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Evaluating the Combined Optimization of Oxygenation and Ventilation in a Patient Simulator

J. Kretschmer, C. Bibiano, P. Stehle, K. Möller

Institute of Technical Medicine, Furtwangen University, Villingen-Schwenningen, Germany
Email: krj@hs-furtwangen.de

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Abstract

The use of mathematical models can aid in optimizing therapy settings in ventilated patients to achieve certain therapy goals. Especially when multiple goals have to be met, the use of individualized models can be of great help. The presented work shows the potential of using models of respiratory mechanics and gas exchange to optimize minute ventilation and oxygen supply to achieve a defined oxygenation and carbon dioxide removal in a patient while guaranteeing lung protective ventilation. The ventilator settings are optimized using respiratory mechanics models to compute a respiration rate and tidal volume that keeps the maximum airway pressure below the critical limit of 30 cm H_2O while ensuring a sufficient expiration. A three-parameter gas exchange model is then used to optimize both minute ventilation and oxygen supply to achieve defined arterial partial pressures of oxygen and carbon dioxide in the patient. The presented approach was tested using a JAVA based patient simulator that uses various model combinations to compute patient reactions to changes in the ventilator settings. The simulated patient reaction to the optimized ventilator settings showed good agreement with the desired goals.

Keywords

Physiological Model, Model Based Optimization, Decision Support, Patient Simulator

1. Introduction

Mechanical ventilation is a life-saving intervention, routinely used in intensive care. It provides breathing support in critically ill patients that are not able to maintain sufficient oxygenation. However, if the ventilator settings are not properly adapted to the individual patient physiology, it can cause injuries to the lung tissue through barotrauma or collaps of alveoli [1]. Optimizing ventilator settings in patients with critically poor lung function poses a trade-off between multiple conflicting goals, such as applying high airway pressures and tidal volumes to ensure sufficient oxygenation versus using low airways pressures to protect healthy lung tissue [2]. Mathematical models of the human physiology can be adapted to the individual physiological properties of a patient and thus can be used to predict reactions of that patient to changes in the ventilator settings. Those predictions can aid in providing decision-making support by using optimization algorithms to calculate ventilator settings that lead to achieving the goals defined by the clinician [3]. Model based decision support in ventilated patients should consider the effect of air volume on the air pressure in the lung, but should also consider other physiological processes that are influenced by the ventilation. The most critical goals to achieve in a ventilated patient are a sufficient minute volume with low air pressures, avoiding intrinsic PEEP (positive end-expiratory pressure) by setting an expiration time that allows the patient to exhale the air before starting with the next inspiration phase and to apply enough oxygen to secure a sufficient oxygenation in the blood. Thus, gas exchange in the patient has to be taken into account when calculating the optimal ventilator settings. The following example should therefore demonstrate how to exploit information from different mathematical models to optimize ventilator settings individually for a patient. The goal was to calculate the necessary minute volume (MV) and inspiratory oxygen fraction (FiO_2) to achieve a desired partial pressure of oxygen and carbon dioxide in arterial blood (PaO_2, $PaCO_2$) while keeping the maximum airway pressure below a critical limit and avoiding the build-up of intrinsic PEEP through a sufficient expiration time. The presented approach is evaluated using a patient simulator that has been presented previously [4]. It incorporates models of respiratory mechanics, gas exchange and cardiovascular dynamics to simulate mechanically ventilated patients with various diseases.

2. Methods

2.1. Respiratory Mechanics Models

The presented approach for combined optimization of ventilation and oxygenation includes four different models of respiratory mechanics that can be used to predict patient behavior. Thus, depending on the individual patient physiology and the available data detail the model that fits the given data best can be used to calculate optimal ventilator settings. The implemented models are ordered hierarchically, *i.e.* all models are related to each other with models of higher order being derived from models of lower order by adding additional elements or by changing linear elements into nonlinear elements. This hierarchy can be exploited for parameter identification when the parameter values of the models of lower order are used as a basis for selecting appropriate initial guesses for the identification of the more complex models [5]. To select the model that fits the given data best, an algorithm has been introduced previously that selects the best model based on fit quality and the number of parameters in the models

[6]. The models available for the presented optimization approach are a model of first order (FOM) [5], a viscoelastic model (VEM) [5], a recruitment model (PRM) [7] and a recruitment model with viscoelastic elements (PRVEM) [8]. Input to the models is air flow, output is air volume and airway pressure.

2.2. Gas Exchange Model

The presented optimization approach uses a three-parameter gas exchange model that allows simulating different ventilation to perfusion ratios (V/Q) to predict the effect of oxygen supply and minute volume on PaO_2 and $PaCO_2$ [9]. The model consists of two alveolar compartments, each of which are provided with a fraction of the inspired air. Parameter fA defines the fraction of air that reaches one of the compartments while the other compartment receives the rest. Venous blood coming from the body is partly shunted away and mixed with the oxygenated blood coming from the capillaries. The non-shunted blood is then distributed among the two alveolar compartments. Parameter fs defines the amount of shunted blood, parameter fQ defines the amount of blood reaching the alveolar compartment that receives the fraction of air defined by fA. Inputs to the model are the measured end-tidal oxygen and carbon-dioxide gas fractions ($FetO_2$, $FetCO_2$) and blood gas parameters such as Hemoglobin concentration, body temperature, base excess and pH. The outputs of the model then are the arterial partial pressures of oxygen and carbon dioxide (PaO_2, $PaCO_2$). To improve the quality of parameter identification, a hierarchical approach has been used here as well. **Figure 1** shows a schematic overview of the identification of the three-parameter gas exchange model. An initial estimate of the shunt is calculated using a simple shunt-model that consists of only one alveolar compartment [10]. This estimate is then used as an initial guess in the identification of a two-parameter model that is derived from the three- parameter model. In the two-parameter model, fQ is fixed to a certain value (fQi = 0.1, 0.2, 0.3, ⋯, 0.9). Parameters fs and fA of the two parameter model are then identified for the specific fQi. The combination of fs, fA and fQi, where the parameter identification received the best fit to the data are finally used as initial estimates for the identification of the three-parameter model. The simple shunt model requires one measured PaO_2 and $PaCO_2$ together with the FiO_2 that was supplied, while the two- and the three-parameter models require four measurements of PaO_2 and $PaCO_2$ and different levels of FiO_2.

2.3. Optimization Algorithm

To achieve a specific PaO_2 and $PaCO_2$ in the patient, both minute ventilation (MV) and supplied oxygen (FiO_2) need to be optimized. Simultaneously, the minute ventilation needs to be calculated with regards to the underlying respiratory mechanics so that the peak airway pressure (P_{peak}) does not lead to additional lung injury and the expiration time is enough to avoid intrinsic PEEP. A study by the ARDS network has shown that ventilation with a peak pressure of 30 cmH_2O instead of 50 cm H_2O leads to a reduction of mortality rate from 39.8% to 31% [2]. To allow an almost complete expiration,

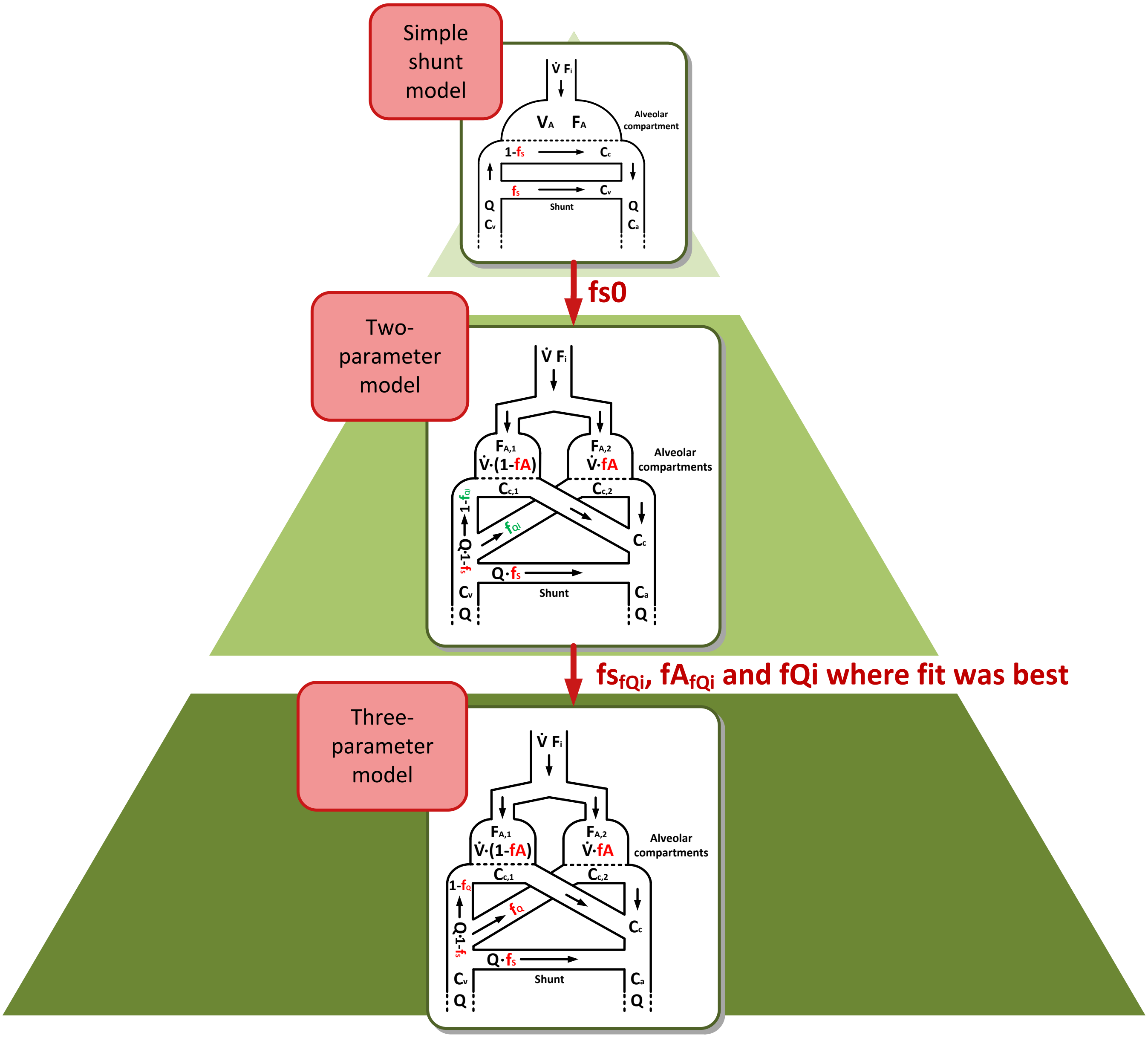

Figure 1. Hierarchical order of the gas exchange models. The simple shunt model is used to calculate an initial shunt estimate, the two-parameter model is used to calculate appropriate initial guesses for the identification of the three-parameter model by testing different blood distributions (fQi) and the fitting shunt fs and alveolar distribution fA to it. The combination of fs, fA and fQi that leads to the model reproducing recorded data best is then used.

expiration time should be at least 3 times the expiratory time constant (τ_E) [3]. The optimization thus starts with finding the maximum respiratory frequency that still allows a complete expiration by using

$$t_{\text{exp, min}} = \tau_E \cdot 3 \tag{1}$$

$$t_{\text{in, total, max}} = t_{\text{exp, min}} \cdot I/E \tag{2}$$

$$f_{\text{R, max}} = 60 \Big/ \left(t_{\text{in, total, max}} + t_{\text{exp, min}} \right) \tag{3}$$

where $t_{exp,min}$ is the minimum expiration time necessary for a complete expiration, $t_{in,total,max}$ is the derived maximum inspiration time using a given inspiration to expiration ratio (I/E) and $f_{R,max}$ is the resulting maximum respiration rate. I/E is given as a goal by the user, while τ_E is calculated using an exponential fit of the recorded expiration phase. The maximum tidal volume ($V_{tid,max}$) is then found by tuning tidal volume (V_{tid}) so that the forward simulation of the respiratory mechanics model results in a peak pressure of 30 cm H_2O. Subsequently, both MV and FiO_2 are tuned to achieve the PaO_2 and $PaCO_2$ goals in the forward simulation of the gas exchange model using MV_{max} derived from the previously calculated $V_{tid,max}$ and $f_{R,max}$ as a boundary condition. The optimal tidal volume ($V_{tid,opt}$) then is the quotient of MV_{opt} and $fR_{,max}$:

All models and algorithms were programmed in MATLAB (R2015a, The Mathworks, Natick, MA, USA). Parameter identification and tuning of V_{tid}, MV and FiO_2 was done using a Nelder-Mead Simplex Search method, realized in MATLAB as *fminsearch* function. **Figure 2** gives an overview of the optimization algorithm.

2.4. Data

The proposed algorithm was tested using a patient simulator that has been published previously. The simulator allows calculating real time reaction of a ventilated patient to changes in the ventilator settings. It combines models of respiratory mechanics, gas exchange and cardiovascular dynamics to achieve a global simulation of physiological interactions caused by applying mechanical ventilation. It allows simulating various model combinations and different parameter settings. Four different model combinations have been tested with the proposed optimization algorithm (Permutations of the

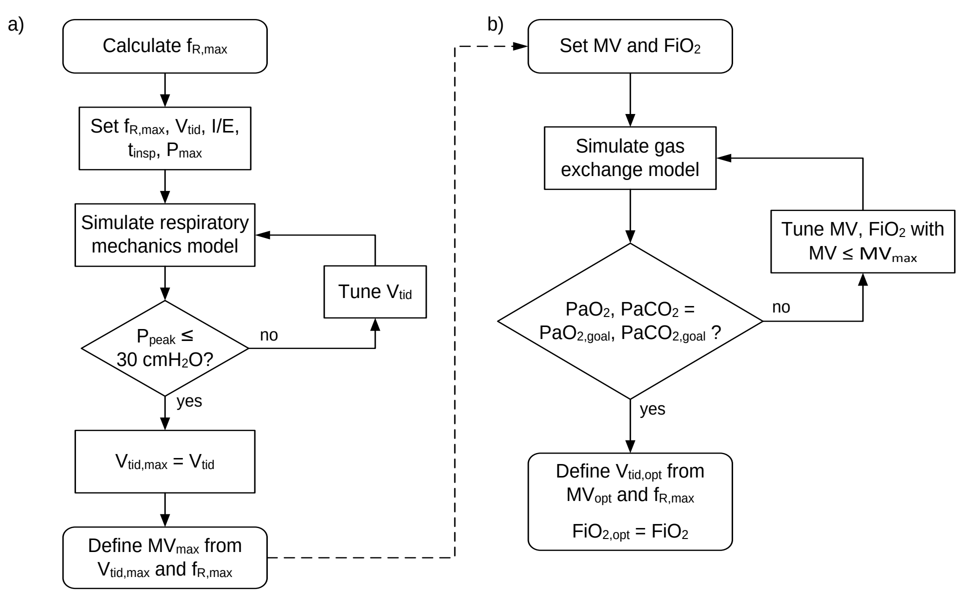

Figure 2. Optimization algorithm to tune MV and FiO_2 to achieve specific PaO_2 and $PaCO_2$ while protecting lung tissue from exceedingly high airway pressures. (a) Algorithm to calculate $f_{R,max}$ and $V_{tid,max}$; (b) Algorithm to calculate optimal MV and FiO_2.

viscoelastic and the recruitment model with a constant flow and a tidal breathing model of gas exchange). **Table 1** shows the relevant parameters that have been used in the models. To identify the respiratory mechanics models, flow, volume and airway pressure (P_{aw}) were recorded, for the gas exchange models $FetO_2$, $FetCO_2$, PaO_2 and $PaCO_2$ was recorded at four different levels of FiO_2 (30%, 50%, 70% and 90%). For a realistic scenario, the recorded data for P_{aw}, flow, volume, $FetO_2$, $FetCO_2$, PaO_2 and $PaCO_2$ were superimposed with white noise with an amplitude of ±3%.

The viscoelastic model (VEM) and the recruitment model (PRM) used to simulate the respiratory mechanics reaction coincide with the models described in 2.2. To simulate gas exchange reactions, models need to comprise body gas exchange, therefore the models used to create the patient data differed from the model used for optimizing MV and FiO_2. The models used for creating the patient data and subsequent evaluation of the optimized ventilator settings are based on the model presented by Chiari *et al.* [11] but were extended to comprise two alveolar compartments [9] [12]. One of the models assumes constant air flow into the lungs, the other comprises a dead space compartment to simulate distinct inspiration and expiration phases [12].

3. Results

Table 2 shows the results of the parameter identification, **Table 3** shows the response to optimized ventilator settings as computed in the patient simulator. Parameter identification of the respiratory mechanics model resulted in a maximum deviation of the identified parameters from their true value of 40% and a minimum deviation of 0% when the VEM was used to create the patient data, and a maximum deviation of 19% with a minimum deviation of 8.9% when the PRM was used to simulate the patient. The identification of the gas exchange model resulted in a maximum deviation of 32% for fs and fQ when using the tidal breathing model for simulating the patient and a maximum deviation of 12% for fs and fQ when using the constant breathing model in the patient simulator. Identified values for parameter fA did show no match (>50% deviation) with the value used to create the data.

Table 1. Parameters used in the respiratory mechanics and gas exchange models. C—Compliance, R—Resistance, K—Overdistention factor, NOpen—Number of recruited alveoli at the beginning of simulation, TOP/TCP—Threshold opening and closing pressure at which alveoli open and close, V_{ds} = Dead space volume.

Model	Parameters							
	C_1 [ml/mmHg]	C_2 [ml/mmHg]	R_1 [mmHg*s/ml]	R_2 [mmHg*s/ml]				
VEM	60	150	0.005	0.005				
	C [ml/mmHg]	R [mmHg*s/ml]	K [1/mmHg]	NOpen [%]	TOP [mmHg]		TCP [mmHg]	
PRM	100	0.01	0.025	40	10		2	
	fs [%/100]	fA [%/100]	fQ [%/100]	V_{ds} [ml]	T [˚C]	CHb [g/L]	pH	BE
Constant flow	0.05	0.8	0.6	0	37	150	7.45	0
Tidal breathing	0.05	0.8	0.6	150	37	150	7.45	0

Table 2. Parameter identification results.

Model used to create patient data		Parameters							
Respiratory mechanics	Gas exchange	C_1 [ml/mmHg]	C_2 [ml/mmHg]	R_1 [mmHg*s/ml]	R_2 [mmHg*s/ml]		fs [%/100]	fA [%/100]	fQ [%/100]
VEM	Constant flow	55.9	185.7	0.007	0.005		0.045	0.104	0.467
	Tidal breathing						0.034	0.108	0.528
		C [ml/mmHg]	R [mmHg*s/ml]	K [1/mmHg]	NOpen [%]	TOP [mmHg]	fs [%/100]	fA [%/100]	fQ [%/100]
PRM	Constant flow	108.9	0.009	0.028	34	11.9	0.050	0.120	0.550
	Tidal breathing						0.036	0.116	0.481

Table 3. Patient response to the optimized ventilator settings as computed in the simulator.

Model used to compute response		Response		
Respiratory mechanics	Gas exchange	P_{peak} [cmH_2O]	PaO_2 [mmHg]	$PaCO_2$ [ml/mmHg]
VEM	Constant flow	16.2	278	33
	Tidal breathing	12.2	264	35
PRM	Constant flow	24.3	280	32
	Tidal breathing	29	271	35

The resulting patient responses show a maximum airway pressure below 30 cm H_2O in all tested combinations, a maximum deviation of 20% and a minimum deviation of 5.6% in the PaO_2 response and a maximum deviation of 8.6% and a minimum deviation of 0% in the $PaCO_2$ response.

4. Discussion

Despite its regular use, individually optimizing mechanical ventilation in patients on the ICU is a challenging task. Multiple conflicting goals need to be weighed against each other while the patient response can predicted on a limited basis only. Using mathematical models helps to not only predict those responses and compute optimal ventilator settings to achieve certain therapy goals but also allow a more detailed insight into the patient's physiology through the identified model parameters. The presented work aims at showing the potential of using such models, especially when multiple goals need to be achieved.

The parameter identification showed a good agreement (≤10% deviation) with the values used to create the patient data in the patient simulator in most of the parameters while some identified parameter values showed a deviation of 20% and more. In the respiratory mechanics models that can be explained by the noise applied to the patient data in the simulator and the data itself used for identifying the parameters. A single standard breath usually is not sufficient to provide enough information to identify the parameters correctly. Instead, multiple maneuvers should be applied to reveal the underlying parameter values. Still, the peak pressures resulting from the optimized settings were all below the critical limit of 30 cm H_2O. The identification of shunt and blood distribution in the gas exchange models mostly showed a good agreement with the values used in the simulator, while the identification of the air distribution seems to have failed. However, the models used to create the data and to compute the patient response differed from the model that was used to calculate the optimal ventilator settings, thus the results of parameter identification should not be used a quality measure for the proposed algorithm. Here, the desired $PaCO_2$ was achieved with only a small deviation while the resulting PaO_2 did not deviate more than 20% from the desired value. The reason for the deviation seems to be that model used to optimize the ventilator settings shows a stronger decrease in oxygenation when the minute ventilation is reduced than the models used in the simulator.

The presented evaluation of the optimization algorithm is purely simulation based and thus can only be used to show the potential of such an approach, a subsequent evaluation with real patient data is therefore planned for the future.

5. Conclusion

The use of mathematical models can aid in optimizing therapy settings in ventilated patients to achieve certain therapy goals. Especially when multiple goals have to be met, the use of individualized models can be of great help. The presented work shows the potential of using models of respiratory mechanics and gas exchange to optimize minute ventilation and oxygen supply to achieve a defined oxygenation and carbon dioxide removal in a patient while guaranteeing lung protective ventilation.

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