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Review

Use of impulse oscillometry to assess lung function in prematurely born children and young people: Comparisons with spirometry

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Educational aims

The reader will come to appreciate that:

- Prematurity is associated with obstructive airway disease, as detected by spirometry or impulse oscillometry measurements.
- Prematurely born individuals may have fixed and/or reversible obstructive airway disease.
- Impulse oscillometry can be used to determine the response to bronchodilator therapy.
- Impulse oscillometry has been validated in children as young as three years of age with the results correlating with those of spirometry.

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ABSTRACT

Premature birth is a risk factor for bronchopulmonary dysplasia (BPD); both of which are associated with obstructive airway disease throughout childhood. Impulse oscillometry (IOS) is an effort-independent, passive measure of tidal breathing, which could have benefits in assessing lung function amongst younger patients unable to perform valid spirometry. A literature search was conducted to investigate the use of IOS in prematurely born children and young people. IOS results correlate with those of spirometry. Reversibility of airway obstruction in children with BPD is variable. IOS could have benefits in assessing individual patient response and suitability for bronchodilator therapy. More work, however, is required to establish multi-ethnic reference ranges and standardise commercially available devices prior to its routine incorporation into clinical practice.

INTRODUCTION

More than 95% of prematurely born infants now survive into adulthood [1], but many will develop bronchopulmonary dysplasia (BPD) (chronic oxygen dependency). It affects 38% of very preterm babies born less than 32 weeks of gestational age (GA) in England and Wales [2]. Prematurity and BPD can result in chronic respiratory morbidity in childhood and young adulthood [3,4]. The EPICure study reported that, although mortality has improved in extremely prematurely born infants, the proportion developing BPD has remained constant [5]. Thus, the numbers of BPD survivors are increasing, hence, understanding their long-term lung function is of importance to paediatric and adult respiratory physicians and the parents of affected infants.

Prematurely born individuals can have obstructive airway disease during childhood and early adulthood [6–10]. Kotecha et al. performed spirometry in children aged 8–9 years [6]. They demonstrated that children born at 33–34 weeks of gestational age (GA)

Abbreviations: BPD, bronchopulmonary dysplasia; GA, gestational age; IOS, Impulse oscillometry; RDS, respiratory distress syndrome.

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had lower *z*-scores of forced expiratory volume in one second (FEV_1), forced vital capacity (FVC) and FEV_1/FVC compared to term-born peers [6]. Obstructive airway disease in prematurely born children is worse in those who had BPD [7–9]. The EPICure Study showed that amongst children born extremely prematurely, BPD children had lower z scores of FEV_1, FVC and FEV_1/FVC than their non-BPD counterparts [7]. Vollsaeter et al. examined 11-year-old children born either extremely prematurely or very low birth weight (VLBW) in 1991–1992 or 1999–2000 [11]. The latter cohort were more likely to have had postnatal surfactant and exposure to antenatal corticosteroids and had less obstructive airway disease, but still greater obstruction than age-matched term controls, FEV_1 *z*-scores (−0.65 vs −0.31, $p = 0.04$), FEV_1/FVC *z*-scores (−0.8 vs −0.3, $p = 0.005$) of the 1999–2000 preterm and term controls, respectively.[11]. Despite those perinatal advances, at 4–12 years of age, those with BPD had worse lung function trajectories than their preterm counterparts without BPD [12]. Doyle et al. followed three cohorts of extremely prematurely born children born in 1991–1992, 1997 and 2005 respectively [13]. Despite increased use of antenatal corticosteroids, postnatal surfactant and less invasive ventilation (nasal continuous positive airway pressure) there were no significant improvements in lung function. Conversely, the *z*-scores of FEV_1 (−1.19 versus −0.65, $p < 0.05$) and FEV_1/FVC (−0.77 versus −0.3, $p < 0.05$) were lower in the 2005 cohort as compared to the 1997 cohort [13]. These surprising findings could be due to halving use of postnatal glucocorticoids from 1997 to 2005. The authors also suggested that prolonged periods of oximetry could account for the increased rate of oxygen dependence in 2005 and may explain the poorer lung function in the latter cohort.

In term born individuals, maximum lung function is achieved between 20 and 25 years of age, after which there is a gradual decline in both FEV_1 and FVC [14]. Those born prematurely are at risk of not reaching their full lung potential in early adulthood [15]. There is conflicting evidence of the effect of puberty on lung growth in prematurely born young people [8,10,16,17]. Some studies have shown 'tracking' of lung function, defined as children with reduced lung function growing into adults with reduced lung function [8,17]. A Norwegian group demonstrated that spirometry results in extremely prematurely born (those born at less than 28 weeks of GA) or very low birth weight (VLBW) children tracked between 10 and 18 years of age for FEV_1 ($r^2 = 0.637$) and FEF_{25-75} ($r^2 = 0.745$) [8]. More recently, the group published longitudinal spirometry data in extremely premature survivors at 25 and 35-years of age [17]. They identified similar declines in FEV_1% from the expected peak, between term (98.8–95.21%) and extremely preterm (86.3–81%), with the mean absolute difference in the decline being 1.7% ($p = 0.4$), supporting the 'tracking' theory [17]. In contrast, an Australian group described worsening spirometry results between 8 and 18 years of age in extremely preterm or VLBW survivors [18]. The authors hypothesized that these children are unlikely to reach the normal peak of airway growth by their mid-20s as compared to individuals born at term. They noted that amongst premature/VLBW individuals, this decline was more prominent in BPD survivors than in the non-BPD group [18].

Narang et al. used spirometry to demonstrate ~~d~~ 'catch up' lung function in a group of prematurely born 21-year-old subjects [10]. 'Catch up' lung function is defined as children with reduced lung function growing into adults with normal lung function. They showed that despite increased self-reported respiratory symptoms, there was no significant difference in lung function between the term and preterm groups, in FEV_1, forced mid-expiratory flow and FVC [10]. Our group recently described the results at 11–14 and 16–19 years of age of prematurely born young people from the United Kingdom Oscillation Study (UKOS), who had been randomised to receive either high frequency oscillation (HFO) or conventional ventilation (CV) from birth [16]. Different trajectories were noted in FEV_1/FVC results (interaction test $p = 0.02$), whereby *z*-scores remained similar over time in the HFO group (−0.01 *z*-score/year) but increased in the CV group (+0.08 *z*-score/year). The FEV1/FVC results were similar at 16–19 years in the HFO and CV groups having been lower in the CV group at 11- to 14-years [19], which suggested 'catch up' growth during adolescence in the CV group [16]. The lung function trajectory of prematurely born individuals during adolescence and early adulthood remains unclear.

Although spirometry is frequently used to assess lung function it requires volitional effort and the ability to produce maximal forced expirations, thus acceptable quality results are usually found only in children over five years of age [20,21]. Premature birth can be associated with adverse neurodevelopmental outcomes [22] and affected individuals may also be unable to perform spirometry. Therefore, techniques such as impulse oscillometry (IOS) which are non-effort dependent could be useful in those populations [23]. This review will evaluate IOS in the assessment of lung function at follow up of prematurely born children and young people and, in particular, discuss its role in longitudinal studies and assessment of airway obstruction reversibility.

Impulse oscillometry (IOS)

IOS is a variant of the forced oscillometry technique (FOT), first described by Dubois et al. To perform FOT, external sinusoidal pressure waves are superimposed on passive tidal breathing to measure properties of the respiratory system [24]. From the relationship between external pressure waves and resultant airflows, the impedance (*Z*, forces opposing external pressure waves) can be derived and from this the reactance (*X*, a measure of elastic recoil of lung tissue) and resistance (*R*, a measure of airway calibre) can be derived [25,26]. External waves that are mono or multifrequency are used and applied continuously or in a time-discrete manner [23]. IOS is a variant of FOT distinguished by application of time-discrete pressure *pulses*, rather than pseudo-random noise (PRN) or sinusoidal waves, which allows for analysis of intra-breath variation of impedance [23,26] (Fig. 1). A Fast Fourier transformation is then applied to decipher the data, such that the impedance can be calculated at multiple frequencies [23,27]. Lower frequencies (5 Hz) are transmitted throughout the pulmonary system to reflect total resistance (R5, resistance at 5 Hz), while higher frequencies (20 Hz) remain in the larger airways and reflect central resistance (R20, resistance at 20 Hz) [26]. The reactance at 5 Hz (X5) predominantly characterises the elastance (inverse of capacitance) and to a lesser degree the inertance of the lung peripheries [23]. At lower frequencies, the negative capacitive reactance dominates, whilst at higher frequencies, the positive inertive reactance dominates. Therefore, the point at which the inertance and capac-

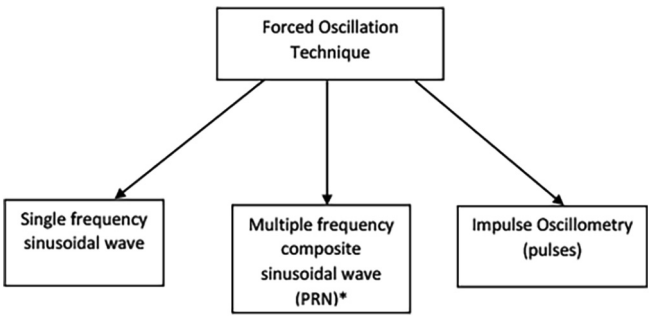

Fig. 1. Different FOT modalities. *PRN FOT can be generated by different devices, including loudspeakers and vibrating mesh.

itance are equal (and total reactance is zero) is the resonant frequency (fres) [23]. Finally, AX (area under the reactance curve) is a summative measure of the degree of peripheral airway obstruction, reflecting as it does frequency dependence of compliance [23].

Comparison to spirometry

Several groups have compared IOS and spirometry to assess lung function at follow up in prematurely born children and young people [28–33]. (Tables 1 and 2) IOS was reported to be better tolerated than spirometry, with higher success rates (87–93% versus 36–67%) [28,29,33] (Table 3). Lung function at seven years of age in VLBW children, was worse in those who had had BPD (mean GA 27 weeks) compared to those without BPD (mean GA 28 weeks) and the control group (R5 (1.35 versus 1.09 versus 0.95 kPa/(L/s), $p < 0.001$) and R20 (0.89 versus 0.78, versus 0.66 kPa/(L/s), $p = 0.001$), X20 (−2.62 versus −0.84 versus 0.65 kPa/(L/s), $p < 0.001$)). Significant differences in spirometry results were lost after adjustment to *z*-scores [14], which the authors attributed to the low numbers of acceptable spirometry results ($n = 4$ in the BPD group and $n = 15$ in the non-BPD group) compared to IOS ($n = 11$ in the BPD group and $n = 29$ in the non-BPD group) [28]. A drawback of the improved feasibility of IOS is that comparisons between the techniques may be biased by a broader IOS study population including patients with intellectual disability related to prematurity, syndromes, or other causes. None of the described studies state intellectual disability or congenital syndromes as exclusion criteria.

Malmberg et al. reported in prematurely born (<30 weeks GA) 7- to 9-year old children that both R5 ($r = -0.55$, $p < 0.0001$) and X5 (r = 0.76, $p < 0.0001$) correlated significantly with % predicted FEV_1 [31]. In contrast, Brostrom et al. showed a greater correlation between FEV_1 and R5 than X5 amongst six to eight year-old VLBW children [32]. It has been suggested that at very high airway resistances, the sensitivity of X5 may be reduced [25]. Furthermore, young children have respiratory rates more than 20–30 breaths/minute which may cause greater variability at the lower frequencies of X5 and R5, which might account for the variability in whether R5 or X5 better correlate with FEV_1 [23,34]. Lundberg et al. demonstrated in six year old children born at less than 27 weeks of GA and term controls significant correlations between R5 and $FEV_{0.75}$ (r −0.43, $p = 0.002$) and $FEV_{0.75}$/FVC ($r = -0.39$, $p = 0.006$), but not FVC ($r = -0.18$, $p = 0.21$ [29]. Lundberg et al. compared the z scores of IOS and spirometry results that were 'within-' and 'outside-' the reference range. The authors defined 'outside reference-' as more extreme than +/− 1.64 z -scores [29]. They described a low positive predictive value (PPV) (22.2%) and a high negative predictive value (NPV) (87.2%) of AX to predict 'outside reference' $FEV_{0.75}$/FVC [29]. This might suggest that IOS had greater sensitivity than spirometry in assessing airway dysfunction, particularly in peripheral airways. This study did not report the PPV and NPV of spirometry to predict IOS variables. In contrast, amongst six-year old children born at less than 27 weeks of GA, the FEV_1 *z*-score differed significantly between those born at 22–24 weeks versus 25–26 weeks of GA and FEV_1/FVC differed between those who had moderate rather than severe BPD, whilst IOS results did not differ significantly between those groups. Amongst the extremely prematurely born group, however, R5-20 results were worse for those born small rather than appropriate for gestational age, which was not detected by spirometry [33]. Overall, IOS is better tolerated than spirometry and the parameters of X5 and R5 have been shown to correlate with FEV_1 and $FEV_{0.75}$ in prematurely born children.

Longitudinal studies

There is only one longitudinal study that used IOS in prematurely born children and young people [35]. Amongst children born at 24–31 weeks of GA with BPD or without BPD between 6 to 8 [32] and 13 to 17 years of age [35], there were higher R5-20 results in the BPD compared to the non-BPD group. This correlated with deterioration in FEV_1/FVC *z*-scores in the BPD group. There was a larger increase of R5-20 over time in the severe BPD group compared to the non-BPD group (beta + 0.11 kPa/(L/s), $p = 0.011$), which suggests worsening longitudinal lung function in this cohort. No significant differences were noted between the other BPD and non-BPD groups [35]. Further longitudinal studies using IOS to assess lung function in prematurely born children are required.

Table 1
IOS studies comparing former pretermers to term controls.

Author, year	Country, Study type	Sample (n)		Gestational Age (weeks)		Age (years)		Results
		Preterm Group (F/M)	Control Group (F/M)	Preterm Group (Mean ± SD)	Control Group (Mean ± SD)	Preterm Group (Mean ± SD)	Control Group (Mean ± SD)	
Lundberg et al., 2020 [29]	Sweden, case-control	49 (22/27)	54 (23/31)	25.1 ± 0.89	39.4 ± 1.18	6.6 ± 0.20	6.6 ± 0.19	Moderate correlation between spirometry and IOS (Spearman's $r = -0.31$ to -0.56)
Dantas, 2021 [43]	Brazil, case-control	52 (40/12)	71 (40/29)	34.0 ± 1.68	Not reported	7.86 ± 1.41	7.69 ± 1.61	No difference between preterm and term groups in IOS results
Thunqvist, 2016 [30]	Sweden, prospective cohort study (BAMSE)	149 (73/76)	2472 (1287/1185)	F: 34.9 (32–36)*M: 35.1 (32–36)*	F: 39.6 (37–41)*M: 39.6 (37–41)*	F: 8.4 ± 0.5 M: 8.4 ± 0.4 F: 16.7 ± 0.4 M:16.7 ± 0.4	F: 8.3 ± 0.5 M: 8.4 ± 0.5 F: 16.7 ± 0.4 M:16.7 ± 0.4	Higher resistance at R5 ($p = 0.003$–0.14) and R5-R20 (males only, $p < 0.001$) and lower FEV_1 (p = 0.02) in preterm than term groups
Thunqvist, 2018 [33]	Sweden, prospective cohort study (EXPRESS)	153 (71/82)	157 (67/90)	25.0 (22–26)*	39.8 (37–41)*	6.6 ± 0.2	6.6 ± 0.2	Preterm children had higher R5, R5-20, larger AX ($p < 0.001$), lower FVC and lower FEV_1 ($p < 0.001$) than term children

PS: passive smoking. NPS: non-passive smoking.
*Reported as median (range).
**Reported as median (25^{th}–75th percentiles).
*** Reported as mean (range).

Table 2
IOS studies comparing children with bronchopulmonary dysplasia (BPD) to former pretermers with no history of BPD.

Author, year	Country, Study type	Sample (n)		Gestational Age (weeks)		Age (years)		Results
		BPD Group (F/M)	Non-BPD Group (F/M)	BPD Group (Mean ± SD)	Non-BPD Group (Mean ± SD)	BPD Group (Mean ± SD)	Non-BPD Group (Mean ± SD)	
Broström, 2010 [32]	Sweden, case-control	Mild: 20Mod: 8 Severe: 4 (Not reported)	28 (Not reported)	Mild: 27 (24–30) *Mod: 27.5 (25–30) *Severe: 28 (25–29)*	30 (38–31)*	Mild: 7.4 (6.3–8.3) *Mod: 7.3 (6.6–7.9) *Severe: 7.1 (6.9–7.5)*	7.6 (6.5–8.0) *	Significant correlation between FEV_1 and X5-10, R5-10 (r = 0.43–0.79, p < 0.002), most significant for R5 and FEV_1 (r = 0.79, p < 0.0003)
Durlak, 2021 [28]	Poland, prospective cohort study	11 (3/8)	VLBW Non-BPD: 29 (13/16) Term controls: 30 (13/17)	27.3 ± 4	VLBW Non-BPD: 28 ± 5 Control: (Not reported)	6.0 ± 1	VLBW Non-BPD: 7.0 ± 0 Control: 7.0 ± 0	R5, R5-20, Fres and AX higher in BPD children than controls (p < 0.001, p = 0.009, p < 0.001, p < 0.001). No statistically significant difference in spirometry z-scores
Malmberg, 2000 [31]	Finland, case-control	15 (8/7)	Non-BPD preterm: 34 (19/15) Term controls: 18 (9/9)	26.9 (24.1–30.7)***	Non-BPD preterm: 28.0 (25.3–30.9)***	8.4 (7.8–9.2)***	Non-BPD preterm: 8.1 (7.3–9.0)***Term controls: 8.2 (5.3–10.7)***	R5 and X5 correlated with % predicted FEV_1 (r = −0.55, p < 0.0001) and r = 0.76, p < 0.0001). BPD group had lower X5, X10 (p < 0.0001) and higher fres (p < 0.008) than the non-BPD preterm group
Manti, 2021 [42]	Italy, case-control	16 (7/9)	14 (8/6)	26.4 ± 0.5	27.9 ± 0.5	5.9 ± 0.3	6.0 ± 0.1	No difference in IOS parameters between BPD and non-BPD groups. Significant difference by comparing all included ELBW infants with reference values
Suursalmi, 2015 [41]	Finland, case-control	21 (Not reported)	Non-BPD VLBW: 19 Term control: 19	26.6 ± 1.6	Non-BPD VLBW: 28.9 ± 1.8	Not reported	Not reported	% predicted R5 higher in BPD vs non-BPD vs term groups (92% vs 79% vs 70%, p = 0.011), greater bronchodilator response of R5 in non-BPD vs BPD vs term groups (-21% vs −17% vs −11% p = 0.010)
Um-Bergström, 2017 [35]	Sweden, case-control	28 (7/21)	23 (11/12)	27 (24–30)***	30 (28–31)***	14.5 (13.2–17)***		R5-20 increasing resistance values with BPD severity (P trend = 0.029)

* Assessed neonatal chronic lung disease rather than BPD.
** Presented as median (10th–90th percentile).
*** Presented as median (range).

Table 3
Comparison of success rates of IOS and spirometry.

Author	Age of cohort	Cohort characteristics	IOS success rate (%)	Spirometry success rate (%)
Durlak et al. [28]	7-years-old	VLBW children and term controls	93	36–67
Lundberg et al. [29]	6-years-old	Children born less than 27 weeks GA and term controls	92	56
Thunqvist et al. [33]	6.5-years-old	Children born less than 27 weeks GA and term controls	87	54

Assessment of reversibility of airway obstruction

A recent statement from the ERS Technical Standards for Respiratory Oscillometry recommends bronchodilator response cut-offs as 40% (R5) and 50% (X5) in children [36] others, however, have considered lower values of 28–36% [37–40]. The use of IOS to assess reversibility of airway obstruction by bronchodilator challenge in BPD premature survivors has been assessed by several groups with variable findings [28,31,32,41–43]. Amongst 6 to 14 year-old VLBW children, a greater proportion response to a bronchodilator was noted in the non-BPD group, next in the BPD group and lowest in the term controls, as indicated by changes in R5 [41]. In contrast, others reported a greater bronchodilator response in seven year old children who were BPD survivors, compared to those without BPD and the least response in term controls [28]. Another study using IOS in 6–8 year old children, did not find significant differences in the proportions with bronchodilator responsiveness using R5 between non-BPD (21%), mild-moderate BPD (26%) and severe BPD (24%) groups [32]. There was, however, significant differences in bronchodilator response as assessed by FEV_1 in those three groups (3.5% versus 8.2% versus 12.4%, p = 0.04 [32]. Dantas et al. found no significant differences in airway reversibility between 5 and 10 year old children born between 32 and 37 weeks of GA and term controls [43]. They reported similar IOS results in the groups at baseline, R5 (0.8 versus 0.82, p = 0.594), R5-20 (0.26 versus 0.27, p = 0.615), AX (2.7 versus 2.5, p = 0.626), and a similar change post-bronchodilator, R5 (−0.11 versus −0.11, p = 0.904), R5-20 (−0.07 versus −0.07, p = 0.923), AX (−0.97 versus −0.71, p = 0.378). The authors postulated that a small sample size (n = 49 cases, n = 70 controls) and being born moderate-to-late- preterm might contribute to the lack of differences compared to term controls [43]. IOS has detected variable bronchodilator responses amongst prematurely born children, with and without BPD, which suggests that some of these individuals may have fixed airway obstruction. Future research

directions should evaluate the role of IOS in the outpatient department to distinguish individual patient responses to bronchodilator.

IOS results in randomised controlled trial (RCTs)

There are only two RCTs that have used IOS to investigate lung function at follow up in prematurely born children, who received either inhaled nitric oxide [44] or dexamethasone [45]. Both studies showed no significant differences in IOS results between the treatment and placebo groups. There was agreement between spirometry and IOS in finding no significant difference between the iNO and placebo groups. FVC was lower in the dexamethasone group than placebo ($p = 0.04$), but no other spirometry or IOS variable differed between the two groups. IOS appears to be comparable to spirometry in assessing outcomes in RCTs.

Passive smoking

In three to seven year old children born at 34 to 36 + 7 weeks of GA [46], passive smoking was associated with worse R5 (0.95 vs 0.84, $p = 0.007$), X10 (−0.15 vs −0.12, $p = 0.049$) and Z5 (1 vs 0.9, $p = 0.007$) results. IOS has a role in observational studies to assess lung function in children and young people.

Limitations of IOS in clinical practice

One of the major drawbacks of IOS is an absence of comprehensive reference ranges. There are, however, reference ranges from healthy children from several countries, including Sweden [47], North America [48], Mexico [49], Finland [37], Korea [50], Taiwan [51] and Turkey [52]. A further drawback is the larger inter-subject variability of results [25], although, the within- and between day variability of IOS measures on an individual level has been low (intraclass correlation coefficient >0.6–0.8) [40]. Finally, there are reports of differences between commercially available oscillometric devices [53–55]. New techniques have been developed to reduce the size of oscillometers, which enables lung function assessment within the clinic room using a small, handheld, portable device. Rather than using the traditional speaker/pulse method, airwave oscillometry (AOS) uses a smaller vibrating mesh [54] and uses multifrequency composite sinusoidal waves rather than pressure pulses, to generate a PRN FOT [23,53]. Comparative studies report statistically significant, although perhaps not clinically significant differences in parameters of resistance, and to a greater extent, reactance [53–57]. Soares et al. used a large asthma population (*in vivo*), phantom three-dimension printed airway resistance model and a standard volume reactance (*in vitro*) to demonstrate that the Jaeger Masterscope IOS had higher resistance values and less negative reactance results than those of the Thorasys tremoFlo C-100 AOS (mean difference in R5 0.04 kPa/(L/s) $p < 0.0001$; X20 0.06 kPa/(L/s) $p < 0.0001$; AX −0.81 kPa/(L/s) $p < 0.0001$) [53]. Another group also compared these two devices in adults with asthma and COPD and highlighted lower values with IOS of AX and Fres and higher values for X5 [53]. A further group compared the devices in 3 to 17-year old children with asthma and showed high (ICC 0.88–0.91) and good (ICC 0.69–0.87) agreement in resistance and reactance, respectively [55]. While the raw value within-patient differences between devices were small, a significant proportional difference was observed for most oscillometry results. These findings highlight the need for standardisation of normative values for different commercially available devices.

Future directions

IOS is a promising tool to assess lung function. Given the high inter-subject variability in IOS results, further work is needed to establish comprehensive multi-ethnic reference ranges, as exists for spirometry. Furthermore, there must be standardization between commercially available IOS and other FOT devices to ensure comparability on a population level. More work is also required to evaluate the role of IOS in longitudinal lung function studies. We have described the use of IOS to detect variable bronchodilator responses amongst prematurely born children, with and without BPD. Future studies should investigate IOS in an outpatient department setting, specifically whether IOS can distinguish pre-school and school aged children with wheeze who might benefit from bronchodilator therapy.

CONCLUSION

We have found that IOS has some benefits over spirometry in assessing lung function in prematurely born children and young people, which include its greater tolerability in young children. The lung function trajectories of BPD survivors, and in particular the extent to which they have fixed airway obstruction, has not been fully elucidated. IOS has promising performance in research settings and should now be evaluated in clinical practice. There is potential for IOS to be used for the rapid assessment of an individual patient response to a bronchodilator challenge within an outpatient setting. This would have utility in highlighting preschool children with wheeze who might benefit from bronchodilator therapy. Prior to its routine incorporation into clinical use, more research should be done to produce comprehensive reference ranges and standardise commercially available devices.

DIRECTIONS FOR FUTURE RESEARCH

- There is a high inter-subject variability in IOS results, further work is needed to establish comprehensive multi-ethnic reference ranges, as exists for spirometry.
- There are several commercially available IOS devices, research is required to ensure standardisation and comparability between devices.
- The usefulness of IOS in longitudinal studies to assess lung function trajectories in prematurely born children and young people merits evaluation.

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AUTHOR CONTRIBUTIONS

All authors were involved in conceptualization. SG wrote the original draft, which was revised and edited by AG and CH.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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