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The Reliability of a Novel Structured Testing Device for Single-breath Lung Carbon Monoxide Uptake: A Randomized Comparison Crossover Study

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Abstract

Background With the development and market launch of several new domestic lung diffusing capacity testing instruments, the clinical reliability of the MeHow MeAir 9000 spirometer, featuring a novel turning valve structure, needs to be validated.

Objective To evaluate the clinical reliability of lung diffusing capacity measurements using the MeHow MeAir 9000 spirometer.

Methods This study included 166 participants: 30 healthy individuals, 68 with interstitial lung disease (ILD), and 68 with chronic obstructive pulmonary disease (COPD). Using a crossover design, participants underwent lung diffusing capacity tests with both the MeHow MeAir 9000 and Jaeger MasterScreen Diffusion spirometers, following the 2017 ERS/ATS standards. The primary indicator was the diffusing capacity for carbon monoxide (D_{LCO}), with the diffusion capacity of carbon monoxide as a percentage of the predicted value (D_{LCO} %pred) as the main categorical indicator. Secondary indicators included D_{LCO} to alveolar volume ratio (D_{LCO} / V_A), alveolar volume (V_A), inspired volume (V_I), breath-hold time (tBH), fractional concentration of inhaled carbon monoxide (F_{ICO}), fractional concentration of inhaled methane (F_{ICH4}), fractional concentration of carbon monoxide in the alveolar space (F_{ACO}), and fractional concentration of methane in the alveolar space (F_{ACH4}). Consistency analysis was performed on the measurements and the classification of lung diffusing capacity impairment severity from both instruments. Additionally, scatter plots and coefficient of variation (CV%) for inhaled carbon monoxide (CO) and methane (CH4) concentrations were analyzed, along with simulator (Hans Rudolph, Kansas City, MO) test results.

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Results D_{LCO}'s Bland-Altman plot showed 95.0% of data points within the 95% CI, with a CCC of 0.988. In the D_{LCO} %pred classification, the ICCs for the ILD group and the COPD group were 0.940 and 0.975, respectively, while the ICC for the healthy subject group was 0.931. These results indicate good consistency for the primary outcome measures. Secondary indicators had varying CCCs, indicating fair to poor consistency ($P < 0.05$). Scatter plots and CV% for inhaled CO and CH4 concentrations suggested better stability of MeAir over MasterScreen. Simulator test results showed MeAir had a CO error range of -3.80% to -1.00% and CH4 error range of -0.50–1.00%, while MasterScreen had a CO error range of -2.53–0.00% and CH4 error range of -1.83% to -0.63%, indicating superior CO detection by MasterScreen and better CH4 detection by MeAir.

Conclusion The MeHow MeAir 9000 spirometer provides high accuracy measurements of lung diffusing capacity and reliable assessment of the severity of diffusing capacity impairment, making it suitable for clinical use.

Clinical trial number Not applicable.

Keywords Pulmonary diffusion function, D_{LCO}, D_{LCO} %pred, Measurement accuracy, Degree of pulmonary dispersion dysfunction, Novel structure, Equipment

Introduction

Pulmonary diffusion capacity refers to the process where gases such as oxygen diffuse through the alveolar-capillary membrane from the alveoli to the capillaries, eventually entering the bloodstream and binding with hemoglobin in red blood cells. Clinically, carbon monoxide(CO) is commonly used as a test gas to assess this function [1], and in diffusion function tests, the tracer gases commonly used are helium (He) and methane (CH4) [2]. The key indicator of diffusion function testing is the Diffusing Capacity of the Lung for Carbon Monoxide (D_{LCO}). The factors affecting it include the concentration of the test gas as well as the inspired volume (V_I), breath-hold time (tBH), environmental factors (including ambient temperature (T), barometric pressure (PB), and the partial pressure of water vapor (PH2O)), and alveolar volume (V_A) [2, 3].

Diffusion function testing of the lungs is widely used in the medical field to assess the condition of lung diseases [4–6]. As the application scope of this test continues to expand, it has been used for diagnosing and monitoring early chronic obstructive pulmonary disease (COPD) [7], distinguishing COPD from asthma [8], and evaluating the therapeutic effects and predicting the prognosis of interstitial lung disease (ILD) [9]. Therefore, the importance of lung diffusion function testing is increasingly highlighted.

Currently, although the market relies heavily on imported lung diffusion function testing equipment, especially the Jaeger MasterScreen Diffusion device (Vyaire Medical, Germany) (hereafter referred to as MasterScreen), which is widely used for its high reliability and authority, domestic lung function equipment is also continuously improving. Now, there are domestic lung function testing systems capable of performing lung diffusion function tests. Unlike the traditional imported MasterScreen, the new domestic MeHow MeAir 9000 device (MeHow Medical Technology Co., China) (hereafter referred to as MeAir) adopts an innovative valve-turning diffusion function module and is equipped with a software system that assists with an exhalation platform and indicator lines. The system can display the auxiliary line of the expiratory platform and automatically control the steering valve when the expiratory flow velocity drops to 0.025 L/s. When the residual gas volume is reached, the air valve is closed, and the diffusion test gas valve is opened. This system can not only standardize the standard of cooperative inspection between the operator and the subject, but also ensure the stability of the inhaled gas concentration, to ensure the accuracy of the measurement of pulmonary dispersion function. The purpose of this study is to comprehensively evaluate the applicability of the MeAir lung diffusion function system in different populations. We plan to perform lung diffusion function tests with the MeAir lung function device and the German MasterScreen lung diffusion function device in populations with restrictive ventilatory dysfunction, obstructive ventilatory dysfunction, respiratory diseases, and healthy individuals. The results will be analyzed and compared to assess the effectiveness of this new lung function instrument's diffusion function system in clinical use.

Methods

According to the established inclusion and exclusion criteria, a single-center randomized crossover trial was conducted among pulmonary function test subjects at the First Affiliated Hospital of Guangzhou Medical University from June 15, 2023, to September 1, 2023.

Participants

The plan is to recruit 166 participants, divided into a COPD group with 68 cases, an ILD group with 68 cases, and a healthy control group with 30 cases who have no pulmonary diseases. There are no restrictions on the severity or the state of respiratory diseases of the

participants. According to the 2017 European Respiratory Society/American Thoracic Society (ERS/ATS) technical standards for lung diffusion function testing, participants who meet the indications for pulmonary function testing and are excluded from the contraindications for pulmonary function testing will be enrolled [10]. According to the randomized crossover procedure, lung diffusion function tests will be completed using both the MasterScreen device and the MeAir device.

Randomization and single-blind

We used simple randomization to assign study participants to begin measurements with either the MasterScreen or MeAir device. A computer-generated list of random numbers was created by an independent person not involved in the study, using the randomization tool in SPSS version 26.0. The list contained a total of 166 numbers, which were either 1 or 2. The number 1 indicated that the participant started with the MasterScreen device, while the number 2 indicated that the participant started with the MeAir device. In this study, a single-blind method was also used for the examination of participants, meaning that the participants were unaware of their randomization numbers under which the tests were conducted. Additionally, in the study design, participants were eventually able to learn the results of their own pulmonary function test from either lung function device.

Quality control

Before the start of the study, both lung function devices underwent technical checks and rigorous quality control by the technicians or service providers. To ensure the acquisition of high-quality measurement results, we calibrated both devices according to the 2017 ERS/ATS technical standards for lung diffusion function testing before each day's measurements [10]. Before starting the examination each day, we first calibrated the environmental factors such as PB, T, and PH2O. Subsequently, both lung function devices were manually calibrated using three-flow measurements and a standard 3.0 L syringe. In addition to volume calibration, the gas concentrations of the test gases, carbon monoxide and methane, were also calibrated.

All pulmonary function tests were completed by 9 senior technicians specialized in pulmonary function, with each participant's two tests conducted by the same professional. The testing process was carried out according to the 2017 ERS/ATS technical standards for lung diffusion function testing [10].

Measurement protocol

All measurements were conducted on both MasterScreen and MeAir devices. During the assessment of lung ventilation and diffusion functions, participants were asked to maintain a seated position to avoid any effects on diffusion capacity measurements due to changes in cardiac output [11, 12]. In accordance with the 2017 ERS/ATS technical standards for lung diffusion function testing, the quality control criteria for the lung diffusion function test are as follows [10]:

Acceptability

- The V_I must be ≥ 85% of the vital capacity (VC).
- The V_A must be within 200 ml or 5% of the V_A from the previous acceptable diffusion maneuver (whichever is larger).
- The inhalation of the test gas to achieve 85% must be completed within 4.0 s.
- The tBH should be 10 ± 2 s without leaks, Muller maneuvers (increasing negative thoracic pressure by forcefully inhaling with the glottis closed), and Valsalva maneuvers (increasing positive thoracic pressure by forcefully exhaling with the glottis closed). The oral pressure change during the breath hold should not exceed ± 3 kPa.
- The exhalation time should be less than 4.0 s to exclude anatomical dead space and allow for appropriate alveolar gas sampling.

Repeatability

- At least two acceptable D_{LCO} measurements should be within 2 $mL{\cdot}min^{-1}{\cdot}mmHg^{-1}$ of each other.
- No more than five measurements should be taken.
- The inhalation of the test gas to achieve 85% must be completed within 4.0 s.
- There should be at least a 4-minute interval between two measurements on the same spirometer.

Study end-points

To analyze the consistency of the diffusion function systems of the two lung function devices, we need to collect and analyze factors that affect the outcomes. According to the formulas for calculating D_{LCO} and V_A (Eqs. 1 and 2), we can understand that the main influencing factors include: volume of equipment dead (Vdequip), volume of anatomical dead (Vdanat), fractional concentration of inhaled carbon monoxide (F_{ICO}), fractional concentration of inhaled methane (F_{ICH4}), fractional concentration of carbon monoxide in the alveolar space (F_{ACO}), fractional concentration of methane in the alveolar space (F_{ACH4}), and environmental factors such as T and PB.

It is worth noting that there are some unavoidable human factors during the diffusion function check that may lead to uncontrollable differences in tBH between MeAir and MasterScreen, and we have indeed found such a situation in our statistics (Table 1). Although tBH

Table 1 Intrasession variability characteristics and compliance rates for the F_{ICO} and F_{ICH4} of Masterscreen and MeAir

Gas	Variables	MasterScreen	MeAir
F_{ICO}	Measured value	0.295(0.291,0.299)	0.298(0.296,0.300)
	Min-Max	0.262–0.310	0.287–0.305
	CV	2.6%	1.2%
	Measurement error	-12.667%~1.667%	-4.333%~1.667%
	The proportion of acceptable	57/160(35.63%)	101/160(63.13%)
F_{ICH4}	Measured value	0.301(0.297,0.305)	0.299(0.295,0.301)
	Min-Max	0.266–0.314	0.287–0.304
	CV	3.0%	1.2%
	Measurement error	-11.333%~4.667%	-4.333%~1.333%
	The proportion of acceptable	69/160(43.13%)	107/160(66.88%)

The target gas concentration is 0.3%. As the data distribution of inhaled gas (both the two devices) do not conform to the normal distribution, so data are presented as median (P25,P75) and minimum to maximum. F_{ICO} (%): fractional concentration of Inspired carbon monoxide; F_{ICH4} (%): fractional concentration of Inspired methane; CV: coefficient of variation; The measurement error is calculated by the difference between the minimum gas concentration and maximum gas concentration to the target gas concentration as a percentage of the target gas concentration. The proportion of acceptable is the ratio where the measurement error is within 1%

is an influencing factor in the D_{LCO} calculation formula, our previous research has found that after a breath-hold time of 8 s, the D_{LCO} results show no significant relationship with tBH [13, 14]. Moreover, by ensuring that all participants have a stable breath-hold time of over 8 s, tBH does not affect the comparison of the main observation index, D_{LCO}, between the two devices.

$$D_{\mathrm{LCO}} = \frac{V_{\mathrm{ASTPD}}}{t_{\mathrm{BH}} \cdot (P_{\mathrm{B}} - 47)} \cdot \ln\left(\frac{F_{\mathrm{ICO}}}{F_{\mathrm{ACO}}} \cdot \frac{F_{\mathrm{ATr}}}{F_{\mathrm{ITr}}}\right) \cdot 60,000 \quad (1)$$

$$V_{\mathrm{ABTPS}} = (V_{\mathrm{IATPD}} - V_{\mathrm{Dequip}} - V_{\mathrm{Danat}}) \cdot \frac{F_{\mathrm{ITr}}}{F_{\mathrm{ATr}}} \cdot \frac{P_{\mathrm{B}}}{(P_{\mathrm{B}} - 47)} \cdot \frac{310}{(273 + T)} \quad (2)$$

To integrate the clinical application of lung diffusion function tests, we referred to international technical guidelines for lung diffusion function and graded the diffusion dysfunction severity of the D_{LCO} %pred measured in the two disease groups into four levels: normal (D_{LCO} %pred ≥ 80%), mild (80% > D_{LCO} %pred ≥ 60%), moderate (60% > D_{LCO} %pred ≥ 40%), and severe (40% > D_{LCO} %pred) [10].

Ultimately, we identified the main quantitative observation indicators for comparing the accuracy of the diffusion checks of the two lung function devices as follows: D_{LCO}; secondary quantitative observation indicators include: D_{LCO} to alveolar volume ratio (D_{LCO} /V_A), V_A, F_{ICO}, F_{ICH4}, F_{ACO}, F_{ACH4}, tBH, and V_I.

The main qualitative observation indicator for assessing the diffusion dysfunction of pulmonary disease is the grade of diffusion dysfunction based on the percentage of the measured carbon monoxide diffusing capacity to the predicted value (D_{LCO} %pred).

Statistical analysis and sample size calculation

We utilized MedCalc and SPSS 26.0 statistical software for data analysis. The normality of the data was tested using the Kolmogorov-Smirnov test. If the data conform to a normal distribution, the quantitative data are represented as (x ± s); if it does not conform to a normal distribution, they are represented as M (P25, P75).

For quantitative data such as test results, we used the concordance correlation coefficient (CCC) to analyze and compare the results of the Primary and Secondary end-points. Bland-Altman plots were also analyzed the Primary end-point with bias estimates and 95% limits of agreement.

The interpretation of correlation from the CCC is as follows: a value less than 0.90 indicates poor strength of agreement, 0.90–0.95 indicates moderate strength of agreement, 0.95–0.99 indicates high strength of agreement, and greater than 0.99 indicates almost perfect agreement. Additionally, if the 95% confidence interval of the result includes 0, it indicates that the result is not statistically significant [15].

For categorical data such as the severity of disease diffusion, we used the intraclass correlation coefficient (ICC) (model: two-way mixed; type: absolute agreement) for analysis and comparison. Values less than 0.5 indicate poor reliability, values between 0.5 and 0.75 indicate moderate reliability, values between 0.75 and 0.9 indicate good reliability, and values greater than 0.90 indicate excellent reliability, with $p < 0.05$ considered statistically significant [16]. Additionally, we compared the recognition ability of the two lung function devices for the concentration of inhaled gases through the central tendency of the scatter plots and by calculating the coefficient of variation (CV) using the root mean square (RMS) method.

With the CCC for Power set at 0.95 and the Lower Boundary at 0.9, and the statistical power reaching 0.99, we need to include at least 124 participants for the analysis of the observation indicators (calculated using PASS 2021). Furthermore, considering a dropout rate of 20%, our goal is to recruit at least 150 participants in total.

Results

This study included a total of 136 patients and 30 normal individuals (Fig. 1). Among them, 68 were patients with ILD and 68 were patients with COPD. Among these patients, one ILD patient was excluded due to low lung capacity (< 1 L) which resulted in an inability to tolerate the breath-holding time, one COPD patient was excluded due to poor cooperation as they could not provide valid data on the Jaeger device, and one COPD patient

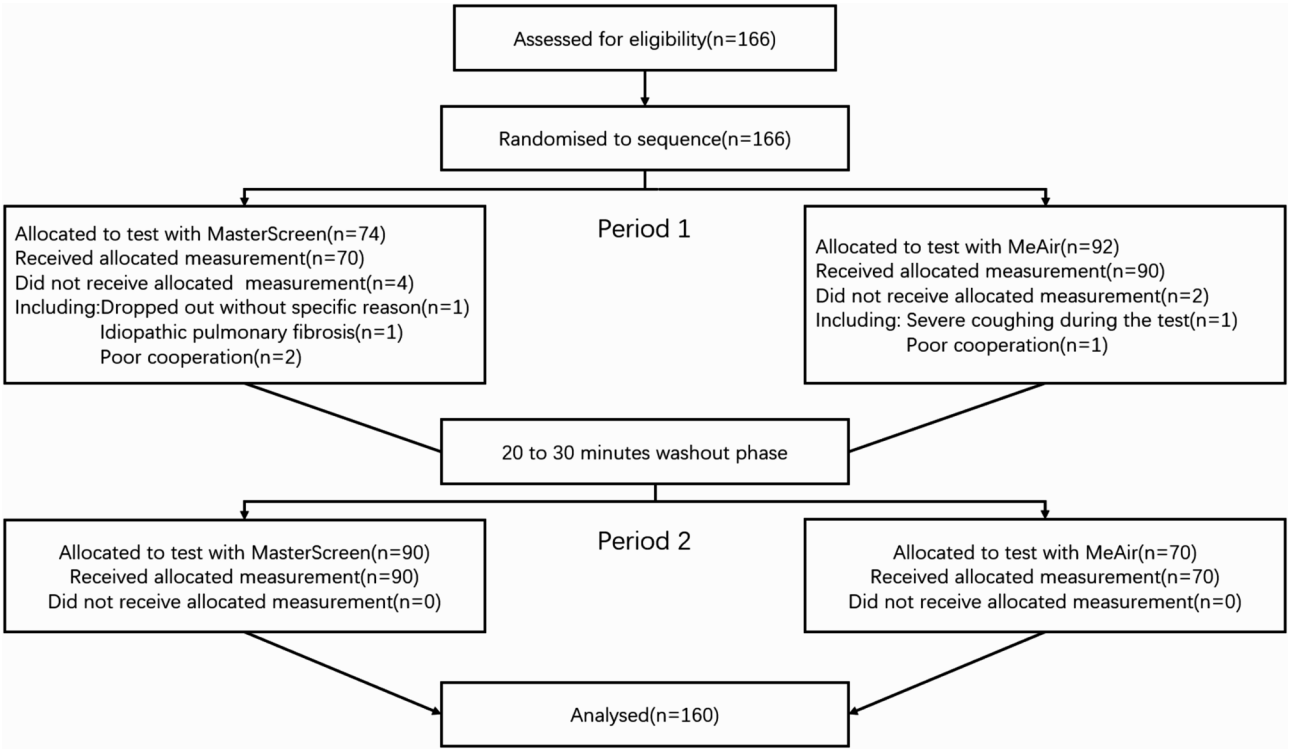

Fig. 1 MeAir flow chart

Table 2 Baseline demographic and clinical characteristics by sequence and by total

Characteristics	MasterScreen-MeAir	MeAir-MasterScreen	*P*-value	Overall
Participants, n (%)	70 (43.8)	90 (56.2)	N/A	160 (100)
Sex, n (%)				
Male	43 (61.4)	60 (66.7)	0.468	103 (64.4)
Female	27 (38.6)	30 (33.3)		57 (35.6)
Age years (Min ~ Max)	55.4 ± 15.2 (24 ~ 82)	52.7 ± 15.6 (19 ~ 84)	0.278	53.9 ± 15.4 (19 ~ 84)
Height cm	161.7 ± 7.3	162.9 ± 6.4	0.282	162.4 ± 6.8
Weight kg	59.3 ± 10.8	61.7 ± 12.0	0.196	60.6 ± 11.5
BMI $kg{\cdot}m^{-2}$	22.6 ± 3.4	23.2 ± 4.0	0.340	22.9 ± 3.7
Disease status, n (%)				
Health	10 (14.3)	17 (18.9)	0.549	27 (16.9)
ILD	28 (40.0)	39 (43.3)		67 (41.9)
COPD	32 (45.7)	34 (37.8)		66 (41.2)

Data are presented as mean ± SD, unless otherwise stated. BMI: body mass index; ILD: interstitial lung disease; COPD: chronic obstructive pulmonary disease. Health: no pulmonary diseases

withdrew midway and did not complete the test. Among the 30 normal individuals, 3 participants were unable to complete the examination due to poor cooperation. Therefore, a total of 160 participants' data were included in the analysis, and no adverse events occurred throughout the study process. The characteristics of the study population are shown in Table 2.

In this clinical study, there were 67 participants in the interstitial lung disease group with respiratory diseases, including 36 male participants (53.73%) and 31 female participants (46.27%), with an average age of 54.6 ± 12.9 years. The COPD group had 66 participants, including 59 male participants (89.39%) and 7 female participants (10.61%), with an average age of 63.3 ± 7.9 years. The health control group consisted of 27 participants, including 17 males (62.96%) and 10 females (37.04%), with an average age of 29.6 ± 5.7 years.

The Bland-Altman plot (Fig. 2) was used to perform a consistency statistical analysis of the main diffusion function observation indicator, D_{LCO} test results. The results showed that 95.0% (152/160) of the observations were within the 95% confidence interval (CI). This indicates

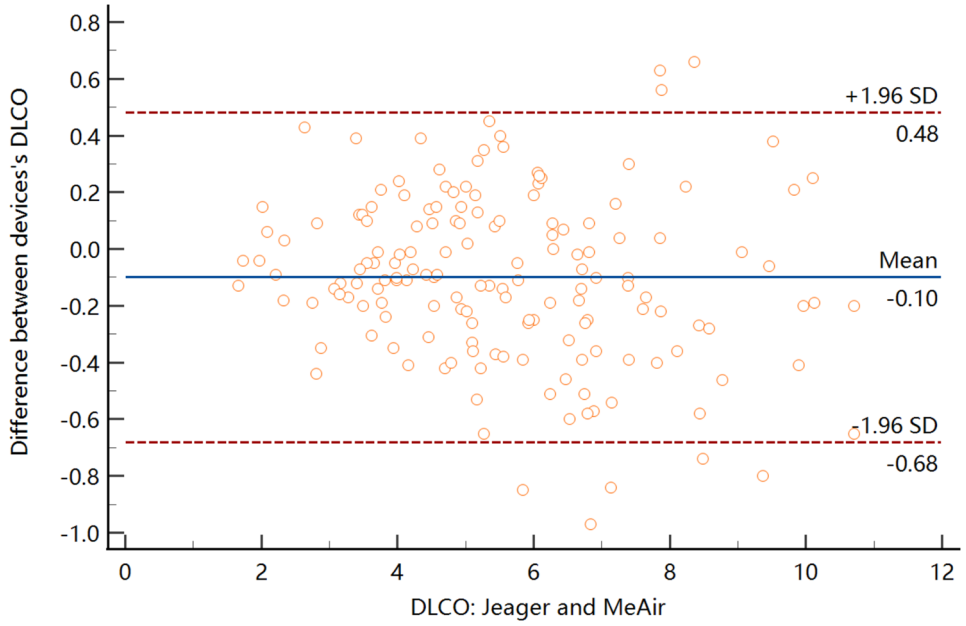

Fig. 2 Comparison of raw data distribution for Bland-Altman scatter plot of D_{LCO} between MasterScreen and MeAir

a high level of agreement between the measurements obtained from the two lung function devices, as most data points fall within the expected range of consistency.

The main observation indicator D_{LCO} and the distribution of secondary observation indicators on the MeAir 9000 lung function device and the MasterScreen lung function device, as well as their consistency correlation coefficient statistical analysis, are detailed in Table 1.

Data conform to a normal distribution, the quantitative data are represented as ($x \pm s$); if it does not conform to a normal distribution, it is represented by M (P25, P75). Absolute value of difference is calculated by the difference between the data in accordance with normal distribution unless otherwise stated. D_{LCO}: diffusing capacity of the lung for carbon monoxide; D_{LCO}/V_A: transfer coefficient of the lung for CO; V_A: alveolar volume; V_I: inspired volume; tBH: Breath-hold time; V_A/t_{BH}: ratios of alveolar volume to breath-hold time; F_{ICO} (%): fractional concentration of Inspired carbon monoxide; F_{ICH4} (%): fractional concentration of Inspired methane; F_{ACO} (%): fractional concentration of carbon monoxide in the alveolar space; F_{ACH4} (%): fractional concentration of methane in the alveolar space; $\frac{F_{ICO}}{F_{ACO}}$: ratio of inspired to expired carbon monoxide concentration; $\frac{F_{ACH4}}{F_{ICH4}}$: ratio of expired to inspired methane concentration; $\frac{F_{ICO}}{F_{ACO}} \cdot \frac{F_{ACH4}}{F_{ICH4}}$: Product of $\frac{F_{ICO}}{F_{ACO}}$ and $\frac{F_{ACH4}}{F_{ICH4}}$; $\mathrm{Ln}\left(\frac{F_{ICO}}{F_{ACO}} \cdot \frac{F_{ACH4}}{F_{ICH4}}\right)$: logarithmic function of $\frac{F_{ICO}}{F_{ACO}} \cdot \frac{F_{ACH4}}{F_{ICH4}}$. Pc: the concordance correlation coefficient (CCC). Pc (95% CI): the 95% confidence interval of CCC. Strength of agreement: the rank of the concordance correlation coefficient between the results of the two datasets.

In accordance with the 2017 ERS/ATS technical standards for lung diffusion function testing, the identification error for the concentration of the standard inhaled test gases by the lung function device must not exceed 1% [10]. In this study, both lung function devices were configured to check the inhaled gases CO and CH4 at a concentration of 0.3%, therefore the passing concentration range is between 0.297% and 0.303%. The distribution of the test gas results for CO and CH4 from the two lung function devices, and the statistical scatter plots can be seen in Table 1; Fig. 3.

Simulator testing

Among the various observational indicators in the subjects, the main difference lies in the ability to recognize gas concentrations. Therefore, in the simulator test, we focused on the identification capability for checking gas concentrations, specifically analyzing and comparing F_{ACO} and F_{ACH4}.

All D_{LCO} test simulations were conducted using the Single Breath Diffusing Capacity of the Lung for Carbon Monoxide (SB D_{LCO}) method. We used the same simulator (Hans Rudolph, Kansas City, MO) for both lung function devices. The specific operation involved connecting the simulator to the mouthpiece of the device under test and using two precision syringes in conjunction with precise gases to simulate a single breath D_{LCO} check operation.

In the simulator test, to compare the identification capability of the check gases at different volumes between

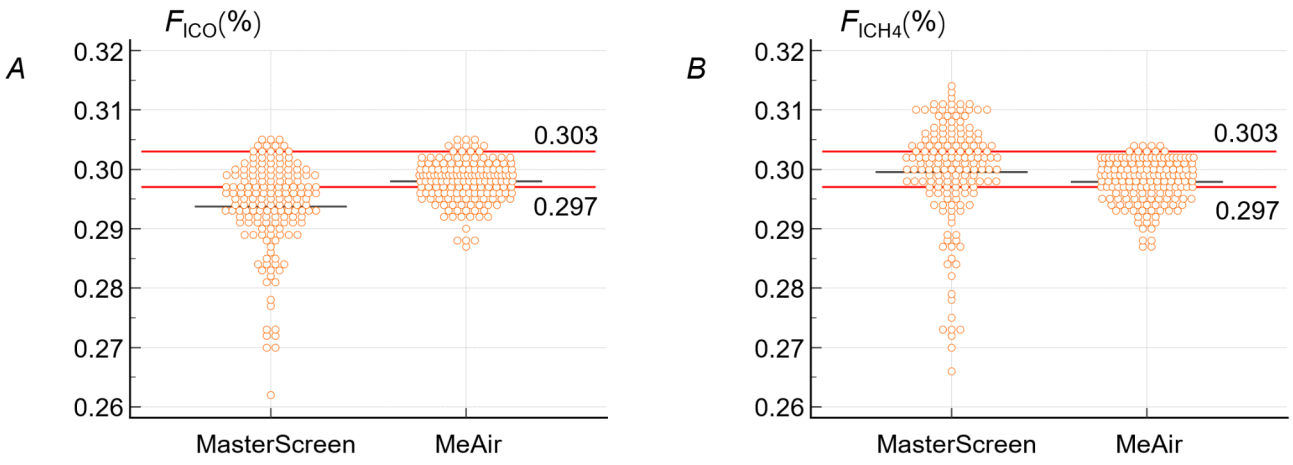

Fig. 3 Comparison of raw data distribution for F_{ICO} and F_{ICH4} between MeAir and MasterScreen in the D_{LCO} tests(A: F_{ICO},B: F_{ICH4})

Table 3 The data distribution of gas CO and CH4 of the simulator in meair and masterscreen

Gas	Group (%)	Volume(L)	MasterScreen		MeAir		
			Mean (Min-Max)(%)	Measurement error (%)	Mean (%) (Min-Max)	Measurement error (%)	*P*-value
CO	Low (0.079)	2.0	0.078(0.077–0.078)	-2.53- -1.27	0.076(0.076–0.076)	-3.80- -3.80	<0.01
		3.0	0.078(0.078–0.078)	-1.27- -1.27	0.076(0.076–0.077)	-3.80- -2.53	
	Middlle (0.100)	2.0	0.100(0.099-0.100)	-1.00- 0.00	0.098(0.097–0.099)	-3.00- -1.00	<0.01
		3.0	0.099(0.099-0.100)	-1.00- 0.00	0.098(0.098–0.099)	-2.00- -1.00	
	High (0.130)	2.0	0.129(0.129–0.129)	-0.77- -0.77	0.128(0.127–0.128)	-2.31- -1.54	<0.01
		3.0	0.129(0.129–0.129)	-0.77- -0.77	0.128(0.128–0.128)	-1.54- -1.54	
CH4	Low (0.218)	2.0	0.215(0.214–0.215)	-1.83- -1.38	0.218(0.218–0.218)	0.00–0.00	<0.01
		3.0	0.215(0.215–0.215)	-1.83- -1.38	0.218(0.218–0.218)	0.00–0.00	
	Middlle (0.201)	2.0	0.198(0.198–0.199)	-1.49- -1.00	0.201(0.200-0.203)	-0.50- 1.00	<0.01
		3.0	0.198(0.198–0.199)	-1.49- -1.00	0.202(0.201–0.203)	-0.50- 1.00	
	High (0.159)	2.0	0.157(0.157–0.157)	-1.26- -1.26	0.160(0.159–0.160)	0.00- 0.63	<0.01
		3.0	0.158(0.158–0.158)	-0.63- -0.63	0.160(0.159–0.160)	0.00- 0.63	

Data are presented as mean and minimum to maximum, unless otherwise stated. The gas concentrations are categorized into low, medium, and high groups based on CO as the standard; the measurement error is calculated by the difference between the minimum and maximum gas concentrations and the target gas concentration, expressed as a percentage of the target gas concentration

the two sets of lung function devices, and the main inspiratory volume in the subjects is mainly between 2.0 L and 3.0 L, we used two different volumes (2.0 L, 3.0 L) with three concentrations of gases to test the MeAir and MasterScreen lung function devices. The standard concentrations of the three check gas groups were as follows: the low concentration group (c(CO%): 0.079%, c(CH4): 0.218%), the medium concentration group (c(CO%): 0.100%, c(CH4): 0.201%), and the high concentration group (c(CO%): 0.130%, c(CH4): 0.159%)). The specific execution method was to perform four simulations at each gas concentration (a total of 12 times for each device); the first simulation at each gas concentration for the device was discarded to ensure that each device system had been completely flushed [3], so the number of tests for each concentration was 3 times. At the same time, before conducting tests at different concentrations, we calibrated the machine for environmental coefficients and the gas concentrations to ensure that each test could obtain results that truly reflected the condition of the machine. The acceptable standard for the simulator gas concentration test was that the measured F_{ACO} and F_{ACH4} had an average relative error within ± 10.0% of the standard gas concentration [17]. The distribution of the simulator test results can be seen in Table 3.

Diffusion function grade of the disease and health population groups subjects

The distribution of the grading results for the extent of lung diffusion dysfunction among the observed indicators in the ILD group and the COPD group and the health group, as well as the statistical analysis, can be found in Tables 4 and 5. The ICC values for the grading of lung diffusion dysfunction in these groups are 0.940 and 0.975 and 0.931, respectively, the above results were statistically significant ($P < 0.05$).

Table 4 The degree of pulmonary dispersion dysfunction in meair and masterscreen of interstitial lung disease and COPD lung disease and health

Variables (rank of D_{LCO} %pred)	ILD		COPD		Health	
	MasterScreen	MeAir	MasterScreen	MeAir	MasterScreen	MeAir
Normal	19.4% (13/67)	17.9% (12/67)	22.7% (15/66)	24.2% (16/66)	85.2% (23/27)	81.48% (22/27)
Mild	32.8% (22/67)	34.3% (23/67)	36.4% (24/66)	33.3% (22/66)	14.8% (4/27)	18.5% (5/27)
Moderate	35.8% (24/67)	35.8% (24/67)	30.3% (20/66)	33.3% (22/66)	0	0
Severe	11.9% (8/67)	11.9% (8/67)	10.6% (77/66)	9.1% (6/66)	0	0

Rank of D_{LCO} %pred: Normal (D_{LCO} %pred ≥ 80%), Mild (80% > D_{LCO} %pred ≥ 60%), Moderate (60% > D_{LCO} %pred ≥ 40%), and Severe (40% > D_{LCO} %pred)

Table 5 ICC analysis of the degree of pulmonary dispersion dysfunction in interstitial lung and COPD lung disease groups

Variables		ICC	95%IC	*P*-value	Strength of agreement
rank of D_{LCO} %pred	Group of ILD	0.940	0.904 ~ 0.963	<0.001	excellent
	Group of COPD	0.975	0.954 ~ 0.986	<0.001	excellent
	Group of Health	0.931	0.849 ~ 0.969	<0.001	excellent

Discussion

This randomized crossover study aims to evaluate the reliability of a new structural diffusion function testing device in measuring lung diffusion function test results and assessing dysfunction grades in both respiratory disease patients and healthy populations by directly comparing two commercially available devices. Bland-Altman 95% confidence interval analysis showed good agreement in the primary indicator D_{LCO} test results between the MeAir and MasterScreen devices, and CCC analysis also indicated a high level of agreement (CCC = 0.988). Based on the excellent agreement of D_{LCO} and the moderate agreement of the related indicator VA, the D_{LCO} / V_A results also demonstrated moderate agreement. All statistical analysis results were statistically significant ($P < 0.05$). Additionally, ICC analysis revealed that the two devices also exhibited a high level of absolute agreement in assessing lung diffusion function grades (COPD group ICC = 0.940, ILD group ICC = 0.975, health group = 0.931).

Due to the poor consistency correlation of tBH, V_A, F_{ICO}, F_{ICH4}, F_{ACO} and F_{ACH4} (Table 6), any differences in these indicators could affect the numerical results of the lung diffusion function D_{LCO}.

Therefore, we considered the possibility of special circumstances arising from internal factor differences that may offset each other. We need to conduct an in-depth analysis of the data of each factor in the calculation

Table 6 Descriptive analysis and concordance correlation coefficient of primary and secondary end-points between masterscreen and meair

Variables	MasterScreen	MeAir	Absolute value of difference	Pc (95% CI)	Pc	Strength of agreement
Primary end - point						
D_{LCO} (mL·min^{-1}·mmHg^{-1})	5.527 ± 1.981	5.627 ± 2.030	0.100 ± 0.296	0.984–0.991	0.988	Substantial
Secondary end-points						
D_{LCO}/V_A (mL·min^{-1}·mmHg^{-1}·L)	1.235(0.990, 1.495)	1.400(1.090, 1.650)	N/A	0.915–0.949	0.934	Moderate
V_A (L)	4.450 ± 1.068	4.148 ± 1.077	0.302 ± 0.218	0.924–0.955	0.942	Moderate
V_I (L)	2.687 ± 0.785	2.786 ± 0.827	0.099 ± 0.180	0.957–0.976	0.968	Substantial
tBH (s)	11.900(11.360,12.970)	11.435(11.120,12.030)	N/A	0.663–0.790	0.733	Poor
V_A/t_{BH} (L·s^{-1})	0.365 ± 0.100	0.354 ± 0.100	0.011 ± 0.023	0.957–0.976	0.968	Substantial
F_{ICO} (%)	0.295(0.291,0.299)	0.298(0.296,0.300)	N/A	0.261–0.423	0.344	Poor
F_{ACO} (%)	0.080 ± 0.018	0.085 ± 0.019	0.005 ± 0.007	0.856–0.918	0.891	Poor
F_{ICH4} (%)	0.301(0.297,0.305)	0.299(0.295,0.301)	N/A	0.225–0.405	0.318	Poor
F_{ACH4} (%)	0.162(0.136,0.181)	0.176(0.151,0.189)	N/A	0.794–0.879	0.842	Poor
$\frac{F_{ICO}}{F_{ACO}}$	3.647(3.177,4.329)	3.488(3.062,4.160)	N/A	0.856–0.919	0.892	Poor
$\frac{F_{ACH4}}{F_{ICH4}}$	0.540(0.467,0.598)	0.599(0.508,0.642)	N/A	0.791–0.873	0.837	Poor
$\frac{F_{ICO}}{F_{ACO}} \cdot \frac{F_{ACH4}}{F_{ICH4}}$	1.896(1.721,2.165)	1.986(1.767,2.224)	N/A	0.921–0.956	0.941	Moderate
$\mathrm{Ln}\left(\frac{F_{ICO}}{F_{ACO}} \cdot \frac{F_{ACH4}}{F_{ICH4}}\right)$	0.655 ± 0.175	0.689 ± 0.175	0.035 ± 0.044	0.933–0.963	0.950	Substantial

process, including the calculation combinations between factors (Table 6). We found that these differences offset each other in the process of calculating the diffusion function results and the results show good consistency. This phenomenon of internal differences offsetting each other has also been found in previous instrument studies [14, 18].

Analysis of the differences in CO and CH4 concentrations

From the statistical analysis of the two inhaled test gases (Tables 1, 3, and 6), it is apparent that the consistent correlation between MeAir and MasterScreen regarding the concentrations of CO and CH4 in the test gases is not satisfactory. The scatter plots (Figs. 2 and 3) and the concentration data distribution tables (Tables 1 and 3) of the results from a sample of 160 subjects indicate that both pulmonary function devices experienced fluctuations in the detection results of inhaled gas concentrations during continuous examination of a large population. According to the 2017 ERS/ATS technical standards for lung diffusion function testing, the pass rates for MeAir's analysis of F_{ICO} and F_{ICH4} are 63.13% and 66.88%, respectively; while the pass rates for MasterScreen's gas analysis are 35.63% and 43.13%, respectively (Table 3) [10]. This means that MeAir's detection of the concentration of inhaled standard gases is superior to MasterScreen, and the precision is better.

Furthermore, in the simulator test results, we can ascertain that in the detection of the gas CO, the MasterScreen device's margin of error fluctuates between −2.53% and 0.00%, while the MeAir device's margin of error fluctuates between −3.80% and −1.00%. Regarding the detection of the CH4, the MasterScreen device's margin of error fluctuates between −1.83% and −0.63%, whereas the MeAir device's margin of error fluctuates between −0.50% and 1.00%. Overall, this indicates that the MasterScreen is more proficient in analyzing CO compared to the MeAir, whereas the MeAir exhibits a stronger capability in recognizing the concentration of CH4 than the MasterScreen.

In summary, regarding the ability to recognize gas concentrations, the MasterScreen lung function instrument is more precise in analyzing CO concentrations, while the MeAir is better at analyzing CH4 concentrations. In the context of extensive examination scenarios, the MeAir is more precise and accurate overall compared to the MasterScreen. Given that both lung function devices are calibrated daily for environmental conditions, inhaled gas concentrations, and flow rates and speeds before conducting examinations, and only proceed with diffusion function testing on subjects after passing quality checks. We can draw a conclusion that the valve-turning structure of the MeAir does indeed ensure the stability of inhaled gas concentrations.

Analysis of the differences in alveolar volume (V_A)

From the V_A calculation formula, we understand that the factors involved include V_{dequip}, V_{danat}, and the concentration ratio of the tracer gas methane (F_{ACH4}/F_{ICH4}), V_I, and environmental coefficients. Since both lung function devices were calibrated for environmental factors before the examination, the environmental factors are consistent. In this project's research, we used the FOWLER method to calculate the dead space volume, and the results for V_{danat} were the same.

In terms of V_{dequip}, as it serves as the system dead space, it should be set constant by the manufacturer. We found that the V_{dequip} in the MeAir test results is consistently 283 ml, but the V_{dequip} results from the MasterScreen show an unstable situation, fluctuating between 142 ml and 172 ml.

Regarding the V_I, the MeAir operating system is equipped with a visual exhalation platform assist line, and its diffusion test module is equipped with a new valve-turning structure, which allows the MeAir system to more accurately ensure that the subject exhales to the residual volume position. In the comparison of the observed indicator V_I data results, the overall mean of MeAir is 0.99 L larger than that of MasterScreen. The results prove that the new module and exhalation platform assist line effectively standardize the operation of the diffusion function test.

Additionally, through our previous analysis of the differences in CH4 concentration between the two devices (Table 6), the consistency correlation of F_{ACH4}/F_{ICH4} for both MasterScreen and MeAir is also poor. Combined with the results of methane concentration detection from the simulator, it indicates that MeAir has a stronger ability to recognize CH4 concentration than MasterScreen.

Therefore, even though the current consistency correlation strength of V_A between MeAir and MasterScreen is moderate, we consider the results from MeAir to be more credible.

Limitations of the study

We acknowledge that there are certain limitations to this study. Firstly, in our experimental design, our research was conducted as a single-center study, and only one device each of MeAir and MasterScreen was used, which limits our ability to comprehensively evaluate the consistency of these two series of devices in diffusion function testing. Future research plans will involve multi-center studies, expand the sample size, and increase the number of MeAir and MasterScreen devices to further explore the differences between the two.

Secondly, the subjects of this study were limited to adult patients with COPD and ILD, as well as healthy adults, and did not cover other respiratory diseases or the pediatric population. In subsequent studies, we will

broaden the sample range to include subjects from more age groups and disease types to further verify the wide applicability of the MeAir pulmonary function device.

Conclusions

The comprehensive analysis indicates that the MeAir lung function device and the MasterScreen lung function device both demonstrate good consistency in the measurement of key primary observation indicators for lung diffusion function tests and in the clinical assessment of the extent of lung diffusion dysfunction. It is particularly noteworthy that the MeAir lung function device shows superior stability when dealing with large populations and prolonged examination periods.

Therefore, based on the above circumstances, we believe that the diffusion function measurement system of the MeAir lung function device has met the standards for clinical application, possesses a high degree of reliability, and is suitable for widespread promotion and use.

Abbreviations

ERS	European Respiratory Society
ATS	American Thoracic Society
D_{LCO}	Diffusing capacity for carbon monoxide
D_{LCO} %pred	Diffusion capacity of carbon monoxide as a percentage of the predicted value
V_A	Alveolar volume
D_{LCO} / V_A	D_{LCO} to alveolar volume ratio
V_I	Inspired volume
VC	Vital capacity
Vdequip	Volume of equipment dead
Vdanat	Volume of anatomical dead
tBH	Breath-hold time
F_{ICO}	Fractional concentration of inhaled carbon monoxide
F_{ICH4}	Fractional concentration of inhaled methane
F_{ACO}	Fractional concentration of carbon monoxide in the alveolar space
F_{ACH4}	Fractional concentration of methane in the alveolar space
CO	Carbon monoxide
CH4	Methane
He	Helium
CV%	Coefficient of variation
T	Ambient temperature
PB	Barometric pressure
PH2O	Partial pressure of water vapor
CCC	Concordance correlation coefficient
ICC	Intraclass correlation coefficient

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Author contributions

Shihua Yao, Jinping Zheng, Yi Gao, and Yanqing Xie were responsible for proposing the research concept and designing the study protocol, including establishing observational indicators, setting inclusion and exclusion criteria, and determining the methods for group allocation. Shihua Yao was in charge of communicating with the participants and obtaining informed consent. Kuiqing Lin, Zhongping Wu, Shubing Chen, Yanqing Xie, Beilan Shen, Liping Zhong, Jiaying An, Xudong Wang, Wenting Liu, and Xinxin Yu were responsible for the study implementation, including diffusion capacity tests and participant screening. Shihua Yao handled data collection, acquisition, and cleaning. Shihua Yao and Tuping Fu conducted the statistical analysis. Shihua Yao drafted the manuscript, while Shihua Yao, Jinping Zheng, and Yi Gao revised the final version and are accountable for the accuracy and integrity of the work.

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Data availability

The pulmonary function test data and clinical information in the current study are not publicly available due to patient privacy obligations but are available from the corresponding authors on reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the First Affiliated Hospital of Guangzhou Medical University (ES-2023-126-02), and all participants were informed of the details of the trial and have signed informed consent forms before the experiment.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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