A comparison of respiratory oscillometry and spirometry in idiopathic pulmonary fibrosis: performance time, symptom burden and test–retest reliability

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Shareable abstract (@ERSpublications)
Oscillometry is quicker to perform and provokes fewer symptoms than spirometry in patients with IPF https://bit.ly/4aYPZv5

Cite this article as: Patel S, Sylvester KP, Wu Z, *et al*. A comparison of respiratory oscillometry and spirometry in idiopathic pulmonary fibrosis: performance time, symptom burden and test–retest reliability. *ERJ Open Res* 2024; 10: 00227-2024 [DOI: 10.1183/23120541.00227-2024].

Received: 8 March 2024
Accepted: 21 March 2024

Abstract

Study question In large multinational patient surveys, spirometry (which requires repeated, reproducible maximal efforts) can be associated with cough, breathlessness and tiredness, particularly in those with idiopathic pulmonary fibrosis (IPF). Oscillometry is an effort-independent test of airways resistance and reactance. We hypothesised that oscillometry would take less time to perform and would be associated with reduced symptom burden than spirometry.

Patients and methods Spirometry and oscillometry were performed in 66 participants with IPF and repeated 2 weeks later. We compared time taken to perform tests, symptom burden and test–retest reliability with Bland–Altman plots and intraclass correlation coefficients (ICCs).

Results Oscillometry took significantly less time to perform than spirometry (mean −4.5 (99% CI −6.0 to −3.0) min) and was associated with lower symptom burden scores for cough (−1.3, 99% CI −1.7 to −0.8), breathlessness (−1.0, 99% CI −1.4 to −0.5), and tiredness (−0.5, 99% CI −0.9 to −0.2). On Bland–Altman analysis, all measures showed good agreement, with narrow limits of agreement and the mean bias lying close to 0 in all cases. The ICCs for forced expiratory volume in 1 s and forced vital capacity were 0.94 and 0.89, respectively, and ranged between 0.70 and 0.90 for oscillometry measures.

Conclusion Oscillometry is quicker to perform and provokes less symptoms than spirometry in patients with IPF.

Introduction

Respiratory oscillometry measures the mechanical properties of the respiratory system during tidal breathing by the application of an oscillating pressure signal, usually at the mouth. Improvements in computer processing speed have led to the development of commercial devices. Together with the publication of technical performance standards [1], there has been interest in the wider use of oscillometry in research settings and clinical practice [2], particularly in those who cannot perform spirometry.

As oscillometry does not require repeated maximal efforts and is independent of patient effort, potential advantages over spirometry might be a shorter time to perform the test and placing less symptomatic burden upon patients. In a large multinational patient survey, issues that were frequently rated as moderately or severely problematic with spirometry included cough, feeling tired and concerns about shortness of breath [3].

In people with idiopathic pulmonary fibrosis (IPF), decline in spirometry, particularly forced vital capacity (FVC), is associated with disease progression, and has frequently been adopted as a clinical trial end-point [4]. However spirometry may be particularly burdensome in IPF, with some patients unable to complete the manoeuvre at all and 26.7% reporting difficulty with spirometry [3]. FVC has also been used as a regulatory gatekeeper for therapy, meaning patients unable to perform the manoeuvre effectively can be denied therapy [5]. In IPF, it has been proposed that oscillometry may have potential value in staging disease severity and prognosis [6, 7].

The aims of the current study were to compare the performance time, symptom burden and test–retest reliability of oscillometry and spirometry in people with IPF referred for lung function testing. We hypothesised that oscillometry would take less time to perform and would be associated with reduced symptom burden than spirometry.

Materials and methods

Study subjects

Potential participants were screened from those referred for pulmonary function testing at the Royal Brompton Hospital between November 2020 and March 2022. The study was approved by the London Bridge Research Ethics Committee (20/LO/0970) and registered on ClinicalTrials.gov (NCT04572971). All participants gave written informed consent. Inclusion criteria were: 1) a diagnosis of IPF made by a specialist multidisciplinary team according to international standards [8]; and 2) ability to provide written informed consent. Exclusion criteria were any contraindication to performing conventional lung function tests [9].

Study design

Participants were asked to attend two research visits. Visit 1 was the day of scheduled spirometry performed as part of their routine clinical care. Respiratory oscillometry was conducted at the same visit and always prior to spirometry at every visit. Visit 2 was scheduled 2 weeks after visit 1. Oscillometry and spirometry assessments were repeated. The performance time of each assessment was recorded, and participants completed the same symptom burden questionnaire immediately after oscillometry and spirometry.

Based on previous local audit data, the performance time of a spirometry session was mean±SD 15±8 min. We estimated that 49 participants would be required to have a 95% chance of detecting, as significant at the 1% level, a decrease in performance time from 15 min for spirometry to 10 min for oscillometry. This significance level was chosen to account for the pre-planned multiple comparisons. To take into account 25% drop out, the minimum recruitment target was 66 participants.

Methods

Baseline spirometry was performed using Vyaire Vyntus BODY equipment (Vyaire Medical, Inc., Mettawa, IL, USA). Spirometry was performed according to American Thoracic Society/European Respiratory Society (ERS) 2019 updated Spirometry Technical Statement [10]. Per cent predicted and standardised residuals were calculated using (ethnicity-adjusted) reference equations from the Global Lung Function Initiative [11].

Impulse oscillometry (Vyaire Vyntus iOS; Vyaire Medical, Inc.) was performed according to ERS technical standards for respiratory oscillometry [1]. iOS equipment was verified using a 3-L syringe and reference module prior to each testing session. Participants were asked to make a tight seal with the lips on a mouthpiece whilst they wore a nosepeg and with their hands supporting their cheeks and the floor of the mouth. Acquisitions were made over 30 s during tidal breathing according to technical standards [1] with the view to recording at least three acceptable attempts (no leak at mouthpiece, occlusion from tongue, coughing or swallowing during recorded portion). Acquisitions were repeated until three attempts with a coefficient of variation <10% in area under the reactance curve (AX), resistance of the respiratory system at 5 Hz (R5) and resistance of the respiratory system at 20 Hz (R20) were recorded. The mean of these three attempts was used in the analysis. Variables recorded from oscillometry were: R5, R20, AX, reactance at 5 Hz (X5), resonant frequency (Fres) and total respiratory impedance (Z5). Per cent predicted and standardised residuals were calculated, where available, from the reference equations from Oostveen and colleagues [12]. All oscillometry measurements were performed by the same operator.

Performance time of the assessment was recorded using a stopwatch. Timing for each test was started when the instructions were given to the participant, and stopped when an acceptable test was obtained.

The symptom burden questionnaire was created and designed by eight members of a patient advisory group, all of whom had chronic respiratory disease and had undergone previous spirometry testing. The patient advisory group used the results of a previous multi-country survey conducted by the European Lung Foundation [3] to develop the components of the questionnaire. The design was determined by presenting the patient advisory group with five established and validated respiratory health related quality of life questionnaires to review: the COPD Assessment Test, Chronic Respiratory Questionnaire, King's Brief Interstitial Lung Disease, St. George's Respiratory Questionnaire and the Leicester Cough Questionnaire. The final questionnaire was designed to be self-administered on paper, and comprised six simple statements relating to cough, breathlessness, clarity on how to perform the test, tiredness, ease of performing the test and confidence in the technician. The design was based on the COPD Assessment Test but comprised a scale from 1–5 (rather than 0–5 in the COPD Assessment Test), where 1 was lowest level of symptoms and 5 was the highest level of symptoms (figure 1).

Impulse oscillometry (iOS)

Didn't make me cough	1 2 3 4 5	Made me a cough a lot
Didn't make me feel breathless	1 2 3 4 5	Made me feel very breathless
I was clear about what I was expected to do	1 2 3 4 5	I was not clear about what I was expected to do
Didn't make me feel tired	1 2 3 4 5	Made me feel very tired
I found it easy to perform the test	1 2 3 4 5	I found it difficult to perform the test
I felt confident in the technician	1 2 3 4 5	I didn't feel confident in the technician

Spirometry

Didn't make me cough	1 2 3 4 5	Made me a cough a lot
Didn't make me feel breathless	1 2 3 4 5	Made me feel very breathless
I was clear about what I was expected to do	1 2 3 4 5	I was not clear about what I was expected to do
Didn't make me feel tired	1 2 3 4 5	Made me feel very tired
I found it easy to perform the test	1 2 3 4 5	I found it difficult to perform the test
I felt confident in the technician	1 2 3 4 5	I didn't feel confident in the technician

FIGURE 1 Symptom Burden Questionnaire.

Analysis

Statistical analysis was performed using Graphpad Prism 10 (GraphPad Software, Boston, MA, USA) and Stata 18 BE (StataCorp LLC, College Station, TX, USA).

Performance time and symptom burden for spirometry and iOS were compared using paired-t-test. The relationship between oscillometry and spirometry variables were analysed using Pearson R correlation coefficient. Agreement between measures taken at visit 1 and visit 2 were assessed using Bland–Altman plots, and correlations between the measures taken at the two timepoints. Intraclass correlation coefficients (ICCs) were calculated for spirometry measures (FVC and forced expiratory volume in 1 s (FEV_1)) and for all oscillometry measures. To compare the test–retest reliability of FVC (the spirometric variable most widely used to assess disease severity and progression in IPF) with iOS variables, we performed a z-test on Fisher z-transformed correlation coefficients [13].

Results

201 people with a diagnosis of IPF were approached. Reasons for non-recruitment included: death or hospitalisation before first visit (n=10), declined to participate in research (n=36), did not want to attend two visits (n=38), unable to contact (n=12), clinical lung function appointment cancelled (n=16), unable to provide informed consent (n=7), unable to perform spirometry (n=1), researcher unavailable (n=3). 66 participants consented and returned for visit 2, with a mean±SD of 18±7 days between visits. Two of the 66 participants who returned for visit 2 were unable to provide spirometry values: one due to recent cataract surgery (contraindicated: <1 week since procedure), and one due to persistent cough during all spirometry attempts resulting in no accurate results being obtained.

Baseline characteristics of the 66 participants are described in table 1.

TABLE 1 Baseline characteristics (n=66)

Age years	73.2±7.6
Sex, male	56 (85)
Body mass index kg·m^{-2}	27.6±5.0
MRC dyspnoea score	3±2
Antifibrotic use	37 (56)
Smoking history	
Never	31 (46)
Current	3 (4.5)
Ex-smoker	32 (48.5)
FEV_1 L	2.21±0.53
FEV_1 % predicted	83.8±21.6
FEV_1 SR	−1.00±1.20
FVC L	2.74±0.77
FVC % predicted	79.8±22.3
FVC SR	−1.29±1.37
FEV_1:FVC	0.80±0.08
PEF L·s^{-1}	8.32±1.88
Z5 kPa·L^{-1}·s^{-1}	0.40±0.12
X5 kPa·L^{-1}·s^{-1}	−0.12±0.06
X5 % predicted	113.0±55.0
R5 kPa·L^{-1}·s^{-1}	0.38±0.12
R5 % predicted	137.3±42.9
R20 kPa·L^{-1}·s^{-1}	0.28±0.07
R20 % predicted	107.0±23.2
R5-R20 kPa·L^{-1}·s^{-1}	0.10±0.08
AX kPa·L^{-1}	1.02±0.89
Fres Hz	18.90±5.47
Fres % predicted	150.9±50.3

Data are presented as n (%) or mean±SD. Per cent predicted and standardised residuals for FEV_1 and FVC were calculated using the Global Lung Function Initiative reference equations. Per cent predicted and standardised residuals for oscillometry measures were calculated, where available, from the reference equations from Oostveen and colleagues [12]. MRC: Medical Research Council; FEV_1: forced expiratory volume in 1 s; SR: standardised residual; FVC: forced vital capacity; PEF: peak expiratory flow; Z5: impedance at 5 Hz; X5: reactance at 5 Hz; R5: resistance at 5 Hz; R20: resistance at 20 Hz; AX: area under the reactance curve; Fres: resonant frequency.

TABLE 2 Comparison between mean patient symptom scores during oscillometry and spirometry, and mean time taken to perform the test

	Oscillometry, mean±SD	Spirometry, mean±SD	Difference mean (99% CI)
Time taken to perform test min	7.0±2.3	11.5±4.5	−4.5 (−6.0 to −3.0)
Cough during test	1.1±0.5	2.4±1.4	−1.3 (−1.7 to −0.8)
Breathlessness during test	1.5±0.1	2.4±1.2	−1.0 (−1.4 to −0.5)
Tiredness during test	1.1±0.6	1.7±1.1	−0.5 (−0.9 to −0.2)
Understanding of how to perform the test	1.0±0.2	1.1±0.3	0.0 (−0.2 to 0.1)
Ease of performing test	1.1±0.4	2.3±1.3	−1.2 (−1.6 to −0.8)
Confidence in technician	1.1±0.5	1.2±0.8	−0.1 (−0.3 to 0.1)

Oscillometry took significantly less time to perform than spirometry (table 2) and was associated with lower symptom burden scores for cough, breathlessness and tiredness (table 2). Oscillometry was also reported by participants as being easier to perform than spirometry (table 2). Subgroup analysis did not see any difference in time taken to perform the tests or symptom burden scores between those with the lowest quartile FVC % predicted (mean FVC 52.9% predicted) and those with FVC % predicted above the lowest quartile (mean FVC 88.6% predicted) (supplementary table S1).

Relationship between oscillometry and spirometry measures

The relationship between the oscillometry and spirometry measures are summarised in table 3. AX was the oscillometry parameter with the strongest correlation with FVC (r= −0.638) and FEV_1 (r= −0.632).

Test–retest reliability

On Bland–Altman analysis, FEV_1, FVC, Z5, X5, R5, R20, AX and Fres showed good agreement of measures taken 2 weeks apart, with narrow limits of agreement and most values lying between this (figure 2). The plots also demonstrated even spread, with no heteroskedasticity and the mean bias lying close to 0 in all cases (table 4).

From the spirometry performed at visit 2 (n=66), mean±SD coefficient of variation of the three closest FEV_1, FVC and peak expiratory flow attempts were 2.35±2.21%, 2.48±2.77% and 6.22±5.62%, respectively. The mean±SD coefficient of variations for oscillometry parameters were 3.51±2.32%, 12.12±10.32%, 4.19±2.56%, 4.88±3.03%, 7.07±2.94% and 3.59±2.44% for Z5, X5, R5, R20, AX and Fres, respectively.

There was also good correlation between the measures taken 2 weeks apart. R (95% CI) for FEV_1, FVC, Z5, X5, R5, R20, AX and Fres were 0.968 (0.947–0.981), 0.957 (0.929–0.975), 0.842 (0.750–0.902), 0.894 (0.829–0.935), 0.828 (0.730–0.893), 0.775 (0.652 to 0.859), 0.877 (0.803–0.924) and 0.781 (0.661–0.863), respectively (figure 3).

The ICCs for FEV_1 and FVC were 0.94 and 0.89, respectively. The ICCs for oscillometry measures Z5, R20, R5, X5, AX and Fres were 0.87, 0.80, 0.74, 0.89, 0.90 and 0.86, respectively. Compared with the ICC for FVC, there were no significant differences in ICC for Z5, R20, X5, AX and Fres (all p>0.05). However the ICC for R5 was lower than for FVC (p=0.0081; 95% CI 0.122–0.675).

TABLE 3 Pearson R correlations between oscillometry and spirometry parameters

	FEV_1 L	FVC L	PEF $L{\cdot}s^{-1}$	FEV_1:FVC	MEF75 $L{\cdot}s^{-1}$	MEF50 $L{\cdot}s^{-1}$	MEF25 $L{\cdot}s^{-1}$
Z5 $kPa{\cdot}L^{-1}{\cdot}s^{-1}$	−0.581**	−0.450**	−0.486**	−0.051	−0.384**	−0.331*	−0.075
R20 $kPa{\cdot}L^{-1}{\cdot}s^{-1}$	−0.331*	−0.195	−0.422**	−0.160	−0.455**	−0.350**	−0.020
R5 $kPa{\cdot}L^{-1}{\cdot}s^{-1}$	−0.507**	−0.391*	−0.448**	0.050	−0.391**	−0.288*	−0.049
X5 $kPa{\cdot}L^{-1}{\cdot}s^{-1}$	0.577**	0.482**	−0.460**	0.046	0.300*	−0.286*	0.150
AX $kPa{\cdot}L^{-1}$	−0.665**	−0.634**	−0.541**	0.132	−0.321*	−0.195	−0.130
Fres Hz	−0.548**	−0.498**	−0.325*	0.111	−0.209	−0.185	−0.085

FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; PEF: peak expiratory flow; MEF75: maximum expiratory flow at 75% vital capacity; MEF50: maximum expiratory flow at 50% vital capacity; MEF25: maximum expiratory flow at 25% vital capacity; Z5: impedance at 5 Hz; R20: resistance at 20 Hz; R5: resistance at 5 Hz; X5: reactance at 5 Hz; AX: area under the reactance curve; Fres: resonant frequency. *: p<0.05; **: p<0.01.

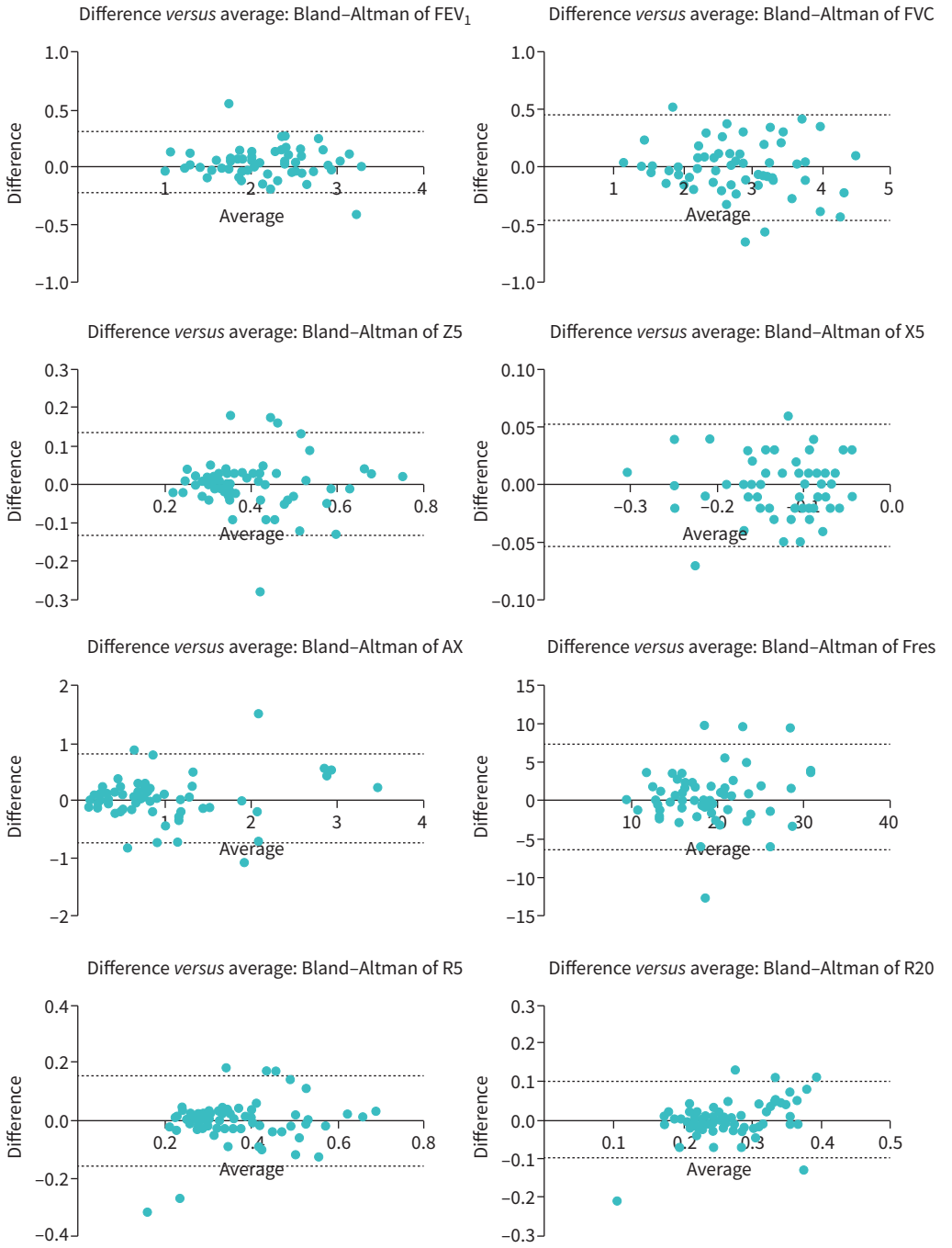

FIGURE 2 Bland–Altman plots to show agreement between oscillometry and spirometry measurements taken 2 weeks apart. FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; Z5: impedance at 5 Hz; X5: reactance at 5 Hz; AX: area under the reactance curve; Fres: resonant frequency; R5: resistance at 5 Hz; R20: resistance at 20 Hz.

Discussion

This study demonstrates that respiratory oscillometry takes less time to perform and provokes less symptoms than spirometry in people with IPF. Test–retest reliability of oscillometry measures were excellent, with reactance measures having a similar ICC to FVC. Due to the simplicity and low patient burden associated with the procedure, the data would support further exploration of the potential of respiratory oscillometry as a longitudinal measure of lung mechanics in people with IPF.

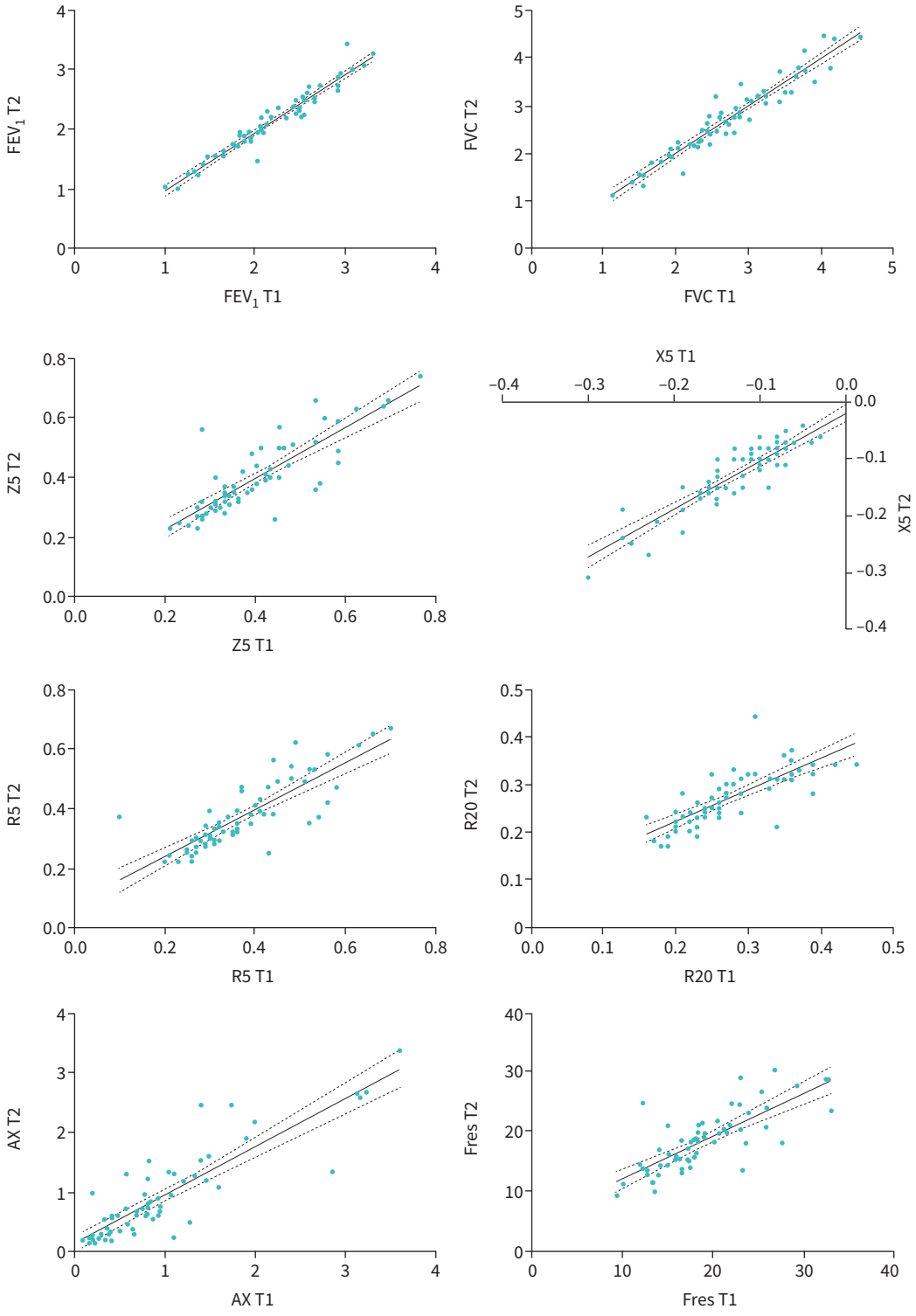

FIGURE 3 Correlations between measurements taken at visit 1 (T1) and visit 2 (T2). FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; Z5: impedance at 5 Hz; X5: reactance at 5 Hz; AX: area under the reactance curve; Fres: resonant frequency; R5: resistance at 5 Hz; R20: resistance at 20 Hz.

In individuals with IPF, there is an excessive production of extracellular matrix within the lungs, resulting in a gradual development of fibrosis, the loss of lung units and increased stiffness of the lung tissue. These factors collectively contribute to a reduction in FVC, and change in FVC is the most commonly used

TABLE 4 Bland–Altman mean±SD bias and 95% limits of agreement for measures taken 2 weeks apart

Variable	Mean±SD bias	95% limits of agreement
FEV_1 L	0.043±0.137	−0.225 to 0.311
FVC L	−0.001±0.231	−0.452 to 0.451
Z5 $kPa \cdot L^{-1} \cdot s^{-1}$	0.001±0.068	−0.133 to 0.135
X5 $kPa \cdot L^{-1} \cdot s^{-1}$	−0.0003±0.027	−0.053 to 0.053
R5 $kPa \cdot L^{-1} \cdot s^{-1}$	−0.005±0.079	−0.160 to 0.151
R20 $kPa \cdot L^{-1} \cdot s^{-1}$	0.001±0.051	−0.098 to 0.100
AX $kPa \cdot L^{-1}$	0.042±0.391	−0.723 to 0.808
Fres Hz	0.538±3.498	−6.318 to 7.393

FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; Z5: impedance at 5 Hz; X5: reactance at 5 Hz; R5: resistance at 5 Hz; R20: resistance at 20 Hz; AX: area under the reactance curve; Fres: resonant frequency.

end-point in clinical trials [4]. Although it is a noninvasive measure, spirometry does require repeated forced maximal manoeuvres and is dependent on patient effort.

X5, the reactance at 5 Hz and AX, the area of reactance, are parameters that comprise two components, inertance and elastance. Reactance refers to how easily the lung can respond to changes in airflow during breathing; inertance is related to the lung's resistance to changes in airflow velocity, especially during quick breaths, and elastance refers to the elastic properties of the lung, that is, the lung's ability to bounce back or resist stretching when air is breathed in. As the elastic properties of the lung are predominantly impacted in the peripheral airways, X5 is dependent on lung volume and X5 becomes "more negative" in fibrotic lung diseases when compared to health [14]. AX is an integrative measure that evaluates reactance over a range of frequencies, but is dominated by the lower frequency components of reactance and therefore determined predominantly by elastance. It has the advantage of having positive rather than negative units, and increases with fibrotic lung disease [15]. Therefore, a loss of lung volume on spirometry, *e.g.* fall in FVC, would also result in a more negative X5 or more positive AX. Our study confirms previous findings to demonstrate moderate strength correlations between spirometric variables and X5 and AX in IPF [7, 15–17].

Limited research has been performed on the burden of spirometry from a patient-focused perspective. Qualitative work from a primary care setting in France reported participants describing the spirometry test as "strange, unsettling and painful" [18]. In an international survey organised by the European Lung Foundation, a significant proportion of the 1760 respondents rated several symptoms as moderately or seriously problematic during spirometry: "being told to keep blowing when they felt nothing is coming out" (31.4%), coughing (30.4%), tiredness (26.3%) and shortness of breath (20.1%) [3]. In this survey, people with IPF were particularly highlighted as a group who found spirometry problematic, with 26.7% finding it not acceptable (compared with 17% for all respondents) [3]. This is corroborated by observations from clinical trials where missing follow-up FVC data occurs in about 20% of participants with IPF [19, 20].

Respiratory oscillometry measures the mechanical properties of the respiratory system during quiet tidal breathing by the application of an oscillating pressure signal (input or forcing signal), most commonly at the mouth. As it does not require repeated forced manoeuvres, it has been proposed that oscillometry may have some advantages over spirometry in terms of reduced performance time and less burden on the patient. However, until now there has been little objective data to support this claim. To our knowledge, this is the first study to quantitatively compare performance time and symptom burden of oscillometry and spirometry, and the first to quantify test–retest reliability of oscillometry specifically in IPF. Other strengths of the study include an adequately powered sample size and the active involvement of patients in the study through the design of the symptom burden questionnaire.

There were limitations. This was a single centre study, using one specific oscillometry measuring device, in people with IPF. Therefore, the results need to be corroborated by data from other centres, on other oscillometry devices and in other patient groups. Due to the nature of the procedures and the outputs from spirometry and oscillometry, it was not possible to blind participants or researchers. As there are no validated instruments to assess symptom burden associated with pulmonary function tests, we used a co-design approach with patients to develop a short questionnaire. This was completed by all the participants in the study without assistance and was sufficiently sensitive to detect a quantifiable difference in symptom burden between oscillometry and spirometry. Whereas participants were naïve to oscillometry,

they were well accustomed to spirometry, and this may have led to a selective study population and introduced bias to our results (but in favour of spirometry). Previous familiarity with spirometry may also potentially explain why the test–retest reliability of oscillometry was not better than spirometry, despite oscillometry being less burdensome for participants. This is confirmed by the few patients unable to perform reproducible spirometry at visit 2 (two out of 66).

Our study has focused on specific aspects of oscillometry testing (namely performance time, symptom burden, test–retest reliability). We also showed that oscillometry parameters show moderate strength correlations with FVC in this cohort of individuals with IPF, corroborating previous cross-sectional observational studies [15, 16, 21]. There is increasing data to support oscillometry as a potentially useful clinical tool in IPF. Mori and colleagues [6] demonstrated that reactance measures may predict lung function decline in patients with IPF, whilst Ishikawa *et al.* [7] demonstrated that X5, Fres and AX had a significant impact on survival independent of age, sex and other prognostic factors. Further studies are needed to establish the potential clinical value of oscillometry in IPF. However, given the simplicity of the procedure as well as the low symptom burden for patients, we speculate that oscillometry may find a role providing supplementary information to spirometry (for example regarding prognosis), or as an alternative means of monitoring lung function in patients with IPF unable to perform spirometry.

In summary, our study has demonstrated that respiratory oscillometry is quicker to perform and provokes less symptoms (such as cough, shortness of breath and fatigue) than spirometry in people with IPF and has excellent test–retest reliability. We propose that oscillometry has potential as a longitudinal measure of lung mechanics in IPF.

Provenance: Submitted article, peer reviewed.

Ethics statement: Research ethics committee and health research authority approval was sought and obtained prior to the start of the study (20/LO/0970). The study was registered at www.clinicaltrials.gov prior to starting (NCT04572971).

Conflict of interest: S. Patel reports a National Institute for Health and Care Research Clinical Doctoral Fellowship (NIHR 300566) paid to their institution since the initial planning of this work. K.P. Sylvester reports the loan of a Resmon Pro FOT device to their institution *via* ResTech in the past 36 months. Z. Wu has nothing to disclose. S. Rhamie has nothing to disclose. P. Dickel has nothing to disclose. T.M. Maher reports consulting fees from Boehringer Ingelheim, Roche/Genetech, AstraZeneca, Bayer, Blade Therapeutics, Bristol-Myers Squibb, CSL Behring, Galapagos, Galecto, GlaxoSmithKline, IQVIA, Pfizer, Pliant, Respivant, Sanofi, Theravance, Trevi, Veracyte and Vicore; and participation on data safety monitoring or advisory boards for Fibrogen, Blade Therapeutics and Nerre, all in the past 36 months. P.L. Molyneaux reports a grant from AstraZeneca paid to his institution since the planning of this work; advisory board fees from Hoffman–La Roche, Boehringer Ingelheim, AstraZeneca, Trevi and Qureight, and speaker fees from Boehringer Ingelheim and Hoffman–La Roche, in the past 36 months; and is an associate editor of this journal. P.M.A. Calverley has nothing to disclose. W.D-C. Man reports a National Institute for Health Research Artificial Intelligence Award paid to his institution since the initial planning of this work; and is Honorary President of the Association of Respiratory Technology and Physiology, and an associate editor of this journal.

Support statement: This research was supported by the National Institute for Health and Care Research Clinical Research Facility at Guy's and St Thomas' NHS Foundation Trust. Funding information for this article has been deposited with the Crossref Funder Registry.

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