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EXPERIMENTAL

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

Accuracy depends on continuous dynamic compensation for changes of gas sampling delay time

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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 (T_D) relative to gas flow signal and the influence of baseline FIO_2 was investigated.
Design: Laboratory study and measurements in mechanically ventilated patients.
Setting: Experimental laboratory and anesthesiological 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 FIO_2 from baseline to 1.0.
Measurements and main results: FRC was determined by MBNW using continuous viscosity correction of T_D (T_{Ddyn}), a constant T_D based on the viscosity of a calibration gas mixture (T_{D0}) and a constant T_D referring to the mean viscosity between onset and end of MBNW (T_{Dmean}). Using T_{Ddyn}, the mean deviation between 15 measurements of three different lung model FRCs ($FRC_{measured}$) and absolute volumes (FRC_{model}) was 0.2 %. For baseline FIO_2 ranging from 0.21 to 0.8, the mean deviation between $FRC_{measured}$ and FRC_{model} was –0.8 %. However, depending on baseline FIO_2, the calculation of FRC using T_{Dmean} and T_{D0} 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 T_{Dmean} and T_{D0} were 0.8–13.3 % and 4.2–23.9 % (median 2.7 % and 8.7 %) smaller than those calculated with $T_{Ddyn.}$
Conclusion: A dynamic viscosity correction of T_D improves the accuracy of FRC determinations by MBNW considerably, when gas concentrations are measured in a sidestream. If dynamic T_D correction cannot be performed, the use of constant T_{Dmean} 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

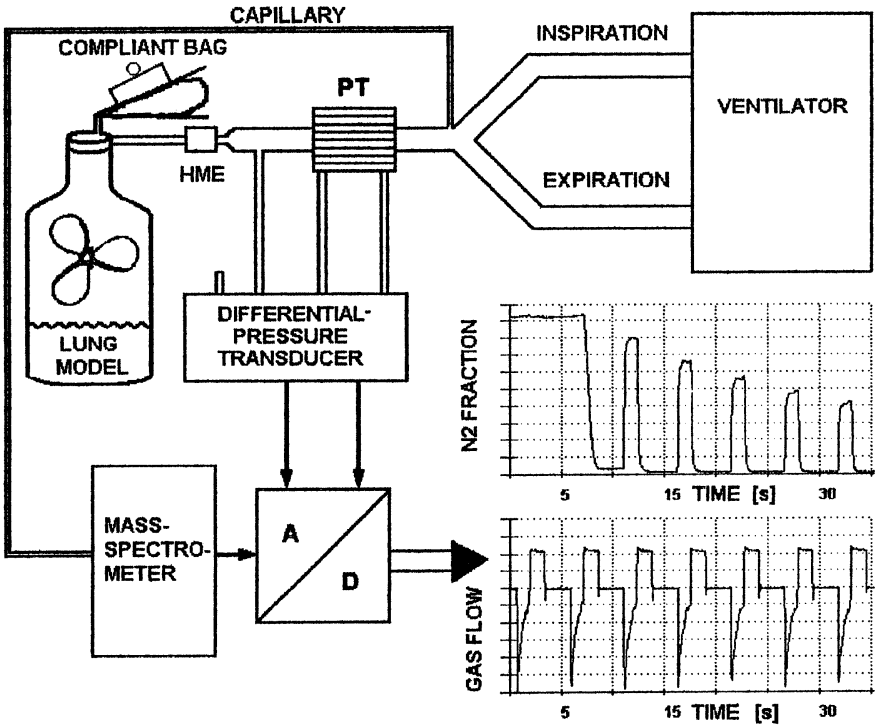

Fig. 1 General schematic diagram of the open circuit multiple breath nitrogen washout system (see text for details). (*PT* pneumotachograph, *A/D* analog/digital converter, *HME* heat and moisture exchanger) An original tracing of nitrogen fraction and gas flow is shown as an example for the output of the personal computer (not shown)

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 multi-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 (T_D) 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 T_D 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 (N_2) volume calculation during MBNW, we used a continuous off-line correction of gas flow and T_D 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 T_D and different baseline FIO_2 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, Väsby, 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. During patient measurements the pneumotachograph was connected to the HME at the proximal end of the endotracheal tube. 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 N_2, oxygen (O_2) and carbon dioxide (CO_2) 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 % N_2, 30 % O_2 and 5 % CO_2) 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 inbuilt 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 N_2 washout maneuver was started by changing the FIO_2 from baseline to 1.0. The calculation of FRC was performed off-line. The N_2 fraction (F_{N2}) at baseline was determined as the average N_2 concentration before the start of washout. The FRC calculation procedure was started with the first O_2 washin breath. As the first breath usually still contains a certain amount of N_2, this inspired N_2 volume was subtracted from the cumulative N_2 volume calculated from the washout procedure. Furthermore, total re-inspired N_2 resulting from incomplete separation of the inspired and expired N_2 volumes at the Y-piece during the washout was measured and subtracted during the integration of flow and N_2 signals. The results of FRC determination with and without subtraction of re-inspired N_2 were compared. To reduce the influence of N_2 washed out from body tissues and of signal noise, the calculation from the measurement was finished at 3 % of the baseline F_{N2}. Additionally, a correction for tissue N_2 by Cournand et al. [12] was used in all patient measurements:

$$V_{N_2,\,added} = \frac{t_{washout}\ [s^{-1}]}{420} \cdot (body\_surface\ [m^{-2}] \cdot 96.5 + 35)\ [ml]$$

The body surface is estimated from

$$body\_surface = \frac{(body\_weight\ [kg^{-1}])^{0,425} \cdot (body\_height\ [cm^{-1}])^{0,725} \cdot 71.84}{10\,000}\ [m^2]$$

FRC was determined by the equation:

$$FRC = \frac{\int_{t_B}^{t_E} -\dot{V}(t) \cdot F_{N_2}(t)dt}{F_{N_2}(t_B) - F_{N_2}(t_E)}$$

where $\dot{V}$ is gas flow, t_B is the time at the beginning of the washout and t_E the time at the end of the calculation; $F_{N2}(t_E)$ was defined as 3 % of $F_{N2}(t_B)$. Note that expiratory flow is negative by definition.

Delay time and viscosity corrections

The entire time delay (T_D) between gas sampling and data output of the mass spectrometer consists of a viscosity-dependent part and a viscosity-independent part (internal delay time, T_m), 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 (T_m) is the time necessary for analysis and output of the signals. For the computation of T_D of the individual capillary, multiple measurements were performed with different gas mixtures of N_2/O_2 revealing a linear relationship between dynamic viscosity and the corresponding delay time ($T_D = 2.07\ \eta + 89$ [ms]; $r^2 = 0.998$). T_m was defined as the time at the intersection with a viscosity of zero in the time-viscosity diagram (89 ms). The delay time (T_D) corresponding to the viscosity (η_0) of the test gas (65 % N_2, 30 % O_2 and 5 % CO_2) used for calibration of the pneumotachograph at 295.5 ° K was taken from the time-viscosity diagram and defined as instantaneous T_{D0} of the individual capillary. During the washout the momentary delay time $T_D(t_i)$ with the momentary gas viscosity $\eta(t_i)$ is [10]:

$$T_D(t_i) = (T_{D0} - T_m) \cdot \frac{\eta(t_i)}{\eta_0} + T_m$$

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 T_D corrections: 1) using the instantaneous T_D at η_0 (constant T_{D0}), 2) using the constant T_D referring to the mean viscosity during MBNW (T_{Dmean} at η_{mean}: mean of η_0 and viscosity of the gas present at the end of MBNW in patients [2 % N_2, 5 % CO_2 and 93 % O_2]) and 3) using the T_D correction for every sampled data point (dynamic correction, T_{Ddyn}). 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.

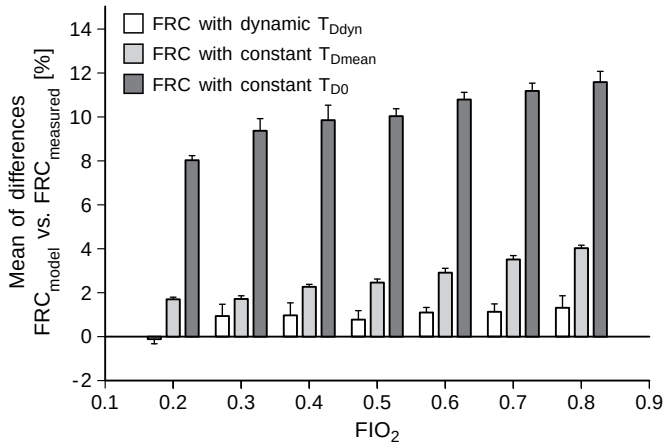

Fig. 2 Mean of differences of model volume (2600 ml) versus five FRC determinations depending on different baseline FIO_2 MBNW was started with. The *light boxes* represent FRC determinations with continuous correction of mass spectrometer delay time (T_{Ddyn}) for changes in dynamic viscosity; the *hatched boxes* represent FRC determinations from the same data without viscosity correction of T_D using two different constant delay times (see text for details)

Experimental setting

Lung model measurements

Three different volumes for FRC_{model} were chosen: 2600 ml, 5100 ml and 7600 ml. FRC was determined at a baseline FIO_2 of 0.3 five times each. To test the accuracy of the N_2 washout method during ventilation with different FIO_2, five determinations of lung model FRC were performed at FIO_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_T 6–12 ml/kg and FIO_2 0.3–0.7 depending on the individual pulmonary status and needs. After each measurement a N_2 washin lasting 15–20 min was performed to regain baseline conditions. To investigate the influence of different baseline FIO_2 on the reproducibility of the FRC measurement, MBNW was started from four different baseline FIO_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].

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

FRC_{model} [ml]	n	Differences of FRC_{model} vs. $FRC_{measured}$ [ml]		Differences of FRC_{model} vs. $FRC_{measured}$ [%]	
		mean	2 SD	mean	2 SD
2600	5	39.8	86	1.5	3.4
5100	5	−4.2	142	−0.08	2.8
7600	5	−9.0	134	−0.12	1.8
Total	15	8.9	123	0.2	2.4

Results

Lung model measurements

Using the delay time and dynamic viscosity correction (T_{Ddyn}), mean deviation of $FRC_{measured}$ and FRC_{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_2 (0.21–0.8) in the lung model revealed no obvious differences in the accuracy of FRC determination. The FRC_{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_2, FRC_{model} was overestimated by 12.4 ± 0.9 %.

Using the constant delay times T_{Dmean} and T_{D0} without viscosity correction, the FRC determination by off-line analysis of the same MBNW curves resulted in systematic differences compared with real lung model FRC (Fig. 2). Relative deviations of $FRC_{measured}$ and FRC_{model} were 2 % and 8 %, respectively, during measurements with FIO_2 of 0.21, increasing to 4 % and 12 % with FIO_2 of 0.8 calculated with constant T_{Dmean} and T_{D0}. Plots of gas flow and N_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_2 of 0.3, compared with FRC measured with higher baseline FIO_2 (0.6, 0.7, 0.8) in seven NORM are shown in Table 3. FRC calculated with two different constant delay times (T_{Dmean} and T_{D0}) were 4.1 ± 6.0 % and 10.9 ± 4.2 %

Table 2 Demographic characteristics, FIO_2 and PEEP of the 30 patients enrolled in the study (*NORM* postoperative patients without significant lung pathology, *ALI* acute lung injury, *COPD* chronic obstructive pulmonary disease)

Group	Age mean (range)	FIO_2 mean (range)	PEEP mean (range)	Diagnosis	
NORM	43.1	0.31	3.8	Abdominal surgery	(9)
(n = 16)	(18–68)	(0.3–0.4)	(0–6)	Bone surgery	(4)
				ENT surgery	(3)
ALI	58.0	0.45	6.8	Sepsis	(5)
(n = 8)	(32–75)	(0.4–0.6)	(5–8)	Pneumonia	(2)
				Near drowning	(1)
COPD	68.6	0.40	5.4	Respiratory failure due to:	
(n = 6)	(57–85)	(0.3–0.6)	(5–8)	-bronchopulmonary infection	(4)
				-respiratory muscle fatigue	(2)
Total	52.9	0.36	4.9		
(n = 30)	(18–85)	(0.3–0.6)	(0–8)		

Table 3 Repeatability of FRC measurements in seven postoperative patients (NORM) depending on baseline FIO_2 at beginning of N_2 washout. Differences of FRC measured with baseline FIO_2 of 0.6, 0.7 and 0.8 versus FRC measured with baseline FIO_2 of 0.3 are expressed as absolute and relative means and 2 SD

$FRC_{baseline\ FIO2}$	n	Differences of repeated measures [ml]		Differences of repeated measures [%]	
		mean	2 SD	mean	2 SD
$FRC_{0.6}$ vs. $FRC_{0.3}$	7	–11	99	–0.4	3.8
$FRC_{0.7}$ vs. $FRC_{0.3}$	7	23	147	0.9	5.6
$FRC_{0.8}$ vs. $FRC_{0.3}$	7	32	203	1.2	7.8

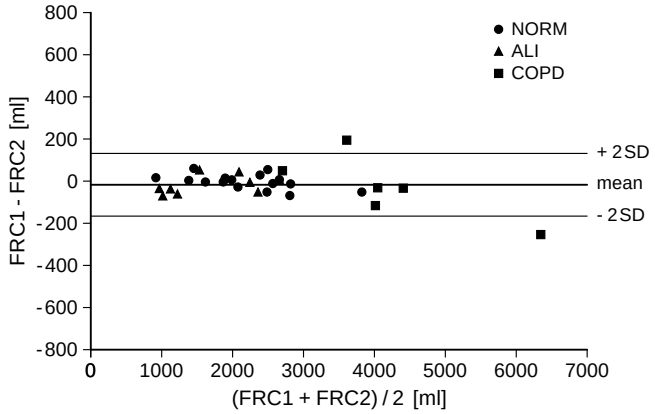

Fig. 3 Repeatability of duplicate FRC measurements in 30 patients with different pulmonary status. Absolute differences of FRC values against their means are plotted according to Bland and Altman [14]. (*NORM* postoperative patients, *ALI* patients with acute lung injury, *COPD* patients with chronic obstructive pulmonary disease)

(mean ± SD) smaller than that using dynamic adjustment of T_D for viscosity changes (T_{Ddyn}). These deviations varied in different patient groups (NORM 2.2 ± 1.1 % and 6.4 ± 1.0 %; ALI 9.3 ± 3.5 % and 13.7 ± 3.0 %, COPD 4.2 ± 2.3 % and 14.5 ± 2.5 % for FRC determined with T_{Dmean} and T_{D0}, respectively, data not shown). The FRC values of all patients calculated with T_{Ddyn}, but without subtraction of re-inspired N_2, were 33.2 ± 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_{D0} 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 η_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 η_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 FIO_2.

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 fulfils 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 maneuver in these patients was further influenced by ventilation inhomogenities, 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 FIO_2 of 0.6, the FRC measurement is known to be well reproducible [16]. We investigated the repeatability of FRC measurements depending on FIO_2 in a subgroup of seven patients (NORM). In our patients 2 SD of differences of FRC measurements with an FIO_2 of 0.3 versus 0.6 were 3.8 % on average. MBNW started from a higher baseline FIO_2 than 0.6 resulted in a decrease in repeatability of about 2 % for each increase in baseline FIO_2 of 0.1 (up to 0.8) in these postoperative patients. Although the mean 2 SD of FRC differences measured with a baseline FIO_2 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 O_2 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 N_2 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 N_2 is subtracted and a viscosity correction of the sidestream sampling delay time (T_D) is carried out. Dynamic viscosity correction improves the accuracy of FRC determination considerably. If a dynamic T_D correction cannot be performed, the authors suggest the use of constant T_{Dmean}. However, this will result in an unpredictable underestimation of the patient's FRC which can exceed 10%.

References

1. Hedenstierna G (1993) The recording of FRC – is it of importance and can it be made simple? Intensive Care Med 19: 365–366
2. Darling RC, Richards DW, Cournand A (1940) Studies on intrapulmonary mixture of gases. Open circuit method for measuring residual air. J Clin Invest 19: 609–618
3. Saidel GM, Salmon RB, Chester EH (1975) Moment analysis of multibreath lung washout. J Appl Physiol 38: 328–334
4. Brunner JX, Wolff G (1988) Pulmonary function indices in critical care patients. Springer Verlag, Berlin Heidelberg New York
5. Huygen PE, Feenstra BW, Holland WP, Ince C, Stam H, Bruining HA (1990) Design and validation of an indicator gas injector for multiple gas washout tests in mechanically ventilated patients. Crit Care Med 18: 754–759
6. Kox WJ, Mills CJ, Hale T (1991) Correction of pneumotachograph signal for changes in viscosity during nitrogen washout. Clin Phys Physiol Meas 12: 359–365
7. Fretschner R, Deusch H, Weitnauer A, Brunner JX (1993) A simple method to estimate functional residual capacity in mechanically ventilated patients. Intensive Care Med 19: 372–376
8. Sullivan WJ, Peters GM, Enright PL (1984) Pneumotachographs: Theory and clinical application. Respir Care 29: 736–749
9. Brunner JX, Langenstein H, Wolff G (1983) Direct accurate gas flow measurement in the patient: compensation for unavoidable error. Med Prog Technol 9: 233–238
10. Brunner JX, Wolff G, Cumming G, Langenstein H (1985) Accurate measurement of N_2 volumes during N_2 washout requires dynamic adjustment of delay time. J Appl Physiol 59: 1008–1012
11. Kreit JW, Sciurba FC (1996) The accuracy of pneumotachograph measurements during mechanical ventilation. Am J Respir Crit Care Med 154: 913–917
12. Cournand A, Yarmouth IG, Riley RL (1941) Influence of body size on gaseous nitrogen elimination during high oxygen breathing. Proc Soc Exp Biol 48: 280–284
13. Bernard GR, Artigas A, Brigham KL, Carlet J, Falke K, Hudson L, Lamy M, LeGall JR, Morris A, Spragg R (1994) Report of the American-European consensus conference on ARDS: definitions, mechanisms, relevant outcomes and clinical trial coordination. Intensive Care Med 20: 225–232
14. Bland JM, Altman DG (1986) Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1: 307–310
15. Quanjer PH (1983) Standardized lung function testing; report of working party "standardization of lung function tests". Bull Eur Physiopathol Respir 19 (Suppl 5): 1–95
16. Kox WJ, Mills CJ (1992) Measurement of alveolar gas mixing in mechanically ventilated patients. Crit Care Med 20: 924–927
17. Guisan M, Tisi G, Ashburn W, Moser K (1972) Washout of ^{133}xenon gas from the lungs: Comparison with nitrogen washout. Chest 62: 146–151
18. Cumming G, Guyatt R (1982) Alveolar gas mixing efficiency in the human lung. Clin Sci 62: 541–547
19. Jonmarker C, Jansson L, Jonson B, Larsson A, Werner O (1985) Measurement of functional residual capacity by sulfur hexafluoride washout. Anesthesiology 63: 89–95