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Spirometry Measurement Model – the Diagnostic Purpose Support

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The paper presents a new model of respiratory mechanism based on the spirometry measurements. The spirometry test assesses efficiency of the lung ventilation. The respiratory system functioning is based on the ventilation mechanism. Thus the quality of the lung depends on the quality of lung ventilation. Respiratory system modelling supports a diagnostic process. The model parameter estimates are obtained on the basis of the spirometry test results. The model parameters enable us to obtain the new information concerning breathing conditions. These parameters make it also possible to distinguish between healthy and diseased subjects. The spirometry measurement model presents itself as a new diagnostically helpful aid.

Keywords: respiratory mechanism, spirometry, modelling

1. Introduction

The process of tissue oxygen supply is a fundamental process of the human life. The quality of the pulmonary ventilation has a strong influence on a patient's health condition. Numerous limitations are imposed on the conditions of the lung quality measurement; the most common concerns the anatomic shape of the respiratory system. Advanced mathematical modelling and identification methods seem to be necessary for improving the diagnostic purposes. The modelling results improve the investigation of respiratory mechanism and therapy process. The aim of this paper is to present a new spirometry measurement model and the usability of its parameter estimates for diagnostic purposes.

Lung functioning consists of three processes: the ventilation, the perfusion and the diffusion. The pulmonary ventilation, the alveolar perfusion with blood and the

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alveolar-capillary membrane diffusion are responsible for the red blood cells oxygenation and carbon dioxide elimination. The paper deals with one of these processes, the ventilation process. The spirometry test is common method of the respiratory system measurement. It assesses the efficiency of the pulmonary ventilation. Interpretation of the spirometry results uses the reference values of the respiration parameters, which were obtained for a representative healthy population. Modelling of the respiratory system helps us to acquire better knowledge and understand the system; therefore it may be helpful in a diagnostic process as well. An additional important piece of information can be required when the modelling results are applied to the choice of an appropriate treatment.

The most popular is the dynamic spirometry, which allows us to measure volume $V(t)$ and airflow $Q(t)$ during the inhalation and the exhalation [1]. The volume and the airflow are measured with a pneumotachometer. The measured quantity is the airflow $Q(t)$, which is given in $[l \cdot s^{-1}]$. The relation between the airflow $Q(t)$ and the air volume $V(t)$ is [2, 3, 4]:

$$V(t) = \int Q(t)\,dt. \tag{1}$$

The volume $V(t)$ is obtained by electronic integration of the airflow $Q(t)$.

The changes of the volume $V(t)$ during the spirometry test are presented in Fig. 1. The spirometry test demands some specific respiratory manoeuvres of the patient. The examination of the ventilation mechanism is preceded by the time periods of quiet breathing-in and breathing-out. Then the patient expires to the maximal breath-out. Next, the rapid inspiration to the maximal breath-in comes before the forced exhalation to the maximal breath-out. During the test, a nose clip is used to prevent air from escaping through the nose. The most important parts of the spirometry test are the maximal breath-in and forced maximal breath-out manoeuvres.

The respiration parameters are calculated on basis of the volume-time curve $V(t)$ [5] shown in Fig. 1:

VC [l] (vital capacity) is the maximum volume of air that can be exhaled or inspired during either a forced (FVC) or a slow (VC) manoeuvre,

TV [l] (tidal volume) is the volume of air moved during either the inspiratory or expiratory phase of each breath,

FEV_1 [l] is the forced expiratory volume during the first second of expiration,

$TPEF$ [s] is the peak expiratory flow time,

FET [s] is the forced expiratory time,

FIT [s] is the forced inspiratory time.

The dynamic spirometer produces a graph named *the flow-volume curves* $Q(t)$ (see Fig. 2). It depicts graphically the airflow compared to the total volume of the inspired air or expired air. The additional respiration parameters are defined on basis of flow-volume curves [5]:

PIF [$l \cdot s^{-1}$] (peak inspiratory flow) is the maximal inspiratory flow rate achieved in the forced inspiratory manoeuvre,

PEF [$l \cdot s^{-1}$] (peak expiratory flow) is the maximal expiratory flow rate achieved and this occurs very early in the forced expiratory manoeuvre,

FVC [*l*] (forced vital capacity) is the maximum volume of air that can be exhaled or inhaled during the forced manoeuvre.

The spirometry results are given in both the raw data and the percentage of reference values, which are standardized. The reference values depend on anthropometric data of the subject such as age, height and gender. The European Respiratory Society

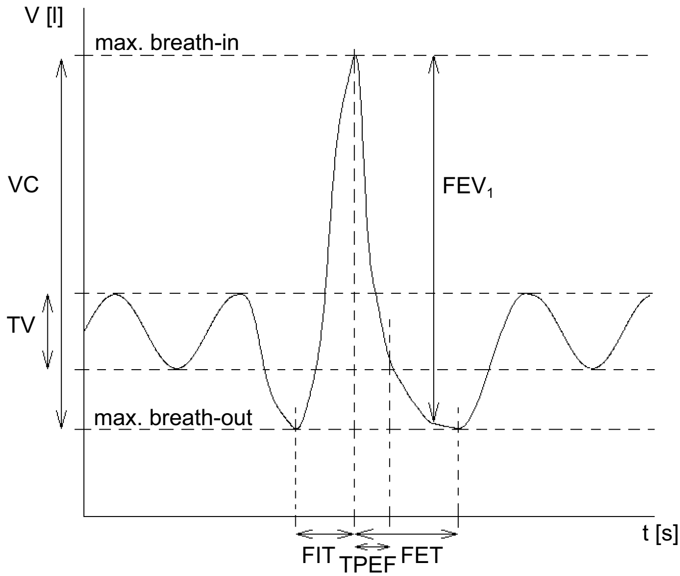

Fig. 1. The volume–time curve *V*(*t*) during quiet breathing, maximal breath-out and maximal breath-in

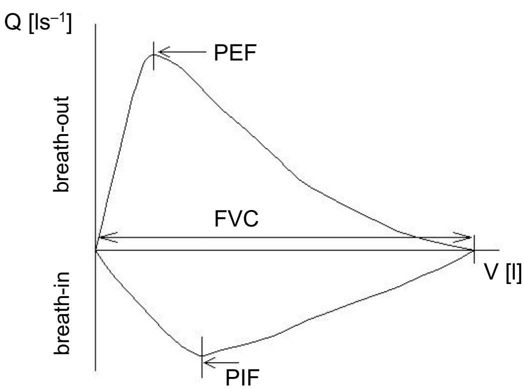

Fig. 2. The result of spirometry tests: the flow-volume curves *Q*(*V*)

published the norms, which are generally used during spirometry test [6]. The Polish Spirometry Recommendations are based on the European ones [7].

Let us concentrate on three respiratory parameters (y_j, j = 1,2,3): *FVC, FEV_1* and *PEF.* The reference value of the particular parameter y_j, j = 1,2,3 for a patient of age $A[years]$ and height $H[meters]$ is obtained in the following way [6, 7]:

$$\begin{aligned} y_j &= R_1^j \cdot H + R_2^j \cdot A + R_3^j, j = 1,2,3, \\ y_1 &= FVC, y_2 = FEV_1, y_3 = PEF. \end{aligned} \tag{2}$$

The norms provide the values of the coefficients R_1^j, R_2^j, R_3^j for each parameter. The coefficients for *FVC, FEV_1* and *PEF*, published by the European Respiratory Society [6, 7], are presented in Table 1. According to the norms, the age range is from 25 to 70 years and the height range is from 1.55 to 1.95 meters (for men) and from 1.45 to 1.80 meters (for women). The same range of age and height is considered in the paper. The respiratory parameters demonstrate stronger dependence on the height (large absolute value of R_1^j) than on the age (small absolute value of R_2^j).

The individual spirometry results vary depending on condition of the ventilation mechanism. In general, the results close to 100% of the nominal values are interpreted as normal. The results that differ 20% and more from the nominal value are considered abnormal [8].

Table 1. The coefficients R_1^j, R_2^j, R_3^j of the reference equation (2) for the respiratory parameters *FVC, FEV_1* and *PEF* according to the European Respiratory Society [6, 7]

Coefficients	R_1^j	R_2^j	R_3^j
	For men		
$FVC, j = 1$	5.760	−0.026	−4.340
$FEV_1, j = 2$	4.300	−0.029	−2.490
$PEF, j = 3$	6.140	−0.043	0.150
	For women		
$FVC, j = 1$	4.430	−0.026	−3.280
$FEV_1, j = 2$	3.950	−0.025	−2.600
$PEF, j = 3$	5.500	−0.030	−1.110

2. Spirometry Model

The spirometry lung functioning test is based on the flow measurement. The breath-in flow is different from the breath-out flow. The airflow depends both on the respiratory system condition and the respiratory manoeuvre. The essence of respiratory manoeuvre during the spirometry test is the maximal expiration and the maximal inspiration. The flow-time curves are the spirometry results. Our point is to model the respiratory volume-time curves.

The presented model of spirometry describes the airflow during maximal inspiration $Q_{in}(t)$ and during maximal forced expiration $Q_{out}(t)$ (see Fig. 3) [9, 10]. For modelling of the process the spline functions were used. The spline functions consist of piecewise lengths of regression functions that give the best fit to localized sections of the data. The particular sections are joined together smoothly. The smooth joining of the sections is ensured mathematically by making the value and the slope of the function at the end of one section identical to that of the next part. The first-derivative continuity of the spline functions is kept.

The maximal inflow $Q_{in}(t)$ has been modelled with the regression function:

$$Q_{in}(t) = A_{in} \cdot \sin\left(\varpi \cdot (t - t_0)\right) \qquad t_0 \le t \le t_1 \tag{3}$$

where A_{in} [$l \cdot s^{-1}$] is amplitude, ϖ [s^{-1}] is pulsation and (t_0, t_1) is the time of breath-in duration. The maximal outflow $Q_{out}(t)$ has been modelled by the two exponential spline functions:

$$Q_{out}(t) = \begin{cases} -A_{out1} \cdot \left(1 - e^{-B_{out1} \cdot (t - t_1)}\right) & t_1 < t \le t_2 \\ -A_{out2} \cdot e^{-B_{out2} \cdot (t - t_2)} + const & t_2 < t \le t_3 \end{cases} \tag{4}$$

where A_{in} [$l \cdot s^{-1}$], B_{out1} [$l \cdot s^{-1}$], A_{out2} [$l \cdot s^{-1}$], B_{out2} [$l \cdot s^{-1}$] are parameters of the regression function. The constant *const* plays only a secondary role in the modelling process. It is used for mathematical reason, namely for keeping the spline functions continuity. It is not a key to explanation of the ventilation mechanism.

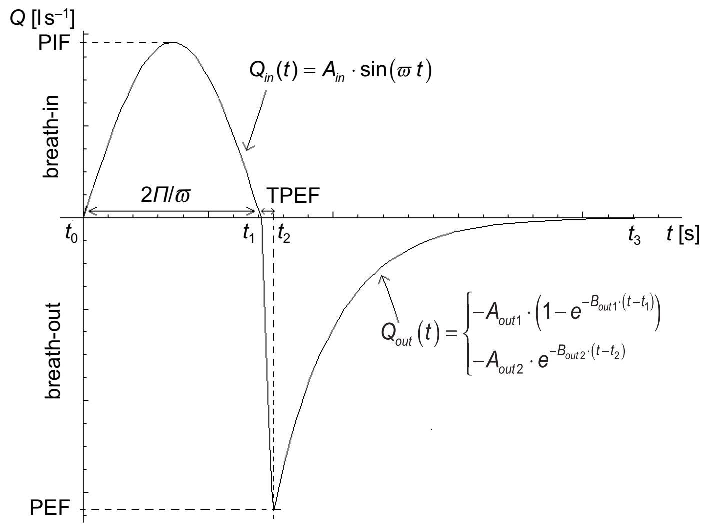

Fig. 3. The modelled flow-time curves $Q_{in}(t)$ and $Q_{out}(t)$

3. Methods

The parameters of the model, which is described by equations (3) and (4), are arranged in a parameter vector $\mathbf{p} = [p_i] = [A_{in}, \varpi, A_{out1}, B_{out1}, A_{out2}, B_{out2}]$ where $i = 1,...,6$ and spirometry measurements are arranged in the vector of measurements $\mathbf{y} = [y_j] = [FEV_1, FVC, PEF, FIT, FET]$ where $j = 1,...,5$.

The flow-time regression functions, given by the equations (3) and (4), were fitted to the flow-time curve $Q(t)$ obtained as the spirometry measurement result. The fitting procedure, by adjusting the parameters of regression functions, assures the equality of the parameters FEV_1, FVC, PEF, FIT, FET calculated on the basis of the spirometry measurements with the same ones resulting from the model functions. The values of the parameters FEV_1, FVC, PEF, FIT, FET based on the measurements y_j^{meas} and the values of the parameters resulting from the procedure of fitting regression functions to the measurements y_j^{fit}, differ not more than 1%, i.e. $\left(\left|y_j^{meas} - y_j^{fit}\right| / y_j^{meas}\right) \leq 1\%$.

The model parameter estimates p_i are calculated on the basis of the measurements y_i therefore they can be shown as functions of the measurements $p_i = p_i(y_j)$. The model parameters cannot be measured directly so their accuracies cannot be calculated by replication of a parameter measurement. Therefore it is necessary to estimate their accuracies on basis of the uncertainty of respiratory parameter measurements via the propagation of an error formula [11]. The formula gives an estimate of the standard deviation of p_i. The standard deviation depends both on sensitivities of the parameter p_i with respect to the measurements y_j and standard deviation s_{y_j} of each measurement y_j.

$$s_{p_i} = \sqrt[2]{\sum_{j=1}^{5} \left(\frac{\partial p_i}{\partial y_j} \right)^2 \cdot s_{y_j}^2}, \; i = 1,..,6 . \tag{5}$$

Similarly as it was made for respiratory parameters, the reference values for model parameters are designed. The reference values of the model parameters $\mathbf{p} = [p_i] = [A_{in}, \varpi, A_{out1}, B_{out1}, A_{out2}, B_{out2}]$ were obtained with the use of the reference equation (2) with coefficients R_1^j, R_2^j, R_3^j, (for standardized respiratory parameters FEV_1, FVC and PEF) shown in Table 1. The two additional respiratory parameters employed for model identification, i.e. FIT and FET, are not standardized. We assume that the parameter $FET = 6$ *sek* (which is the minimal, correct value) and the ratio of $FIT : FET = 1:2$ [6, 7]. The results, i.e. the graphical representation of the equations giving the base for reckoning reference values of the model parameters, are presented in Fig. 4. The ranges of age and height, taken into consideration in the paper, were the same as those provided by the European Respiratory Society norms: the age range was from 25 to 70 years and the height range was from 1.55 to 1.95 for men and from 1.45 to 1.80 meters for women.

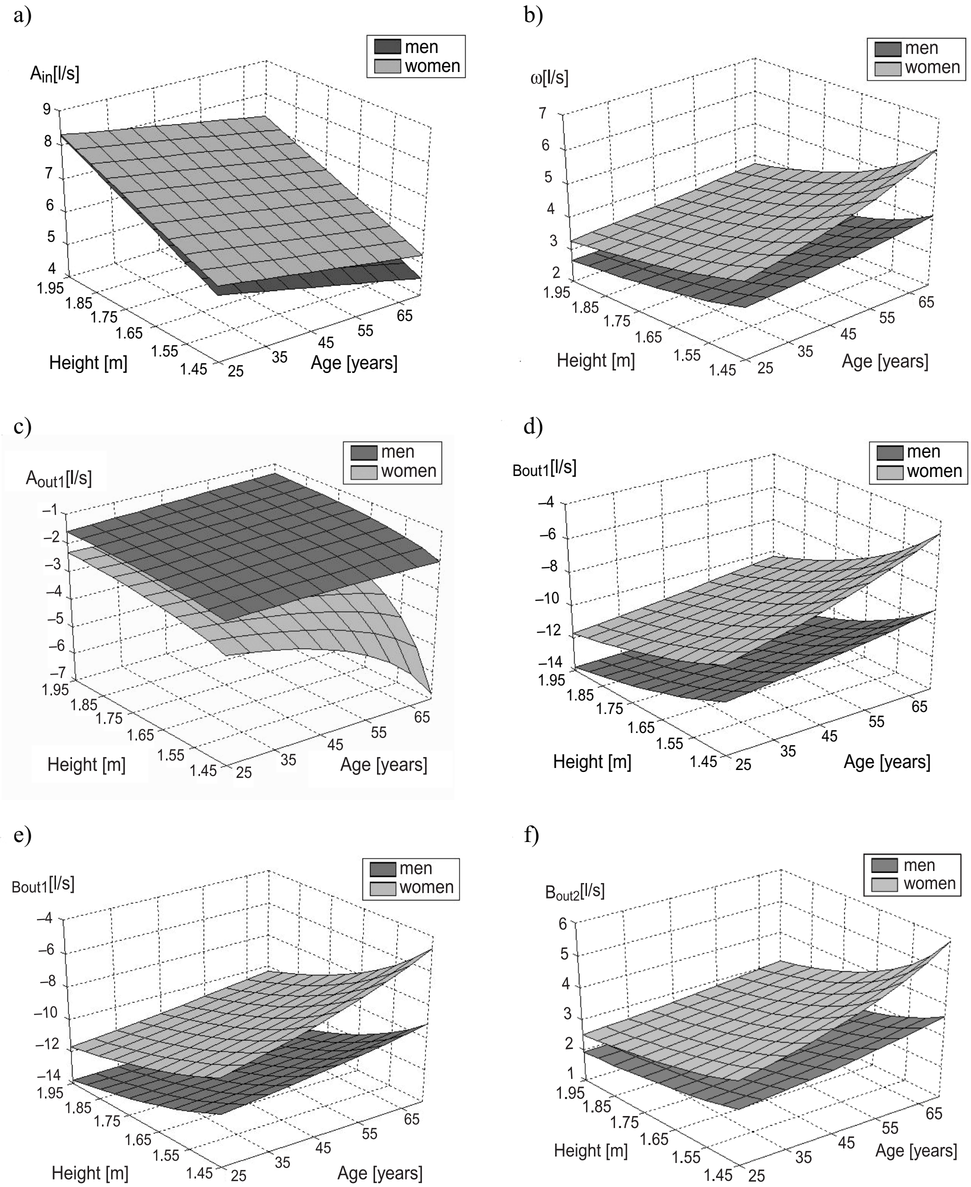

Fig. 4. The reference values of the model parameters: a) A_{in}, b) ϖ, c), A_{out1} d) B_{out1}, e) A_{out2}, f) B_{out2}

The varied health conditions cause a change in the values of the ventilation parameters FEV_1 and FVC when compared to the standardized reference values. The degradation of the patient's breathing condition causes a decrease in the respiration parameters value. The 20% decrease from the nominal value is considered abnormal [8].

The obstructive pulmonary disease leads to the decrease of FEV_1. The restrictive lung changes result in the decrease of FVC. When for both the parameters there is the decrease below 80% of the reference values, the mixed changes are diagnosed.

The model parameter susceptibility, in respect to different health conditions, was verified by means of evaluation the influence of 20% decrease in standardized respiration parameter value on the model parameter estimates. The nominal model parameters $\mathbf{p}_{NOM}$ were estimated on the basis of the nominal values of FEV_1 and FVC. The 20% decrease of FEV_1, FVC, and both FEV_1 and FVC, simulates various health conditions: obstructive, restrictive and mixed disease respectively. Then, on the basis of simulated diseased cases (obstructive, restrictive and mixed), the model parameter estimates were calculated: $\mathbf{p}_{obstr.}$, $\mathbf{p}_{restr.}$, and $\mathbf{p}_{mix.}$. For each parameter p_i, $i = 1,2...6$ a relative change in the parameter value was calculated as follows:

$$\begin{gathered} p_i = p_i\left(FEV_1, FVC\right) = p_i\left(y_1, y_2\right), \\ \frac{\Delta p_i}{p_i} = \left|\frac{\partial p_i\left(y_1, y_2\right)}{\partial y_1}\right| \cdot \frac{\Delta y_1}{y_1} + \left|\frac{\partial p_i\left(y_1, y_2\right)}{\partial y_2}\right| \cdot \frac{\Delta y_2}{y_2}. \end{gathered} \tag{6}$$

The degree to which relative changes in measurements $\Delta y_j/y_j$, $j = 1,2$ influence a relative change in parameters $\Delta p_i/p_i$, $i = 1 \div 6$ depends on the sensitivity $S_{y_j}^{p_i} = \partial p_i\left(y_j\right) / \partial y_j$. The larger the sensitivity is**,** the more dependent on change in measurement the parameter is.

4. Results

The model parameter estimates $\mathbf{p} = [p_i] = [A_{in}, \varpi, A_{out1}, B_{out1}, A_{out2}, B_{out2}]$ were obtained making use of measurements y_j.

Below there are the exemplary parameter vectors for women, $H = 1.95[meters]$, $A = 25[years]$, $\mathbf{p}$ = [8.31, 3.26, –2.32, –11.71, 16.21, 2.49] and $H = 1.55[meters]$, $A = 70[years]$, $\mathbf{p}$ = [5.24, 6.11, –6.79, –4.71, 17.82, 5.89] and for the same age and height for men respectively, $\mathbf{p}$ = [8.29, 2.65, –1.59, –13.81, 14.76, 1.94] and $\mathbf{p}$ = [4.53, 4.13, –2.04, –9.17, 11.06, 3.59]. Then the model parameter estimates usefulness for diagnostic purposes was verified. At first, accuracy of the parameter estimates was analysed. Next the reference values of the model parameters were calculated. The susceptibility of the model parameters to wide-ranging health conditions was also investigated.

The measurement error, given by the producer of the measuring device, is 3% [12, 13]. The error propagation method (see equation (5)) was used for obtaining the relative accuracy $s_{pi}/p_i[\%]$ of the parameter estimates p_i, resulting from the measurement error. The results are presented in Table 2. The relative accuracies of B_{out1} and A_{in} model parameters are the best and equal 2.81% and 3.00% respectively, while

A_{out1} accuracy is the worst and equals 7.27%. The model parameter estimates were not found particularly sensitive to the measurement error. Their errors are of the same order of magnitude as the measurement error, and accuracies are reasonable and acceptable.

Table 2. The relative accuracy of the model parameter estimates obtainable for 3% measurement error

p_i	$\frac{s_{pi}}{p_i}$[%]
A_{in}	3.00
ϖ	4.42
A_{out1}	7.27
B_{out1}	2.81
A_{out2}	5.21
B_{out2}	5.04

Next the reference values of the model parameters $\mathbf{p} = [p_i]$ were calculated. They were obtained with the use of the reference equations (2) giving the reference values for respiratory parameters over the analysed range of age $A \in (25,70)$ [years] and height $H \in (1.45,1.80)$ [meters]. For each point of coordinates (a_r,h_k), $a_r \in A$ and $h_k \in H$, $a_{r+1} - a_r = 0.5$ year, $h_{k+1} - h_k = 0.05$ meter, $r = 1,...,80$, $k = 1,...,50$, on the basis of the reference respiratory parameters, the reference model parameters were calculated. The results obtained are presented in Fig. 4. As the figure shows, the parameters obtained for men and women differ noticeably, in particular for older and shorter population.

Then, for the graphical form of the model parameters dependence on age, height and gender shown in Fig. 4, we sought for a mathematical formula able to describe the dependence. We adopted the regression function for model parameters as follows:

$$p_i = R_1^i \cdot H + R_2^i \cdot A + R_3^i, i = 1,..,6\,. \tag{7}$$

The references values of the coefficients R_1^i, R_2^i, R_3^i were calculated for six model parameters $\mathbf{p} = [p_i] = [A_{in}, \varpi, A_{out1}, B_{out1}, A_{out2}, B_{out2}]$. Six sets of the coefficients were obtained: one for each model parameter. The obtained R_1^i, R_2^i, R_3^i coefficients are presented in Table 3. The research was made for men and women separately. The coefficients obtained for men differ much from those obtained for women. The analysis reveals that the dependence of the model parameters' reference values on height (R_1) is stronger than on age (R_2). The value and the influence of the coefficient are also significant.

Table 3. The coefficients R_1^i, R_2^i, R_3^i of the reference equation for the model parameters A_{in}, ϖ, A_{out1}, B_{out1}, A_{out2}, B_{out2}

Coefficients	R_1^i	R_2^i	R_3^i
For men			
A_{in}, $i = 1$	4.605	–0.032	0.113
ϖ, $i = 2$	–1.878	0.003	6.125
A_{out1}, $i = 3$	0.677	0.005	–2.970
B_{out1}, $i = 4$	–6.333	0.011	–2.070
A_{out2}, $i = 5$	4.945	–0.035	5.842
B_{out2}, $i = 6$	–1.851	0.007	5.264
For women			
A_{in}, $i = 1$	4.125	–0.022	0.832
ϖ, $i = 2$	–4.032	0.023	9.777
A_{out1}, $i = 3$	6.609	–0.030	–12.622
B_{out1}, $i = 4$	–10.253	0.058	5.159
A_{out2}, $i = 5$	–1.828	0.017	17.643
B_{out2}, $i = 6$	–4.695	0.027	10.019

For men, the parameters B_{out1}, A_{out2} and A_{in} show the strong dependence on the height: the absolute value of the coefficient R_1 is equal to 6.333, 4.945 and 4.605 respectively for the parameters. The smallest value of R_1, which is equal to 0.677, indicates the parameter A_{out1} as the less dependent one on the height of a male patient. The age coefficients R_2, for A_{out2} and A_{in}, are equal to –0.035 and –0.032 respectively. The other age coefficients R_2 are positive and smaller than the former two. The coefficient R_3 has the strongest influence on ϖ, A_{out2} and B_{out2} (6.125, 5.842 and 5.264 respectively) while its influence on A_{in} (0.113) is the smallest.

Both for men and women $|R_1| > |R_2|$, which means that the influence of height on the reference value of the model parameters is larger than the influence of age. The highest $|R_1| = 10.253$ was obtained for women B_{out1} and the lowest $|R_1| = 0.677$ for men A_{out1}. The strongest dependence on the age was for women B_{out1} as $|R_2| = 0.058$. The coefficient R_3 has the strongest influence on the woman reference values of model parameters A_{out2} and A_{out1}: $|R_3| = 17.643$ and $|R_3| = 12.622$ respectively.

The linear reference equation (2), recommended by the European Respiratory Society, does not seems to be the only choice for the results presented in Fig. 4, in particular for woman plots c) and d) which become non-linear for smaller *H* (height) and bigger *A* (age). In further works we will attempt to find a more fitting mathematical description of the model parameter changes in the full range of *A* and *H*. It seems doubtless whether the regression function will be a non-linear one. As it results from our work, no single non-linear function adopted for all model parameters gives a better fit to the data than the linear one. This is because of distinctly linear and non-linear parts of the plots that can be distinguished. Possibly the spline will be the more suitable solution.

The model parameter susceptibility, for different health conditions, was also verified. The model parameters for the three simulated diseased cases, obstructive, restrictive and mixed, were calculated. The results obtained are presented in Table 4 and shows that the model parameters ϖ, A_{out1} and B_{out2} are more vulnerable to obstructive changes than the respiratory parameter *FVC*: the 20% decrease in *FVC* causes 25.11%, 36.67% and 21.94% changes in ϖ, A_{out1} and B_{out2}, respectively. The 20% change in FEV_1 (restrictive change) causes a change only in the two model parameters: the 10.97% change in and the 18.88% change in B_{out2}. The mixed lung changes (20% decrease of FEV_1 and *FVC*) cause the 25.11%, 36.67%, 32.65% changes in the model parameters ϖ, A_{out1} and B_{out2}. Thus, it has been shown above that the susceptibility of ϖ, A_{out1}, B_{out2} to obstructive changes is more significant than the susceptibility of respiratory parameter assumed at 20%.

The attained outcomes allow us to postulate that the model parameter estimates could be successfully applied for diagnostic purposes. It provides new information concerning breathing conditions compared with the traditional diagnostic parameters. So far the breath–in parameters have been not adopted for diagnosis. The parameter ϖ refers to the breath–in and it occurred to be a sensitive candidate for a new diagnostically useful parameter of the lung condition, which relates to inhalation.

Table 4. The susceptibility of the model parameters to varied health conditions: $\frac{\Delta p_i}{p_i}[\%]$ for obstructive, restricted and mixed changes

p_i	$\frac{\Delta p_i}{p_i}$ $\frac{p_i^{obstr} - p_i^{refer}}{p_i^{refer}}$ $[\%]$	$\frac{\Delta p_i}{p_i}$ $\frac{p_i^{restr} - p_i^{refer}}{p_i^{refer}}$ $[\%]$	$\frac{\Delta p_i}{p_i}$ $\frac{p_i^{mix} - p_i^{refer}}{p_i^{refer}}$ $[\%]$
A_{in}	0.00	0.00	0.00
ϖ	25.11	0.00	25.11
A_{out1}	36.67	0.00	36.67
B_{out1}	–8.52	0.00	–8.52
A_{out2}	–6.51	10.97	7.81
B_{out2}	21.94	18.88	32.65

The parameters A_{out1} and A_{out2} describe the breath-out interval, in which two internals are distinguished. The parameters refer to the first and the second part of the exhalation separately. The first one is the fast exhalation, which is a rapid increase of the inflow. The second one is the decreasing exhalation, which is a slow decrease of the outflow. The traditional parameters do not describe these parts of the breath-out separately. Thus the parameters A_{out1} and A_{out2} could be also used for diagnostic purposes as well.

5. Conclusions

The spirometry measurements of the respiratory system quality, together with the modelling and simulation of disease states have been presented in the paper. The model parameter estimates, obtained on the basis of dynamic spirometry measurements, were evaluated with respect to their accuracy, with the use of the error propagation method. The reference values of the model parameters were established. Then, for the reference values of the parameters, the coefficients that describe the influence of the height and the age on the model equation were also found. Three groups of patients, with the obstructive, the restrictive and the mixed lung disorder, were considered. Their lung's health occurred to be unmistakably identified with the help of the model parameter estimates.

The model parameters provide also new information concerning breathing conditions. The traditional diagnostic parameters, which describe the breath-in interval, were not used as a clue for diagnosis. The parameter ϖ presents itself as a new, sensitive and diagnostically useful respiratory parameter.

The acquired outcomes allow us to postulate that the spirometry respiratory model parameter estimates could be successfully applied for diagnostic purposes.

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