Determination of functional residual capacity (FRC) by multibreath nitrogen washout in a lung model and in mechanically ventilated patients

Abstract  Objective: Validation of an open-circuit multibreath nitrogen washout technique (MBNW) for measurement of functional residual capacity (FRC). The accuracy of FRC measurement with and without continuous viscosity correction of mass spectrometer delay time (TD) relative to gas flow signal and the influence of baseline FIO2 was investigated.

Design: Laboratory study and measurements in mechanically ventilated patients.

Setting: Experimental laboratory and anaesthesiological intensive care unit of a university hospital.

Patients: 16 postoperative patients with normal pulmonary function (NORM), 8 patients with acute lung injury (ALI) and 6 patients with chronic obstructive pulmonary disease (COPD) were included.

Interventions: Change of FIO2 from baseline to 1.0.

Measurements and main results: FRC was determined by MBNW using continuous viscosity correction of TD (TD dyn), a constant TD based on the viscosity of a calibration gas mixture (TD0) and a constant TD referring to the mean viscosity between onset and end of MBNW (TDmean). Using TD dyn, the mean deviation between 15 measurements of three different lung model FRCs (FRC measured) and absolute volumes (FRC model) was 0.2 %. For baseline FIO2 ranging from 0.21 to 0.8, the mean deviation between FRC measured and FRC model was −0.8 %. However, depending on baseline FIO2, the calculation of FRC using TD mean and TD0 increased the mean deviation between FRC measured and FRC model to 2–4 % and 8–12 %, respectively. In patients (n = 30) the average repeatability coefficient was 6.0 %. FRC determinations with TD mean and TD0 were 0.8–13.3 % and 4.2–23.9 % (median 2.7 % and 8.7 %) smaller than those calculated with TD dyn.

Conclusion: A dynamic viscosity correction of TD improves the accuracy of FRC determinations by MBNW considerably, when gas concentrations are measured in a sidestream. If dynamic TD correction cannot be performed, the use of constant TD mean might be suitable. However, in patient measurements this can cause an FRC underestimation of up to 13 %.

Key words  Aged  Functional residual capacity  Lung volume measurement  Mechanical ventilation  Critical care  Chronic obstructive pulmonary disease  Acute lung injury
Introduction

The monitoring of end-expiratory lung volume (functional residual capacity, FRC) is an important tool with which to assess the pulmonary status and the effect of the ventilator setting in patients with acute respiratory failure requiring mechanical ventilation [1]. Since the open-circuit multiple breath nitrogen washout method (MBNW) was first established by Darling et al. in 1940 [2], several investigators have used washout techniques to measure FRC in ventilated patients [3–7]. Although MBNW can be performed easily, a significant problem with this method is the considerable changes in gas viscosity during the washout maneuver, which affect the accuracy of the gas flow measurement by pneumotachography [8, 9]. Sidestream analysis of gas fractions (e.g. by mass spectrometry) via a capillary and mainstream gas flow measurement result in a substantial delay (TD) between the two signals, mainly caused by the transport time of the sampled gas. Thus, for further evaluation the signals must be synchronized. Additionally, the gas flow through the sampling capillary is viscosity-dependent and TD has to be corrected for the momentary viscosity of the gas mixture to determine specific gas volumes exactly at each time during the washout. To improve the accuracy of nitrogen (N₂) volume calculation during MBNW, we used a continuous off-line correction of gas flow and TD for changes in dynamic gas viscosity (slightly modified from [10]). The purpose of this study was the evaluation of the accuracy and repeatability of FRC determinations by MBNW maneuvers and the influence of the dynamic adjustment of TD and different baseline FIO₂ on FRC measurements in a lung model and in mechanically ventilated patients.

Materials and methods

Measurement equipment

The measurement apparatus is shown in Fig. 1. Gas flow was measured with a heated pneumotachograph (Fleisch no. 2, Fleisch, Lausanne, Switzerland) and a differential pressure transducer (Huba Control, Würenlos, Switzerland). The pneumotachograph was directly connected to a heat and moisture exchanger, HME (Humid-Vent 2, Gibeck Respiration, Väby, Sweden) at the proximal end of the inlet of the lung model. The HME was used to minimize the influence of water vapor on gas viscosity. Tracheal pressure was determined at the same position with a second differential pressure transducer. Inspiratory and expiratory gases were continuously sampled via a capillary (length: 3.09 m) connected to the Y-piece of the breathing circuit. Concentrations of N₂, oxygen (O₂) and carbon dioxide (CO₂) were measured with a mass spectrometer (MGA 1100, Perkin-Elmer, Pomona, CA, USA; response time: < 70 ms) which operated in the ratio mode resulting in a display of the gases as a fraction of 1.0 excluding water vapor. After zero point adjustment, a two-point calibration of the mass spectrometer was performed. Linearity of the mass spectrometer was checked over the whole range of the used gas concentrations for all measured gases using commercially available calibration gas mixtures (Messer-Griesheim, Duisburg, Germany). All data were
sampled on-line by an analog/digital converter (DT 2801-A, Data Translation, Marlboro, MA, USA) at a rate of 40 Hz and processed by an IBM AT compatible personal computer. The data acquisition and processing software were programmed with a commercially available software program (Asyst® 4.0, Keithley Asyst, Taunton, MA, USA).

The flow measuring system was calibrated with a gas mixture of known gas concentrations (65 % N₂, 30 % O₂ and 5 % CO₂) and definite viscosity using a precision calibration pump (Engström Megamed 05, Engström, Stockholm, Sweden) that produces a sinusoidal flow pattern. The same tube system was used during the calibration of the flow and the measurements [11]. The repeatability (2 SD of differences) of 10 calibration procedures was 0.2 % for the flow calibration factor. During calibration measurement the instantaneous gas viscosity was determined from the analyzed gas fractions to correct the measured flow signal [9]. The volume was then obtained from the corrected flow signal by off-line analysis. To minimize a drift of the volume signal by an off-set of the flow signal, the pressure transducer was adjusted meticulously during zero flow conditions before each measurement. Furthermore, a flow off-set was estimated after that and subtracted from the flow signal during off-line analysis. Thus, the PT signal showed no appreciable shift during the measuring period.

Lung model

The custom-made lung model consisted of a 10 l glass bottle and a 1.5 l rubber bag representing the compliant part of the lung for tidal breathing. The bag was placed between two perspex plates with a weight on top of the upper plate to provide complete emptying of the bag during expiration. The compliance of the test lung model was 40 ml/mbar. Different lung model volumes (FRC model) were achieved by using different water levels in the bottle. The exact FRC model was measured by volume replacement, i.e. by filling of the entire bottle with water at the beginning and the end of each measurement series. Changes of model volumes by water vaporizing during the experiments were avoided by the use of the HME. Gas mixing inside the lung model was optimized by an in-built fan. The dead space volume (HME, pneumotachograph, connectors) between the Y-piece and the lung was 80 ml. The lung model was mechanically ventilated in a volume-controlled mode with constant inspiratory flow using an EVITA 2 ventilator (Drägerwerke, Lübeck, Germany). The inspiratory flow was set at 40 l/s, the respiratory rate at 10/min, the inspiratory : expiratory time ratio (I : E) was 1 : 2 and the tidal volume 800 ml for all settings.

Determination of FRC

The N₂ washout maneuver was started by changing the FIO₂ from baseline to 1.0. The calculation of FRC was performed off-line. The N₂ fraction (F,N₂) at baseline was determined as the average N₂ concentration before the start of washout. The FRC calculation procedure was started with the first O₂ washin breath. As the first breath usually still contains a certain amount of N₂, this inspired N₂ volume was subtracted from the cumulative N₂ volume calculated from the washout procedure. Furthermore, total re-inspired N₂ resulting from incomplete separation of the inspired and expired N₂ volumes at the Y-piece during the washout was measured and subtracted during the integration of flow and N₂ signals. The results of FRC determination with and without subtraction of re-inspired N₂ were compared. To reduce the influence of N₂ washed out from body tissues and of signal noise, the calculation from the measurement was finished at 3 % of the baseline FNC₂. Additionally, a correction for tissue N₂ by Courant et al. [12] was used in all patient measurements:

\[ V_{N_2,\text{added}} = \frac{V_{\text{washout}}}{s^{-1}} \times \frac{\text{body_surface} \times [m^2]}{420} \]

The body surface is estimated from

\[ \text{body_surface} = \frac{\text{body_weight} \times [kg^{-1}]^{0.425} \times \text{body_height} \times [cm^{-1}]^{0.725} \times 71.84}{10000} \]

FRC was determined by the equation:

\[ FRC = \frac{t_f}{t_0} - \frac{\int -V(t) \cdot F_{N_2}(t)dt}{F_{N_2}(t_B) - F_{N_2}(t_E)} \]

where \( V \) is gas flow, \( t_f \) is the time at the beginning of the washout and \( t_0 \) the time at the end of the calculation; \( F_{N_2}(t_B) \) was defined as 3 % of \( \text{FNC}_2(t_E) \). Note that expiratory flow is negative by definition.

Delay time and viscosity corrections

The entire time delay (TD) between gas sampling and data output of the mass spectrometer consists of a viscosity-dependent part and a viscosity-independent part (internal delay time, Tm), both contributing to the time between gas analysis and data output. The viscosity-dependent part depends on the pressure gradient through the sampling system of the gas analyzer as well as on the diameter and length of the capillary. The viscosity-independent part (Tm) is the time necessary for analysis and output of the signals. For the computation of TD of the individual capillary, multiple measurements were performed with different gas mixtures of N₂/O₂ revealing a linear relationship between dynamic viscosity and the corresponding delay time (TD = 2.07 \( \eta \) + 89 [ms]; \( \eta \) = 0.0998). \( F_{N_2}(t) \) was defined as the time at the intersection with a viscosity of zero in the time-viscosity diagram (89 ms). The delay time (TD) corresponding to the viscosity (\( \eta(t) \)) of the test gas (65 % N₂, 30 % O₂ and 5 % CO₂) used for calibration of the pneumotachograph at 295.5 K was taken from the time-viscosity diagram and defined as instantaneous TD of the individual capillary. During the washout the momentary delay time TD(t) with the momentary gas viscosity \( \eta(t) \) is [10]:

\[ TD(t) = (TD_0 - T_m) \times \frac{\eta(t)}{\eta_0} + T_m \]

The method described by Brunner et al. [10] was slightly modified: a linear interpolation between sampled data points was used to allow shifts on the time scale below the sampling interval time.

Off-line FRC determinations were performed by three different TD corrections: 1) using the instantaneous TD at \( \eta_0 \) (constant TD0), 2) using the constant TD referring to the mean viscosity during MBNW (TDmean at \( \eta_{mean} \); mean of \( \eta_0 \) and viscosity of the gas present at the end of MBNW in patients [2 % N₂, 5 % CO₂ and 93 % O₂]) and 3) using the TD correction for every sampled data point (dynamic correction, TDdyn). The three methods were compared in order to investigate the influence of viscosity-dependent error in the synchronization of flow and gas signals on FRC.
Experimental setting

Lung model measurements

Three different volumes for FRC\textsubscript{model} were chosen: 2600 ml, 5100 ml and 7600 ml. FRC was determined at a baseline FIO\textsubscript{2} of 0.3 five times each. To test the accuracy of the N\textsubscript{2} washout method during ventilation with different FIO\textsubscript{2}, five determinations of lung model FRC were performed at FIO\textsubscript{2} of 0.21, 0.3, 0.4, 0.5, 0.6, 0.7 and 0.8 at an end-expiratory volume of 2600 ml.

Patient measurements

To test the reproducibility of the method, we performed duplicated MBNW measurements in 30 mechanically ventilated adult intensive care patients. Sixteen postoperative adults (NORM) without history or evidence of lung pathology were studied in the first 4 h after major non-thoracic surgery. Fourteen critically ill patients with either acute lung injury (ALI; \(n = 8\)) or acute decompensation of chronic obstructive pulmonary disease (COPD, \(n = 6\)) were included. ALI was defined by the recent definitions [13]. COPD was diagnosed by clinical examination and from previous pulmonary function tests from the medical records. Patients were mechanically ventilated with continuous positive pressure ventilation (CPPV), 10–20 breaths/min, constant inspiratory flow, \(V\textsubscript{T} = 6–12\) ml/kg and FIO\textsubscript{2} 0.3–0.7 depending on the individual pulmonary status and needs. After each measurement a N\textsubscript{2} washin lasting 15–20 min was performed to regain baseline conditions. To investigate the influence of different baseline FIO\textsubscript{2} on the reproducibility of the FRC measurement, MBNW was started from four different baseline FIO\textsubscript{2} levels (0.3, 0.6, 0.7 and 0.8) in seven NORM patients. The study protocol was approved by the Ethical Committee of the University of Göttingen and informed consent was given by the patients or their next of kin.

Descriptive statistical analysis was performed according to Bland and Altman [14].

### Results

#### Lung model measurements

Using the delay time and dynamic viscosity correction (TD\textsubscript{dyn}), mean deviation of FRC\textsubscript{measured} and FRC\textsubscript{model} (2600 ml, 5100 ml, 7600 ml) was 0.2 % (9 ml) with a doubled standard deviation (2 SD) of 2.4 % (123 ml) as shown in Table 1.

Washout maneuvers at different FIO\textsubscript{2} (0.21–0.8) in the lung model revealed no obvious differences in the accuracy of FRC determination. The FRC\textsubscript{model} was slightly underestimated (average less than 1 %) and the 2 SD of differences was 1.2 % on average (data not shown). Without subtraction of re-inspired N\textsubscript{2}, FRC\textsubscript{model} was overestimated by 12.4 \(\pm\) 0.9 %.

Using the constant delay times TD\textsubscript{mean} and TD\textsubscript{0} without viscosity correction, the FRC determination by offline analysis of the same MBNW curves resulted in systematic differences compared with real lung model FRC (Fig. 2). Relative deviations of FRC\textsubscript{measured} and FRC\textsubscript{model} were 2 % and 8 %, respectively, during measurements with FIO\textsubscript{2} of 0.21, increasing to 4 % and 12 % with FIO\textsubscript{2} of 0.8 calculated with constant TD\textsubscript{mean} and TD\textsubscript{0}. Plots of gas flow and N\textsubscript{2} signals during MBNW demonstrated that the curves shift to relation to each other.

#### Patient measurements

Patients characteristics are shown in Table 2. In patients the relative coefficient of repeatability (2 SD of differences between repeated measures) for 30 duplicate FRC measurements was 3.8 % (NORM), 5.2 % (ALI), 7.3 % (COPD) and 6.0 % in all patients (Fig. 3). Deviations of FRC measured with a baseline FIO\textsubscript{2} of 0.3, compared with FRC measured with higher baseline FIO\textsubscript{2} (0.6, 0.7, 0.8) in seven NORM are shown in Table 3. FRC calculated with two different constant delay times (TD\textsubscript{mean} and TD\textsubscript{0}) were 4.1 \(\pm\) 6.0 % and 10.9 \(\pm\) 4.2 %.

### Table 1: Validity of FRC measurements in a lung model with three different volumes. Differences of FRC\textsubscript{model} (2600 ml, 5100 ml, 7600 ml) and FRC\textsubscript{measured} are expressed as absolute and relative means and 2 SD of number of MBNW procedures

<table>
<thead>
<tr>
<th>FRC\textsubscript{model} [ml]</th>
<th>n</th>
<th>Differences of FRC\textsubscript{model vs. FRC\textsubscript{measured}} [ml]</th>
<th>Differences of FRC\textsubscript{model vs. FRC\textsubscript{measured}} [%]</th>
</tr>
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<tr>
<td></td>
<td></td>
<td>mean 2 SD</td>
<td>mean 2 SD</td>
</tr>
<tr>
<td>2600</td>
<td>5</td>
<td>39.8 86</td>
<td>1.5 3.4</td>
</tr>
<tr>
<td>5100</td>
<td>5</td>
<td>4.2 142</td>
<td>0.08 2.8</td>
</tr>
<tr>
<td>7600</td>
<td>5</td>
<td>9.0 134</td>
<td>0.12 1.8</td>
</tr>
<tr>
<td>Total</td>
<td>15</td>
<td>8.9 123</td>
<td>0.2 2.4</td>
</tr>
</tbody>
</table>

### Table 2: Patient characteristics

<table>
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<th>Groups</th>
<th>(n)</th>
<th>(FRC\textsubscript{model} [ml])</th>
<th>(FRC\textsubscript{measured} [ml])</th>
<th>(%)</th>
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<td>2700</td>
<td>9.0</td>
</tr>
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<td>ALI</td>
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<td>2700</td>
<td>9.0</td>
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<tr>
<td>COPD</td>
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<td>2600</td>
<td>2700</td>
<td>9.0</td>
</tr>
<tr>
<td>All</td>
<td>30</td>
<td>2600</td>
<td>2700</td>
<td>9.0</td>
</tr>
</tbody>
</table>

### Table 3: FRC calculated with two different constant delay times (TD\textsubscript{mean} and TD\textsubscript{0})

<table>
<thead>
<tr>
<th>FRC\textsubscript{model} [ml]</th>
<th>n</th>
<th>Differences of FRC\textsubscript{model vs. FRC\textsubscript{measured}} [ml]</th>
<th>Differences of FRC\textsubscript{model vs. FRC\textsubscript{measured}} [%]</th>
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smaller than that using dynamic adjustment of $T_D$ for viscosity changes ($T_D^{dyn}$). These deviations varied in different patient groups (NORM $2.2 \pm 1.1\%$ and $6.4 \pm 1.0\%$; ALI $9.3 \pm 3.5\%$ and $13.7 \pm 3.0\%$, COPD $4.2 \pm 2.3\%$ and $14.5 \pm 2.5\%$ for FRC determined with $T_D^{mean}$ and $T_D^0$, respectively, data not shown). The FRC values of all patients calculated with $T_D^{dyn}$, but without subtraction of re-inspired $N_2$, were $33.2 \pm 17.7\%$ higher on average.

**Discussion**

This study clearly shows that the determination of end-expiratory lung volume by multibreath $N_2$ washout is valid and accurate if the delay time of sidestream sampled gas analysis is continuously corrected for gas viscosity changes during the measurement. The difference of only $2.4\%$ of $2$ $SD$ on average between FRC measured and FRC model demonstrates the high accuracy of our method. The absence of systematic differences in measured lung model FRC during ventilation with different $FIO_2$ (range 0.21–0.8) indicates very exact compensation for viscosity changes influencing the gas flow measurement and $T_D$.

On the other hand, assuming a constant $T_D$ resulted in incorrect synchronization of flow and gas concentration signals and, thus, the FRC$_{model}$ was underestimated by $8$–$12\%$ with the constant $T_D^0$ used in this study. This error increased gradually with increasing the baseline $FIO_2$ (see Fig. 2) although differences in gas viscosity during MBNW with higher baseline $FIO_2$ decreased. Consequently, the lower difference between the inspiratory and expiratory gas viscosity should result in a lower
influence of viscosity changes on FRC determination. However, in our measurement set-up the error using constant T_D0 increases, because constant T_D0 refers to the corresponding viscosity $\eta_0$ of the calibration gas consisting of 30% O_2, 65% N_2 and 5% CO_2. The use of a constant T_Dmean, referring to the mean of $\eta_0$ and the viscosity present at the end of the washout, was able to reduce the underestimation of FRC_model to 2–4 %, depending on baseline FIO2.

Brunner et al. validated FRC determinations by N_2 washout using different dynamic and constant T_D corrections in a lung model [10]. They concluded from their data, that breath-to-breath and continuous dynamic T_D correction are able to increase the accuracy of lung model FRC determinations. Although they used an argon-oxygen mixture, instead of pure O_2, for the washout and their algorithm did not correct for re-inspired N_2, Brunner et al. found comparable deviations between FRC_measured and FRC_model (~1.8% vs 2–4% [T_Dmean] and 14.5% vs 8–12% [T_D0]) in this study). The good results with constant T_Dmean were explained by a summation of overestimation of the N_2 volume in the first, and underestimation in the second, part of the washout of a lung model FRC resulting in a smaller total error. However, our study demonstrates that, in patients with inhomogeneous ventilation and non-ideal washouts, the second part of the washout seems to dominate and, consequently, the underestimation of FRC is more pronounced.

The differences of patients FRCs determined by constant versus dynamic T_D showed a wide range (0.8–13.3%, median 2.7% with T_Dmean and 4.2–23.9%, median 8.7% with T_D0) which varied between patients and between lung function groups. Plotting flow and nitrogen signals with constant T_D during the washout procedure revealed that the N_2 signal lags behind the flow signal. This time shift varied over the period of the washout, because the dynamic viscosity of the gas mixture increased with lower F_N2 (the viscosity of O_2 is higher than the viscosity of N_2 at body temperature). This incorrect signal synchronization leads to underestimation of expiratory N_2 amounts and overestimation of inspiratory N_2 volumes (which are erroneously subtracted from exhaled N_2 volumes). Consequently, FRC was underestimated by constant T_D determination. Interindividual differences of the N_2 slope and the flow signal, depending on the lung status and ventilator settings of our patients, might explain the variability in FRC underestimation due to the incorrect synchronization of signals and make it unlikely that an optimal constant T_D for all settings and patients can be found. This confirms the need for accurate synchronization of gas and flow signals at any time during the washout. Moreover, if inspiratory and expiratory gases are not perfectly separated, the re-inspired N_2 amount results in an overestimation of FRC, which would have been 33% on average of all the patients investigated.

Our method fulfills the proposed requirements for standardized pulmonary function tests of 10% [15] since the reproducibility was 6.0% on average for all lung function groups. However, there were considerable differences between the groups, revealing a higher deviation of the repeated measures in ALI and COPD patients. This might partly be explained by less stable pulmonary conditions over the period of time required for analysis. In COPD patients the mean FRC was nearly twice as high as in the other groups. Consequently, a higher number of breaths and a longer duration of measurement was necessary to remove the nitrogen. Additionally, the washout maneuvers in these patients was further influenced by ventilation inhomogeneities, which could have changed during the study period. These factors might have caused a summation of small systematic errors potentially present during MBNW and a lower reproducibility of FRC measurements in COPD patients.

Up to a baseline FIO2 of 0.6, the FRC measurement is known to be well reproducible [16]. We investigated the repeatability of FRC measurements depending on FIO2 in a subgroup of seven patients (NORM). In our patients 2 SD of differences of FRC measurements with an FIO2 of 0.3 versus 0.6 were 3.8% on average. MBNW started from a higher baseline FIO2 than 0.6 resulted in a decrease in repeatability of about 2% for each increase in baseline FIO2 of 0.1 (up to 0.8) in these postoperative patients. Although the mean 2 SD of FRC differences measured with a baseline FIO2 of 0.8 versus 0.3 were still less than 10% in NORM, one might expect higher deviations in critically ill patients.

Validation of the accuracy of FRC determinations by comparison of the lung model and patient measurements is limited. The laboratory set-up used for validation in this study consists of a single compartment lung model with almost ideal gas-mixing properties. This hardly reflects the clinical situation, especially in COPD. Trapped air or airway closure is not detected by MBNW and the incomplete recovery of N_2 due to inhomogeneous ventilation [17] and gas-mixing inefficiency [18] is another potential source of error, in COPD as well as in ALI patients, which might cause an underestimation of the FRC determined by MBNW. Additionally, there is no N_2 washed out from body tissues in lung model measurements. Although we used a generally accepted algorithm for the correction of tissue N_2, this algorithm might not exclude the total influence caused by tissue N_2 (namely in critically ill patients) and thus increase the error, particularly during long washout periods, e.g. in COPD patients with long ventilatory time constants.

Unfortunately, until now no ‘gold standard’ exists for FRC determination in mechanically ventilated patients. FRC measured by washout techniques reflects only the intrapulmonary gas volume, which is accessible to the current ventilation. FRC determined by a washout of
tracer gases, therefore, cannot be directly compared with methods like body plethysmography [4]. In comparison with previously published results obtained with tracer gas washout methods, which avoid dramatic viscosity changes, e.g. by using small amounts of foreign tracer gases such as helium or sulfur hexafluoride, the accuracy and reproducibility of the method described are in the same range [5, 19]. However, the advantages of the method described for FRC determination compared with other open circuit washout methods are: there is no need to disconnect the patient from the ventilator or to interrupt the actual breathing cycle and no additional indicator gases, injector devices or mechanical ventilators are necessary.

An interesting and simple O2 washin device has recently been described [7], unfortunately, the method is only sensitive to detect FRC changes of about 20%. Considering the important role of lung volume in acute respiratory failure, the method described may stimulate a more accessible use of FRC determination in intensive care patients.

In conclusion, multibreath N2 washout maneuvers are of acceptable accuracy and repeatability to measure FRC in a clinical setting at the bedside in ICU patients, on condition that re-inspired N2 is subtracted and a viscosity correction of the sidestream sampling delay time (TD) is carried out. Dynamic viscosity correction improves the accuracy of FRC determination considerably. If a dynamic TD correction cannot be performed, the authors suggest the use of constant TDmean. However, this will result in an unpredictable underestimation of the patient’s FRC which can exceed 10%.

References