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SERIES "ATS/ERS TASK FORCE: STANDARDISATION OF LUNG FUNCTION TESTING"
Edited by V. Brusasco, R. Crapo and G. Viegi
Number 3 in this Series

Standardisation of the measurement of lung volumes

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BACKGROUND AND PURPOSE

Inspired and expired lung volumes measured by spirometry are useful for detecting, characterising and quantifying the severity of lung disease. Measurements of absolute lung volumes, residual volume (RV), functional residual capacity (FRC) and total lung capacity (TLC) are technically more challenging, which limits their use in clinical practice. The role of lung volume measurements in the assessment of disease severity, functional disability, course of disease and response to treatment remains to be determined in infants, as well as in children and adults. Nevertheless, in particular circumstances, measurements of lung volume are strictly necessary for a correct physiological diagnosis [1].

In contrast to the relative simplicity of spirometric volumes, a variety of disparate techniques have been developed for the measurement of absolute lung volumes. These include the following: body plethysmography (using various methodologies), nitrogen washout, gas dilution, and radiographic imaging methods.

The present document integrates and consolidates the recommendations of the current American Thoracic Society (ATS)/European Respiratory Society Task Force on pulmonary function standards, and the recommendations from an earlier National Heart, Lung, and Blood Institute (NHLBI) workshop convened by the ATS. The NHLBI workshop participants, who were experts with considerable adult and paediatric experience, published their input in the form of background papers in the *European Respiratory Journal* between 1995 and 1999 [2–12]. Later, a NHLBI workshop consensus document was written, which can be found on the ATS website [13], for those who require more in-depth descriptions, discussion and a fuller derivation of equations.

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 contrast, lung volumes derived from conventional chest radiographs are usually based on the volumes within the outlines of the thoracic cage, and include the volume of tissue (normal and abnormal), as well as the lung gas volume. Lung volumes derived from computed tomography (CT) scans can include estimates of abnormal lung tissue volumes, in addition to normal lung tissue volumes and the volume of gas within the lungs. In this statement, previously accepted definitions will be used (fig. 1) [14–18].

The FRC is the volume of gas present in the lung at end-expiration during tidal breathing.

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

The maximum volume of gas that can be inspired from FRC is referred to as the inspiratory capacity (IC).

The inspiratory reserve volume is the maximum volume of gas that can be inhaled from the end-inspiratory level during tidal breathing.

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

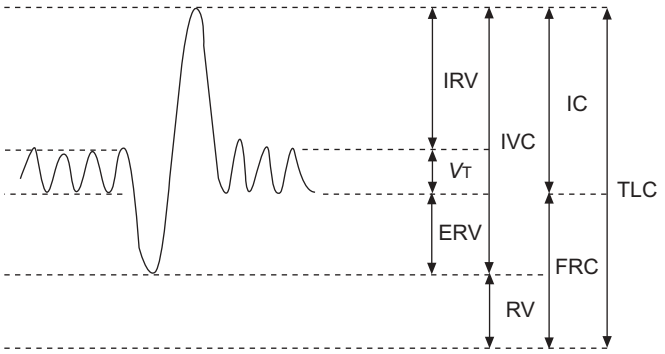

FIGURE 1. Static lung volumes and capacities based on a volume–time spirogram of an inspiratory vital capacity (IVC). IRV: inspiratory reserve volume; V_T: tidal volume (TV); ERV: expiratory reserve volume; RV: residual volume; IC: inspiratory capacity; FRC: functional residual capacity; TLC: total lung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

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

The thoracic gas volume (TGV or V_{TG}) is the absolute volume of gas in the thorax at any point in time and any level of alveolar pressure. Since this term is too nonspecific, it is recommended that its use should be discontinued and replaced with more specific terminology, for example, plethysmographic lung volume (abbreviated at $V_{L,pleth}$), and FRC by body plethysmography or TGV at FRC (FRC_{pleth}).

TLC refers to the volume of gas in the lungs after maximal inspiration, or the sum of all volume compartments.

The vital capacity (VC) is the volume change at the mouth between the positions of full inspiration and complete expiration. The measurement may be made in one of the following ways: 1) inspiratory vital capacity (IVC), where the measurement is performed in a relaxed manner, without undue haste or deliberately holding back, 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) forced vital capacity, 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.

PATIENT PREPARATION

Guidelines for patient preparation are included in the statement on general considerations for lung function testing in this series of documents [19].

DERIVATION OF LUNG SUBDIVISIONS

No matter what technique is used to measure FRC (see sections entitled Measurement of FRC using body plethysmography, Measurement of FRC using nitrogen washout, and Measurement of FRC using helium dilution), two subdivisions of the VC (IC and ERV) will have to be measured in order to calculate the TLC and RV (fig. 1). It has proved difficult to reach a consensus on whether the RV should be the minimal value as would most probably be obtained by performing the ERV manoeuvre from FRC and then subtracting ERV from the measured value for FRC, or the approaches which would likely result in higher RVs in those with obstructive lung disease

when RV was defined from either slow or forced expirations starting from the point of maximal inspiration. It was also difficult to identify a single method for measuring RV and TLC that was efficient for clinical use and performable by those with severe obstructive lung disease. While future studies are needed to provide better scientific rationale, two methods are recommended for computations of related lung volumes once FRC has been determined.

The first and preferred method is to measure ERV immediately after the acquisition of the FRC measurement(s), followed by slow IVC manoeuvres, all performed as ''linked'' manoeuvres (*i.e.* without the patient coming off the mouthpiece prior to the completion of the manoeuvres; fig. 2). The reported value for the FRC is the mean of the technically satisfactory FRC measurements, linked to the technically satisfactory ERV and IVC manoeuvres used for calculating the RV and TLC. The reported value for RV is the reported value for FRC minus the mean of the technically acceptable ERV measurements, linked to technically acceptable FRC determinations. The reported value of TLC is the reported value for RV plus the largest of the technically acceptable IVCs.

The second recommended method utilises the performance of IC manoeuvres immediately after the acquisition of the FRC measurement(s) to measure the TLC. This method may be necessary in those with severe obstructive dysfunction or severe dyspnoea who are unable to follow the FRC measurements with a linked ERV manoeuvre as a result of dyspnoea. The patients may come off the mouthpiece between successive linked FRC and IC determinations, and also between the separate VC manoeuvres that are required to calculate RV as the mean TLC minus the largest VC measured. The VC measurement can be derived from either the IVC manoeuvre that follows an ERV manoeuvre (as used in the first method), or from a slow EVC that follows an IC manoeuvre after the FRC determination. The slow EVC can be linked with the FRC/IC measurements if patient discomfort does not preclude optimal performance. 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 three largest sums of technically acceptable FRC values and linked IC manoeuvres.

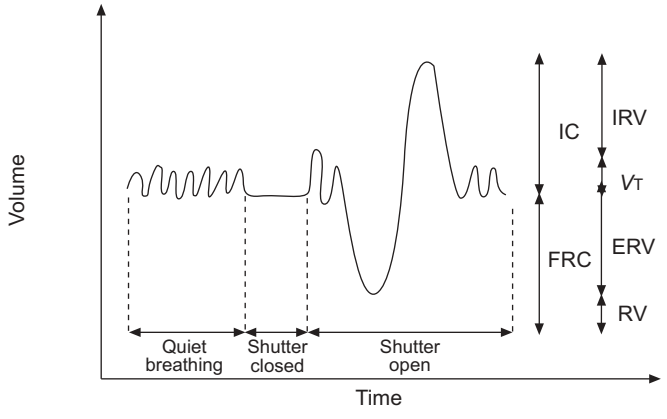

FIGURE 2. Volume–time display showing the sequence of quiet breathing and after stable end-expiratory level is achieved, a short period when the shutter is closed for determination of the thoracic gas volume, followed by an open-shutter period during which the patient stays on the mouthpiece and performs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

Recommendations for the measurement of VC are presented in the document on the standardisation of spirometry in this series [20]. There is insufficient evidence regarding optimal recommendations for the reproducibility criteria of the ERV and IC, which are used in computing TLC and RV.

The determination of FRC is the key component in the measurement of lung volumes, and can be assessed by body plethysmography, gas washout or gas dilution methods, or using radiography. The FRC_{pleth} includes nonventilated, as well as ventilated, lung compartments, and, thus, yields higher results than the gas dilution or washout methods [3, 11]. The FRC_{pleth} may be further increased by gas that is present in the abdomen. In cases of severe airflow obstruction, FRC_{pleth} may be overestimated when panting rates are >1 Hz [21]. In patients with severe airflow obstruction or emphysema, the true value of the FRC is underestimated by the gas dilution or washout methods. Despite this fact, the gas dilution/washout methods are widely used because they are simple to perform and the instrumentation is relatively inexpensive.

MEASUREMENT OF FRC USING BODY PLETHYSMOGRAPHY

Introduction and theory

The term TGV (or V_{TG}) 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 volume of intrathoracic gas measured when airflow occlusion occurs at FRC.

In healthy individuals, there are usually minimal differences in FRC measured by gas dilution/washout techniques and plethysmography. However, in patients with lung disease associated with gas trapping, most, but not all, studies indicate that FRC_{pleth} often exceeds the FRC measured by gas dilution [3, 11].

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 [11, 22]. More detailed reviews of the theory are available [11, 13].

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 body plethysmograph by measuring the changes in the following: 1) pressure within a constant-volume chamber (variable-pressure plethysmograph); 2) volume within a constant-pressure chamber (volume-displacement plethysmograph); or 3) airflow in and out of a constant-pressure chamber (flow plethysmograph). A flow plethysmograph can be converted into a variable-pressure

plethysmograph by simply occluding the pneumotachograph orifice, making it adaptable to the respiratory manoeuvre of interest.

Regardless of the plethysmograph type, a transducer capable of measuring mouth pressure $\geq \pm 5$ kPa ($\geq \pm 50$ cmH_2O), with a flat frequency response in excess of 8 Hz, is essential. Spirometers or pneumotachographs that are used for the measurement of lung volumes and forced inspiratory and expiratory volumes should meet published standards for the accuracy and frequency response of spirometric devices [16, 23]. The transducer measuring changes in the chamber pressure must be capable of accurately measuring a range of ± 0.02 kPa (± 0.2 cmH_20) [16]. Thermal drift may give rise to a pressure change of as much as 1.0 kPa (10 cmH_20), which may necessitate a larger working range of the transducer. A time constant of 10 s for a controlled leak (which minimises slowly occurring pressure changes) is ideal.

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 [11]. A second approach for compensation is to use an iterative method [24].

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 [11]. 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 fidelity of the signal at 5 Hz. To ensure that panting frequencies slightly above 1 Hz will not lead to problems, the minimum acceptable frequency response should result in accuracy at 8 Hz.

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. 2) The equipment is set up for testing, including calibration, according to manufacturer's instructions. 3) The equipment is adjusted so that the patient can sit comfortably in the chamber and reach the mouthpiece without having to flex or extend the neck. 4) The patient is seated comfortably, with no need to remove dentures. The procedure is explained in detail, including that the door will be closed, the patient's cheeks are to be supported by both hands, and a nose clip is to be used. 5) The plethysmograph door is closed, and time is allowed for the thermal transients to stabilise and the patient to relax. 6) The patient is instructed to attach to the mouthpiece and breathe quietly until a stable end-expiratory level is achieved (usually 3–10 tidal breaths). 7) When the patient is at or near FRC, the shutter is closed at end-expiration for ~2–3 s, and the patient is instructed to perform a series of gentle pants (~± 1 kPa (~± 10 cmH_2O)) at a frequency between 0.5 and 1.0 Hz [21, 25]. Panting frequencies of >1.5 Hz may lead to errors, and those <0.5 Hz may cause problems with the controlled leak of the body plethysmograph system. A metronome can be used to assist patients with this manoeuvre. 8) A series of 3–5 technically satisfactory panting manoeuvres should be recorded (*i.e.* a series of almost superimposed straight lines separated by only a small thermal drift on the pressure–volume plot; fig. 3), after which the shutter is opened and the patient performs an ERV manoeuvre, followed by a slow IVC manoeuvre (or, as a second priority, an IC manoeuvre followed by a slow EVC manoeuvre). If needed, the patient can come off the mouthpiece and rest between TGV/VC manoeuvres. Patients with severe dyspnoea may have difficulty performing the preferred VC method (*i.e.* ERV immediately after TGV, followed by a slow IVC; fig. 2). To overcome this, the patient can be instructed to take two or three tidal breaths after the panting manoeuvre, prior to performing the linked ERV and IVC manoeuvres. 9) For those unable to perform appropriate panting manoeuvres (*e.g.* young children), an alternative is to perform a rapid inspiratory manoeuvre against the closed shutter. In this situation, it is essential that the complete rather than the simplified version of the TGV computation equation [11] is used in the calculation of TGV. The user should confirm that the complete equation is used by the computer during such measurements. 10) With regards to repeatability, at least three FRC_{pleth} values that agree within 5% (*i.e.* difference between the highest and lowest value divided by the mean is ≤ 0.05) should be obtained and the mean value reported. If there is a larger deviation, additional values should be obtained until three values agree within 5% of their mean, and the mean value should be reported.

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 document in this series [20]. The mouth pressure transducer should be physically calibrated daily. The plethysmograph signal should also be calibrated daily, using a volume signal of similar magnitude and frequency as the respiratory manoeuvres during testing.

A validation of accuracy using a known volume should be performed periodically. This can be carried out using a ''model'' lung or container of known volume [11, 26]. Filling a flask with thermal mass (*e.g.* copper wool) is essential in

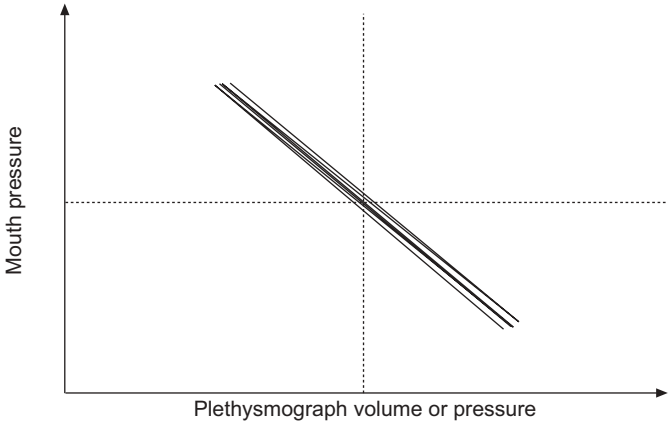

FIGURE 3. Display of a properly performed panting manoeuvre as a series of almost superimposed straight lines separated by only a small thermal drift.

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. 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 [11].

At least monthly, or whenever plethysmographic errors are suspected, two reference subjects (biological controls) should have their FRC_{pleth} and related RV and TLC measured. Values that differ significantly (*e.g.* >10% for FRC and TLC, or >20% for RV) from the previously established means for measurements on the same subject suggest errors of measurement. These criteria are approximately twice the reported coefficients of variation for repeat measurements of these parameters; hence, tighter standards can be adopted at the cost of more frequent ''false alarms'' that suggest equipment malfunction.

Calculations

The calculation of V_{TG} is based on Boyle's Law, which states:

$$P_{alv1} \times V_{TG1} = P_{alv2} \times V_{TG2} \quad (1)$$

P_{alv1} and V_{TG1} are the absolute pressure and lung volumes before the compression/rarefaction manoeuvre, and P_{alv2} and V_{TG2} are the absolute pressure and lung volumes after the manoeuvre. Water vapour pressure needs to be subtracted from all pressures, but this is not shown for the sake of simplicity. Expressed as a change from the baseline, the equation becomes:

$$V_{TG} = -(\Delta V/\Delta P) \times P_{alv2} \quad (2)$$

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:

$$V_{TG} = -(\Delta V/\Delta P) \times P_B \quad (3)$$

$\Delta V/\Delta P$ 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:

$$V_{TG} = -(\Delta V/\Delta P) \times P_{alv2} \times (P_{alv1}/P_B) \quad (4)$$

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 paper [11, 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 rarefaction and compression manoeuvre). For panting frequencies in the order of 1 Hz, this assumption is valid. However, slow rarefaction 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, as mentioned previously, the use of the simplified version of Boyle's Law would be inappropriate.

Along the same line, it is customary to subtract the volume of the apparatus between the mouth and the occluding valve from the TGV. However, rarefaction and compression of this volume are not isothermal, and if the volume is large in relation to TGV 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.

MEASUREMENT OF FRC USING NITROGEN WASHOUT

Introduction and theory

This technique is based on washing out the N_2 from the lungs, while the patient breathes 100% O_2. The initial alveolar N_2 concentration and the amount of N_2 washed out can then be used to calculate the lung volume at the start of washout. The technique originally utilised gas collections for a 7-min period, a period deemed adequate for washout of N_2 from the lungs of healthy subjects. The technique has the disadvantage that an inaccuracy in the measurement of the expired volume or the final N_2 concentration will cause a significant error. The availability of rapidly responding N_2 analysers and computers has further refined the technique. Additional details and literature citations regarding various N_2 washout techniques and washout measurements using other gases are available in a background paper [12].

A modification of the 7-min N_2 washout method, which monitors N_2 excretion over 5 min and then extrapolates the late exponential component of the continuous N_2 excretion curve, has been proposed [27], which avoids underestimating the true alveolar N_2 concentration in patients with obstructive lung disease and eliminates the need for longer washout times. The current authors are unaware of any commercial pulmonary function testing system that uses this approach; therefore, manufacturers are encouraged to offer it as an option in the future. Due to existing variations in currently available commercial systems and the absence of studies comparing accuracy, reproducibility and efficiency, no single method for the measurement of FRC using nitrogen washout (FRC_{N_2}) can be recommended at this time. The following recommendations are for methods used most commonly in clinical pulmonary function laboratories.

Equipment

N_2 analysers should be linear with an inaccuracy $\leqslant 0.2\%$ of full range throughout the measuring range (0–80%), have a resolution of $\leqslant 0.01\%$, and a 95% analyser response time of

<60 ms to a 10% step change in N_2 concentration (after correction for phase shift). Compliance with these performance specifications should be confirmed by the manufacturers, since few clinical laboratories have the resources required for such evaluations [13].

If measurements of N_2 concentration are made indirectly by subtracting measurements of O_2 and CO_2, the accuracy, drift and linearity characteristics of the O_2 and CO_2 analysers should result in indirect calculations of N_2, with comparable performance characteristics to the direct measurements of N_2 specified previously. Mass spectrometers should meet the previously outlined specifications for all three gases, have a molecular weight resolution of <1.0, and have <1% drift over 24 h, or at least be stable for the measurement period after calibration (which should be carried out immediately before use).

Pneumotachographs or other flow-measuring devices (*e.g.* ultrasonic flow meters, turbines, *etc.*) incorporated into the breathing circuits to measure gas flows should comply with the recommendations from the standardisation of spirometry document in the present series [20], but they only require a flow range of 0–6 $L \cdot s^{-1}$. Factors that must be considered and controlled to ensure that the previously highlighted performance specifications are met include: the performance characteristics of specific flow-measuring devices; potential inaccuracies from the condensation of water from expired gases; changes in gas temperature; and changes in gas viscosity or density over the range of O_2/N_2 mixtures.

The system should have a sampling rate of $\geqslant$40 samples$\cdot s^{-1}$ per channel for flow and N_2 signals. Amounts of exhaled N_2 should be calculated every 25 ms (or less), with appropriate corrections for phase differences between flow and N_2 measurements [28].

The breathing valve for switching the patient from breathing room air to 100% O_2 should have a dead space <100 mL for adults and <2 $mL \cdot kg^{-1}$ in smaller children. Oxygen can be provided either from a gas-impermeable bag filled with dry 100% O_2, or a source of O_2 connected to a demand valve. As a result of the effects of inspiratory resistance on FRC, triggering pressures from demand valves during tidal breathing should ideally be smaller than those pressures that are acceptable in IVC manoeuvres occurring during single-breath carbon monoxide diffusing capacity ($D_{L,CO}$) measurements. This is especially important in patients with neuromuscular weakness. However, until data that define the magnitude of errors with lower demand-valve pressures are available, the same maximal demand-valve pressures that are required for $D_{L,CO}$ measurements (<1 kPa (<10 cmH_20)) are acceptable.

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, with calibration as instructed by the manufacturer. 2) The patient should be asked if he/she has a perforated eardrum (if so, an earplug should be used). 3) The patient is seated comfortably, with no need to remove dentures. The procedure is explained, emphasising the need to avoid leaks around the mouthpiece during the washout and using a nose clip. 4) The patient breathes on the mouthpiece for ~30–60 s to become accustomed to the apparatus, and to assure a stable end-tidal expiratory level. 5) When breathing is stable and consistent with the end-tidal volume being at FRC, the patient is switched into the circuit so that 100% O_2 is inspired instead of room air. 6) The N_2 concentration is monitored during the washout. A change in inspired N_2 of >1% or sudden large increases in expiratory N_2 concentrations indicate a leak; hence, the test should be stopped and repeated after a 15-min period of breathing room air. A typical profile is shown in figure 4. 7) The washout is considered to be complete when the N_2 concentration is <1.5% for at least three successive breaths. 8) At least one technically satisfactory measurement should be obtained. If additional washouts are performed, a waiting period of $\geqslant$15 min is recommended between trials. In patients with severe obstructive or bullous disease, the time between trials should be $\geqslant$1 h [27]. If more than one measurement of FRC_{N_2} is made, the value reported for FRC_{N_2} should be the mean of technically acceptable results that agree within 10%. If only one measurement of FRC_{N_2} is made, caution should be used in the interpretation.

Quality control

Before each patient is tested, the N_2 analyser should be set to zero using 100% O_2, and then exposed to room air to confirm calibration. The percentage of N_2 for room air should be within 0.5% of the expected reading for room air (*i.e.* 78.08%). If a needle valve is used to create a sufficient vacuum to measure N_2 by emission spectroscopy, it should be regularly inspected and cleaned. Before the initial use and once every 6 months thereafter, the linearity of the N_2 analyser should also be confirmed by measuring the N_2 percentage of a calibration gas mixture, where the expected N_2 concentration is ~40%, either from a certified calibration tank or created using precision dilution techniques. Observed values should be within 0.5% of expected, and readings must be corrected for nonlinearity greater than this.

The accuracy of the flow and volume output of the flow-measuring device should be confirmed at least daily with a calibrating syringe, using pumping frequencies that will result

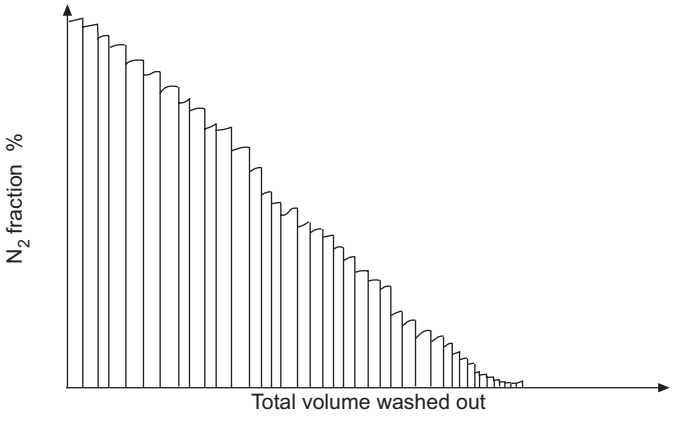

FIGURE 4. Display of a normal profile of a multiple-breath N_2 washout with the patient breathing 100% O_2. The area under the curve is the N_2 volume washed out, which, divided by the total volume washed out, gives the fractional concentration of N_2 in the volume of gas washed out at the end of the test or in the end-tidal gas of the last breath at the end of the test.

in flows of the same range as tidal flows, and should comply with the recommendations made in a previous document in this series [20]. Initially and monthly, exhalation volumes should be checked with the syringe filled with room air, and inhalation volumes with the syringe filled with 100% O_2. The temperature should be validated as described previously [19]. Testing of biological controls should be performed at least monthly.

Calculations

FRC_{N_2} is computed from the following equation:

$$FRC_{N_2} \times F_{N_2}1 = (FRC_{N_2} \times F_{N_2}2 + N_2 \text{ volume washed out}) - (N_2 \text{ volume from tissue}) \quad (5)$$

Solving for FRC_{N_2}, this becomes:

$$FRC_{N_2} = (N_2 \text{ volume washed out} - N_2 \text{ volume from tissue})/(F_{N_2}1 - F_{N_2}2) \quad (6)$$

where $F_{N_2}1$ and $F_{N_2}2$ are the fractions of N_2 in the end-tidal gas before the washout, and in the end-tidal gas of the last breath at the end of the test, respectively. The N_2 volume washed out is the volume in the bag multiplied by the N_2 fraction of the mixed gas in the bag, or it is calculated on-line as the sum of $F_{N_2} \times V_T$ for all the breaths, with F_{N_2} being the mixed expired fraction of N_2 in the individual breath and V_T the volume of that breath. This sum equals the area under the curve in figure 4. This value of FRC_{N_2} should be corrected to BTPS conditions, and the volume of the equipment dead space must be subtracted.

N_2 excreted from the tissues can be estimated from tables or complex exponential equations. Since the difference in the correction when these different sources are used is small, it is recommended that the following relatively simple equation for estimating tissue excretion, adjusted for body size as a result of N_2 eliminated after a 7-min washout period, is used [29]. As the largest fraction of the N_2 is excreted in the first phase of the washout, this equation can be assumed to be appropriate for washout times of <7 min:

$$N_2 \text{ tissue excretion (mL)} = ((BSA \times 96.5) + 35)/0.8 \quad (7)$$

where BSA is the body surface area in m^2, and is determined by using weight in kg and height in cm in the following equation [30]:

$$BSA = 0.007184 \times \text{weight}^{0.425} \times \text{height}^{0.725} \quad (8)$$

MEASUREMENT OF FRC USING HELIUM DILUTION

Introduction and theory

The method for measuring lung volumes is based on the equilibration of gas in the lung with a known volume of gas containing helium [31, 32]. The test gas consists of air with added oxygen of 25–30%, but higher concentrations are acceptable. Helium is added to a concentration of ~10% (full scale) [9]. 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:

$$V_{app} \times F_{He1} = (V_{app} + FRC_{He}) \times (F_{He2}) \quad (9)$$

$$FRC_{He} = V_{app}(F_{He1} - F_{He2})/F_{He2} \quad (10)$$

where lung volume includes the dead space of the valve and mouthpiece, which must be subtracted, and FRC_{He} should be corrected to BTPS conditions.

Equipment

For systems that utilise a volume-displacement spirometer, the capacity of the spirometer should be ⩾7 L. It should be noted, however, that the larger the spirometer is, the higher is the required resolution of the helium measurements. The specifications for the volume measurements should comply with the recommendations in a previous document in this series [20]. Furthermore, the V_{app} with the bell at zero volume, including the circuit tubing to the mouthpiece valve, should not exceed 4.5 L, since the smaller the V_{app} is at the time that the patient is switched into the circuit, the larger (and more accurate) the measured changes in helium concentration during the FRC measurement will be.

The spirometer should be equipped with a mixing fan, CO_2 absorber, O_2 and helium supply, a gas inlet and outlet, and a water vapour absorber in the line to the helium analyser. Before the measurements, enough 100% helium should be added to the system to give a helium reading of ~10%. The remainder of the gas added to the system can be room air or a mixture of room air and O_2. If room air is used, it is important to ensure adequate O_2 replacement during the test. The mixing fan should mix the gas throughout the circuit within 8 s after the end of exhalation into the circuit. Typically, breathing-circuit flows of ~50 $L \cdot min^{-1}$ are utilised to ensure adequate mixing of helium concentration measurements, which are reported every 15 s. If pneumotachometers or other flow devices are used instead of volume-displacement spirometers, and if they are not isolated from variations in gas properties (*e.g.* by bag-in-box systems), then appropriate calibrations and corrections may be necessary to accommodate the changes in gas properties.

A thermal-conductivity helium analyser is the type utilised most commonly, but other types of helium analysers may be used [33]. The helium analyser should have a range of ~0–10% helium, a resolution of ⩽0.01% helium over the entire range, and a 95% response time of <15 s to a 2% step change in helium concentration in the breathing circuit. The meter should be stable with a drift of ⩽0.02% for measurement periods of up to 10 min. For systems in which O_2 concentration changes substantially because of O_2 consumption during the measurement of FRC, the helium analyser must be calibrated over the range of O_2 concentrations encountered. Since thermal-conductivity helium analysers are sensitive to temperature changes, it should be ensured that the temperature of the gases entering the helium analyser is the same as that during calibration.

A small pump samples gas from the breathing circuit just beyond the CO_2 absorber, and pushes it through a desiccant chamber, through the helium analyser and back into the main

circuit; for most analysers, a flow of $\geqslant 200\ mL \cdot min^{-1}$ is necessary. Since changes in the flow of gas through the analyser or in the pressure of gas in the analyser circuit will affect response time or accuracy, variations in flow and pressure should be minimised. Similarly, since thermal-conductivity analysers also respond to changes in concentration of CO_2, O_2, N_2 and water vapour pressure, CO_2 and water are removed before the sample is introduced into the helium analyser, and the O_2 concentration is maintained relatively constant by adding O_2 to the circuit as necessary. The activity of the CO_2 and water absorbers should be ensured before each test (either from visual or photocell detection of indicator colour changes, or by replacing the absorbent after a specified number of tests (or accumulated minutes of equilibration time)). The breathing-circuit CO_2 level during testing should be kept below 0.5% to avoid patient discomfort and hyperventilation.

Lung volumes are reported at BTPS conditions. When TLC and subdivisions thereof are measured, the temperature of gas inside the system differs from both BTPS and the ambient temperature and pressure, saturated with water vapour (ATPS) conditions computed using room temperature, since the conditions are variably affected by exhaled warm gas, room temperature, and heat generated by absorption of CO_2 in the soda lime canister. Therefore, the temperature of the gas in the breathing circuit should be measured so that these lung volumes can be corrected to BTPS conditions. The temperature sensor should have an accuracy of better than 0.5℃ over the range of 12–30℃, and should have a 90% response time of $<$30 s to a 5℃ step change of temperature of the gas inside the breathing circuit.

The breathing valve and mouthpiece should have a combined dead space of $<$100 mL, and should be easy to disassemble for sterilisation. The size of this dead space should be available from the manufacturer or measured by water displacement.

Continuous measurement of the O_2 concentration ensures a satisfactory O_2 supply and also provides a means to adjust the output of thermal-conductivity helium analysers for the effect of different O_2 concentrations.

Measurement technique

Specific details of procedures will vary with different types of equipment and degrees of automation [9], but the basic procedure is as follows. 1) The equipment should be turned on and allowed an adequate warm-up time. 2) The equipment should be set up for testing, including calibration, according to manufacturer's instructions. 3) The patient should be asked if he/she has a perforated eardrum (if so, an earplug should be used). 4) The patient is seated comfortably, with no need to remove dentures. The procedure is explained, emphasising the need to avoid leaks around the mouthpiece during the test and to use a nose clip. 5) The patient breathes for ~30–60 s on the mouthpiece to become accustomed to the apparatus, and to ensure a stable end-tidal expiratory level. 6) The patient is turned ''in'' (*i.e.* connected to the test gas) at the end of a normal tidal expiration. 7) The patient is instructed to breathe regular tidal breaths. 8) The O_2 flow is adjusted to compensate for O_2 consumption (significant errors in the calculation of FRC can result if O_2 consumption is not adequately accounted for). 9) The helium concentration is noted every 15 s. 10) 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 gas-exchange abnormalities [9]. 11) Once the helium equilibration is complete, the patient is turned ''out'' (*i.e.* disconnected from the test gas) of the system. If the measurements of ERV and IC are to be linked to the FRC measured, it should be ensured that the spirometer has an adequate volume for the full ERV and IVC manoeuvres (fig. 5). 12) At least one technically satisfactory measurement should be obtained. Due to the extra costs and time in making multiple measurements, and the relatively good inter-day variability in adults, two or more measurements of FRC_{He} need to be made only when necessitated by clinical or research need [9]. If only one measurement of FRC_{He} is made, caution should be used in the interpretation. For younger children, however, it is recommended that at least two technically satisfactory measurements be performed. If more than one measurement of FRC_{He} is carried out, the value reported for FRC_{He} should be the mean of technically acceptable results that agree within 10%.

Quality control

Before each patient is tested, the following items should be checked: water level of water-sealed spirometers (if applicable); status of all CO_2 and water absorbers; operation of the circuit fan (assessed by listening); and the baseline stability of helium and volume signals. Systems that can be pressurised conveniently (*e.g.* by placing a weight on top of an upright

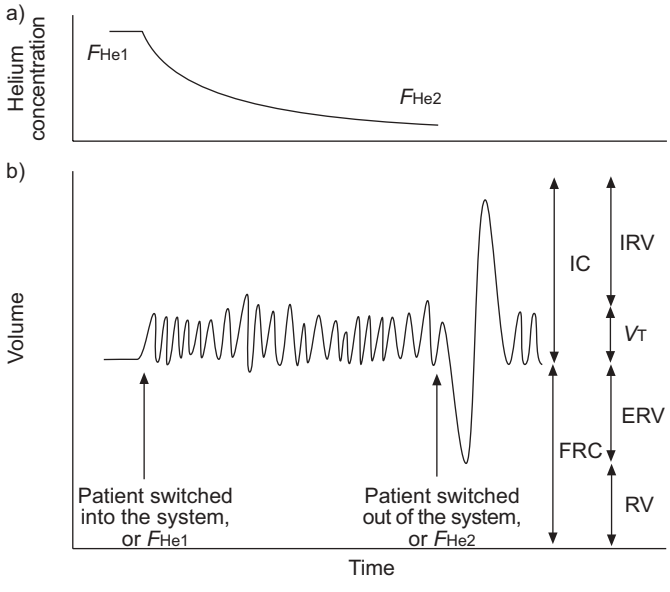

FIGURE 5. Display of an acceptable profile for a helium dilution test to determine functional residual capacity (FRC), in which O_2 is continually added to compensate for O_2 consumption. As the helium concentration falls (a), it corresponds to the time course of the volume change (b). To obtain ''linked'' expiratory reserve volume (ERV) and inspiratory vital capacity manoeuvres, the patient should not be switched out of the system as shown. F_{He1}: helium fraction at the time that the subject is connected to the apparatus; F_{He2}: helium fraction at the time of equilibration; IC: inspiratory capacity; IRV: inspiratory reserve volume; V_T: tidal volume (TV); RV: residual volume.

water-sealed spirometer) should be checked for leaks at least once during the 24 h prior to patient testing, and after tubing or canister changes.

The stability of the helium meter should be confirmed weekly (it should not drift >0.02% in 10 min). The temperature should be validated as described previously [19].

It is necessary to check the linearity of the helium meter periodically or when erroneous results are suspected. This is accomplished by diluting a measured helium concentration with known volumes of air (maximum error of 0.5% of full scale, which would be 0.05% for 10% helium). However, contemporary helium meters have very stable linearity. If the stability of the helium meter linearity has been demonstrated (*e.g.* by weekly checks over a few months), then quarterly or semi-annual checks seem sufficient, as there are no available data to support more frequent linearity checks for all instruments. Monthly testing of biological controls is recommended and useful, in that it tests not only the equipment, but also the procedures used by the technicians.

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 ATPS and BTPS, and should be corrected to BTPS. 2) It is recommended that no corrections for helium absorption be made. 3) 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 [9]. 4) With regards to switching errors, in practice, patients are not always at FRC when they are switched into the spirometer circuit. Corrections for this should be made from the spirometer trace when reporting FRC_{He} (fig. 6). Some computerised systems report and account for the switch-in error automatically, 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 by the technologist.

MEASUREMENT OF LUNG VOLUMES USING IMAGING TECHNIQUES

In subjects with a limited ability to cooperate, radiographic lung volumes may be more feasible than physiological measurements. The definition of the position of lung inflation at the time of image acquisition is clearly essential. Volumes measured this way carry their own assumptions and limitations, and cannot be directly compared with volumes measured by the techniques mentioned previously. Imaging techniques for use in children and adults have been reviewed in a previous report [4], from where the following information is derived.

Conventional radiographs

The principle is to outline the lungs in both anteroposterior and lateral chest radiographs, and determine the outlined areas either by assuming a given geometry or by using planimeters in order to derive the confined volume. Adjustments are made for magnification factors, volumes of the heart, the intrathoracic tissue and blood, and infradiaphragmatic spaces. In the determination of TLC, 6–25% of subjects differed by >10% from plethysmographic measurements in adult subjects [34]. For paediatric applications, studies are more problematic [35].

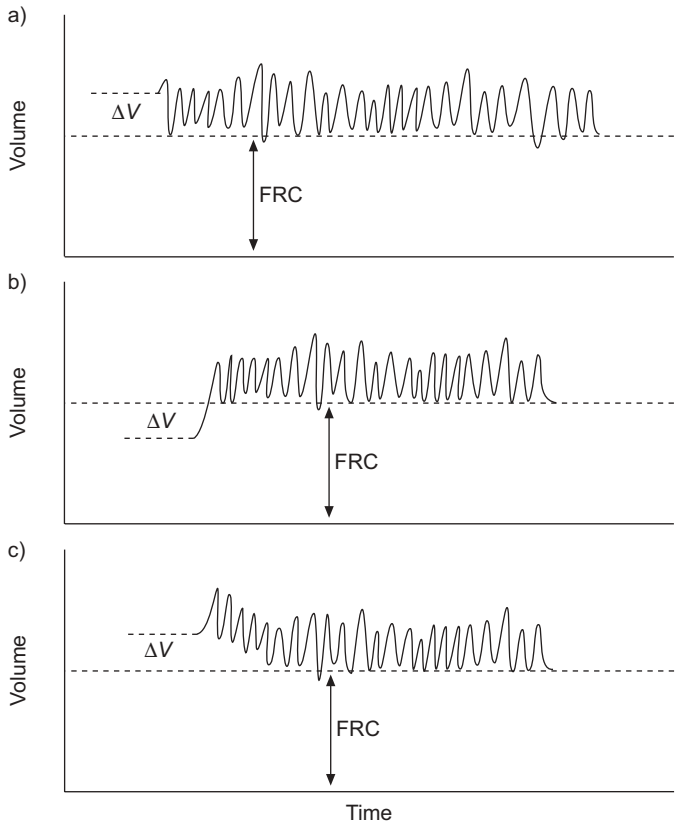

FIGURE 6. Display of volume–time spirograms, showing examples when the patient is not switched into the spirometer circuit. a) The patient was turned into the circuit at a lung volume higher than the functional residual capacity (FRC), and the volume difference (ΔV) would be subtracted. b) The patient is turned into the circuit at a lung volume below FRC, and the ΔV would be added. c) The patient was turned into the circuit above the true FRC, and the ΔV would be subtracted. Modified from [16].

Computed tomography

In addition to thoracic cage volumes, CTs can provide estimates of lung tissue and air volumes, and can also estimate the volume of lung occupied by increased density (*e.g.* in patchy infiltrates) or decreased density (*e.g.* in emphysema or bullae). In a study of children, comparable correlations were observed for CT and radiographic measurements as compared with plethysmographic TLC [36–38]. A disadvantage of using CT is the high radiation dose. This dose can probably be considerably diminished by modifying the technique.

Magnetic resonance imaging

Magnetic resonance imaging (MRI) offers the advantage of a large number of images within a short period of time, so that volumes can be measured within a single breath. As with CT,

MRI offers the potential for scanning specific regions of the lung, as well as the ability to adjust for lung water and tissue. However, despite the advantages of an absence of radiation exposure, the use of MRI for measuring thoracic gas volume will be limited by its considerable cost.

Controversies and critical questions

There are inadequate data in the literature to support recommending one specific technique over the other, or to standardise imaging techniques for measurement of thoracic gas volumes. It is a question of whether TLC values obtained during routine chest radiographs are sufficiently close to those achieved in pulmonary function laboratories. A few studies indicate that radiographic TLC is slightly smaller than the latter [39, 40], but this may relate to a lack of proper coaching in enabling the patient to reach TLC during the radiographic procedure. The larger standard deviations of radiographic measurements may limit their clinical usefulness. In patients with lung disease, the difference between radiographic measurements and lung function measurements may be due to differences in the ability to include airspace-occupying tissue, leading to a tendency for the radiographic method to give higher values. CT and MRI techniques offer the potential for measuring intrathoracic volumes and estimating lung gas volumes after subtraction of estimates of fluid and tissue volumes derived from measurements of image density.

REFERENCE VALUES

Lung volumes are related to body size, with standing height being the most important factor. In children and adolescents, lung growth appears to lag behind the increase in standing height during the growth spurt, and there is a shift in relationship between the lung volume and height during adolescence [41, 42].

A number of factors must be considered when selecting predictive values for absolute lung volumes including: matching of the reference and patient populations; appropriate extrapolation of regression equations, when considering the size and age range of subjects actually studied; and differences in testing methodology between clinical laboratories and studies from which predicted reference values are derived. Additional information is provided elsewhere [1].

INFECTION CONTROL

This subject is discussed in more detail in a previous document from this series [19].

ABBREVIATIONS

Table 1 contains a list of abbreviations and their meanings, which will be used in this series of Task Force reports.

TABLE 1 List of abbreviations and meanings

ATPD	Ambient temperature, ambient pressure, and dry
ATPS	Ambient temperature and pressure saturated with water vapour
BTPS	Body temperature (*i.e.* 37℃), ambient pressure, saturated with water vapour
C	Centigrade
CFC	Chlorofluorocarbons
cm	Centimetres
COHb	Carboxyhaemoglobin
$D_{L,CO}$	Diffusing capacity for the lungs measured using carbon monoxide, also known as transfer factor
$D_{L,CO}/V_A$	Diffusing capacity for carbon monoxide per unit of alveolar volume, also known as K_{CO}
D_M	Membrane-diffusing capacity
DT	Dwell time of flow >90% of PEF
EFL	Expiratory flow limitation
ERV	Expiratory reserve volume
EV	Back extrapolated volume
EVC	Expiratory vital capacity
$F_{A,X}$	Fraction of gas X in the alveolar gas
$F_{A,X,t}$	Alveolar fraction of gas X at time t
$FEF_{25–75\%}$	Mean forced expiratory flow between 25% and 75% of FVC
$FEF_{X\%}$	Instantaneous forced expiratory flow when X% of the FVC has been expired
FEV_1	Forced expiratory volume in one second
FEV_t	Forced expiratory volume in t seconds
$F_{E,X}$	Fraction of expired gas X
$FIF_{X\%}$	Instantaneous forced inspiratory flow at the point where X% of the FVC has been inspired
$F_{I,X}$	Fraction of inspired gas X
FIVC	Forced inspiratory vital capacity
FRC	Functional residual capacity
FVC	Forced vital capacity
H_2O	Water
Hb	Haemoglobin
Hg	Mercury
Hz	Hertz; cycles per second
IC	Inspiratory capacity
IRV	Inspiratory reserve volume
IVC	Inspiratory vital capacity
K_{CO}	Transfer coefficient of the lung (*i.e.* $D_{L,CO}/V_A$)
kg	Kilograms
kPa	Kilopascals
L	Litres
$L \cdot min^{-1}$	Litres per minute
$L \cdot s^{-1}$	Litres per second
lb	Pounds weight
$MEF_{X\%}$	Maximal instantaneous forced expiratory flow where X% of the FVC remains to be expired
MFVL	Maximum flow–volume loop
mg	Milligrams
MIF	Maximal inspiratory flow
mL	Millilitres
mm	Millimetres
MMEF	Maximum mid-expiratory flow
ms	Milliseconds
MVV	Maximum voluntary ventilation
P_{A,O_2}	Alveolar oxygen partial pressure
P_B	Barometric pressure
PEF	Peak expiratory flow
P_{H_2O}	Water vapour partial pressure
P_{I,O_2}	Inspired oxygen partial pressure
θ (theta)	Specific uptake of CO by the blood
RT	Rise time from 10% to 90% of PEF
RV	Residual volume
s	Seconds

TABLE 1 (Continued)

STPD	Standard temperature (273 K, 0℃), pressure (101.3 kPa, 760 mmHg) and dry
TB	Tuberculosis
TGV (or V_{TG})	Thoracic gas volume
t_I	Time taken for inspiration
TLC	Total lung capacity
Tr	Tracer gas
t_{tot}	Total time of respiratory cycle
TV (or V_T)	Tidal volume
V_A	Alveolar volume
$V_{A,eff}$	Effective alveolar volume
VC	Vital capacity
V_c	Pulmonary capillary blood volume
V_D	Dead space volume
V_I	Inspired volume
V_S	Volume of the expired sample gas
μg	Micrograms

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