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Medical decision support in mechanical ventilation employing combined model information of gas exchange and respiratory mechanics

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Abstract: Mechanical ventilation has become a routine therapy that is mostly applied in critical clinical conditions. It allows a patient to overcome the physiological impact of trauma, critical illness or surgeries by providing sufficient oxygenation and carbon dioxide removal. Though being such a lifesaving intervention, mechanical ventilation may also cause further impairment of the lung tissue if ventilator settings are chosen inappropriately. Moreover, without titration the clinician usually is not able to find suitable settings to reach a desired oxygenation in the patient. We are therefore proposing a concept to implement a model based medical decision support system that is able to provide appropriate settings for FiO_2, minute ventilation, respiration rate, I:E, peak inspiratory pressure and inspiration time to reach a desired level of PaO_2 and $PaCO_2$ based on patient specific physiological properties. Hierarchically ordered models of gas exchange are employed to ensure a robust identification of model parameters from patient data. Currently, performance of the model based predictions is evaluated in a clinical application test, but preliminary results are physiologically correct.

Keywords: Decision support system, mechanical ventilation, mathematical models.

1. INTRODUCTION

Mechanical ventilation is a life-saving therapy that allows a patient to overcome the physiological impact of trauma, critical illness or surgeries. The primary goal of the clinician is to achieve a sufficient oxygenation and appropriate carbon dioxide removal in the patient. Additionally, the clinician will try to minimize the physical impact of this therapy on the patient's lung tissue, which could be harmed furthermore by inappropriate ventilator settings. Both the lack of time to constantly monitor the patient's disease state and the complex interactions between the various ventilator settings and the physiological outcome make finding optimal settings for an individual patient challenging.

We therefore propose to employ medical decision support to provide appropriate ventilator settings that help to pursue therapeutical strategies defined by the clinician. These strategies might include a certain level of oxygenation, fast weaning from the ventilator or tight lung-protective ventilation. Decision making should be model based as opposed to knowledge based systems, which do not include the patient specific properties. Model based systems allow calibration based on patient data and therefore provide individual optimization of ventilator settings. Mathematical models for optimization of ventilator settings should not be solely based on pulmonary mechanics, but should also include other physiological processes that are influenced by artificial ventilation. We have therefore developed a system of interacting models that include pulmonary mechanics, gas exchange and cardiovascular dynamics (Kretschmer, et al. 2011). Each of these model families comprises multiple model versions, which are suitable for different clinical questions and contain a various number of free parameters. All models are ordered hierarchically, i.e. each model is related to its next simpler predecessor and its more complex successor.

The aim of the proposed concept is to demonstrate how information obtained from different mathematical models can be exploited to provide medical decision support on a global physiological scale. The presented example combines a hierarchically ordered family of gas exchange models with a lung mechanics model in order to get both advice on how to set minute ventilation and inspired oxygen fraction (FiO_2) to achieve a certain oxygenation and carbon dioxide removal in the patient and at the same time computing an optimal minute inspiration to expiration (I:E) ration that allows both full expiration and a minimal inspiratory peak pressure.

2. METHODS

2.1 Models of gas exchange

The presented system comprises a family of mathematical models that focus on gas exchange. Each model differs in simulation focus and complexity, i.e. the number of differential equations defining the model and the quantity of model parameters that need to be identified when calibrating the model. Moreover, the implemented models include different representations of ventilation and perfusion distribution. Figure 1 shows a schematic overview of the model family. Here, model complexity rises from top to bottom.

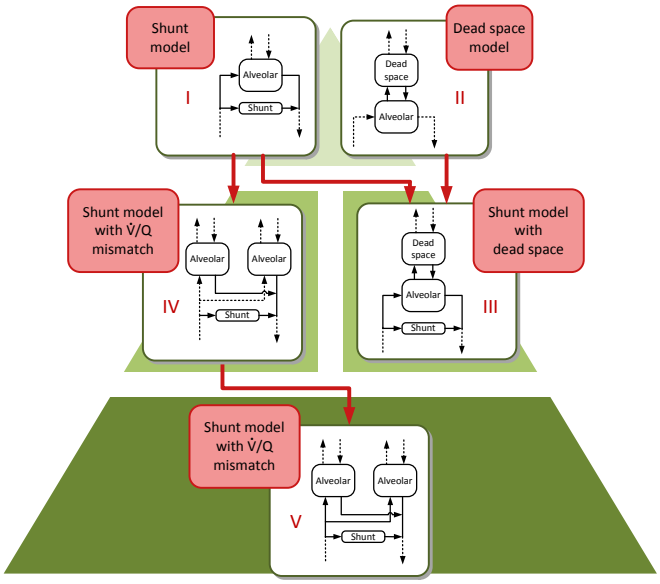

Fig. 1. Schematic overview showing the family of gas exchange models that is used in the proposed decision support system. Each model is related to its simpler predecessor and its more complex successor. (I) Shunt model, (II) Dead space model, (III) Shunt model with dead space, (IV) Shunt model with V̇/Q mismatch and fixed perfusion distribution, (V) Shunt model with V̇/Q mismatch and variable perfusion distribution

Model I consists of an alveolar compartment receiving 100% of ventilation and a shunt compartment with no ventilation, i.e. it defines the amount of venous blood that does not participate in gas exchange but is mixed directly into the oxygenated end-capillary blood. This model can be calibrated with only one blood gas measurement and showed good results when comparing simulated with clinical PaO_2 (arterial partial pressure of oxygen) data (Kretschmer, et al. 2013a). However, reproducing measured $PaCO_2$ (arterial partial pressure of carbon dioxide) is not possible in this model (Kretschmer, et al. 2013b). Model II comprises a different approach; it includes a dead space compartment, i.e. a compartment with ventilation but no perfusion instead of the shunt compartment in model I. The model is derived from the three compartment model proposed by Riley (Riley 1980). It allows simulation of $PaCO_2$ in the patient, tests with measured data showed consistent results in a comparable version of this model (Kretschmer, et al. 2013b). Both of the above models include one model parameter that needs to be identified. Combining both models allows simulation of both PaO_2 and $PaCO_2$; the resulting model (III) now comprises two parameters (Riley 1980). Although comprising compartments with different distributions of ventilation and perfusion, this model is not able to reproduce effects of ventilation/perfusion (V̇/Q)-mismatch. Such may be achieved by extending model I by an additional alveolar compartment, allowing ventilation to be distributed among the two compartments. Fixing perfusion distribution to 10% in one compartment (low perfusion) and 90% in the other compartment (high perfusion), results in a model (IV) that still includes only two model parameters (Karbing, et al. 2011, Kjaergaard, et al. 2001). Finally, model V includes a variable perfusion distribution among the alveolar compartments, thus three model parameters need to be identified (Karbing, et al. 2011, Melo, et al. 1993). Karbing et al. showed that model V is superior to model IV in reproducing PaO_2 and $PaCO_2$ at different levels of FiO_2 (Karbing, et al. 2011).

2.2 Respiratory mechanics model

Respiratory mechanics are simulated by an RC-model of first order. The electrical analogue thus includes a serial arrangement of a resistance to reproduce the resistive effects and a capacitor to reproduce the compliant effects of the lung tissue. Figure 2 shows a representation of the electrical analogue. The model comprises three parameters, i.e. R, C and τ_E which represents the expiratory time constant (Schranz, et al. 2013).

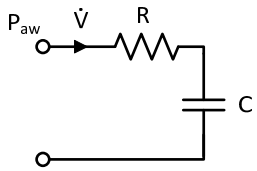

Fig. 2. Electric analogue of the first order RC-model to simulate respiratory mechanics. R – lung resistance, C – lung compliance, P_{aw} – airway pressure, V̇ – air flow.

2.3 Parameter identification

Model calibration to patient-specific properties is necessary to ensure calculation of individually optimized ventilator settings. The presented models of gas exchange are identified hierarchically, i.e. parameter values of simple models are exploited as initial values for the identification of complex models. This approach has proven to be beneficial to avoid reaching global minima in the error surface, thus increasing robustness of the identification process (Riedlinger, et al. 2013a, Schranz, et al. 2011). Figure 3 schematically describes the identification process of the applied models of gas exchange. Model I is calibrated directly by calculating shunt fraction from measured patient data (Kretschmer, et al. 2013a). Models II-V are identified employing the Nelder-Mead Simplex Method (Lagarias, et al. 1998) to minimize the summed squared difference between measured and simulated PaO_2 and $PaCO_2$. Following the hierarchical structure, models I and II are identified using average values of healthy subjects as the initial values. Results for shunt fraction (f_S) and ventilation distribution to dead space (f_A) are then used as initial values to calibrate model III. Ventilation distribution in model II is not equivalent to ventilation distribution among the compartments in model IV, thus calibration of model IV can only exploit shunt fraction of model I. The initial value for ventilation distribution is set to 50%. Finally, calibration of model V employs parameter values for ventilation distribution and shunt as identified in model IV, initial value for perfusion distribution (f_Q) is set to 50%.

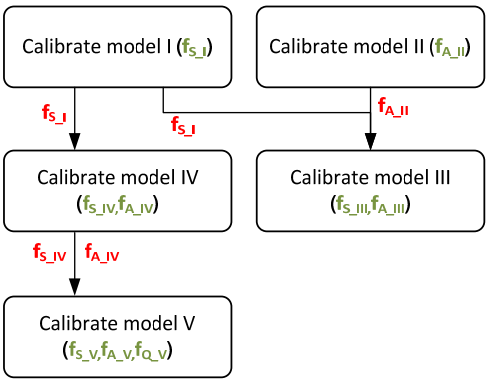

Fig. 3. Schematic description of hierarchical parameter identification of the gas exchange model family. Complex models exploit identified model parameters of their simpler predecessors as initial values for parameter identification. Green – Model parameters that are calibrated, Red – Model parameters that are used as initial values in the next hierarchy layer. f_S – shunt fraction, f_A – ventilation distribution, f_Q – perfusion distribution.

The data used for calibration includes $FetO_2$ and $FetCO_2$ (end-tidal gas fraction of oxygen and carbon dioxide, respectively), SpO_2 (peripheral oxygen saturation) at four different FiO_2 levels. Additionally, measurements or estimates of current minute ventilation, dead space volume, respiration rate, cardiac output, CO_2 production and respiratory quotient as well as blood gas data from one blood gas sample is needed, including pH, base excess, Haemoglobin concentration, temperature, PaO_2, and $PaCO_2$ are necessary. All of the aforementioned data needs to be recorded at a steady state, i.e. after each change in FiO_2, the clinician needs to until equilibrium is achieved in the patient.

Resistance and compliance of the respiratory mechanics model are identified by fitting it to inspiratory data of measured ventilation cycles (pressure controlled mode) using multiple linear regression, τ_E is determined by fitting an exponential function to the expiratory flow data (Schranz, et al. 2013).

2.4 Optimization of ventilator settings

The proposed system is intended to find appropriate ventilator settings to reach certain levels of PaO_2 and $PaCO_2$ in the patient defined by the clinician. Additionally, the clinician is asked to define the PEEP that should be used as well as the ramp time (t_{Ramp}) that should be applied during inspiration. Based on these parameters, the system is defined to find suitable values for FiO_2, minute ventilation (MV), respiration rate (f_R), inspiration to expiration ratio (I:E), inspiratory peak pressure (P_{Insp}) and total inspiration time (t_{Insp}).

FiO_2 can either be calculated directly using model I (Kretschmer, et al. 2013a) or be identified by tuning it to minimize the quadratic difference between desired PaO_2 and simulated PaO_2 using models III-V with the tested FiO_2. Optimal minute ventilation may be calculated analogously, i.e. by tuning it to minimize the quadratic difference between desired $PaCO_2$ and the $PaCO_2$ that is simulated by models II-V. In models III-V, influence of FiO_2 and MV is not limited to PaO_2 or $PaCO_2$, respectively. Thus tuning of those parameters has to be done synchronously. The applied penalty function is stated in eq. 1.

$$E = \left(PaO_2 - PsO_2\right)^2 + k \cdot \left(PaCO_2 - PsCO_2\right)^2 \quad (1)$$

Here, PaO_2 and $PaCO_2$ are the desired oxygen and carbon dioxide partial pressures in arterial blood, while PsO_2 and $PsCO_2$ are the simulated values. The difference between desired and simulated $PaCO_2$ is multiplied by a factor (k=2) to account for its lower value.

Optimal P_{Insp} is chosen as the minimal peak inspiratory pressure that is necessary to ensure the MV calculated by the gas exchange models. Additional boundary conditions are the PEEP and ramp time defined by the clinician as well as a fixed expiration time of three times the identified expiratory time constant τ_E to ensure an expiration of at least 95% (Lourens, et al. 2000). Given the just mentioned boundary conditions, P_{Insp} can be expressed as a function of t_{Insp} (Schranz, et al. 2013):

$$P_{Insp} = \frac{RC^2\left(e^{\frac{t_{Ramp}}{RC}} - 1\right)PEEP - t_{Ramp} \cdot e^{\frac{t_{Insp}}{RC}}\left(C \cdot PEEP + V_T\right)}{C\left[RC\left(e^{\frac{t_{Ramp}}{RC}} - 1\right) - t_{Ramp} \cdot e^{\frac{t_{Insp}}{RC}}\right]} \quad (2)$$

Here, V_T is the tidal volume that can be derived from minute ventilation, the current dead space and the sum of inspiration and expiration time. Plotting the above function as a relation between t_{Insp} and P_{Insp} reveals a unique minimum allowing selection of an appropriate t_{Insp} that ensures minimal pressure while avoiding the build-up of intrinsic PEEP. f_R and I:E can then be derived from the selected t_{Insp}.

Using gas exchange models II and III allows a stepwise optimization of parameters, i.e. optimal MV is calculated before optimizing P_{Insp} and t_{Insp}. Models IV and V however require input signals of $FetO_2$ and $FetCO_2$, which are functions of f_R. Thus, in models IV and V optimization is done synchronously using the algorithm described in Figure 4.

3. RESULTS

3.1 Graphical user interface

The above described method for optimizing ventilator settings has been implemented in a graphical user interface programmed in MATLAB® (R2012a, The Mathworks®, Natick, USA) to provide the clinician with a tool to enter the measured patient data and to retrieve the recommended ventilator settings. In addition, the user interface shows the identified model parameters, thus providing the clinician with additional information about the patient's disease state. The user interface requires the user to manually enter results from

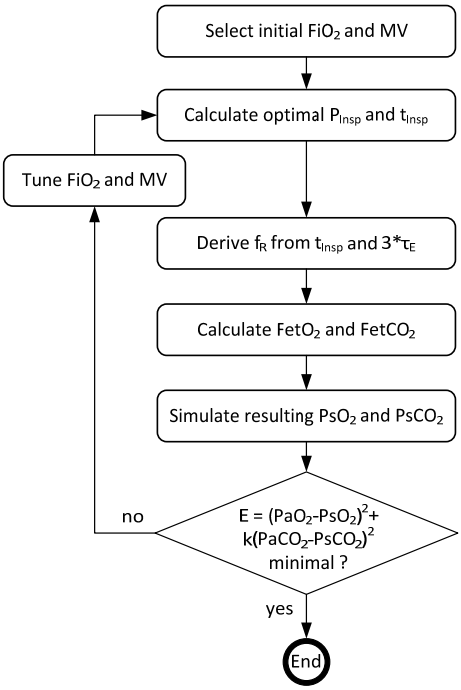

Fig. 4. Schematic description of synchronous optimization of FiO_2, MV, P_{Insp} and t_{Insp}. Models IV and V require $FetO_2$ and $FetCO_2$ as input signals. Both are functions of f_R, thus MV and P_{Insp}/t_{Insp} cannot be optimized sequentially.

blood gas analysis and measurements at four different levels of FiO_2. Respiration data is taken directly from the ventilator. The current setup is intended for a clinical application study, thus it shows recommended ventilator settings based on each of the gas exchange models presented above. Additionally, the interface displays the remaining error after parameter identification and allows the user to specify the O_2 and CO_2 dissociation curves to be employed in simulation of gas exchange. Figure 5 shows a screenshot of the user interface.

3.2 Simulation results and predicted ventilator settings

Each of the presented models has been tested in isolation before and has proven to be physiologically plausible with the ability to reproduce clinical data (Karbing, et al. 2011, Kretschmer, et al. 2013a, Kretschmer, et al. 2013b, Schranz, et al. 2013). Ventilator settings calculated by proposed system employing the various gas exchange models were also physiologically plausible. The recommended FiO_2 that has been computed by the gas exchange models differed by a maximum of 6%. Models II and III showed a difference in the recommended minute ventilation compared to MV recommended by models IV and V. Models II and III proposed a higher MV to reach the desired $PaCO_2$ than models IV and V.

4. DISCUSSION

Selecting appropriate ventilator settings in patients admitted to intensive care is a challenging task due to both a lack in

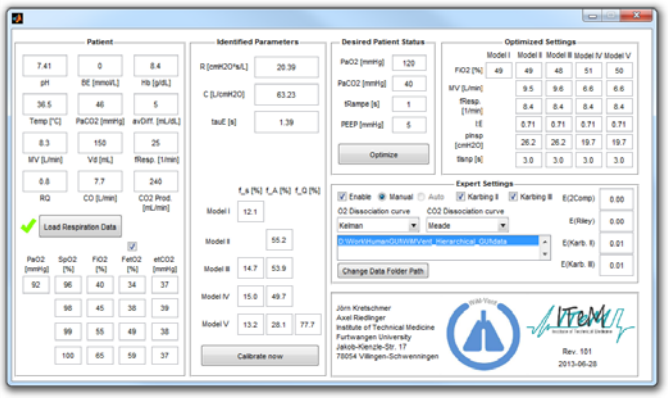

Fig. 5. Screenshot of the graphical user interface. It allows the user to enter results from blood gas analysis and measurements of SpO_2, $FetO_2$ and $FetCO_2$ at four different levels of FiO_2. It shows the results of parameter identification to provide the user with additional information about the patient's disease state and shows recommendations for ventilator settings based on each of the implemented gas exchange models.

deeper insights into the patient's physiology as well the inability to predict complex physiological interactions and thus the outcome of a certain ventilation strategy. Several researches have tackled this task in the past. However, they were based on knowledge based systems (Campbell, et al. 2001, Dojat, et al. 1997, Lozano, et al. 2008, Shahsavar, et al. 1994), thus not including the possibility to adapt the decision support to an individual patient, did not have any anatomical or physiological relation (Rudowski, et al. 1991, Tehrani and Roum 2008) or were limited to one physiological domain or a fixed combination of models (Rees, et al. 2006, Rutledge, et al. 1993), thus inhibiting the possibility of adapting the simulation to changes in the patient's disease state. The proposed system includes both a combination of different physiological domains to allow a global simulation of the patient and enables a decision support system to adapt itself to changes in the patient by providing different models of the same family. It thus provides the required tools for optimizating FiO_2 and minute ventilation to provide sufficient oxygenation and carbon dioxide removal in the patient. Additionally, it implements a lung-protective strategy, i.e. a minimal inspiratory peak pressure to achieve the recommended minute ventilation. The lung is thus protected from high mechanical stress as well as intrinsic PEEP build-up.

Moreover, the hierarchical structure of the presented family of gas exchange models allows robust identification of model parameters by exploiting the existing model relations (Riedlinger, et al. 2013b). Identification results are shown on a graphical interface to provide the clinician with additional information on the patient's disease state.

However, the proposed system includes some limitations. In order to employ the optimization of inspiratory peak pressure, patients need to be ventilated in pressure controlled mode, thus the system can neither be applied to patients ventilated

in volume controlled modes nor in assistive modes. Moreover, the current system provides multiple recommendations, each using a different model of gas exchange, thus leaving it to the clinician to select one of the suggested ventilator settings. Future versions need to implement an algorithm to select the best model in terms of agreement with patient data, number of model parameters and the current clinical question.

Although computing physiologically sound recommendations, the proposed system still needs to be evaluated in a clinical setting comparing model predictions with real patient outcome. The presented graphical user interface is currently employed in a clinical application study to evaluate the predictive performance of the proposed system. Nonetheless, the implemented models have been evaluated in isolation before, thus promising accurate results in the presented system.

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