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Extrapolation of a non-linear autoregressive model of pulmonary mechanics

Ruby Langdon[a,*], Paul D. Docherty[a], Yeong Shiong Chiew[a,b], J. Geoffrey Chase[a]

[a] Department of Mechanical Engineering, University of Canterbury, Christchurch, New Zealand
[b] School of Engineering, Monash University Malaysia, Bandar Sunway, Malaysia

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ABSTRACT

For patients with acute respiratory distress syndrome (ARDS), mechanical ventilation (MV) is an essential therapy in the intensive care unit (ICU). Suboptimal PEEP levels in MV can cause ventilator induced lung injury, which is associated with increased mortality, extended ICU stay, and high cost. The ability to predict the outcome of respiratory mechanics in response to changes in PEEP would thus provide a critical advantage in personalising and improving care. Testing the potentially dangerous high pressures would not be required to assess their impact.

A nonlinear autoregressive (NARX) model was used to predict airway pressure in 19 data sets from 10 mechanically ventilated ARDS patients. Patient-specific NARX models were identified from pressure and flow data over one, two, three, or four adjacent PEEP levels in a recruitment manoeuvre. Extrapolation of NARX model elastance functions allowed prediction of patient responses to PEEP changes to higher or lower pressures.

NARX model predictions were more successful than those using a well validated first order model (FOM). The most clinically important results were for extrapolation up one PEEP step of 2 cmH_2O from the highest PEEP in the training data. When the NARX model was trained on one PEEP level, the mean RMS residual for the extrapolation PEEP level was 0.52 (90% CI: 0.47–0.57) cmH_2O, compared to 1.50 (90% CI: 1.38–1.62) cmH_2O for the FOM. When trained on four PEEP levels, the NARX result was 0.50 (90% CI: 0.42–0.58) cmH_2O, and was 1.95 (90% CI: 1.71–2.19) cmH_2O for the FOM.

The results suggest that a full recruitment manoeuvre may not be required for the NARX model to obtain a useful estimate of the pressure waveform at higher PEEP levels. The methodology could thus allow clinicians to make informed decisions about ventilator PEEP settings while reducing the risk associated with high PEEP, and subsequent high peak airway pressures.

1. Introduction

Acute respiratory distress syndrome (ARDS) requires mechanical ventilation (MV) in the intensive care unit (ICU) [1,2]. ARDS can involve elements of inflammation in the lungs and fluid accumulation in airways, and has a high mortality rate [3]. Positive end-expiratory pressure (PEEP) is a ventilator setting used to prevent de-recruitment of lung units at the end of expiration. However, suboptimal PEEP settings can lead to ventilator induced lung injury (VILI) [4,5]. VILI in turn increases mortality and morbidity of ARDS patients [4]. When PEEP levels are too high, over distension of alveoli may cause VILI. Low PEEP levels are known to cause atelectrauma, and thus further damage. Hence, setting optimal PEEP levels is necessary to minimise the incidence of VILI, and reduce morbidity and mortality [6].

Physiological modelling can be used to capture patient-specific pulmonary mechanics to aid determination of optimal ventilator settings for each patient [7,8]. There have been a wide range of physiologically and clinically relevant models [9–14]. Models of pulmonary mechanics range from very simple models [15] to complex descriptive models [16]. Both modelling strategies have offered clinical benefit in different situations. However, simpler models are limited in their abilities to describe all respiratory mechanics, and more complex models can suffer from non-identifiability [14,17]. Predicting pulmonary behaviour beyond the clinical conditions for which a model was identified or trained requires a highly robust, yet descriptive, model that can be evaluated on the data typically available in real time. Overall, while there is debate around which models are suitable for various modes of ventilation,

* Corresponding author.
E-mail address: ruby.langdon@pg.canterbury.ac.nz (R. Langdon).

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there is also a real lack of research on the extrapolation of any such models across PEEP levels.

We have previously proposed a nonlinear autoregressive (NARX) model of respiratory mechanics [18–20]. The NARX model has successfully captured airway pressure waveforms in ARDS patients during recruitment manoeuvres [18,20]. The model uses pressure-dependent basis functions to capture pulmonary system elastance, and multiple time-dependent resistance coefficients to capture lung relaxation and viscoelastic effects.

The aim of this research is to determine the ability of the NARX model to extrapolate and predict the effects of changes in PEEP settings beyond those for which the model was trained. If successful, it would allow clinicians to determine whether or not to alter, and in particular raise, the PEEP setting for a particular patient without the need for actually trialling these alternative settings. Hence, the ability to extrapolate and predict the outcomes of changes could reduce the risk of testing higher, or lower, PEEP levels and thus reduce the incidence of VILI, which overall would improve patient outcomes.

2. Materials and methods

2.1. Data

Data from a pilot Clinical Utilisation of Respiratory Elastance (CURE) software trial [21] was used in this analysis. Airway pressure and flow data were collected from ten fully sedated ARDS patients. Seven patients were ventilated in pressure controlled mode, and three were ventilated in volume controlled mode. The patient age ranged from 18 to 88, with a mean of 55 years. The breathing rate was approximately 3.3 s, with no end-expiratory pause. 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 via spline correction to maintain a volume of zero at PEEP.

As patients sometimes underwent multiple recruitment manoeuvres during the trial, 19 sets of data were obtained. PEEP at the beginning of the recruitment manoeuvre varied between 8 cmH_2O and 16 cmH_2O for different patients. During a recruitment manoeuvre, PEEP was increased in steps of 2 cmH_2O. The recruitment manoeuvres of different patients contained different numbers of PEEP steps. All 19 data sets contained at least four PEEP step increases, so the first five PEEP levels of each data set were used in this analysis. This limit was chosen to allow a concise and simple analysis.

2.2. Respiratory models

The first order model (FOM) of pulmonary mechanics forms the basis of the NARX model. The FOM contains single resistive and elastic components:

$$P(t) = R\dot{V}(t) + EV(t) + P_0(t) \tag{1}$$

where P is the measured airway pressure (cmH_2O), t is time (s), R is the airway resistance (cmH_2Os/L), $\dot{V}$ is the airway flow rate (L/s), E is the pulmonary elastance (cmH_2O/L), V is the inspired volume (L), and P_0 is the offset pressure (cmH_2O).

The NARX model builds upon the FOM by incorporating pressure dependent basis functions to describe elastance, and multiple time dependent terms that represent the effect of airway resistance to flow and changes in flow. The NARX model is defined:

$$P(t) = \sum_{i=1}^{M} a_i \phi_i(P(t))V(t) + \sum_{j=0}^{L} b_j \dot{V}(t_{-j}) + P_0(t) \tag{2}$$

where $\phi_i(P(t))$ is the particular basis function value for a given pressure measurement (dimensionless); a_i is the coefficient for a given basis function (cmH_2O/L), M is the number of basis functions used, b_j is a series of terms that capture resistance and inertance of the flow (cmH_2Os/L); L is the number of resistive terms. The subscript $-j$ in the second term refers to the previous time samples. Thus, each $P(t)$ is calculated from information from the previous L data points. The sum of the basis functions multiplied by their a_i coefficients represent elastance through pressure. The FOM can be replicated with $M=L=1$, and zero order basis functions.

2.3. Basis function modification

The original NARX model [18] used first order b-spline basis functions to capture the elastance pressure shape [22]. However, such functions are not suitable for extrapolation beyond the range of data used to train the model. To extrapolate the NARX model, elastance basis functions must extend to cover pressures not present in the training data.

When the pressure dependent elastance profiles were identified for the entire recruitment manoeuvre, several different type of pressure-elastance shapes were observed (Fig. 1). It was determined that the range of profiles observed could be constructed with linear combinations of constant, linear, exponential, and sigmoidal functions (Fig. 2):

$$\phi_1 = 1 \tag{3a}$$

$$\phi_2 = \frac{P}{50} \tag{3b}$$

$$\phi_3 = e^{-0.04P} \tag{3c}$$

$$\phi_4 = \frac{1}{1 + e^{-0.25(P-28)}} \tag{3d}$$

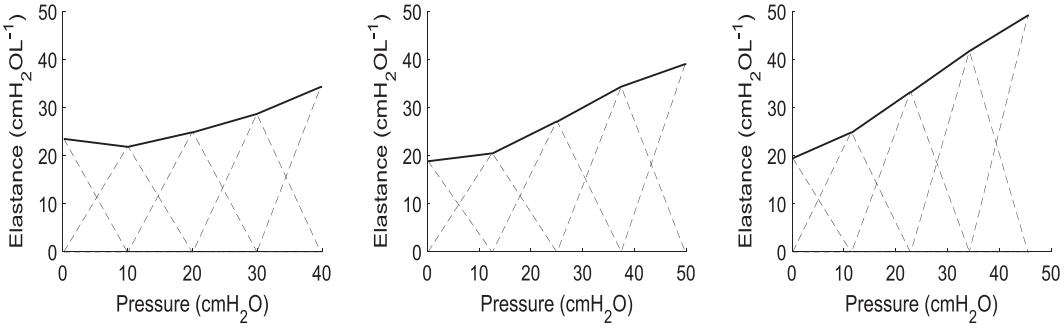

Fig. 1. Five first order basis functions multiplied by the coefficients a_1–a_5, identified for three indicative patient responses over 100% of the available data.

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