Constrained Optimization for Noninvasive Estimation of Work of Breathing

Francesco Vicario, Antonio Albanese, Dong Wang,
Nikolaos Karamolegkos, and Nicolas W. Chbat, *Members, IEEE*

***Abstract*— This paper presents a technique for noninvasive estimation of respiratory muscle effort (also known as work of breathing, WOB) in mechanically ventilated patients. Continual and real-time assessment of the patient WOB is desirable, as it helps the clinician make decisions about increasing or decreasing mechanical respiratory support. The technique presented is based on a physiological model of the respiratory system, from which a cost function is constructed as the sum of squared errors between model-based airway pressure predictions and actual measurements. Quadratic programming methods are used to minimize this cost function. An experimental example on animal data shows the effectiveness of the technique.**

I. Introduction

The need for estimation of the respiratory mechanics and patient inspiratory effort is well-known in the medical community [1]-[2]. The clinical parameter commonly used to assess the effort made by the patient at each breath is known as work of breathing (WOB). WOB is defined as the mechanical work done by the respiratory muscles during inhalation. Knowing the patient WOB is especially important in partially assisted mechanical ventilation modes such as pressure support ventilation (PSV), where patient and ventilator share the mechanical work performed on the respiratory system. Moreover, in critical care medicine the popularity of this type of ventilation modes has recently increased. These modes, in fact, are believed to promote patient respiratory muscles activation and weaning, thus resulting in better outcomes and reduced hospitalization costs [3]-[4]. In particular, the quantitative assessment of WOB is valuable to clinicians to help them select the appropriate level of ventilation support in order to prevent both atrophy and fatigue of the patient respiratory muscles, typically due to too high and too low ventilator support, respectively. The state of the art for WOB estimation requires measurement of the esophageal pressure via the insertion of a balloon-tipped catheter in the patient's esophagus. Not only is this technique invasive, but it also needs characterization of the mechanical properties of the chest wall, which generally requires the patient to be made passive (e.g., via sedation or hyperventilation). These drawbacks limited the popularity of the technique. Alternative methods that do not require invasive measurements have been proposed, such as artificial neural networks [5]. However, they do not provide information on the underlying physiological mechanisms associated with WOB.

The new technique presented in this paper is noninvasive and based on a physiological model of the respiratory system, from which a cost function is constructed as the sum of squared errors between model-based airway pressure predictions and actual measurements. Physiological considerations are translated into mathematical constraints that restrict the space of feasible solutions and make the resulting optimization problem strictly convex, i.e., with a unique minimizing solution. Existing quadratic programming techniques are used to efficiently find such a minimizing solution, which yields an estimate of the respiratory mechanics (resistance and elastance) as well as an estimate of the equivalent pressure exerted by the respiratory muscles over the breath. The mathematics behind the method is described in detail in [6], where the method is shown to successfully provide estimates for the respiratory resistance and elastance in spontaneously breathing ventilated patients. In this paper, we focus on the estimation of the respiratory muscle pressure waveform and use it to estimate WOB. We demonstrate on animal data that the method is suitable for continual, real-time, and noninvasive assessment of WOB.

II. Method

The problem addressed in this paper can be stated as follows. Given measurements of pressure and flow at the patient airway opening (i.e., at the mouth or, for patients ventilated with an endotracheal tube, at the so-called Y-juncture), estimate the WOB done by the patient at each breath. Pressure and flow waveforms are typically available for mechanically ventilated patients, hence the solution to this problem is noninvasive.

A. Mathematical Model

The lungs are traditionally represented as an elastic compartment (balloon) served by a single resistive pathway (airways). Despite its simplicity, this lumped model is representative of the real lung mechanics and accepted in the respiratory research community. The pressure at the entrance of the resistive pathway represents the airway opening pressure (P_{ao}), whereas the pressure inside the balloon corresponds to the alveolar pressure (P_{al}). The balloon, in turn, is enclosed in the chest wall that is represented as an additional elastic compartment whose internal pressure corresponds to intrapleural pressure (P_{pl}). The system is subject to an external pressure (P_{mus}) that represents an equivalent pressure of the force exerted by the respiratory muscles (mainly the diaphragm). The electrical analogue corresponding to this schematic representation of the respiratory system is shown in Fig. 1a. R_{aw} and E_L denote

F. Vicario (corresponding author, phone: +1-914-945-6151; fax: +1-914-945-6014; e-mail: francesco.vicario@philips.com), A. Albanese (antonio.albanese@philips.com), D. Wang (dong.wang@philips.com), N. Karamolegkos (nikolaos.karamolegkos@philips.com), and N. W. Chbat (chbat@philips.com) are with Acute Care Solutions, Philips Research North America, Briarcliff Manor, NY 10510 USA.

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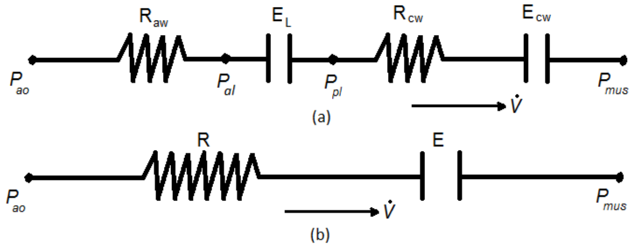

Figure 1. Schematic representation of respiratory mechanics: (a) electrical analogue; (b) lumped electrical analogue.

the airways/lungs resistance and elastance, respectively, whereas E_{cw} denotes the elastance of the chest wall. Mechanical dissipation (friction) within the chest wall is taken into account by an additional resistance R_{cw}. The simplest model assumes that the resistive and elastic elements in the above electrical analogue are described by constant parameters (linear model).

The number of parameters in the electrical analogue in Fig. 1a can be reduced to two, namely the overall resistance R and elastance E of the respiratory system (Fig. 1b) to obtain what is known in the literature as the linear first-order single-compartment model of respiratory mechanics [7]. The air flow $\dot{V}(t)$ through the resistive and elastic elements is driven by the pressure difference $P_{ao}(t) - P_{mus}(t)$. The equation governing its dynamics, known as the equation of motion of the respiratory system, is

$$P_{ao}(t) = R\dot{V}(t) + EV(t) + P_{mus}(t) + P_0 \quad (1)$$

where $V(t)$ represents the volume of air inhaled from the beginning of inhalation ($t = 0$), and P_0 is a constant pressure term balancing the pressure at the airway opening at $t = 0$ ($V(0) = \dot{V}(0) = P_{mus}(0) = 0$).

As explained in detail in [6], the estimation of $P_{mus}(t)$ without knowing R and E is an underdetermined problem, i.e., there exist infinitely many solutions of triplets R, E, $P_{mus}(t)$ satisfying (1). Only one of them is the physiological solution that we are after.

B. Estimation Method

To overcome the underdetermined nature of the mathematical problem, we introduce physiological constraints on the unknowns to be estimated. For instance, the signal profile of the pressure exerted by the respiratory muscles does not change arbitrarily over one breath. It typically monotonically decreases at the beginning of a spontaneous breath, then monotonically returns to zero as the muscles relax. Finally, in conditions of passive exhalation, this pressure remains zero until the next breath is initiated. This physiological knowledge can be infused in the estimation algorithm in the form of regional constraints where the monotonicity of $P_{mus}(t)$ is enforced via inequalities and equalities. For simplicity, the estimation algorithm is formulated below replacing $P_{mus}(t)$ with $\tilde{P}_{mus}(t) = P_{mus}(t) + P_0$, since P_0 is constant over the breath. The estimation problem can then be cast as a constrained optimization problem with cost function

$$J = \sum_{k=1}^{k=N} \left(P_{ao}(k) - \left(R\dot{V}(k) + EV(k) + \tilde{P}_{mus}(k) \right) \right)^2 \quad (2)$$

to be minimized subject to the following constraints

$$\tilde{P}_{mus}(k+1) - \tilde{P}_{mus}(k) \le 0 \quad \text{for } k = 1,2,\dots,m-1 \quad (3a)$$
$$\tilde{P}_{mus}(k+1) - \tilde{P}_{mus}(k) \ge 0 \quad \text{for } k = m,m+1,\dots,q-1 \quad (3b)$$
$$\tilde{P}_{mus}(k+1) - \tilde{P}_{mus}(k) = 0 \quad \text{for } k = q,q+1,\dots,N \quad (3c)$$

where k denotes the kth time sample, since the data are typically collected via sampling devices, and N is the total number of time samples in the breath. The time samples m and q define the borders of the 3 regions with different monotonicity. The cost function is of least-squares (LS) type, since the squared terms in (2) correspond to the difference between the measured P_{ao} and the one estimated from the model in (1) at each time sample. The unknowns over which J is minimized are R, E, $\tilde{P}_{mus}(1)$, $\tilde{P}_{mus}(2)$, …, $\tilde{P}_{mus}(N)$.

The constrained optimization problem in (2)-(3) is characterized by a quadratic cost function and linear constraints. It belongs to the class of so-called quadratic programs, which are a mature mathematical technique [8]. Well-established algorithms such as the interior-point and active-set methods exist to solve this class of optimization problems and routines are available in most commercial software, e.g. Matlab®. In the quadratic program (2)-(3), the parameters m and q need be specified. A search for the optimal m and q is then necessary. Because in normal conditions the ventilator cycles off when or after the patient effort terminates, we fix $q = SOE$ (SOE stands for start of exhalation and denotes the time sample when the ventilator stops supporting the breath, a.k.a. cycling off) and perform a search for m over the interval $1 \le m < SOE$. For each candidate value for m, we solve a quadratic program in the form of (2)-(3) and obtain a corresponding minimized value J_{min} of the cost function (2). The solution arising from the m giving the minimum among all the J_{min}'s provides the desired estimate for R, E, and $P_{mus}(t)$.

Finally, the estimate of WOB is obtained by integration of $P_{mus}(t)$ over the inhaled volume

$$WOB = \frac{1}{V_T}\int_0^{t_{V_T}} P_{mus}(t)\dot{V}(t)dt = \frac{1}{V_T}\int_0^{V_T} P_{mus}(t)dV \quad (4)$$

where V_T is the tidal volume, or maximum volume of air inhaled over the breath. Note that WOB is usually defined as the respiratory muscle mechanical work normalized over the tidal volume. This is the most common definition adopted in mechanical ventilation practice, hence it is our choice in this study, too. As an aside, (4) is also at the core of the so-called Campbell diagram, i.e., the state-of-the-art tool used in the medical community to compute WOB graphically from measurements of the esophageal pressure.

III. Results

To verify the effectiveness of the proposed technique in real case scenarios, the estimation method has been retrospectively tested on available experimental data. The data were collected as part of an educational study performed at the Pulmonary Research and Animal Laboratory at Duke University Medical Center on a 44 kg adult male pig. The experimental protocol was approved by the local institutional review board committee. During the study, a pig was anaesthetized, intubated and connected to an Esprit ventilator with NM3 respiratory monitor (Philips-Respironics). Airway pressure (P_{ao}) and flow ($\dot{V}$) were measured at the Y-juncture between the breathing circuit and the endotracheal tube, via the standard proximal sensors of the NM3 monitor. The pressure inside the esophagus (P_{es}) was measured as a surrogate of intrapleueral pressure using an esophageal balloon connected to a differential pressure transducer (Model PS309D, Validyne Engineering, Northridge, CA). Occlusion tests were performed to assess the correct positioning of the balloon as described in [9]. Data were acquired and collected at 100 Hz using a dedicated system for real-time data acquisition and computation. The datasets used to demonstrate the proposed algorithm are related to periods during which the pig was subject to continuous positive airways pressure (CPAP) with variable levels of pressure support ventilation (PSV). A dataset with 453 consecutive breaths, corresponding to about 30 minutes of data, was considered. The performance of the proposed algorithm was evaluated by comparing the WOB that was noninvasively estimated via the presented constrained optimization method with the WOB that was invasively calculated from the measured P_{es} over the same dataset. The invasive estimates were obtained according to the following procedure. *(1)* At the end of the study, the pig was placed on volume control ventilation (VCV) in order to be ventilated passively with moderate to high tidal volumes such that its spontaneous respiratory drive was temporarily inhibited ($P_{mus} = 0$ in (1)). The flow ($\dot{V}$) and pressure (P_{ao} and P_{es}) data from five such passive breaths were then used to compute the resistance and elastance of the chest wall (R_{cw} and E_{cw}). Particularly, the LS method was used to fit the data via the equation describing the portion of the electrical analogue in Fig. 1a that pertains to the chest wall (i.e., from P_{pl} to P_{mus})

$$P_{es}(t) = R_{cw}\dot{V}(t) + E_{cw}V(t) + P_0{}' \qquad (5)$$

where $P_{mus} = 0$ and P_{pl} is replaced by P_{es}. This yielded values of R_{cw} and E_{cw} for each selected passive breath. Final estimates of R_{cw} and E_{cw} were then obtained by averaging across five individual VCV breaths. *(2)* The equation of motion of the chest wall for active patient, again with P_{pl} replaced by P_{es}, was then used to compute the invasive estimate of $P_{mus}(t)$

$$P_{mus}(t) = P_{es}(t) - R_{cw}\dot{V}(t) - E_{cw}V(t) - P_0{}' \qquad (6)$$

over the 453 PSV breaths. Finally, the invasive estimate of WOB was obtained by integrating $P_{mus}(t)$ from (6) over the inhaled volume in accordance with (4).

Fig. 2 compares the invasive and noninvasive sequences of estimates over the dataset across different PSV levels. The estimates follow the same trends as the PSV level is changed. As expected from physiological intuition, higher PSV generally corresponds to lower WOB, and vice versa. A thorough analysis of the invasively estimated P_{mus} waveforms reveals that anomalous breathing conditions occur and explain part of the difference between the curves in Fig. 2. For instance, between 100 and 550 seconds the majority of the breaths show that the animal respiratory muscles were active during exhalation. The PSV level over this time range is highest (20 cmH_2O) and so is the inhaled volume of air. Hence the animal makes a respiratory effort to enhance the exhalation of such a high volume. Breaths with active exhalation violate the assumptions made in defining the constraints (3), hence the corresponding noninvasive estimates are expected to be affected. Another anomaly that occurs in the dataset shown in Fig. 2, although more sporadically, is the so-called patient double effort, i.e., the respiratory muscles exert force to inhale into two separate segments of the same breath. Also this condition violates the assumptions behind (3) and is then likely to generate estimation error. Additionally, numerical simulations have revealed that early cycling-off of the ventilator (i.e., the ventilator's SOE occurring before the patient has completely relaxed the respiratory muscles) is a critical condition for the estimation method based on constrained optimization (see [6] for more details). Early ventilator cycling-off occurs in three breaths in the dataset shown in Fig. 2. To give an idea of the above-mentioned anomalies and to show a few examples of noninvasively estimated P_{mus} waveforms for both anomalous breaths and normal breaths, Fig. 3 reports four snapshots from different segments of the dataset, each with three breaths. Figs. 4 and 5 summarize the comparison between invasive and noninvasive WOB estimates via linear regression and Bland-Altman plots. Every data point in these plots represents a breath and is displayed with a different marker to indicate whether the breath is considered to be normal or is characterized by early SOE, active exhalation or double effort.

IV. Discussion

The paper presented a method for the estimation of work of breathing in mechanically ventilated patients. Compared to existing techniques, the new method is noninvasive and

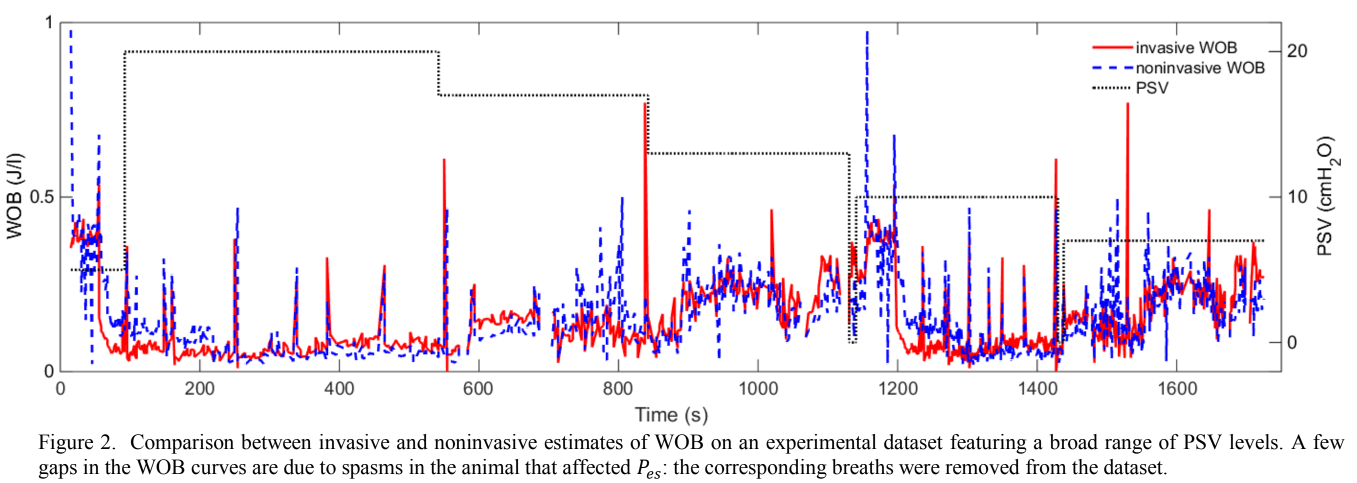

Figure 2. Comparison between invasive and noninvasive estimates of WOB on an experimental dataset featuring a broad range of PSV levels. A few gaps in the WOB curves are due to spasms in the animal that affected P_{es}: the corresponding breaths were removed from the dataset.

does not require maneuvers interfering with the desired ventilation patterns. Additionally, it is based on a physiological model and as such provides the clinicians with more insight into respiratory mechanics. Continual noninvasive assessment of respiratory effort holds the promise that clinicians will be able to better provide mechanical ventilator support with fewer adverse effects and ultimately better outcomes.

The plots in Figs. 4 and 5 showed how detection of some mechanical ventilation anomalies would be beneficial for the performance of the proposed estimation technique. The estimates from normal breaths match over a relatively broad range of WOB, as shown in Fig. 4 by the proximity of the data points plotted as circles to the bisector. Conversely, the data points from anomalous breaths tend to spread farther from the bisector. Fig. 5 highlights how the one-sigma confidence interval of the error between invasively and noninvasively estimated WOB for normal breaths is significantly smaller than the one for anomalous breaths. Detecting the above-mentioned ventilation anomalies would then have a twofold advantage. First of all, discarding the noninvasive estimates of WOB from anomalous breaths improves the overall performance of the proposed estimation technique, preventing the clinicians from making non-optimal decisions based on potentially erroneous estimates. Secondly, and perhaps even more importantly, the above-mentioned ventilation anomalies represent undesirable clinical conditions. Upon their detection, the clinician would normally change the ventilator settings to return to normal conditions. As a consequence, anomaly detection would solve at its root the problem of anomalies potentially affecting the presented noninvasive technique. Future work will then focus on developing algorithms able to automatically detect such anomalies from P_{ao} and $\dot{V}$ measurements.

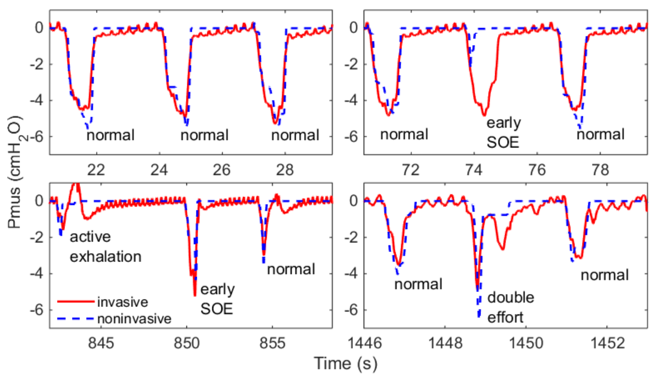

Figure 3. Examples of P_{mus} estimates from the experimental dataset shown in Fig. 2.

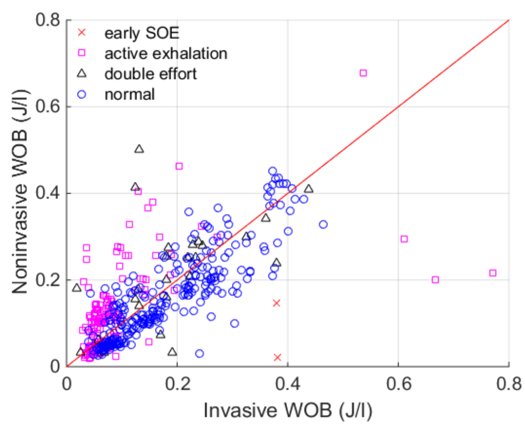

Figure 4. Linear regression plot for the WOB estimates reported in Fig. 2.

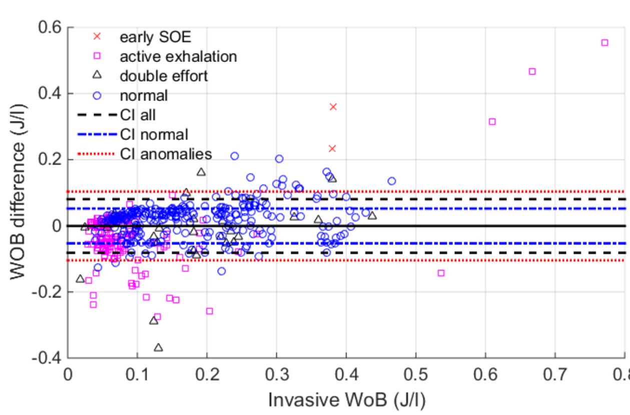

Figure 5. Bland-Altman plot for the WOB estimates reported in Fig. 2.

As a final comment, it is important to note that the invasive estimate of WOB is used in this study as the state-of-the-art benchmark to assess the performance of the proposed noninvasive estimation technique. However, the use of the esophageal pressure as a surrogate for the intrapleural pressure is, as well as modeling error, a source of error in the benchmark. To the knowledge of the authors, no better technique to measure P_{mus} is available to compute a real WOB gold standard. The comparison provided in this paper is then to be intended as an assessment of the agreement between two different estimation techniques, one invasive, the other noninvasive, rather than an assessment of the absolute performance of the new technique.

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