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Model-based Respiratory Mechanics to Titrate PEEP and Monitor Disease State for Experimental ARDS Subjects

Erwin J. van Drunen, Yeong Shiong Chiew, J. Geoffrey Chase, Bernard Lambermont, Nathalie Janssen, Thomas Desaive

Abstract— **Modelling the respiratory mechanics of mechanically ventilated (MV) patients can provide useful information to guide MV therapy. Two model-based methods were evaluated based on data from three experimental acute respiratory distress syndrome (ARDS) induced piglets and validated against values available from ventilators. A single compartment lung model with integral-based parameter identification was found to be effective in capturing fundamental respiratory mechanics during inspiration. The trends matched clinical expectation and provided better resolution than clinically derived linear model metrics. An expiration time constant model also captured the same trend in respiratory elastance. However, the assumption of constant resistance and a slightly higher fitting error results in less insight than the single compartment model. Further research is required to confirm its application in titrating to optimal MV settings.**

I. Introduction

Modelling the respiratory mechanics of mechanically ventilated (MV) patients suffering from acute respiratory distress syndrome (ARDS) potentially provides a non-invasive method to obtain clinically and physiologically useful information to guide MV therapy [1-4]. Clinicians offer a supportive environment to ARDS patients by applying positive end expiratory pressure (PEEP). It is hypothesised that monitoring model-based respiratory mechanics throughout treatment for an ARDS patient in real-time will provide unique descriptions of the patient's disease progression, and response to MV [5-8].

Two model-based approaches are investigated on their ability to capture the respiratory mechanics of experimental ARDS subjects. One model uses only inspiration data and the other only expiration data. The inspiration portion of the breathing cycle can only be used if the subject/patient is fully sedated. For spontaneously breathing (SB) subjects/patients, oesophageal pressure measurements are required. However, it is hypothesised that expiration is primarily or completely passive, regardless of whether the subject/patient is sedated or SB. Determining lung parameters for a SB subject/patient without additional measuring tools will open up the clinical applicability of a model-based approach to guiding MV.

E. J. D.[a] (erwin.vandrunen@pg.canterbury.ac.nz) Corresponding Author,
Y. S. C.[a] (yeong.chiew@pg.canterbury.ac.nz),
J. G. C.[a] (geoff.chase@canterbury.ac.nz),
B. L.[b] (b.lambermont@chu.ulg.ac.be),
N. J.[b] (njanssen@chu.ulg.ac.be),
T. D.[c] (tdesaive@ulg.ac.be).

[a] University of Canterbury, Christchurch, 8041, New Zealand
[b] University Hospital of Liège, Liège, Belgium
[c] University of Liège, Liège, Belgium

II. Methods

A. Inspiration: Single Compartment Lung Model

During controlled positive pressure ventilation, the most commonly used model in clinical practice is the single compartment linear lung model [9]:

$$P_{aw}(t) = R_{rs} \times Q(t) + E_{rs} \times V(t) + P_0 \quad (1)$$

where P_{aw} is the airway pressure, t is time, R_{rs} is the conducting airway resistance, Q is the air flow, E_{rs} is the elastic property of the lung, V is the lung volume and P_0 is the offset pressure [10]. The integral-based method [11] is used to estimate values of E_{rsIB} (elastance) and R_{rsIB} (resistance) that best fit Equation 1. Integral-based parameter identification is similar to multiple linear regression where using integrals increases robustness to noise [11, 12]:

$$\int P_{aw}(t) = R_{rsIB} \times \int Q(t) + E_{rsIB} \times \int V(t) + \int P_0 \quad (2)$$

The application of this model is limited to fully sedated subjects/patients dependant on MV. SB subjects/patients have individual breathing efforts aside from ventilator support, altering the respiratory mechanics [13, 14].

B. Expiration: Time Constant Model

Expiration is effectively the passive (ventilator applied pressure = $P_0 \approx$ PEEP) unloading of a capacitor over a resistance. Thus, some of the energy provided by the ventilator during inspiration is stored in the form of elastic extension of the lung and chest wall, and is unloaded via the bronchial and tube resistance [15, 16]. The system time constant, τ in expiratory flow data is hypothesised to capture the subject's/patient's disease state. Thus, in expiration, Equation 1 becomes:

$$PEEP = R_{rs} \times Q(t) + E_{rs} \times \int_0^t Q(\varphi)\, d\varphi + PEEP \quad (3)$$

Differentiating Equation 3 yields:

$$0 = R_{rs} \times \frac{dQ(t)}{dt} + E_{rs} \times Q(t) \quad (4)$$

Dividing Equation 4 by the resistance, R_{rs} yields:

$$\frac{dQ(t)}{dt} + \frac{E_{rs}}{R_{rs}} \times Q(t) = 0 \quad (5)$$

Solving this differential equation yields:

$$Q(t) = Q_{\max} e^{-t/\tau} \quad (6)$$

where Q_{max} is the value of maximum expiratory flow. As the lung becomes stiffer due to ARDS, the value of τ is expected to decrease where $\tau = 1/K = R_{rs}/E_{rs}$. If the resistance is assumed constant [12], then K is directly proportional to E_{rs}. K is determined during expiration and may be used to capture ARDS disease progression in both SB and sedated subjects/patients assuming the expiration process is similar.

C. Experimental Data

Three experimental ARDS piglets were ventilated using Engström CareStation ventilators (Datex, General Electric Healthcare, Finland) with a volume controlled, square flow profile. The subjects underwent two experimental phases. Phase 1 was a progression from a healthy sedated state to an oleic acid induced ARDS state at a constant PEEP of 5 cmH_2O. Phase 2 was a staircase recruitment maneuver after the subject was diagnosed with ARDS.

D. Validation

The estimated parameters from the models are compared with conventional clinically derived metrics of respiratory mechanics. The Engström CareStation ventilator (Datex, General Electric Healthcare, Finland) automates a short end-inspiratory pause (EIP) during controlled MV [17-19]. The zero-flow phase during EIP omits the resistance component in Equation 1. The resulting pressure after EIP (plateau pressure, P_{plat}) can be used to estimate static ventilation elastance, E_{static} [20]. Equally, the pressure difference between peak pressure (PIP) and P_{plat} can be used to calculate airway resistance, R_{static}.

$$E_{static} = (P_{plat} - PEEP) / V_t \quad (7)$$

$$R_{static} = (PIP - P_{plat}) / Q \quad (8)$$

Both E_{static} and R_{static} can be derived directly from modern ventilators with an automated EIP feature. This feature allows model-based estimates of E_{rsIB}, R_{rsIB} and K to be compared with E_{static} and R_{static}.

III. RESULTS AND DISCUSSION

A. Fitting Errors

The model-based methods estimate values of E_{rsIB} and R_{rsIB} for inspiration data and values of K for expiration data. Median and inter-quartile (IQR) absolute percentage fitting errors relative to recorded data are reported in Table 1 for one representative subject. Overall, the single compartment model had a lower fitting error than the time constant model over both phases. However, both models were able to identify the trends and fundamental changes in respiratory mechanics as determined by the EIP method. All model errors were within likely measurement errors of 3-10%.

TABLE I. MODEL FITTING ERRORS FOR EACH METHOD

Model	Absolute Percentage Fitting Error (Median [IQR]) [%]		
	Phase 1	Phase 2	Overall
Single Compartment Lung Model	2.12 [0.98-4.30]	2.58 [1.21-4.45]	2.14 [0.99-4.31]
Time Constant Model	3.96 [1.90-6.86]	2.99 [1.40-5.03]	3.92 [1.87-6.79]

B. Disease Progression – Phase 1

Disease progression was captured in this study by tracking calculated model parameters. After oleic acid injection, it was found that both the respiratory elastance and system time constant follow the same trend. Both parameters show a slow and then rapid change as ARDS develops as shown in Figure 1 for one representative subject. It is observed that E_{rs} increases with time, suggesting that the lung becomes stiffer as ARDS develops in the subject [21]. A similar trend was found when monitoring K during phase 1. Thus, K is an alternative parameter that captures the subject's disease state progression.

C. Recruitment Maneuver – Phase 2

PEEP induced recruitment is time dependant where increased values of E_{rs} and K are observed at the start of every PEEP increase. As the breathing pattern stabilises, respiratory elastance slowly decreases to a specific minimum at that PEEP level as shown in Figure 2 for one representative subject. Decrease of elastance over time to a specific minimal can be described by recruitment and/or the lung's viscoelastic properties, which cause hysteresis [22, 23].

D. Comparing Models and PEEP Titration

It was found that decreasing PEEP titration resulted in lower overall E_{rs} and K compared to increasing PEEP titration, as shown in Figure 2. When PEEP is increased to a higher level (at 20 cmH_2O), recruitment, as well as potential lung overstretching occurs. However, after PEEP is reduced, the lung remains more compliant, which is an expected response from such a maneuver. During PEEP titration E_{rs} and K drop to an overall minimum at a PEEP of 15 cmH_2O. Setting PEEP at minimum elastance theoretically benefits ventilation by maximising recruitment, reducing work of breathing and avoiding overdistension [5, 7, 8, 24]. Both models show this trend and so could potentially aid in guiding MV therapy.

Recruitment is a function of PEEP and time [25, 26]. Therefore, the true minimal E_{rs} and K can be determined after a stabilisation period is provided at each PEEP level. This study found that minimum E_{rs} and K occur at a similar PEEP in both increasing and decreasing PEEP titration. Thus, the authors hypothesise that PEEP can be titrated to a minimum E_{rs} and K either way. These results provide first insight into how the models can be used to capture relevant dynamics and subsequently guide decision making.

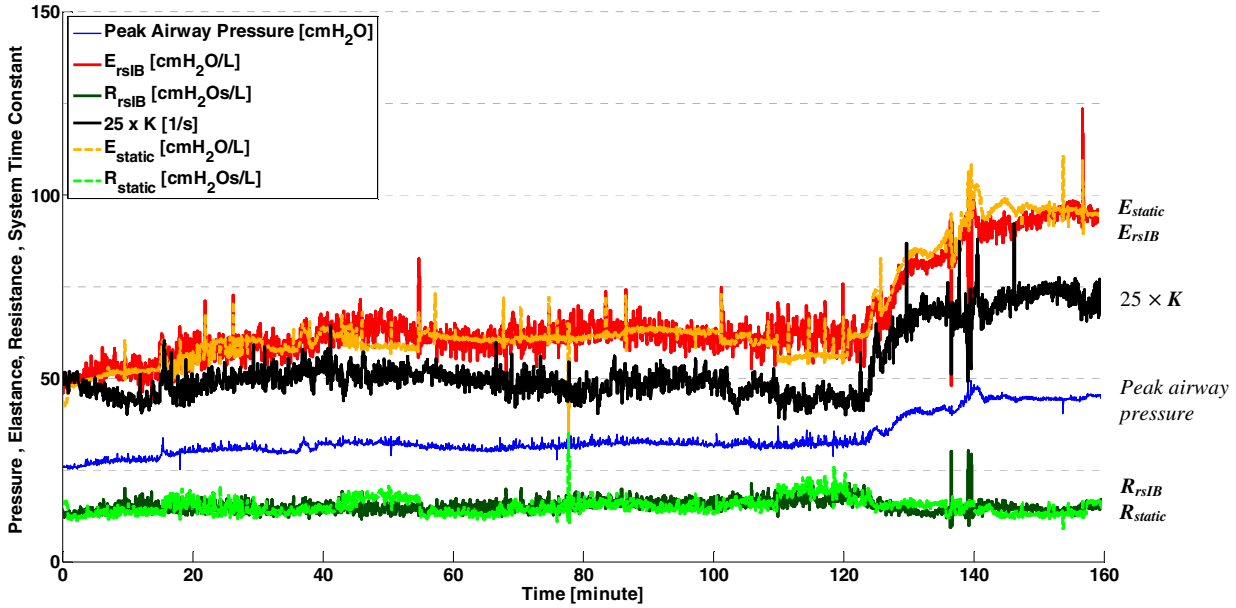

Figure 1. Respiratory system mechanics monitoring for a representative subject during Phase 1, ARDS progression. Note that values of *K* have been scaled for clarity and serve as an indication of trend comparison.

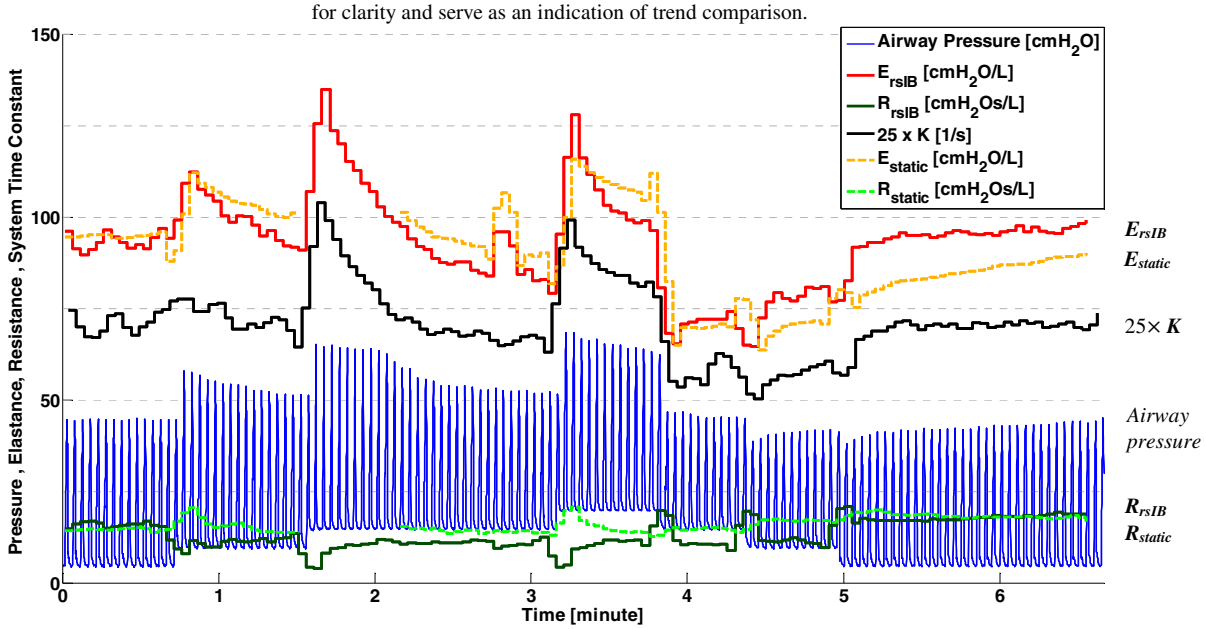

Figure 2. Respiratory system mechanics monitoring for a representative subject during Phase 2, ARDS recruitment maneuver. Note that values of *K* have been scaled for clarity and serve as an indication of trend comparison.

The single compartment lung model is limited to subjects/patients who are fully sedated and dependant on MV [13]. However, the method presented is still viable for a large portion of the most ill and costly MV patients. This method also gives more insight into the respiratory mechanics than the time constant model which lumps the respiratory resistance and elastance into one parameter, *K*. However, the values of R_{rs} and R_{static} were shown to remain relatively constant throughout both phases resulting in the similar trend observed between respiratory elastance and *K*.

E. Limitations

The finite pause at the end of inspiration enables a zero-flow phase that prolongs inspiration. The prolonged inspiration time allows the inspired tidal volume to distribute evenly in the lung and results in improved alveolar ventilation [18, 19, 27-29]. This mode of ventilation is not normally available in many ventilators and may be erroneous when the automated end inspiratory pause is too short and does not allow peak pressure to drop to the true plateau pressure [30].

Pathogenesis of ARDS animal models are more consistent where the methods of developing ARDS is known and controlled. ICU patients, in contrast, are more variable as the causes of disease are different with greater inter-patient variability in response to treatment. Thus, the application of these two models for respiratory mechanics monitoring in human patients warrants investigation.

IV. CONCLUSION

Respiratory system mechanics vary with disease state development and in response to MV settings. A single compartment lung model with integral-based parameter identification was effective in capturing fundamental respiratory mechanics. Trends matched clinical expectation and provided better resolution than clinically derived linear metrics demonstrating robustness and potential for guiding MV therapy. An expiration time constant model also captured the same trend in respiratory elastance. However, the assumption of constant resistance and a slightly higher fitting error leads to less insight than that provided by the single compartment model. Further research is required to confirm its use in actual ARDS patients. Both methods were able to capture respiratory mechanics similar to modern ventilators, thus further validating the model-based findings and its application to titrate care.

REFERENCES

[1] A. M. Lauzon and J. H. Bates, "Estimation of time-varying respiratory mechanical parameters by recursive least squares," Journal of Applied Physiology, vol. 71, pp. 1159-1165, September 1, 1991 1991.

[2] A. Sundaresan, T. Yuta, C. E. Hann, J. Geoffrey Chase, and G. M. Shaw, "A minimal model of lung mechanics and model-based markers for optimizing ventilator treatment in ARDS patients," Computer Methods and Programs in Biomedicine, vol. 95, pp. 166-180, 2009.

[3] B. Ma and J. Bates, "Modeling the Complex Dynamics of Derecruitment in the Lung," Annals of Biomedical Engineering, vol. 38, pp. 3466-3477, 2010.

[4] A. Sundaresan and J. G. Chase, "Positive end expiratory pressure in patients with acute respiratory distress syndrome - The past, present and future," Biomedical Signal Processing and Control, vol. 7, pp. 93-103, 2011.

[5] A. Carvalho, F. Jandre, A. Pino, F. Bozza, J. Salluh, R. Rodrigues, et al., "Positive end-expiratory pressure at minimal respiratory elastance represents the best compromise between mechanical stress and lung aeration in oleic acid induced lung injury," Critical Care, vol. 11, p. R86, 2007.

[6] U. Lucangelo, F. Bernabè, and L. Blanch, "Lung mechanics at the bedside: make it simple," Current Opinion in Critical Care, vol. 13, pp. 64-72 2007.

[7] F. Suarez-Sipmann, S. H. Bohm, G. Tusman, T. Pesch, O. Thamm, H. Reissmann, et al., "Use of dynamic compliance for open lung positive end-expiratory pressure titration in an experimental study," Critical Care Medicine, vol. 35, pp. 214 - 221, 2007.

[8] B. Lambermont, A. Ghuysen, N. Janssen, P. Morimont, G. Hartstein, P. Gerard, et al., "Comparison of functional residual capacity and static compliance of the respiratory system during a positive end-expiratory pressure (PEEP) ramp procedure in an experimental model of acute respiratory distress syndrome," Critical Care, vol. 12, p. R91, 2008.

[9] J. Mead and J. L. Whittenberger, "Physical Properties of Human Lungs Measured During Spontaneous Respiration," Journal of Applied Physiology, vol. 5, pp. 779-796, June 1, 1953 1953.

[10] J. H. T. Bates, Lung Mechanics: An Inverse Modeling Approach: Cambridge University Press, 2009.

[11] C. E. Hann, J. G. Chase, J. Lin, T. Lotz, C. V. Doran, and G. M. Shaw, "Integral-based parameter identification for long-term dynamic verification of a glucose-insulin system model," Computer Methods and Programs in Biomedicine, vol. 77, pp. 259-270, 2005.

[12] Y. S. Chiew, J. G. Chase, G. Shaw, A. Sundaresan, and T. Desaive, "Model-based PEEP Optimisation in Mechanical Ventilation," BioMedical Engineering OnLine, vol. 10, p. 111, 2011.

[13] L. Brochard, G. Martin, L. Blanch, P. Pelosi, F. J. Belda, A. Jubran, et al., "Clinical review: Respiratory monitoring in the ICU - a consensus of 16," Critical Care, vol. 16, p. 219, 2012.

[14] D. Grinnan and J. Truwit, "Clinical review: Respiratory mechanics in spontaneous and assisted ventilation," Critical Care, vol. 9, pp. 472 - 484, 2005.

[15] K. Möller, Z. Zhao, C. Stahl, and J. Guttmann, "Seperate analysis of respiratory system mechanics in inspiration and expiration," in 55. GMDS-Jahrestagung, Mannheim, Germany, 2010, pp. 566-7.

[16] K. Möller, Z. Zhao, C. A. Stahl, and J. Guttmann, "On the analysis of dynamic lung mechanics separately in ins- and expiration,", IFMBE Proceedings, Chalkidiki, Greece, 2010, pp. 164-7.

[17] S. Ingelstedt, B. Jonson, L. Nordström, and S.-G. Olsson, "A Servo-Controlled Ventilator Measuring Expired Minute Volume, Airway Flow and Pressure," Acta Anaesthesiologica Scandinavica, vol. 16, pp. 7-27, 1972.

[18] S. F. Fuleihan, R. S. Wilson, and H. Pontoppidan, "Effect of Mechanical Ventilation with End-inspiratory Pause on Blood-Gas Exchange," Anesthesia & Analgesia, vol. 55, pp. 122-130, January/February 1976 1976.

[19] O. Pillet, M. L. Choukroun, and Y. Castaing, "Effects of inspiratory flow rate alterations on gas exchange during mechanical ventilation in normal lungs. Efficiency of end-inspiratory pause," CHEST Journal, vol. 103, pp. 1161-1165, 1993.

[20] K. K. Shiu and M. J. Rosen, "Is There a Safe Plateau Pressure Threshold for Patients with Acute Lung Injury and Acute Respiratory Distress Syndrome?," American Journal of Respiratory and Critical Care Medicine, vol. 173, p. 686, March 15, 2006 2006.

[21] Y. S. Chiew, T. Desaive, B. Lambermont, N. Janssen, G. M. Shaw, C. Schranz, et al., "Performance of lung recruitment model in healthy anesthetized pigs," in 2012 World Congress of Medical Physics and Biomedical Engineering, Beijing, China, 2012, pp. 1-page.

[22] S. Ganzert, K. Möller, D. Steinmann, S. Schumann, and J. Guttmann, "Pressure-dependent stress relaxation in acute respiratory distress syndrome and healthy lungs: an investigation based on a viscoelastic model," Critical Care., vol. 13, p. R199, 2009.

[23] S. Andreassen, K. L. Steimle, M. L. Mogensen, J. B. d. l. Serna, S. Rees, and D. S. Karbing, "The effect of tissue elastic properties and surfactant on alveolar stability," Journal of Applied Physiology, vol. 109, pp. 1369-1377, November 1, 2010 2010.

[24] Z. Zhao, D. Steinmann, I. Frerichs, J. Guttmann, and K. Moller, "PEEP titration guided by ventilation homogeneity: a feasibility study using electrical impedance tomography," Critical Care, vol. 14, p. R8, 2010.

[25] S. P. Albert, J. DiRocco, G. B. Allen, J. H. T. Bates, R. Lafollette, B. D. Kubiak, et al., "The role of time and pressure on alveolar recruitment," Journal of Applied Physiology, vol. 106, pp. 757-765, March 2009 2009.

[26] C. S. l. V. Barbas, G. F. J. de Matos, M. P. Pincelli, E. da Rosa Borges, T. Antunes, J. M. de Barros, et al., "Mechanical ventilation in acute respiratory failure: recruitment and high positive end-expiratory pressure are necessary," Current Opinion in Critical Care, vol. 11, pp. 18-28, 2005.

[27] S. Lindahl, "Influence of an end inspiratory pause on pulmonary ventilation, gas distribution, and lung perfusion during artificial ventilation," Critical Care Medicine, vol. 7(12), pp. 540-546, 1979.

[28] S. Baehrendtz, "The Influence of an end-inspirtory pause on fas exchange and central haemodynamics in patients with acute respiratory failure," Clinical Physiology, vol. 5, pp. 93-98, 1985.

[29] J. Devaquet, B. Jonson, L. Niklason, A.-G. Si Larbi, L. Uttman, J. Aboab, et al., "Effects of inspiratory pause on CO2 elimination and arterial PCO2 in acute lung injury," Journal of Applied Physiology, vol. 105, pp. 1944-1949, December 2008 2008.

[30] L. Barberis, E. Manno, and C. Guérin, "Effect of end-inspiratory pause duration on plateau pressure in mechanically ventilated patients," Intensive Care Medicine, vol. 29, pp. 130-134, 2003.