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Model-Based Analysis of Ventilation Inhomogeneity in Respiratory Mechanics

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ABSTRACT

Individualized models of respiratory mechanics help to reduce potential harmful effects of mechanical ventilation by supporting the evaluation of patient-specific lung protective ventilation strategies. Assessing ventilation inhomogeneities might be an important aspect in optimizing ventilator settings. The aim of this study is to capture and analyze ventilation inhomogeneity by a mathematical model using clinical data. The results show that the lung physiology of mechanically ventilated patients without lung condition can be described by an inhomogeneity model revealing two alveolar compartments with median time constants of 0.4 and 3.9 s. Thus, the IHM in combination with specific ventilation maneuver might be suitable to capture lung physiology for model-based optimization of ventilator settings but requires additional image-based investigations to further support the validity of the model.

Keywords: Respiratory Mechanics; Inhomogeneity Model; Parameter Identification; Model-Based Therapy

1. Introduction

Non-adapted ventilator settings risks are severe side effects in intensive care patients during mechanical ventilation [1]. Optimized patient-specific settings can be obtained by individualizing physiological models using clinical data and parameter identification methods. Individualized models provide insight into patient's physiology that is not directly measurable. Thus, they offer significant potential to evaluate and guide personalized lung protective ventilator strategies on intensive care units [2-4]. The concept of model-based therapy applicable at the bedside of the patient requires models that are as simple as possible, while capturing all relevant dynamics and being identifiable with limited available measurement set.

Relevant dynamics of lung mechanics are significantly affected by ventilation inhomogeneity [5]. Thus, inhomogeneities in lung mechanics might provide useful information on the lung tissue response to modified ventilator settings. Currently, ventilation inhomogeneity can be captured by computed tomography (CT) [6] or by electro impedance tomography [7]. An alternative approach involves the Inhomogeneity Model (IHM) of respiratory mechanics [8], which has been a strong force in the field of pulmonary physiology ever since [5].

This paper presents the assessment and analysis of the inhomogeneity model in mechanically ventilated patients to evaluate its potential for model-based therapy.

2. Material & Methods

2.1. Models and Parameter Identification

First Order Model (*FOM*): The FOM is the simplest representation of lung mechanics and considers homogeneous ventilation. The equation of motion is given in (1) and the electrical analog is shown in **Figure 1**. The resistive element R ($cmH_2O \cdot s/L$) corresponds to the resistance of the central and peripheral airways and the compliant compartment C (mL/cmH_2O) represents the elasticity of alveolar tissue and the chest wall [5] defining the respiratory time constant $\tau = R \cdot C$. The patient-specific parameters R and C are determined by Multiple Linear Regression using measured data samples of flow rate ($\dot{V}$) as model input and airway pressure (p_{aw}) as model output [9]. p_C represents the pressure in the elastic compartment.

$$\dot{p}_C = \frac{1}{C}\dot{V}$$
$$p_{aw} = p_C + R\dot{V} \quad (1)$$

Inhomogeneity Model (*IHM*): The IHM is a two-compartment model representing two different alveolar regions by two compliances ($C1$, C_2 in mL/cmH_2O) with their own local airway ($R1$, $R2$ in $cmH_2O \cdot s/L$) connected to the airway opening. This model assumes parallel ventilation inhomogeneity in the lungs described by the two

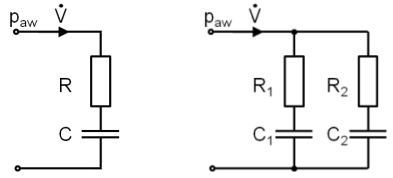

Figure 1. Electrical analog of respiratory mechanics models. Left: First Order Model—FOM, Right: Inhomogeneity Model—IHM.

time constants $\tau_1 = R_1 \cdot C_1$ and $\tau_2 = R_2 \cdot C_2$. Thus, this model is able to simulate redistribution processes between these two compartments (Pendelluft) [5]. The electrical analog is given in **Figure 1**, and the mathematical description is presented in state-space representation in (2)

$$\begin{bmatrix} \dot{p}_{C1} \\ \dot{p}_{C2} \end{bmatrix} = \begin{bmatrix} -\dfrac{1}{C_1(R_1+R_2)} & \dfrac{1}{C_1(R_1+R_2)} \\ \dfrac{1}{C_2(R_1+R_2)} & -\dfrac{1}{C_2(R_1+R_2)} \end{bmatrix} \begin{bmatrix} p_{C1} \\ p_{C2} \end{bmatrix} + \begin{bmatrix} \dfrac{R_2}{C_1(R_1+R_2)} \\ \dfrac{R_1}{C_1(R_1+R_2)} \end{bmatrix} \dot{V}$$

$$p_{aw} = \begin{bmatrix} 1-\dfrac{R_1}{R_1+R_2} & \dfrac{R_1}{R_1+R_2} \end{bmatrix} \begin{bmatrix} p_{C1} \\ p_{C2} \end{bmatrix} + \frac{R_1 R_2}{R_1+R_2}\dot{V} \qquad (2)$$

where p_{C1} and p_{C2} (cmH_2O) are state-signals corresponding to the pressure components generated by the volumes stored in the compliant compartments C_1 and C_2. Parameter identification is performed by minimizing the sum of squared error (SSE) between measured ($p_{aw,meas}$) and simulated airway pressure using the iterative Integral-Method (IIM) [10,11]:

2.2. Clinical Data

Measurement sets of ten mechanically ventilated patients without lung conditions were selected from a previous study [12], where Super-Syringe Maneuvers were performed. During the Super-Syringe Maneuver small volume portions (100 mL) are administered with a constant flow rate (30 L/min), followed by an airway occlusion of 3 s allowing a static pressure-volume relation. Each portion increments the alveolar pressure in the lungs. Measured airway pressure and flow were sampled at 125 Hz and are shown exemplarily in **Figure 2**.

Informed consent was obtained from patients or their legally authorized representative.

2.3. Analysis

Each inspiration cycle was selected and referenced to its plateau pressure (p_{Plat}), reached at the end of occlusion. Patient-specific FOM parameters (R, C) and IHM parameters (R_1, C_1, R_2, C_2) were identified for each cycle. The identified parameters of the cohort were plotted in boxplots illustrating the median and interquartile range (IQR) to present general trends with respect to plateau pressure.

3. Results

3.1. Model Individualization

Overall 381 breathing cycles were available to identify model parameters. FOM identification leads to physiological plausible values in every case tested, whereas IHM identification revealed partly negative and un-phy-

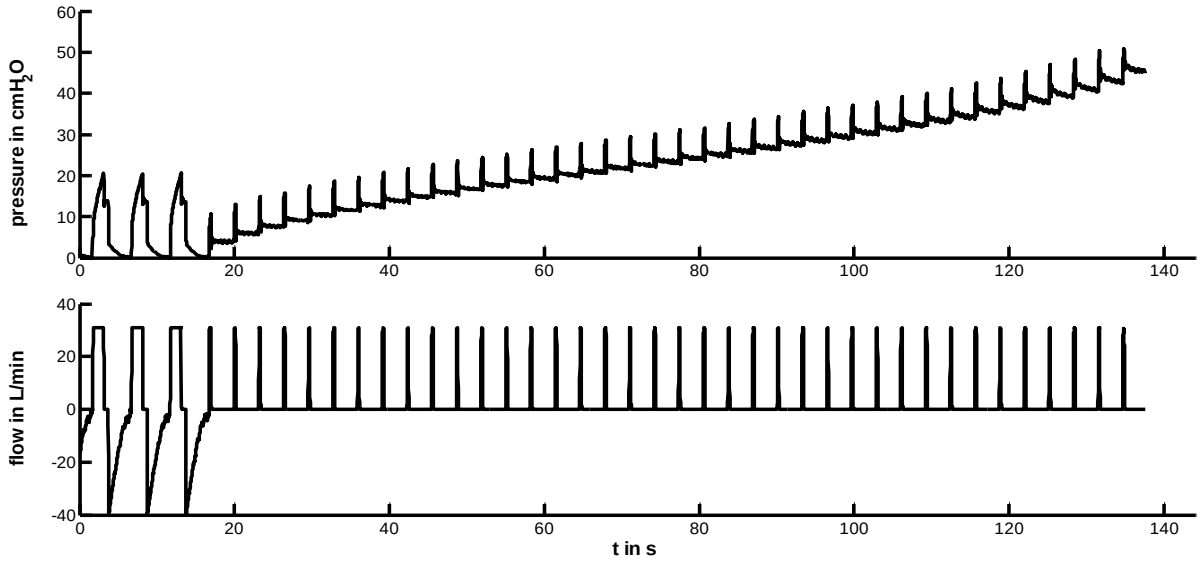

Figure 2. Airway pressure and flow rate during a Super-Syringe Maneuver, initiated after baseline ventilation.

siological parameter values in 39 cases. These erroneous identifications occurred mainly in breathing cycles in low pressure regions. **Figure 3** shows comparisons of measured and simulated model responses of the FOM and IHM in low and high pressure regions. Obviously, the pressure relaxation during the occlusion is more pronounced in higher pressure regions. Fitting the IHM to the data assigns these relaxation effects to redistribution processes. Pressure responses at low plateau pressure show no relaxation effects and thus impair IHM identification.

The identified parameters resulting from the successfully fitted cycles are summarized in a statistical analysis and presented as overall cohort medians and IQR in **Table 1** and in terms of plateau pressure in **Figure 4**. Generally, the individualized IHM parameters indicate two heterogeneous compartments with significant different time constants of τ_1 = 3.9 s (IQR: 2.1 - 7.7) and τ_2 = 0.4 s (IQR: 0.2 - 0.5). In addition the global median time constant of the FOM equals 0.9 s (IQR: 0.6 - 1.1).

The pressure dependency of the FOM parameters show a constant trend in terms of resistance, and a parabolic trend for the compliance with a maximum value at p_{Plat} = 20 cmH_2O. The IHM parameter of compartment 1 reveal an increase in R_1 and a parabolic trend of C_1 similar to C. R_2 and C_2 tend to remain constant, with R_2 being in the same orders of magnitude as R.

4. Discussion

The presented analysis shows the pressure dependency of the identified parameters of the FOM and IHM in patients without lung condition.

FOM identification shows a parabolic trend in compliance C increasing by more than factor 2 with increasing pressure. The maximal compliance was reached at 20 cmH_2O.

IHM identification reveals inhomogeneous ventilation represented by two compartments with significant different time constants. The compartment with the larger compliance shows similar behavior as the global compliance trend of the FOM. Simultaneously, the compliance of the second compartment is smaller by factor 3. Similar findings of inhomogeneity of two different compartments with various time constants were obtained with EIT, where inhomogeneity was related to regional dynamics differences in ventral and dorsal areas in patients under general anesthesia without lung condition [13].

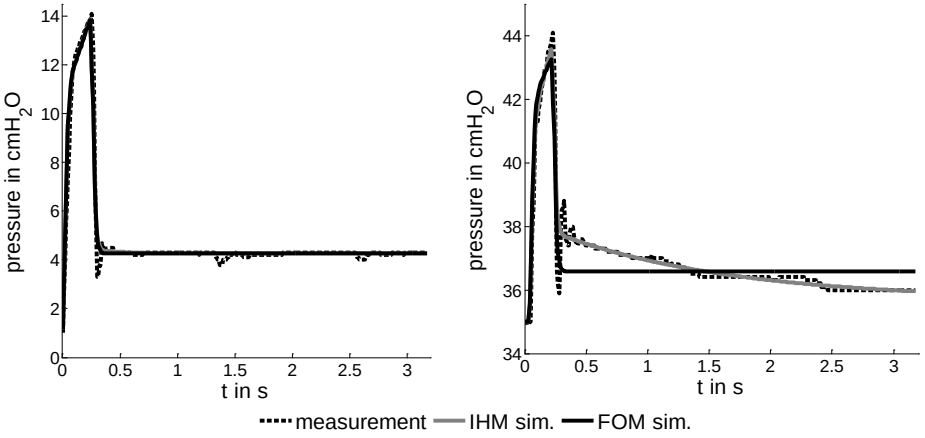

Figure 1. Measured and simulated pressure of First Order Model (FOM) and Inhomogeneity Model (IHM) at various plateau pressures of 4 and 36.5 cm H_2O.

Table 1. Medians and IQR from FOM and IHM identified parameters

Model	Parameter	Value[a]
FOM	R (cmH_2O·s/L)	11.6 (11.2 - 12.1)
	C (mL/cmH_2O)	78.8 (52.9 - 93.7)
IHM	R_1 (cmH_2O·s/L)	41.0 (39.0 - 59.6)
	C_1 (mL/cmH_2O)	96.0 (53.3 - 128.7)
	R_2 (cmH_2O·s/L)	15.4 (13.0 - 17.0)
	C_2 (mL/cmH_2O)	29.3 (18.5 - 30.7)

[a]median and interquartile range

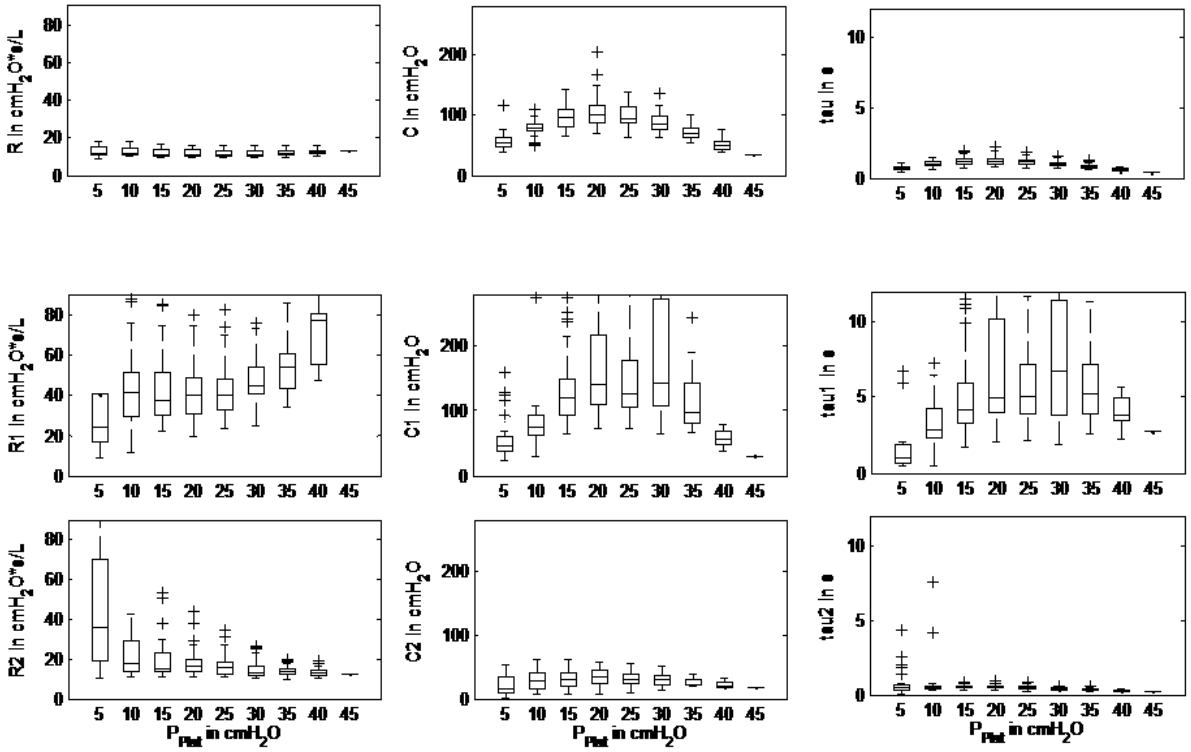

Figure 4. Statistical analysis of identified model parameters in terms of plateau pressure (p_{Plat}). Top line: FOM parameters, Bottom lines: IHM parameters.

Thus, these model-based results may indicate the IHM as an alternative approach to obtain measures of dynamic changes of inhomogeneous lung aeration. Still, the interpretation of model parameters, in particular, the validity of the identified compartments are only valid if the model assumption is correct.

However, the same model prediction quality could be obtained by the viscoelastic model (VEM), which describes the observed by the same equation but different coefficients [5,14]. In this case, measured data of flow rate and airway pressure lead to the problem of undistinguishable models. It is unclear whether the observed dynamics can be assigned to viscoelastic or inhomogeneity characteristics. Thus, further investigations combined with imaging methods are necessary to analyze both dynamics separately to further validate the model assumptions of the IHM.

Once the IHM is fully validated, it might offer a new possibility to easily assess ventilation inhomogeneities to evaluate and guide personalized lung protective ventilator strategies on intensive care units.

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REFERENCES

[1] A. S. Slutsky, "Lung Injury Caused by Mechanical Ventilation," *Chest*, Vol. 116, 1999, pp. 9-15. http://dx.doi.org/10.1378/chest.116.suppl_1.9S-a

[2] A. Sundaresan, J. G. Chase, G. M. Shaw, Y. S. Chiew and T. Desaive, "Model-Based Optimal PEEP in Mechanically Ventilated ARDS Patients in the Intensive Care Unit," *Biomed Eng Online*, Vol. 10, 2011, p. 64. http://dx.doi.org/10.1186/1475-925X-10-64

[3] S. Lozano, K. Möller, A. Brendle, D. Gottlieb, S. Schumann, C. A. Stahl, *et al.*, "AUTOPILOT-BT: A system for Knowledge and Model Based Mechanical Ventilation," *Technol Health Care*, Vol. 16, 2008, pp. 1-11.

[4] S. E. Rees, C. Allerød, D. Murley, Y. Zhao, B. W. Smith, S. Kjaergaard, *et al.*, "Using Physiological Models and Decision Theory for Selecting Appropriate Ventilator Settings," *Journal of Clinical Monitoring and Computing*, Vol. 20, 2006, pp. 421-429. http://dx.doi.org/10.1007/s10877-006-9049-5

[5] J. H. Bates, "Lung Mechanics: An Inverse Modeling Approach," 1st Edition, Cambridge University Press, New York, 2009.

[6] K. Markstaller, B. Eberle, H. U. Kauczor, A. Scholz, A. Bink, M. H. Thelen, W., *et al.*, "Temporal Dynamics of Lung Aeration Determined by Dynamic CT in a Porcine

Model of ARDS," *British Journal of Anaesthesia*, Vol. 87, 2001, pp. 459-468. http://dx.doi.org/10.1093/bja/87.3.459

[7] Z. Zhao, K. Möller, D. Steinmann, I. Frerichs and J. Guttmann, "Evaluation of an Electrical Impedance Tomography-Based Global Inhomogeneity Index for Pulmonary Ventilation Distribution," *Intensive Care Medicine*, Vol. 35, 2009, pp. 1900-1906. http://dx.doi.org/10.1007/s00134-009-1589-y

[8] A. B. Otis, C. B. McKerrow, R. A. Bartlett, J. Mead, M. B. McIlroy, N. J. Selver-Stone, *et al.*, "Mechanical Factors in Distribution of Pulmonary Ventilation," *Journal of Applied Physiology*, Vol. 8, 1956, pp. 427-443.

[9] C. Schranz, C. Knöbel, J. Kretschmer, Z. Zhao and K. Möller, "Hierarchical Parameter Identification in Models of Respiratory Mechanics," *IEEE Transactions on Biomedical Engineering*, Vol. 58, 2011, pp. 3234-3241. http://dx.doi.org/10.1109/TBME.2011.2166398

[10] C. Schranz, P. D. Docherty, K. Möller and J. G. Chase, "Integral-Based Identification of an Inhomogeneity Model in Respiratory Mechanics," 6*th International Conference on Bioinformatics and Biomedical Engineering*, Shanghai, 2012, pp. 575-578. http://dx.doi.org/10.1186/1475-925X-11-38

[11] C. Schranz, P. D. Docherty, Y. S. Chiew, K. Möller and J. G. Chase, "Iterative Integral Parameter Identification of a Respiratory Mechanics Model," *BioMedical Engineering OnLine*, Vol. 11, 2012.

[12] C. A. Stahl, K. Möller, S. Schumann, R. Kuhlen, M. Sydow, C. Putensen, *et al.*, "Dynamic versus Static Respiratory Mechanics in Acute Lung Injury and Acute Respiratory Distress Syndrome," *Critical Care Medicine*, Vol. 34, 2006, pp. 2090-2098. http://dx.doi.org/10.1097/01.CCM.0000227220.67613.0D

[13] S. Pulletz, M. Kott, G. Elke, D. Schädler, B. Vogt, N. Weiler, *et al.*, "Dynamics of Regional Lung Aeration Determined by Electrical Impedance Tomography in Patients with Acute Respiratory Distress Syndrome," *Multidisciplinary Respiratory Medicine*, Vol. 7, 2012, p. 44. http://dx.doi.org/10.1186/2049-6958-7-44

[14] G. Avanzolini and P. Barbini, "Comments on "Estimating Respiratory Mechanical Parameters in Parallel Compartment Models", *IEEE Transactions on Biomedical Engineering*, Vol. 29, 1982, pp. 772-774. http://dx.doi.org/10.1109/TBME.1982.324873

