Review Article

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TANAFFOS

A Review on Human Respiratory Modeling

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Input impedance of the respiratory system is measured by forced oscillation technique (FOT). Multiple prior studies have attempted to match the electromechanical models of the respiratory system to impedance data. Since the mechanical behavior of airways and the respiratory system as a whole are similar to an electrical circuit in a combination of series and parallel formats some theories were introduced according to this issue. It should be noted that, the number of elements used in these models might be less than those required due to the complexity of the pulmonary-chest wall anatomy. Various respiratory models have been proposed based on this idea in order to demonstrate and assess the different parts of respiratory system related to children and adults data. With regard to our knowledge, some of famous respiratory models in related to obstructive, restrictive diseases and also Acute Respiratory Distress Syndrome (ARDS) are reviewed in this article.

Key words: Respiratory impedance, Respiratory resistance, Respiratory reactance, Compliance, Respiratory modeling, Forced oscillation technique

INTRODUCTION

The evaluation of respiratory system with regards to electrical analogue (1) can resolve many problems in behavior of lungs and chest (2) that presented by Otis et al. (3) and others (4-14). Many authors assessed the resistive, inertial and elastic characteristics of respiratory system comparable to RLC electrical model (series format of resistance-inductance-capacitance) or to a resistance-mass-spring mechanical system (4-7). It should be noted that there are many designs for investigating characteristics of physical systems (15). Previous studies have shown that evaluation of respiratory function by forced oscillation technique (FOT) needs minimal patient collaboration (5, 16). Dubois et al. (5) developed the forced oscillation technique (FOT) in 1956 as a non-invasive procedure, using sinusoidal signals to the respiratory system, to calculate the impedance of the respiratory system. They utilized forced sinusoidal pressure oscillation to evaluate induced flow at the adult patients' mouth. The magnitude and phase angle of impedance of respiratory system were assessed at various frequencies (3-10 Hz) in relation to those of induced pressure and flow oscillation (5). It was shown that the respiratory system behaves in a similar way to a second-order system, such that at low frequencies the phase angle was negative because of the elasticity and compliance of the respiratory system, and at higher frequencies the phase angle reach to positive values due to the inertial characteristics of respiratory system (5).

Forced oscillation technique could be a useful method for evaluation of lung function in infants (17) and could be used in intubated patients as well (18, 19). It should be emphasized that measurements in newborns cannot be

done with adult equipment and are difficult to perform due to technical problems such as application of the test signal, apparatus dead space, and assessment of low frequencies due to high respiratory rates (17). Therefore a computer simulation of the input impedance is recommended in order to better interpret respiratory impedance measurements in newborns using various lung models (17). It is clear that oscillations can be generated by pumps or loudspeakers (5, 20, 21). The respiratory impedance could be calculated by measuring the ratio of Fourier-transformed air pressure and the rate of air flow signal at the entrance of the respiratory system (17). It should be noted that signal patterns other than sinusoidal oscillations are also utilized to measure respiratory impedance. Evaluation of lung mechanics using pulse mode was expressed by Muller and Vogel (22) in adults and Sullivan et al. (23) used short sinusoidal pulses to calculate respiratory impedance in intubated infants.

Since the mechanical behavior of respiratory system is analogous to an electrical circuit, respiratory impedance (including real and imaginary part) can be interpreted with electrical models which are comparable to the resistances, compliances, and inertances inherent to the respiratory system (5, 24, 25). Proper computational processing was applied in order to estimate respiratory model component for better detection, diagnosis, and treatment of various diseases/pathologies (26). Some studies have been accomplished in line with this issue (24, 27, 28), but further investigations are needed for forced oscillation measurements. Diong et al. (26) assessed five human respiratory models including Resistance-Inductance-Capacitance (RIC), viscoelastic, DuBois, Mead, and extended RIC models. The evaluation was performed by estimation of their parameters and estimation of error techniques. Many authors have used the DuBois method or some variation of it in order to evaluate respiratory mechanics in both humans and animals (4, 6, 7, 9, 10, 12, 29-36). Michaelson et al. (2) measured the magnitude and phase angle of total respiratory impedance in normal subjects, smokers, and those with chronic obstructive pulmonary disease (COPD) in frequency range of 3-45Hz and observed small differences in impedance between healthy subjects and smokers. However, these two groups showed the behavior similar to that of a second-order system for 0 degree phase angle in the range of 5-9 Hz, 40 degree at 20 Hz and 60 degree at 40 Hz. It is interesting to note that the phase angle in COPD group was more negative compared to those in healthy subjects and smokers for all frequencies (2). Investigations of total respiratory resistance and reactance by forced oscillation technique have been performed in patients with diffuse interstitial lung disease. Total respiratory impedance in 15 patients with restrictive lung disease was evaluated at frequency of 6Hz and showed increased values in 60% of the patients (30). It should be emphasized only a weak correlation was observed between impedance and airway resistance (30). It is interesting that three of nine patients with diffuse pulmonary disease showed increased respiratory resistance (6). Muller and Vogel assessed total respiratory resistance and reactance in frequency range of 5-30Hz in 12 patients with restrictive defects and observed variations in total respiratory resistance and reactance, similar to those of patients with COPD (37). Van Noord et al. evaluated 54 patients with interstitial lung disease by FOT in frequency range of 4-26Hz (25). The patients had no signs of airway obstruction. In patients with total lung capacity (TLC) less than 80% of expected, total respiratory reactance was diminished especially at low frequencies. However, the variation in total respiratory resistance was small. It was notable that there were no variations in total respiratory resistance or reactance in patients with TLC > 80% of expected value (25).

In the following, we briefly review the Otis et al. (3) approach for evaluation of mechanical lung behavior, and then the famous respiratory modeling related to adult and children data with regard to obstructive and restrictive diseases as well as acute respiratory distress syndrome (ARDS).

OTIS APPROACH TO LUNG FUNCTION

Rohrer showed that volume-elastic and flow-resistive properties of lungs can be evaluated by dividing lung

pressures to static and dynamic components (38). A similar expression was utilized by Otis et al. between pressure, volume and flow according to equation 1 (39).

$$\Delta P = KelV + K1\dot{V} + K2\dot{V}^2 \quad (1)$$

ΔP indicates the pressure difference across the lung, Kel is the ratio of variation of pressure to the variation of volume (V) when no flow exist, and the other variables explain the pressure-flow properties of the airway and tissue resistance in the span of lung volume, V, and $\dot{V}$ is the flow rate (39). Otis et al. stated that lungs can consider as a system with a single volume-elastic and a single flow resistance unit (3). However in some situations it is not convenient to utilize this simple model, but it can be perceived for any single pulmonary pathway in the lungs region (3). Otis et al. modeled the behavior of a single pathway and illustrated it by a volume-elastic part having compliance and a resistance in series configuration (Figure 1a). Therefore, at any time the total pressure across the system can be expressed by ΔP according to equation 2:

$$\Delta P = P_1 + P_2 = \frac{V}{C} + R\dot{V} \quad (2)$$

In this theory, driving pressure is restricted to a sine wave and considered as the equation 3 to solve the equation 2 (3).

$$\Delta P = \Delta P_m \sin(2\pi ft) \quad (3)$$

So flow can be calculated by equation 4:

$$\dot{V} = \dot{V_m} \sin(2\pi ft + \theta) \quad (4)$$

Where

$$V_m = \frac{\Delta P_m}{\sqrt{R^2 + \left(\frac{1}{2\pi fRC}\right)^2}} \quad (5)$$

$$\theta = \tan^{-1}\frac{1}{2\pi fRC} \quad (6)$$

RC is the time constant of the system (3). Otis et al. explained that increasing of compliance, frequency, and resistance decreases the phase angle between driving pressure and flow (3). Therefore for a system with no resistance (purely elastic) phase angle would be 90 degrees and for a system with no elastance (infinite compliance) phase angle would be 0 degree. It should be noted that at very high and low frequencies the phase angle could reach 0 and 90 degrees respectively (3). In a system with two or more separate pathways that are arranged in parallel (figure1b), if separate impedances operate in the same phase with each other, the total impedance of the system is expressed according to equation 7.

$$\frac{1}{Z} = \frac{1}{Z_1} + \frac{1}{Z_2} \quad (7)$$

Where Z_1 and Z_2 are each pathway's impedance in parallel configuration. This proves that if the time constants of the individual pathways are the same, the variation of impedance with frequency is the same in different pathways. However, if the individual pathways have different time constants the flows will be out of phase with each other due to different phase angles between flow and pressure (3).

It should be emphasized that the simple model represented in figure 1a can illustrate the mechanical behavior of the lungs when the time constants of each pathway are equal because effective resistance and compliance of the system will be the same for all frequencies (3).

Otis et al. showed that pulmonary compliance in normal young adults does not change over a wide range of respiratory rates therefore the time constants for different pathways were noticeable the same in normal lungs and the distribution of ventilation was independent of the respiratory rate (3). However, pulmonary compliance declined with increasing respiratory rate in normal subjects with induced bronchospasm and in patients with asthma and emphysema (3).

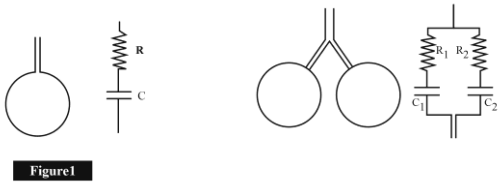

Figure1

(a) (b)

Figure1. Comparision between (a) a single pulmonary pathway (resistor and condenser are in series format) and (b) two pulmonary pathways(two series of resistor and condenser are in parallel format), with electrical circuits (3).

RESPIRATORY IMPEDANCE MODELING

Below famous respiratory models related to obstructive and restrictive diseases, as well as ARDS are reviewed:

1- RC Model

In this simple model airway resistance (R in cmH2O/L/s) and alveolar compliance (C in L/cmH2O) are assigned as a simple RC circuit (Figure 2a) with impedance (Z) calculated by equation 8 (17):

$$Z = R - \frac{j}{\omega C} \qquad (8)$$

Where ω is the angular frequency in radians/second. The RC model is recommend for tidal breathing measurements, but is not proper for breathing at higher respiratory rates (17).

2- RIC Model

In the RIC model lung inertance (*I* in cmH2O/L/s2) is added to the RC model (Figure 2b) with impedance (Z) calculated by equation 9 (27):

$$Z = R + j\left(wI - \frac{1}{wC}\right) \qquad (9)$$

3- Extended RIC model

This model was introduced as an improved version of the RIC model and is recommend by Woo et al. (40). The added peripheral resistance is in parallel with the compliance (Figure2c), which can lead to the frequency dependence of real impedance. It can also indicate the resistance produced by the small airways (26). The extended RIC model is called the DuBois model when I_t and C_t approach zero and infinity, respectively, and is called the Mead model when C_l and C_w approach infinity and Ce approaches zero (26). In the extended RIC model impedance (Z) is calculated by equation 10 (27):

$$Z = R + \frac{R_P}{1 + (\omega R_P C)^2} + j\left(wI - \frac{\omega R_P^2 C}{1 + (\omega R_P C)^2}\right) \qquad (10)$$

4- Mead Model

This model includes seven parameters: Inertance (*I*), central and peripheral resistances (*Rc* and *Rp*), lung, chest wall, bronchial tube, and extrathoracic compliances (*Cl*, *Cw*, *Cb*, *Ce*), which are used for lung and chest wall modeling (17) as shown in Figure 2d. This model explains various mechanical behaviors of the lungs and chest wall (17). Total impedance (Z) is calculated by equation 11 (17):

$$Z = \frac{-j}{\omega C_e} || Z_m \qquad (11a)$$

$$Z_m = \frac{R_P C_l^2}{\omega^2 R_P^2 C_b^2 C_l^2 + (C_b + C_l)^2} + R_C + j\left(-\frac{\omega^2 R_P^2 C_b C_l^2 + C_b + C_l}{\omega[\omega^2 R_P^2 C_b^2 C_l^2 + (C_b + C_l)^2]} + \omega I - \frac{1}{\omega C_w}\right) = R_m + jX_m \qquad (11b)$$

$$R_e(Z) = \frac{R_m}{1 - 2\omega C_e X_m + \omega^2 C_e^2 (R_m^2 + X_m^2)} \qquad (11c)$$

$$I_m(Z) = \frac{X_m - \omega C_e (R_m^2 + X_m^2)}{1 - 2\omega C_e X_m + \omega^2 C_e^2 (R_m^2 + X_m^2)} \qquad (11d)$$

5- Dubois Model

This model was introduced by Dubois et al (5). Airway, tissue, and alveolar properties are separated into various segments (Figure 2e). DeBois model includes airway and tissue resistance (R_{aw}, R_t), airway and tissue inertance (I_{aw}, I_t), and tissue and alveolar compliance (C_t, C_g). Impedance (Z) is expressed by equation 12 (27):

$$Z = R_{aw} + j\omega I_{aw} + \frac{R_t C_t^2 \omega^2}{(C_g C_t I_t)^2 \omega^6 + \left[C_g C_t \left(C_g C_t R_t^2 - 2I_t (C_g + C_t)\right)\right]\omega^4 + (C_g + C_t)^2 \omega^2} - \frac{j\omega\left[C_g C_t^2 I_t^2 \omega^4 - C_t\left(2C_g I_t + C_t I_t - C_g C_t R_t^2\right)\omega^2 + (C_g + C_t)\right]}{(C_g C_t I_t)^2 \omega^6 + \left[C_g C_t \left(C_g C_t R_t^2 - 2I_t (C_g + C_t)\right)\right]\omega^4 + (C_g + C_t)^2 \omega^2} \qquad (12)$$

6- Viscoelastic Model

In the viscoelastic model the human respiratory system is modeled based on overall airway resistance (R_{aw}), static compliance (C_s), and viscoelastic tissue resistance and compliance (R_{ve}, C_{ve}) (Figure 2f) (28). Impedance is calculated according to equation 13 (27):

$$Z = R_{aw} + \frac{R_{ve}}{1 + (\omega R_{ve} C_{ve})^2} - j\left(\frac{1}{\omega C_s} + \frac{\omega R_{ve}^2 C_{ve}}{1 + (\omega R_{ve} C_{ve})^2}\right) \qquad (13)$$

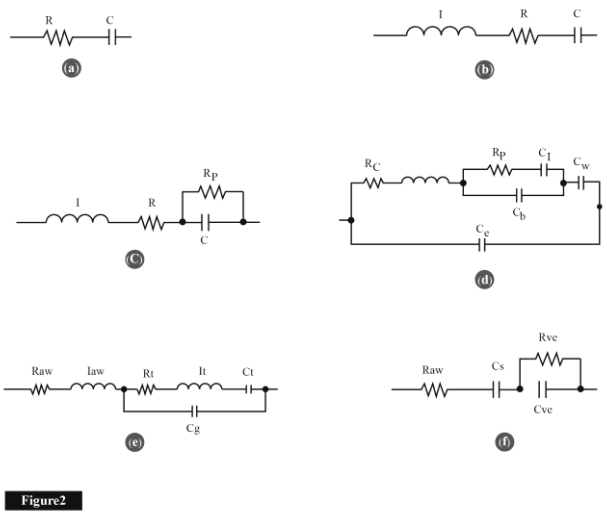

Figure2

Figure 2. Illustration of Six respiratory models. (a) RC model, (b) RIC model, (c) Extended RIC model, (d) Mead model, (e) DuBois model, (f) Viscoelastic model (27).

Schmidt et al. evaluated the RC, the RIC (figure 3a, 3b) and the Mead models in infants and explained that pulmonary inhomogeneity in lung mechanics cannot be assessed by a one-compartment model (17). .Peripheral obstruction of the airways or restriction on lung elasticity can generate uneven alveolar distribution that is well explained by the two-compartment model illustrated in figure 3c. The respiratory impedance $Z_{rs}(j\omega)$ expressed by this model is described according to equation 14 with the real and imaginary parts (17).

$$Z_{rs}(j\omega) = R_c + j\omega I + \left[R_{P1} + \frac{1}{(j\omega C_{P1})}\right] \| \left[R_{P2} + \frac{1}{(j\omega C_{P2})}\right] (14a)$$

$$R_e(Z_{rs}) = \frac{\omega^2 T_{P1} T_{P2}(T_{P1}C_{P2} + T_{P2}C_{P1}) + T_{P1}C_{P1} + T_{P2}C_{P2}}{\omega^2 C_{P1}^2 C_{P2}^2 (R_{P1} + R_{P2})^2 + (C_{P1} + C_{P2})^2} + R_C (14b)$$

$$I_m(Z_{rs}) = -\frac{\omega^2 (T_{P1}^2 C_{P2} + T_{P2}^2 C_{P1}) + C_{P1} + C_{P2}}{\omega[\omega^2 C_{P1}^2 C_{P2}^2 (R_{P1} + R_{P2})^2 + (C_{P1} + C_{P2})^2]} + \omega I (14c)$$

$$Z_{rs}(j\omega) = \frac{1}{j\omega C_e} || Z_m (14d)$$

Where *T*p1 = *R*p1 ·Cp1 and *T*p2 = *R*p2 ·Cp2.

In the Mead model (Figure 3d) extrathoracic compliance (Ce) by the mouth and the face mask, the chest wall characteristics, leakage of air around face masks or endotracheal tubes can assess (17). Schmidt et al. (17) explained that in healthy full-term newborns, as the imaginary part of impedance in RC model (as the one-compartment model) is not sufficiently stated for higher respiratory rates and since there is no resonant frequency, the RC model is not proper for modeling the respiratory impedance. The RIC model (one-compartment model) introduces a convenient expression of the respiratory impedance and this model is well described for simulating improvement and growth of the lung. The two-compartment model is usually appropriate for explaining pulmonary inhomogeneity (17). Three asthmatic children (aged 6.5–9 years) and one normal child (aged 7 years) were evaluated by Diong et al. in order to compare the five models of respiratory impedance (RIC, viscoelastic, DuBois, Mead and the extended RIC model) (26). The Mead model illustrated the best fit but the overestimation of lung compliance Cl and chest wall compliance Cw (means of 5,129 L/cmH2O and 1,064 L/cmH2O, respectively) were observed in this model (26). They also stated that the behavior of extended RIC model was slightly inferior to that of the DuBois model and noticeably better than the RIC model (26).

Diong et al. used the IOS data for five adults with mild obstructive lung disease (bronchiectasis) and five normal adults (adult cohort 1 data set) to analyze the real impedance ZR, and the imaginary impedance ZX at discrete frequencies of 5, 10, 15, 20, 25, and 35 Hz (26). They also evaluated another group to estimate of parameters models, including 105 adults (expressed as cohort 2) with respiratory disorder of both obstructive and restrictive disease; consist of asthma, chronic obstructive pulmonary disease (COPD) and sarcoidosis. While Mead model can reach to minimal errors, overestimation of lung compliance Cl was observed for patients with mild airflow obstruction. This behavior is shown for chest wall compliance Cw as well. It is interesting that the R (is similar to central airway resistance) and the Rp values in the extended RIC model better correspond with the expected values for patients with mild airflow obstruction. Furthermore, the C value calculated by the extended RIC model is nearly in line with the capacitance of the small

airways in patients with mild airflow obstruction (26). Because reactance (ZX) is most sensitive to small airway obstruction in patients with chronic airflow obstruction it is obvious that this parameter is the essential parameter and should not be ignored while evaluating various respiratory models (26). Diong et al. concluded that in comparison of respiratory models, while the DuBois model can generate the second lowest mean total error, the reactance error observed in the extended RIC model was much lower, which can be beneficial for this model (26).

For five healthy adults and cohort 2 patient data, Diong et al. (26) showed that the Mead model obtained the lowest mean total error value and the DuBois model had the second lowest level, while the viscoelastic model yielded the worst fit and noticeable overestimations of lung compliance Cl and chest wall compliance Cw were observed when evaluated the Mead model (26).

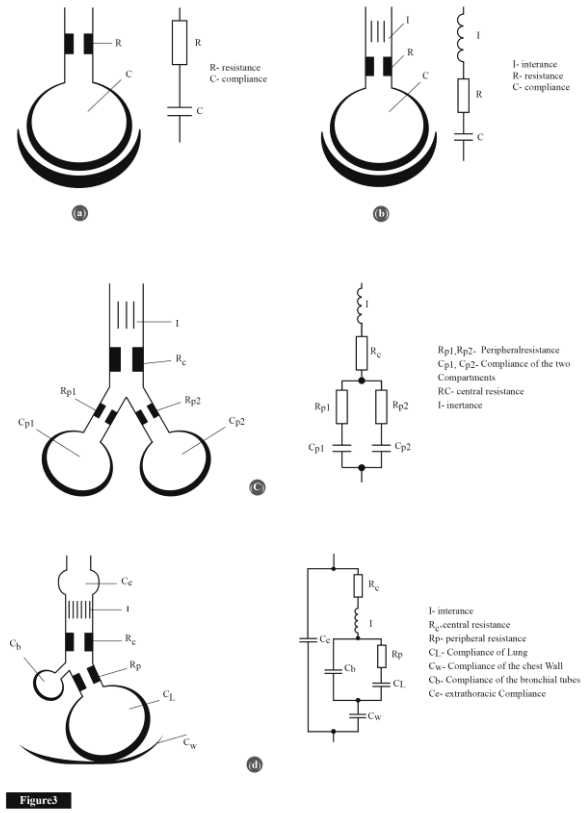

Figure 3. Linear lung models used for simulation of input impedance: (a) RC model, (b) RIC model, (c) two-compartment model and (d) lung model related to Mead model (17).

Diong et al. explained that the different ranges of R, Rp, I, and, C parameters are observed for both patients and healthy groups. So the individual parameter values that are determined by IOS data cannot discriminate between patients with obstructive lung diseases and normal group (26). Accordingly, the combination of two or more parameters can be a useful method for discrimination between patient and healthy adults (26).

It should be noted that mathematical models that are used for respiratory mechanics could be useful for different ventilator settings and supported ARDS (41, 42). The proposed models might be useful for obtaining of limited information such as flow rate and airway pressure in real time situation at the bedside(43). In ARDS patients' alveolar recruitment (44) and alveolar distension effects are important. Obtaining these data requires invasive procedures and imaging that may not be practical in monitoring therapy so simulation could be presented as a non-invasive alternative (43). Hickling's model was used for patients with ARDS to assess pressure-volume properties (45). Some investigators utilized this model for various purposes such as finding the proper lung predictive airway pressure (46) and opening pressure for measurement of convenient value of positive end expiratory pressure (PEEP)(47). The pressure-dependent recruitment model (PRM) that stated by Schranz et al. (43) was a consideration of the Hickling model (45) and alveolar distention effects (48) that is based on resistance (mbar.s/ml) and compliance (ml/mbar) being present in the serial format. It should be noted that in the Hickling model(45) the lung was considered to have 30 horizontal layers in order to obtain various levels of pressure and alveolar distention explained the stiffness of lung so that with increasing pressure, the compliance reduced in exponential manner (48). Schranz et al. (43) utilized the hierarchical parameter identification (49) in order to precise initial parameters for patient-specific of PRM model. Schranz et al. illustrated that the PRM model received the observed dynamics of ARDS patients and the measured data were compatible with the PRM model (43).

They stated that the parameters used in this model can introduce the valuable information for therapy monitoring in patients with respiratory diseases (43).

CONCLUSION

In this article, several investigations that evaluated and measured the respiratory impedance were reviewed and also, with regard to our knowledge, various respiratory modelling impedance are stated for obstructive, restrictive diseases and also Acute Respiratory Distress Syndrome (ARDS).Advantage and disadvantage of several respiratory modelling were also demonstrated. It would be interesting that, some modification in respiratory modeling related to ARDS patients will be performed in our center in near future.

REFERENCES

1. Olson, H.F., Dynamical Analogies. 2nd edition ed. 1958, New York: Van Nostrand Reinhold Co.
2. Michaelson ED, Grassman ED, Peters WR. Pulmonary mechanics by spectral analysis of forced random noise. ***J Clin Invest*** 1975; 56(5):1210-30.
3. Otis AB, Mckerrow CB, Bartlett RA, Mead J, Mcilroy MB, Selver-Stone NJ, Radford EP Jr. Mechanical factors in distribution of pulmonary ventilation. ***J Appl Physiol*** 1956;8(4):427-43.
4. Brody AW, Dubois AB, Engelberg J, Nisell OI. Natural frequency, damping factor and inertance of the chest-lung system in cats. ***Am J Physiol*** 1956;186(1):142-8.
5. Dubois AB, Brody AW, Lewis DH, Burgess BF Jr. Oscillation mechanics of lungs and chest in man. ***J Appl Physiol*** 1956;8(6):587-94.
6. Fisher AB, DuBois AB, Hyde RW. Evaluation of the forced oscillation technique for the determination of resistance to breathing. ***J Clin Invest*** 1968;47(9):2045-57.
7. Grimby G, Takishima T, Graham W, Macklem P, Mead J. Frequency dependence of flow resistance in patients with obstructive lung disease. ***J Clin Invest*** 1968;47(6):1455-65.
8. Grimby G, Takishima T, Graham W, Macklem P, Mead J. Frequency dependence of flow resistance in patients with obstructive lung disease. ***J Clin Invest*** 1968;47(6):1455-65.
9. Hull WE, Long EC. Respiratory impedance and volume flow at high frequency in dogs. ***J Appl Physiol*** 1961;16:439-43.
10. Maslin, K.R. and G.F. Rowlands, A new method of measuring the impedance of the human respiratory system at moderate frequencies. 1966: Farnborough, Hants. p. 1-41.
11. Mead J. Contribution of compliance of airways to frequency-dependent behavior of lungs. ***J Appl Physiol*** 1969;26(5):670-3.
12. Rowlands, G.F., K.R. Maslin, and L.H. Hutton, Frequency response of the human breathing system, to an input oscillating pressure-wave. 1964: Farnborough, Hants. p. 1-28.
13. Shephard RJ. Dynamic characteristics of the human airway and the behavior of unstable breathing systems. ***Aerosp Med*** 1966;37(10):1014-21.
14. Vandenberg J. An electrical analogue of the trachea, lungs and tissues. ***Acta physiologica et pharmacologica neerlandica*** 1960;9(3):361-85.
15. Cuenod M, Sage AP. Comparison of some methods used for process identification. ***Automatica*** 1968;4(4):235-69.
16. Smith HJ, Reinhold P, Goldman MD. Forced oscillation technique and impulse oscillometry. ***European Respiratory Monograph*** 2005;31:72.
17. Schmidt M, Foitzik B, Hochmuth O, Schmalisch G. Computer simulation of the measured respiratory impedance in newborn infants and the effect of the measurement equipment. ***Med Eng Phys*** 1998;20(3):220-8.
18. Farré R, Ferrer M, Rotger M, Navajas D. Servocontrolled generator to measure respiratory impedance from 0.25 to 26 Hz in ventilated patients at different PEEP levels. ***Eur Respir J*** 1995;8(7):1222-7.
19. Peslin R, Felicio da Silva J, Duvivier C, Chabot F. Respiratory mechanics studied by forced oscillations during artificial ventilation. ***Eur Respir J*** 1993;6(6):772-84.
20. Michaelson ED, Grassman ED, Peters WR. Pulmonary mechanics by spectral analysis of forced random noise. ***J Clin Invest*** 1975;56(5):1210-30.

21. Sly PD, Hayden MJ, Peták F, Hantos Z. Measurement of low-frequency respiratory impedance in infants. ***Am J Respir Crit Care Med*** 1996;154(1):161-6.
22. Müller E, Vogel J. Modelling and parameter estimation of the respiratory parameters using oscillatory impedance data and results of modelling. ***Bull Eur Physiopathol Respir*** 1980;16:189-90.
23. Sullivan KJ, Durand M, Chang HK. A forced perturbation method of assessing pulmonary mechanical function in intubated infants. ***Pediatr Res*** 1991;29(1):82-8.
24. Peslin R, Papon J, Duviver C, Richalet J. Frequency response of the chest: modeling and parameter estimation. ***J Appl Physiol*** 1975;39(4):523-34.
25. van Noord JA, Clément J, Cauberghs M, Mertens I, Van de Woestijne KP, Demedts M. Total respiratory resistance and reactance in patients with diffuse interstitial lung disease. ***Eur Respir J*** 1989;2(9):846-52.
26. Diong B, Nazeran H, Nava P, Goldman M. Modeling human respiratory impedance. Comparing the best method with the least estimation errors. ***IEEE Eng Med Biol Mag*** 2007;26(1):48-55.
27. Baswa S, Nazeran H, Nava P, Diong B, Goldman M. Evaluation of respiratory system models based on parameter estimates from impulse oscillometry data. ***Conf Proc IEEE Eng Med Biol Soc*** 2005;3:2958-61.
28. Lutchen KR, Costa KD. Physiological interpretations based on lumped element models fit to respiratory impedance data: use of forward-inverse modeling. ***IEEE transactions on biomedical engineering*** 1990;37(11):1076-86.
29. Atlan G, Varène P, Jacquemin C, Pouliquen R, Boisvieux JF, Richalet J. Critical study of forced oscillation methods in respiratory mechanics. ***Bull Physiopathol Respir (Nancy)*** 1971;7(1):63-80.
30. Obol BJ. Tests of ventilatory function not requiring maximal subject effort. II. The measurement of total respiratory impedance. ***Am Rev Respir Dis*** 1968;97(5):868-79.
31. Dubois AB, Ross BB. A new method for studying mechanics of breathing using cathode ray oscillograph. ***Proc Soc Exp Biol Med*** 1951;78(2):546-9.
32. Goldman M, Knudson RJ, Mead J, Peterson N, Schwaber JR, Wohl ME. A simplified measurement of respiratory resistance by forced oscillation. ***J Appl Physiol*** 1970;28(1):113-6.
33. Grimby G. Measurement of respiratory resistance with forced oscillations. ***In Scandinavian Journal of Clinical & Laboratory Investigation*** 1969 Jan 1 (p. 37).
34. Hyatt RE, Zimmerman IR, Peters GM, Sullivan WJ. Direct writeout of total respiratory resistance. ***J Appl Physiol*** 1970;28(5):675-8.
35. Sharp JT, Henry JP, Sweany SK, Meadows WR, Pietras RJ. Total Respiratory Interance and its Gas and Tissue Components in Normal and Obese Men. ***J Clin Invest*** 1964;43:503-9.
36. Zechman FW Jr, Peck D, Luce E. Effect of vertical vibration on respiratory airflow and transpulmonary pressure. ***J Appl Physiol*** 1965;20(5):849-54.
37. MUller E, Vogel J. Messung und Modellinterprctation neurer atemm echanischer Parameter. Z Erkrank. Atm Org. 1981;157:340-4.
38. Rohrer F. Flow resistance in human air passages and the effect of irregular branching of the bronchial system on the respiratory process in various regions of the lungs. ***Arch Ges Physiol*** 1915;162:225-99.
39. Otis AB, Fenn WO, Rahn H. Mechanics of breathing in man. ***J Appl Physiol*** 1950;2(11):592-607.
40. Woo T, Diong B, Mansfield L, Goldman M, Nava P, Nazeran H. A comparison of various respiratory system models based on parameter estimates from impulse oscillometry data. ***Conf Proc IEEE Eng Med Biol Soc*** 2004;5:3828-31.
41. Lozano S, Möller K, Brendle A, Gottlieb D, Schumann S, Stahl CA, et al. AUTOPILOT-BT: a system for knowledge and model based mechanical ventilation. ***Technol Health Care*** 2008;16(1):1-11.
42. Sundaresan A, Chase JG, Shaw GM, Chiew YS, Desaive T. Model-based optimal PEEP in mechanically ventilated ARDS patients in the intensive care unit. ***Biomed Eng Online*** 2011;10:64.
43. Schranz C, Docherty PD, Chiew YS, Chase JG, Möller K. A time-continuous model of respiratory mechanics of ARDS patients. In World Congress on Medical Physics and

Biomedical Engineering May 26-31, 2012, Beijing, China 2013 (pp. 2166-2169). Springer Berlin Heidelberg.

44. Gattinoni L, Caironi P, Cressoni M, Chiumello D, Ranieri VM, Quintel M, et al. Lung recruitment in patients with the acute respiratory distress syndrome. ***N Engl J Med*** 2006; 354(17): 1775-86.
45. Hickling KG. The pressure-volume curve is greatly modified by recruitment. A mathematical model of ARDS lungs. ***Am J Respir Crit Care Med*** 1998;158(1):194-202.
46. Markhorst DG, van Genderingen HR, van Vught AJ. Static pressure-volume curve characteristics are moderate estimators of optimal airway pressures in a mathematical model of (primary/pulmonary) acute respiratory distress syndrome. ***Intensive care medicine*** 2004;30(11):2086-93.
47. Sundaresan A, Yuta T, Hann CE, Chase JG, Shaw GM. A minimal model of lung mechanics and model-based markers for optimizing ventilator treatment in ARDS patients. ***Comput Methods Programs Biomed*** 2009;95(2):166-80.
48. Salazar E, Knowles JH. An Analysis of Pressure-Volume Characteristics of the Lungs. ***J Appl Physiol*** 1964;19:97-104.
49. Schranz C, Knöbel C, Kretschmer J, Zhao Z, Möller K. Hierarchical parameter identification in models of respiratory mechanics. ***IEEE Trans Biomed Eng*** 2011;58(11):3234-41.