

Fundamentals of Spirometry with general considerations for Lung function testing in General Practitioner`s Offices (GPO) and recommendations for proper operation of PC based diagnostic devices for examination of pulmonary diseases.

Background: Lung function testing, defined as well as spirometry is a simple and widely used lung function test. A spirometry is a test that measures airflow when the patient is breathing and possible abnormalities in the airways and lung tissue can be detected and recorded. Respiratory functions and differences between normality and pulmonary diseases causing obstructive and possibly restrictive effects can be assessed by a measurement routine which is easily to be performed.

Spirometry is becoming more and more important as respiratory tract diseases are increasing rapidly based by different factors. Additionally spirometry is the method of choice for a fast and reliable screening of COPD (Chronic Obstructive Pulmonary Disease).

The patients entering the General Practitioner`s Offices are predestinated for this kind of basic examinations like blood pressure measurement, ECG, spirometry and other analysis methods for assessment of the general patient`s status. This kind of patient screening is essential for to continue the differential diagnosis and for to organize other investigations and treatments.

More and more the diagnostic tools for lung function testing and other essential diagnostic examinations are PC based devices as the common advantages are fast results and recording of patient examination data, paperless documentation ability, possibility of data transfer, USB or Bluetooth™ operation modes, mobile operation and easy to be operated light weight modules. For to guarantee a possibility of simple operation most of the devices are operated by WINDOWS™ OS or predestinated for mobile operation, ANDROID™ OS. Another argument for use of these kind of PC based spirometers is the data exchange and resulting out of it the ability of communication between General Practitioners and the specialists in the internal medicine and pneumology. This kind of cooperation and interaction between GPs and specialists is of utmost importance for to assure the exact diagnosis and the selection of an efficient therapy with correct medication. These factors are providing the very best treatment of the patients.

Keywords: General Practitioner (GP), General Practitioner`s Office (GPO), Respiratory Tract Diseases, Pulmonary Diseases, asthma, Chronic Obstructive Pulmonary Disease (COPD), Disease Management Program (DMP), PINK FLOW PC based Spirometer, Universal Serial Bus (USB), WINDOWS™, Operation System (OS), Medical Device Regulations (MDR), European Norm (EN), International Standard Organization (ISO), Certificate Europe (CE) Notified Body (NB), Post Market Surveillance (PMS), Post Market Clinical Follow Up (PMCF).

Definitions: The joint guidelines concerning lung function testing prepared by the European Respiratory Society (ERS) and the American Thoracic Society (ATS) are describing precisely the procedures and parameters that are common for many methods of spirometry:

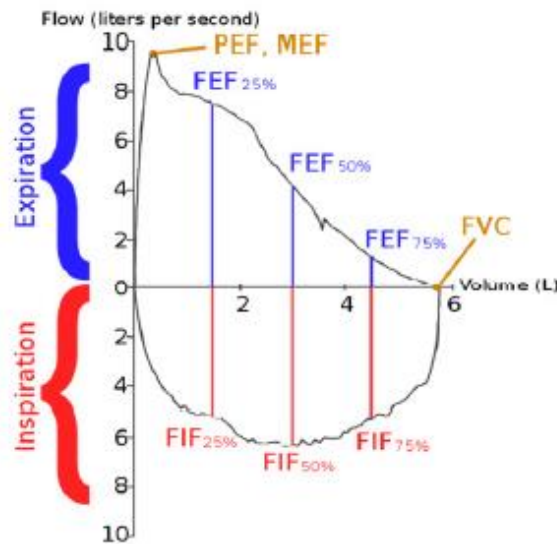
List of description of the most common measured parameters and abbreviations used in this document and also included as part of this abstract. These parameters are content of respiratory measurement analysis of an innovative PC based spirometer operated by ultrasonic flow volume measurement - **Overview of parameters:**

- FVC procedure: FVC, FEV1, FEV1/FVC, FEV6, FIVC, FIV1, EV, PEF, PIF, FEF25, FEF50, FEF75
- FIF25, FIF50, FIF75, MMEF2550, MMEF2575, FET, ELA, ZeroTime, EOTV, PEFT
- VC procedure: VC, IVC, IC, ERV, TV, TI, TE, VE, RR, TV/TI, TE/TI
- MVV procedure: MVV

Forced Vital Capacity (FVC) curve main values (Picture 1):

- FVC: Forced vital capacity
- PEF: Peak expiratory flow
- PIF: Peak inspiratory flow
- FEV1: Forced expiratory volume in one second
- FEV6: Forced expiratory volume in sixth second
- FET: Peak expiratory time
- FEF25%: Instantaneous forced expiratory flow when 25% of the FVC has been expired
- FEF50%: Instantaneous forced expiratory flow when 50% of the FVC has been expired
- FEF75%: Instantaneous forced expiratory flow when 75% of the FVC has been expired
- FIF25%: Instantaneous forced inspiratory flow at the point where 25% of the FVC has been expired
- FIF50%: Instantaneous forced inspiratory flow at the point where 50% of the FVC has been expired

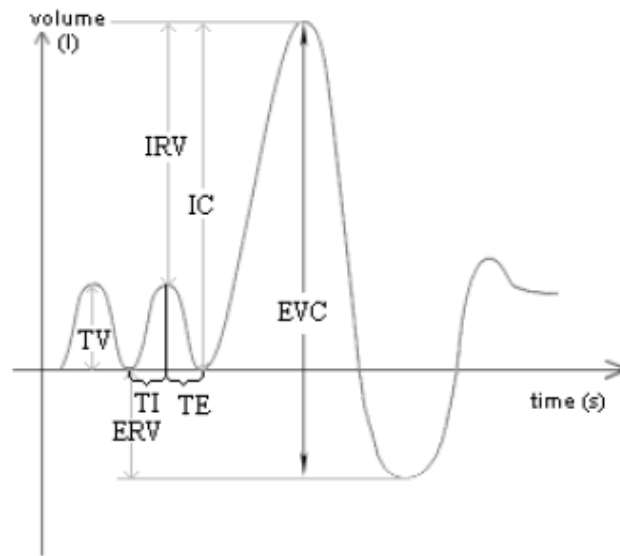
- FIF75%: Instantaneous forced inspiratory flow at the point where 75% of the FVC has been expired
- MMEF25%-50%: Maximum mid-expiratory flow between 25% and 50% of
- VCMMEF25%-75%: Maximum mid-expiratory flow between 25% and 75% of FVC



Picture 1

Vital Capacity (VC) session values (Picture 2):

- VC: Vital capacity
- IVC: Inspiratory vital capacity
- EVC: Expiratory vital capacity
- IC: Inspiratory capacity
- ERV: Expiratory reserve volume
- IRV: Inspiratory Reserve Volume
- TV: Tidal Volume
- TI: Time measured for inspiration
- TE: Time measured for expiration



Picture 2

Description of Analysis:
 VC Curve Analyzer (VCCA) calculates the VC parameters and makes notes on the quality of the VC curve. The notes are visible under “maneuver quality (Automatic)” in the result page and under “VC maneuver” on report templates.

While VC Curves are stored in the database in unchanged format the Curve Analyzer interprets them in its latest version. This means that if there is a new version of the software, which contains an update of the VC Curve Analyzer, the VC curves are re-evaluated with that latest version of the Curve Analyzer. This is done when the trials are loaded from the database in VC Result Page. New version of the VC Curve Analyzer are usually smarter (detect errors / non-conformances more sophisticatedly) and they may calculate parameters from curves, on which former VCCA versions failed.

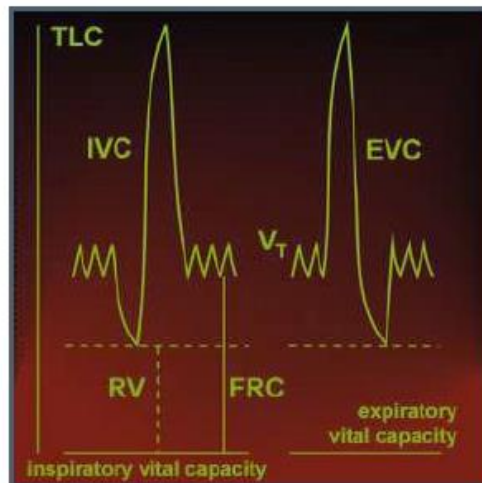
If the curve is still not “usable” by the latest VCCA message “VC Session migration failed” is displayed and the VC parameters are still undefined (0.0) on the VC result page.

Types of VC curves (Picture 3):

The vital capacity is assessed during an inspiratory maneuver. Starting from end-tidal volume the subject expires maximally and subsequently makes a full inspiration. This is the inspiratory vital capacity (IVC).

The vital capacity is assessed during an expiratory maneuver. Starting from end-tidal volume the subjects makes a full inspiration and subsequently exhales maximally. This represents the expiratory vital capacity (EVC), or ‘slow vital capacity’ in the Anglo-American literature.

Source: <http://www.spirxpert.com/indices2.htm>



Picture 3

VC curve

A VC curve consists from three different sections:

- leading tidal breaths
- full expiration / inspiration and returning to the tidal breath
- finishing tidal breaths

Description of correct parts and failure analysis of a VC curve:

- Difference between real and ideal VC curves
- In an ideal VC curve the tidal breaths are the same and the expiration volumes are always the same and the inspiration volumes. In real VC curve the tidal breaths follow a (normal) distribution (in terms of inspiration volume, expiration volume, inspiration time and expiration time).
- In an ideal VC curve a tidal breath ends with no offset (the curve returns to the same volume level). So the baselines (functional residual volume - FRC) of the tidal breaths are the same before and after full expiration-inspiration pair. In a real curve due to different sources this is not true:
 - flow-meter device has inaccurate calibration (not of interest if device has AUTOCAL mode)

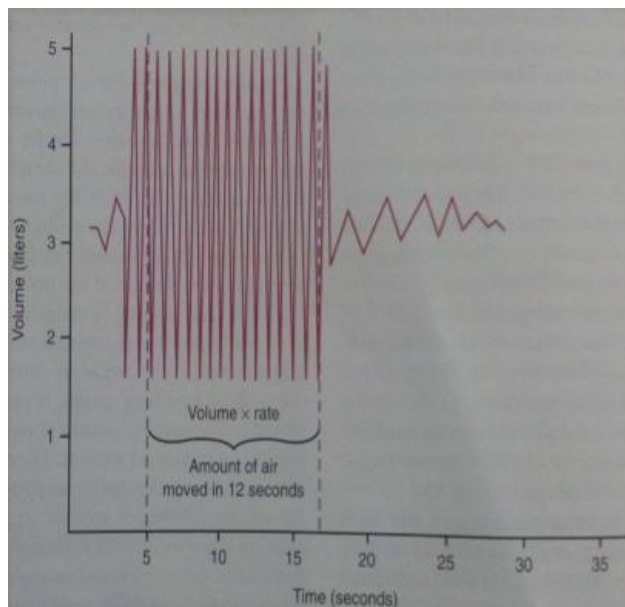
Prosecution of Description of correct parts and failure analysis of a VC curve:

- ➤ patient as a flow generator is not ideal (to be taken care about anamnesis)
- ➤ room ambient conditions are not set properly in the Software (temperature, humidity and air pressure)
- A real VC curve usually does not have finishing tidal breath
- The returning from full expiration / inspiration to the tidal breath occurs without transition (immediately) in an ideal curve. In a real curve this is not true

- Considering A) and C) and D). The tidal breaths are averaged (in terms of expiration volume, inspiration volume, expiration time, inspiration time), however only the leading tidal breaths.
- Considering B) we need a volume Base Point related to tidal breath. Without this base point we are not able to calculate parameters other than VC (IVC/EVC)
- Place of Base Point:
EVC: end of last tidal expiration (before starting full inspiration)
IVC: end of last tidal inspiration (before starting full expiration)

Maximum Voluntary Ventilation (MVV) Session can interpret these values (Picture 4):

MVV: Maximum voluntary ventilation (MVV) is a measure of the maximum amount of air that can be inhaled and exhaled within one minute. For the comfort of the patient this is done over a 15 second time period before being extrapolated to a value for one minute expressed as liters/minute. Average values for males and females are 140–180 and 80–120 liters per minute respectively.



Picture 4

The currently implemented Predictive Algorithms are (overview):

- Knudson
- E.R.S. 2010 / Knudson
- Crapo & Bass / Knudson
- E.R.S. 2010 / Zapetal
- Barcelona / Zapetal
- NHANES III
- Crapo
- Hsu
- Swiss Adult 1996
- Chinese Hong Kong

- Gore 1995 – Australia
- Stanojevic 2009
- Swedish/Hedenström
- Pneumobill / Knudson /Austrian / Polgar for children
- ERS/Polgar(Argentina)
- SER 2009 (Chile)
- Pereira 2008 (Brazil)
- Perez-Padilla(PLATINO)
- Perez-Padilla(Mexico)
- Global Lung Initiative(ERS)

Terms and definition of generally relevant parameters with cross reference to standards and harmonized norms:

Accuracy is defined as the closeness of agreement between the result of a measurement and the conventional true value.

Repeatability is defined as the closeness of agreement between the results of successive measurements of the same item carried out. This repeatability is an important parameter not only for clinical evaluation, it should even be subject to all of the following conditions: Same method, same observer (means physician), same device, same location, same condition of use, and repeated over a certain space of time. Especially for drug monitoring and drug titration repeatability becomes an important parameter to be taken care about. PRE and POST measurements are to be done for to find out the correct and individual dosage (drug titration) for a drug, especially when treating COPD by medication with Anticholinergics (Beta-2-Mimetics), by Corticoides or, since a few years, PDE-4-Inhibitors.

Reproducibility is the closeness of agreement of the results of successive measurements of the same item where the individual measurements are carried out with changed conditions, such as: Method of measurement, observer (means physician), same device, location, conditions of use, and time. Thus when technician is testing devices, it has to be done by respecting all the relevant parameters necessary for testing and calibration. Testing has to be done for most of the spirometers within an approval interval of 24 months (MDD 92/42/EEC).

Risk Management and Clinical Evaluation – Directives and Norms: For manufacturers of spirometers and there is required a product Technical File Documentation including all the documents for Risk Management (EN 14971:2019) and the Clinical Evaluation routine in accordance to the directives of the MDR (EU) 2017/745. The terms accuracy, repeatability and reproducibility are very important and represent the relevancy towards bringing these product related documents in conformity with the Medical Device Regulation MDR (EU) 2017/745 and the harmonized European Norms (EN) and norms of the International Standard Organization (ISO). It must noted, that diagnostic spirometers are classified as Class IIa devices as amended by the directives of MDR (EU) 2017/745 Article 51, Annex VII and the guidelines of MDCG 2019-11 for classification of medical devices.

As result of this classification and the harmonized norm EN ISO 13485 including the Annex directives the Notified Bodies (NBs) do have to check and approve the Technical Documentation Files of the medical products in accordance to the MDR (EU) 2017/745. The successful approval is documented by the Technical Documentation approval report issued by the NB. In accordance, the manufacturer is then authorized to issue the EC Declaration of Conformity. The medical product is labelled with the CE mark showing the Notified Bodies Code-No. CEXXXX (a CE Mark with four digits).

Description of Spirometry Measurement Method of the PRO SPIRO N PC based Spirometer:

Different manufacturers are using different methods for measuring the lung function testing results. Most methods measure the volume indirectly: The volume is calculated from the measured flow.

One of the most reliable methods for measurement of the respiratory functions is:

- **The PinkFlow* flow-meter** is the newest innovation of the PC-based spirometer of our partner company. The PinkFlow* flow-meter is the ideal flow-meter for the most demanding pulmonary function tests: Hygienic single-use application - No moving parts - Insensitive against condensation and vapour -Integrated gas sampling port - Fully interchangeable flow-meters -No need for recalibration after changing -Quick pneumatic coupling Fully recyclable made from homogenous polystyrene. The PinkFlow* flow-meter fully complies with the specifications and requirements of the Standardization of Lung Function Testing ATS/ERS Task force (European Respiratory Journal)

Features and benefits of the PRO SPIRO N PC-Spirometer:

- Sleek design ergonomic form and just one USB connection to the PC
- The PRO SPIRO N version has built-in ambient temperature, pressure and humidity sensors for the full automatic BTPS correction
- The spirometer is the basic device of the functional lung diagnostics It is inevitable in detecting the early malfunction of the respiratory system:
- COPD
- Asthma
- Chronic bronchitis
- Obstructive ventilation disorder
- Emphysema
- The PINK FLOW flow-meter and the spirometer fully complies with the specifications and requirements of the Standardization of Lung Function Testing ATS/ERS Task force (European Respiratory Journal)
- Connecting to a laptop or PC the system provides full portability in battery mode as well

**Picture of PRO SPIRO N PC based USB Spirometer
with PINK FLOW sensor and bacterial- / viral filter**

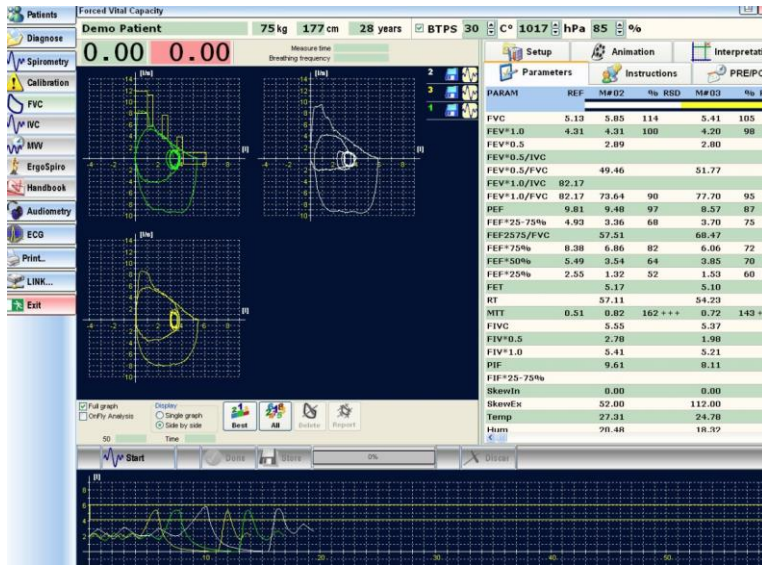


Flow meter..... PPF-18 PinkFlow
Flow measurement range ± 18 l/s
Flow measurement accuracy..... $\pm 2\%$ or ± 10 ml/s
Flow measurement resolution 10 ml/s
Linearity $\pm 2\%$
Volume measurement range..... ± 20 l
Volume measurement accuracy..... $\pm 2\%$ or ± 10 ml
Volume measurement resolution 10 ml

**Picture of calibration pump PCS-3000
(recommended for most accurate calibration)**



Pictures of screen: Lung function treatment results



FVC measurement



IVC measurement



MVV measurement

Whole list of PRO SPIRO N Pulmonary Function Tests' parameters:

<u>Forced ex and inspiration:</u>	
FVC	Forced Vital Capacity
FEV*0.5	Forced Expiratory Volume in 0.5 second
FEV*1.0	Forced Expiratory Volume in 1.0 second
FEV*0.5/IVC	Ration of FEV*0.5 and IVC in %
FEV*0.5/FVC	Ration of FEV*0.5 and FVC in %
FEV*1.0/IVC	Ration of FEV*1.0 and IVC in %
FEV*1.0/FVC	Ration of FEV*1.0 and FVC in %
PEF	Peak Expiratory Flow
FEF*25-75%	Forced mid-Expiratory Flow rate
FEF*75%	Forced Expiratory Flow at 75% lung volume
FEF*50%	Forced Expiratory Flow at 50% lung volume
FEF*25%	Forced Expiratory Flow at 25% lung volume
FET	Forced Expiratory Time
MTT	Mean Transit Time
FIVC	Forced Inspiratory Vital Capacity
FIV*0.5	Forced Inspiratory Volume in 0.5 sec
FIV*1.0	Forced Inspiratory Volume in 1.0 sec
PIF	Peak Inspiratory Flow rate
FIF*25-75%	Forced mid-Inspiratory Flow rate
<u>Static vital capacity</u>	
IVC	Inspiratory Vital Capacity
IRV	Inspiratory Reserve Volume
ERV	Expiratory Reserve Volume
TV	Tidal Volume
SVC	Slow Vital Capacity
<u>Maximal Voluntary Ventilation</u>	
MVV	Maximal Voluntary Ventilation
MVV*f	Maximal Voluntary Ventilation Frequency

Measurement of Respiratory Flow is an accurate and reproducible method, however attention has to be taken care about hygienic directives: Beside easy operation of this spirometer all the advantages as fast detection and recording of patient data it has to be taken care about the hygienic way of operating spirometers for to guarantee to avoid cross contaminations.

Hygienic operation methods during lung function testing: Weekly at least 1 billion microorganisms can be detected in a dry closed spirometer system after having done 100 measurements. **The most characteristics ones are:**

Acinetobacter calcoaceticus (var Anitratus), Acinetobacter calcoaceticus (var Lwoffii)
Achromobacter xylosoxidans, Alkaligenes denitrificans, Alkaligenes spp,
Citrobacter freundii, Aerobic spore bearing bacillus, Coliform Gram negative bacilli
Enterobacter agglomerrans, Flavobacterium spp, Klebsiella pneumoniae
Pseudomonas fluorescens, Pseudomonas spp, Staphylococcus aureus
Staphylococcus albus, Streptococcus spp (haemolytic), Xanthomonas spp,

Penicillium spp

Using Bacterial and Viral filter prevents cross-contamination and is therefore recommended when doing lung function tests!



Picture of Bacterial and Viral Filter with integrated elliptic mouthpiece



The bacterial and viral filtration efficiency of the recommended bacterial and viral filters type is validated.

Picture of Nose Clip



Using a nose clip guarantees an optimal routine of breathing by the patient!

Breathing routine during lung function testing: As the patient will do several different breathing tests the routine of these tests will be different, too. The physician does have to explain the routine before each test. A good effort during the lung function test will assure good results. A proper explanation of the breathing routine before the real test is a security for a successful test as evidence of correct analysis and diagnosis.

Considerations concerning contraindications of spirometry: Doing spirometry examinations can be a physical provocation for some few patients. Within one month after a myocardial infarct the recommendation is not to test the patient. Additionally, it must be taken care about the guidelines of contraindications for lung function tests which are described in several abstracts. The expert opinion from more than 25 years ago are that high risk contraindications are, as mentioned before, associated with cardiovascular problems as myocardial infarct, pulmonary embolism or ascending aortic aneurysm. Some less risk but still remarkable contraindications are prevalent focused on recovery from abdominal or head or major thoracic surgery. Of course, even less grave surgeries might represent a potential risk. The physician must to distinguish between the sincerity of the surgery as it may be at risk of complication from testing. In general, the previous recommendation of waiting for six weeks after having

surgical procedures or medical complications before performing lung function can often now be reduced to less than 3 weeks with less invasive surgical techniques.

Final comments, statements and conclusion:

Empirical Value:

Since many years we evaluated a lot of sales of the PRO SPIRO PC based spirometers. These devices have been sold in Germany, Austria, Switzerland and internationally, too. We filed the very low rate of reclamations, the device measurement accuracy, the device performance concerning patient compliance and detection of Customer Satisfaction by doing additional filing of Post Market Surveillance (PMS), Post Marketing Clinical Follow Up (PMCF), Clinical Assessments and Clinical Evaluation Reports.

Conclusion:

Spirometry is essentially important in the diagnosis and follow-up of asthma and other respiratory diseases like mentioned before. Considering the importance of respiratory diseases on public healthcare and the economy, clear is that spirometry deserves a lot more attention as it is a very simple and inexpensive test. Lung function testing is highly recommended to be a basic examination in general medicine for to avoid subsequent follow-up expenses based by a not being provided efficient and meaningful diagnostic screening test.

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www.mesamed.de

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