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Inverse Modeling Supports Quantification of Pressure and Time Depending Effects in ARDS Patients

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Abstract—**The application of respiratory mechanics models combined with standardized ventilation maneuvers enable investigations of patients' lung mechanics at the bedside in order to optimize ventilation therapy. Therefore, the underlying dynamic effects of respiratory mechanics (viscoelasticity, inhomogeneity and recruitment) are uncovered by applying various ventilation maneuvers and subsequently captured by the corresponding model via parameter identification methods.**

Data sets of patients undergoing quasi-static and dynamic ventilation patterns are available along with a hierarchical model structure for parameter identification and simulation purposes. The applicability of the basic 1st order model (FOM) of respiratory mechanics for various flow rates proved to be critical and patient dependent, since distinctive time-depending effects could not be considered. To improve this, a 2nd order model (SOM), individualized using data of a SCASS maneuver (Static Compliance Automated Single Step), enables successful simulations of respiratory mechanics in dynamic and quasi-static conditions. Pressure dependent effects such as static recruitment, can be captured by Hickling's nonlinear compliance model.

This research illustrates the applicability of various models of respiratory mechanics within the model hierarchy in various circumstances and the ability to distinguish between dynamic and static effects.

I. Introduction

RESPIRATORY therapy of ARDS patients (Acute Respiratory Distress Syndrome) poses a dilemma to clinicians: Large regions of the patient's lung are collapsed and require high ventilation pressures to be opened and stabilized. On the other hand these high ventilation pressures may deploy additional damage to the lung by overstretching initially opened regions [1]. As this conflict remains unresolved, model-based ventilation seems a promising approach in order to provide an individual lung protective compromise [2].

Therefore, models of respiratory mechanics support the investigation of lung mechanics at the bedside of the patient where usually the measurable information is limited to airway pressure and airflow. Certain underlying effects of respiratory mechanics such as viscoelasticity, inhomogeneity (pendelluft) or alveolar recruitment can be uncovered by the application of standardized ventilation maneuvers. Until now a distinction between these effects is not possible with the limited information of airway pressure and flow rate. Therefore, other partly invasive measurement techniques, such as microscopy, electro impedance tomography or sound analysis, must be applied.

The presented work avoids extensive investigations using additional measurement equipment to ensure straightforward bedside applicability. Therefore investigations based on models of respiratory mechanics should provide more insight into these mechanisms allowing differentiation between static and dynamic effects.

These investigations are based on measured data of ARDS patients undergoing various ventilation maneuvers. The applied models are arranged in a hierarchical structure to ensure the distinction of linear and nonlinear effects and to support the parameter identification processes [3]. To guarantee bedside application, the used models are supposed to be as simple as possible and only as complex as necessary.

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II. Materials and Methods

A. Models

The applied models of respiratory mechanics are hierarchically arranged (Fig. 1). The first level includes the basic linear 1st Order Model (FOM) of respiratory mechanics. The FOM consists of a serial arrangement of a resistance R (airway resistance) and a compliance C (elasticity of the respiratory system). Linear regression is used for parameter identification of this model.

The models in the second level are enhancements of the FOM, which are accomplished either by adding another compartment leading to a 2nd Order Model (SOM) or by requiring nonlinear models for the resistance or compliance of the FOM [4] (Fig. 1).

A variety of SOMs exist with the two most prominent being the Viscoelastic Model (VEM) and the Inhomogeneity Model (IHM), both are physiologically plausible and lead to the same mathematical description [5]. The following investigations are based on the VEM since a robust approach for its parameter identification was already developed [3].

The applied nonlinear compliance model is based on the pressure depending recruitment model developed by Hickling [6]: The lung represents a collection of multiple alveolar units being recruited or not at any given pressure. The lung is divided into 30 layers consisting of an evenly distributed amount of alveolar units. The lung volume can be increased by recruiting alveolar units. Recruitment is controlled by the Threshold Opening Pressure (TOP), which has to be exceeded to open up and stabilize alveolar units. At the beginning of inspiration a certain amount of alveolar units are open, holding the residual volume. The compliance of each layer corresponds to the compliance of recruited alveoli [7, 8]. Once an alveolar unit is recruited it's compliance saturates exponentially with increasing pressure according to Salazar and Knowles [9].

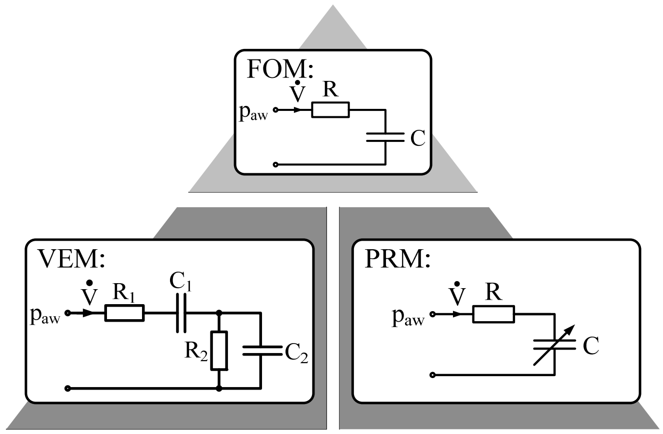

Fig. 1. Model hierarchy supporting parameter identification in order to analyze effects in respiratory mechanics. 1st Order Model of respiratory mechanics (FOM), Viscoelastic Model (VEM) and Pressure depending Recruitment Model (PRM).

B. Data

This study is based on clinical data from a previous study where standardized ventilation maneuvers were performed on mechanically ventilated patients with ARDS syndrome using an Evita4Lab-System (Dräger Medical, Lübeck, Germany). The maneuvers were performed at a Positive End Expiratory Pressure (PEEP) of 0 mbar.

Airway pressure (pressure transducer 1790, Si-instruments, Nördlingen, Germany) and flow rate (pneumotachograph Fleisch No. 2, F+G GmbH, Hechingen, Germany) were measured at a sampling rate of 125 Hz [10]. Exemplary results of two patients out of 12 are depicted.

Low-Flow (LF) maneuver: The lung is inflated by an extremely low constant gas flow of 35 mL/s over 55 s, which enables a quasi-static pressure/volume relationship.

Dynamic-Slice (DS) maneuver: Extracting the first of five sequent respiratory cycles with a gas flow of 600 mL/s for 2 s, which appear during baseline ventilation and are used for quantifying lung dynamics.

Static Compliance Automated Single Step (SCASS) maneuver: After reaching a randomized amount of volume within the inspiration, the airway is occluded for 5 s to obtain a quasi-static pressure/volume relationship [11].

III. RESULTS

The models of the hierarchy are identified using data from two patients. A measure of the goodness-of-fit of the model is provided by the *coefficient of determination* (*CD*).

$$CD = 1 - \frac{SSE}{\sum_1^n (p_{meas} - \bar{p}_{meas})^2} \tag{1}$$

$$SSE = \sum_1^n (p_{meas} - p_{sim})^2 \tag{2}$$

The CD can take a value anywhere from 1, which corresponds to a perfect fit, to 0, which signifies the model has absolutely no relation to the data [4].

A. FOM: Parameter Identification and Simulation

The parameters of FOM from two patients are identified using data from the DS maneuvers leading to FOM_{DS}. These parameter values are given in Table I. Since the model parameter seems to be maneuver-dependent the indexing of the model refers to the underlying data set (e.g. FOM_{DS}). The corresponding pressure response of both patients is depicted as black curves in Fig. 2a and Fig. 2d respectively.

TABLE I
FOM_{DS} PARAMETER VALUES BASED ON THE DS MANEUVER

Parameter	Patient 1	Patient 2
R (mbar·s/mL)	0.0092	0.0162
C (mL/mbar)	38.9	38.1
CD^{DS}	0.9967	0.9559
CD^{LF}	0.7199	0.8648

Resulting parameter values of the FOM identification process based on data of DS maneuvers and resulting CD values when simulating the FOM_{DS} with flow profiles of other maneuvers.

Using the identified FOM_{DS} to predict the pressure response during the LF maneuver leads to the predicted pressure responses shown as grey curves in Fig. 2a and Fig. 2d.

B. VEM: Parameter Identification and Simulation

The parameters of the identified VEM_{SCASS} of both patients are shown in Table II. The simulation results of the identified VEM_{SCASS} during DS and LF situations of Patient 1 and Patient 2 are illustrated in Fig. 2b and Fig. 2e respectively. The VEM_{SCASS} is able to reproduce the pressure responses with minimized error independently on the ventilation maneuver. The average CD of both pressure responses could be improved against the FOM and equals 0.99.

C. PDR: Parameter Identification and Simulation

The identified PDR_{LF} parameter values are shown in Table III and the measured and simulated pressure responses of the LF and DS maneuver are plotted in Fig. 2c and Fig. 2f.

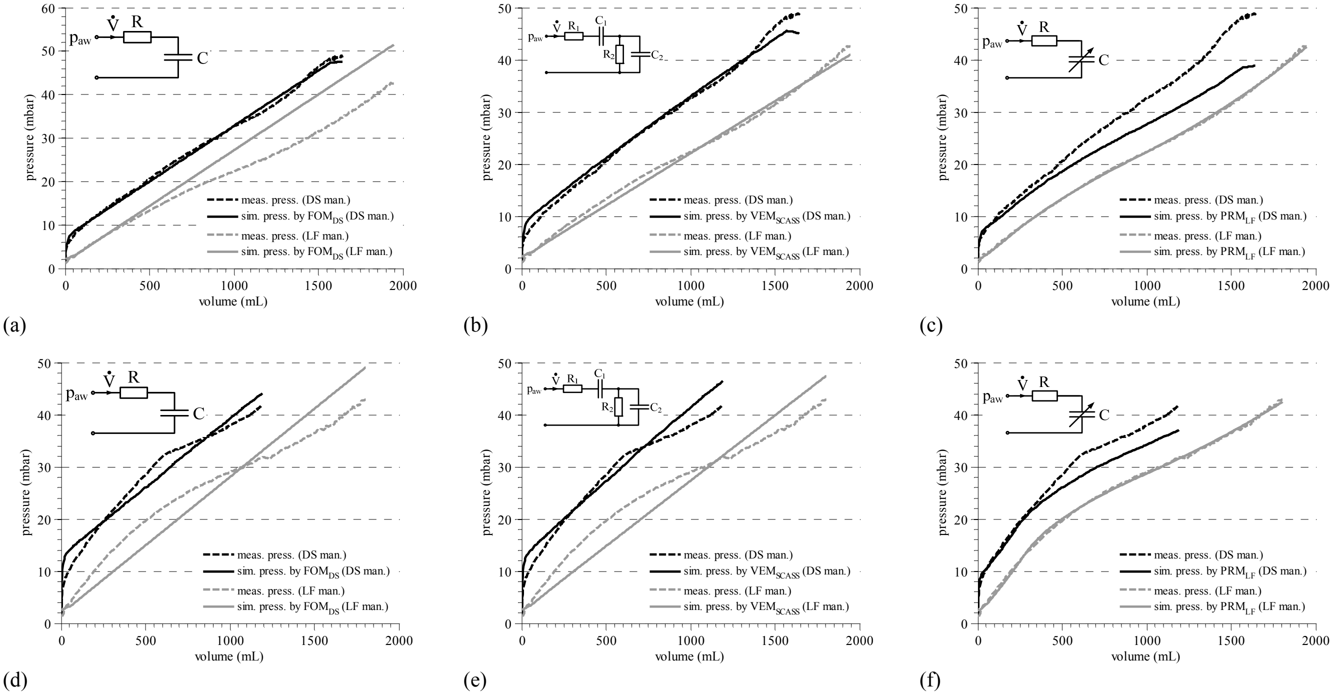

Fig. 2. Measured (dashed lines) and simulated (solid lines) pressure responses of the Dynamic-Slice (black) and Low-Flow (grey) maneuver of Patient 1 (a-c) and Patient 2 (d-f) using various models: (a), (d) Simulating the 1st Order Model of Respiratory Mechanics (FOM_{DS}), identified by a Dynamic-Slice maneuver; (b), (e) Simulating the Viscoelastic Model of Respiratory Mechanics (VEM_{SCASS}), identified by a SCASS maneuver; (c), (f) Simulating the Pressure Depending Recruitment Model (PRM_{LF}), identified by a Low-Flow maneuver;

TABLE II

VEM_{SCASS} PARAMETER VALUES BASED ON THE SCASS MANEUVER

Parameter	Patient 1	Patient 2
R_1 (mbar·s/mL)	0.0112	0.0154
C_1 (mL/mbar)	49.9	39.8
R_2 (mbar·s/mL)	0.0133	0.0115
C_2 (mL/mbar)	148.8	181.8
τ_{VE} (s)	2.0	2.1
CD^{SCASS}	0.9912	0.9813
CD^{DS}	0.9891	0.9404
CD^{LF}	0.9935	0.8916

Resulting parameter values of the VEM_{SCASS} identification process based on data of SCASS maneuvers and resulting CD values when simulating the VEM_{SCASS} with flow profiles of other maneuvers.

TABLE III

PRM_{LF} PARAMETER VALUES BASED ON THE LF MANEUVER

Parameter	Patient 1	Patient 2
R (mbar·s/mL)	0.0033	0.0129
m_{TOP} (mbar)[a]	5.7	14.1
$NOpen$ (%)[b]	48.1	30.5
C (mL/mbar)	85.3	97.5
K (mbar^{-1})[c]	0.025	0.025
CD^{DS}	0.6758	0.9262
CD^{LF}	0.9996	0.9984

Resulting parameter values of the PRM_{LF} identification process based on data of LF maneuvers and resulting CD values when simulating the PRM_{LF} with flow profiles of other maneuvers. [a] mean TOP, [b] initial percentage of open alveolar units before inflation, [c] saturation factor according to Salazar-Knowles

IV. DISCUSSION

The predictions of the FOM_{DS} during LF situation of Patient 1 present a strong mismatch to the measurement set concerning the slope of the increase in pressure. The prediction of the correct pressure response for two various flow rates leads to the assumption that additional underlying dynamic effects which are present in the patient's lung mechanics are not captured within this basic model.

This mismatch is not that significant in the data of Patient 2. The average prediction of the FOM_{DS} seems to be still valid for Patient 2 but provides only rough estimates since the measured response shows strong deviations to the linear predictions of the model. Regarding the average *CD* value, the individualized FOM_{DS} shows better agreement to Patient 2 (CD^{mean} = 0.91) than to Patient 1 (CD^{mean} = 0.86). The mentioned dynamic effects in the measurement set seems to have additional effects besides the FOM characteristic, most likely related to the flow rate. These dynamic effects can be quantified by higher order linear models, e.g. VEM, to simulate respiratory mechanics. Thereby data from SCASS maneuvers, with the emergence of these dynamics during the end-inspiratory hold period, is used to individualize the VEM by assigning the dynamic effect to viscoelastic tissue properties.

As shown in Fig. 2b the VEM_{SCASS} reproduces accurate prediction of the pressure response independently on the applied flow rate leading to an improvement of the CD^{mean} to 0.99 in Patient 1. Since the mean tendencies of the pressure responses of Patient 2 were already roughly determined by the FOM_{DS} the identification of a VEM_{SCASS} did not lead to a significant improvement of the average CD^{mean} (from 0.91 up to 0.92). This suggests the dynamic effects are not that distinctive in the measured data of Patient 2. Thus the simulated pressure responses of the VEM_{SCASS} of Patient 2 are almost equal to the ones of the FOM_{DS} in Fig. 2d.

In the case of Patient 1 the FOM shows good correlation between the single flow rate and the VEM, even for multiple flow rates by reaching high *CD* values. The *CD* values regarding the data of Patient 2 were lower. Regarding the plotted pressure responses there seem to be strong deviations of the measurement around the simulated pressures calculated by linear models (FOM, VEM). These deviations from the linear behavior (Fig. 2b, Fig. 2e) can be attributed to recruitment effects that are quantified by a pressure depending compliance model. Based on the LF maneuver data, the PRM_{LF} is individualized and enables predictions of the curved pressure responses with minimized error (Fig. 2c, Fig. 2f).

Simulation of the PRM_{LF} in the DS maneuver showed that the model's predictions do not match the measurements. This leads to the conclusion that pressure depending recruitment models are able to minimize the SSE in static conditions but are not able to explain the differences in increase of pressure during various ventilation maneuvers. To improve on this, a third layer of the model hierarchy combining nonlinear compliance models in a SOM may be a promising approach.

The two exemplary data sets demonstrated predominantly linear behavior (Patient 1), with good agreement of the measurement to the results of the VEM simulations (Fig. 2c) and nonlinear behavior (Patient 2, Fig. 2e). Within the data of 12 ARDS patients, the predominantly linear behavior was found in 4 and the nonlinear behavior in 8 patients.

V. Conclusion

The introduced hierarchical model structure allows meaningful investigations in underlying effects of respiratory mechanics, allowing dynamic and static effects to be distinguished.

Acknowledgment

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References

[1] L. Gattinoni, P. Caironi, M. Cressoni, D. Chiumello, V. M. Ranieri, M. Quintel *et al.*, "Lung recruitment in patients with the acute respiratory distress syndrome," *N Engl J Med.,* vol. 354, no. 17, pp. 1775-1786, 2006.

[2] 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, no. 1, pp. 1-11, 2008.

[3] C. Schranz, J. Guttmann, and K. Möller, "An Approach towards Parameter Identification in Hierarchical Models of Respiratory Mechanics," *Biomed Tech.,* vol. 55 (Suppl. 1), 2010.

[4] J. H. Bates, *Lung Mechanics: An Inverse Modeling Approach*, 1 ed.: Cambridge University Press, 2009.

[5] T. Similowski, and J. H. Bates, "Two-compartment modelling of respiratory system mechanics at low frequencies: gas redistribution or tissue rheology?," *Eur Respir J,* vol. 4, no. 3, pp. 353-358, 1991.

[6] K. G. Hickling, "The pressure-volume curve is greatly modified by recruitment. A mathematical model of ARDS lungs," *Am J Respir Crit Care Med.,* vol. 158, no. 1, pp. 194-202, 1998.

[7] T. Yuta, J. G. Chase, G. M. Shaw, and C. E. Hann, "Dynamic Models of ARDS Lung Mechanics for Optimal Patient Ventilation."

[8] C. Schranz, J. Guttmann, and K. Möller, "Fitting respiratory mechanics in ARDS by a nonlinear recruitment model with viscoelastic component," *Biomed Tech.,* vol. 55 (Suppl. 1), 2010.

[9] E. Salazar, and J. H. Knowles, "An analysis of pressure-volume characteristics of the lungs," *J Appl Physiol.,* vol. 19, pp. 97-104, 1964.

[10] 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," *Crit Care Med.,* vol. 34, no. 8, pp. 2090-2098, 2006.

[11] "Dräger Medical AG & Co: Evita 4 Lab, PC - Fernsteuerung für Messmanöver und spezielle Beatmungsmuster in Evita 4, Gebrauchsanweisung," 2001.