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Reformulation of the pressure-dependent recruitment model (PRM) of respiratory mechanics

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ABSTRACT

Background: The pressure dependent recruitment model (PRM) is a comprehensive mathematical description of pulmonary mechanics in acute respiratory distress syndrome (ARDS). However, previous investigations of the PRM implied that the number of model parameters may cause inaccurate parameter estimation.
Methods: PRM models were evaluated for 12 ARDS patients that underwent a low-flow recruitment manoeuvre. The identified parameter set formed the basis of a parameter reduction investigation of the PRM. The parameter reduction investigation measured the mean cohort residual error (ψ) yielded by each possible combination of identified parameter set with the non-identified parameter values set to *a priori* population constants.
Results: Reducing the five variable PRM to a particular three variable model configuration produced a limited increase in model fit to data residuals ($\psi_5 = 22.68$, $\psi_3 = 29.21$ mbar). The reduced model evaluates airway-resistance, compliance and distension as model variables and uses population values for alveoli opening pressure and the ratio of open alveoli at end expiratory.
Conclusions: The reduced PRM model captures all major pressure–volume response features in the ARDS patients. Reduced parameterisation allows more robust parameter identification and thus more reliable parameter estimates that may prove more useful in a clinical setting.

1. Introduction

Model-based decision support has been applied to respiratory support in critical care and has provided improved patient outcomes and healthcare cost-efficiency [1]. The methodology typically characterises patient-specific pressure–volume (PV) responses mathematically and uses this characterisation to predict the response to therapy [2–4]. Hence, therapeutic choices can be assessed prior to application and the risk of excessive pressure harming alveoli or insufficient tidal volume and oxidation can be mitigated [5,6].

Mathematical characterisation of the patient's PV response is achieved by fitting a model of PV mechanics to patient data [7,8]. Respiratory mechanics models differ in their level of parameterisation and their ability to describe the characteristics that occur in typical PV response curves [2,3,9]. The most clinically useful model formulations are capable of capturing the patient characteristics that are important for modelling the potential patient responses to particular therapeutic choices. However, ascertaining the ideal model formulation or level of parameterisation is difficult process and may be different for different patient groups [2,8]. In particular, increasing the parameterisation of the model typically increases the models ability to exactly capture all of the PV characteristics that appear in data. However, increased parameterisation also increases parameter trade-off, and potentially limits the parameter estimation accuracy and predictive capability of the model for different respiratory loading conditions [10,11].

This investigation re-parameterises the pressure-dependent recruitment model (PRM) defined by Schranz *et al.* The PRM model is a mathematical formulation of the Hickling description of respiratory mechanics [12]. Hickling described lung recruitment as a discrete process in which layers of alveoli open at particular

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evenly distributed opening pressures. The Schranz *et al.* formulation includes compliance and distension characteristics to fully model the mechanics through a broad pressure range. However, the model requires identification of five model parameters. Although theoretical structural parameter identifiability has been proven in a third order Taylor Series approximation to the model [7], the practical identifiability of the model has proven troublesome [7,13,14] due to the similarity in model input–output roles [10].

2. Methods

2.1. Pressure-dependent recruitment model (PRM)

Schranz et al. [7] applied the Hickling description of the pulmonary mechanics of acute respiratory distress syndrome (ARDS) patients [12] into a PV model that includes distension characteristics. The model relates the airway pressure (p_{aw}) to the induced lung volume for ARDS patients undergoing mechanical ventilation. The bronchial path resistance (R) models the 'Poiseuille' resistance to pressure induced flow. The increased resistance to expansion at higher volumes is quantified with the distension parameter (k). The linear expansion of the lung with respect to increasing pressure is determined via the compliance term (C). ARDS patients often have sections in the lung that are not available at end expiration. Hence, the ratio of the alveoli that are open at the end of expiration is a modelled parameter (θ). Finally, the pressure threshold (TP) at which the closed alveoli start to become available is incorporated into the model. The PRM equations are defined:

$$p_{aw} = R\dot{V} + p_a \tag{1}$$

$$\dot{p}_a = \dot{V}e^{kp_a}\left(C\theta + C(1-\theta)e^{kTP}\sum_{P_R=0,0.5,1,\ldots}^{14.5} H_{PR}e^{kP_R}\right)^{-1} \tag{2}$$

where

$$H_{PR} = \begin{cases} 0 & p_a < TP + P_R \\ 1 & p_a \geq TP + P_R \end{cases} \tag{3}$$

and p_{aw} is the airway pressure [mbar]; R is the airway resistance [mbar·s·mL^{-1}]; V is the induced volume [mL]; p_a is the alveolar pressure [mbar]; k defines the distension characteristics of the lung [mbar^{-1}]; C defines the compliance of the bronchial path and alveoli [mL·mbar^{-1}]; θ is the proportion of alveoli that are open at the end of expiration [1]; TP is the threshold opening pressure of the first layer of recruitable alveoli [mbar]; P_R is the airway pressures above TP that are required for layers of the lung to open [mbar].

The airway pressure and the air flow-rate are measured, and the identified model parameter set ($\mathbf{X}$) that defines the patient-specific response to the low flow inflation (LF) manoeuvre is:

$$\mathbf{X} = \{R, C, \theta, k, TP\} \tag{4}$$

2.2. Experimental methods

Twelve patients with acute respiratory distress syndrome (ARDS) that required mechanical ventilation in intensive care were recruited to undergo a LF manoeuvre. The LF was performed using an Evita4Lab-System to induce a flow rate of 33 mL s^{-1} until airway pressure reached 45 mbar. Thus, a quasi-static PV curve can be measured. Measurements of pressure (piezoresistive pressure transducer–1790 SI-special instruments, Nördlingen, Germany) and air flow rate (Fleisch No2 pneumotachograph, F+G GmbH, Hechingen, Germany) were taken at 125 Hz.

All experiments were undertaken under informed consent signed by the patient or their legally authorised representative. Ethical consent was provided by the local ethics committee. Patient characteristics are given in Table 1. For more experimental details please refer to Stahl *et al.* [15].

Table 1
Demographic data of the cohort.

Pat. Nr.	Gender	Age	BMI	Diagnose
1	m	37	28.7	Pneumonia
2	f	50	23.0	Pancreatitis, pneumonia
3	f	30	23.8	Peritonitis, sepsis
4	f	50	39.1	Pneumonia
5	m	40	20.8	Perforated sigma, Peritonitis
6	m	42	27.2	Pneumonia, Pancreatitis
7	m	51	27.8	Traumatic Brain Injury, Pneumonia
8	m	45	26.1	S/P Neck Dissection
9	m	38	24.6	Traumatic Brain Injury
10	m	73	26.6	S/P coronary-bypass grafting, Pneumonia
11	m	60	22.8	ARDS
12	m	45	26.8	Blunt abdominal trauma, pneumonia
Mean (SD)		47 (11)	26.4 (4.6)	

2.3. Computational application

2.3.1. Stage one – model identification

The full model parameter set $\mathbf{X}$ (Eq. (4)) was identified for each data set using the Matlab (R2012a; 7.14.0.79; 64-bit) function lsqnonlin.m using the 'Trust-region reflective' algorithm. The function was set to declare convergence when the change in $\mathbf{X}$ or the change in the function was less than 10^{-8}. The maximum number of allowed forward simulations was 1000 and the minimum $\Delta\mathbf{X}$ allowed when computing the Jacobian was set as 0.1% of the median population values for $\mathbf{X}$. This approach ensured successful convergence of the parameter TP, which could contribute to erroneous objective function gradient directions at very small $\Delta\mathbf{X}$ values. The identified parameters were constrained to positive values, and had no effective upper limit.

The model fit to data objective function value (ψ) was defined:

$$\psi = \left\| p_{aw,model} - p_{aw,data} \right\|_2 \tag{5}$$

The forward simulations of the model were completed using the error-stepping method [13]. This method is similar to the Picard iteration [16], as it iteratively reduces error in a simulation, rather than performing numerical integration through time-steps. The method used the following steps:

(1) Assume a pressure curve $p_a = V/C$.
(2) Evaluate $H_{0,\,0.5,\,1,\,\ldots,\,14.5}$ using p_a.
(3) Evaluate Eq. (2) for $\dot{p}_a$ using $\mathbf{X}$.
(4) Integrate $\dot{p}_a$ for p_a.
(5) Iterate about steps 2–4 for 30 iterations by which time the model simulation has fully stabilised.

Model parameter values are presented for each patient. To assess robustness of identified model parameters, the change in objective function for a ±10% change in each element of $\mathbf{X}$ was assessed.

2.3.2. Stage two – model pruning

Previous studies of the PRM model generated parameter estimates for some patients that were not considered physiologically plausible [7]. Although the model parameters are all structurally identifiable, the model roles may be similar in respect to their effects on the PV response curve and thus inaccuracies in the measured data had an effect on practical model identification [10]. Hence, the effect of reducing the degree of model parameterisation is tested.