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Evaluating the Suitability of a Neonatal Respiratory System Model for the Simulation of Arterial Partial Pressures

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Abstract: Blood gas analyses (BGAs) are used during mechanical ventilation as a diagnostic tool for partial pressures of gases in the blood, but deliver only spot measurements due to their invasive nature. We evaluate an established neonatal pulmonary model on its suitability to estimate partial pressures of oxygen and carbon dioxide to bridge the gap between BGAs. The evaluation is twofold. First, we conduct a comparison to the model's original evaluation, using five patients with one simulation each, to underline the importance of reproducibility of implementations. Second, we perform an evaluation based on a collected dataset of 11 patients and 452 simulations, comparing the simulated partial pressures of O_2 and CO_2 to BGA measurements. We report considerable deviations from real measurements and propose adaptations to improve the simulation.

Keywords: Physiological model, respiratory model, neonate

1 Introduction

Mechanical ventilation is a life-saving intervention in the neonatal intensive care unit (NICU). During mechanical ventilation, blood gas analyses (BGA) are used to monitor acid-base status and gas exchange. Partial pressures of oxygen and carbon dioxide are used to adjust ventilator settings. However, BGAs are spot measurements which can only be obtained at the cost of patient stress and blood loss. They cannot be used for continuous control of ventilator settings. To address this limitation, it is common to use a model of the respiratory system to continuously simulate arterial partial pressures and thus provide the basis for the development and use of ventilator control. While numerous approaches exist for modeling adult

respiratory systems [1], there are very few that focus specifically on neonates such as [2] and [3], neither including O_2 and CO_2 partial pressures. Notably, Tehrani presented a neonatal respiratory model [4], which has been further evaluated in subsequent studies [5] and used to develop supportive systems for NICUs [6]. The applications of such models extend further to form a basis for closed-loop controllers, e.g. a CO_2 controller for ventilated neonates [7], or serve more generally as a patient simulator to guide therapeutic interventions or act as training tools.

This study contributes a comprehensive evaluation of an implementation of the neonatal respiratory model presented by Tehrani [5]. We established a test environment to compare simulated arterial partial pressures against the model's original evaluations and further BGA measurements. This latter part of the evaluation was performed on our own dataset comprising 11 patients and 452 simulations, providing valuable insights into the model's accuracy and applicability in clinical settings.

2 Evaluation Setup

This work evaluates a mathematical model of the respiratory system in ventilated neonates which was presented by Tehrani in [5]. Similarly to Tehrani, we focused on ventilation with pressure control, taking the following ventilator settings as part of the model's inputs: peak inspiratory pressure (PIP), positive end-expiratory pressure ($PEEP$), respiratory rate (RR) and fraction of inspired oxygen (F_{iO_2}). Further inputs are the patient's weight, dynamic lung compliance (C_{dyn}) and shunt fraction, describing the fraction of blood which is not oxygenated. Based on these inputs the model simulates values for arterial and mixed arterial partial pressures of oxygen and carbon dioxide, which we will refer to as P_{aO_2} , P_{aCO_2} and P_{amO_2} , P_{amCO_2} . Fig. 1 shows a block diagram of the model, which we implemented in MATLAB Simulink¹. The model's evaluation is divided into two parts: the reconstruction of a previous evaluation and an evaluation on new patient data.

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¹ Model implementation available at <https://git.rwth-aachen.de/informatik11/model-of-neonatal-respiratory-system>

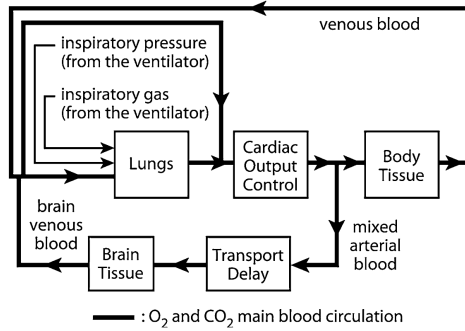


Fig. 1: Block diagram of the evaluated respiratory system model, taken from [5]

We performed a reconstruction of Tehrani’s evaluation from [5], which used data from five neonates presented previously in [6] and had two consecutive blood gas analysis available per patient. The model was run from the first BGA to the next. The simulated P_{aO_2} (transformed to saturation) and P_{aCO_2} were compared against measured oxygen saturation and carbon dioxide partial pressure from the BGA. We replicated the procedure, by using the provided data as model input and compared our results to Tehrani’s simulations.

Next, we evaluated the model by performing a patient-data based evaluation in a similar manner to [5] with our own data. We ran the model for the time span between two consecutive BGA and compared the simulated P_{amO_2} and P_{amCO_2} to the partial pressures from the second BGA. We chose to compare the arterial mixed partial pressure instead of arterial partial pressure, as most of our BGAs are from capillary blood, which are closer to mixed arterial blood. The data were collected in the RWTH Aachen University Hospital and include records of ventilation data from the neonatal intensive care unit. From the dataset we extracted patients with available entries for RR , PIP , $PEEP$, F_{iO_2} and blood gas analyses. The dynamic compliance is partially available in the dataset and is otherwise computed through an estimation based on weight from [8]. The extraction resulted in a set of 11 patients, five male and six female. A statistical description of the patients with their simulation parameters is presented in Table 1. In total 452 pairs of consecutive BGAs were available, resulting in 452 simulations. For the simulations we didn’t use the patient’s birth weight, but the weight averaged over the time period of available BGAs. To run the model automatically on the collected data, we set up a simulation environment in MATLAB. The model is initialized with O_2 and CO_2 values from one BGA. The model is run until the next available BGA. As the used ventilator parameters are recorded at a frequency of 1Hz, we can capture changes in the parameters between the BGAs and feed these to the model. The output consists of the simulated P_{amO_2} and P_{amCO_2} .

3 Results

The original results from [5] together with our reconstructed results are shown in Table 2. For three out of the five patients we achieved similar values to Tehrani for both P_{aO_2} and P_{aCO_2} . However, the simulation of the other two patients deviated considerably from the original values, patient three having the highest deviation.

During the patient data-based evaluation, 18 of the 452 performed simulations reached extremely high values for P_{amO_2} and P_{amCO_2} (over 2000mmHg and up to 3.8×10^{15} mmHg), showcasing scenarios in which the implemented equations reached an unstable state. These simulations were excluded from the following visualizations.

The absolute errors for simulated P_{amO_2} and P_{amCO_2} are visualized as a histogram in Fig. 2. As the available blood gas data was unevenly distributed among patients, the results are grouped by weight as follows: (0, 1]kg, (1, 1.5]kg, (1.5, 2.5]kg and (2.5, 4]kg. From this plot we observe that P_{aCO_2} exhibits higher errors than P_{aO_2} , the highest errors resulting solely from the lowest weight class.

Our input data for PIP , $PEEP$, RR and F_{iO_2} contained continuous measurements between two BGAs. Thus, we wanted to display how changes in a parameter during a simulation would influence the error in the O_2 and CO_2 partial pressures. A considerable impact of parameter change could only be observed for F_{iO_2} as shown in Fig. 3.

4 Discussion

The reconstructions of the evaluation from [5] matched the original values for three patients, while the results for the other two patients diverged considerably. Neither for the simulations that were reconstructed well, nor for the two that diverged could a common characteristic be found to justify the difference between the two outcomes. This deviation could hint to either different settings of the model, such as differential equations solver due to the different implementations or to possible numerical instabilities in the model. The results show that not only the model’s description but also implementation details are important for reproducibility.

From the patient-based evaluation we observed that both static high F_{iO_2} input values as well as changes in F_{iO_2} between BGAs can cause extreme and implausible simulated oxygen and carbon dioxide partial pressures. On the one hand, these deviations can result from a simplified modeling of the effect F_{iO_2} has on P_{aO_2} . On the other hand, F_{iO_2} is changed as a result of the patient’s state change, such as dropped oxygen saturation. This state change is however not captured by the model.

Tab. 1: Patient description, values for C_{dyn} , PIP , $PEEP$, RR and F_{iO_2} are given as mean $\pm$ std. BW stands for birth weight. Only measured C_{dyn} is shown.

Pat. ID	PIP (mmHg)	$PEEP$ (mmHg)	RR (b/min)	F_{iO_2} (%)	BW class (g)	C_{Dyn} (ml/cmH ₂ O)	Gestational age (weeks)	Simulation count
1	17 $\pm$ 3.2	4.8 $\pm$ 0.9	48.1 $\pm$ 12	25.6 $\pm$ 5.3	(600, 800]	0.4 $\pm$ 0.4	(24, 26]	74
2	19.1 $\pm$ 2.3	5.9 $\pm$ 0.6	43.7 $\pm$ 8.4	24.6 $\pm$ 5.7	(3400, 3600]	1.9 $\pm$ 2.2	(36, 38]	46
3	15.4 $\pm$ 1.3	5.9 $\pm$ 0.4	15 $\pm$ 0	23.3 $\pm$ 4.6	(2000, 2200]	-	(38, 40]	15
4	19 $\pm$ 3	5.8 $\pm$ 0.2	51.5 $\pm$ 10.4	27 $\pm$ 9.2	(800, 1000]	0.1 $\pm$ 0.1	(28, 30]	15
5	18.2 $\pm$ 1.6	4.9 $\pm$ 0.4	46.9 $\pm$ 6.7	27.9 $\pm$ 7.7	(600, 800]	0.4 $\pm$ 0.6	(24, 26]	17
6	22.9 $\pm$ 3.3	1.1 $\pm$ 1.6	52.5 $\pm$ 5	35.1 $\pm$ 10.5	(600, 800]	-	(22, 24]	96
7	23.9 $\pm$ 3.4	5.9 $\pm$ 0.3	55.6 $\pm$ 6	39.1 $\pm$ 15.8	(600, 800]	-	(24, 26]	142
8	3.6 $\pm$ 0.4	6.5 $\pm$ 0.1	41.2 $\pm$ 13.1	21.2 $\pm$ 2.1	(2800, 3000]	0.9 $\pm$ 17.6	(38, 40]	11
9	19.6 $\pm$ 2	-	48.5 $\pm$ 3.3	30.5 $\pm$ 8.6	(2000, 2200]	-	(32, 34]	12
10	14.9 $\pm$ 0.5	5.9 $\pm$ 0.2	17 $\pm$ 4.9	26.4 $\pm$ 4.3	(400, 600]	0.7 $\pm$ 0.2	(24, 26]	1
11	18.8 $\pm$ 01.7	5.8 $\pm$ 0.4	41 $\pm$ 4.6	27.9 $\pm$ 6.7	(3400, 3600]	1.7 $\pm$ 0.5	(38, 40]	23

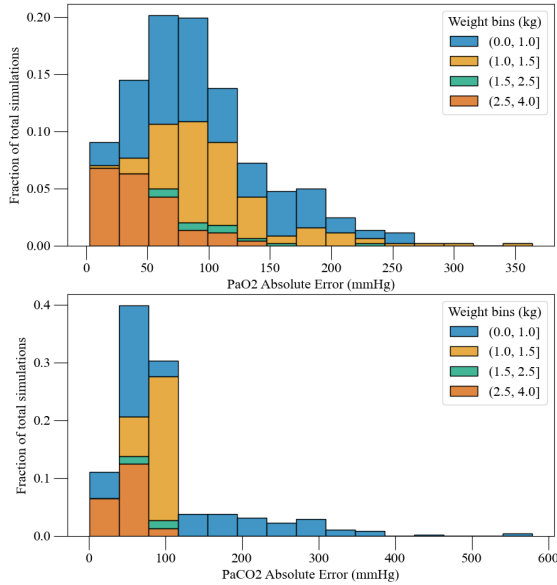


Fig. 2: Distribution of absolute error for simulated P_{aO_2} and P_{aCO_2} of the 11 patients grouped by weight.

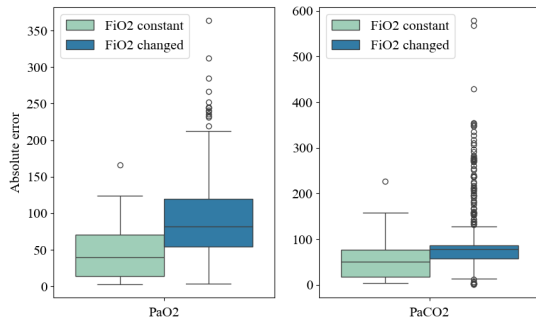


Fig. 3: Absolute error in P_{aO_2} and P_{aCO_2} for simulations where F_{iO_2} stayed constant vs. where it changed.

Tab. 2: Reproduction of Tehrani's simulation [5] (orig) and our reconstruction (recon).

Patient ID	P_{aO_2} orig. (mmHg)	P_{aO_2} rec. (mmHg)	P_{aCO_2} orig. (mmHg)	P_{aCO_2} rec. (mmHg)
1	90	87.23	40	38.11
2	109	108.55	41	44.67
3	68	14.75	48	110.15
4	87	83.51	40.5	41.63
5	148	122.44	51.3	89.93

Low-weight patients stood out with high errors, especially neonates with weights under 1kg. This effect was even greater for P_{amCO_2} compared to P_{amO_2} . This could be linked to the modeled production of CO_2 as there is no differentiation in metabolic rates between patients. Further, the weight is used in the model only to determine the physiological dead space, which does not take part in gas exchange and has no further effects on other parameters. Especially linking dynamic compliance to weight is an important step, as the same absolute compliance represents different lung states for patients of different weights. Overall we consider the model currently unsuited for the simulation of extreme and very low birth weight patients, as multiple model-internal parameters are not adjusted between weight groups nor do they distinguish between the patient's health states.

To improve the modeling of arterial partial pressures multiple changes could be made. First, the model needs an extension which limits the direct influence an increase in F_{iO_2} has on the oxygen partial pressure. Such a limitation would also reflect data reported on the ratio of P_{aO_2}/F_{iO_2} , which is not linear in contrast to the model and varied depending on the F_{iO_2} level [9]. A further improvement could be brought by adjusting the relationship between the alveolar partial pressure P_{AO_2} and P_{aO_2} , which is modeled by a constant subtrahend of 20mmHg, representing the alveolar-arterial gradient for oxy-

gen. This value has been shown to differ between newborns [10] and can reach values of over 600mmHg [11]. Adapting the dissociation curves for the relationship between concentration and partial pressure of gases used in the model, could also offer an improvement, as the ones employed in the original publication [4] are computed from adult data. A further parameter which greatly influences the oxygen levels in neonates is the shunt describing the mixing of arterial and venous blood [3]. The shunt was set to 0.1, meaning 10% of the blood was not oxygenated, similar to Tehrani's evaluations [4, 5]. Trying to parametrize the shunt to individual patients could also improve the model. Ultimately, the model could be augmented by a cardiovascular component to account for blood pH, as has been done in [12]. An extension of the model to include even more parameters could however also add new errors, as measurements for neonates are not as widely available as for adults and a thorough evaluation is harder.

After adaptations to the model, its evaluation could be extended from the point-wise blood gas analysis-based evaluation to a continuous comparison of the modeled partial pressures by considering transcutaneous measurements of gases.

Limitations. Most of the used blood gas analyses in the patient-based evaluation are from capillary blood samples, but are compared to arterial mixed gases, between which a known difference exists [13]. The patients' weights used in the simulation were averaged over the time span of available BGAs due to privacy concerns.

5 Conclusion

In this work we evaluated the simulated arterial partial pressures for oxygen and carbon dioxide using a model of the neonatal respiratory system. Through a two-fold evaluation we identified potential improvements of the model, to overcome implausibly high simulated carbon dioxide partial pressures and simulate low birth weight neonates more accurately. We conclude, that the model needs further development before it can be used as a developmental basis across all neonatal patient groups at least for the CO₂-based control of ventilator settings.

Author Statement

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Declaration, and has been approved by the Ethics Committee of the Medical Faculty, RWTH Aachen University (EK 118-19).

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