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# Incomplete Forced Expiration – Estimating Vital Capacity by a Mathematical Method

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**Key Words**
Lung function · Multi-exponential modelling · Spirometry · Vital capacity

**Abstract**
***Background:*** Vital capacity is a key parameter in the determination of lung function, usually assessed by means of a forced expiration maneuver. This maneuver can be exhausting, and patients often cannot complete it. ***Objectives:*** This study evaluates a method to estimate forced vital capacity (FVC) based on the extrapolation of volume-time curves from forced expiration. ***Methods:*** The algorithm was applied to 2,363 volume-time curves from patients with and without respiratory disease. 416 of these spirograms originated from incomplete maneuvers. For each spirogram, estimated ($FVC_{est}$) and measured FVC were compared with inspiratory vital capacity. ***Results:*** Reliable $FVC_{est}$ were obtained for 82% of all and for 76% of the incomplete maneuvers. Regardless of the category of respiratory disease and acceptability of forced expiration, $FVC_{est}$ were close to inspiratory vital capacities. ***Conclusions:*** When assessing the lung function of patients who cannot complete forced expiration, this method could help to reduce the duration of maneuvers required to provide a reliable estimate for vital capacity.



## Introduction

Spirometry is one of the most widely applied clinical tests in respiratory medicine to diagnose obstructive and to rule out restrictive pulmonary diseases. A key parameter of spirometric lung function tests is vital capacity, usually assessed by measuring forced vital capacity (FVC). This requires a forced expiration maneuver leading to nearly complete emptying of the lungs, an effort that may be exhausting or even impossible to perform for elderly subjects or patients with severely impaired lung function, in particular for individuals suffering from a severe obstructive pulmonary disease. Inspiratory vital capacity (IVC) can be measured more easily in many of these subjects; however, assessment of IVC requires an additional maneuver and is often not measured because of a suspected risk of infection.

These difficulties have led to new approaches aiming at the identification of alternative measures of vital capacity that can also be obtained from incomplete forced expiration maneuvers. Swanney et al. [1] concluded that the forced expiratory volume in 6 s ($FEV_6$) proposed by the National Lung Health Education Program [2] represents an acceptable surrogate for FVC, using the reference values presented by Hankinson et al. [3]. This approach requires 6 s of forced expiration, not necessarily an expiratory plateau as demanded by the American Thoracic

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Society in 1995 [4]. Jensen and Crapo [5] have developed a linear model to predict $FEV_6$ from a weighted sum of $FEV_3$, $FEV_{3.5}$, and $FEV_4$. Following a different approach, Desmond et al. [6] used mono- and bi-exponential functions to extrapolate volume-time curves in order to develop new end-of-test criteria for spirometry in children.

Recently, we have developed a method for automatic analysis of volume-time curves obtained by forced expiration [7]. The procedure uses all the available volume-time data, regardless of expiratory time, and provides an estimate for FVC ($FVC_{est}$) together with a corresponding uncertainty ($\sigma_{est}$) that indicates the reliability of the estimate. The expiratory time needed to provide a reliable $FVC_{est}$ depends on the appearance of a specific volume-time curve. Usually, more than 2 s are required to obtain $\sigma_{est}$ of less than 0.1 liters.

The aim of this study is to evaluate the performance of this method by applying it to a large number of clinically obtained spirometric data sets from patients without and with different underlying respiratory diseases.

## Methods

*Data Selection*

Anonymously spirometric data sets were selected, following the alphabetical order of the patients' identification, from the database of the Department of Pneumology at the University Hospital of Freiburg. The database contained data from all tests performed in the Lung Function Laboratory between August 1990 and October 2000. All data originated from routine medical examinations in the Lung Function Laboratory. Since no supplementary tests were performed, and individuals were not identified, approval by the Ethics Review Board and informed consent were not required.

Spirometric data were recorded using the Jaeger Masterlab (Jaeger, Hoechberg, Germany). The device incorporates a heated pneumotachograph and includes software correction to BTPS. The calibration of the device is routinely checked for inspiratory versus expiratory flow accuracy once daily. Each data set contained at least three measurements of IVC and volume-time curves from subsequent forced expiration maneuvers, total lung capacity, and maximum expiratory airway resistance ($R_{aw}$) derived from a plethysmographic measurement. IVC was carried out before the forced exhalation in all measurements.

Spirograms were selected and classified according to the criteria described in the following. For each data set, only the spirogram that resulted in the largest expiratory volume was analyzed, representing the best available maneuver following the acceptability guidelines for FVC measurements published by the American Thoracic Society in 1995 [4], except for the criteria concerning exhalation time (forced expiration time, FET: the time from the back-extrapolated 'time zero' until FVC is exhaled, expressed in seconds) and end-of-test criteria.

Spirograms were rejected if at least one of the following conditions was observed: (1) an unsatisfactory start of expiration, characterized by excessive hesitation, false start, or back-extrapolated volume >5% of the total expiratory volume or 0.15 liters, whichever was greater; (2) any discernible cough or varying effort during the maneuver, or (3) leakage or an obstructed mouthpiece.

The remaining spirograms were visually classified into three categories: *acceptable, short* or *incomplete.* For acceptable spirograms, the exhalation time was at least 6 s, and an end-expiratory plateau in the volume-time curve was observed, defined as no change in volume for at least 1 s. Short spirograms did not meet the above criterion for acceptable maneuvers but otherwise resembled a completed forced expiration smoothly arriving at the final exhaled volume. The maneuver was abruptly terminated in incomplete spirograms.

Following the recommendations of the American Thoracic Society from 1991 [8] and the European Respiratory Society from 1993 [9], measured lung function values were compared with limits of normal from reference equations based on a cross-sectional study of the local population [10]; each spirogram was classified into one of two categories with respect to the kind of respiratory disease, depending on the presence or absence of an obstructive component: (i) *mixed or obstructive* (decreased $FEV_1$/IVC or increased $R_{aw}$) and (ii) *normal or restrictive* (normal $FEV_1$/IVC and normal $R_{aw}$).

*Mathematical Analysis*

The selected spirograms were subjected to a recently developed algorithm that provides an $FVC_{est}$ together with a $\sigma_{est}$. The method is described in more detail in the Appendix. Briefly, it is based on bi- or tri-exponential extrapolation of a volume-time curve. For a given spirogram, extrapolation relies on all data with volumes smaller than the final expired volume ($FEV_{end}$), i.e. a possible end-expiratory plateau is not used. Moreover, data from the beginning of the maneuver are automatically ignored if a late or slow start of expiration is detected.

The magnitude of the $\sigma_{est}$ of $FVC_{est}$ decreases with increasing duration of the spirogram. The value of $\sigma_{est}$ for a given volume-time curve mainly depends on this duration in proportion to the time constants of the respective bi- or tri-exponential fitting function. Since the values of time constants may be considerably different for different spirograms, the duration necessary for a reliable $FVC_{est}$ varies from patient to patient. In a previous study [7], we truncated complete spirograms at different times and found that $FVC_{est}$ was most often close to the FVC measured if $\sigma_{est}$ was less than 0.1 liters. On the other hand, uncertainties of less than 0.1 liters were rarely achieved for spirograms shorter than 2 s. Therefore, $FVC_{est}$ was judged unreliable if less than 2 s of spirometric data were available or if $\sigma_{est}$ of $FVC_{est}$ was greater than 0.1 liters, corresponding to a confidence interval $FVC_{est} \pm \sigma_{est}$ of a width of more than 0.2 liters.

Figure 1 schematically shows the volume tracings of spirometric maneuvers as well as the different pulmonary gas volumes that were either measured or estimated by mathematical analysis.

For each acceptable volume-time curve, $FVC_{est}$ was compared with IVC on the one hand and with the FVC measured on the other hand. In the case of short or incomplete spirograms where FVC was not available, $FEV_{end}$ was considered instead of FVC.

*Statistics*

The SAS software package (version 8.2) was used for statistical analysis. For each group and category, t tests were applied to evaluate whether the volume differences $FVC_{est}$ – FVC, IVC – FVC or $FVC_{est}$ – IVC (FVC being replaced by $FEV_{end}$ for incomplete and short spirograms) were significantly different either from 0 or smaller than IVC – FVC for acceptable spirograms from normal subjects or

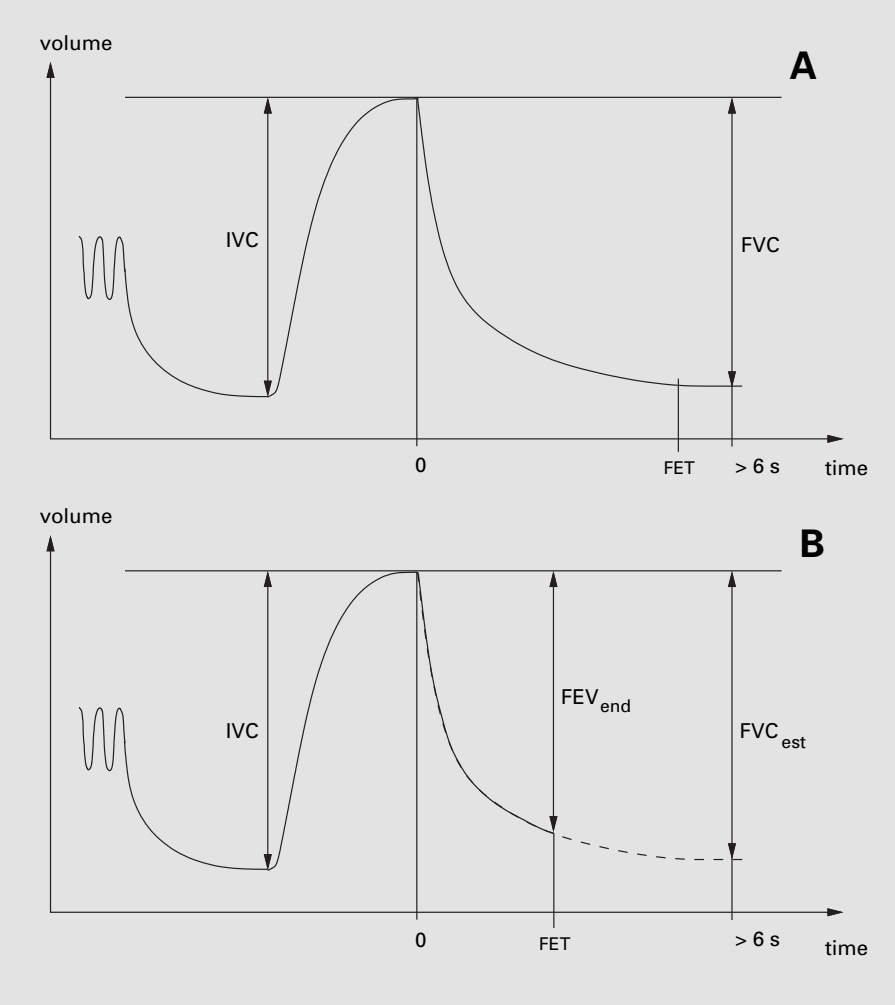


**Fig. 1.** Schematic volume-time tracings illustrating the respiratory maneuvers. Following normal breathing, the IVC maneuver starts with a deep expiration and a subsequent deep inspiration. The volume decrease following the inspiratory plateau reflects the forced expiration maneuver that is completed after 6 s (**A**). In the case of an incomplete maneuver (**B**), the spirogram is mathematically extrapolated (dashed line). The following pulmonary gas volumes and time points are determined: IVC and FVC (measured on the basis of complete spirograms, **A**); $FEV_{end}$ (short or incomplete spirograms, **B**); $FVC_{est}$ (estimated using the mathematical method), and FET.

patients with purely restrictive lung disease; adjustment for multiple comparisons was performed using Dunnett's method [11].

Finally, FET, i.e. the time from the start of forced expiration when $FEV_{end}$ was reached, was evaluated for all incomplete maneuvers.

## Results

The numbers of spirograms investigated in the different groups are given in table 1. From a total of 2,363 spirograms, values of $FVC_{est}$ with low uncertainties ($\sigma_{est}$ <0.1 liters) were obtained for 82% of volume-time curves with expiratory times greater than 2 s. The percentage of spirograms leading to elevated uncertainties is higher in the groups of incomplete and short volume-time curves than in the group of acceptable maneuvers.

A comparison of the different measures of vital capacity for the spirograms analyzed is depicted in figure 2. Means, standard deviations, medians and 95% quantiles of $FVC_{est}$ – FVC, IVC – FVC and $FVC_{est}$ – IVC are shown for the group of acceptable spirograms. For short and incomplete volume-time curves, $FVC_{est}$ – $FEV_{end}$, IVC – $FEV_{end}$ and $FVC_{est}$ – IVC are displayed. In each group of spirograms, the respective volumes originating from subjects with and without an obstructive component are presented separately.

All volume differences except for $FVC_{est}$ – IVC in the group of incomplete spirograms from non-obstructive subjects and in both groups of short spirograms were significantly different from 0 ($p < 0.0001$). On the other hand, comparing the volume differences with IVC – FVC for acceptable spirograms from non-obstructed individuals, $FVC_{est}$ – IVC was significantly closer to 0 for all

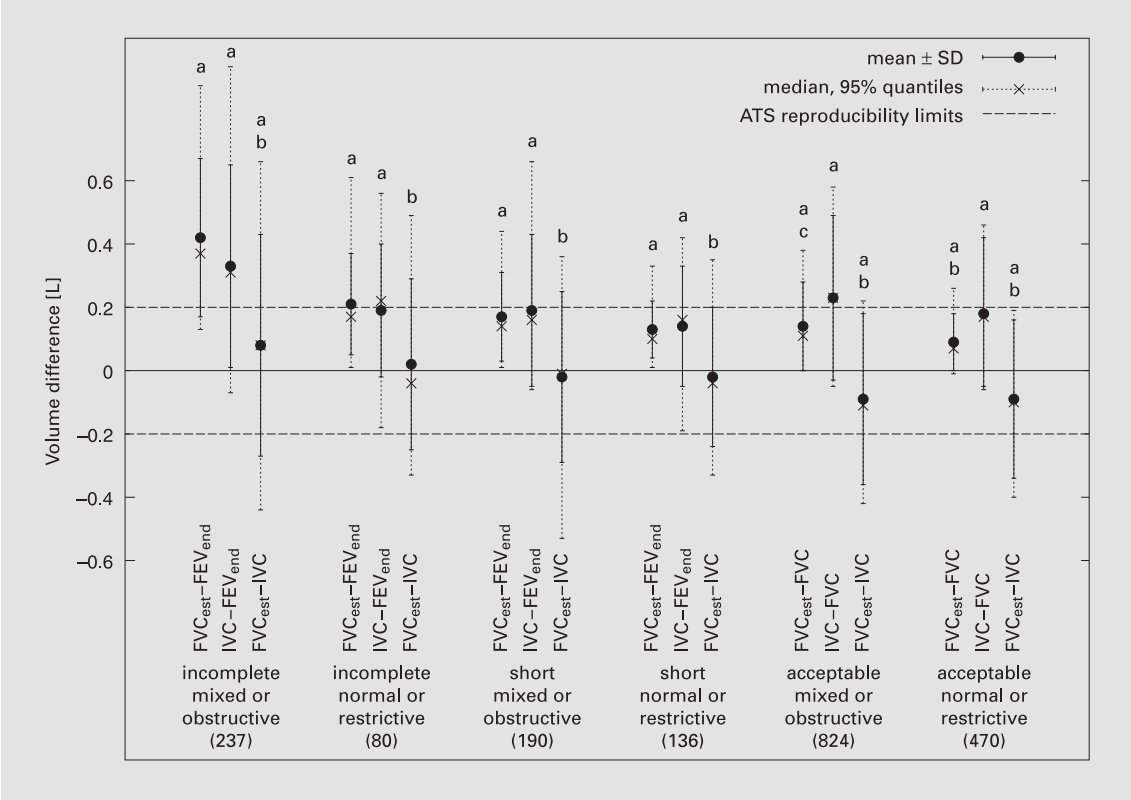


**Fig. 2.** Comparison of the different measurements of vital capacity: $FVC_{est}$, $FEV_{end}$ (for incomplete and short spirograms), FVC (for acceptable maneuvers), and IVC. Means, standard deviations, medians and 95% quantiles of the respective differences are displayed; the numbers of volume-time curves in the respective groups are indicated in parentheses; [a] $p < 0.0001$ vs. 0; [b] $p < 0.0001$ and [c] $p < 0.05$, vs. acceptable spirograms from normal subjects and patients with purely restrictive pulmonary disease, respectively. ATS = American Thoracic Society.

groups ($p < 0.0001$). The same is observed for $FVC_{est}$ – FVC in the group of acceptable spirograms from patients with mixed or obstructive pulmonary disease ($p < 0.05$) and from normal subjects or patients with restrictive pulmonary disease ($p < 0.0001$).

Generally, differences between $FVC_{est}$ and FVC or $FEV_{end}$ are most often larger than discrepancies between $FVC_{est}$ and IVC. For all groups and categories, $FVC_{est}$ is on average within 0.2 liters of IVC. Moreover, IVC is on average higher than FVC or $FEV_{end}$ for all groups. A considerable variability in the differences between FVC and IVC is observed, even for patients with restrictive lung disease and normal subjects who visually seemed to have achieved a complete forced expiration.

Our data confirm the finding that the difference between IVC and FVC is usually larger for patients with an obstructive component than for normal subjects or patients suffering from a restrictive respiratory disease, even if the forced expiration maneuver appears to be complete.

For *acceptable spirograms*, $FVC_{est}$ most often lies between FVC and IVC. $FVC_{est}$ and FVC are closer for normal subjects and patients with restrictive pulmonary disease than for patients with an obstructive component. The same observations are made for *short spirograms*. $FVC_{est}$ and IVC are even slightly closer than for acceptable volume-time curves. The same holds for IVC and $FEV_{end}$.

The highest differences between $FVC_{est}$ and $FEV_{end}$ as well as between IVC and $FEV_{end}$ are observed for *incomplete spirograms*. Like in the other groups, these differences are larger for patients with an obstructive or mixed pulmonary disease than for normal subjects or patients with restrictive lung disease. On the other hand, incom-

**Table 1.** Demographic data and partition of investigated volume-time curves into different categories with respect to measurement acceptability and respiratory disease

| Spirogram category | Respiratory disease | $\sigma_{est} < 0.1$ liters M/F (total) | Age, years (mean ± SD) M/F | $\sigma_{est} \geq 0.1$ liters M/F (total) | Age, years (mean ± SD) M/F |
|---|---|---|---|---|---|
| Incomplete | Normal or restrictive | 68/12 (80) | 42.4 ± 14.8/38.9 ± 15.7 | 16/9 (25) | 41.9 ± 12.7/37.3 ± 15.5 |
| | Mixed or obstructive | 197/40 (237) | 58.4 ± 15.7/37.1 ± 15.5 | 54/20 (74) | 59.0 ± 14.0/49.0 ± 14.8 |
| Short | Normal or restrictive | 105/31 (136) | 42.8 ± 15.3/44.6 ± 13.3 | 30/34 (68) | 43.0 ± 14.3/39.6 ± 13.8 |
| | Mixed or obstructive | 107/83 (190) | 52.4 ± 17.6/45.2 ± 18.2 | 30/51 (81) | 52.0 ± 17.6/45.0 ± 15.0 |
| Acceptable | Normal or restrictive | 354/116 (470) | 48.8 ± 14.1/46.9 ± 14.3 | 36/26 (62) | 38.8 ± 14.3/42.7 ± 16.2 |
| | Mixed or obstructive | 466/358 (824) | 58.0 ± 14.6/53.1 ± 16.3 | 56/64 (120) | 56.5 ± 14.4/48.1 ± 19.1 |

plete spirograms from patients with an obstructive component represent the only category where $FVC_{est}$ is on average slightly larger than IVC.

Overall, $FVC_{est}$ and IVC in each single group are closer than FVC and IVC for acceptable spirograms from normal subjects or patients with restrictive lung disease.

The results of the analysis of FET for incomplete maneuvers are summarized in table 2. For all subcategories, FET was on average less than 6 s, and $FEV_6$ was available in only 23.3% of incomplete spirograms. On the other hand, reliable $FVC_{est}$ were provided for 77.9% of these abruptly terminated maneuvers.

**Table 2.** Partition of FET for incomplete maneuvers

| Patient category | Total | $\sigma_{est}$ < 0.1 liters | FET ≥ 6 s | FET, s average | SD |
|---|---|---|---|---|---|
| Normal | 83 | 67 | 1 | 3.50 | 1.09 |
| Restrictive | 22 | 16 | 0 | 2.81 | 0.57 |
| Mixed | 37 | 26 | 4 | 3.93 | 2.10 |
| Obstructive | 274 | 215 | 92 | 5.47 | 2.20 |

## Discussion

In this study, we estimated vital capacity from volume-time curves obtained during forced expiration maneuvers using a recently developed method based on bi- or tri-exponential functions. The algorithm has been implemented on a standard PC; computation time was typically of the order of 3 s. As a main result, we found that the method provides reliable estimates for vital capacity in the majority of cases when the forced expiration lasts longer than 2 s.

In particular, regardless of the category of spirograms or of underlying pulmonary disease, deviations in $FVC_{est}$ from IVC are on average less pronounced than differences between FVC and IVC measurements for acceptable spirograms from individuals without obstructive pulmonary disease. This is especially surprising because we would have expected IVC and FVC in this group to produce the smallest differences of all measures for vital capacity and all groups of spirograms, in particular in the light of the finding of Baur et al. [12] that IVC and FVC values are not significantly different in healthy subjects. However, it cannot be excluded that a volume-time curve visually appeared to be acceptable although the cooperation decreased at the end of a forced expiration maneuver. This would have resulted in an underestimation of FVC and, as a consequence, of $FVC_{est}$, too.

A decrease in cooperation at the end of a forced expiration maneuver could also explain the fact that acceptable spirograms from normal subjects and from patients with restrictive pulmonary disease led to smaller differences between $FVC_{est}$ and FVC than acceptable volume-time curves from patients with an obstructive component in their pulmonary disease. It could be speculated that the decrease in effort is more pronounced in obstructive patients.

It could also be supposed that individuals who are able to complete their forced expiration within less than 6 s are less prone to a decrease in effort at the end of the maneuver. This would explain the lower differences between the different measurements for vital capacity in the case of short spirograms.

As a conjectural explanation for the finding that $FVC_{est}$ is on average slightly higher than IVC for incomplete spi-

rograms originating from patients with an obstructive component, it could be suspected that patients with a severe airway obstruction who cannot complete a forced expiration maneuver might also have difficulties to accomplish the slow expiration preceding the measurement of IVC, which would lead to underestimation of IVC. In cases of severe obstruction and relatively short FET, the application of our method to the truncated spirogram might result in a slight overestimation of vital capacity by $FVC_{est}$, due to the increased spreading of time constants of different pulmonary compartments [13]. However, the requirement that $\sigma_{est} < 0.1$ liters, explicitly introduced to avoid overfitting, was found to be a reliable cutoff criterion [7], so that we expect this situation to be extremely rare.

Summarizing our results, we hypothesize that IVC, $FVC_{est}$ and FVC basically reflect the same physiological variable and that underestimation of vital capacity by measurement of FVC is mainly caused by the inability of an individual to perform a complete forced expiration maneuver with optimal effort. Possible reasons for incomplete forced expiration are long time constants in obstructive diseases and premature glottic closure, for example. On the other hand, $FVC_{est}$ obtained by patient-specific data-driven multi-exponential extrapolation of forced expiratory spirograms provides estimates of vital capacity that are consistent with IVC.

All aspects considered, we conclude that the method yields trustworthy estimates for vital capacity even when it is applied to volume-time curves from forced expiration maneuvers abruptly terminated at an early stage, i.e. between 2 and 6 s after the start of the maneuver. In clinical practice, this method could simplify forced expiration without considerable loss of information. However, it might not be desirable to shorten the duration of acceptable forced expiration maneuvers to less than 6 s by default. On the other hand, when assessing the lung function of patients who cannot easily achieve an end-expiratory plateau, the algorithm could help to obtain reliable estimates of vital capacity while reducing the required duration or the necessary number of maneuvers.

We expect the model-based Tiffeneau index $FEV_1/FVC_{est}$ to improve the diagnostic impact of forced expiration in patients with airflow obstruction. Furthermore, taking into account the conclusions drawn by Permutt and Menkes [13] on the sensitivity of $FEV_3/FVC$ to changes in small airway function associated with smoking, the usefulness of $FEV_3/FVC_{est}$ as an indicator of early manifestations of chronic obstructive pulmonary disease could also be investigated.


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## Appendix

*Algorithm for Multi-Exponential Analysis of Spirograms*

Negative volumes representing expiration by convention, multi-exponential functions of the equation:

$$\hat{V}_M(t) = -FVC_{est}(M) + \sum_{j=1}^{M} A_j e^{-\mu_j t},\ M = 2 \text{ or } 3 \qquad (1)$$

with positive constants $A_1, \ldots A_M$ and $\mu_1, \ldots \mu_M$ are used to model the expiratory volume $V(t)$. Let $[V(t_i),\ i = 1, \ldots N]$ be a time series of volume measurements and $\sigma$ the standard deviation of the measurement error. The Levenberg-Marquardt method is applied to find the set of $(2M + 1)$ parameters $[FVC_{est}(M), A_1, \ldots A_M, \mu_1, \ldots \mu_M]$ that minimizes the quantity

$$\chi^2(M) = \sum_{i=1}^{N} \left[ \frac{V(t_i) - \hat{V}_M(t_i)}{\sigma} \right]^2,$$

first for $M = 2$, then for $M = 3$. The magnitude of $\chi^2(M)$ reflects how close the bi- or tri-exponential model is to the measured data.

After completion, the Levenberg-Marquardt method also provides the estimated covariance matrix $Cov(M)$ of the corresponding parameters. The covariance matrix is transformed into the correlation matrix $Corr(M)$ by normalization:

$$Corr(M)_{ij} = \frac{Cov(M)_{ij}}{\sqrt{Cov(M)_{ii}\, Cov(M)_{jj}}}.$$

The ratio of the highest and the lowest eigenvalue of $Corr(M)$, the condition number $c(M)$, reveals the adequacy of the model used in the fitting procedure. If all parameters are identifiable, $c(M)$ should be close to one, whereas high values of $c(M)$ indicate overfitting.

The optimum number of exponentials for a given spirogram is chosen as $M = 2$ or $M = 3$, depending on which one yields the lower value of $\chi^2 c/[N - (2M + 1)]$. Vital capacity is then estimated by $FVC_{est} = FVC_{est}(M)$ from equation 1. $\sigma_{est}$ of $FVC_{est}$ is obtained from the corresponding component of the covariance matrix. A detailed description of the procedure has been given previously [7].

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