Open Access

Ruby Langdon*, Paul D. Docherty and Knut Möller

Inspiratory and expiratory elastance in a non-linear autoregressive model of pulmonary mechanics

DOI 10.1515/cdbme-2016-0138

Abstract: For patients with acute respiratory distress syndrome (ARDS), the use of mathematical models to determine patient-specific ventilator settings can reduce ventilator induced lung injury and improve patient outcomes. A non-linear autoregressive model of pulmonary mechanics was used to identify inspiratory and expiratory pressure-dependent elastance (E_i and E_e) as independent variables. The analysis was implemented on 19 data sets of recruitment manoeuvres (RMs) that were performed on 10 mechanically ventilated patients. At pressures $p = 15–20$ cmH_2O the agreement between E_i and E_e was low. However, E_i was a well-matched predictor of E_e for $p = 25–40$ cmH_2O, with $R^2 \geq 0.78$, and there was no significant bias in the difference between E_i and E_e. Since many other models cannot uniquely identify E_i and E_e, the outcome may provide further insight into the characteristics of ARDS lungs in sedated patients.

Keywords: autoregressive models; parameter identification; pulmonary modelling.

1 Introduction

Acute respiratory distress syndrome (ARDS) is a condition treated via mechanical ventilation in the intensive care unit (ICU). ARDS generally involves inflammation in the lungs and excess fluid in the airspaces, which increases elastance. While ventilation is necessary, it can sometimes cause ventilator induced lung injury (VILI) [1]. Excessively high airway pressure or high tidal volumes can cause distension and sometimes rupture of alveoli. Low pressures cause the cyclical opening and closing of alveoli with each breath that can damage healthy alveoli, known as atelectrauma [2].

The use of patient specific ventilator settings can help to avoid VILI [3]. As each patient and their disease state are unique, the optimal ventilator settings are patient specific. Mathematical models that describe the physiology of ARDS lungs can allow these optimal patient specific ventilator settings to be found. VILI is associated with a high mortality rate [4], thus a model that effectively describes lung behaviour and reduces the chances of VILI could significantly improve patient outcomes and reduce morbidity and mortality.

While there are a wide range of physiologically and clinically relevant models [5–7], in general these models are not able to uniquely identify inspiratory elastance E_i, and expiratory elastance E_e as independent variables. This is because the flow and volume both follow exponential decays during relaxed expiration of the sedated lung. As flow and volume are not linearly independent, single elastance and resistance terms are non-identifiable.

A nonlinear autoregressive (NARX) model of pulmonary mechanics has been described by Langdon et al. [8]. The NARX model uses basis functions to describe a pressure-dependent elastance, allowing it to describe recruitment and distension effects across recruitment manoeuvres (RMs). The model also uses time-dependent, flow-dependent terms to fit the passive lung relaxation during an inspiratory pause.

The aim of this paper is to determine the ability of the NARX model to identify independent inspiratory and expiratory elastances, and show the relationship between E_i and E_e. This will help to further validate the NARX model and its usefulness in accurately describing patient physiology.

2 Material and methods

2.1 Data

Data from a pilot clinical utilisation of respiratory elastance (CURE) software trial was used in this analysis.

***Corresponding author: Ruby Langdon,** Department of Mechanical Engineering, University of Canterbury, New Zealand, E-mail: ruby.langdon@pg.canterbury.ac.nz
Paul D. Docherty: Department of Mechanical Engineering, University of Canterbury, New Zealand, E-mail: paul.docherty@canterbury.ac.nz
Knut Möller: Institute of Technical Medicine, Furtwangen University, Germany, E-mail: moe@hs-furtwangen.de

© 2016 Ruby Langdon et al., licensee De Gruyter.
This work is licensed under the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 License.

Airway pressure and flow data were collected from ten fully sedated ARDS patients, seven of which were ventilated in pressure controlled mode, and three of which were ventilated in volume controlled mode. Patient age ranged from 18 to 88 with a mean of 50.3 years. The breathing rate was approximately 18 breaths per minute. Pressure and flow were recorded from a Puritan Bennett 840 ventilator at a sampling rate of 50 Hz. Volume was calculated from continuous integration of the flow, with compensation for volume drift to maintain a volume of zero at PEEP.

As patients often underwent multiple RMs during the trial, 19 sets of data were obtained. PEEP at the beginning of the RM varied between 8 cmH_2O and 16 cmH_2O for different patients. During each RM, PEEP was increased in steps of 2 cmH_2O. The RMs of different patients contained between four and nine PEEP step increases. The maximum pressure reached for each patient ranged between 36 cmH_2O and 52 cmH_2O.

Ethics approval for the study and use of collected data was granted by the New Zealand South Regional Ethics Committee. Informed consent was obatined from all individuals.

2.2 Respiratory models

The NARX model contains first order b-spline basis functions that describe a pressure dependent elastance, and time dependent terms that capture the pressure responses that occur due to changes in flow:

$$\begin{aligned} P_{aw}(t) &= \sum_{k=1}^{4} a_{ik} \emptyset_k \left(P_{aw_i}(t)\right) V_i(t) \\ &+ \sum_{k=1}^{4} a_{ek} \emptyset_k \left(P_{aw_e}(t)\right) V_e(t) \\ &+ \sum_{j=1}^{170} b_j \dot{V}(t_{-j}) + P_0(t) \end{aligned} \tag{1}$$

where: P_{aw_i} and P_{aw_e} are the measured inspiratory and expiratory airway pressure (cmH_2O), $\dot{V}$ is the airway flow rate (l/s), V_i and V_e are the inspiratory and expiratory volume (l), and P_0 is the end-expiratory pressure (cmH_2O). There are four first order basis-functions to be used, k is the index of a particular basis function, a_k is the coefficient for a given basis function (cmH_2O/l), and $\emptyset_k(P_{aw}(t))$ is the basis function value for a given pressure measurement. The sum of the basis functions multiplied by their a_k coefficients defines elastance. There are 170 b_j coefficients (cmH_2Os/l) that capture airway resistance, viscoelastic effects, and expiratory relaxation. The subscript $-j$ in the third term refers to the previous time samples. Thus, each $P_{aw}(t)$ is calculated from information from the previous 170 data points.

The optimal number of basis functions and b_j terms was determined in previous analyses of the NARX model fit for this data set [9].

To identify the NARX model coefficients, a linear system of equations must be generated and inverted to find:

$$\mathbf{x} = \left[a_{i1} \ \ldots \ a_{i4} \ a_{e1} \ \ldots \ a_{e4} \ b_1 \ \cdots \ b_{170} \right]^{\mathrm{T}} \tag{2}$$

where: a_{i1}–a_{i4} are the inspiratory elastance coefficients, and a_{e1}–a_{e4} are the expiratory elastance coefficients.

The inspiratory elastance coefficients are identified based on inspiratory data only, and the expiratory elastance coefficients are identified on expiratory data only. The b coefficients are identified on both inspiratory and expiratory data.

2.3 Analysis

The a_i, a_e, and b coefficients were identified for each data set. The basis functions multiplied by the a terms gives a continuous elastance across pressure between the minimum and maximum pressures present in each data set. The coefficient of determination (R^2) was calculated for the linear relationship between E_e and E_i at different pressures. Bland-Altman analysis was performed to determine any bias in the difference between E_e and E_i as pressure increased. To further quantify intra-patient versus inter-patient variability, the variance of E_i, E_e, and (E_i–E_e) were calculated. All analysis was undertaken on an i7 quad core PC with 16GB RAM using MATLAB 2014a 64 bit functions and the statistical toolbox (Mathworks, Natick, MA, USA).

3 Results

The inspiratory and expiratory elastances were determined for each of the 19 data sets. The agreement between E_i and E_e was generally poor at low pressure, and good at pressures greater than the second basis function knot. The behaviour of a typical patient is shown in Figure 1.

The relationship between E_i and E_e at various pressures is shown in Figure 2. The plot at $p = 15$ cmH_2O contains 18 data points because one data set did not contain pressures as low as 15 cmH_2O. Similarly, two data sets did not contain pressures at 40 cmH_2O or greater.

The R^2 value for the E_i to E_e linear relationship describes how well the E_i value predicts the E_e value. Figure 2 shows the strength of prediction is weak at $p = 15$ cmH_2O, but strong for $p \geq 25$ cmH_2O, with $R^2 \geq 0.78$. The 1:1 lines

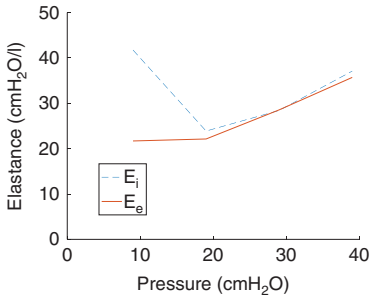

Figure 1: Inspiratory and expiratory elastance across pressure for one patient.

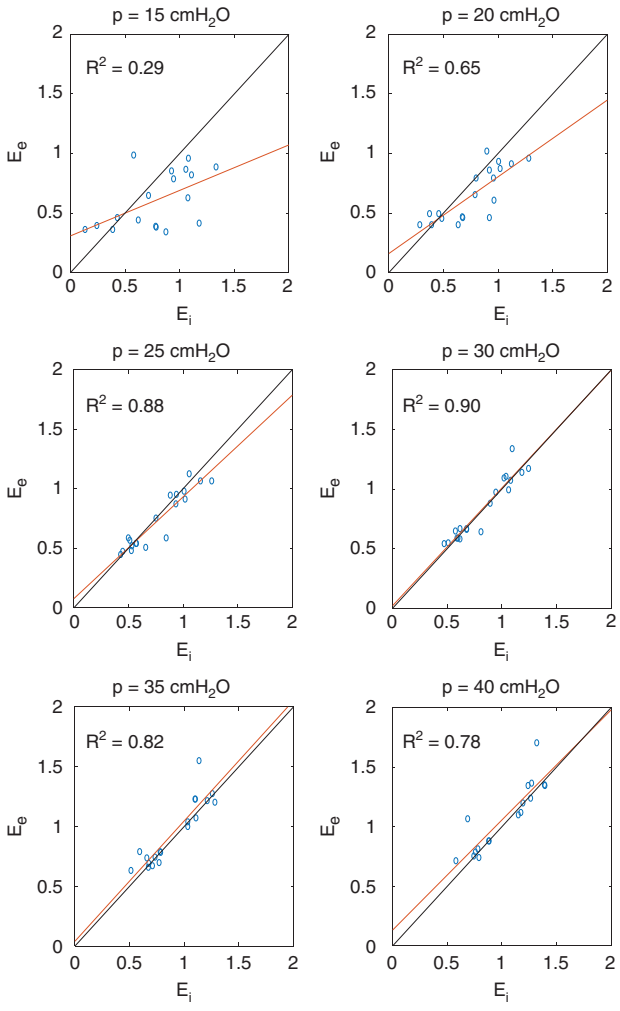

Figure 2: Expiratory elastance vs. inspiratory elastance for p = [15 20 25 30 35 40] cmH_2O. R^2 values are given for the linear relationship between E_e and E_i, plotted in red. The 1:1 line is plotted in black.

plotted plotted on Figure 2 show that there is a tendency for E_i to be $> E_e$ at low pressures, and for E_e to be slightly higher than E_i at high pressures.

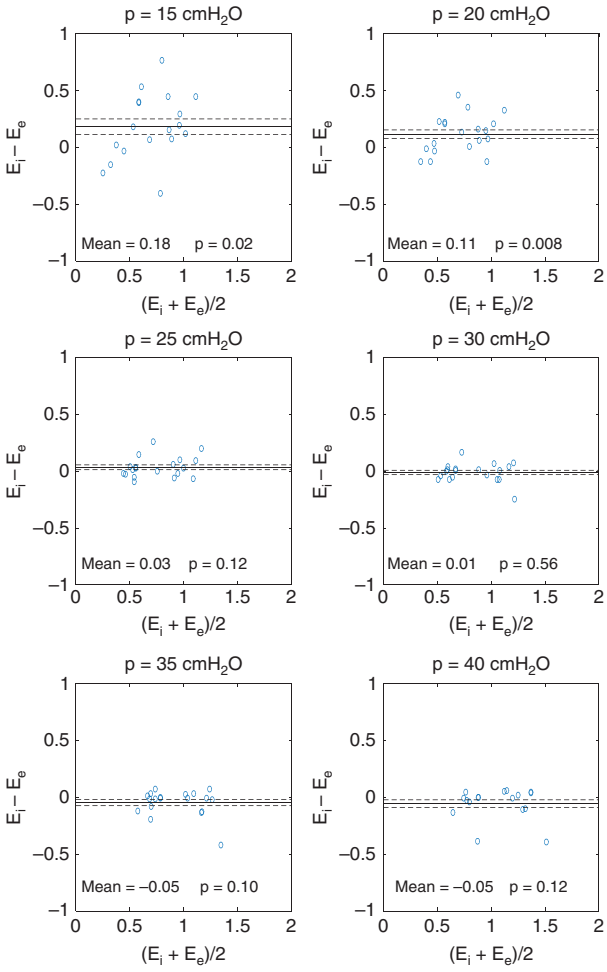

Figure 3: Bland-Altman plots for p = [15 20 25 30 35 40] cmH_2O. Solid line = the mean of the difference. Dotted lines = standard error of the mean difference.

Bland-Altman plots allow any fixed bias between E_i and E_e to be more easily observed. Figure 3 shows the Bland-Altman plots for pressures 15–40 cmH_2O. The mean and corresponding p value are specified on each plot. A p value > 0.05 indicates that the mean difference is not significantly different from zero, based on a one sample t-test, thus there is no significant difference between E_i and E_e for this pressure. The analysis found that there is a significant difference between E_i and E_e for p = 15 cmH_2O and p = 20 cmH_2O only. The bias is towards E_i being larger than E_e.

Variances of E_i, E_e, and (E_i–E_e) were calcualted to determine intra-patient versus inter-patient variability. For pressures of 20 cmH_2O and above, the variance of (E_e–E_i) was smaller than the variance of both E_i and E_e at each measured pressure. Based on the t-test, the variance of E_i and E_e were not significantly different. The variance of (E_e–E_i) was significantly smaller than the variance of

E_i (t-test, $p = 0.0007$) and significantly smaller than the variance of E_e (t-test, $p = 0.03$).

4 Discussion

This analysis shows that the NARX model is capable of identifying unique inspiratory and expiratory elastance profiles. E_i was a well-matched predictor of E_e for $p = 25$–40 cmH_2O (Figure 2). There was no significant bias in the difference between E_i and E_e for $p = 25$–40 cmH_2O (Figure 3). The intra-patient variability was significantly lower than the inter-patient variablility for $p = 20$–40 cmH_2O. Overall, this indicates that for this cohort, E_i and E_e were comparable for $25 \leq p \leq 40$ cmH_2O, and thus may be equally valuable as an indicator of patient condition.

There was low agreement between E_i and E_e at low pressures (Figure 1). E_i was a bad predictor of E_e at $p = 15$ cmH_2O. There was a significant positive bias in (E_i–E_e) at $p = 15$ cmH_2O and $p = 20$ cmH_2O. In addition, the variance of (E_i–E_e) was larger than the variance of E_e at $p = 15$ cmH_2O. The cause of this behaviour relates to the use of distinct basis functions used to define elastance. With $M = 4$, the first basis function ($\emptyset_1$) is non-zero for only the lowest third of the pressures present in the data set. Therefore $\emptyset_1$ is identified using only the volume data that exists when these low pressures are present in inspiration.

At the beginning of inspiration, the pressure rises very rapidly. There are relatively few data points here, as the gradient of the pressure increase is so steep. Thus there are relatively few data points used to identify $\emptyset_1$, compared to $\emptyset_2$, $\emptyset_3$, and $\emptyset_4$. There is not enough useful information for determining the elastance in this small portion of inspiratory data. Since the gradient of the pressure drop during expiration is shallower at lower pressures, there is more data available to identify expiratory elastance, and the issue does not occur. Therefore E_e is likely to be more reliable than E_i at low pressure using the method presented in this paper.

A similar problem with inspiratory elastance would be likely to occur if the NARX model was identified using this method on any single PEEP level, where a recruitment manoeuvre was not carried out. In this scenario, either the E_i and E_e should not be identified separately, or the E_i should not be relied on for diagnostic use.

While a strong agreement between E_i and E_e was found for $25 \leq p \leq 40$ cmH_2O, the sample size of 19 data sets is relatively small. Also, due to the limited size of the RMs for some patients, the $p = 15$ cmH_2O analysis was based on 18 data sets, and the analysis at $p = 40$ cmH_2O was based on only 17 data sets. The methods should be tested on a larger patient cohort to verify the results. A larger number of patients with RMs that reached pressures of greater than 40 cmH_2O would also allow an assessment of any possible variability in E_i and E_e at very high pressures.

Separate inspiratory and expiratory elastances may not be currently used as a diagnostic aid by clinicians. However, this analysis has shown that unique E_i and E_e values can be obtained using the NARX model. The outcomes of this type of analysis may provide further insight into sedated ARDS patient conditions that other models cannot accomplish.

Author's Statement

Research funding: The author state no funding involved. Conflict of interest: Authors state no conflict of interest. Informed consent: Informed consent has been obtained from all individuals included in this study. Ethical approval: Ethics approval for the study and use of collected data was granted by the New Zealand South Regional Ethics Committee.

References

[1] Dreyfuss D, Saumon G. Ventilator-induced lung injury. Lessons from experimental studies. Am J Respir Crit Care Med. 1998;157:294–323.

[2] Slutsky AS, Ranieri VM. Critical care medicine: ventilator-induced lung injury. N Engl J Med. 2013;369:2126.

[3] Fenstermacher D, Hong D. Mechanical ventilation: what have we learned? Crit Care Nurs Q. 2004;27:258–94.

[4] Phua J, Badia JR, Adhikari NKJ, Friedrich JO, Fowler RA, Singh JM, et al. Has mortality from acute respiratory distress syndrome decreased over time?: a systematic review. Am J Respir Crit Care Med. 2009;179:220–7.

[5] Chiew YS, Chase JG, Shaw G, Sundaresan A, Desaive T. Model-based PEEP optimisation in mechanical ventilation. BioMed Eng Online. 2011;10:111.

[6] van Drunen E, Chiew YS, Chase J, Shaw G, Lambermont B, Janssen N, et al. Expiratory model-based method to monitor ARDS disease state. BioMed Eng Online. 2013;12:57.

[7] Sundaresan A, Yuta T, Hann CE, Chase GJ, Shaw GM. A minimal model of lung mechanics and model-based markers for optimizing ventilator treatment in ARDS patients. Comput Methods Programs Biomed. 2009;95:166–180.

[8] Langdon R, Docherty PD, Chiew Y-S, Möller K, Chase JG. Use of basis functions within a non-linear autoregressive model of pulmonary mechanics. Biomed Signal Proces. 2016;27:44–50.

[9] Langdon R, Docherty PD, Chiew YS, Damanhuri NS, Chase JG. Implementation of a non-linear autoregressive model with modified Gauss-Newton parameter identification to determine pulmonary mechanics of respiratory patients that are intermittently resisting ventilator flow patterns. 9th IFAC Symposium on Biological and Medical Systems. 2015.