# Automated Positive End-Expiratory Pressure Titration during Mechanical Ventilation

**Philip von Platen** * **Anake Pomprapa** * **Arnhold Lohse** *
**Steffen Leonhardt** * **Philipp A. Pickerodt** ** **Martin Russ** **
**Mahdi Taher** ** **Emilia Boerger** ** **Roland C. E. Francis** **
**Marian Walter** *

* *Medical Information Technology, RWTH Aachen University, Aachen, Germany (e-mail: platen@hia.rwth-aachen.de).*
** *Department of Anesthesiology and Operative Intensive Care Medicine CCM/CVK, Charité - Universitätsmedizin Berlin, Corporate member of Freie Universität Berlin, Humboldt Universität zu Berlin, and Berlin Institute of Health, Berlin, Germany (e-mail: philipp.pickerodt@charite.de)*

**Abstract:** Optimizing the positive end-expiratory pressure remains challenging for any clinician treating a patient with acute respiratory distress syndrome. This paper presents an approach to automate a PEEP titration maneuver and identify the best PEEP according to maximal compliance. The respiratory system was modeled by a single-compartment model, and parameters were estimated using multiple linear regression. A classifier identified the *best* PEEP using the scaled relative change in compliance between PEEP levels based on empirical data from previous manual PEEP titrations. An experimental system allows the *in vivo* testing of the automated PEEP titration, including additional safety measures. The complete system was tested in a single animal experiment and correctly identified the *best* PEEP. The introduced system is a step closer towards an automated, standardized PEEP optimization and closed-loop control of mechanical ventilation.

*Keywords:* critical care, feedback control, mechanical ventilation, decision support systems, artificial intelligence

## 1. INTRODUCTION

Acute Respiratory Distress Syndrome (ARDS) is a severe form of respiratory failure with a high mortality rate (Bellani et al., 2016). Patients suffering from ARDS have insufficient oxygen in their blood, a stiffer lung (reduced lung compliance), and collapsed lung regions (atelectasis). Positive pressure mechanical ventilation is the current therapy of choice, which supplies supplementary oxygen and ventilation to improve gas exchange. A positive end-expiratory pressure (PEEP) is applied to keep the lung open, thereby reducing atelectasis and increasing the functional residual capacity of the lung, which can lead to improved oxygenation. Conversely, PEEP can also lead to overdistension of lung regions and increase right heart load. Hence, choosing an optimal PEEP level remains a challenging task for any clinician.

Different approaches for optimizing PEEP have been proposed, but there is currently no consensus on the optimal method (Hess, 2015). An early landmark study by Suter et al. (1975) proposed titrating PEEP such that the oxygen delivery is maximized. However, the calculation of oxygen delivery requires invasive measurement of cardiac output and oxygen tension. The respiratory system compliance was proposed as a substitute, since it correlated well with oxygen delivery. As such, many PEEP optimization methods include titrating the PEEP until maximum compliance is reached. Suarez-Sipmann et al. (2007) showed that compliance could identify the beginning of collapse after recruitment and confirmed these findings with oxygenation and computed tomography scans. Other methods include finding the lower point of inflection in the pressure-volume curve in a low-flow inflation maneuver or calculating a stress index, as described in Hess (2015). A model-based PEEP optimization based on intra-breath compliance was proposed by Chiew et al. (2011).

Imaging techniques, such as Computed Tomography (CT) Scan and Electrical Impedance Tomography (EIT), have also been used for offline PEEP optimization. Gattinoni et al. (2006) considered lung density from CT scans at different PEEP levels. Different EIT features, such as the global in-homogeneity and hyperdistension indices (Hochhausen et al., 2017) or the overdistended and collapsed zones (Zhao et al., 2020) were also used to adjust the PEEP.

Optimizing PEEP by finding the maximum compliance remains a widely researched method; it requires no additional devices (CT and EIT), specialized mechanical ventilators (low-flow method), and is not limited to volume-

controlled ventilation (stress-index). The standard procedure for finding the maximum compliance, as shown in Fig. 1, involves first increasing the level of the end-expiratory pressure to a specific value and then stepwise reducing, or titrating, the PEEP and observing the compliance at every level. Hickling (2001) argued that due to the known hysteresis of the respiratory system, a decremental PEEP titration should be used instead of an incremental titration. This type of PEEP optimization method was used in a clinical study performed by the Writing Group for the Alveolar Recruitment for Acute Respiratory Distress Syndrome Trial (ART) Investigators (2017).

Despite its simplicity, such a PEEP optimization maneuver is not performed routinely in the clinical setting, as it is time-consuming and requires the full attention of the clinician. The clinician needs to manually adjust the PEEP while closely observing the dependent variable (the compliance). At the same time, adjusting PEEP can lead to critical events, such as hypoxemia and hypercapnia, due to reduced tidal volumes caused by small lung compliance. Contrarily, large lung compliance can lead to very large tidal volumes, possibly inducing volutrauma (Acute Respiratory Distress Syndrome Network, 2000). Finally, varying the level of PEEP will affect the patient's hemodynamic stability and needs to be closely observed by the clinician.

An automated PEEP titration method would reduce the clinician's workload during such maneuvers, allowing more focused monitoring of the patient. It would also benefit the patient, as it could lead to the more routine use of titrations and superior, standardized choices of PEEP. We will introduce an algorithm to automate the titration and optimize PEEP according to maximal compliance. Data from 21 manual PEEP titrations, performed in a porcine model of ARDS, are used to design the algorithms. The system is evaluated online in a single animal experiment.

## 2. METHODS

### *2.1 Data and Experimental Setup*

The available PEEP titration data was gathered from eight adolescent pigs (German landrace, male, approx. 40 kg). All animals were put under general anesthesia and respiratory failure was induced either by surfactant depletion using saline-based lung lavages, see Russ et al. (2016), or surfactant depletion combined with injurious ventilation, as shown in Russ et al. (2021). The animals remained deeply sedated throughout the experiment and had no spontaneous breathing. Both models produced a severe form of ARDS according to the Berlin definition ($PaO_2/FiO_2$ of less than 100). In this work, no differentiation was made between the two models and all data was pooled together.

Following the induction of respiratory failure, a PEEP titration was performed manually, followed by a three-hour phase of protective ventilation, according to the autoARDSNet protocol introduced by Pomprapa et al. (2014). This process was repeated up to three times per animal. The settings for the manual PEEP titrations are given in Table A.1. A total of 21 PEEP titrations from eight animals were used in the subsequent analysis.

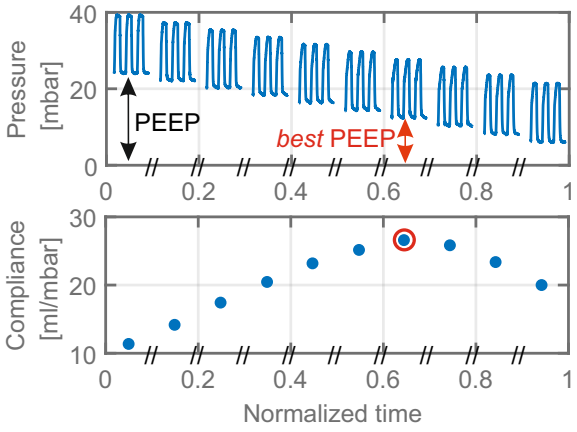


Fig. 1. A decremental PEEP titration. The *best* PEEP and maximum compliance are shown in red.

An experimental system was developed that contains all the sensors and actuators required for automated control of a mechanical ventilator. All algorithms ran on a real-time PC (MicroLabBox, dSPACE GmbH, Paderborn, Germany) which communicated with a medical panel PC (THA.leia$^3$, MCD Medical Computers Deutschland GmbH, Mönchengladbach, Germany) running MATLAB 2017b (The MathWorks Inc., Natick, USA) and dSPACE Control Desk ver. 7.1 (dSPACE GmbH, Paderborn, Germany). A modified respirator (EVE, Fritz Stephan GmbH, Gackenbach, Germany) received remote commands and sent all measurement data via a custom RS232 protocol to the real-time PC. The respirator has a built-in pulse oximeter (MASIMO Rainbow, Irvine, USA) and capnograph (MASIMO IRMA $CO_2$, Irvine, USA). All ventilation data (pressure and flow) were sampled at 100 Hz, whilst the other variables, such as oxygen saturation ($SpO_2$), heart rate, and end-tidal carbon dioxide concentration ($etCO_2$) were sampled at 1 Hz. The data were recorded and processed on the real-time PC.

### *2.2 Estimation of Lung Mechanics*

The respiratory system can be modeled as a single-compartment, comprising a resistance and a compliance. More complex respiratory system models exist, such as the non-linear single-compartment model (Morton et al., 2018) or multi-compartment models (Bates, 2009) that achieve higher accuracy in modeling the respiratory system. However, the current manual PEEP titrations also use a single-compartment model, and as such, the definition of *best* PEEP, as used here, was based on that assumption. If a more complex model were used, the physiological meaning of the different respiratory parameters would need to be re-evaluated and a new definition of *best* PEEP would need to be found. We, therefore, used the single-compartment model to retain clinical acceptance and physiological transparency.

The differential equation for the single-compartment model is given by:

$$P_{\mathrm{aw}}(t) = R_{\mathrm{rs}} \cdot \dot{V}_{\mathrm{aw}}(t) + \frac{1}{C_{\mathrm{rs}}} \cdot V_{\mathrm{aw}}(t) + P_0, \qquad (1)$$

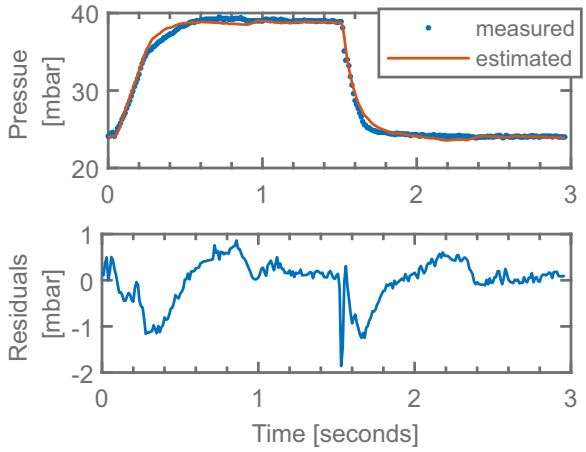


Fig. 2. Measured and estimated data for one breath.

where $P_{\text{aw}}$ is the airway pressure, $\dot{V}_{\text{aw}}$ is the flow, $V_{\text{aw}}$ is the volume found by integrating the flow, and $P_0$ is the end-expiratory pressure. The parameters resistance ($R_{\text{rs}}$) and compliance ($C_{\text{rs}}$) were estimated using multiple linear regression on a breath-by-breath basis, as described in Bates (2009). An exemplary measured breath, along with the estimate and the residual, is shown in Fig. 2.

The *coefficient of determination* ($CD$) presents the goodness-of-fit of the estimate, see Bates (2009), and is given by:

$$CD = 1 - \frac{\sum_{i=1}^{N} \left(P_{i,\text{aw}} - \hat{P}_{i,\text{aw}}\right)^2}{\sum_{i=1}^{N} \left(P_{i,\text{aw}} - \bar{P}_{\text{aw}}\right)}, \tag{2}$$

where $\bar{P}_{\text{aw}}$ is the mean pressure over one breath, $P_{i,\text{aw}}$ is the measured and $\hat{P}_{i,\text{aw}}$ the estimated airway pressure at sample $i$. The closer the $CD$ is to one, the better the model accounts for the variation in the data, see Bates (2009). A low $CD$ value for a given breath, therefore, expresses a poor fit. For all available data the $CD$ was found to be $0.9863 \pm 0.0055$, which is a sufficiently good fit for the automated PEEP titration.

### *2.3 Classification of Best PEEP*

The large signal hysteresis behavior of the lung needs to be considered regarding the direction of the titration and in determining the *best* PEEP.

In the current manual methods, the PEEP is reduced until a peak in the compliance curve becomes obvious; thereby requiring going over the peak in order to be sure that the maximum value has passed. However, simply re-setting the PEEP to the (previously) identified *best* PEEP would not return the compliance to the previous maximum value. Instead, by moving from the expiratory limb (decreasing PEEP) towards the inspiratory limb (increasing PEEP) of the lung hysteresis curve, the obtained result would take on an entirely different value. In the study by the Writing Group for the Alveolar Recruitment for Acute Respiratory Distress Syndrome Trial (ART) Investigators (2017), a recruitment maneuver was performed after the maximum compliance was found, but before setting the *best* PEEP. Recruitment maneuvers, however, require clinical exper-

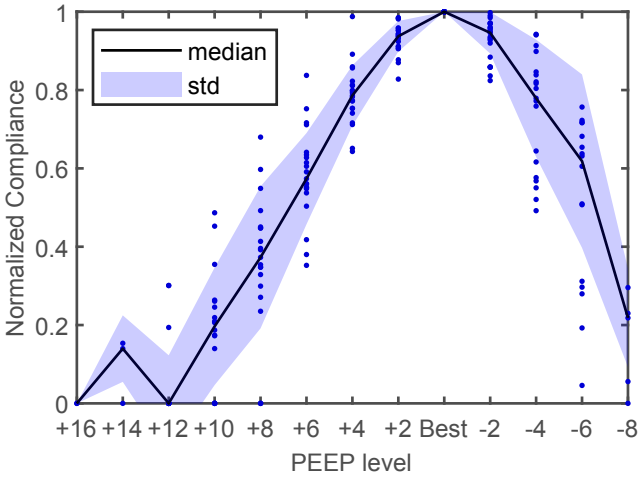


Fig. 3. Normalized PEEP titration data from 21 titrations from eight animals; centered around their individual *best* PEEP.

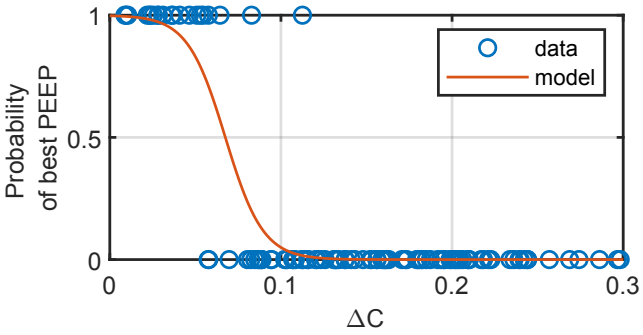


Fig. 4. Logistic model used for the classification of PEEP levels.

tise and can lead to severe hemodynamic instability and a possible pneumothorax.

In this work, we show that the *best* PEEP can be identified with a large degree of accuracy and without surpassing the compliance peak by using logistic regression.

All available PEEP titrations are first centered around the *best* PEEP and subsequently normalized, as shown in Fig. 3. Then, for each titration, the different PEEP levels prior to and including the *best* PEEP are labeled. In total there were 118 available PEEP levels, with 21 *best* and 97 *not best* PEEP levels, classified as a 1 or a 0, respectively.

Fig. 3 shows all 21 PEEP titrations having a similar shape. Hence, the scaled relative increase in compliance ($\Delta C$) as given by (3) is used as a predictor.

$$\Delta C_i = \frac{\bar{C}_i - \bar{C}_{i-1}}{\bar{C}_{i-1}}, \tag{3}$$

where $i$ is the index of the current PEEP level, $\bar{C}_i$ is the median compliance at the current level, and $\bar{C}_{i-1}$ is the median compliance at the previous level.

Logistic regression models the probability that a measurement ($X$) belongs to a certain class ($Y$) (James et al., 2013). In our case, we used the scaled relative compliance as a predictor ($\Delta C$). The model was trained using the labeled data above and a five-fold cross-validation method. The resulting logistic regression model is shown in Fig. 4.

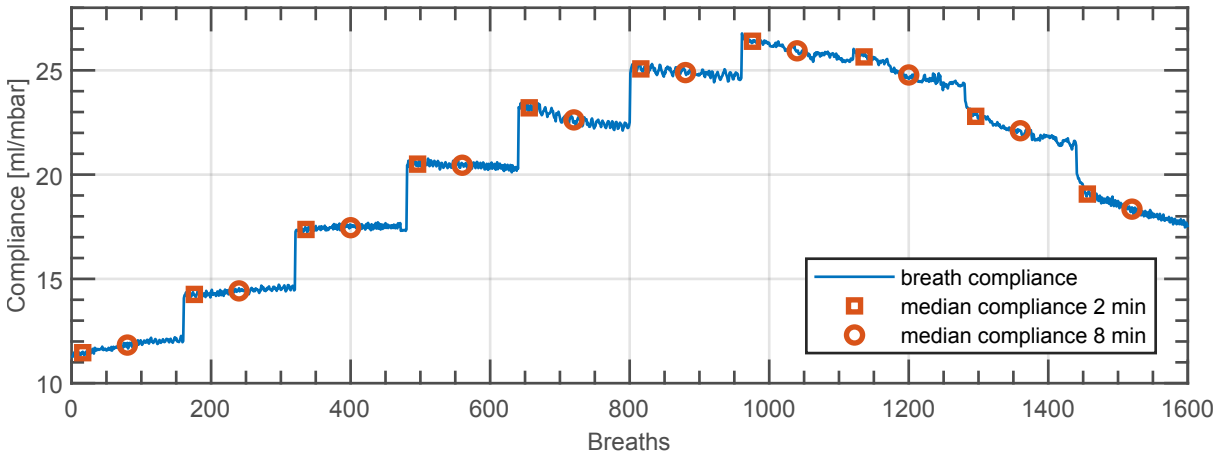


Fig. 5. The continuous estimation of the compliance during a complete titration.

The threshold for predicting the *best* PEEP was set at 0.5 ($p(\Delta C) > 0.5$). The classifier achieved an accuracy of 95 % for classifying a random PEEP level as either *best* PEEP or *not best* PEEP.

If the prediction of the *best* PEEP fails and we have passed the maximum compliance, the $\Delta C$ will be negative and the PEEP should be increased again. This class is classified as $-1$. The classifier is therefore combined into the following form:

$$f(\Delta C_i) = \begin{cases} 0, & \text{if } \Delta C_i \geq 0.067 \\ -1, & \text{if } \Delta C_i < 0 \\ 1, & \text{otherwise} \end{cases} \quad (4)$$

### *2.4 Control of mechanical ventilator*

The algorithm to perform the automated *best* PEEP identification was designed as a state machine. The conditions to transition to the next state are shown in the flowchart in Fig. 6.

A pressure-controlled ventilation mode was chosen for the maneuver, with a constant driving pressure $\Delta P$:

$$\Delta P = P_{\text{insp}} - PEEP = 14\,\text{mbar}, \quad (5)$$

with $P_{\text{insp}}$ the set point for the inspiratory pressure. A driving pressure of 14 mbar was chosen, as it was shown by Amato et al. (2015) that keeping the driving pressure below 15 mbar correlates with a reduced risk of mortality. Other mechanical ventilator settings, such as the breathing rate and inspiration to expiration ratio, are set by the clinician prior to starting the maneuver and kept constant throughout. The fraction of inspired oxygen ($FiO_2$) is set to 1.0 for the entire maneuver to prevent hypoxemia. This is in line with current clinical ARDS treatment, where periods with $FiO_2$ equal to 1.0 are used during interventions such as suction or disconnection, see Acute Respiratory Distress Syndrome Network (2000).

Several automated safety measures were implemented as well. Sufficient alveolar ventilation and gas exchange were ensured by preventing very low tidal volumes, even with severe decreases in compliance. The algorithm automatically increases the driving pressure if the tidal volume; scaled to predicted body weight ($V_{\text{T,pbw}}$); drops below a lower threshold of 4 ml kg$^{-1}$. If a significant increase in compliance causes the tidal volume to increase above

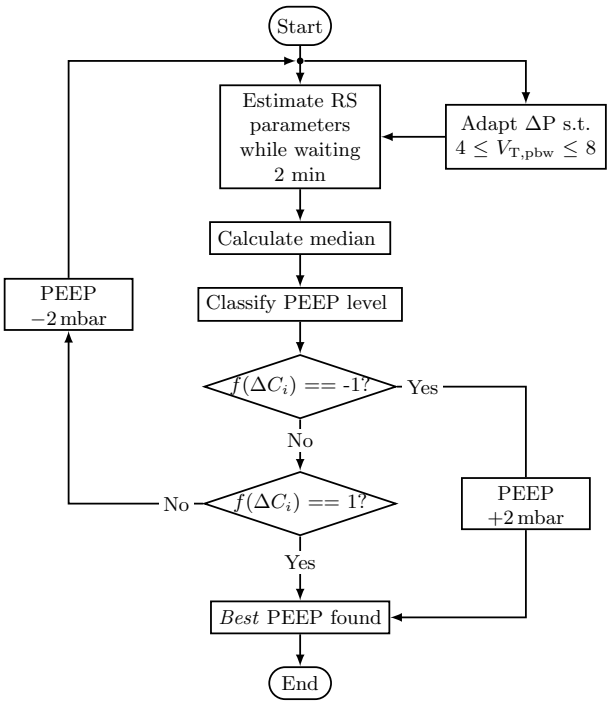


Fig. 6. Flowchart for the automated PEEP titration.

the upper threshold of 8 ml kg$^{-1}$, the driving pressure automatically decreases. If the $SpO_2$ drops by more than 3 % compared to the start of the downward titration, the titration is automatically stopped. The clinician is alerted and control is returned to the clinician.

Deciding on the required duration of each PEEP step was crucial. A compromise between evaluating each PEEP level at a quasi-stationary point and reducing the total time of the maneuver was required. Chiumello et al. (2013) studied the time required to reach a steady-state for both gas exchange and respiratory mechanics, among others, after a PEEP change. They found that after a PEEP decrease, the oxygenation had stabilized at 5 min, possibly earlier, but this was not evaluated. The respiratory mechanics could take up to 60 min to reach an equilibrium. As can be seen in Fig. 5 the compliance on each step had not reached a true steady-state after eight minutes

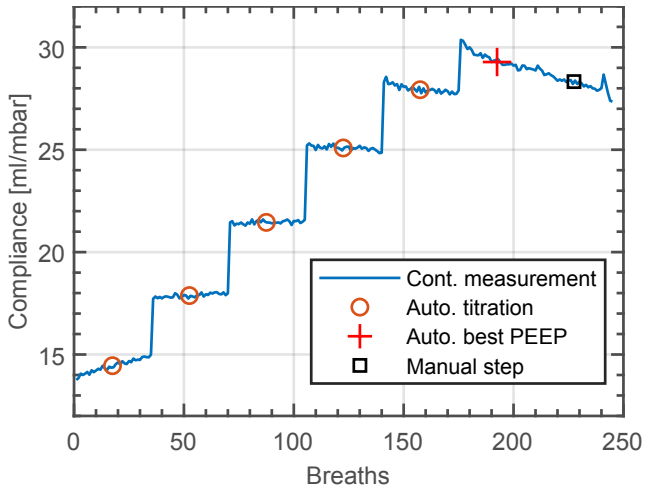


Fig. 7. Result of the automated PEEP titration maneuver. After the system had found the *best* PEEP, the PEEP was reduced manually to confirm that the maximum compliance had been found.

(160 breaths). However, the change in compliance between steps is substantially more significant than the relative compliance change on each step. An evaluation of the *best* PEEP found using the median compliance of the first two minutes compared to the median compliance of the complete eight minutes showed no difference. Therefore, a decrease in PEEP is programmed to occur every two minutes until the *best* PEEP has been identified.

## 3. RESULTS AND DISCUSSION

The automated PEEP titration was tested during a single animal experiment. First, a clinician ensures the animal is hemodynamically stable and in deep anesthesia. Then, using the available user interface, the clinician started the automated PEEP titration protocol. Fig. 7 shows the trajectory of the breath-by-breath compliance changes during the maneuver. At 190 breaths the *best* PEEP had been automatically determined and the control of the mechanical ventilator was returned to the clinician.

To validate that this was the *best* PEEP, the clinician subsequently manually reduced the PEEP even further, which caused a reduction in compliance. As such, the automated system correctly identified the *best* PEEP. The system performed the maneuver without requiring the clinician to intervene and adapt mechanical ventilator settings, allowing him to focus on monitoring the patient and keeping the hemodynamics stable during the maneuver.

Our implementation automates the currently applied clinical procedure of PEEP titrations by finding the maximum compliance. This procedure is understood and used by clinical staff and may lead to faster acceptance. At the same time, however, we made the assumption, based on clinical feedback, that the PEEP with the maximum compliance is the *best* choice. However, there is no consensus on what the optimal PEEP truly is, see Hess (2015). Benefits of finding the PEEP with maximum compliance (or equivalently, the minimum elastance) have been shown in experimental studies (Suarez-Sipmann et al., 2007). A prospective study is proposed by Kim et al. (2020), but the study is still ongoing and no results have been published.

The system incorporates artificial intelligence in the decision-making process of adapting mechanical ventilator settings. By using a single predictor and logistic regression for the classification, the decision of the *best* PEEP is comprehensible, transparent and can be easily retraced. Furthermore, logistic regression performs well, even with limited data. If clinical data on PEEP titrations becomes available, further artificial intelligence algorithms could be used to predict the *best* PEEP for a patient. A similar approach was used to optimize other mechanical ventilator settings for weaning (Prasad et al., 2017). A limitation exists due to the available data being restricted to an artificially induced ARDS in a porcine model. Before being transferred to a patient, the classification requires adaptation to real clinical data.

The current system is limited to performing an automated PEEP titration if initiated by the clinician. Before and after the maneuver, the clinician or other automated system (Platen et al., 2020) have to adapt the other mechanical ventilator settings, such as the breathing frequency, driving pressure or fraction of inspired oxygen. Once an optimized PEEP level has been determined, it should remain fixed for up to 24 h, as is outlined in the Acute Respiratory Distress Syndrome Network (2000) guidelines. Then the clinician could initiate another automated PEEP titration if required.

The system can be extended to include further parameters to evaluate the *best* PEEP online. Firstly, the single-compartment model is a first approximation of the respiratory system, which was chosen for its simplicity and clinical transparency. Higher order models could be used to gain further insight into the changes in lug dynamics during these titrations. Furthermore, the system only considers the global lung mechanics; however, the benefit of local information, by using EIT, for example, could further improve the system. Finally, the goal of mechanical ventilation is to provide sufficient gas exchange; therefore physiological variables such as $SpO_2$, end-tidal $CO_2$, or derived variables, such as shunt, dead-space and ventilation efficiency, should be included in the decision process.

## 4. CONCLUSION

In this work, we presented an automated PEEP titration maneuver that is able to identify the *best* PEEP. In addition, a classifier was developed and trained using empirical data to evaluate if the current PEEP level is the *best*. Finally, the system was validated during a single animal experiment, whereby it automatically performed the entire titration and correctly identified the *best* PEEP without clinician input.

## ACKNOWLEDGEMENTS

This work has been funded by the Federal Ministry of Education and Research (BMBF, Germany) and is part of the project SOLVe with grant number 13GW0240. The authors gratefully acknowledge the support provided by L. Hinken and W. Braun, Fritz Stephan GmbH, for their

invaluable assistance during the animal trial and provision of the modified mechanical ventilator.

## REFERENCES

Acute Respiratory Distress Syndrome Network (2000). Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med*, 342, 1301–1308.

Amato, M.B.P., Meade, M.O., Slutsky, A.S., Brochard, L., Costa, E.L.V., Schoenfeld, D.A., Stewart, T.E., Briel, M., Talmor, D., Mercat, A., Richard, J.C.M., Carvalho, C.R.R., and Brower, R.G. (2015). Driving pressure and survival in the acute respiratory distress syndrome. *N Engl J Med*, 372, 747–755.

Bates, J.H.T. (2009). *Lung Mechanics: An Inverse Modeling Approach*. Cambridge University Press.

Bellani, G., Laffey, J.G., Pham, T., Fan, E., Brochard, L., Esteban, A., Gattinoni, L., van Haren, F., Larsson, A., McAuley, D.F., Ranieri, M., Rubenfeld, G., Thompson, B.T., Wrigge, H., Slutsky, A.S., Pesenti, A., LUNG SAFE Investigators, and ESICM Trials Group (2016). Epidemiology, patterns of care, and mortality for patients with acute respiratory distress syndrome in intensive care units in 50 countries. *JAMA*, 315, 788–800.

Chiew, Y.S., Chase, J.G., Shaw, G.M., Sundaresan, A., and Desaive, T. (2011). Model-based PEEP optimisation in mechanical ventilation. *Biomed Eng Online*, 10, 111.

Chiumello, D., Coppola, S., Froio, S., Mietto, C., Brazzi, L., Carlesso, E., and Gattinoni, L. (2013). Time to reach a new steady state after changes of positive end expiratory pressure. *Intensive Care Med*, 39, 1377–1385.

Gattinoni, L., Caironi, P., Cressoni, M., Chiumello, D., Ranieri, V.M., Quintel, M., Russo, S., Patroniti, N., Cornejo, R., and Bugedo, G. (2006). Lung recruitment in patients with the acute respiratory distress syndrome. *N Engl J Med*, 354, 1775–1786.

Hess, D.R. (2015). Recruitment maneuvers and PEEP titration. *Respir Care*, 60, 1688–1704.

Hickling, K.G. (2001). Best compliance during a decremental, but not incremental, positive end-expiratory pressure trial is related to open-lung positive end-expiratory pressure: A mathematical model of acute respiratory distress syndrome lungs. *Am J Respir Crit Care Med*, 163, 69–78.

Hochhausen, N., Biener, I., Rossaint, R., Follmann, A., Bleilevens, C., Braunschweig, T., Leonhardt, S., and Czaplik, M. (2017). Optimizing PEEP by electrical impedance tomography in a porcine animal model of ARDS. *Respir Care*, 62, 340–349.

James, G., Witten, D., Hastie, T., and Tibshirani, R. (2013). *An Introduction to Statistical Learning*. Springer Texts in Statistics. Springer-Verlag, New York.

Kim, K.T., Morton, S., Howe, S., Chiew, Y.S., Knopp, J.L., Docherty, P., Pretty, C., Desaive, T., Benyo, B., Szlavecz, A., Moeller, K., Shaw, G.M., and Chase, J.G. (2020). Model-based PEEP titration versus standard practice in mechanical ventilation: A randomised controlled trial. *Trials*, 21, 130.

Morton, S.E., Dickson, J.L., Chase, J.G., Docherty, P.D., Howe, S.L., Shaw, G.M., and Tawhai, M. (2018). Basis function identification of lung mechanics in mechanical ventilation for predicting outcomes of therapy changes: A first virtual patient. *IFAC-PapersOnLine*, 51, 299–304.

Platen, P.v., Pomprapa, A., Lachmann, B., and Leonhardt, S. (2020). The dawn of physiological closed-loop ventilation-a review. *Crit Care*, 24, 121.

Pomprapa, A., Schwaiberger, D., Pickerodt, P., Tjarks, O., Lachmann, B., and Leonhardt, S. (2014). Automatic protective ventilation using the ARDSNet protocol with the additional monitoring of electrical impedance tomography. *Crit Care*, 18, R128.

Prasad, N., Cheng, L.F., Chivers, C., Draugelis, M., and Engelhardt, B.E. (2017). A reinforcement learning approach to weaning of mechanical ventilation in intensive care units. *arXiv:1704.06300 [cs]*.

Russ, M., Boerger, E., von Platen, P., Francis, R.C.E., Taher, M., Boemke, W., Lachmann, B., Leonhardt, S., and Pickerodt, P.A. (2021). Surfactant depletion combined with njurious ventilation results in a reproducible model of the acute respiratory distress syndrome (ARDS). *J Vis Exp*.

Russ, M., Kronfeldt, S., Boemke, W., Busch, T., Francis, R.C.E., and Pickerodt, P.A. (2016). Lavage-induced surfactant depletion in pigs as a model of the acute respiratory distress syndrome (ARDS). *J Vis Exp*.

Suarez-Sipmann, F., Böhm, S.H., Tusman, G., Pesch, T., Thamm, O., Reissmann, H., Reske, A., Magnusson, A., and Hedenstierna, G. (2007). Use of dynamic compliance for open lung positive end-expiratory pressure titration in an experimental study. *Crit Care Med*, 35, 214–221.

Suter, P.M., Fairley, B., and Isenberg, M.D. (1975). Optimum end-expiratory airway pressure in patients with acute pulmonary failure. *N Engl J Med*, 292, 284–289.

Writing Group for the Alveolar Recruitment for Acute Respiratory Distress Syndrome Trial (ART) Investigators (2017). Effect of lung recruitment and titrated positive end-expiratory pressure (PEEP) vs low PEEP on mortality in patients with acute respiratory distress syndrome: A randomized clinical trial. *JAMA*, 318, 1335–1345.

Zhao, Z., Lee, L.C., Chang, M.Y., Frerichs, I., Chang, H.T., Gow, C.H., Hsu, Y.L., and Möller, K. (2020). The incidence and interpretation of large differences in EIT-based measures for PEEP titration in ARDS patients. *J Clin Monit Comput*, 34, 1005–1013.

## Appendix A. TABLES

Table A.1. Ventilator settings for the PEEP titration

| Setting | Value |
|---|---|
| $\Delta$P | 14 mbar |
| PEEP | 24 mbar to 6 mbar |
| f | 20 $min^{-1}$ |
| $FiO_2$ | 1.0 |
| I:E | 1:1 |