



Comparison of forced oscillation technique and spirometry in paediatric asthma

To the Editor:

The Global Initiative for Asthma report emphasises the use of spirometry in diagnosing and monitoring asthma in children from 6 years of age onwards [1]. Spirometry requires good cooperation and younger children are sometimes unable to perform repeated forced expiratory blows [2]. Alternative pulmonary function measurements, such as the forced oscillation technique (FOT), are increasingly available for children at preschool age [3]. FOT measures lung function by imposing small soundwaves over tidal breathing through a mouthpiece, where pressure and flow changes in the airways are measured to derive respiratory system properties [4, 5]. The first study on bronchodilator responses by FOT in preschool-aged children was published already two decades ago [6]. Guidelines endorse the use of respiratory oscillometry in diagnosing and following up asthma in young children [3, 7], and it has shown potential in predicting loss of asthma control in older children and adolescents [8]. However, little is known of how FOT indices correlate with flow–volume indices when this technique is used in adjunct with conventional spirometry.

The children's respiratory assessment laboratory in Evelina London Children's Hospital (London, UK) has been using a commercial FOT application with fixed frequency at 8 Hz oscillation input. We hypothesised that baseline and post-bronchodilator lung function measurements by FOT would have a mutual relationship with spirometry measurements obtained at the same visit, in children with moderate to severe asthma. In addition, we aimed to investigate agreement between the two methods regarding bronchodilator responsiveness (BDR).

Measurements were collected from a tertiary level asthma clinic between January and June in 2017. The data consisted of 72 sequential clinic visits from an ethnically diverse regional population. First, baseline FOT (Resmon Pro; MGC Diagnostics, USA) measurement at 8 Hz was performed with patient's cheeks supported by a technician, according to current guidelines [3]. Respiratory system resistance at 8 Hz ($R_{rs,8}$) was expressed as age-specific height-adjusted reference values (Z-scores) using two different reference equations for 3–12-year-olds [9] and for 13–17-year-olds [10]. Then, baseline spirometry (EasyOne Pro Lab; NDD, Switzerland) was obtained [3], and forced vital capacity (FVC), forced expiratory volume in 1 s (FEV_1), FEV_1 /FVC ratio and forced expiratory flow at 25–75% FVC ($FEF_{25-75\%}$) were expressed as multiethnic reference values (Z-scores) [11]. 15 min after salbutamol (400 µg) administration, the children were studied repeatedly with FOT and spirometry. Relative increases in $FEV_1 \geq 12\%$ from baseline [12] or relative decreases in $R_{rs,8} \leq -32\%$ from baseline defined abnormal BDR [9]. Clinical data on age, sex, ethnicity and use of asthma medication prior the testing were available. Statistical analyses were performed with SPSS (version 26; IBM, USA). The results are expressed as means and standard deviations for continuous, and numbers and frequencies for categorised variables. ANOVA was used in the analysis of continuous, and Fisher's exact or Chi-squared tests in the analysis of categorised variables, as appropriate. Bivariate correlations (R) were reported with Pearson coefficients for normally distributed and with Spearman coefficients for non-normally distributed data.



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Evaluation of airway obstruction with forced oscillation technique can be an adjunct to spirometry or even used as a primary method in those children unable to perform spirometry
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All data were extracted retrospectively from de-identified clinical physiology reports. Ethical approval and data protection were provided by the Evelina London Children's Hospital local directorate review board (Guy's and St Thomas' NHS Foundation Trust, registration number 8901).

72 patients were measured during uninterrupted maintenance medication for asthma. Mean \pm SD age was 10.9 \pm 3.6 years with range from 3.8 to 17.7 years. All 72 children were able to perform baseline FOT measurement. Six children (7.9 \pm 5.0 years) were not able to produce repeatable spirometry, resulting in 66 (91.6%) measurements with both baseline tests. 18 children were unable to proceed to post-bronchodilator measurements due to clinical reasons (poor baseline performance, lack of time or non-cooperation). These children were on average younger (8.8 \pm 3.7 years) compared to the 54 (75%) children who were able to perform both baseline and post-bronchodilator tests (11.6 \pm 3.3 years, $p=0.003$). In these 54 cases (51.9% male), reported ethnicities were 41% black, 46% Caucasian and 13% Asian; measured height 146 \pm 17.4 cm; and weight 43 \pm 18.0 kg. 13 (24.1%) reported use of bronchodilator within the last 12 h before BDR testing.

In 54 children with both lung function tests available, baseline spirometric indices were abnormal (≤ -1.65 Z-scores) for FEV₁ in 21 (38.9%), FVC in six (11.1%), FEV₁/FVC in 26 (48.1%) and FEF_{25-75%} in 21 (38.9%) cases. After bronchodilation, abnormal FEV₁ was found in nine (16.7%), FVC in five (9.3%), FEV₁/FVC in nine (16.7%) and FEF_{25-75%} in 11 (20.4%) cases. Bronchodilator administration increased FEV₁ on average from -1.19 ± 1.44 to -0.40 ± 1.21 Z-scores, FVC from -0.33 ± 1.14 to -0.01 ± 1.07 Z-scores, FEV₁/FVC from -1.64 ± 1.71 to -0.71 ± 1.24 Z-scores and FEF_{25-75%} from -1.45 ± 1.48 to -0.47 ± 1.53 Z-scores. In FOT, R_{rs} was abnormal ($\geq +1.65$ Z-scores) at baseline in 20 (37.0%) cases and after

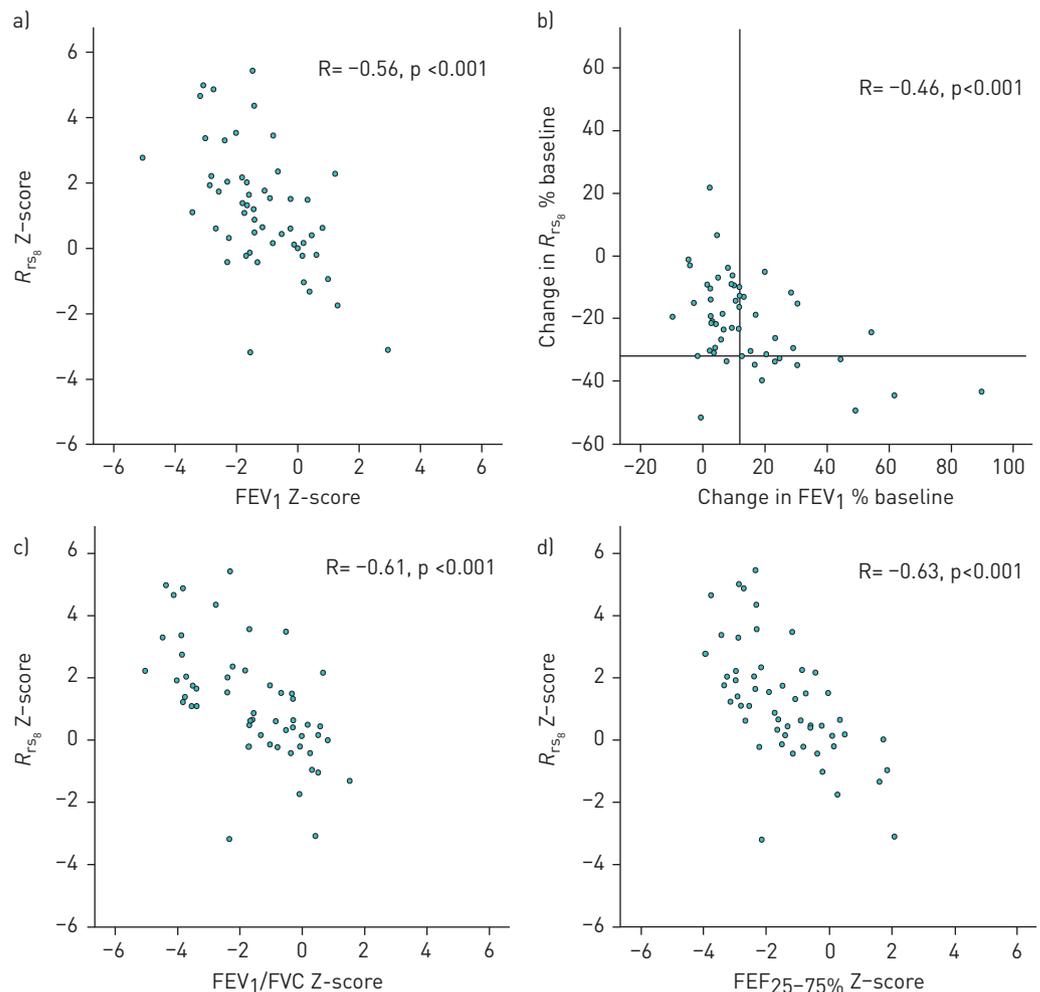


FIGURE 1 a) Bivariate correlation of baseline resistance of the respiratory system at 8 Hz (R_{rs}) with forced expiratory volume in 1 s (FEV₁), b) change in R_{rs} from baseline (cut-off -32%) and change in FEV₁ from baseline (cut-off $+12\%$), c) R_{rs} and FEV₁/forced vital capacity (FVC) and d) R_{rs} and forced expiratory flow at 25-75% FVC (FEF_{25-75%}) in 54 children with moderate to severe asthma at a mean age of 11.6 years.

bronchodilation in five (9.3%) cases. R_{rs} decreased on average from 1.21 ± 1.85 to -0.73 ± 1.87 Z-scores, respectively.

Statistically significant baseline FOT and spirometry bivariate correlations are presented in figure 1. Baseline R_{rs} was significantly related with FEV_1 ($R = -0.56$, $p < 0.001$), FEV_1/FVC ($R = -0.61$, $p < 0.001$) and $FEF_{25-75\%}$ ($R = -0.63$, $p < 0.001$) but not with FVC. Post-bronchodilator R_{rs} was related with FEV_1 ($R = -0.38$, $p = 0.005$), FEV_1/FVC ($R = -0.35$, $p = 0.01$) and $FEF_{25-75\%}$ ($R = -0.36$, $p = 0.008$) but not with FVC. In BDR comparisons, decrease in R_{rs} was related with increase in FEV_1 ($R = -0.46$, $p < 0.001$) (figure 1).

There were 11 (20.4%) children positive for BDR by FOT and 20 (37.0%) positive for BDR by spirometry. BDR tests were in concordance in 76% (41 versus 13 out of 54, $p < 0.001$). Two cases (3.7%) were negative by spirometry but positive by FOT and 11 (20.4%) positive by spirometry but negative by FOT. There were no significant differences in age, sex, ethnicity, height, weight, body mass index or use of any bronchodilator before the BDR between cases with test agreement and disagreement (data not shown).

There were three main findings when evaluating the relationship between FOT and spirometry in asthmatic children. Firstly, baseline lung function tests showed moderate correlations between R_{rs} and FEV_1 , FEV_1/FVC and $FEF_{25-75\%}$ but not with FVC. Secondly, there was a fair consistency between BDR defined by relative change in R_{rs} and change in FEV_1 from baseline. Thirdly, all children were able to perform FOT whereas the younger children were not able to perform spirometry.

The linear relationship between FOT and spirometry was strongest in baseline indices describing peripheral obstruction, *i.e.* FEV_1/FVC and $FEF_{25-75\%}$. This reflects our study population demonstrating significant reversible obstruction. Similar magnitudes of correlation (-0.51 – -0.71) have been described between baseline FEV_1 and R_{rs} using impulse oscillometry [13, 14] but literature comparing FOT and spirometry in children is scarce. For BDR, a negative correlation of -0.46 was in line with previously reported relationship between R_{rs} and FEV_1 [15].

There was a moderate agreement with BDR comparisons between FOT and spirometry, with 13 outliers having either a pathological response in R_{rs} or FEV_1 , but not both. No clear demographic factor was found to be associated with test disagreement. BDR by spirometry seemed to pick up more cases, and discrepancies in BDR between two methods may be related to technical and physiological factors. Bronchodilation changes in oscillometric indices are mathematically more dependent from baseline than spirometric indices. For example, when airway obstruction is present, FOT baseline R_{rs} is higher and the decrease due to bronchodilation is relatively smaller in percentage, whereas FEV_1 shows more marked improvement in relation to baseline. However, oscillometry is thought to be more sensitive to peripheral airway obstruction than spirometry, and previously baseline measurements rather than BDR with impulse oscillometry were more effective in distinguishing uncontrolled asthma status in children [16]. As a limitation to more specific FOT analysis, reactance data were not available in this study.

We aimed to look at clinical performance and consistency of FOT and spirometry findings in children followed up at a tertiary level asthma clinic. Both baseline tests were available from 92% of children and 75% of children had both tests accepted after bronchodilation. The time to obtain two consequent measurements was limited and performance at baseline may have been affected if testing was continued further. These data were not fully recorded and thus direct feasibility comparisons were not available.

In conclusion, FOT showed moderate correlation with spirometry indices and was accessible to children with moderate to severe asthma. The findings support the use of FOT in adjunct with spirometry and even as a primary method in younger asthmatics unable to perform spirometry.

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