

MBW Phase-III Slope Analysis

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1. Introduction

Phase-III analysis of nitrogen washout is an advanced method for the study of ventilation distribution in the lung. A description of this method can, for example, be found in [1]. The method basically performs a Phase-III Slope Analysis of each expiratory N₂ trace registered during the multi-breath N₂ washout.

This method is still relatively new and has not yet been implemented in the clinical software of EasyOne Pro LAB. In a first step MBW Phase-III Slope Analysis is implemented in the 'research software' WBreath that accompanies the clinical software of EasyOne Pro LAB. Tests performed in the clinical software EasyOne Connect can either be opened directly in WBreath, or these tests can be exported in WBreath format and can then be analyzed on a separate PC using WBreath.

This Application Note details how Phase-III Slope Analysis can be performed with EasyOne Pro LAB and the software WBreath.

2. Prerequisites

This description is based on the following software versions:

- EasyWarePro **V 3.1.0.1**
- WBreath **V 3.48.0**

The most recent version of the programs can be downloaded from the ndd website at <http://www.ndd.ch/index/downloads-software>

Please note that you also need Access codes provided by ndd in order to perform the MBW analysis including phase-III analysis. Installation of WBreath on a separated PC and entering of the access codes is described in the Application Note 'Installation of WBreath', also available from the ndd website at www.nddmed.com.

Please note that Phase-III Slope Analysis in the above mentioned WBreath version is not yet validated and in a prototype state. In this phase, changes in the software may alter the computed values of the parameters.

Please also note that the algorithm for MBW analysis used for phase-III computation differs from the officially released version in EasyOne Pro LAB. FRC and LCI values therefore can differ when compared to the results in EasyOne Pro LAB. For details, please refer to our Application Note 'Measurement Technology Background' available on our website.

3. Workflow

In order to perform a phase-III analysis of a nitrogen multiple-breath washout (N₂ MBW) the following steps have to be executed:

Start a normal MBW test using EasyOne Pro LAB. Please note that according to [2] an expired volume of 0.95 to 1.4 liters (for adult patients) should be achieved during the washout phase if Phase-III Slope Analysis is going to be performed. EasyWarePro contains an incentive display that allows to check the inspired volume of each breath.

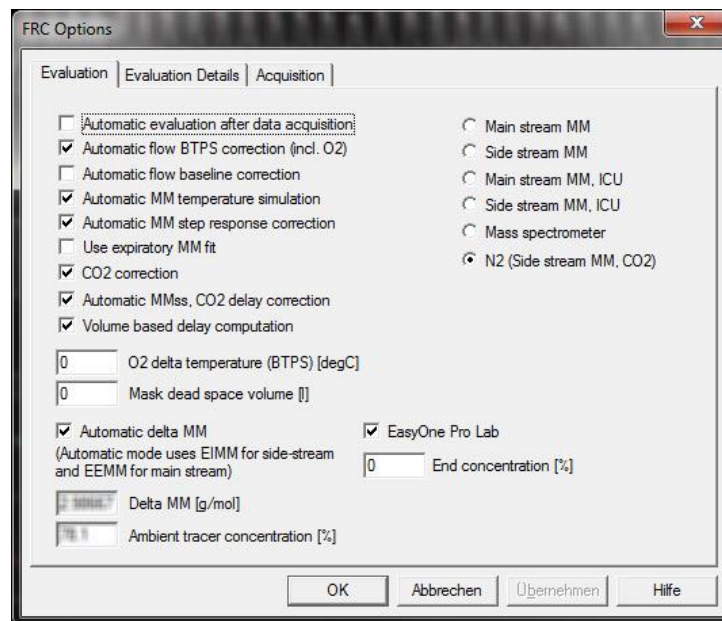
When the test has been performed, a single trial can be opened directly in WBreath:

- a) Display *Patient History* and select the small button with the three dots. New buttons appear; select *Open WBreath*.
- b) The complete raw data of the first trial is opened in the scientific software WBreath.
- c) In order to select other trials of this MBW test, select *File / Open* and move to the folder *Application Data / n d d / EasyOnePro / WB-Export*. Each trial is available there. The file name consists of the Patient ID combined with test's date and time.

As an alternative, all trials of an MBW test can be exported:

- a) Plug a memory stick into the back of your EasyOne Pro LAB.
- b) Display *Patient History* and select the small button with the three dots. New buttons appear; select *WBreath Export*. Select an appropriate folder on the memory stick.
- c) The files can now be opened in WBreath on your PC (the software can be downloaded using the link indicated above).

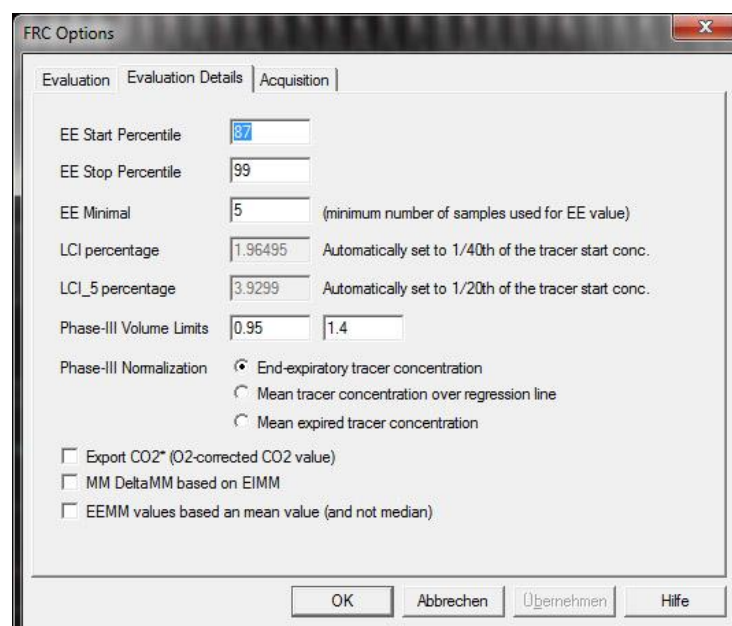
An MBW test is now opened in To perform the MBW phase-III analysis, check that the following options are correctly set: Go to *Analysis / FRC Options*:



Phase-III MBW analysis can only be performed using the 'N2 (Side stream MM, CO2)' method. Please also make sure that the 'EasyOne Pro LAB' and the 'Automatic MMs, CO2 delay correction' checkmarks are set.

Remark: The settings of WBreath can be saved in a configuration file by selecting *File / Save Configuration as...* The default configuration loaded while starting WBreath can be specified in *File / Preferences / Default configuration*.

Furthermore, the tab *Evaluation Details* allows to set more options, especially the type of N₂ tracer concentration normalization used for the analysis:

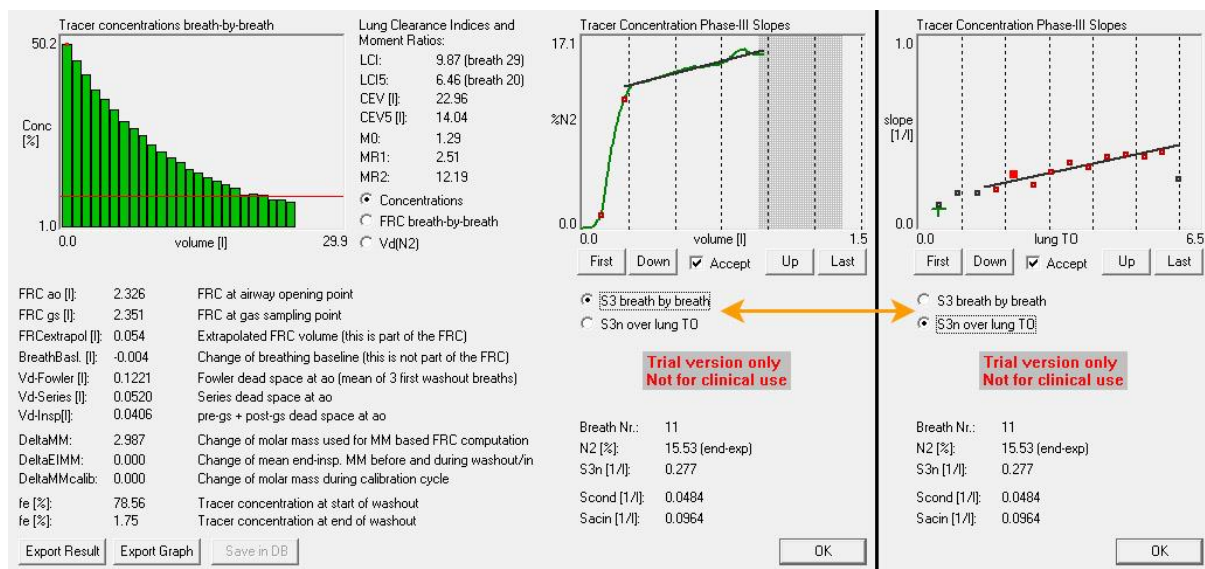


Three different types of normalization can be selected:

1. Normalization by end-expiratory tracer concentration.
2. Normalization by mean tracer concentration over the phase-III regression line.
3. Normalization by mean expiratory concentration over the entire expiration (see [4, 5]).

Please note that, in most cases, the phase-III analysis strongly depends on the method chosen for normalization. Please refer also to the Consensus Statement [2] and the additional papers [4, 5] for the selection of the appropriate method.

The MBW phase-III analysis is performed by selecting *Analysis / FRC* or by pressing the appropriate icon on the toolbar. The following result window is shown:



The left side of the window shows the result parameters of the FRC computation including LCI (at $1/40^{\text{th}} = 2.5\%$ and at $1/20^{\text{th}} = 5\%$ of the tracer gas) and Moment Ratios in the center between the two graphs.

The right side of the window shows the phase-III analysis. Depending on the selected mode the right side shows one of the following two diagrams:

1. S3 breath by breath: In this mode the N₂ concentration over the expired volume can be displayed for each breath of the MBW. The target volume is marked in grey (the area is adapted according to the patient data; see above). The two breakpoints between phases I, II, and III of the expiration are shown with small red rectangles on the N₂ curve. The actual phase-III slope is shown as a straight line on the N₂ graph.

With the buttons *Up*, *Down*, *First*, and *Last*, each breath of the washout can be visually inspected. The N_2 curve is automatically scaled. With decreasing end-expiratory N_2 values, the noise on the displayed curve increases.

2. S3n over lung TO: In this graph the normalized phase-III slopes are plotted over the lung turn-over (CEV divided by FRC). The type of normalization can be selected in the FRC options (see above). Acceptable S3n values are marked in dark red rectangles, unacceptable breaths are marked with black rectangles. The selected S3n breath value is marked in bright red. By using the *Up*, *Down*, *First*, and *Last* buttons the selected breath can be moved and the individual values can be inspected.

Independently of the selected graph, the *Accept* flag signals if the selected breath has been considered for the computation of the S_{cond} parameter; this flag has been set using the criteria defined in [2] (see also next section). Due to the restrictions described above the acceptability flag can only be changed if the S_{cond} value of a breath is within these limits. The value for S_{cond} changes automatically if the acceptability flag is changed.

Below the graph on the right side, the following information is displayed:

- The selected breath number (changes with the *Up/Down* buttons).
- The N_2 concentration used for slope-III normalization of the selected breath. Please note that this value depends on the normalization method selected in the window as described above. The selected normalization method is shown in parentheses.
- The normalized phase-III slope of the selected breath (S3n).
- The actual values of S_{cond} and S_{acin} .

4. Background Information

Phase-III analysis is based on the 'Consensus statement for inert gas washout measurement using multiple- and single-breath tests' [2]; automated determination of the phase-III slope is based on a publication by Ch.R Stuart-Andrews et al. [3] using a break-point analysis.

1. Inclusion criteria for S3n values: At present, the automatic selection (reflected by the acceptability flag) of S3n values is based upon the criteria defined in the Consensus Statement (see [2]):
 - a. Lung turn-over of breath between 1.45 and 1.65.
 - b. The computed S3n value is >0 , i.e., negative or horizontal slopes are not taken into account.
 - c. A first regression line is computed based on the criteria listed above. All breaths that are not within the 95% CI of this regression line are rejected and a final regression line is computed.

- d. If required, more breaths can be excluded manually; the computation of S_{cond} and S_{acin} will be adapted accordingly.
2. Display of N_2 and O_2 channels: Computation of S_{3n} is based upon the N_2 concentration trace. After computing phase-III slopes, an additional N_2 (and also O_2) channel is available and can be displayed. Go to *View / Channels...* and select the channels N_2 and/or O_2 .
3. Exporting result data: As in previous versions of WBreath, MBW result data can be exported using the *Export Result* button in the FRC result window. If this button is pressed, the file *ResultFRC-N₂.csv* is written into the working folder (which can be defined under *File / Preferences*). For each FRC test that is exported, a new line with result data is added to that file. Batch evaluation (*File / Batch Evaluation*) can be used as in previous versions of WBreath.
4. Exporting the Breath table: The Breath table (*Analysis / Breath Table*) now also contains the values of the normalized slope $\bar{3}$ (S_{3n}) and the acceptability criteria for each breath. The new parameters are called 'Trace S_{3n} ' and 'TraceAccept'. These values are also available in the export of the Breath table (*File / Export Breath Table...*).
5. Tracer start and tracer end concentrations: The start concentration is the N_2 concentration before the washout started; the end concentration is the concentration of N_2 of the last recorded breath. Please note that both LCI and FRC are computed at the point where three consecutive breaths are below $1/40^{\text{th}}$ of the start N_2 concentration.

5. References

- [1] S. Verbanck, D. Schuermans, A. Van Muylem, M. Paiva, M. Noppen, W. Vincken. Ventilation distribution during histamin provocation. *J Appl Physiol* 83(6): 1907-1916, 1997.
- [2] Consensus statement for inert gas washout measurement using multiple- and single- breath tests. *Eur Respir J* 2013; 41: 507-522.
- [3] Ch.R. Stuart-Andrews, V.J. Kelly, S.A. Sands, A.J. Lewis, M.J. Ellis, B.R. Thompson. Automated detection of phase III slope during inert gas washout testing. *J Appl Physiol* 112: 1073-1081, 2012.
- [4] A.B.H. Crawford, M. Makowska, M. Paiva, L.A. Engel. Convection- and diffusion-dependent ventilation maldistribution in normal subjects. *J Appl Physiol* 59(3): 838-846, 1985.

- [5] S. Verbanck, M. Paiva, D. Schuermans, S. Hanon, W. Vincken, A.V. Muylem. Relationships between the lung clearance index and conductive and acinar ventilation heterogeneity. *J Appl Physiol* 112: 182-190, 2012.