

Power-Based Optimization of Ventilation Frequency Without Compliance or Resistance Measurements: A Simulation Study

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Abstract

Background: Mechanical ventilation remains a life-saving intervention but carries risks such as barotrauma, volutrauma, ergotrauma, and hemodynamic disturbances. Modern ventilators incorporate adaptive strategies to minimize the work of breathing (WOB), often relying on measurements of respiratory resistance and compliance. However, such measurements are prone to error and often unavailable in real time. This study presents a novel adaptive ventilation concept that dynamically identifies the optimal ventilation frequency minimizing WOB per minute without requiring resistance or compliance measurements.

Material and methods: Using a validated hybrid respiratory simulator, we conducted simulation experiments across three representative lung conditions: normal mechanics, decreased compliance, and increased resistance. The system conceptually searched for the ventilation frequency minimizing WOB/min while maintaining constant alveolar ventilation, with the optimization process emulated manually in this proof-of-concept study.

Results: Results confirmed that WOB/min follows a parabolic function of frequency, with optimal frequencies found at 18, 21, and 12 breaths per minute for normal, restrictive, and obstructive patterns, respectively. Importantly, the optimal frequencies aligned with ranges observed in clinical studies of adaptive support ventilation. Furthermore, the system demonstrated natural variability in ventilation rate and tidal volume, which may contribute to alveolar recruitment.

Conclusion: Our findings validate the concept of energy-based optimization of ventilation independent of online lung mechanics assessment. The proposed method is robust, physiologically grounded, and may become suitable for integration into next-generation intelligent ventilators after full automation of the adaptive algorithm. Future work will focus on full automation of the adaptive algorithm and its evaluation in preclinical and clinical studies targeting WOB and mechanical power minimization.

Introduction

According to the World Health Organization, COVID-19, chronic obstructive pulmonary disease (COPD), respiratory infections and respiratory tract cancers were among the most common causes of death in the world in 2021, accounting for 12.9%, 5.1%, 3.7% and 2.8% of deaths, respectively¹. In many cases of threats to health and life patients require treatment with mechanical lung ventilation. In many situations, these are cases of lung inhomogeneity and asymmetric respiratory pathology, in which there are significant differences in the mechanical properties of different areas of the lungs. This applies especially to patients with acute respiratory distress syndrome (ARDS)^{2,3}, lung cancer⁴, COPD⁵, pneumothorax⁶, and post-accident injuries⁷ as well as with bronchopulmonary dysplasia².

Ventilators used in clinical practice today are technologically advanced devices that usually provide effective respiratory therapy for patients with specific lung conditions. The operating parameters of these devices (tidal volume, ventilation frequency) are set manually by the operator, most often an anesthesiologist, who also decides whether to change these settings during respiratory therapy in accordance with commonly accepted protocols and recommendations for particular respiratory diseases and the progression of therapy.

In recent years, ventilators with the function of automatic adaptive ventilation frequency adjustment have been introduced into clinical practice, aiming to minimize the respiratory work as the mechanical properties of the respiratory system change during long-term lung ventilation^{8,9}. However, mechanical ventilation remains an invasive therapy with side effects

that can be harmful to the patient including barotrauma, volutrauma, ergotrauma, and hemodynamic disturbances¹⁰. For many years, it has been accepted that the optimal ventilation frequency, which minimizes the work of breathing (WOB), is the most beneficial for patients undergoing respiratory therapy¹¹. Experimental and clinical studies are conducted at leading research centers on the effectiveness of adaptive lung ventilation, including adaptive support ventilation (ASV)¹², INTEL-LiVENT-ASV¹³ and adaptive pressure control-continuous mandatory ventilation¹⁴. Other ventilation modes are also being explored for specific lung pathologies, including COPD¹⁵, ARDS¹⁶ and neonatal bronchopulmonary dysplasia¹⁷. The greatest challenge for those providing respiratory therapies, however, is the emergence of a new and unknown lung disease. In the case of the outbreak of the COVID-19 pandemic, it was initially assumed that COVID-19-induced lung pathology resembled classical ARDS. Established lung protection strategies for ARDS – such as low tidal volumes, deep sedation and positive end-expiratory pressure – were applied¹⁸. However, these strategies proved effective in only 20-30% of patients, who developed type H COVID-19, which behaves similarly to typical ARDS^{18,19}. The remaining 70% of patients developed type L COVID-19, for which the therapy for classical ARDS was inappropriate^{20,21}. In Germany, on the other hand, Groeneveld proposed a different treatment approach, utilizing larger tidal volumes and zero positive end-expiratory pressure (PEEP) pressure, with much better outcomes²².

The lesson from the tragic fatalities caused by the COVID-19 pandemic is the necessity to test and compare various ventilation therapy protocols on simulators, under experimental and ultimately in clinical settings. To facilitate this, it is essential to develop an appropriate tool for research, ultimately leading to the development of a new ventilation system with multiple options for ventilation procedures, utilizing findings from the latest clinical trials on adaptive lung ventilation²³ and alveolar recruitment methods²⁴.

Analyzing the current state of knowledge presented above and the existing technological solutions used in lung ventilators, the following conclusions can be drawn: a) conventional ventilators do not always provide effective respiratory therapy, b) adaptive ventilation as it is performed nowadays requires additional on-line measurements of respiratory parameters of the respiratory system, c) other solutions used in practice, which enable, for example, separate ventilation of the lungs in patients with lung inhomogeneity, also do not allow for effective control of respiratory therapy with the use of two ventilators.

The purpose of using adaptive lung ventilation is to increase the patient's safety by limiting the possibility of respiratory damage to the lungs (barotrauma, volumetric trauma or ergotrauma), the so-called VILI (ventilator-induced lung injury). It is generally proved that this can be achieved by setting a ventilation rate for which the respiratory work (or power) is minimal. This ventilation rate is called optimal for a given moment of a patient ventilation.

The starting point for the assumptions we made in our study was an original article by Otis²⁵, which was a key paper

for many considerations on the issue of adaptive lung ventilation. He showed, using mathematical analysis (assuming a sinusoidal shape of the respiratory flow), that WOB per minute (i.e. de facto respiratory power) as a function of respiratory rate shows the shape of a parabola, with a clear minimum with a frequency similar to the spontaneous respiration rate. Therefore, the frequency with which we breathe is evolutionarily related to respiratory power minimization, which is generally consistent with the common principle of energy minimization in biological systems. The assumption that Otis made was also to keep alveolar ventilation on constant value while changing the ventilation rate. The minute ventilation (MV) is equal to ventilation of dead space (mainly airways not involved in gas exchange) and ventilation of alveoli (**Equation 1**). The latter is related to gas exchange in the lungs, so it is important for the delivery of oxygen to the circulatory system.

$$MV = f \cdot V_D + f \cdot V_A \quad (\text{Equation 1})$$

where:

f – respiratory rate (breaths per minute);

V_D – dead space volume (the volume of air in a single inhalation that is not involved in gas exchange).

V_A – alveolar volume (air volume in a single breath, involved in gas exchange).

The parabolic shape of the WOB per minute as a function of f has its justification. With constant alveolar ventilation, low f means deep inhalations and increased respiratory work must be done to overcome elastic resistance (lung compliance). On the other hand, a high f means that dead space ventilation has an increasing share in a single inhalation and that the MV must be increased more and more to keep alveolar ventilation constant.

The considerations from the above article by Otis were also the starting point for the development of Tehrani works (patent US4,986,268²⁶ and paper²⁷) concerning the following relationship (**Equation 2**) on the basis of which the adaptive algorithm was to find the optimal ventilation frequency:

$$f = \frac{\sqrt{1 + 2aRC \frac{V_{AR}}{V_{DR}}} - 1}{aRC} \quad (\text{Equation 2})$$

where:

RC – time constant as the product of lung resistance (R) and compliance (C), expressed in sec.;

$a = 2\pi^2$ – the constant a is equal to the assumption of sinusoidal respiratory flow;

V_{AR} – alveolar ventilation ($f \cdot V_A$);

V_{DR} – dead space ventilation ($f \cdot V_D$), in l/min.

It is also worth mentioning that this solution is used in a modified way by the Hamilton company in one of the ventilators^{28–30}.

The above equation has the following features: the equation is not explicitly given, f appears on the left-hand side as a result, but also appears on the right side in V_{AR} factor, and

instant information on dead space volume is required. Information is also required about the R and C of the lungs (more precisely, of the lung system respiratory tract). Knowledge of V_D is necessary to know what the patient's alveolar ventilation will be when setting $MV = f \cdot VT$ (where VT is the tidal volume) on the ventilator.

One of the main challenges, however, is that R and C must be determined based on actual measurements. These indicators are only a representation of the mechanical properties of the lungs (resistance properties and elastic properties). In addition, in the event of rapid changes in these properties (e.g., the endotracheal tube clogging with the patient's secretions), the optimal f will change, but the adaptive algorithm based on the above equation will by default not take this into account. There is a need for manual correction for a new R and C measurement or cyclical automatic measurements of these parameters. The accuracy of R and C determination is an additional problem.

The goal of the paper is to develop and test a novel solution of adaptive, variable ventilation on a simulation platform that would create alveolar recruitment and simultaneously optimize lung ventilation by rate adaptation without the need to make measurements that are difficult in clinical conditions. Due to the constant monitoring of the effectiveness of the therapy, the control system will allow for a quick change of the ventilation procedure. This will reduce the negative side effects of mechanical ventilation especially in the setting of lung pathology, as well as time and costs of therapy. Our task was to analyze if the optimal ventilation rate realizing minimum power of breathing (WOB/time [J/min]) for a given patient lies in the clinically acceptable range of ventilation frequency changes and if the WOB/min changes so significantly by applying adaptive lung ventilation that it is worth using it as an optimization criterion.

Material and Methods

Our concept of the system with cyclically changing respiratory rate is presented in **Figure 1**. The ventilator is equipped with an extreme regulator that automatically seeks, from the respiratory cycle to the next respiratory cycle, the minimum value of the respiratory power (work of breathing per minute), which causes the cyclically variable ventilation rate, and thus the tidal volume, to stabilize the value of minute ventilation required for the patient.

In this proof-of-concept study, we propose a semi-automated approach that emulates the operation of an adaptive ventilation algorithm. The method involves stepwise changes in ventilation frequency to identify the setting that minimizes WOB per minute, while maintaining constant (set) alveolar ventilation. Although the algorithm has not yet been fully implemented, its function was simulated manually to demonstrate the feasibility of this strategy. By circumventing the need for real-time measurements of respiratory system resistance (R) and compliance (C), this approach offers a simplified yet effective means of frequency optimization. Moreover, ventilation

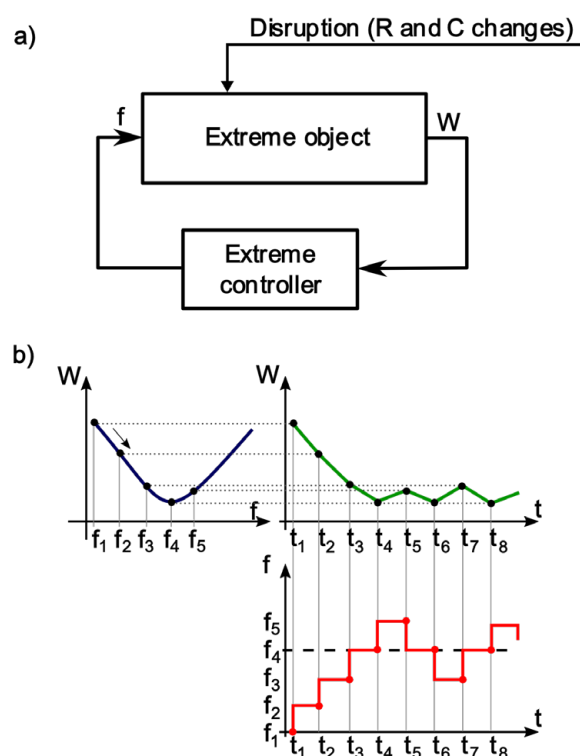


Figure 1. The idea of a system with cyclically changing tidal/respiratory volume. R – respiratory resistance; C – respiratory compliance; W – work of breathing; f – respiratory rate; t = time.

near the optimal respiratory rate allows for natural variability in tidal volume, which may be more physiologically favorable than conventional ventilation with fixed tidal volumes^{31,32}.

We decided to take an in-depth look at this problem by conducting simulation studies on the previously developed Hybrid (pneumatic-numerical) Respiratory Simulator (HRS – **Figure 2a**) using the above-mentioned criterion of ventilation frequency optimization. The HRS was successfully verified to simulate the ventilator-lungs interaction in cases of adults³³ as well as infants lung pathology³⁴⁻³⁶. More details about the HRS both hardware and software were described previously^{33,37}. Briefly, the HRS used in this study is composed of two interactive and cooperating parts (**Figure 2b**). One part is a numerical model of the respiratory system mechanics. It is divided by the trachea, main bronchi, chest wall and 80 compartments representing 80 lung regions (bronchial tree and parenchyma). It is worth mentioning that this model is nonlinear and takes into account phenomena such as bronchial flow limitation or collapsing of alveoli. It enables simulations of both obstructive and restrictive respiratory system pathologies and accounts for lung position during ventilation (including the effect of gravity). It is executed in real-time on an industrial PC based computer (PXI-1042, National Instruments, Austin, TX). The second part of this HRS is a pneumatic-numerical interface. Based on the impedance transformation theory, this interface enables interaction between real devices (such as a ventilator) and a digital model of the respiratory system through mutual signal transformation between the real and virtual (numerical) domains (**Figure 2b**). The pressure (P) beyond the Y-piece of the breathing circuit is measured by a sensor (143SC01D-

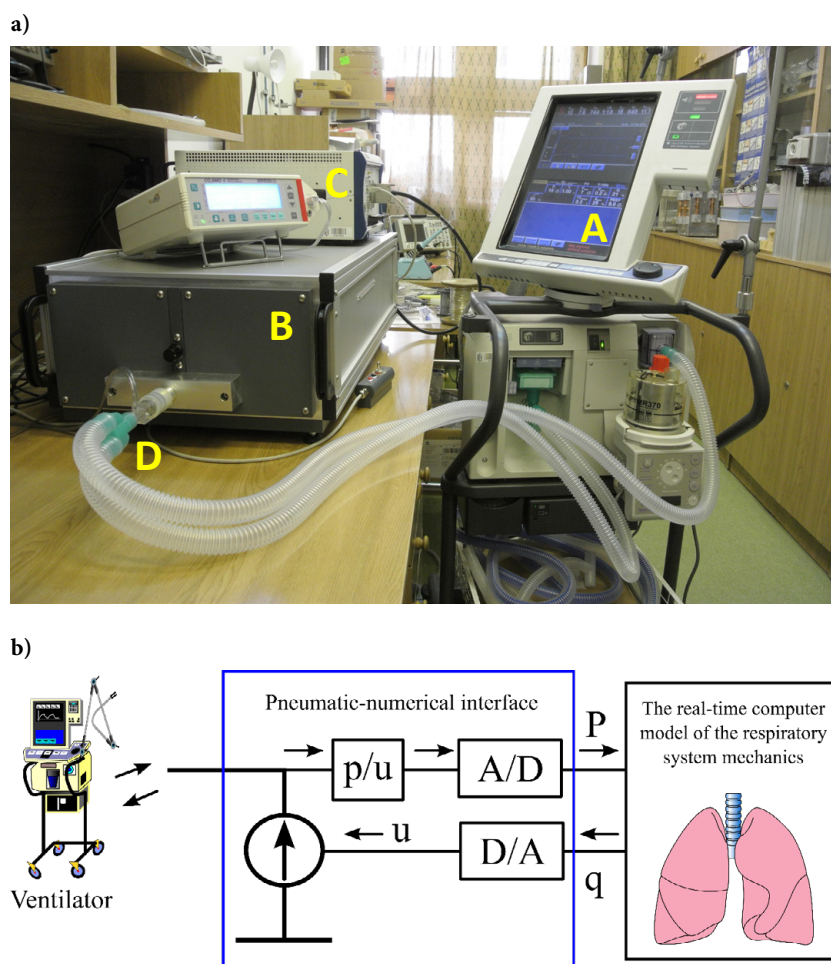


Figure 2. Measuring set-up: a) The photo of the hybrid (pneumatic-numerical) adult respiratory system simulator HRS as an artificial patient, connected to the ventilator; (A) Puritan Bennett 840 Ventilator System. (B) Pneumatic-numerical interface of the respiratory simulator, (C) PXI – a real time industrial computer numerically simulating the physiology of the respiratory system, (D) Y-piece of the breathing circuit. b) The scheme of the hybrid respiratory simulator. A/D – analog-to-digital converter, D/A – digital-to-analog converter, p/u – pressure transducer, P – pneumatic pressure, q – pneumatic flow.

PCB, Sensortech GmbH, Germany) installed in the HRS and is treated as an input pressure in the mouth-trachea (P_{aw}) and the input variable for the respiratory system numerical model (analog-to-digital conversion). The result of the whole numerical calculations is the flow in the trachea (q) – the output variable. This flow value is transferred (digital-to-analog conversion) as the voltage to the electrically-controlled pneumatic flow source to generate the flow q, and then the whole process is repeated. Finally, we observe the artificial patient's (HRS) response to the actions of the ventilator. The HRS pneumatic flow source is composed of two pistons driven by a DC brush motor (RE65, Maxon Motor, Switzerland). The whole HRS software was developed in LabVIEW™ 2013 (National Instruments, Austin, TX).

The simulation protocol:

The HRS-system was used to perform all simulations. A clinical ventilator Puritan Bennett 840 (Medtronic, Minneapolis, MN) was connected to the HRS. Mandatory ventilation mode of operation was assumed (no spontaneous “patient’s” breaths, breaths are performed only by the ventilator) and the

volume-controlled ventilation mode was set in the ventilator (MV is set in the ventilator through the f task and the VT task). A constant alveolar ventilation level of 6 l/ min was assumed in all simulations. Since the dead space volume was constant and known (150 ml) from the HRS numerical model, it was known what VT would be set to obtain a constant alveolar ventilation for a given f.

WOB was online calculated in the HRS software, based on the Otis formula²⁵ (Equation 3):

$$WOB = \int_0^{T_i} (P_{aw} \cdot q) dt \quad (\text{Equation 3})$$

where:

T_i – inspiration time

P_{aw} – Artificial Patient's (HRS) upper airway pressure, related to support pressure

q – inspiratory flow in the Artificial Patient's (HRS) upper airways

The simulation of the adaptive ventilation process consisted of a stepwise but manual change of f (and adjusting the MV

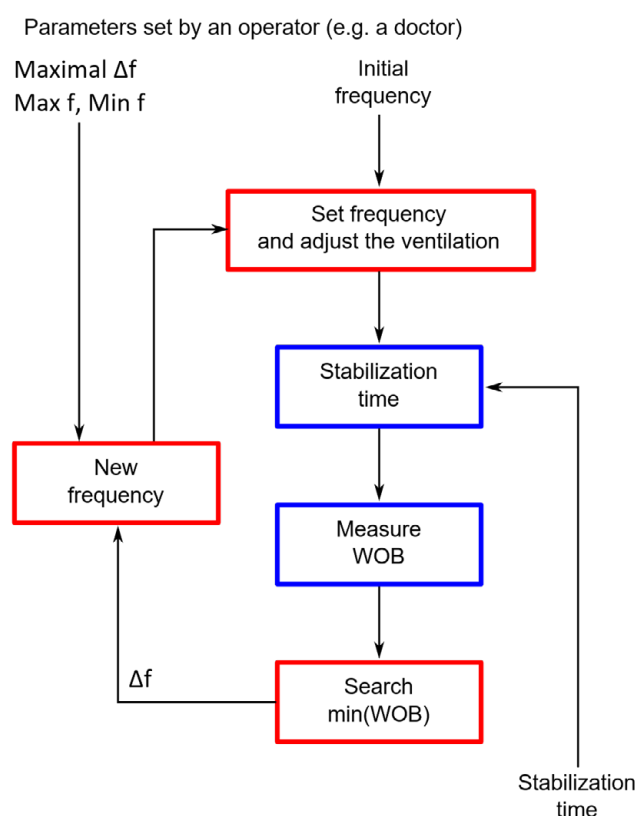


Figure 3. The conceptual algorithm of the adaptive search process of the minimal work of breathing WOB. Red blocks indicate manual operations, while blue blocks indicate automatic operations; f – the ventilation frequency (respiratory rate); Δf – the ventilation frequency step size.

to keep alveolar ventilation constant) in order to find the f to minimize the WOB per minute. The simulation consisted of three distinct respiratory system conditions: a) with resistance and compliance values falling within the broad normative ranges reported in the literature³⁸⁻⁴⁰, arbitrarily selected as representative of a healthy individual, b) with decreased respiratory compliance, c) with increased respiratory resistance. The mechanical properties of the digital respiratory system were changed in the HRS system, but were also measured with a ventilator using the end-inspiratory pause maneuver for this purposes.

The simulation procedure was initiated with a baseline respiratory rate of 8 breaths/min. At each iteration (step), the ventilation frequency was manually increased or decreased by $\Delta f = 1-13$ breaths/min (mostly 1-3), while the minute ventilation was simultaneously adjusted to maintain constant alveolar ventilation (6 L/min). This Δf step size was chosen as a preliminary compromise between sufficient resolution to identify the WOB minimum and to demonstrate WOB increasing when the frequency is too low or too high, as well as to identify a realistic number of steps reflecting potential clinical adaptation speed. After the algorithm implementation in the new generation of ventilators, the initial frequency and the maximal frequency step size can be set individually by the operator, whereas Δf range will be further refined through algorithm optimization for its automatization.

For each lung condition (normal, restrictive, and obstructive), a full search was performed within the range of discrete frequency values from 8 to 25 breaths/min, depending on the parabolic shape of the WOB/ f curve, until a clear minimum was identified. Each frequency step was maintained for approximately 1-2 minutes of simulated ventilation to ensure signal stabilization and accurate computation of mean WOB/min. This stabilization time is also an internal parameter for further algorithm's optimization.

The adjustment of frequency and minute ventilation was performed manually by the operator according to a predefined algorithmic logic, while WOB/min computation and data acquisition were executed automatically by the HRS control software in real time. **Figure 3** summarizes the conceptual algorithm of the adaptive search process, highlighting manual and automated elements.

Results

Figure 4 presents the results of simulations performed under three different conditions of respiratory mechanics, illustrating the relationship between WOB per minute and respiratory rate (left panels), as well as the behavior of a semi-automated frequency adjustment algorithm (right panels).

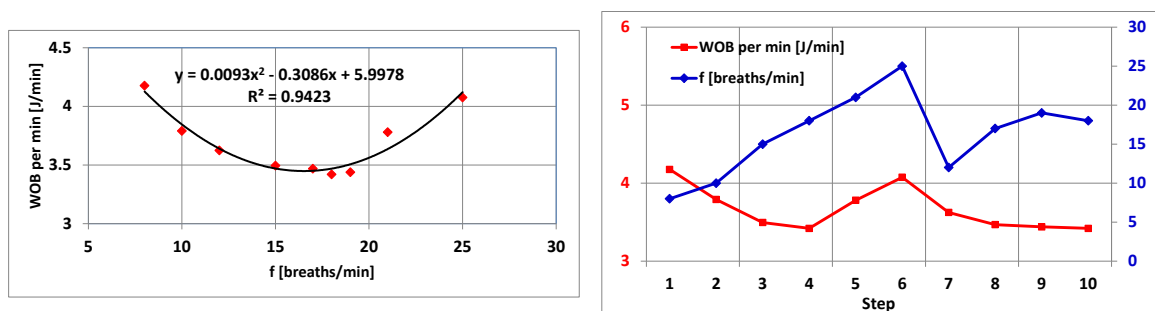
Top row (normal resistance and compliance, $R = 1.8$ cmH₂O/L/s; $C = 119$ ml/cmH₂O):

The left panel shows a parabolic relationship between WOB per minute and ventilation frequency, with a clear minimum at approximately 18 breaths per minute, suggesting this rate minimizes respiratory effort when lung mechanics are normal. The right panel confirms this result by simulating the behavior of an adaptive algorithm that progressively approaches the optimal frequency through stepwise adjustments. Red lines indicate WOB per minute, which shows a distinct decrease and then increase across steps, while blue lines show the corresponding ventilation frequency selected at each step.

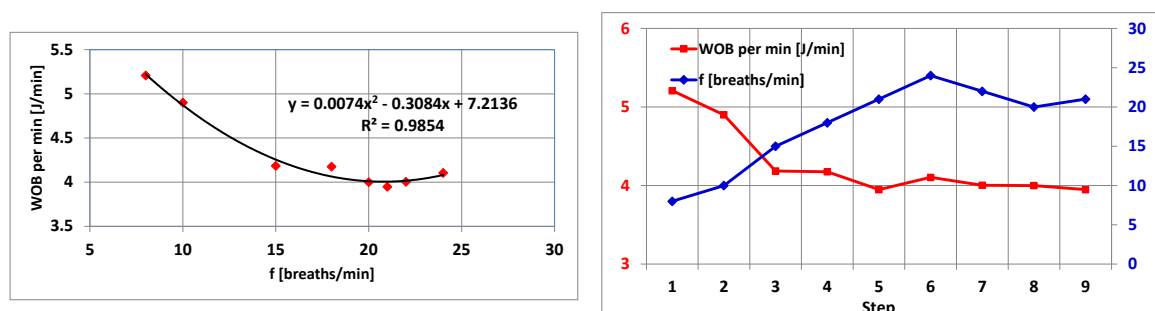
Middle row (decreased compliance, $C = 82$ ml/cmH₂O): In the left panel, the WOB-frequency curve shifts, and the minimum WOB occurs at a higher frequency of approximately 21 breaths per minute. This indicates that in a stiffer lung, a faster respiratory rate is energetically more efficient for maintaining the same alveolar ventilation. The right panel shows that the algorithm successfully converges toward this higher frequency, with a corresponding reduction in WOB over the steps.

Bottom row (increased resistance, $R = 3.5$ cmH₂O/L/s): In this condition, the left panel displays a U-shaped WOB curve with the minimum occurring at a lower frequency – around 12 breaths per minute – suggesting that slower ventilation is more favorable when airway resistance is elevated. The right panel again demonstrates the adaptive algorithm's ability to adjust iteratively toward the optimal frequency, with a marked reduction in WOB across the steps, before increasing again beyond the optimum.

Respiratory resistance and compliance within the normal range

 $R = 1.8 \text{ [cmH}_2\text{O/L/s]}; C = 119 \text{ [ml/cmH}_2\text{O]}$ 

Decreased respiratory compliance

 $R = 1.8 \text{ [cmH}_2\text{O/L/s]}; C = 82 \text{ [ml/cmH}_2\text{O]}$ 

Increased respiratory resistance

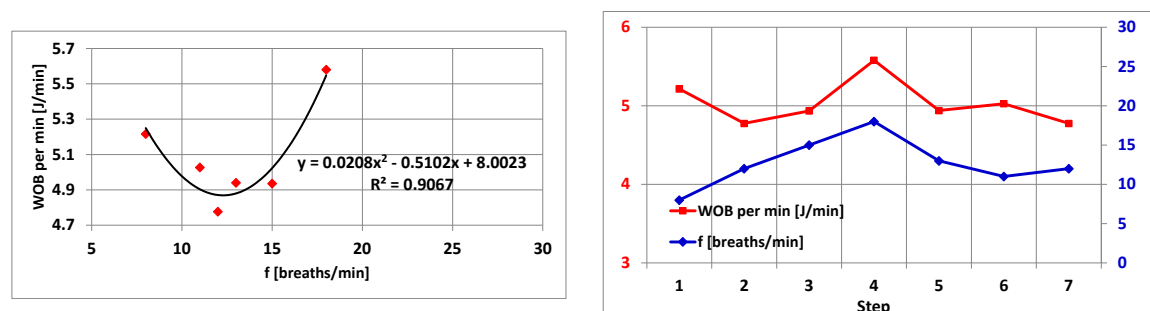
 $R = 3.5 \text{ [cmH}_2\text{O/L/s]}; C = 115 \text{ [ml/cmH}_2\text{O]}$ 

Figure 4. Optimization of the WOB under varying respiratory system conditions using a stepwise frequency adjustment algorithm. Each row represents a different mechanical scenario: Top row – normal respiratory mechanics; Middle row – decreased respiratory compliance; Bottom row – increased respiratory resistance. Left panels: Polynomial fits of WOB per minute as a function of ventilation frequency, illustrating the existence of a frequency at which WOB is minimized. Right panels: Simulation of a semi-automated algorithm that searches for the frequency minimizing WOB while maintaining constant alveolar ventilation. Red lines show WOB per minute; blue lines indicate the corresponding ventilation frequency across iterative steps.

C – respiratory compliance, R – respiratory resistance, WOB – work of breathing.

In all three cases, polynomial fits (second-degree) were used to approximate the WOB curves and identify the frequency associated with the minimum WOB. The resulting R^2 values (displayed on the plots) confirm the appropriateness of the parabolic model. These simulations collectively demonstrate that the energetically optimal ventilation frequency depends on the underlying mechanical properties of the respiratory system and that the proposed approach can effectively identify it through stepwise adjustment without requiring direct measurement of resistance or compliance.

Discussion

The simulations confirmed that the proposed system can dynamically adjust the ventilation rate to minimize WOB per minute. We observed the decrease in optimal f for increased R and the increase in optimal f for decreased C , which is consistent with the analysis of optimal respiration rate from an energetic point of view conducted by Bates⁴¹. **Figure 4** shows that for the assumed criterion – minimal value of WOB/min – so called optimal ventilation rate is situated in the clinically

acceptable range of frequency changes⁴². It applies to patients with healthy lungs and also to those with restrictive (with decreased compliance) and obstructive pulmonary diseases (with increased resistance). This can be proved by comparing our simulation results (**Figure 4**) with the results of prospective observational studies conducted by Arnal et al. on 100 consecutive patients ventilated in ASV-mode⁴³. They observed the following ranges of optimal ventilation: $f=15-21$ breaths/min for healthy lung, $f=12-15$ breaths/min for obstructive lung and $15-20$ breaths/min for restrictive lung, which are consistent with our findings.

As can be seen from the simulation results, actual values of WOB/min do not increase dramatically with ventilation rate changes above or below its optimal value. But it is only true if the patient's lung condition does not change, otherwise, WOB/min may increase much more. An increase in R causes the shape of the parabola to narrow, which gives a smaller range for changes "around optimal f ", which should be accounted for in the automatic adaptive algorithm. If, e.g., a healthy lung condition during long-term ventilatory therapy, worsens to an obstructive pattern) then WOB/min increases more profoundly (**Figure 4**), especially when the ventilation rate is not optimized according to the assumed criterion. A decrease in C causes the shape of the parabola to expand, resulting in a wider range of frequencies that give WOB per minute close to optimal, which is valuable information and can be used by an automatic adaptive algorithm for a different criterion.

These observations align with a broader trend in ventilator design, where control systems are becoming increasingly adaptive and personalized. For example, Sheltag and Kadhim demonstrated that nonlinear Proportional Integral-Derivative (PID) controllers can significantly improve pressure regulation performance in ventilator systems⁴⁴. Compared to classical PID, the nonlinear controller showed enhanced responsiveness to rapid changes in patient demand and better robustness to external disturbances⁴⁴. While our approach focuses on minimizing WOB/min through frequency adaptation, both strategies reflect the shift toward real-time, physiology-driven control, moving away from fixed-parameter settings toward flexible algorithms responsive to individual lung dynamics. In a complementary direction, Deepa et al. proposed the use of cycloidal pressure and flow waveforms, which offer smoother transitions and more natural respiratory profiles by minimizing higher-order pressure derivatives⁴⁵. Although not adaptive in terms of frequency, their approach aligns with the goal of improving patient-ventilator synchrony and reducing discomfort through waveform shaping, and it may be considered as a potential enhancement in adaptive ventilatory strategies.

VILI has been investigated for last years in many experimental and clinical studies. Cressoni et al. in the study on 15 ventilated piglets managed to find the threshold of WOB/min = 12 J/min, above which 60% of animals developed VILI.⁴⁶ For patients the threshold value of WOB/min for VILI has not been established yet, mainly for ethical reasons (no acceptance of invasive maneuvers on lungs) and because of the very complex issue of VILI detection and analysis. So if we cannot

quantitatively evaluate a value of WOB/min that may cause VILI in a particular patient an automatic searching for a ventilation rate that minimizes WOB/min by an extreme controller is reasonable. In line with our approach to dynamic respiratory rate control minimizing WOB/min, Alkhalifah et al. proposed a data-driven, real-time adjustment of mechanical ventilation settings based on mechanical power and hypoxemia severity⁴⁷. Their machine learning model successfully predicted ICU mortality and supported personalized thresholds of safe mechanical power⁴⁷. In line with this perspective, Wu et al. applied causal inference and simulation modeling to a large ICU cohort and demonstrated that median mechanical power has a significant negative impact on ventilator-free days⁴⁸. They emphasized that no universal mechanical power threshold exists, reinforcing the need for personalized, dynamically adjusted ventilation strategies to minimize VILI⁴⁸. These findings further support our concept of WOB/min-minimizing control and motivate future developments in adaptive, patient-specific ventilation profiles. Moreover, recent modeling by Marini et al. emphasized that not only the total mechanical power but also its intracycle distribution – particularly power applied above a damaging pressure threshold – can influence VILI risk⁴⁹. Building on these insights, our future work will focus on optimizing pressure waveform profiles to further reduce intracycle power and enhance lung protection.

Figure 4 shows that automatic searching for an optimal ventilator rate causes the actual ventilation frequency changes from one ventilatory cycle to another which results in automatic changes of tidal volume to keep minute alveolar ventilation on the same level. In this way so called uneven or variable ventilation is automatically realized what is supposed to recruit alveoli according to some investigations. The mechanism of variable ventilation resembles the strategy proposed by Depta et al., where the cyclic modulation of ventilatory parameters (including PEEP levels and frequency) aims to recruit slow-filling lung compartments and protect well-ventilated regions from overdistension²⁴. A similar concept was presented by Candik et al., who applied programmed multilevel ventilation (3-LV) in clinical settings⁵⁰. Their approach involved alternating respiratory cycles with variable pressure, frequency, and tidal volume, which resulted in improved compliance and gas exchange in postoperative cardiac surgery patients, without requiring high PEEP levels⁵⁰. They concluded that variability in ventilatory parameters contributes to more effective alveolar recruitment and enhanced adaptation to spontaneous breathing after extubation⁵⁰. Additionally, Beda et al. developed and validated an adaptive control system for noisy pressure-controlled ventilation, which introduces breath-to-breath variability of tidal volume by automatically adjusting driving pressures using a least mean squares-based approach⁵¹. Their simulation and bench test studies demonstrated that this form of biologically inspired variability improves recruitment and ventilatory efficiency while adapting to rapid changes in lung mechanics without manual input⁵¹. These findings support our concept, in which variability in frequency and tidal volume arises naturally from the optimization process around

the minimum WOB/min, potentially offering lung-protective benefits similar to those of explicitly programmed variable ventilation strategies.

This study has several limitations. First, it represents a proof-of-concept simulation rather than a clinical validation; therefore, the findings cannot be directly generalized to patient populations. The hybrid respiratory simulator, although previously validated for realistic mechanical behavior, simplifies certain physiological phenomena such as surfactant effects and patient-ventilator asynchrony. Second, the adaptive algorithm was implemented manually, and its fully automated performance under dynamic conditions (e.g., abrupt changes in resistance or compliance) has not yet been tested. Third, only three representative mechanical conditions were evaluated, which may not fully capture the diversity of real-world lung pathologies. Finally, the study focused exclusively on minimizing mechanical power (i.e., the work of breathing per minute), without assessing gas exchange efficiency or hemodynamic effects. Future experimental and clinical research should address these aspects using automated implementations and extended physiological monitoring.

It should also be noted that in this study, the work of breathing was calculated only for the inspiratory phase. This approach reflects the energy delivered by the ventilator to the respiratory system and is consistent with standard definitions of mechanical power in controlled ventilation, which account for positive (inspiratory) pressure-volume work⁵². The expiratory phase was not included, as in passive expiration the flow reversal typically involves minimal energy expenditure from the ventilator and mainly reflects the elastic recoil of the respiratory system⁵³. However, in situations where expiratory flow limitation, intrinsic PEEP, or active expiratory muscle activity occurs, additional resistive losses and dissipated energy may contribute to the total mechanical load⁵³. Therefore, extending the model to include the expiratory phase could provide a more complete picture of total energy dissipation within the lung and chest wall system, particularly in obstructive conditions or during partial patient effort. Future algorithmic implementations could incorporate bidirectional pressure-volume integration to capture both inspiratory and expiratory components of mechanical power.

The next stage of development will focus on implementing a fully automated version of the adaptive algorithm within a modern ventilator control system. This will involve integration of continuous real-time mechanical power computation directly from airway pressure and flow signals, enabling the ventilator to autonomously adjust the respiratory rate on a breath-by-breath basis. Incorporating machine learning methods or model-predictive control may further enhance responsiveness to abrupt mechanical changes, such as secretion buildup or recruitment/derecruitment events. Another direction will be to expand the optimization criterion to include additional physiological endpoints – such as gas exchange efficiency, driving pressure, and dynamic compliance – allowing

for multi-objective optimization that balances energy delivery, oxygenation, and lung protection. Ultimately, validation on physical test lungs and preclinical models will precede pilot clinical trials assessing the safety, stability, and lung-protective potential of the system under dynamic respiratory conditions.

Conclusions

Based on the results of the simulation tests, the following conclusions can be drawn:

1) For constant alveolar ventilation WOB per minute follows a parabolic function of ventilation rate, allowing the optimal rate to be found through stepwise adjustments.

2) Changes in lung resistance and compliance affect the optimal ventilation rate, which is consistent with the findings of Otis²⁵ and Tehrani²⁷. Increased resistance leads to a lower optimal frequency, while decreased compliance increases the optimal frequency. These effects correspond to the narrowing or widening of the WOB/frequency parabola and must be considered when designing adaptive control algorithms

3) The proposed adaptive ventilation system effectively minimizes WOB per minute without the need for continuous monitoring of lung resistance and compliance. It remains sensitive to mechanical property changes and enables indirect tracking of respiratory system status through the shape of the WOB curve.

4) The natural variability introduced by continuously adjusting ventilation rate around the optimal WOB/min value may have beneficial effects on alveolar recruitment.

The general conclusion from the conducted research is the correctness of the proposed concept of searching for the optimal ventilation frequency with the given criteria, with simultaneous independence from the R and C parameters and no need to determine them. However, knowing the dead space volume is still necessary. We must point out, that the proposed adaptive algorithm in this study was implemented manually. In order to analyze the dynamics of the lungs-ventilator system future work should focus on implementing this concept in a modern generation of automatic adaptive ventilators for testing in simulations (hybrid respiratory simulator) and clinical settings.

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Ethics Statement

This study did not involve human participants or animals. Therefore, ethical approval was not required

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