



European Respiratory Society/American Thoracic Society technical statement: standardisation of the measurement of lung volumes, 2023 update

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Shareable abstract (@ERSpublications)

This document provides updated technical standards for measurement of lung volumes, developed by the European Respiratory Society (ERS) and American Thoracic Society (ATS) <https://bit.ly/474TxuC>

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Abstract

This document updates the 2005 European Respiratory Society (ERS) and American Thoracic Society (ATS) technical standard for the measurement of lung volumes. The 2005 document integrated the recommendations of an ATS/ERS task force with those from an earlier National Heart, Lung, and Blood Institute workshop that led to the publication of background papers between 1995 and 1999 and a consensus workshop report with more in-depth descriptions and discussion. Advancements in hardware and software, new research and emerging approaches have necessitated an update to the 2005 technical standard to guide laboratory directors, physiologists, operators, pulmonologists and manufacturers. Key updates include standardisation of linked spirometry, new equipment quality control and validation recommendations, generalisation of the multiple breath washout concept beyond nitrogen, a new acceptability and grading system with addition of example tracings, and a brief review of imaging and other new techniques to measure lung volumes. Future directions and key research questions are also noted.

Key updates

- Emphasis on importance of linked manoeuvres for determining lung volumes after measurement of functional residual capacity (FRC).

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- For standardisation of linked spirometry, the method that is expected to be achievable by most patients is recommended.
- Emphasis on importance and limitations of biological controls for quality assurance assessment.
- New equipment quality control and validation recommendations, including a requirement for isothermal lung mechanical models for calibration and verification of body plethysmographs.
- Emphasis on pant frequency and recommendations on measuring airway resistance using body plethysmography. Comment on panting *versus* tidal breathing.
- Generalised concept of multiple breath washout (MBW) beyond nitrogen (N₂)
- Updates on MBW technique based on recently published technical standards.
- Differentiation between inert-gas dilution equipment that use volume-based *versus* flow-based spirometers.
- A new acceptability and grading system for assessment of the quality of lung volume measurements. Examples of tracings distinguishing manoeuvres of different grades.
- Recommendation for using Global Lung Initiative (GLI) lung volume reference values.
- Updates on measurement of lung volumes by imaging and other new techniques.
- Data file requirements, standardised operator comments and sequence of lung function measurements.

Background and purpose

Determination of lung volumes – measurements of FRC with calculation of total lung capacity (TLC) and residual volume (RV) – add important diagnostic information to what can be deduced from spirometry alone [1, 2]. A reduced forced vital capacity (FVC) on spirometry may be due to a restrictive ventilatory defect, air trapping in the setting of an obstructive ventilatory defect, or the combined presence of obstructive and restrictive defects. A reduced TLC establishes the presence of a restrictive ventilatory defect [3]. RV and FRC can help identify the cause of a reduced FVC or TLC. Lung volume measurements may enhance the assessment of obstructive ventilatory defects through the detection of air trapping and hyperinflation.

Unlike spirometry, which utilises only one methodology, lung volumes can be measured using a variety of techniques. These include body plethysmography, MBW and inert gas dilution. In health these approaches yield similar results, but results can be quite disparate in disease. In addition, lung volumes can be obtained from imaging techniques which are also briefly covered by this document.

Methods

A proposal was submitted to update the 2005 lung volumes standards by a joint ERS and ATS task force [4]. Co-chairs and members were approved by the ATS and ERS, the latter of which managed disclosure of conflicts of interest. Task force members were physicians and scientists with research publications in relevant areas and experience in directing pulmonary function laboratories, clinical use of lung volumes, and development of guidelines. A medical librarian (S.L. Knight) designed search strategies related to lung volumes using medical subject headings and text words, and limited to human studies and articles with English abstracts, from 2004 through August 2021 (supplementary material). Ovid databases included MEDLINE, In-Process and Non-indexed Citations, Embase and Cochrane Registry of Controlled Trials (CENTRAL). Literature known to the panel, but not identified by the systematic literature search was also included.

At each stage of review, at least two task force members reviewed each entry for relevance by focusing on articles with information on technical performance of lung volumes rather than only clinical application, and on tests performed volitionally by adults or children. From 9779 abstracts after the initial search, 296 were selected for review of full-text articles, yielding 77 articles. An additional 30 were hand-searched (nine in the main document, 21 in the supplementary material), which includes some articles cited in the 2005 standard.

Task force members used published data and their expertise to make modifications, additions and deletions to the 2005 standards. A standardised survey of equipment details was created with separate sets of questions for body plethysmography, MBW and helium dilution. ERS staff distributed and collected the surveys from manufacturers identified by the task force. In addition, the task force reviewed equipment specifications published on the manufacturers' websites. Survey responses and online data were not informative enough to report survey data for all specifications in this standard. Where neither data nor expertise suggested a change, prior recommendations were retained.

Definitions and subdivisions of lung volume

The term "lung volume" usually refers to the volume of gas within the lungs, as measured by body plethysmography, gas dilution or washout. In this statement, previous definitions of lung volumes are used

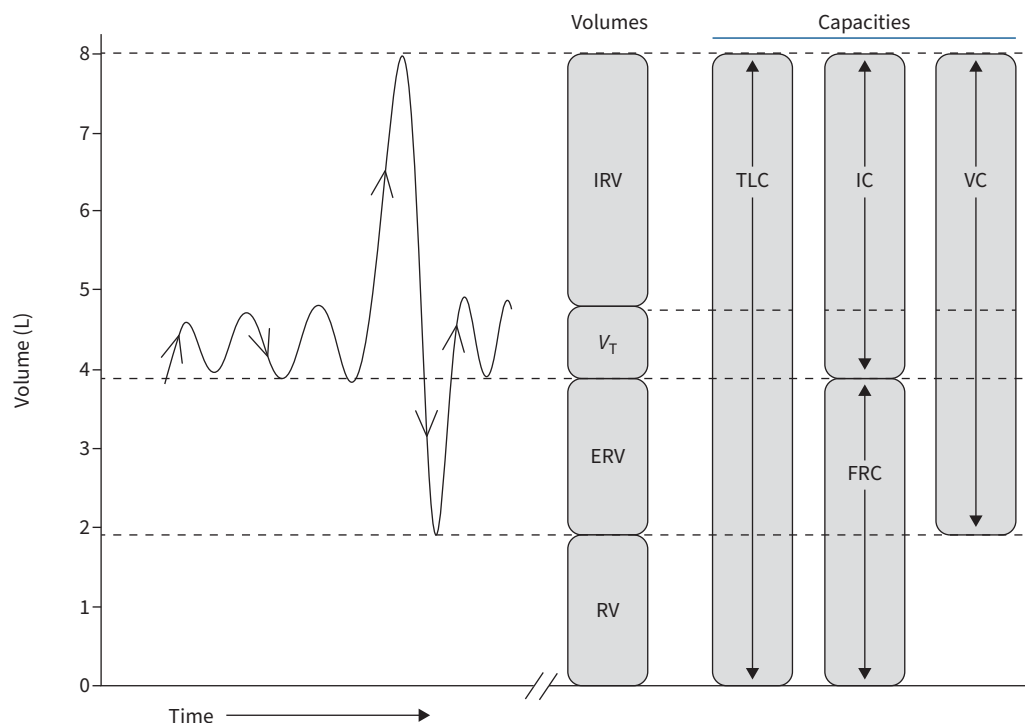


FIGURE 1 Static lung volumes and capacities based on a volume-time spirogram of an expiratory vital capacity (VC). IRV: inspiratory reserve volume; V_T : tidal volume; ERV: expiratory reserve volume; RV: residual volume; TLC: total lung capacity; IC: inspiratory capacity; FRC: functional residual capacity.

(figure 1) [5–9]. The total volume of the lung at maximal inspiration is the TLC and can be divided into subdivisions which are either volumes or capacities. The four unique lung volumes are RV, expiratory reserve volume (ERV), tidal volume (V_T) and inspiratory reserve volume (IRV). The lung volumes can be combined to form lung capacities, which include vital capacity (VC), inspiratory capacity (IC), FRC and TLC (figure 1).

The volume of gas inhaled or exhaled during the respiratory cycle is called the tidal volume (V_T).

FRC is the volume of gas present in the lung at passive end-expiration during tidal breathing, or the sum of ERV and RV.

ERV is the volume of gas that can be maximally exhaled from the end-expiratory lung volume during tidal breathing (*i.e.* from FRC to RV).

RV refers to the volume of gas remaining in the lung after maximal exhalation (regardless of the lung volume at which exhalation was started).

The maximum volume of gas that can be inspired from FRC to TLC is referred to as the IC.

IRV is the maximum volume of gas that can be inhaled from the end-inspiratory lung volume during tidal breathing.

The VC is the volume change at the mouth between the positions of full inspiration (TLC) and full expiration (RV). The measurement may be made in one of the following ways: 1) inspiratory vital capacity, where the measurement is performed in a relaxed manner, without undue haste, from a position of full expiration to full inspiration; 2) expiratory vital capacity (EVC), where the measurement is similarly performed from a position of full inspiration to full expiration; or 3) FVC, which is the volume of gas that is exhaled during a forced expiration, starting from a position of full inspiration and ending at complete expiration [10].

TLC refers to the volume of gas in the lungs after maximal inspiration, or the sum of all volume compartments (RV+ERV+ V_T +IRV). TLC is also the sum of IC and FRC or RV and VC.

Measurement of FRC

The determination of FRC is the key component in the measurement of lung volumes, and can be assessed by body plethysmography, gas dilution or washout methods, or using radiography. To obtain an accurate FRC, ERV, IC and IRV, a stable FRC should be achieved during tidal breathing. In alignment with the 2019 spirometry standard, a stable end-expiratory V_T may be defined as having at least three tidal breaths with the difference between maximum and minimum end-expiratory lung volume within 15% of the tidal volume [10]. The FRC measured by plethysmography (FRC_{pleth}) includes nonventilated, as well as ventilated, lung compartments, and thus may yield higher results than the gas dilution or washout methods in some patients with certain lung diseases [11–13]. Although theoretically FRC_{pleth} may be further increased by gas that is present in the abdomen, the amount of abdominal gas is small (~100 mL) and even larger volumes appear to have no effect on measurement of FRC [14]. In cases of severe airflow obstruction, FRC_{pleth} may be overestimated when panting rates are >1 Hz (60 breaths·min⁻¹) because mouth pressure underestimates the absolute change in alveolar pressure during both inhalation and exhalation [15–17]. In patients with severe airflow obstruction, bullae or emphysema, FRC is underestimated by the gas dilution or washout methods. Despite this fact, the gas dilution/washout methods are widely used because the instrumentation can be less costly. Table 1 lists advantages and disadvantages of plethysmography, gas dilution and washout methods. Single-breath gas dilution methods as used in the determination of alveolar volume during measurement of diffusing capacity are not covered in this standard. They are more susceptible to the problem of underestimation of TLC when there is regional ventilation inhomogeneity, are not linked with spirometric manoeuvres that allow determination of other lung volumes, do not primarily measure FRC and do not include anatomical dead space. Although there is improvement in estimation of TLC from the single-breath method by using total exhaled breath as noted in the 2017 ERS/ATS standard for carbon monoxide uptake in the lung (D_{LCO} standard), the limited evidence available nonetheless shows underestimation [18, 19].

Derivation of lung subdivisions

No matter what technique is used to measure FRC (see sections Measurement of FRC using body plethysmography, Measurement of FRC using MBW and Measurement of FRC using helium dilution), VC and one of its subdivisions, IC or ERV, will have to be measured to calculate the TLC and RV (figure 1). The 2005 standard detailed two methods for measuring IC or ERV after determination of FRC, followed by calculation methods unique to each method. A subsequent study found that the two calculation methods were equivalent, and although one method yielded higher values for TLC and VC in those without a ventilatory defect, the differences were small and may not be clinically significant [20].

For standardisation, the method that is expected to be achievable by most patients is recommended here. Immediately after the acquisition of the FRC measurement(s) an IC manoeuvre is performed to measure

TABLE 1 Advantages and disadvantages of lung volume measurement techniques

	Advantages	Disadvantages
Body plethysmography: measures volume of all compressible gas	Shorter testing period Measures all thoracic gas Requires only short time to repeat measurements	Technically challenging to administer and perform Potential for claustrophobia Can overestimate FRC in severe obstruction Higher equipment cost and space requirements Cabin may not accommodate patient's weight or size
Multiple breath washout: measures volume of gas in ventilated areas	Quiet breathing technique for measurement of FRC	Requires slightly larger tidal volumes Longer testing period Requires more time to repeat measurements Can underestimate FRC in obstructive lung disease Potential risk to patients with ventilation sensitive to high level of inspired oxygen
Helium dilution: measures volume of gas in ventilated areas	Quiet breathing technique for measurement of FRC	Longer testing period Requires CO ₂ absorber, desiccant and O ₂ bleed-in Requires more time to repeat measurements Can underestimate FRC in obstructive lung disease

FRC: functional residual capacity; CO₂: carbon dioxide; O₂: oxygen.

the TLC in a “linked” manner (*i.e.* without the patient coming off the mouthpiece prior to the completion of the manoeuvres) (figure 2). The IC manoeuvre is followed by a linked slow EVC manoeuvre to RV. Care must be taken to coach patients through a slow EVC because, commensurate with any degree of obstructive ventilatory defect, there is potential for air trapping and overestimation of RV with a forced manoeuvre that can cause premature dependent airway closure (figure 3). Some patients may need to take tidal breaths immediately after the determination of FRC, and this is acceptable as long as they remain on the mouthpiece. The reported value for the FRC is the mean of technically acceptable FRC measurements used for the calculation of TLC. The TLC is the mean of the sums of technically acceptable FRC values and linked IC manoeuvres. The RV is the reported value for TLC minus the largest VC measured. While recognising that manufacturers currently may have recommendations for measurement of static lung volumes without linked manoeuvres, it is recommended that all methods link the spirometry manoeuvres with the FRC measurement to calculate TLC and/or RV.

Linked spirometry is optimal. However, some patients may have difficulty with linked spirometry after many minutes on the mouthpiece during measurement of FRC by MBW or helium dilution. In these cases, unlinked spirometry is an alternative after re-establishing a resting FRC with tidal breathing. Results that incorporate unlinked manoeuvres should be reported with caution (useable rather than acceptable). Differences in FRC between linked and unlinked manoeuvres are likely to be small relative to the TLC, which is often the primary outcome of the test. Unlinked spirometry is not a recommended option for plethysmography.

Recommendations for the measurement of IC and unforced VC (slow vital capacity) are presented in the document on the standardisation of spirometry [10]. Repeatability of the IC and ERV, which are used in computing TLC and RV, are determined in part by the repeatability of FRC, which is covered later.

General patient preparation

The patient's age, height and sex are used in the reference equations to calculate predicted values. Age should be expressed in years to one decimal point. Height should be measured in centimetres to one decimal place, without shoes, and with the back flat against a surface, ideally using a stadiometer (supplementary material). For patients with a deformity of the thoracic cage, such as kyphoscoliosis, the

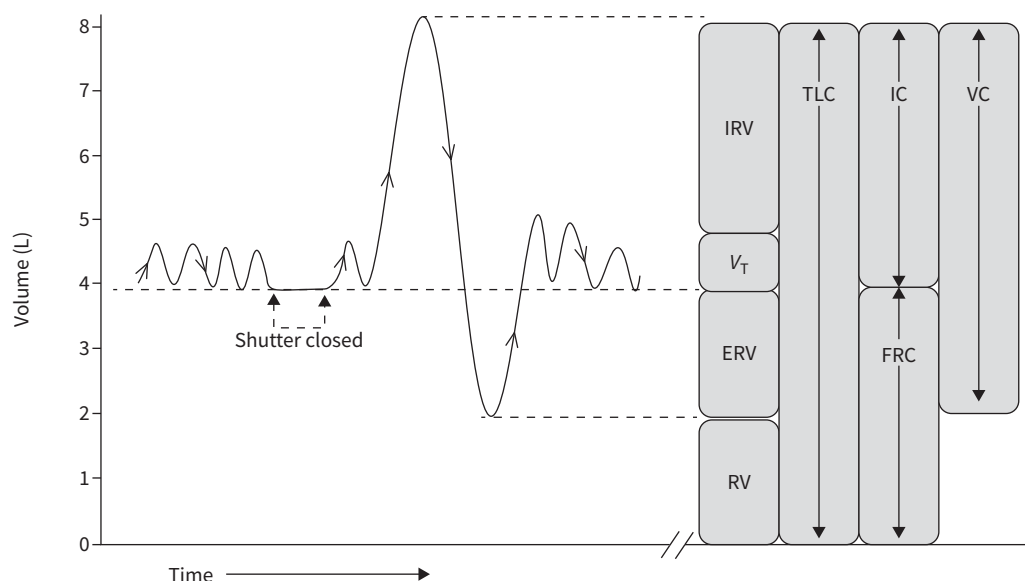


FIGURE 2 Volume–time display showing the sequence of quiet breathing and, after stable end-expiratory level is achieved, a short period when the shutter is closed for determination of the thoracic gas volume, followed by an open-shutter period during which the patient stays on the mouthpiece and performs an inspiratory capacity (IC) manoeuvre followed by a slow expiratory vital capacity (VC) manoeuvre. In a linked manoeuvre, all volumes are determined without the patient coming off the mouthpiece. IRV: inspiratory reserve volume; V_T : tidal volume; ERV: expiratory reserve volume; RV: residual volume; TLC: total lung capacity; FRC: functional residual capacity.

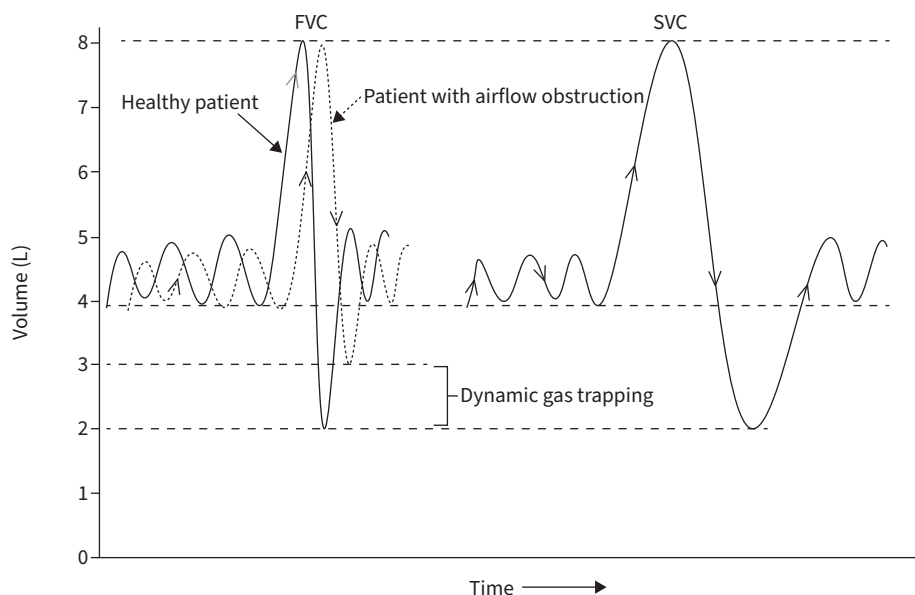


FIGURE 3 In a healthy patient, expiratory vital capacity manoeuvres performed in a forced (FVC) or slow (SVC) manner are expected to yield the same result. However, in a patient with an obstructive ventilatory defect, there is potential for dynamic gas trapping and overestimation of residual volume with a forced manoeuvre.

arm span from fingertip to fingertip, or ulna length, can be used in regression equations which provide adjustments for age and sex to estimate height. Details are available in the 2019 ERS/ATS standardisation of spirometry technical statement [10]; diagrams detailing best practices can be found in the supplementary material. Technical comments should be available on the report when standing height cannot be measured but is instead estimated, for example: “Predicted values have been calculated using an estimate of standing height and should be used with caution”. Weight should be measured to the nearest 0.5 kg, as plethysmographic systems use weight to calculate body volume in the calibration software. Weight is also used as a guide to anatomical dead space in some systems, but is inferior to direct measurement *via* the Fowler method [21].

Activities that should be avoided before testing and instructions on withholding medications are included in the spirometry 2019 update. The operator should record the type and dosage of any (inhaled or oral) medication that may alter lung function and when the drugs were last administered. The decision to avoid long- and short-acting bronchodilators is a clinical one, dependent on the question being asked. Patients should be asked to wear loose-fitting clothing and refrain from eating a large meal or drinking large volumes of liquid prior to testing. Dentures should normally be left in place; however, if they are loose, they may interfere with performance and should be removed. Special considerations in children are covered in recent statements on pulmonary function testing [10, 22]. Protection of patients and staff from infection through pre-testing patient evaluation, cleaning of testing rooms and equipment and management of the laboratory environment are covered elsewhere [23].

Sequence of lung function measurements

Previous standards suggested that the order for performing lung function tests should consider the optimal workflow in the laboratory, potential influences of one test on another and the ability of the patient to undertake the test. The order of tests should be kept constant to avoid introducing unanticipated variability to test results [24]. There is no recommendation for or against use of a bronchodilator prior to measurement of the diffusing capacity of the lung for carbon monoxide (D_{LCO}) [18]. An example order of performing tests is spirometry, static lung volumes, inhalation of bronchodilator agent (if used), diffusing capacity, repeat spirometry and repeat static lung volumes (if required).

It is recommended that D_{LCO} measurements be made before any multibreath N_2 washout tests, as residual oxygen may result in underestimation of D_{LCO} [24]. Therefore, an alternative order of performing lung

function tests would be spirometry, D_{LCO} , N_2 MBW test, inhalation of bronchodilator agent (if used), repeat spirometry.

Measurement of FRC using body plethysmography

Introduction and theory

The term thoracic gas volume (VTG or TGV) refers to the plethysmographic measurement of intrathoracic gas at the time of airflow occlusion. The volume is the compressible gas within the thorax. The term FRC_{pleth} refers to the FRC during relaxed tidal breathing prior to measurement of VTG as obtained by applying a correction if needed for any difference between VTG and FRC.

Plethysmographic measurements are based on Boyle's law, which states that, under isothermal conditions, when a constant mass of gas is compressed or decompressed, the gas volume decreases or increases and gas pressure changes such that the product of volume and pressure at any given moment is constant [13, 14]. More detailed reviews of the theory are available [25].

Equipment

The changes in thoracic volume that accompany a compression or decompression of the gas in the lungs during respiratory manoeuvres can be obtained using a constant volume body plethysmograph by measuring the changes in box pressure. The body plethysmograph is a cabin with a total cabin volume of 700–1200 L. A larger cabin may be needed for very tall or obese patients. Some large cabins are accessible for patients in a wheelchair. A bidirectional intercom should be available for communication between patient and operator.

A transducer capable of measuring mouth pressure $\geq \pm 5$ kPa ($\geq \pm 50$ cmH₂O), with a flat frequency response of > 8 Hz, is essential. All nine current manufacturers of plethysmography equipment surveyed reported that the mouth pressure transducer could measure this range and three reported meeting or exceeding the minimum frequency response. Flow measuring devices that are used for the measurement of lung volumes and maximal inspiratory and expiratory volumes should meet published standards for the accuracy and frequency response of spirometric devices [10]. The transducer measuring changes in the cabin pressure must be capable of accurately measuring a range of ± 0.02 kPa (± 0.2 cmH₂O) [7]. Thermal drift may give rise to a pressure change of as much as 0.1 kPa (1 cmH₂O), which may necessitate a larger working range of the transducer [13]. Equipment from eight out of nine manufacturers surveyed meet this larger range for cabin pressure measurement. Cabin pressure transducer accuracy and resolution should be maintained across the measurement range. Manufacturers' responses for cabin pressure transducer accuracy and resolution varied and warrant standardised reporting. A time constant of 10 s (range 5–25 s) for a controlled leak (which minimises slowly occurring pressure changes) is ideal. Out of the nine current manufacturers surveyed, five reported a value of ≤ 10 s. Thermal drift due to temperature changes in the interior of the plethysmograph is common to all types of equipment and can be detected and compensated for from the volume–pressure plot during an occlusion showing a systematic difference in slope between compression and expansion [13].

Manufacturers should state the frequency response of their plethysmographic systems and provide instructions for the user on how to verify it. The verification of frequency response is most commonly accomplished by the application of a sinusoidal volume signal, where the frequency can be varied [13]. It is generally recommended that the minimum adequate frequency response should be five times the frequency of the signal being measured. For a pant at 1 Hz, this means accuracy of the signal at 5 Hz. For panting frequencies slightly above 1 Hz, the minimum acceptable frequency response is 8 Hz.

Patient preparation

The measurement procedure must be thoroughly explained, demonstrated and practised with the patient. This must include practising 1) mouthpiece and nose clip placement; 2) panting by putting the hand over the mouth; 3) supporting the cheeks, *i.e.* flat of the hands against the cheeks, without raising the arms; 4) tight lip seal throughout the measurement and specifically while shutter is closed; and 5) closing the door. Supporting the cheeks is particularly important in the setting of airflow obstruction, where it reduces but does not eliminate the impact of higher panting frequencies [17]. For patients with claustrophobia, it is important to explain that the door can be released at any time from both the outside and inside.

Measurement technique

The measurement technique requires the following steps:

- 1) Equipment should be:
 - a) turned on and allowed an adequate warm-up time (as specified by the manufacturer);

- b) set up for testing, including calibration, according to manufacturer's instructions. During calibration and use, rapid changes in room pressure and vibrations should be avoided (*e.g.* doors shutting abruptly, changes in room air currents from heating, ventilation, and air conditioning and high-efficiency particulate air filter systems). Gusty winds and direct sunlight may also affect measurements;
 - c) adjusted so that the patient can sit comfortably in the cabin and reach the mouthpiece without having to flex or extend the neck.
- 2) The plethysmograph door is closed, and time is allowed for the thermal transients to stabilise (approximately 30 s to 2 min) and the patient to relax.
 - 3) The patient is instructed to attach to the mouthpiece (flange-type preferred), and breathe quietly until a stable end-expiratory lung volume, *i.e.* FRC is reached (usually three to 10 tidal breaths; see Measurement of FRC).
 - 4) The shutter is closed at or near end-expiration for $\sim 2\text{--}3$ s, during which time the patient is instructed to perform a series of gentle pants against the closed shutter ($\sim \pm 1$ kPa ($\sim \pm 10$ cmH₂O)) at a frequency between 0.5 and 1.0 Hz, $\sim 30\text{--}60$ pants per minute. Panting frequencies of >1.5 Hz may lead to overestimation of FRC. This effect increases as obstruction worsens. Panting frequencies of <0.5 Hz may cause problems with the controlled leak of the body plethysmograph system. Acceptable panting manoeuvres should be recorded (*i.e.* a series of two to three almost superimposed straight lines separated by only a small thermal drift on the pressure–volume plot; figure 4).
 - 5) Next, the shutter opens and the patient performs a linked IC manoeuvre followed by an EVC (figure 2). Patients with severe dyspnoea may have difficulty performing linked spirometry immediately after closed shutter panting. To overcome this, the patient can be instructed to stay on the mouthpiece and take two or three tidal breaths after the panting manoeuvre, prior to performing the linked IC and EVC manoeuvres.
 - 6) The operator must review the placement of tangent lines on the panting loops. Adjust the tangent lines only if the software placement appears to be in error. Tracings for plethysmograph tests should be shown graphically in the report to aid quality assessment [26]. Similarly, the operator must verify automatic adjustment for differences between VTG and FRC_{pleth} on the spirometer tracing. Panting frequency for each manoeuvre should be displayed within the data acquisition software for assessment of quality. Technical comments should be added if panting frequency for trials selected is outside the target range to inform interpretation of results.
 - 7) Measurement of airway resistance must not be performed during the same manoeuvre performed to measure lung volumes because the optimal panting frequencies are different and increased time on the mouthpiece increases opportunity for leak which can compromise accurate measurement of lung volumes (supplementary material).

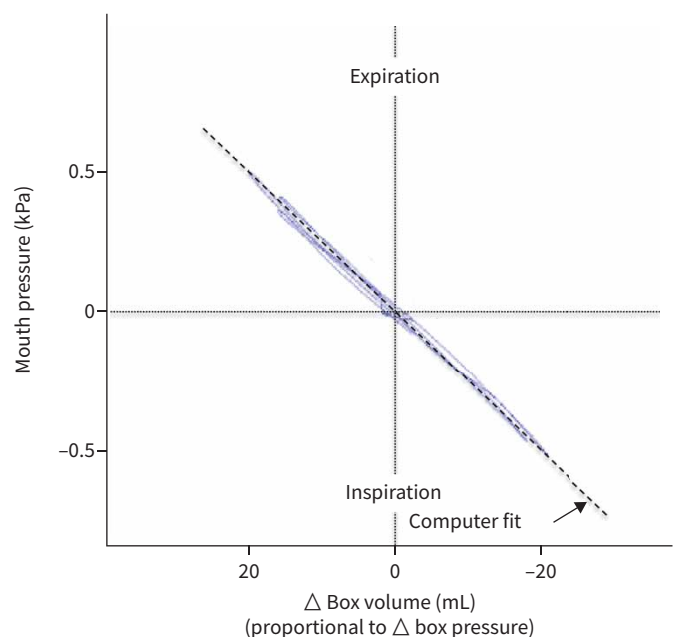


FIGURE 4 Display of a properly performed panting manoeuvre as a series of almost superimposed straight lines separated by only a small thermal drift. The target panting frequency is between 0.5 and 1 Hz. Δ : change.

Quality control

The accuracy of the flow and volume output of the mouth flow-measuring device should comply with the recommendations made in the spirometry 2019 document [10].

The mouth pressure transducer should be physically calibrated daily or prior to use. The plethysmograph signal should also be calibrated daily, using a volume signal of similar magnitude and frequency as the respiratory manoeuvres during testing. Calibration must be performed more frequently when temperature or pressure are changing (*e.g.* twice a day).

A validation of accuracy using a known volume must be performed monthly, when new software is uploaded, or a problem is suspected. This can be carried out using a model lung or container of known volume, ideally of two different sizes [13, 27]. Filling a flask with thermal mass (*e.g.* copper wool) and using the proper frequency of air movement (0.5–1 Hz) are essential in order to simulate the isothermal conditions within the lung; care should be taken to adjust the calculated volumes to ambient (or model) temperature and saturated conditions, rather than to body temperature and ambient pressure, saturated with water vapour (BTPS) conditions, during the calculations. If a person is required to be in the cabin during use of the model lung, their anthropomorphic data should be entered into the software to get accurate measurements. The accuracy of adult plethysmographs in measuring the gas volume of the container should be ± 50 mL or 3%, whichever is greater, based on a mean of five determinations [13].

At least monthly, or whenever errors are suspected, two healthy nonsmoking reference subjects (biological controls) should undergo body plethysmography. Previously established baseline data from the biological controls should have a coefficient of variation of $<5\%$ for both FRC and TLC. Values that differ significantly from the baseline means on the same subject suggest errors of measurement. A suggested threshold above which the difference is significant is two standard deviations above the mean, with the standard deviation calculated from the baseline data points. A large multilaboratory study of repeat measurements found that this threshold is $\sim 4\%$ for TLC and $\sim 7\%$ for FRC [28]; tighter standards can be adopted at the cost of more frequent false alarms that suggest equipment malfunction. Biological controls can identify problems missed during *in vitro* testing such as if an incorrect mouthpiece is being used [29]. If the operator is a biological control, they can provide acute evaluation of equipment suspected to have a problem during patient testing. The task force recognises that although experience supports the value of biological controls, evidence for the practice is lacking, there are challenges with variability (*e.g.* ageing, low *versus* high natural individual variability), a range of values tested that do not include extremes of disease, laboratory efficiency, timely analysis of data, turnover and availability of staff, and concerns with privacy if staff serve as biological controls (see supplementary material for data analysis spreadsheet).

A validation process for onboarding new, repaired equipment, or significantly updated software has been defined in the supplementary material. This process assists the laboratory management team in identifying bias or shifts in clinical results related to an equipment change.

Calculations

The calculation of VTG is based on Boyle's law, which states:

$$P_{av1} \times VTG_1 = P_{av2} \times VTG_2 \quad (1)$$

P_{av1} and VTG_1 are the absolute pressure and lung volumes before the compression/decompression manoeuvre, and P_{av2} and VTG_2 are the absolute pressure and lung volumes after the manoeuvre. Water vapour pressure needs to be subtracted from all pressures, because it does not behave as a compressible gas in that its partial pressure is determined only by temperature, but this is not shown for the sake of simplicity. Expressed as a change from the baseline, the equation becomes:

$$VTG = \left(\frac{\Delta V}{\Delta P} \right) \times P_{av2} \quad (2)$$

Since the panting manoeuvre is intended to occur with small changes in pressure around barometric pressure (P_B), the simplified and widely used version is:

$$VTG = \left(\frac{\Delta V}{\Delta P} \right) \times P_B \quad (3)$$

$\Delta V/\Delta P$ represents the slope of the simultaneous changes in body volume, which, in a pressure plethysmograph, are the tiny changes in pressure within the box, calibrated to reflect changes in the volume of the subject *versus* the change in pressure at the mouth. When a rapid inspiratory manoeuvre is performed, the complete version must be used, as follows:

$$VTG = \left(\frac{\Delta V}{\Delta P} \right) \times P_{alv2} \times \left(\frac{P_{alv1}}{P_B} \right) \quad (4)$$

If the panting manoeuvre begins with a P_{alv1} that is different from P_B , as occurs if the occlusion takes place at a volume other than FRC, the volume will need to be corrected to FRC, but P_{alv1} will also need to be corrected for P_B . Details of the complete derivation of the equations are given in both a web-based document and background article [13].

The underlying assumption of the technique is that the pressure–volume changes in the body are isothermal, and any heat generated by compression is instantaneously lost to the surrounding tissue. However, changes in pressure and volume within the plethysmograph are assumed to be adiabatic (*i.e.* there is insufficient time for heat exchange to occur between the air within the plethysmograph and either the walls or the subject during the decompression and compression manoeuvre). For panting frequencies on the order of 1 Hz, this assumption is valid. However, slow decompression manoeuvres where the subject is occluded at end-expiration and the pressure–volume changes occur with the normal respiratory effort are to be discouraged, since the time course may allow for heat exchange within the plethysmograph. This would alter the pressure–plethysmograph volume calibration. This would not be a problem if the subject made a rapid inspiratory effort, but the complete version of Boyle’s law should be used [13].

Along the same line, it is customary to subtract the volume of the apparatus between the mouth and the occluding valve from the VTG. However, decompression and compression of this volume are not isothermal, and if the volume is large in relation to VTG due to an excessively large filter, for example, errors will be introduced. In other words, efforts should be made to minimise the volume between the occluding valve and the patient.

Body plethysmography in children

In most children aged ≥ 3 years who have successfully completed spirometry, body plethysmography is possible. This requires staff specially trained to work with children. In one study, 70% of young children aged between 3 and 7 years who successfully performed spirometry were able to tolerate occlusions and sufficiently performed FRC measurements in the body plethysmograph. During each closed-shutter procedure two to three breathing efforts were performed [30]. In order not to disturb the pressure measurements by dangling of the feet, it is important to adjust the height of the seat and use a footrest if necessary. If a footrest is used, box calibration should be performed with the footrest inside the box.

Measurement of FRC using MBW

Introduction and theory

The multiple breath inert gas washout technique (MBW) is based on washing out an inert tracer gas from the lungs over multiple tidal breaths. This tracer gas can either be an endogenous gas (*e.g.* N_2) washed out by breathing 100% oxygen, or an exogenous gas (*e.g.* sulfur hexafluoride) washed out using room air. The initial alveolar tracer gas concentration and the amount of tracer gas washed out can then be used to calculate the lung volume at the start of washout (the breath immediately preceding the washout). FRC measured by MBW (FRC_{MBW}) represents the lung volume at end of expiration in direct communication with the airway opening.

While historical versions of the test were based on a set time period (*e.g.* 7 min), the current consensus guidelines [31] recommend an end-of-test threshold when the end-tidal tracer gas concentration reaches below 1/40th of the start concentration, which corresponds with the threshold used to calculate the lung clearance index.

Additional details and literature regarding various inert gas washout techniques and the calculation of ventilation inhomogeneity indices are available in the ATS/ERS consensus statement and ATS preschool technical statement for MBW testing [31, 32].

Equipment

Flow analysers (*e.g.* pneumotachographs, ultrasonic flow meters, turbines, *etc.*) incorporated into the breathing circuits to measure gas flows should have an instantaneous flow accuracy within 5% across the range of flows encountered during clinical testing and volume accuracy within 3% using a precision calibration syringe [31]. In young children, tidal volume accuracy should be within 3% or 5 mL, whichever is greater [32].

Gas analyser properties should ensure a linear and accurate gas signal. End-tidal tracer gas concentrations should be within $\leq 1\%$ of the tracer gas concentrations at the start of the washout (*e.g.* ± 0.8 at 80% N₂) and within 5% of the tracer gas concentrations at the end-of-test criteria (*e.g.* ± 0.1 at 2% N₂). An analyser rise time of < 100 ms to 90% of the target gas concentration is recommended across all age groups. The system should have a sampling rate of ≥ 100 Hz per channel for flow and gas concentration measurements (met by all nine current manufacturers of MBW equipment surveyed). In systems utilising carbon dioxide (CO₂) and oxygen (O₂) analysers for indirect measurement of N₂, the same requirements noted for N₂ analysers should be met for the calculated N₂ gas concentrations. Manufacturers and users should be aware of the potential for cross-sensitivity between CO₂ and O₂ analysers, which in one system led to overestimation of FRC and was corrected by a software update [33, 34]. Of nine current manufacturers of MBW equipment surveyed, four meet the specification for direct or indirect measurement of N₂ tracer gas concentration and four only reported O₂ analyser accuracy of within 1% and CO₂ accuracy within 0.1%.

Flows and integrated volumes should be reported at BTPS. Signals for flow and gas concentrations should have a temporal alignment accuracy within 10 ms across the duration of the entire washout. Dynamic flow and viscosity dependent delay synchronisation is recommended for testing in young children because the high variability in breathing pattern influences delay between the flow and gas concentration signals. Total equipment dead space should be minimised to < 2 mL·kg⁻¹. Equipment-related resistance should be minimised to avoid the effects on breathing pattern and FRC during testing.

Patient preparation

The measurement procedure should be thoroughly explained, demonstrated and practised with the patient. This must include practising 1) mouthpiece and nose clip placement; 2) tight lip seal throughout the measurement; and 3) relaxed tidal breathing. A flanged or scuba-like mouthpiece or face mask can assist with preventing leaks. If tolerated, patients should not breathe supplemental oxygen for ≥ 10 min prior to an MBW manoeuvre: the operator should confirm that exhaled N₂ is 78% prior to a manoeuvre and wait additional time if it is not. The patient should be asked if they have a perforated eardrum; if so, an earplug should be used.

Measurement technique

The measurement technique should adhere to the following steps.

- 1) The equipment should be turned on and allowed an adequate warm-up time and set up for testing including spirometer and gas calibrations, according to manufacturer's instructions.
- 2) The patient is instructed to breathe regular tidal breaths without sighs, cough or apnoea. Children should perform relaxed tidal breathing, whereas adults can be encouraged to perform fixed-volume tidal breathing (*e.g.* 1 L).
- 3) An adequate time should be allowed (~ 30 – 60 s) before the washout phase to permit the patient to become accustomed to the apparatus and ensure a stable end-tidal expiratory lung volume (see Measurement of FRC).
- 4) Switching to the washout phase:
 - a) for N₂ MBW, the patient breathes room air during a pre-washout phase before being switched to 100% O₂ to wash out the resident N₂ gas;
 - b) for exogenous gas MBW, the patient breathes an inert tracer gas mixture during a wash-in phase until an equilibrium in gas composition is reached between the lung and the tracer gas mixture. The patient is switched to room air to wash out the exogenous tracer gas;
 - c) the switch to 100% O₂ (N₂ MBW) or room air (exogenous gas MBW) should occur at the stable FRC.
- 5) The tracer gas concentration is monitored during the washout. A change in inspired tracer gas or sudden large increases in expiratory tracer gas concentrations can indicate a leak and the test should be stopped. A typical profile is shown in figure 5. If end-tidal CO₂ is available, it should remain in the range of 4–6% to exclude significant hypo/hyperventilation. MBW is a tidal breathing test that should report FRC in ventilated regions of the lung. Breathing deviations outside of this (both immediately before and during washout) should be avoided to prevent the release of trapped gas from under-ventilated regions, which can affect the measurement and repeatability of FRC [31].

- 6) The washout is complete when the end-tidal tracer gas concentration is below 1/40th of the starting concentration for at least three consecutive tidal breaths.
- 7) Once measurement of FRC is complete, the patient is instructed to perform a linked manoeuvre as described in Derivation of lung subdivisions.
- 8) A waiting period of at least twice the washout time is recommended between manoeuvres. Longer waiting periods may be required in patients with severe obstructive or bullous disease [35].

Quality control

Before each patient is tested, the concentration of tracer gas should be within 0.5% of the expected baseline reading (e.g. 78.08% for N₂ in ambient air). The accuracy of the flow and volume output of the flow measuring device should be confirmed at least daily with a calibrating syringe. A two-point calibration of gas analysers is recommended prior to each testing day. Testing of biological controls should be performed monthly and whenever an error is suspected; see plethysmography section for guidance on using biological controls.

Calculations

FRC_{MBW} is computed from the following equation:

$$\text{FRC}_{\text{MBW}} \times \text{Fet}_{\text{start}} = (\text{FRC}_{\text{MBW}} \times \text{Fet}_{\text{end}} + \text{net volume of inert gas exhaled}) \quad (5)$$

Solving for FRC_{MBW}, this becomes:

$$\text{FRC}_{\text{MBW}}^* = \frac{(\text{net volume of inert gas exhaled})}{(\text{Fet}_{\text{start}} - \text{Fet}_{\text{end}})} \quad (6)$$

where Fet is the concentration at end-tidal volume of the tracer gas, at the start (Fet_{start}) and end (Fet_{end}) of the MBW measurement. The net volume of tracer gas exhaled is calculated as the sum of the integral products of exhaled volume and gas concentration for each washout breath. FRC_{MBW}* includes the volume of the equipment dead space between the sensor and the patient, which is subtracted, and the result corrected to BTPS conditions. Correction for potential diffusion of tissue N₂ into the lung is no longer recommended [31].

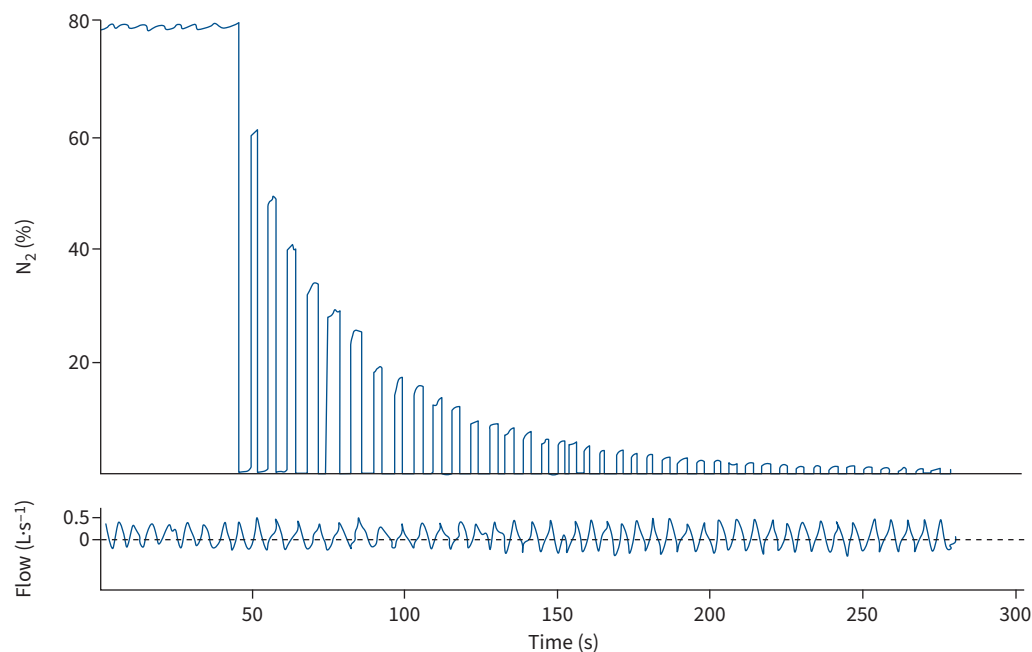


FIGURE 5 Display of the time course of nitrogen (N₂) (%) and flow (L·s⁻¹) throughout the standard multiple breath washout measurement with the patient breathing 100% oxygen. When expressed as N₂% versus volume instead of time (not shown), the area under the curve would be the N₂ volume washed out.

Measurement of FRC using helium dilution

Introduction and theory

The method for measuring lung volumes is based on the mixing and equilibration of the resident gas in the lung with a known volume of gas containing helium. Helium is inert and insoluble so that negligible amounts cross the alveolar membranes into the lung tissue and blood. The test gas typically consists of a concentration of helium and oxygen. During the test the helium concentration falls progressively, stabilising once mixing is complete. During rebreathing the CO₂ is absorbed and oxygen is added continuously to maintain a constant overall volume of the system (equipment and the lungs).

The lung volume (FRC_{He}) at the time the subject is connected to the spirometry apparatus of a known volume (V_{app}) and helium fraction (F_{He1}) is calculated from the helium fraction at the time of equilibration (F_{He2}) as follows:

$$V_{\text{app}} \times F_{\text{He1}} = (V_{\text{app}} + \text{FRC}_{\text{He}}) \times (F_{\text{He2}}) \quad (7)$$

$$\text{FRC}_{\text{He}}^* = \frac{V_{\text{app}}(F_{\text{He1}} - F_{\text{He2}})}{F_{\text{He2}}} \quad (8)$$

FRC_{He}* includes the dead space of the equipment and mouthpiece, which is subtracted, and the result corrected to BTPS conditions.

Equipment

There are typically two main equipment configurations used to perform this test.

The first was described in detail in the 2005 standard utilising a volume displacement spirometer ≥ 8 L, a mixing fan, CO₂ absorber, O₂ and helium supplies, a gas inlet and outlet and a water vapour absorber in line with the helium analyser. Figure 6 is an example of this configuration with the equipment connected to the patient *via* a circuit and tubing. The spirometer is filled with a known concentration of helium (~10%). O₂ is added and mixed using a fan. Any drift because of CO₂ absorption and O₂ consumption is observed in the spirometric baseline trace and can be corrected by the continuous addition of O₂. The time course of helium equilibrium in a normal subject and a patient with COPD is presented in the helium concentration *versus* time graph.

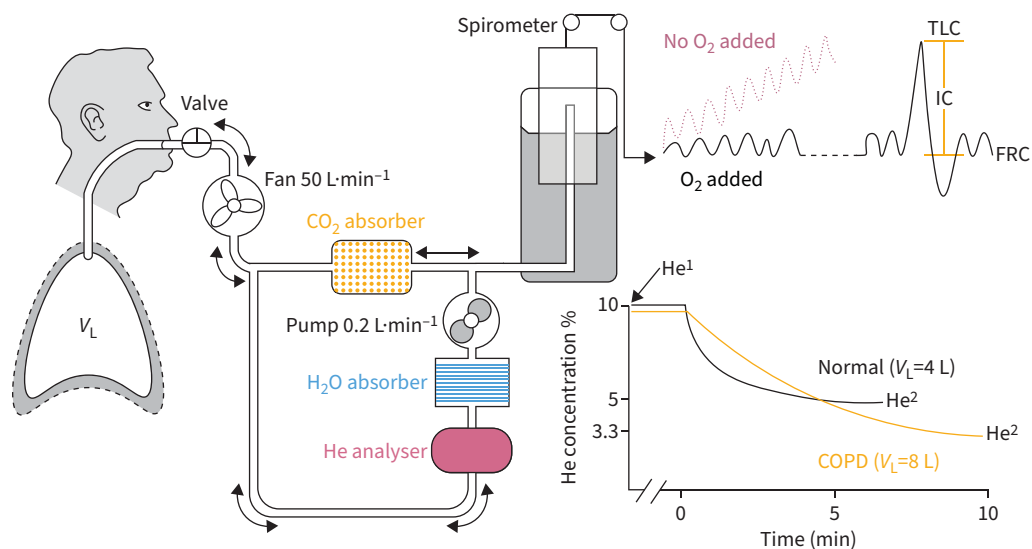


FIGURE 6 Helium (He) dilution setup utilising a volume-displacement spirometry. The spirometric tracing will have a rising baseline as shown in red if carbon dioxide (CO₂) absorption and oxygen (O₂) consumption are not accounted for by continuous addition of an appropriate amount of O₂. TLC: total lung capacity; IC: inspiratory capacity; FRC: functional residual capacity; V_L: lung volume. Reproduced from [36] with permission.

Another commonly available configuration utilises a flow sensing spirometer (pneumotachograph), with a rebreathing bag, CO₂ absorber, mixed O₂ and helium supply, a gas inlet and outlet, an oxygen compensation switch and a water vapour absorber in line with the helium analyser (figure 7). Exact gas concentrations (generally 9–14% helium, 21% oxygen, balance air) from a certified medical gas cylinder are added to a rebreathing bag from which the patient will inhale until equilibration is reached, as determined automatically by the measuring system. The dead-space volume of a pneumotachograph is less than that of a volume displacement configuration, *e.g.* ~1 L instead of ~4 L. The method of gas mixing in this configuration varies by manufacturer. Some manufacturers use a fan to mix the gas prior to and during the helium wash-in phase. Others report that mixing is performed by the subject's tidal ventilation instead of using a fan. Equilibration is also assisted by the gas sampling that comes from the bag, through the analyser and then returned to the bag. The oxygen level is kept constant by injecting oxygen into the circuit when O₂ falls below the threshold level. A stable baseline indicates no dilution of oxygen in the circuit and hence the initial bag volume is maintained. The CO₂ is removed both on expiration and on inspiration using a chemical absorber, *e.g.* soda lime. It is useful to note that an increase in temperature may result from the patient breathing across the CO₂ absorber leading to production of heat and water vapour and can result in water droplets in the rebreathing bag. This may require the use of single-use rebreathing bags. The spirometer should comply with the latest volume measurement standard [10]. Circuit resistance including mouthpiece and filter should be <0.05 kPa·L⁻¹·s⁻¹. The volume of bacterial filters should be minimised (ideally <100 mL). Dead-space details should be available from the manufacturer. The 2005 standard describes helium analysers, gas sampling and absorber requirements.

Patient preparation

The procedure is explained, demonstrated and practised, emphasising the need to avoid leaks around the mouthpiece during the test with a tight lip seal and to use a nose clip. Use of a flanged mouthpiece will assist with preventing leaks. The patient should be asked if they have a perforated eardrum; if so, an earplug should be used.

Measurement technique

Specific details of procedures will vary with different types of equipment and degrees of automation [37], but the basic procedure is as follows.

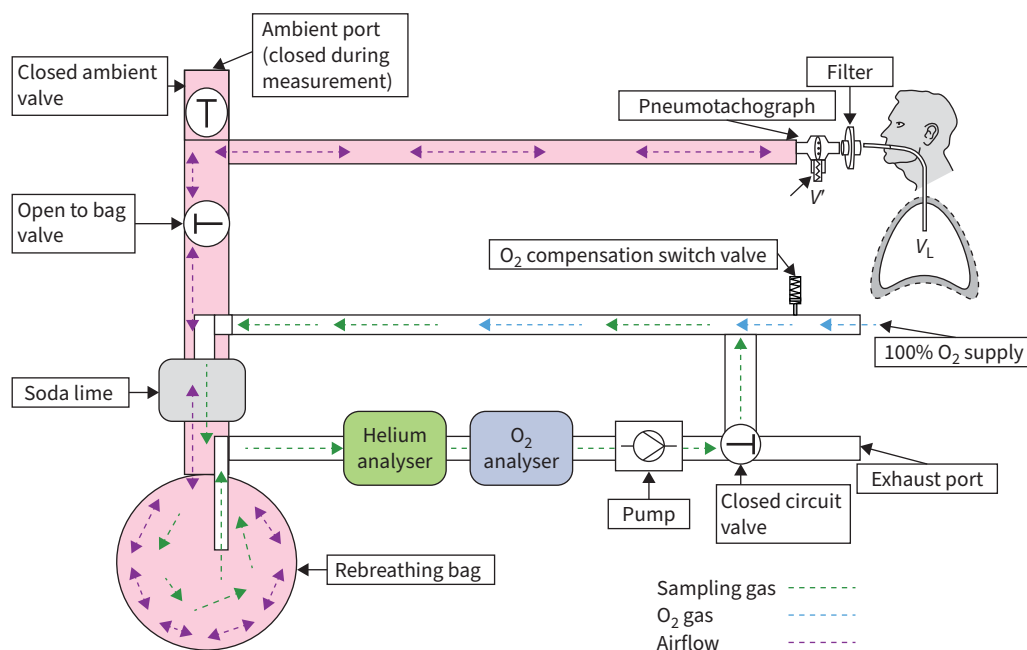


FIGURE 7 Helium dilution setup utilising a pneumotachometer and rebreathing bag. Volumes of 100% oxygen (O₂) are added to the bag to compensate for oxygen consumption to keep the oxygen percentage in the circuit and the circuit volume constant. Helium is analysed by continuously sampling gas that is pumped from the rebreathing bag. V_L : lung volume.

- 1) The equipment should be turned on and allowed an adequate warm-up time and set up for testing including spirometer and gas calibrations, according to manufacturer's instructions.
- 2) The patient breathes on the mouthpiece to achieve a stable tidal expiratory breathing pattern, which typically takes ~30–60 s to become accustomed to the apparatus (see Measurement of FRC).
- 3) The patient is connected to the test gas at the end of a normal tidal expiration.
- 4) The patient is instructed to breathe regular tidal breaths. Continuous measurement of the O_2 concentration ensures a satisfactory O_2 supply and provides a means to adjust the output of thermal-conductivity helium analysers for the effect of different O_2 concentrations. Irregular breathing during dilution may affect the measurement and repeatability of FRC in the setting of heterogeneous ventilation. In some systems, irregular breathing may impact the O_2 supply and thereby potentially affect the measurement of FRC by changing helium concentration through a change in circuit volume.
- 5) The percentage helium concentration and equilibration graph are monitored continuously for potential leaks (figure 8). A sudden drop in helium indicates a system leak and will result in an overestimation of FRC. Helium equilibration is considered to be complete when the change in helium concentration is $<0.02\%$ for 30 s. The test rarely exceeds 10 min, even in patients with severe ventilation inhomogeneity [37].
- 6) Once the helium equilibration is complete, the patient is disconnected from the test gas and measurements of ERV and IC are linked to the FRC measured as described in the Derivation of lung subdivisions section.
- 7) A waiting period of at least twice the dilution time is recommended between manoeuvres. Longer waiting periods may be required in patients with severe obstructive or bullous disease.

Quality control

Before each patient is tested, the following items should be checked: status of all CO_2 and water absorbers; operation of the circuit fan if applicable (assessed by listening); and the baseline stability of helium and volume signals. The reliability of the CO_2 and water absorbers should be checked before each test (either from visual inspection, or by replacing the absorbent after a specified number of tests or accumulated minutes of equilibration time).

Systems that can have gas filling volume checks should be checked for leaks at least once per month, and after tubing or canister changes. The stability of the helium analyser should be confirmed weekly (it should not drift $>0.02\%$ in 10 min; two out of four current manufacturers of helium dilution equipment surveyed reported a 10-min drift of 0.01%). The temperature should be validated as described previously [10]. Monthly testing of biological controls is recommended and useful, in that it tests not only the equipment,

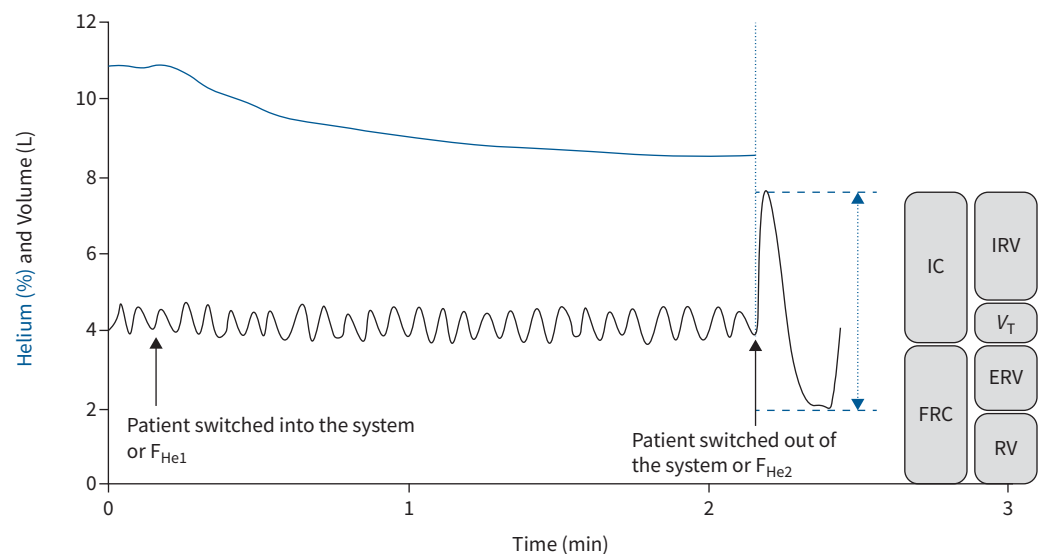


FIGURE 8 Display of an acceptable profile for a helium dilution test to determine functional residual capacity (FRC), in which oxygen (O_2) is continually added to compensate for O_2 consumption. Once equilibration is reached, a patient is switched from breathing helium to room air. F_{He1} : helium fraction at the time that the patient is connected to the apparatus (10.9% in this example); IC: inspiratory capacity; IRV: inspiratory reserve volume; V_T : tidal volume; RV: residual volume; ERV: expiratory reserve volume.

but also the procedures used by the operators; see plethysmography section for guidance on using biological controls.

Calculations

Providing the subject is connected to the spirometer at FRC, FRC_{He} can be calculated from the previously stated equations (included in the introduction and theory of the measurement of FRC using helium dilution). With regards to corrections in calculating FRC_{He} , the following points should be considered.

- 1) FRC_{He} is determined at a condition between ambient temperature and pressure saturated with water vapour and BTPS and should be corrected to BTPS.
- 2) Correction factors for N_2 excretion during the helium equilibration, and corrections for helium concentration when the respiratory quotient differs from 1.0 can be ignored [37].
- 3) With regards to switching errors, in practice, patients are not always at FRC when they are switched into the spirometer circuit. Corrections for this are typically made automatically from the spirometer trace (supplementary figure S5), but it is still preferable for continuous recordings of spirometry to be available so the computer-derived adjustments for switch-in errors can be confirmed (or edited) by the operator.

Measurement of lung volumes using imaging techniques

Physiological tests are preferred to investigate a suspected restrictive disorder or hyperinflation, but in some situations, including research, imaging may be the only source of lung volume information.

Volumes derived from imaging techniques preferably done in the upright position include thoracic cage volume, total lung volume, lung tissue volume and air volume; the latter is most comparable to the results from normal persons using the physiological techniques described earlier. While imaging techniques can provide subdivisions of TLC including FRC and RV with more extensive coaching and pairing with spirometry, typically measurements are made only on images obtained at maximal inflation. In subjects with a limited ability to cooperate, radiographic lung volumes may be more feasible than physiological measurements. However, the extent of lung inflation at the time of image acquisition, body position and image analysis technique influence the measurements and are essential to define. Further consideration of these details and specific imaging methods is provided in the supplementary material.

Repeatability

The goal is to obtain at least three acceptable FRC_{pleth} values that agree within 5% (*i.e.* difference between the highest and lowest value divided by the mean is ≤ 0.05). If there is a larger deviation, additional values should be obtained, until three values agree within 5% of their mean. Patient fatigue may limit the number of manoeuvres. Results with repeatability $>5\%$ may still be of use.

For MBW and helium dilution, operators should strive to obtain at least two technically acceptable trials [37, 38]. FRC_{MBW} and FRC_{He} should be within 10% of the mean of all acceptable or useable trials (*i.e.* difference between the highest and lowest value divided by the mean is ≤ 0.10). Tidal breathing is likely to be variable in young children (aged <7 years) and more lenient test repeatability criteria are recommended [31, 32].

Acceptability and grading

Task force members considered whether to grade individual reported lung function indices as in the 2019 spirometry standard or separate manoeuvres as in the 2017 D_{LCO} standard. The conclusion was to provide a practical classification of FRC and linked spirometry manoeuvres: acceptable (meeting all quality criteria); useable (reported and used with caution); or not useable or acceptable (reject: consider not reporting), which combined with repeatability contribute to grading systems for the lung volume test. These grading systems can provide a level of confidence in the accuracy of lung volume measurements. The decision to grade the lung volume test rather than individual reported indices or separate manoeuvres was based on these considerations: 1) a lower quality of the linked spirometry affects multiple indices simultaneously (*e.g.* VC, RV and TLC) and it is difficult to have more or less caution about one index *versus* another; 2) the quality of the indices is related through shared dependence on the quality of the FRC measurement followed by linked spirometry; and 3) the FRC is seldom used clinically by itself and so there is less of a need to grade it separately as there is for the FVC and forced expiratory volume in 1 s (FEV_1). Separate acceptability and grading systems are given for different methods of measuring lung volumes because 1) each method has unique technical considerations for evaluating quality; 2) the different lung volume methods are reported to have different repeatability standards; and 3) for MBW, from which pulmonary function indices other than lung volumes are also derived, a previously proposed and evaluated grading system provided key criteria [38].

The classification and grading criteria should be incorporated into the software to reduce the implementation burden and potential for error. The acceptability and grading criteria are not validated but are an attempt to codify published data and task force members' experience in what is achievable and best practice, with guidance from recommendations in other statements [10, 18, 31, 37, 39]. The proposed system does not preclude the use of reasonable alternatives such as removing criteria related to stability of pre-shutter closure/pre-switch-in end-tidal lung volume if RV and TLC are the only variables of interest and only linked spirometry is performed. The overriding goal of the operator must be to always achieve the best possible testing quality for each patient.

Table 2 lists acceptability criteria for the measurement of FRC_{pleth} . Table 3 lists acceptability criteria for the linked spirometry manoeuvre. The quality of the FRC_{pleth} manoeuvre, quality of the linked spirometry manoeuvre and the repeatability of the measurements determine the overall grade of a testing session (table 4). Grades D, E and U (useable) tests are reported, but interpreted and used clinically with caution.

For MBW and helium dilution, acceptability criteria are listed in tables 5 and 6. All MBW and helium dilution measurements with leak should be excluded. MBW measurements should be visually inspected for large deviations in breathing pattern that could influence results. Significant deviations (sighs, coughs, very small breaths, apnoeas) in tidal breathing immediately prior to and at the start of the washout will probably influence FRC results and these manoeuvres should be terminated immediately in order to collect additional attempts [38, 40–42]. A separate grading system is presented for MBW and helium dilution in table 7 because it is not easy to obtain multiple acceptable manoeuvres. Difficulty in maintaining a very steady breathing pattern during washout and dilution is expected to frequently yield useable rather than acceptable manoeuvres. This grading system deviates from that published for MBW [38], but is intended to be clinically useful and consistent across all methods in this standard; alternatives may be more appropriate in research settings.

TABLE 2 Acceptability criteria for thoracic gas volume (functional residual capacity) measurement using body plethysmography

Tidal breathing prior to shutter closure and pants/small breaths during shutter closure	
Acceptable	Pre-shutter closure: <ul style="list-style-type: none"> • stable end-tidal lung volume[¶] During shutter closure: <ul style="list-style-type: none"> • closed pants • overlapping straight lines with no thermal drift • straight lines with minimal thermal drift • pant frequency 0.5–1 Hz or pant frequency >1.0–1.5 Hz with no or minimal obstruction on spirometry
Useable[#]	Any of: <ul style="list-style-type: none"> • Pre-shutter closure: <ul style="list-style-type: none"> • unstable end-tidal lung volume[¶] without significant shift in either direction • During shutter closure: <ul style="list-style-type: none"> • portions of closed pants • portions of overlapping straight lines • parallel straight lines (thermal drift) • pant frequency >1.5–2.0 Hz with no or minimal obstruction on spirometry
Not acceptable or useable (reject)	Any of: <ul style="list-style-type: none"> • Pre-shutter closure: <ul style="list-style-type: none"> • unstable end tidal lung volume[¶] with significant shift in either direction (e.g. increase in end-expiratory lung volume with each breath) • During shutter closure: <ul style="list-style-type: none"> • open pants • no straight lines • excessive thermal drift • pants are clipped (mouth pressure transducer range exceeded) • pant frequency <0.5 Hz, >2.0 Hz or >1.5 Hz and evidence of significant obstruction on spirometry

Refer to supplementary figures S1–S3 for examples of normal and abnormal tracings. [#]: interpret with caution; [¶]: stability defined as three or more tidal breaths with the difference between maximum and minimum end-expiratory lung volume within 15% of the tidal volume [10].

TABLE 3 Acceptability and usability criteria for spirometry for calculation of residual volume and total lung capacity

Spirometry manoeuvre after FRC measurement	
Acceptable[#]	Linked spirometry: <ul style="list-style-type: none"> • if aged >6 years, SVC \geq (FVC – 150 mL) • if aged \leq6 years, SVC \geq (FVC – 100 mL) or (FVC – 10% of FVC), whichever is smaller
Useable[¶]	Any of: <ul style="list-style-type: none"> • unlinked spirometry with an MBW or helium dilution FRC measurement with stable pre-phase end-tidal lung volume⁺ • if aged >6 years, SVC \geq (FVC – 250 mL) • if aged \leq6 years, SVC \geq (FVC – 200 mL) or (FVC – 10% of FVC), whichever is smaller
Not acceptable or useable (reject)	Any of: <ul style="list-style-type: none"> • unlinked spirometry in body plethysmography • unlinked spirometry with an MBW or helium dilution FRC measurement with unstable pre-phase end-tidal lung volume⁺ • if aged >6 years, SVC < (FVC – 250 mL) • if aged \leq6 years, SVC < (FVC – 200 mL) or (FVC – 10% of FVC), whichever is smaller

FRC: functional residual capacity; SVC: slow vital capacity; FVC: forced vital capacity; MBW: multiple-breath washout. [#]: meets American Thoracic Society (ATS)/European Respiratory Society (ERS) acceptability criteria for within-manoeuve evaluation of inspiratory capacity and SVC [10]; if forced spirometry is not performed in the same session with lung volumes, an alternative is to require that at least three measures of vital capacity that meet ATS/ERS acceptability criteria for within-manoeuve evaluation are obtained and that the largest of these vital capacities is a substitute for the FVC in this table; [¶]: interpret with caution; ⁺: stability defined as three or more tidal breaths with the difference between maximum and minimum end-expiratory lung volume within 15% of the tidal volume [10].

Reporting

Selection of manoeuvres

The expected higher within-visit variability of lung volume manoeuvres compared to within-visit variability of spirometry manoeuvres and risk of underestimation and overestimation of lung volumes supports averaging of lung volume results prior to reporting. If two or more acceptable manoeuvres that meet the best FRC repeatability criteria in tables 4 and 7 (5% for body plethysmography and 10% for MBW and helium dilution) are obtained, these and their associated spirometry manoeuvres should be used to calculate and report FRC and other lung volumes, per the Derivation of lung subdivisions section. If the operator cannot obtain at least two acceptable and repeatable FRC manoeuvres, all manoeuvres with acceptable or useable FRC and spirometry and meeting the least stringent FRC repeatability (10% for body plethysmography and 25% for MBW and helium dilution), should be used. If three or more manoeuvres (e.g. one acceptable and two useable) are considered and the least stringent FRC repeatability is not met, the manoeuvre with the largest difference from the mean FRC should be discarded with its associated

TABLE 4 Grading system for a lung volume test performed using body plethysmography

Grade [#]	Number of FRC measurements ^{¶,†}	Number of SVC measurements [¶]	Repeatability [§] of FRC
A	\geq 3 acceptable	\geq 3 acceptable	Within 5%
B	\geq 2 acceptable	\geq 2 acceptable	Within 5%
C	\geq 2 acceptable	\geq 2 acceptable	Within 10%
D	1 acceptable and \geq 1 useable	1 acceptable and \geq 1 useable	Within 10%
E	1 acceptable and 0 useable	1 acceptable and 0 useable	NA
U	0 acceptable and \geq 1 useable	0 acceptable and \geq 1 useable	Within 10%
F	0 acceptable or useable		

FRC: functional residual capacity; SVC: slow vital capacity; NA: not applicable. [#]: overall grade is lowest of FRC, SVC and FRC repeatability grades. For example, if number of FRC measurements and repeatability of FRC are both grade A (three acceptable efforts and repeatable), but SVC is grade B (only two acceptable efforts), then the overall grade is B; [¶]: number of measurements refers to the manoeuvres used for calculation of FRC and other lung volumes; [†]: if all spirometry manoeuvres are not acceptable or useable, report FRC only; [§]: difference between the highest and lowest value divided by the mean \times 100.

TABLE 5 Acceptability and grading criteria for functional residual capacity measurement by multiple breath washout (MBW)

Tidal breathing prior to washout and washout phase characteristics	
Acceptable[#]	<p>Pre-switch-in:[†]</p> <ul style="list-style-type: none"> relaxed tidal breathing with stable end-tidal lung volume[§] <p>During washout:^f</p> <ul style="list-style-type: none"> relaxed tidal breathing without sigh, cough, or breath-hold flow is stable with no forced breathing or signs of hyperventilation (CO₂ within 4–6% range if available) no evidence of leak end-of-test criteria met (three consecutive tidal breaths under target concentration) <p>When performed:</p> <ul style="list-style-type: none"> adequate wait time between MBW manoeuvres (at least twice the washout time; longer with obstructive lung disease)
Useable[¶]	<p>As for acceptable except any of:</p> <p>Pre-switch-in:[†]</p> <ul style="list-style-type: none"> unstable end-tidal lung volume[§] without significant shift in either direction irregular tidal breaths (swallow, small breath) in pre-phase <p>During washout:^f</p> <ul style="list-style-type: none"> irregular first breath of washout (swallow, small breath) sigh, cough, or breath-hold in rest of washout but no increase in end-tidal tracer gas concentration end-tidal lung volume is unstable during washout but no increase in end-tidal tracer gas concentration
Not acceptable or useable (reject)	<p>Any of:</p> <p>Pre-switch-in:[†]</p> <ul style="list-style-type: none"> unstable end tidal lung volume[§] with significant shift in either direction (e.g. increase in end-expiratory lung volume with each breath) flow is highly erratic with or without forced breathing or hyperventilation (CO₂ outside 4–6% range if available) sigh, cough, or breath-hold <p>During washout:^f</p> <ul style="list-style-type: none"> sigh, cough, or breath-hold in first breath of washout sigh, cough, or breath-hold in rest of washout resulting in increase in end-tidal tracer gas concentration^{##} significant shifts in end-tidal lung volume during washout resulting in increase in end-tidal tracer gas concentration^{##} flow is highly erratic with or without forced breathing or hyperventilation (CO₂ outside 4–6% range if available) evidence of leak end-of-test criteria not met: manoeuvre does not have three consecutive tidal breaths under target concentration <p>When performed:</p> <ul style="list-style-type: none"> inadequate wait time between MBW manoeuvres for gas concentrations to re-equilibrate (less than twice the washout time or end-tidal tracer gas concentration has not returned to baseline)

Refer to supplementary figures S3 and S4 for examples of normal and abnormal tracings. CO₂: carbon dioxide. [#]: acceptable manoeuvres can be challenging to obtain in MBW, especially in young children; [¶]: interpret with caution; [†]: pre-switch-in (also known as pre-phase) grading criteria are relevant to the last three breaths before the washout phase; [§]: stability defined as three or more tidal breaths with the difference between maximum and minimum end-expiratory lung volume within 15% of the tidal volume [10]; ^f: grading criteria are relevant to all breaths of the washout until the end-of-test criteria are reached; ^{##}: increases in end-tidal tracer gas concentration during the washout in response to irregular breathing pattern can indicate the release of trapped gas from unventilated regions of the lung and is a reason to reject the trial.

spirometry; FRC repeatability is then recalculated and additional manoeuvres discarded in a similar manner until the least stringent repeatability is met. If two manoeuvres that are acceptable or useable do not meet the least stringent FRC repeatability, specific concerns about a manoeuvre should inform the decision on which one to discard prior to reporting FRC and other lung volumes from a single manoeuvre. Two acceptable FRC manoeuvres not meeting the least stringent repeatability criteria is expected to be an infrequent occurrence; in this case, a specific concern about one manoeuvre may not be present and it is recommended to obtain another manoeuvre to determine which is the outlier.

For body plethysmography, if two grade A manoeuvres meeting the best repeatability are not obtained, the report should include a caution to the interpreter that testing was suboptimal (see standardised operator comments in supplementary material). For MBW and helium dilution, only one manoeuvre may be feasible in clinical practice, and this can be reported if acceptable or useable with a note of caution that repeatability could not be assessed. Based on common practice for MBW and the challenge in obtaining acceptable manoeuvres, the mean of all acceptable and useable tests within 25% repeatability can be reported for MBW and helium dilution as an alternative to the preference for two or more acceptable and repeatable manoeuvres noted earlier.

TABLE 6 Acceptability and grading criteria for functional residual capacity measurement by helium (He) dilution

Tidal breathing prior to dilution phase and dilution phase characteristics	
Acceptable	Pre-switch-in: <ul style="list-style-type: none"> stable end-tidal lung volume[¶] During dilution: <ul style="list-style-type: none"> relaxed tidal breathing without sigh, cough, or breath-hold stable end-tidal lung volume no leak end-of-test criteria met: ($\Delta[\text{He}] < 0.02\% \times 30 \text{ s}$) When performed: <ul style="list-style-type: none"> adequate wait time between manoeuvres (at least twice the dilution time; longer with obstructive lung disease)
Useable[#]	As for acceptable except any of: Pre-switch-in: <ul style="list-style-type: none"> unstable end-tidal lung volume[¶] without significant shift in either direction During dilution: <ul style="list-style-type: none"> non-uniform dilution curve minimally unstable end-tidal lung volume sigh, cough or breath-hold with no leak
Not acceptable or useable (reject)	Any of: Pre-switch-in: <ul style="list-style-type: none"> unstable end-tidal lung volume[¶] with significant shift in either direction (e.g. increase in end-expiratory lung volume with each breath) During dilution: <ul style="list-style-type: none"> unacceptable breathing pattern evidence of leak failed end of test When performed: <ul style="list-style-type: none"> inadequate wait time between manoeuvres

[#]: interpret with caution; [¶]: stability defined as three or more tidal breaths with the difference between maximum and minimum end-expiratory lung volume within 15% of the tidal volume [10].

Report format

Laboratories should follow ATS recommendations for reporting of lung volume measurements with additions as noted for specific methods in this document [26]. To achieve interoperability, all pulmonary function devices should have the capability to export standardised pulmonary function test data to electronic medical records [43]. Testing session data file requirements have been listed in the D_{LCO} and spirometry technical standards [10, 18]; additional values specific to lung volume measurement are listed in the supplementary material. Operator comments are a key part of the report (supplementary material). The operator should give

TABLE 7 Grading system for a lung volume test performed by multiple breath washout (MBW) or helium dilution

Grade [#]	Number of FRC ^{¶,†} measurements	Number of SVC [¶] measurements	Repeatability [§] of FRC
A	≥2 acceptable	≥2 acceptable	Within 10%
B	1 acceptable and ≥1 useable	1 acceptable and ≥1 useable	Within 10%
C	≥2 useable	≥2 useable	Within 10%
D	≥2 acceptable or useable	≥2 useable	Within 25%
E	1 acceptable and 0 useable	1 acceptable and 0 useable	NA
U	0 acceptable and 1 useable	0 acceptable and 1 useable	NA
F	0 acceptable or useable		

FRC: functional residual capacity; SVC: slow vital capacity; NA: not applicable. [#]: overall grade is lowest of FRC, SVC and FRC repeatability grades. For example, if number of FRC measurements and repeatability of FRC are both grade A (three acceptable efforts and repeatable), but SVC is grade B (only two acceptable efforts), then the overall grade is B; [¶]: number of measurements refers to the manoeuvres used for calculation of FRC and other lung volumes; [†]: if all spirometry manoeuvres are not acceptable or useable, report FRC only; [§]: difference between the highest and lowest value divided by the mean×100.

comments on the test session and must report any quality issues (tables 2, 3, 5 and 6). Comparison with prior values during interpretation is important. Therefore, reports should always include trends.

Reference values

The GLI reference set provides contemporary sex-specific reference values for TLC and its subdivisions across the age range 5–80 years using data from 11 countries [44]. Currently, the GLI reference values have data only from subjects of European ancestry. There are few published studies of non-European reference values [45]. Due to many concerns with the use of race and ethnicity as a biological variable including their inconsistent definitions, marked heterogeneity within these groups and the risk of contributing to health inequities by normalising differential exposure to social and environmental influences on lung function, race-specific equations are not recommended [46]. However, because multiracial reference equations for lung volumes are not available, we recommend use of the GLI reference equations on an interim basis. The GLI reference equations can be utilised for plethysmographic, washout and dilution test methodologies. Caution is recommended when using GLI reference equations for those of non-European ancestry. For communities where most people are not represented by the GLI reference equations, reference equations meeting rigorous quality standards [47, 48] and representing an average inclusive of the diversity of the local population may be appropriate. Laboratories should ensure that local measurement techniques match those used to generate data used for derivation of reference equations. The taskforce is currently unable to recommend reference equations for imaging methodologies.

Future directions and key research questions

Lung volumes are less repeatable than FEV₁ or FVC from spirometry. Improved repeatability would increase the value of individual and serial lung volume measurements. TLC and RV are derived from FRC and linked spirometry, which each have measurement errors that may add together and contribute to the larger variability compared to FEV₁ and FVC. Analysis of the sources of variability and efforts to reduce the variability of both FRC and linked spirometry can improve repeatability of lung volume measurements. Other techniques such as imaging have different sources of variability and thus there is potential for higher repeatability compared to traditional methods through better characterisation and implementation. The clinical utility of lung volume measurements will be enhanced by having reference data available from populations that are the same or similar to those used for spirometry. Such data can contribute to interpretation of physiological patterns that suggest disease categories by making results concordant between spirometry and lung volumes. The diversity of populations contributing to reference data for both lung volumes and other pulmonary function tests must be increased. The acceptability and grading criteria presented in this document should be evaluated for achievability and performance in yielding accurate and precise results. An understanding of the relationship between acceptability and the likelihood of repeatability is needed. Availability and monetary and environmental costs of helium make the sustainability of the helium dilution technique uncertain.

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