Measurement of Functional Residual Capacity by Sulfur Hexafluoride Washout

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Measurement of functional residual capacity (FRC) by the open-circuit multiple breath tracer gas washout technique is an established method. A system based upon washout of sulfur hexafluoride (SF₆) during mechanical ventilation is described. The central unit in the system is a sensitive and rapid-response infrared SF₆ analyzer. SF₆ is washed in until the alveolar concentration of SF₆ is 0.5%, a concentration so low that the supply of other gases is hardly influenced. During washout, the flow of SF₆ from the lungs is calculated by a computer every 10 ms from signals representing expiratory flow and SF₆ concentration. The total volume of SF₆, washed out, is calculated by integration of SF₆ flow. Since the alveolar concentration at the end of washin is known, the lung volume may be obtained. The measurement procedure is highly automated and the result is presented by the computer immediately after washout. Accurate and reproducible results in model lung tests were obtained during air and N₂O/O₂ ventilation. Comparison with body plethysmography (FRCbody) in eight sitting healthy subjects gave the following: FRCbody = 7 ml + 0.98 × FRCox, r = 0.99. Comparison with nitrogen washout (FRCN₂) in five postoperative patients gave the following: FRCN₂ = 59 ml + 0.97 × FRCox, r = 0.97. FRCbody during N₂O/O₂ ventilation was the same as during air/O₂ ventilation in a group of paralyzed patients.

The measurement system has not been tested in patients with obstructive lung disease. (Key words: Anesthesia. Lung: functional residual capacity. Measurement technique: washout. Ventilation: mechanical.)

Our method is a modification of the open circuit method originally described by Hickam et al. in 1954. However, instead of collecting the expired gas in a bag the volume of washed-out tracer gas is calculated by a computer that receives signals representing tracer gas concentration and expired flow. The central unit in the system is a fast and sensitive analyzer for sulfur hexafluoride (SF₆). The analyzer permits the use of tracer gas concentrations below 0.5%. The system was tested in a model lung, in healthy subjects, and in patients without obstructive lung disease.

Methods

System Description

The equipment (fig. 1) constitutes an infrared SF₆ analyzer, a CO₂ analyzer (CO₂ Analyzer 930, Siemens-Elema Company), a thin catheter connected to a solenoid valve for delivery of SF₆, a ventilator (Servo 900 B or G, Siemens-Elema Company), and a computer (LSI 11/23, Digital Equipment Corporation). The transducers of the SF₆ and CO₂ analyzers are placed over cuvettes in the airway. The SF₆ analyzer automatically resets its zero level at the end of each inspiration. Consequently, no SF₆ can be allowed in the cuvette during that phase of the ventilator cycle. SF₆ is therefore introduced between the transducer and the patient via the catheter. During washing of SF₆ the solenoid valve opens in synchrony with the inspiratory gas flow from the ventilator. Since the variations in airway pressure are negligible in comparison with the driving pressure (about 500 cmH₂O), the flow of SF₆ through the catheter is nearly constant. If the ventilator is also set to a constant inspired flow, the resultant mixture will have a constant concentration of SF₆ throughout the inspiration. The tip of the SF₆ catheter is usually placed at the junction between the heat/moisture exchanger and a connection tube. The sudden change in tubing dimension at this point is thought to cause turbulence and hence good mixing. The transducer of the SF₆ analyzer is placed close to the Y-piece. Although the breathing circuit is of the “nonrebreathing” type, some rebreathing from the Y-piece is unavoidable. To minimize rebreathing, the Y-piece is equipped with valves (fig. 1). The volume,

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which is also taken to be the rebreathed volume, between
the transducer and the valves, is 12 ml. Zero reset,
which takes place at the end of inspiration is not affected
as the rebreathed volume constitutes the first fraction
of the inspired volume.

A signal proportional to CO₂ concentration is sub-
tracted from the SF₆ signal to compensate for the slight
influence CO₂ has on SF₆ measurements. The propor-
tionality factor is adjusted so that measured mean expired
SF₆ concentration is within ±0.001% when actual con-
centration is zero.

**Measurement Sequence.** SF₆ washin is continued at a
constant rate until there is no detectable change in
expired SF₆ concentration over a period of 1 min.
Washout is started simply by stopping SF₆ supply between
one inspiration and the next. Washout is continued until
mean expired concentration of the last five breaths is
below 0.001%. Washin plus washout in an anesthetized
adult usually takes 6–12 min. Figure 2 shows the end
of washin and the start of washout in a patient. The
signal is noisy; we have avoided using analog filtering in
order to retain a fast response. The noise does not
prevent accurate measurement of FRC, since this is
based on calculation of mean SF₆ concentration over an
extended period (see below). In figure 2, SF₆ washin
continues until breath no. 3. In expiration no. 1–3 the
SF₆ concentration curve rises quickly. The initial peak
in the curve is due to inertia in the delivery system for
SF₆ causing a small bolus of SF₆ to be deposited in the
airway just after inspiratory flow has ceased. This artifact
does not affect the calculations. During washout, the
SF₆ signal rises more slowly as the airway dead space
contains no SF₆ at the beginning of expiration.

**Computations.** The computer receives signals from the
SF₆ analyzer and from the expiratory flowmeter of the
ventilator. After linearization of the SF₆ signal, the SF₆
elimination is calculated every 10 ms as the product of
SF₆ concentration and expiratory flow. Tidal SF₆ elim-
ination is obtained by integration. As the system only
measures SF₆ flow from the patient, a correction for
rebreathing of end-tidal gas is made before tidal SF₆ volumes are added to obtain the total amount of washed out SF₆ (Vₛ₆₆₆). FRC is obtained as:

\[ \text{FRC} = \frac{V_{\text{SF₆}}} {C_{\text{SF₆(alv)}}} \times 1.09 - V_{\text{app}} \]  (1)

C_{\text{SF₆(alv)}} is the alveolar concentration of SF₆ at the end of washin. It is obtained as the mean concentration during expiration of the second half of the tidal volume. The mean of the last five breaths of washin is used; 1.09 is the conversion factor to BTPS conditions.¹ The conversion factor may, of course, also be computed each time by entering patient temperature, ambient temperature, etc., into the computer. V_{\text{app}} is the apparatus dead space volume.

Calibrations. The SF₆ signal is calibrated with a known gas mixture using a test gas valve (66 98 393 EO37E, Siemens-Elema Company). As V_{\text{SF₆}} and C_{\text{SF₆(alv)}} are measured by the same transducer, it is evident from equation (1) that measured FRC is not affected by a change in calibration if the SF₆ signal remains linear. Since, in addition, the SF₆ analyzer is quite stable, we have not deemed it necessary to perform daily calibrations. The expiratory flowmeter is calibrated with the relevant O₂:N₂ or O₂:N₂O mixture by comparing expired volume, as measured by the computer, with the value obtained with a wet gas meter. Adding 0.5% SF₆ changes the calibration of the flowmeter by less than 1%. Thus, the performance of the flowmeter is not affected by changes in viscosity during the FRC measurements.

EVALUATION OF SYSTEM PERFORMANCE

In all tests insufflation time was 25% and end-inspiratory pause time 10% of the full ventilatory cycle. N₂O/O₂ was given in the proportions 65/35. The SF₆ calibration was checked repeatedly during the test period, and the reading always varied by less than 4%. The expiratory flowmeter was calibrated with a wet gas meter (Wohlgroth, Zürich) daily and after changing the inspired gas mixture. The day-to-day variation with unchanged gas mixtures seldom exceeded 2%. The linearity of the expiratory flowmeter was established both with air and with nitrous oxide, using a method described by Fletcher et al.¹¹ The human studies were approved by the local Human Investigation's Committee, and informed consent was obtained from all subjects or their guardians.

Model Lung Tests. The model lung consisted of a U-shaped vessel, one limb of which was ventilated. The FRC volume was varied between 500 and 5,000 ml by filling the vessel with water.

Comparison with Body Plethysmographic Measurements. Eight healthy subjects (12–56 yr) were studied. A computerized version of the plethysmographic technique described by Jonson¹² was used. The ventilator tubing and the SF₆ and CO₂ transducer cables were passed through air-tight seals out of the body box and connected to the ventilator and the rest of the measurement system placed outside the box. The test subject was seated in the body box, equipped with a nose clip and connected to the ventilator through a mouth piece. The ventilator was set at 10–15 breaths/min, and the tidal volume was adjusted to give an end-tidal P_{CO₂} of about 35 mmHg. The subjects were allowed to adjust to mechanical ventilation for 5–10 min. At the end of SF₆ washin, the ventilator was stopped during the expiratory phase, a shutter in the airway was closed and the subject was asked to make breathing efforts against the closed shutter at a frequency of 1 Hz or less to allow the thoracic gas volume to be determined. The ventilator was then restarted and washout of SF₆ commenced. Thus, both measurements refer to the same instant.

Comparison with Nitrogen Washout. Five men (38–65 yr) were studied a few hours after cardiac or aortic surgery, while still sedated and mechanically ventilated. Four patients had no history of lung disease; one patient had pulmonary fibrosis secondary to sarcoidosis. Each patient was examined without and with PEEP (5–10 cmH₂O). Two synchronized ventilators, set at 9–14 l/min and 10–20 breaths/min, were used.² One ventilator was used for ventilation with air/oxygen (F_{O₂} 0.30–0.44) and the other for ventilation with oxygen (containing less than 0.02% nitrogen) during nitrogen washout. A cross-over arrangement close to the endotracheal tube allowed a sudden change to oxygen ventilation. The nitrogen analyzer (model 720, Ohio Medical Products) was significantly disturbed by SF₆. Thus, we were not able to obtain simultaneous measurements with both techniques. FRC was therefore first measured with SF₆, then with N₂, and then again with SF₆. All FRC measurements were made in duplicate. The nitrogen washed out during oxygen ventilation was collected in a Douglas bag. Washout was terminated at an end-tidal N₂ concentration of 2%. The N₂ content in the bag, V_{N₂(bag)} (bag), was measured and FRC was obtained as:

\[ \text{FRC} = \frac{V_{N₂(bag)} - V_{N₂(body)}} {C_{N₂(initial)} - C_{N₂(end)}} \times 1.09 - V_{\text{app}} \]  (2)

Here, V_{N₂(body)} is the estimated correction for N₂ evolved from body tissues. Based on a study by Lundin,¹³
this was set to 40, 35, and 28 ml for the first, second, and third minutes of washout respectively. $C_{N_2}$(initial) is the alveolar $N_2$ concentration prior to oxygen breathing; $C_{N_2}$(end) the alveolar $N_2$ concentration at the end of washout; 1.09 the conversion factor from ATPS to BTPS; and $V_{app}$ the apparatus dead space.

**Tests in Paralyzed Patients during Anesthesia.** The reproducibility was assessed by performing duplicate FRC measurements in 11 patients (37–66 yr) while they were prepared for cardiac surgery. None of the patients had signs of pulmonary disease. The patients were anesthetized with droperidol/fentanyl, paralyzed with alcuronium, and ventilated with $N_2O/O_2$ at a rate of 10 breaths/min. The tidal volume was adjusted to give an end-tidal $P_{CO_2}$ of approximately 35 mmHg. In nine of these patients, FRC obtained during $N_2O/O_2$ ventilation was compared with the value obtained with $air/O_2$ at the same $F_{O_2}$ (0.35). Five patients were first ventilated with $air/O_2$, then with $N_2O/O_2$, and then again with $air/O_2$. In the other four, the order was reversed. These measurements were done after surgery while the patient was still heavily sedated.

**Statistics.** Regression lines were obtained by the method of least squares. The residual standard deviation (RSD) around the regression line was calculated. Student’s two-sided $t$ test was used for assessment of significance.

## Results

### Model Lung Tests

The results obtained during air and $N_2O/O_2$ ventilation are shown in figure 3. Each point represents the mean value of two determinations of FRC. On average, the determinations differed by 1.1% (range 0–3.5%).

**Comparison with Body Plethysmographic Measurements ($FRC_{BOX}$)**

The results are shown in figure 4. The equation of regression was: $FRC_{SF_6} = 7 \text{ ml} + 0.98 \times FRC_{BOX}$, $r = 0.99$ and RSD = 126 ml. The slope was not significantly different from 1.0, and the intercept was not significantly different from 0.

**Comparison with Nitrogen Washout ($FRC_{N_2}$)**

The results are shown in figure 5. The equation of regression was as follows: $FRC_{SF_6} = 59 \text{ ml} + 0.97 \times FRC_{N_2}$, $r = 0.97$ and RSD = 225 ml. The slope and the intercept were not significantly different from 1.0 and 0, respectively. The time needed for $N_2$ washout to
the 2% level and for SF₆ washout to 0.001% was 2.3 ± 0.5 and 3.9 ± 0.5 min (mean ± 1 SD), respectively.

**Tests in Paralyzed Patients during Anesthesia**

On average, duplicate determinations differed by 2.4% (range 0.7–6.8%), the range of values for FRC being 1,261 to 2,788 ml. The comparison between measurements obtained during N₂O/O₂ ventilation and measurements obtained during air/O₂ ventilation is shown in figure 6. The equation of regression was as follows: \( \text{FRC}_{SF6}(\text{N}_2\text{O}/\text{O}_2 \text{ vent.}) = -40 \text{ ml} + 1.03 \times \text{FRC}_{SF6} \text{ (air/O}_2 \text{ vent.}, r = 0.99, \text{ RSD} = 72 \text{ ml. The slope and the intercept were not significantly different from 1.0 and 0, respectively.}

**Discussion**

Much is known about FRC changes caused by anesthesia per se, but the knowledge of changes brought about by different surgical interventions is limited. This may be due to the lack of a convenient and unobtrusive measurement equipment that can be used in the operating room during N₂O/O₂ anesthesia. The lack of methods that leave the ventilator treatment and oxygen supply undisturbed has even limited the use of FRC measurements in the intensive care unit, although monitoring of FRC would probably improve the care of severely ill patients. The present system was designed with both these aspects in mind.

SF₆ was selected as a suitable tracer gas for FRC determinations, as it was measurable at low concentrations with a fast infrared analyzer. Some possible sources of error in the SF₆ analyzer have been discussed in a previous communication. SF₆ is an inert, toxic gas with a Bunsen solubility coefficient in bloodless lung tissue of 0.0068, which is slightly lower than that for helium. The solubility in blood is similarly low. Hence, the solubility of SF₆ is not an important source of error during FRC measurements. Although SF₆ is a heavy molecule (MW = 146) and its diffusivity gas-in-gas is only one-seventh of that of helium, mixing of SF₆ in the lungs occurs quickly in healthy individuals. In patients with obstructive disease it may take longer for SF₆ to equilibrate in the lungs than for helium. On the other hand, the low solubility of SF₆ makes it
possible to prolong washin and washout until a stable expired SF₆ concentration indicates that the whole ventilated space is equilibrated. It is, however, important to realize that the method described here will share the limitations of other gas dilution methods—lung units that do not communicate with the airway during the measurement period will not be measured. With the present set-up, the flowmeter is situated at the expiratory port of the ventilator, while the SF₆ transducer is placed at the Y-piece. Part of measured expired flow will thus be due to discharge of gas compressed in the ventilator tubing. This might cause errors similar to those that occur when CO₂ elimination rate is measured with the CO₂ Analyzer 930.† The problem is discussed in detail by Fletcher et al.¹¹ Of course, it may be avoided if the flowmeter is placed close to the SF₆ transducer, but the error may also be corrected for by providing the computer with the airway pressure signal from the ventilator, along with information about tubing compliance. This allows the computer to calculate, at each moment, how much the discharge of compressed gas in the tubing contributes to measured expired flow. For the present experiments, such a modification of the system has not been deemed necessary, since tubing compliance was low (0.7 ml/cmH₂O).

We obtained a close correspondence between body plethysmography and SF₆ washout. This is in agreement with a previous study in which lung volume measurements with body plethysmography were compared with a gas dilution technique in sitting healthy subjects. Thus, Tierney and Nade²¹ observed: FRCN₂ = 222 ml + 0.96 × FRCBOX, r = 0.99. The mean difference between FRCN₂ and FRCBOX was 21 ml (calculated from the original data supplied in their article). There may be a greater difference between the thoracic gas volume and the communicating gas volume in supine patients.³ When FRC is determined by nitrogen washout, washout is usually terminated when the expired concentration of nitrogen is 2%, i.e., at 1/40th of the initial concentration. In contrast, SF₆ washout is continued until mean expired concentration is only 0.001%, i.e., 1/500th of the initial concentration. In spite of this difference between the two methods, FRCSF₆ did not exceed FRCN₂, which one would have expected if contributions from pulmonary units with slow time constants had been important. The possibility remains that the two methods may yield different results in other types of patients, e.g., those with obstructive lung disease.

The measurement system presented was designed to overcome some of the problems associated with FRC measurements during mechanical ventilation and anesthesia. It allows measurements to be performed with relative ease and with good accuracy and reproducibility. FRC is presented immediately after washout on the computer screen. Except for the computer, all equipment is placed on an ordinary ventilator cart (height 125 cm, width 40 cm, length 60 cm). Also, the computations are so simple that a microprocessor could easily be used in a future system built upon the concepts presented here. In this study we have chosen to calculate the volume of tracer gas present in the lungs at the end of washin from the data obtained during a prolonged washout. In theory, this volume could be obtained by studying only the washin phase. Another way of speeding up the measurements would be to stop the washout earlier and complete the calculation by extrapolation.

One disadvantage with the present system for SF₆ delivery is that it can only be used for FRC measurements during volume-controlled mechanical ventilation. This is because SF₆ flow in the catheter is constant during inspiration. Consequently, inspiratory flow from the ventilator must also be constant in order to prevent variations in inspired SF₆ concentration. To make the principle useful during controlled ventilation with other patterns of inspiratory flow and during spontaneous ventilation, the SF₆ supply must be modulated so that it is proportional to instantaneous inspired flow.

Addendum

The CO₂ analyzer is no longer a mandatory part of the set-up (fig. 1) as a recent redesign of the SF₆ analyzer has eliminated the interference from carbon dioxide.

References

during mechanical ventilation with or without PEEP. Crit Care Med 9: 873–877, 1981