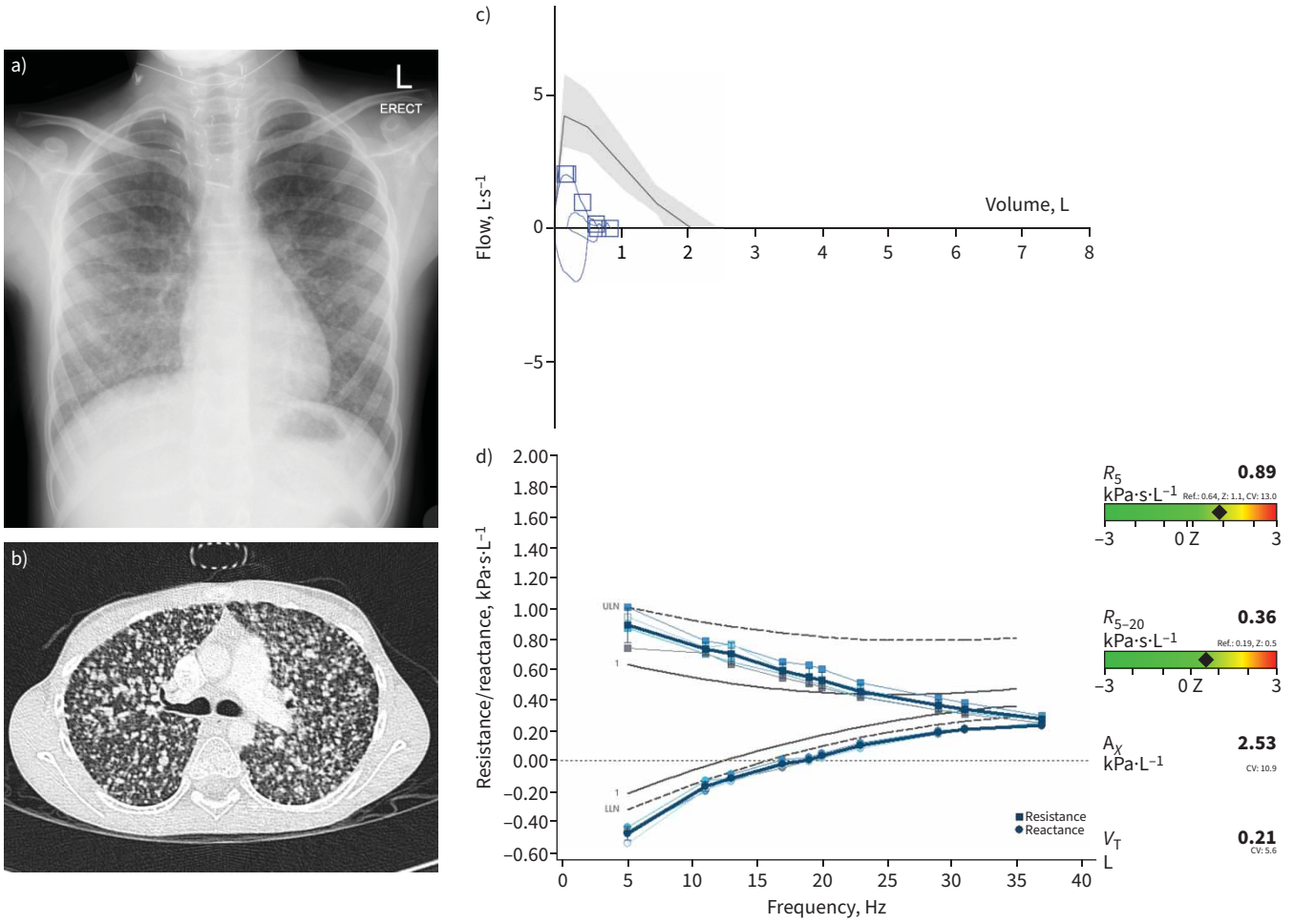

FIGURE 5 Chest imaging, spirometry flow–volume loop and forced oscillation curves for the patient described in case 5. a) Anterior–posterior chest radiograph demonstrating diffuse nodules of varying size with apical-caudal gradient and basal predominance. Additionally, surgical clips are visible at the site of the thyroidectomy. b) Contrast-enhanced axial computed tomography chest image at the level of the carina exhibits the diffuse pulmonary nodules extending to the lung periphery. c) Spirometry flow–volume loop reveals diminished expiratory airflow and volume (normal expected range for age, height and sex shaded grey). d) Forced oscillation resistance and reactance curves, with upper (ULN) and lower limit of normal (LLN) as dashed lines, showing normal respiratory resistance with reactance tracking below the LLN with the most abnormal measurement at X_5 suggesting the most disrupted lung mechanics are in the periphery of the lung. R_5: respiratory resistance at 5 Hz; $R_{5–20}$: resistance change from 5 to 20 Hz; A_X: area under the reactance curve; CV: coefficient of variation (%); V_T: tidal volume; X_5: respiratory reactance at 5 Hz.

One of the strengths of FOT (*i.e.* requiring minimal patient participation) is demonstrated in case 1. This child was incapable of performing spirometry or plethysmography but could perform FOT. However, FOT was unable to demonstrate abnormal lung mechanics despite the extensive DLD and disrupted physiology. FOT could potentially monitor disease progression, but treatment response would be difficult to determine as no abnormalities were demonstrated. FOT performed best when an element of airflow limitation was present (see case 4). In this case (mixed obstructive/restrictive physiology) FOT demonstrated abnormal reactance which may reflect small airway disease. Alternatively, the decreased reactance and increased A_X may reflect disease severity as found in adults with idiopathic lung fibrosis [14, 15].

The use of FOT in DLD is hampered by a lack of data on restrictive physiology. The available paediatric studies are limited to neuromuscular disease, where FOT correlated with disease severity, demonstrating increased resistance, and there was a negative correlation between lung volume and A_X [5]. However, these findings may represent atelectasis or airway obstruction due to mucous plugging rather than the parenchymal disease demonstrated in this case series. In contrast to our findings, in adults with pulmonary fibrosis and restrictive physiology respiratory reactance parameters correlated with disease severity [14, 15].

TABLE 1 Summary of the pulmonary function results for all five cases

Case	Spirometry			Plethysmography		Forced oscillation testing		
	FVC, L	FEV_1, L	FEV_1/FVC, %	TLC, L	RV, L	R_5, kPa·s·L^{-1}	$R_{5–20}$, kPa·s·L^{-1}	A_X, kPa·L^{-1}
1	N/A	N/A	N/A	N/A	N/A	1.15 Z=0.98	0.42 Z=N/A	1.62 Z= −1.7
2	1.03 Z= −3.586	0.95 Z= −3.275	92 Z= −0.508	1.59 Z= −3.121	0.60 Z= −0.045	0.58 Z= −0.31	0.125 Z= N/A	0.68 Z= −1.3
3	1.52 Z= −2.94	1.21 Z= −3.38	79 Z= −1.69	2.11 Z= −3.72	0.63 Z= −0.51	0.801 Z=1.143	0.339 Z=0.7	1.459
4	1.05 Z= −3.711	0.65 Z= −4.604	61 Z= −3.266	N/A	N/A	1.00 Z=1.6	0.444 Z=0.9	5.08 Z>ULN
5	0.83L Z= −4.84	0.65 Z= −4.62	78 Z= −1.75	1.51 Z= −4.09	0.87 Z=0.32	0.89 Z=1.1	0.36 Z=0.5	2.53 Z>ULN

FVC: forced vital capacity; FEV_1: forced expiratory volume in 1 s; TLC: total lung capacity; RV: residual volume; R_5: respiratory resistance at 5 Hz; $R_{5–20}$: resistance change from 5 to 20 Hz; A_X: area under the reactance curve; N/A: not available; ULN: upper limit of normal. Spirometry and plethysmography Z-scores were calculated using Global Lung Function Initiative race neutral (spirometry) and caucasian (plethysmography) reference data and equations. Forced oscillation test Z-scores were calculated by the Tremoflo software using equations by Calogero *et al.* [11] (for cases 1 and 2) and Nowowiejska *et al.* [12] (for cases 3, 4 and 5).

The cases included in this series have significantly impaired PFTs with diffuse parenchymal disease. Clinical examination, chest imaging, and flow- and volume-based PFTs clearly demonstrate lung disease which was either not evident on FOT and/or did not correlate with the disease severity found by clinical examination, chest imaging or other PFTs. This raises the concern that FOT may have limited sensitivity to detect pathology associated with restrictive physiology in paediatric DLD.

FOT is an appealing technique to evaluate paediatric lung function. It is quick to perform, requires little patient participation and can be performed at the bedside. While knowledge of FOT in diffuse airway disease in children is increasing, there remain limitations to the widespread use of FOT in childhood lung disease. Little is known about the FOT findings in diffuse parenchymal disease and how FOT correlates with other PFTs, specifically plethysmography. Further limiting the generalisation of FOT data is that the reference data are device and technique specific [16].

Based on this case series, we caution the use of FOT to establish the presence or severity of lung disease in children with diffuse parenchymal lung disease and restrictive physiology.

Key points

- FOT interrogate the mechanics of the respiratory system by measuring the response of the respiratory system to pressure waves introduced at the mouth during tidal breathing
- FOT may be sensitive to detect small airway disease in children; however, its use in diffuse parenchymal lung disease is not established.
- FOT may not reliably detect disrupted lung physiology in children with restrictive lung physiology and there are limited data on its use in this diverse group of lung diseases.
- FOT findings may not reflect the severity of parenchymal lung disease in children in the absence of small airway pathology.

Self-evaluation questions

1. Is the following statement true or false? FOT lung function testing is sensitive to detect diminished lung volume in children.
2. In children with diffuse parenchymal lung disease, which of the following lung function test(s) is/are indicated?
   a) Spirometry
   b) Plethysmography
   c) Spirometry and plethysmography
   d) FOT
3. Is the following statement true or false? In children with diffuse lung disease FOT correlates well with spirometry.

Conflict of interest: M.M. van der Zalm reports grants from TMA2019SFP-2836 TB lung-FACT2 from EDCTP2 program supported by the European Union, K43TW011028 from the Fogarty International Centre of the National Institutes of Health (NIH). The remaining authors have nothing to disclose.

Support statement: M.M. van der Zalm is supported by a career development grant from the EDCTP2 programme supported by the European Union (TMA2019SFP-2836 TB lung-FACT2), the Fogarty International Centre of the National Institutes of Health (NIH) under Award Number K43TW011028.

References

1 Lombardi E, Fainardi V, Calogero C, *et al.* Lung function in a cohort of 5-year-old children born very preterm. *Pediatr Pulmonol* 2018; 53: 1633–1639.
2 Gunawardana S, Tuazon M, Wheatley L, *et al.* Airwave oscillometry and spirometry in children with asthma or wheeze. *J Asthma* 2023; 6: 1153–1161
3 Ramsey KA, Ranganathan SC, Gangell CL, *et al.* Impact of lung disease on respiratory impedance in young children with cystic fibrosis. *Eur Respir J* 2015; 46: 1672–1679.
4 Domínguez-Martín C, Cano A, Díez-Monge N, *et al.* Spirometry and respiratory oscillometry: feasibility and concordance in schoolchildren with asthma. *Pediatr Pulmonol* 2023; 58: 1896–1903.
5 Veldhoen ES, Roos JH, Bekkema R, *et al.* Oscillometry: a substitute of spirometry in children with neuromuscular diseases? *Pediatr Pulmonol* 2022; 57: 1618–1624.
6 Rachow A, Ivanova O, Bakuli A, *et al.* Performance of spirometry assessment at TB diagnosis. *Int J Tuberc Lung Dis* 2023; 27: 850–857.
7 Graham BL, Steenbruggen I, Miller MR, *et al.* Standardization of spirometry 2019 update. An official American Thoracic Society and European Respiratory Society technical statement. *Am J Respir Crit Care Med* 2019; 200: e70–e88.
8 Wanger J, Clausen JL, Coates A, *et al.* Standardisation of the measurement of lung volumes. *Eur Respir J* 2005; 26: 511–522.
9 Sly PD, Hantos Z, Czövek D. The international collaboration to Improve Respiratory Health in Children (INCIRCLE) ERS clinical research collaboration. *Eur Respir J* 2018; 52: 1801867.
10 Bowerman C, Bhakta NR, Brazzale D, *et al.* A race-neutral approach to the interpretation of lung function measurements. *Am J Respir Crit Care Med* 2023; 207: 768–774.
11 Calogero C, Simpson SJ, Lombardi E, *et al.* Respiratory impedance and bronchodilator responsiveness in healthy children aged 2–13 years. *Pediatr Pulmonol* 2013; 48: 707–715.
12 Nowowiejska B, Tomalak W, Radliński J, *et al.* Transient reference values for impulse oscillometry for children aged 3–18 years. *Pediatr Pulmonol* 2008; 43: 1193–1197.
13 Gie A, Schubert P, Conradie W, *et al.* 'Miliary metastasis' in a child with papillary thyroid cancer. *BMJ Case Rep* 2022; 15: e249598.
14 Mori Y, Nishikiori H, Chiba H, *et al.* Respiratory reactance in forced oscillation technique reflects disease stage and predicts lung physiology deterioration in idiopathic pulmonary fibrosis. *Respir Physiol Neurobiol* 2020; 275: 103386.
15 Yamamoto Y, Miki K, Tsujino K, *et al.* Oscillometry and computed tomography findings in patients with idiopathic pulmonary fibrosis. *ERJ Open Res* 2020; 6: 00391-2020.
16 Chaya S, Macginty R, Jacobs C, *et al.* Normal values of respiratory oscillometry in South African children and adolescents. *ERJ Open Res* 2023; 9: 00371-2022.

Suggested answers

1. False. FOT does not measure lung volumes but rather lung mechanics.
2. c. In children with diffuse parenchymal lung disease spirometry should be used to identify those with restrictive physiology. Plethysmography should be performed to evaluate lung volumes. The use of FOT in children with diffuse parenchymal lung disease remains unclear.
3. False. FOT and spirometry do not correlate well in children with diffuse lung disease, especially in the absence of airway disease and airflow obstruction.