

Multi-Breath Washout FAQ

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1 Introduction

Performing Multiple Breath Washout (MBW) tests with the EasyOne Pro LAB requires the patient to perform tidal breathing over a period of 2 to almost 10 minutes (depending on the patient). Due to the long duration, the test can, in some cases, be challenging to perform.

This document describes problems and errors that can occur during the test procedure. Some of these problems and errors cannot currently be detected automatically by the software. This document is based on V3.2.0.6 of EasyOne Connect, the software used on EasyOne Pro LAB.

Please note that the issues described in this document are not caused by the design of the EasyOne Pro, but are problems generally encountered in MBW tests.

This application note mainly focuses on how to perform good quality MBW tests for the determination of FRC (Functional Residual Capacity) and LCI (Lung Clearance Index)¹.

2 MBW Test Procedure

According to the ‘Consensus Statement for inert gas washout measurement using multiple- and single-breath tests’ [1] LCI is defined as follows:

LCI is the most commonly reported MBW index in current pediatric literature, and defined as the number of FRC lung turnovers (TO; calculated as CEV/FRC) required to reduce alveolar tracer-gas concentration to a given fraction of its starting concentration, historically 1/40 (2.5%).

¹ Computation of S_{cond} and S_{acin} based on N_2 concentration slope analysis is even more challenging and requires steady breathing throughout the washout (see [1] and the Application Note ‘MBW Phase-III Slope Analysis’).

Further on in the text it is described that LCI is normally determined at the point where three consecutive breaths have been detected below 2.5% of the initial tracer (N₂) concentration.

EasyWarePro is based on this definition and only marks a test as acceptable if three consecutive breaths with N₂ concentrations below 2% are detected².

When an MBW test is performed with EasyOne Pro, the end-tidal N₂ concentration is computed on-line (i.e. while the test is performed). The on-line N₂ concentrations are displayed in the bar-graph window. However, these values are not identical to the final end-tidal N₂ concentrations computed at the end of the test, where a more precise 'off-line' computation is used. The error between the 'on-line' values and the final values computed during the final evaluation is normally within $\pm 0.2\%$ N₂.

If the automatic test mode³ is selected, the system ends a test when 5 consecutive N₂ concentration values below 1.8% are detected. This approach makes sure that the LCI criterion (three consecutive N₂ concentrations below 1/40th of the start concentration) is met in almost all cases.

When the manual test mode is selected, please make sure that enough breaths below 2% are recorded and be aware that a maximum error of $\sim 0.2\%$ is possible between on-line and final N₂ concentration computation.

If only one or two consecutive breaths with N₂ concentrations below 2% are measured, then the LCI is still computed, but the test is marked as not acceptable. In this case the error message 'FRC, tracer concentration at end of test is too high' is shown (Message Number 31).

3 Patient Preparation

In order to perform the test with a patient, the patient must be introduced to the system and the MBW procedure has to be explained in detail. We propose performing the following:

- Show the equipment to the patient with focus on the mouth piece and the nose clip.
- Demonstrate what noises are to be expected during the test procedure. For this purpose the valve can manually be closed and opened (Utilities / Configuration / Device / DLCO Valve).
- Explain to the patient that he/she does not feel a difference between breathing 100% oxygen and normal air. The oxygen might feel more 'dry' which can lead to increased saliva production and, in rare cases, coughing.
- Tell the patient that he/she should breathe normally, continuously and steadily. The mouth must be closed and the lips must seal tightly around the Spirette. He/she must not laugh, speak or yawn during the test.
- The teeth must be placed on-top of the Spirette, not biting down on the Spirette.
- Swallowing is OK if necessary.
- According to the Consensus Statement [1] sighing during the washout phase should lead to exclusion of the test (as it may significantly elevate FRC).
- Each test takes about three to five minutes.
- The time between two tests must be twice as long as the test time. During this time the patient should remove the mouth piece and may remove the nose clip

² An N₂ concentration of 2% corresponds to 1/40th = 2.5% of the initial N₂ concentration of ambient air (1/40th of 78.1% equals 2% N₂).

³ For selection of the test mode go into Utilities / Configuration / Test / FRC (MBW).

as well. The patient can drink in between tests, but he/she should not drink carbonated drinks (this can cause artifacts due to CO₂).

4 Errors and Problems in MBW Tests

4.1 Start of Washout

The Consensus Statement states that the pre-washout phase has to have

stable VT and end-expiratory lung volume over the preceding 30 s.

This is also true for the measurements with EasyOne Pro where the first three breaths before the washout are used as a reference.

In the software of EasyOne Pro LAB the start of the washout is controlled by three settings (accessible via Utilities / Configuration / Test / MBW):

Test Mode	This setting defines if the washout start and end are automatically or manually controlled.
Min. No. of Breaths	This setting defines the minimum number of 'stable' breaths before the washout start. Please note that in both manual and automatic mode the number of breaths defined here must fulfil the stability criteria (see below)
Target volume Range	This setting defines if a large tidal volume range is used (i.e. for adults, SnIII analysis) or if a small Vt range is used (i.e. for pediatric applications)

The stability criteria for the tidal volume Vt (in- and expiratory volume) before the washout are as follows:

Large Vt range	<u>Vt min</u>	<u>Vt max</u>	<u>Bar-graph min</u>	<u>bar-graph max</u>
Patient weight available	5 ml/kg (max 350 ml)	30 ml/kg	950 ml	1400 ml
Patient weight not available	250 ml	3000 ml	950 ml	1400 ml
Small Vt range				
Based on ideal body weight [2]	6 ml/kg	16 ml/kg	8 ml/kg	13 ml/kg

Note: For the small Vt range the ideal body weight is determined from height, age and sex of the patient. For details refer to [2].

This stability criteria may lead to the situation where a washout cannot be started. Example for 'Large Vt range': If a patient has a weight of 50 kg, then the Vt is limited to 250 ml to 1500 ml. If the Min. No. of Breaths is set to 5, then all 5 breaths have to be within that limit; even if one out of 5 breaths is slightly above 1500 ml then the test will not start. In order to resolve the problem please ask the patient to breathe with smaller tidal volume.

4.2 Hyperventilation

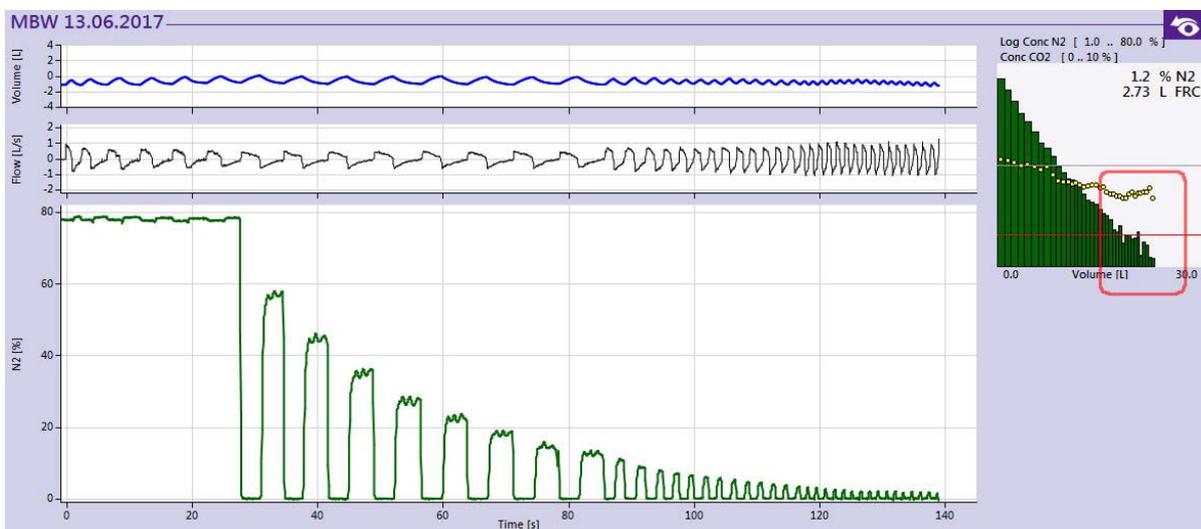
If the patient hyperventilates during the MBW test procedure, the end-tidal N_2 and CO_2 values cannot be determined due to an incomplete phase III of the expirogram. The Consensus Statement says the following regarding this:

If available, monitor end-tidal CO_2 values during MBW to screen for hyperventilation.

In order to monitor end-tidal CO_2 concentration please activate this feature in Utilities / Configuration / Test / MBW / Show CO_2 curve. The end-tidal CO_2 concentration is plotted within the N_2 bar graph display, end the gray line indicates a level of 5% CO_2 .

Hyperventilation can be recognized in two ways: First, the end-tidal CO_2 values will decrease and second, the increased breathing frequency can be recognized in the graphs of flow, volume and N_2 .

The screen shot below shows a test with hyperventilation during the last part of the MBW test:



At the start of the washout the breathing frequency is normal and complete N_2 expirograms can be identified (i.e. N_2 signals with a clearly identifiable phase III). During the above MBW test, the breathing frequency is increased. Due to the increase in frequency and the decrease in tidal volume end-expiratory CO_2 concentrations, indicated as yellow dots on top of the semi logarithmic N_2 concentration plot, and therefore end-expiratory N_2 concentrations, cannot be measured accurately (no clear plateau in phase III). As a result, the end-expiratory N_2 concentrations differ significantly from breath to breath (see diagram on the right side). As a consequence, LCI cannot be measured accurately since there is no clear point where the N_2 concentrations fall below the red line, indicating $1/40^{\text{th}}$ of the initial N_2 concentration.

Recommendation: Make sure that the breathing frequency and the tidal volume are constant throughout most of the test. Apart from the flow, volume and N_2 traces the yellow dots in the N_2 diagram indicate the end-expiratory CO_2 concentration; in the above diagram the falling concentrations of CO_2 can clearly be seen. During the same phase the end-expiratory N_2 concentrations do not decrease in a regular fashion and make a precise determination of LCI impossible.

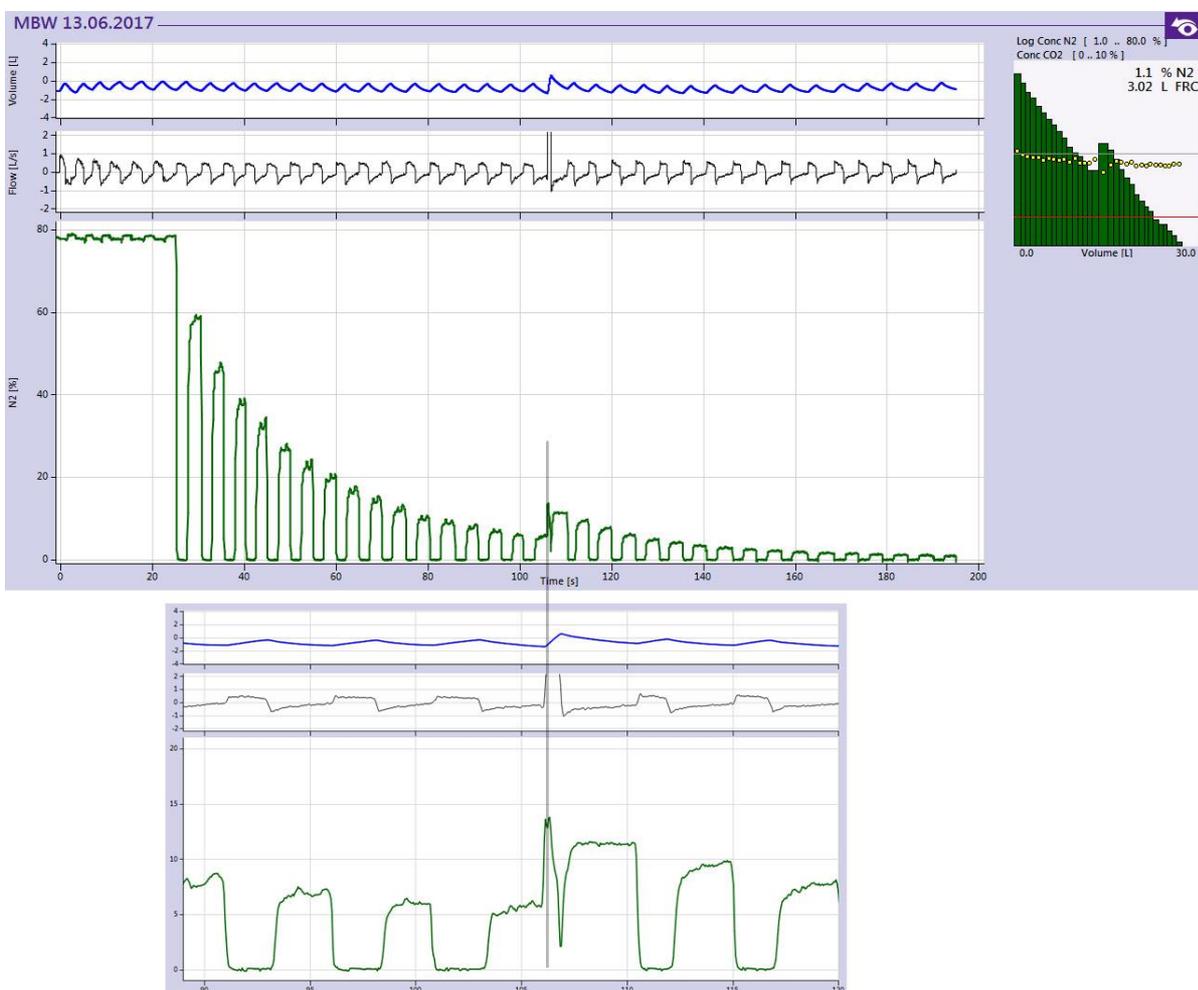
4.3 High inspiratory Flow / Room Air Inspiration

The N_2 MBW test relies on the fact that the patient only inspires 100% O_2 during the washout phase. If the patient inhales room air during the washout, the N_2 concentration will rise again. Inspiration of room air can occur due to several reasons:

- The patient inhales room air due to a leak at the mouth piece.
- The patient inhales room air due to excessive inspiratory flow combined with a leak in the check-valve.

The following two pictures show how inspiration of room air can be detected. At a test time of approx. 105 sec the patient inhales deeply and exceeds the maximum flow level of 2 l/s. The check-valve was blocked manually and due to this additional error inspiration of room air occurred. The excessive flow can also be detected in the flow and volume signals. At the end of the test the warning ‘High inspiratory or expiratory pressure detected’ is displayed and the test is automatically marked ‘not acceptable’.

In the zoomed display mode (shown below the main picture), the inspiratory N₂ can be recognized easily. In addition the end-expiratory N₂ concentrations raise immediately after room air inspiration.



In order to eliminate inspired room air, the following recommendations should be followed:

- Make sure that the pressure of the O₂ supply at EasyOne Pro LAB is set to 4 bar. Also make sure that the pressure does not drop below 3 bar during the washout phase when the patient inhales O₂.
- Make sure that a new spirette and FRC barriette are used. Both items are essential for patient hygiene and for good tightness during a washout test.
- Use a nose-clip and mount it properly.

- Make sure that the patient places the teeth on-top of the spirette and closes the lips tightly around the mouth piece during the entire test.
- Make sure that the patient does not exceed the limits 2 l/s inspiratory flow.

5 MBW Acceptability and Quality Grades

The current software of EasyOne Pro / LAB contains a quality grading system for Spirometry and for DLCO. For Multiple-Breath Washout (MBW) tests, however, a quality grading system has not yet been introduced by ATS/ERS.

For MBW a grading a system similar to those used in spirometry has been implemented in the software of EasyOne Pro LAB in order to allow a defined quality grading system and a defined 'end-of-test' criteria. The grading system is mainly based on the ATS/ERS consensus statement [1]. Based on this publication quality grades A to F will be defined; the trial acceptability and test quality assessment will be explained in the following.

5.1 MBW Acceptability

In order for a trial to be acceptable the following criteria apply:

1. End-of-test criteria for LCI is met (3 consecutive breaths with end-tidal N₂ concentration <1/40th of the starting N₂ concentration).
2. Mouth pressure <±5 mbar detected during the test procedure.
3. Flow < ±2 l/s during the test.
4. Mean inspiratory volume during washout is within limits defined in chapter 4.1.
5. No large volume drift detected.
6. ERV and IRV can be computed when a 'linked' MBW test is performed.

Please note that the following criteria are at the moment not quantified and therefore not considered for test acceptability:

1. Breathing pattern: According to the 'Consensus Statement' the breathing pattern should be similar between patients.
2. Irregular breathing pattern at start of test: The breathing pattern should be similar throughout the washout test.
3. Sighs during the test. According to the Consensus Statement visible sighs should prompt for test exclusion.
4. Leaks causing room air inspiration during washout causing a step in the end-tidal N₂ concentrations during the washout.
5. Hyperventilation may lead to test exclusion (however, this is not mentioned in the Consensus Statement).

Since these criteria are not quantified, they should be checked by the technician performing the tests and the acceptability should be adapted manually when a test has been performed. The quality grading will be recomputed as soon as the acceptability has been changed by the user.

5.2 MBW Quality Grades

The following quality grading system based on the ATS/ERS MBW Consensus Statement [1] is defined:

Grade A	A minimum of 2 acceptable maneuvers with LCI variability <5% and FRC variability <10%	→ Session complete
Grade B	A minimum of 3 acceptable maneuvers with LCI variability < 10% and FRC variability <25%	→ Session complete
Grade C	2 acceptable maneuvers with LCI variability < 10% and FRC variability < 25%	
Grade D	1 acceptable maneuver or multiple maneuvers with LCI variability ≥10% or FRC variability ≥ 25%	
Grade F	no acceptable maneuver	

Remark: FRC and LCI variability are defined as the largest difference to the median FRC respectively LCI value. In statistics and probability theory, the median is the numerical value separating the higher half of a data sample, a population, or a probability distribution, from the lower half. The median of a finite list of numbers can be found by arranging all the observations from lowest value to highest value and picking the middle one (e.g., the median of {3, 3, 5, 9, 11} is 5). If there is an even number of observations, then there is no single middle value; the median is then usually defined to be the mean of the two middle values [1] [2] (the median of {3, 5, 7, 9} is $(5 + 7) / 2 = 6$), which corresponds to interpreting the median as the fully trimmed mid-range. (Wikipedia)

Additional restrictions:

- At the moment the FRC and LCI values are reported as average of all acceptable trials. The additional criteria that only trials within $\pm 25\%$ of the median have to be considered is not implemented.
- There is at the moment no warning message when only 2 acceptable trials are performed (the warning message is suggested in the Consensus Statement [1]).

6 Accuracy

Regarding FRC (and LCI) accuracy, the Consensus Statement states the following:

Formal FRC repeatability criteria for MBW indices should not be routinely applied, but FRC values within 10% should be viewed as encouraging. FRC values differing by more than 25% from the median of three test values should be excluded.

7 Conclusions

All above mentioned recommendations should be followed carefully.

The most important general recommendation is that patients must breathe regularly in order to perform qualitatively acceptable tests (see [1]):

Breathing patterns during testing should be kept similar between subjects to facilitate comparison of results. In adults this is achieved by using strict breathing regimens where feasible and in younger children (aged <16 years) by distraction to encourage relaxed tidal breathing.

For details please refer to the Consensus Statement [1].

8 References

- [1] Consensus statement for inert gas washout measurement using multiple- and single-breath Tests. Eur Respir J 2013; 41: 507–522.
- [2] Estimating physiologically appropriate tidal volume ranges for multiple breath washout tests. E. Horton, R. Jensen, S. Stanojevic, F. Ratjen.