Studia Universitatis "Vasile Goldiş", Seria Ştiinţele Vieţii
Vol. 19, issue 1, 2009, pp. 123-131

ESTIMATING RESPIRATORY MECHANICS WITH CONSTANT-PHASE MODELS IN HEALHTY LUNGS FROM FORCED OSCILLATIONS MEASUREMENTS

Clara IONESCU*[1], Kristine DESAGER[2], Robin DE KEYSER[1]
[1]Ghent University, Department of Electrical energy, Systems and Automation, Gent, Belgium
[2]University Hospital Antwerp, Department of Pulmonary Division, Wilrijk, Belgium

ABSTRACT. Demanding minimal cooperation from the patient, the forced oscillation technique (FOT) is an attractive non-invasive lung function test. Its successful application to assess respiratory mechanics makes it an interesting topic for further investigations. Recent trends in signal processing and modelling techniques play a significant role in improving the assessment of input respiratory impedance. A four-parameter constant-phase model and a five parameter constant-phase model are evaluated here in healthy young females and males. The identification results show that the five parameter constant-phase model delivers better estimates in terms of minimizing modelling errors. The observed model values agree qualitatively with expected values based on previous reports in the specialized literature for healthy subjects.

Keywords: lung function test, non-invasive, forced oscillations, signal processing, modeling, respiratory system, input impedance

INTRODUCTION

Non-invasive lung function tests are broadly used for assessment of respiratory mechanics (Northrop, 2002). Although they require forced manoeuvres from patient side and special training for the technical medical staff, most popular tests in lung function laboratories are spirometry and body plethysmography. Despite its simplicity and minimal cooperation requirements from the patient, forced oscillations technique (FOT) remains a non-routinely performed lung function test in clinical environment, possibly because of lacking ability to characterize specific parts of the respiratory system (Cavalcanti et al., 2006; Navajas and Farré, 1999; Oostveen et al., 2003).

However, when only classification is envisaged, the FOT is suitable to apply and requires minimal effort from both patient and clinical staff (Pham et al., 1995). A recent trend has been observed in the research community in employing mathematical tools for use in biomedicine (Eke et al., 2002). These tools have become available once the technologic advances allowed complex numerical computations for simulation studies. The fractional-order parametric models are such tools, able to capture the viscoelastic properties of the lung parenchyma (Suki et al. 1994). It has been shown in animal studies and excised lungs in humans that the tissue damping and tissue elastance are well characterized using models in which the compliance comprises a term in fractional-order integral (Hantos et al., 1992a,1992b). These models are also known as constant-phase models, due tot their intrinsic property of providing a phase-lock in a limited frequency range (Oustaloup, 1995).

In this study we show the use of such models on a healthy group of subjects, providing model parameter values. The performance with respect to modelling errors is assessed on two constant-phase models, with four and five parameters, respectively. The results show the limitations in the four parameter constant phase model to capture increasing values in the respiratory impedance with frequency.

MATERIALS AND METHODS

Subjects

The group evaluated in this study consists of volunteers without a history of respiratory disease, whose lung function tests were performed in our laboratory, and Table 1 presents their biometric parameters.

Table 1

Biometric parameters of the investigated subjects; values are presented as mean±SD

	male (n=15)	female (n=8)
Age (yrs)	23±0.7	23±1.3
Height (m)	1.76±0.062	1.68±0.032
Weight (kg)	73±5.1	63±2.8

***Correspondence:** Clara Ionescu, Ghent University, Department of Electrical energy, Systems and Automation, Technologiepark 913, 9000 Gent, Belgium; email: clara@autoctrl.UGent.be*
Article received: september 2008; published: march 2009

Measurements

In this study, we evaluate healthy subjects with the Forced Oscillations Technique (FOT) non-invasive lung function test (Oostveen et al., 2003). Air-pressure P and air-flow Q during the FOT lung function test can be measured either at the mouth of the patient, either endotracheal, either at body surface (Desager et al., 1991; Northrop, 2002). If the impedance is measured at the mouth of the patient, then it is called input impedance. In the case when the measurements are done across the body surface, this is then called transfer impedance. Using electrical analogy, where the P corresponds to voltage and Q corresponds to current, the respiratory impedance Zr can be defined as their spectral (frequency domain) ratio relationship (Daroczy et al., 1982; Ionescu and De Keyser, 2003). The present study is restricted to measurements of input respiratory impedance, that is, P and Q are measured at the mouth of the patient with reference to the atmospheric pressure (Oostveen et al., 2003). Typically, the resulted impedance is a frequency dependent complex representation of mechanical properties and defines a real part Rrs – called resistance – and an imaginary part Xrs – called reactance. The real part describes the dissipative mechanical properties, whereas the imaginary part is related to the energy storage capacity and determined by both elastic and inertive properties.

The subject is connected to the typical setup from figure 1 via a mouthpiece, suitably designed to avoid flow leakage at the mouth and dental resistance artefact. The oscillation pressure in most recent FOT devices is generated by a loudspeaker (LS) connected to a chamber (Birch et al., 2001). The LS is driven by a power amplifier fed with the oscillating signal generated by a computer. The movement of the LS cone generates a pressure oscillation inside the chamber, which is applied to the patient's respiratory system by means of a tube connecting the LS chamber and the bacterial filter (bf). A side opening of the main tubing allows the patient to decrease dead space re-breathing. Ideally, this pipeline will have high impedance at the excitation frequencies to avoid the loss of power from the LS pressure chamber. It is advisory that during the measurements, the patient should wear a nose clip and keep the cheeks firmly supported to reduce the artefact of upper airway shunt. Pressure and flow are measured at the mouthpiece, respectively by means of i) a pressure transducer and ii) a pneumotachograph (PN) plus a differential pressure transducer (PT). The FOT pressure signal should be kept within a range of a peak-to-peak size of 0.1-0.3 kPa, in order to ensure optimality, patient comfort and stay within a narrow range in order to assume linearity (Desager et al., 1997). Averaged measurements from 3-5 technically acceptable tests should be taken into consideration for further signal processing. Typical recorded signals are depicted in figure 1-B.

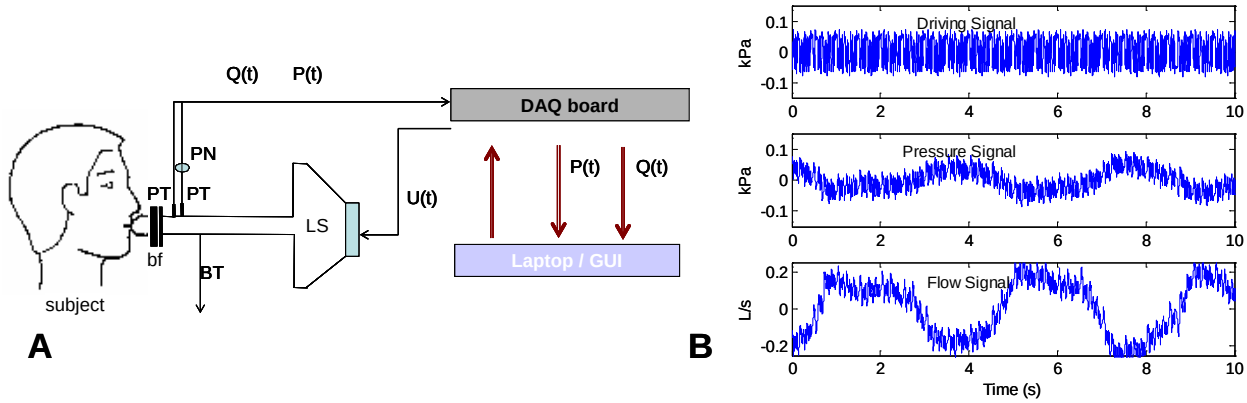

Fig. 1 A schematic overview (A) of the FOT measurement setup. Typical measured signals (B) from one subject: oscillatory driving pressure; trans-respiratory pressure and air-flow. The breathing of the patient (low frequency) can be observed superimposed on the multisine signals. See text for symbol explanations.

Excitation signals

If properly chosen, the excitation signal will provide useful information for the identification task without disturbing the system during its nominal operation (here: normal breathing). A comprehensive and didactical overview on the design algorithms and applications for frequency-domain identification is given in (Schoukens and Pintelon, 2001) for both non-parametric and parametric modelling purposes. The type of signals applied with FOT to assess respiratory mechanics will be briefly enumerated along with their practical use.

No Input Signal: this is the simplest scenario, resulting in a measure of the breathing alone, in terms of pressure and flow. This scenario is used to follow variability of the breathing signal, mechanical tidal parameters at the frequency of breathing (Babik et al., 2002). The advantage of using this signal is that no extra forces are applied to the patient (as in case of any other excitation signal) and no optimal input design is necessary. The drawback is that information is gathered solely at the breathing frequency, and identification of the respiratory function is practically impossible.

Random Oscillation: this is a non-periodic signal characterized by a continuous distribution of the signal power within the defined frequency band, often referred to as random noise. This kind of signal poses the advantage of being un-correlated with the breathing of the patient, making it attractive for low frequency identification, but has the drawback of introducing leakage effects. The reason is that the closer to the breathing frequency of the patient, the higher the danger of breathing harmonics interfering in the identification process. The drawback of this type of signal is a low signal-to-noise ratio, taking into account that the breathing of the patient is regarded as noise for the identification task; the signal-to-noise ratio can partially be improved with suitable filters. For this type of signal a lot of signal power is also generated outside the frequency band of interest, resulting in excited frequency points which the user does not want and distorting the desired information. The wide frequency range has also the drawback that when the respiratory system is assumed to be linear, some errors may be introduced (due to nonlinearity).

Impulse Oscillation: a comprehensive overview of the method using this kind of signal is given in (Smith et al., 2005). For the identification task, however, an impulse type excitation signal is sub-optimal, and prone to give biased estimates (Diong et al., 2007).

Sine Wave: this periodic excitation is of great interest when frequency-domain identification is targeted, providing unbiased estimates. Besides, it allows direct interpretation of the mechanical load and a high signal-to-noise ratio. The drawback is that only one point in the frequency domain is excited, so the information is not sufficient to assess the mechanical properties of the lungs. In order to avoid this drawback, multi-sine waves are applied to excite the system over the whole range of frequencies in one experiment. The limitation, however, is that the amplitude (power) of the signal decreases with frequency, due to the fact that the overall power spectrum of the multi-sine must be kept within the linearity, safety and comfort range for the patient respiration. This constraint leads to limitations in the peak-to-peak amplitude of the FOT signal between 0.1-0.3kPa (Oostveen et al., 2003; Van De Woestijne et al., 1994). In this study, we consider applying multi-sine oscillations to the patient, in a limited frequency range.

Frequency range

There are distinctively three sets of frequency range for characterizing human respiratory input impedance: low, medium and high. There is no consensus on the exact intervals to define a low and a high frequency range. However, in the literature, low frequencies are referred to those smaller than 100 times the breathing frequency (which is typically 0.28Hz), thus up to 30Hz. A commonly used, medium range of frequencies has been defined between 4-50Hz. The high frequency range could then include frequencies up to 5000Hz (e.g. in acoustic impedance, respiratory sounds analysis). Published reports show that if the oscillatory signal is superimposed on spontaneous breathing, oscillation frequencies higher than 4Hz must be used (Navajas et al., 1988). The main reason is the presence of harmonics introduced by the breathing signal, which may corrupt the information measured in response to the excitation signal, but also limitations in the loudspeaker power below 4Hz.

Most studies have used data from 4-16Hz or 3-32Hz, which do not include the spontaneous breathing frequencies. The assessment of the mechanical properties of chest, tissue and airways is therefore specific for the chosen frequency-intervals. The validity of the model parameters (which also depend on the model-complexity) varies with the frequency-range in which data for the identification task is collected (Farré et al., 1989). This observation is also shared by Lutchen and Jackson (Lutchen and Jackson, 1987) in their study on dog input and transfer impedance when comparing three frequency ranges: 4-32, 4-64 and 4-110Hz. It appears that respiratory system parameters can be more accurately extracted in input impedance data which include the first (around 10Hz) and the second resonance frequencies (around 80Hz). In this study, we limit our measurements around the first resonant frequency, i.e. 4-48Hz.

Respiratory input impedance

One of the most common non-parametric representations of the input impedance Zr is obtained assuming a linear dependence between the breathing and superimposed oscillations at the mouth of the patient. Apart from the errors introduced by the linear assumptions, the spectral representation of Zr is a fast, simple and fairly reliable evaluation. The algorithm for estimating Zr can be summarized starting from the corresponding equation for the electrical analogue in figure 1-B:

$$P(s) = Z_r(s)Q(s) + U_r(s) \qquad (1)$$

where s denotes the Laplace operator. If the excitation signal is designed to be uncorrelated with the breathing of the patient and correlation analysis applied to the measured signals, one can estimate the respiratory impedance as:

$$\hat{Z}(j\omega) = \frac{S_{PU_g}(j\omega)}{S_{QU_g}(j\omega)} \qquad (2)$$

where $S_{ij}(j\omega)$ denotes the cross-correlation spectra between the various input-output signals, ω is the angular frequency and $j = (-1)^{1/2}$. From the point of view of the forced oscillatory experiment, the signal components of respiratory origin, (U_r) have to be regarded as pure noise for the identification task. However, to fulfill this condition is necessary that: i) the test signal U_g is designed such that it is not

correlated with the normal respiratory breathing signal U_r and ii) the conversion from voltage to pressure oscillation follows a linear relationship. By definition, the modulus $|Z_r|$ is a measure of the total mechanical load of the respiratory system at the respective oscillation frequencies. The phase of respiratory impedance Φ_r is defined as the phase lag between $P(t)$ and $Q(t)$ and it is computed as the ratio between the time lag and the oscillation period $\Phi_r = 360 \times \Delta t / T$. The frequency where Φ_r =0 is called the *resonance frequency* and it depends on the balance between the different kind of mechanical properties (elastic, inertial). This then allows for differentiating between healthy and pathologic cases, since the resonance frequency changes significantly from typically 8Hz for a healthy adult to 14Hz for a patient with mild airway obstruction and about 20Hz in cases of severe obstruction.

According to (Pasker *et al.*, 1997), the real (*Rrs*) and imaginary (*Xrs*) parts of the impedance can be predicted from their biometric data as given below:

Female
Rrs0f=-0.4300*h+0.00165*w-0.00070*a+0.9312 (RSD=0.0619)
Rrs1f=0.01176*h-0.000106*w-0.000045*a-0.00817 (RSD=0.00256)
Xrs0f=0.2487*h-0.001700*w-0.00053*a-0.2158 (RSD=0.0406)

Male
Rrs0m=-0.2454*h+0.001564*w-0.00055*a+0.5919 (RSD=0.0493)
Rrs1m=0.01176*h-0.000106*w-0.000045*a-0.00817 (RSD=0.00197)
Xrs0m=0.2487*h-0.001700*w-0.00053*a-0.2158 (RSD=0.0306)

where *a* denotes age in *yrs*, *h* denotes height in *m*, *w* denotes weight in *kg* and *RSD* is the residual standard deviation. The *0f* and *1f* coefficients are related to the *E* and *D* coefficients respectively, resulted from fitting the polynomial given by:

$$R_{rs} \text{ (or } X_{rs}) = Df + E \qquad (3)$$

to the real or imaginary data sets, with *D*, *E* identified constants and *f* the oscillatory frequency, in this case between 4-48Hz. Confidence intervals of the identified values for 95% were calculated from RSDx1,96.

The constant-phase models

While fractional-order models seem to be popular in characterizing the viscoelastic properties of materials (Adolfsson *et al.*, 2005) and broadly used to characterize geometrical structures, physical and chemical phenomena, their potential to model biologic systems has only been recently acknowledged (Eke *et al.*, 2002). Until present, there is no fractional-order model presented in the literature to characterize the viscous effects observed in airway disease and particle deposition, in spite of the fractal geometry posed by the respiratory branching tree (Mandelbrot, 1983; Weibel, 2005). It has been shown that fractional orders models outperform integer-order models for characterizing input impedance in humans (Ionescu and De Keyser, 2008).

One of the most striking finding in the specialized literature was that respiratory resistance decrease sharply with increasing frequency in low frequency range. The proportionality between the real and imaginary parts (i.e. constant phase behavior) originates from tissue mechanics: its weakening and subsequent disappearance, indicating the influences of Newtonian resistances and inertances, appear only at higher frequencies. This observation implies the coupling of elastic and dissipative processes in an elementary tissue level. According to the Hildebrandt-model, Laplace transformation of the pressure decay in a rubber balloon can be characterized by the expression of the elastic modulus: $T(s) = sP(s)/V = As^k \Gamma(1-k) + B$, where $s = j\omega$, $\Gamma(1-k)$ is the respective gamma function, with *A* and *k* constants (Hildebrandt, 1969). Division of $T(s)$ by s results in the impedance. Evaluation of impedance data in cats and dogs, invasively applied during tracheostomy in the relaxed (anesthetized) chest wall showed that below 1Hz tissue hysteresivity slightly deviates from constancy (Hantos *et a*l., 1992a;1992b). The tissue hysteresivity (=*G*/*H*) was obtained from Hildebrandt equation for $\beta = 1-k$ and $Z_{ti}(j\omega) = (G - jH)/\omega^{\beta}$. In the time domain, this expression captures the pressure decay after the volume increment as $P(t)/V = At^k$. The invariance of this damping-to-elastance ratio, i.e. the degree of mechanical efficiency, is a remarkable property of the respiratory tissues, with significant implications in the energy balance of respiration. This observation may therefore help discriminate between healthy and various pathologies, since the energy balance is expected to vary considerably with disease. Same studies provided the volume dependence of estimated parameters (resistance, inertance, damping and elastance coefficient) with peak-to-peak oscillation volume. Hantos proposed to find a model characterized by:

$$Z_r(j\omega) = R + I(j\omega) + (G - jH)/\omega^{\beta} \qquad (4)$$

with *R* a Newtonian resistance describing the resistance of the central airways; *I* an inertance representing the inertive properties of the gas in the lungs; *G* denoting the real part of an elastance (1/*C*, with *C* the compliance) and representing tissue

Studia Universitatis "Vasile Goldiş", Seria Ştiinţele Vieţii
Vol. 19, issue 1, 2009, pp. 123-131

damping, reflecting the energy dissipation in lungs and *H* the imaginary part of elastance, denoting tissue elastance and reflecting the energy conservation in the lung tissues. A model including fractional order compliance and inertance appeared to be necessary in order to ensure a reasonably good fit to the impedance data (without significantly increasing the order of the model):

$$Z_r(j\omega) = R + I(j\omega)^{\alpha} + \frac{1}{C(j\omega)^{\beta}} \qquad (5)$$

with α and β sub-unitary independent variables. Along with the corresponding model estimates, the error on the real and imaginary part respectively and the total error between the real patient impedance and the model estimated impedance are calculated according to the formulae:

$$E_r = \sqrt{\frac{1}{N}\sum_{1}^{N}(r-\hat{r})^2}; \quad E_x = \sqrt{\frac{1}{N}\sum_{1}^{N}(x-\hat{x})^2}; \quad E_{Total} = \sqrt{E_r^2 + E_x^2} \qquad (6)$$

with *r* denoting the real part of the impedance, *x* denoting the imaginary part of the impedance and *N* the total number of data samples. Further on, model parameters from the separate groups were evaluated using *boxplots*. The *boxplot* is typically a box and whisker plot for each column of the matrix **M**, whereas here the columns are respectively the parameters for healthy group and for COPD group. The box has lines at the lower quartile, median, and upper quartile values. The whiskers are lines extending from each end of the box to show the extent of the rest of the data. Outliers are data with values beyond the ends of the whiskers.

RESULTS AND DISCUSSIONS

Applying the non-parametric identification using (2) resulted in a set of complex input impedances for each group, in the 4-48Hz frequency range. The standard deviations on the averaged impedance data varied roughly in both groups from a ±17% at 4-6Hz, to ±5% at resonant frequencies (6-10Hz) and to ±12% at 35Hz. Generally, the imaginary part of impedance had lower standard deviations than real part for all subjects.

Since we had no information on the volunteers presumed healthy and therefore predicted values for polynomial terms in (3) were verified with 95% confidence intervals (Quanjer, 1998). In all cases, the identified values of the polynomial coefficients from (7) were close to the predicted values of *Rrs0*, *Rrs1* and *Xrs0*, within the 95% confidence intervals.

Figure 2 provides a comparison between the results of the 4CPM and 5CPM on the best identified patient from the healthy group. The theoretical assumption that the real part of (2) cannot capture the increase in impedance with frequency is therefore experimentally validated.

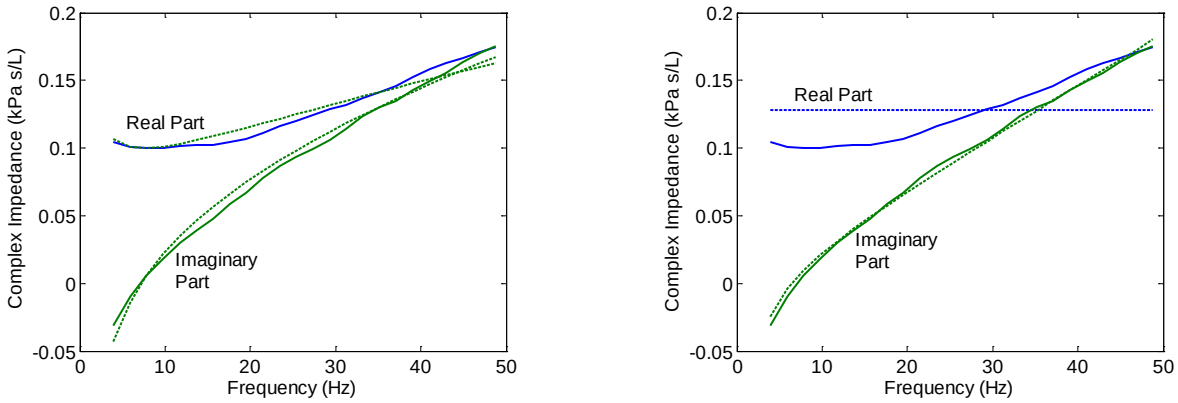

Fig. 2 The healthy subject with the least total error in 5CPM with E_r=0.0059; E_x=0.0057, E_{Total}=0.0082 (left) and the same patient in 4CPM with E_r=0.0263; E_x=0.0125, E_{Total}=0.0291 (right); continuous lines denote the measured impedance with (2) and dashed lines denote the identified impedance

For the two parametric models described by (4) and (5), the corresponding parameter values in terms of their average values and standard deviations, and modeling errors, are given in Table 2. It can be observed that lower error values are provided using the 5CPM, than the 4CPM.

Table 2

Identified model parameters from 4CPM and 5CPM, in healthy groups. Reported values are given in terms of mean and standard deviation values

Model	Parameters	Females	Males
4CPM	*R* (kPa s/L)	0.1795±0.0329	0.1894±0.0705
	L (kPa s²/L)	0.0006±0.0001	0.0006±0.0002
	1/*C* (kPa/L)	0.8088±0.0001	0.89±0.5855
	β	1±0	0.988±0.0278
	E_r	0.0425±0.014	0.043±0.0226
	E_x	0.0128±0.0057	0.011±0.0061
	E_{Total}	0.0445±0.0149	0.0445±0.0231
5CPM	*R* (kPa s/L)	0.0002±0.0002	0.0022±0.0091
	L (kPa s²/L)	0.0277±0.0076	0.0301±0.0304
	1/*C* (kPa/L)	1.4412±0.5537	1.5303±0.0304
	α	0.4082±0.0401	0.4546±1.1461
	β	0.76±0.0785	0.7011±0.1808
	E_r	0.0164±0.0075	0.0184±0.0112
	E_x	0.0126±0.0055	0.0139±0.0046
	E_{Total}	0.0216±0.0071	0.0236±0.0109

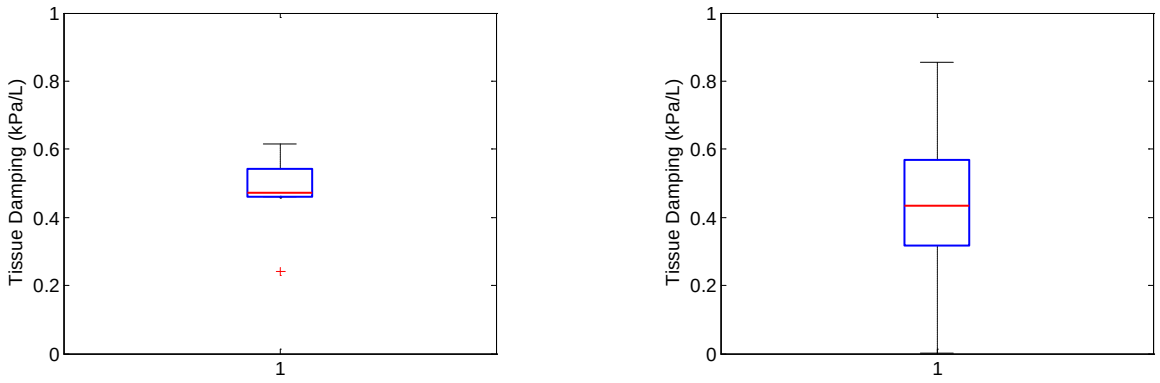

Fig. 3 Tissue damping in healthy females (left) and males (right) with the 5 parameter constant-phase model

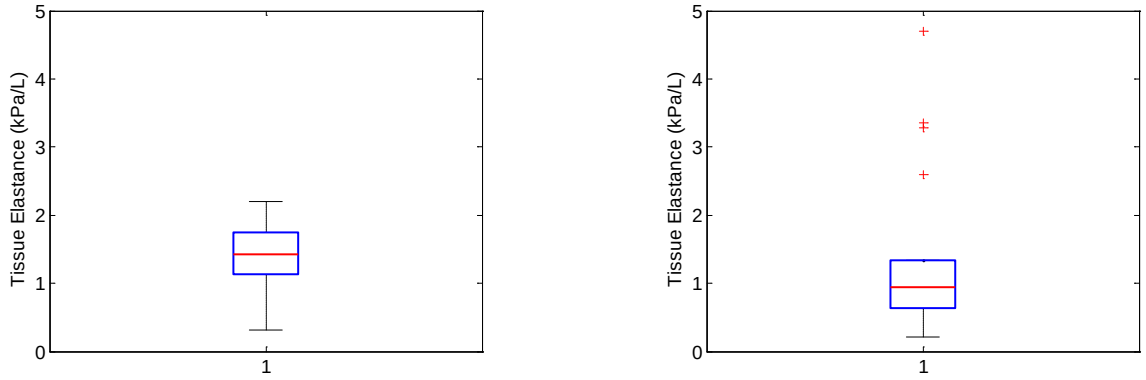

Fig. 4 Tissue elasticity in healthy females (left) and males (right) with the 5 parameter constant-phase model

Studia Universitatis "Vasile Goldiş", Seria Ştiinţele Vieţii
Vol. 19, issue 1, 2009, pp. 123-131

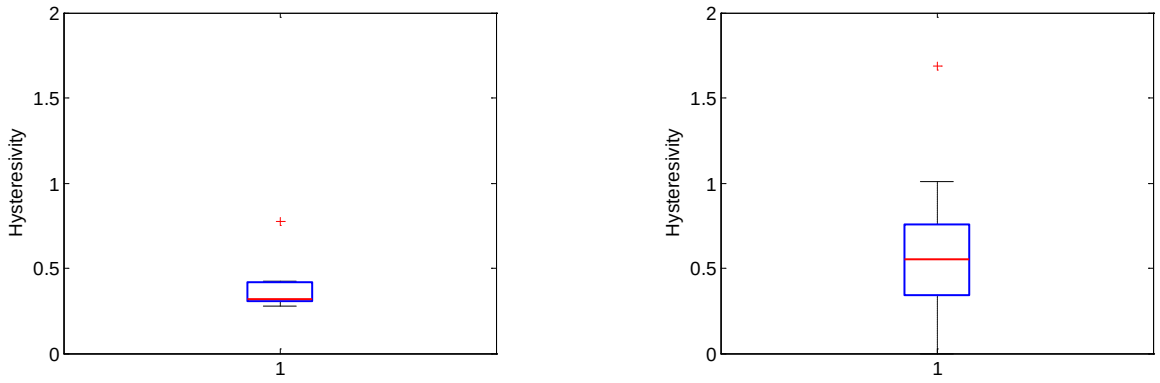

Fig. 5 Tissue hysteresivity in healthy females (left) and males (right) with the 5 parameter constant-phase model

Figures 3-5 depict the comparison between the results obtained with the 5CPM, respectively, in terms of corresponding tissue damping *G*, tissue elastance *H* and tissue hysteresivity $\eta=G/H$ values in healthy females and males.

The original contribution of this study is the proposed constant-phase model with five parameters (5CPM) and its analysis on healthy subjects, compared to the four parameter model (4CPM). From Table 2, one can observe that the 5CPM identified significantly lower low values for the resistance when compared to the 4CPM, within each subject group. The underlying reason for this behavior is that resistance properties are captured by the non-integer orders of the derivative and the integral terms (Oustaloup, 1995). This could be an indication that the model structure in (5) has an unnecessary parameter (*R*), since the real part is well characterized by the real parts of inertance and compliance fractional–order terms. On the other hand, increased values in inertance (I) were obtained with 5CPM than with 4CPM, probably to compensate for the lower resistance values. There were no significant differences between identified model parameters in compliance (C) and β values.

The damping factor is a material parameter reflecting the capacity for energy absorption. In materials similar to polymers, as lung tissue properties are very much alike polymers, damping is mostly caused by viscoelasticity, i.e. the strain response lagging behind the applied stresses (Suki *et al.*, 1994;1997; Yuan *et al.*, 1997). The model given by (2) is derived from the formula used by Hildebrandt to fit the relaxation data of a rubber balloon (Hildebrandt, 1969; Hantos *et al.*, 1992a;1992b). The exponent β governs the degree of the frequency dependence of tissue resistance G/ω^{β} and tissue elastance $H\omega^{1-\beta}$. The hysteresivity coefficient η introduced by Stamenovic (Fredberg and Stamenovic, 1989) is *G*/*H* in this model representation.

It is difficult to provide a fair comparison between the values reported in this study and the ones reported previously for tissue damping and elastance. Firstly, such studies have been previously performed from excised lung measurements and invasive procedures (Suki *et al.* 1997; Brewer *et al.*, 2003; Ito *et al.*, 2007), which related these coefficients with *transfer impedance* instead of *input impedance*. The measurement location is therefore important to determine mechanical properties of lungs. The data reported in our study, has been derived from non-invasive measurements at the mouth of the patients, therefore including upper airway properties. Secondly, the previously reported studies were made either on animal data (Hantos *et al*., 1992a;1992b; Brewer *et al*., 2003; Ito *et al*., 2007), either on other lung pathologies (Kaczka *et al.*, 1999; Hall *et al*., 2000; Brennan *et al.*, 2005). Nevertheless, the values from Table 2 were within the expected range suggested by previously reported studies in literature.

The main limitation of the present study is that both model structures and their corresponding parameter values are valid strictly within the specified frequency interval 4-48Hz. Nonetheless, since only one resonant frequency is measured and is the closest to the nominal breathing frequencies of the respiratory system, we do not seek to develop model structures valid over larger frequency range. Moreover, it has been previously shown that one model cannot capture the respiratory impedance over frequency intervals which include more than one resonant frequency (Farré *et al.*, 1989). A second limitation arises from the parameters of the constant-phase models. The fractional-order operators are difficult to handle numerically. The concept of modeling using non-integer order Laplace (e.g. $s^{\alpha}, \frac{1}{s^{\beta}}$) is rather new in practical applications and has not reached the maturity of integer-order system modeling. This concept has been borrowed from mathematics and chemistry applications to model biological signals and systems only very recently. Even more, in its present form (4), the fractional-order model has never before been employed to model respiratory mechanics. Advances in technology and computation have enabled this topic in the latter decennia and it has captured the interest of researchers. Although the parameters are intuitively related to pathophysiology of respiratory mechanics, the structural interpretation of

the fractional-orders is not deciphered. Finally, the property of constant-phase models is that a phase-lock appears in a limited frequency range (Oustaloup, 1995). It has never been actually shown that the morphology of the respiratory system leads intrinsically to such behavior; although under certain recurrent geometrical conditions this is possible (Mandelbrot, 1983; Weibel, 2005). Viscoelastic properties in lung parenchyma have been assessed in both animal and human tissue strips (Suki *et al*., 1994; Salerno *et al*., 2004) and correlated to fractional-order terms. A relation between these fractional-orders and structural changes in airways and lung tissue has not been found (e.g. airway remodeling). In this line of thought, the mechanical properties of resistance, inertance and compliance have been derived from airway geometry and morphology (i.e. airway radius, thickness, cartilage percent, length, etc) (Ionescu *et al*., in press). These parameters have been employed in a recurrent structure of healthy lungs using analogue representation of ladder networks (Ionescu *et al*., submitted). In the latter contribution, the appearance of a phase-lock (phase-constancy) is shown, supporting the argument that it represents an intrinsic property, leading to fractional values of 0.4 to 0.5. Its correlation to changes in airway morphology is an ongoing research matter. Experimental studies on various groups of patients (*e.g.* asthma *versus* COPD) to investigate a possible classification strategy for the parameters of this proposed model between various degrees of airway obstruction and lung abnormalities may also offer interesting information upon the sensitivity of model parameters.

CONCLUSIONS

This paper presents values for constant-phase models in groups of healthy males and females. A comparison between a reported constant phase model and a newly proposed model is provided, showing the advantages and dis-advantages of both model structures. Discussion on parameter values is also provided, in relation to other reported values from literature. It should be noted that the study here provides physically meaningful model values (always positive). Although the constant-phase model in four parameters became very popular in the last decade, there is a general tendency to accept such models without critical analysis on the model performance in terms of modelling errors. This paper shows that the four parameter constant-phase model so commonly reported in literature is limited to variations in respiratory impedance which decrease with frequency. The alternative model that we propose tackles this limitation, by introducing another parameter, without increasing the overall numerical complexity.

It is generally accepted that with FOT, as well as with other non-invasive lung function tests, the assessed information is a sum of all mechanical properties, and delivers no insight on specific components within the respiratory system. However, this is suitable for classification purposes only, and not in specific investigations. The FOT lung function test is therefore a simple and straightforward tool to assess respiratory mechanics, which can be successfully combined with the use of constant-phase models for assessing respiratory mechanics.

REFERENCES

Northrop R., "Non-invasive measurements and devices for diagnosis", CRC Press, (2002)

Cavalcanti J., Lopes A, Jansen J, Melo P, “Detection of changes in respiratory mechanics due to increasing degrees of airway obstruction in asthma by the forced oscillation technique”, Respiratory Medicine, 100, pp. 2207-2219, (2006)

Navajas R. , Farré R., “Oscillation mechanics”, Eur Resp Mon, 12, pp. 112-140, (1999)

Oostveen E., Macleod D, Lorino H, Farré R, Hantos Z, Desager K, Marchal F, "The forced oscillation technique in clinical practice: methodology, recommendations and future developments", Eur Respir J, 22, pp. 1026-1041, (2003)

Pham Q.T., Bourgkard E, Chau N, Willim G, Megherbi SE, Teculescu D, Bohadana A, Bertrand JP., “Forced Oscillation Technique (FOT): a New Tool for Epidemiology of Occupational Lung Diseases?.” Eur. Resp. J., 8: pp. 1307-1313 (1995).

Eke A., Herman P, Kocsis L, Kozak L, “Fractal characterization of complexity in temporal physiological signals”, Physiological measurement, 23, pp. R1-R38, (2002)

Suki B., Barabasi A.L., Lutchen K., “Lung tissue viscoelasticity: a mathematical framework and its molecular basis”, J Appl Physiol, 76(6), pp. 2749-2759, (1994)

Hantos Z, Adamicza A, Govaerts E, Daroczy B., “Mechanical Impedances of Lungs and Chest Wall in the Cat”, American Physiology Society, 73(2), pp. 427-433, (1992).

Hantos Z, Daroczy B, Suki B, Nagy S, Fredberg J. “Input Impedance and Peripheral Inhomogeneity of Dog Lungs”, American Physiology Society, 72(1), pp. 168-178, (1992).

Oustaloup A., (1995) “La derivation non-entière” (in French), Hermes, Paris

Desager K, Buhr W, Willemen M, Van Bever HP, De Backer W, Vermeire P, Landser F., “Measurement of Total Respiratory Impedance in Infants by the Forced Oscillation Technique”. American Physiological Society, pp. 770-776, (1991)

Daröczy B, Hantos Z, "An improved forced oscillatory estimation of respiratory impedance", Int J Bio-Medical Computing, 13, pp. 221-235, (1982)

Ionescu C, De Keyser R, “A Novel Parametric Model for the Human Respiratory System”. Proc. of the IASTED Int. Conf. on Modelling and Simulation, pp. 246-251 (2003).

Birch M, MacLeod D, Levine M, "An analogue instrument for the measurement of respiratory impedance using the forced oscillation technique", Phys Meas, 22, pp. 323-339, (2001)

Desager D, Cauberghs M, Van De Woestijne K, "Two point calibration procedure of the forced oscillation technique", Med. Biol. Eng. Comput., 35, pp. 561-569, (1997)

Schoukens J, Pintelon R, "System Identification, a frequency-domain approach", IEEE Press, 2001

Babik B, Petak F, Asztalos T, Bogats G, Hantos Z., "Components of Respiratory Resistance Monitored in Mechanically Ventilated Patients". Eur. Respir. J., 20: pp. 1538-1544, (2002)

Smith H, Reinhold P, Goldman M, "Forced oscillation technique and impulse oscillometry", Eur Resp Mon , 31, pp. 72-105, (2005)

Diong B, Nazeran H, Nava P, Goldman M, "Modelling human respiratory impedance", IEEE Engineering in Medicine and Biology, 26:1, pp. 48-55, (2007)

Van De Woestijne K, Desager K, Duiverman E, Marshall F, "Recommendations for measurement of respiratory input impedance by means of forced oscillation technique", Eur Resp Rev, 4, pp. 235-237, (1994)

Navajas D, Farré R, Rotger M, Peslin R, "A new estimator to minimize the error due to breathing in the measurement of respiratory impedance", IEEE Trans Biomed Eng, 35, pp. 1001-1005, (1988)

Farré R, Peslin R, Oostveen E, Suki B, Duvivier C, Navajas D, "Human respiratory impedance from 8 to 256 Hz corrected for upper airway shunt", American Journal of Applied Physiology, 67, pp. 1973-1981, (1989)

Lutchen K, Jackson A., "Reliability of Parameter Estimates from Models Applied to Respiratory Impedance Data". American Physiology Society, pp. 403-413 (1987).

Mandelbrot B., (1983) "The fractal geometry of nature", NY: Freeman &Co

Pasker H, Peeters M, Genet P, Nemery N, Van De Woestijne K., "Short-term Ventilatory Effects in Workers Exposed to Fumes Containing Zinc Oxide: Comparison of Forced Oscillation Technique with Spirometry". Eur. Respir. J., 10: pp. 523-1529 (1997).

Adolfsson K, Enelund M, Olsson P, "On the fractional order model of viscoelasticity", Mechanics of Time-dependent materials, Springer, 9, pp. 15–34, (2005)

Weibel E.R., "Mandelbrot's fractals and the geometry of life: a tribute to Benoît Mandelbrot on his 80th birthday", in Fractals in Biology and Medicine, vol IV, Eds: Losa G., Merlini D., Nonnenmacher T., Weibel E.R., Berlin: Birkhaüser, pp. 3-16 (2005)

Ionescu C., De Keyser R., (2008) "Parametric models for characterizing respiratory input impedance", J Medical Engineering & Technology, 32(4), pp. 315-324

Hildebrandt J., (1969), "Comparison of mathematical models for cat lung and viscoelastic balloon derived by Laplace transform methods from pressure-volume data", Bulletin of Mathematical Biophysics, 31, pp. 651-667

Suki B, Yuan H., Zhang Q., Lutchen K., "Partitioning of lung tissue response and inhomogeneous airway constriction at the airway opening", J Appl. Phys. , 82, pp. 1349-1359, (1997)

Quanjer Ph.H, "Referentiewaarden", in Longfunktie Onderzoek (in Dutch), Demedts M. and Decramer M. (Ed.), Leuven:Garant, pp. 27-37, (1998)

Yuan E, Ingenito P, Suki B "Dynamic Properties of Lung Parenchyma: Mechanical Contributions of Fiber Network and Interstitial Cells". American Physiology Society, pp. 1420-1431 (1997).

Fredberg J, Stamenovic D., "On the imperfect elasticity of lung tissue", J. Appl. Physiol., 67, pp. 2408-2419, (1989)

Brewer K., Sakai H., Alencar A., Majumdar A., Arold S., Lutchen K., Ingenito E., Suki B., "Lung and alveolar wall elastic and hysteretic behaviour in rats: effects of in vivo elastase", J. Appl. Physiol., 95(5): pp. 1926-1936, (2003)

Ito S., Lutchen K., Suki B., "Effects of heterogeneities on the partitioning of airway and tissue properties in mice", J. Appl. Phys., 102(3), pp. 859-869, (2007)

Kaczka D., Ingenito E., Israel E., Lutchen K., "Airway and lung tissue mechanics in asthma: effects of albuterol", Am J Respir Crit Care Med, 159, pp. 169-178, (1999)

Hall G., Hantos Z., Petak F., Wildhaber J., Tiller K., Burton P., Sly P., "Airway and respiratory tissue mechanics in normal infants", Am J Resp Crit Care, 162, pp. 1397-1402, (2000)

Brennan S., Hall G., Horak F., Moeller A., Pitrez P., Franzmann A., Turner S., de Klerk N., Franklin P., Winfield K., Balding E., Stick S., Sly P., "Correlation of forced oscillation technique in preschool children with cystic fibrosis with pulmonary inflammation", Thorax, 60, pp. 159-163, (2005)

Salerno F, Fust A., Ludwig M, "Stretch-induced changes in constricted lung parenchymal strips: role of extracellular matrix", Eur Resp J, 23, pp. 193-198., (2004)

Ionescu C., Segers P., De Keyser R., (in press) "Mechanical properties derived from morphological insight", in IEEE Transactions on Biomedical Engineering, 10 pages, DOI 10.1109/TBME.2008.2007807

Ionescu C., Oustaloup A., Levron F., De Keyser R., (submitted) "Geometrical and structural properties of lungs as fractals", The 15th IFAC Symposium on System Identification, St. Malo, France, 6-9 July 2009