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Inspiratory respiratory mechanics estimation by using expiratory data for reverse-triggered breathing cycles☆

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ABSTRACT

Background and objective: Model-based lung mechanics monitoring can provide clinically useful information for guiding mechanical ventilator treatment in intensive care. However, many methods of measuring lung mechanics are not appropriate for both fully and partially sedated patients, and are unable provide lung mechanics metrics in real-time. This study proposes a novel method of using lung mechanics identified during passive expiration to estimate inspiratory lung mechanics for spontaneously breathing patients.

Methods: Relationships between inspiratory and expiratory modeled lung mechanics were identified from clinical data from 4 fully sedated patients. The validity of these relationships were assessed using data from a further 4 spontaneously breathing patients.

Results: For the fully sedated patients, a linear relationship was identified between inspiratory and expiratory elastance, with slope 1.04 and intercept 1.66. The r value of this correlation was 0.94. No cohort-wide relationship was determined for airway resistance. Expiratory elastance measurements in spontaneously breathing patients were able to produce reasonable estimates of inspiratory elastance after adjusting for the identified difference between them.

Conclusions: This study shows that when conventional methods fail, typically ignored expiratory data may be able to provide clinicians with the information needed about patient condition to guide MV therapy.

1. Introduction

Patients with respiratory failure requiring breathing support are mechanically ventilated. Clinicians must provide patient- and disease-specific mechanical ventilation (MV) therapy to prevent alveoli collapse and improve gas exchange [1,2]. A key component of MV therapy is selecting the ideal postive end expiratory pressure (PEEP) setting. A high PEEP may damage healthy lung tissue, but too little PEEP will reduce gas exchange [3]. Thus, a significant amount of research focuses on identifying the optimum PEEP for each patient [4–6].

Clinically useful information for selecting PEEP settings are provided by model-based lung mechanics monitoring [7,8]. In critical care, any method of measuring lung mechanics must be appropriate for both fully and partially sedated patients, and provide lung mechanics metrics in real-time. At present, many models do not meet these criteria: They are typically too computationally complex for real-time respiratory mechanics monitoring, or may require procedures or measurements unavailable in a typical clinical setting [9–15]. Furthermore, simple lung models are unable to produce accurate measurements for spontaneously breathing (SB) patients. Patient breathing efforts, such as reverse-triggering in response to ventilator driven inhalation, may significantly alter measured ventilator pressure or flow. These changes cannot be fully described without additional invasive measures [9–18].

Abbreviations: ICU, Intensive care unit; MV, Mechanical ventilation; PEEP, Positive end expiratory pressure; SB, spontaneous breathing.

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This study uses a computationally simple model-based method to assess retrospective patient lung mechanics. Specifically, the relationship between inspiratory and expiratory mechanics are assessed, to identify and validate any non-patient specific trends. Muscular breathing effort is assumed to be minimal during passive expiration, and independent of any inspiratory SB efforts such as reverse-triggering [19,20]. Therefore, linking respiratory mechanics captured during expiration in SB patients back to inspiration could extend the ability of respiratory mechanics to titrate MV care.

2. Methodology

2.1. Can expiration be modeled?

A computationally simple, single compartment lung model is able to identify patient- and breath-specific lung mechanics from clinical pressure and flow data [5,7,18]. It is defined:

$$P_{aw}(t) = R_{rs}Q(t) + E_{rs}V(t) + P_0 \tag{1}$$

where P_{aw} is airway pressure, t is time, R_{rs} is resistance of the conducting airways, Q is airflow, E_{rs} is respiratory elastance (inverse of compliance), V is inspired volume, and P_0 is positive end expiratory pressure (PEEP) [7]. This model does not account for any patient breathing effort. Thus, any changes in ventilator pressure or flow caused by SB efforts can result in incorrect measurements of underlying respiratory mechanics [17,20–22].

P_{aw} is equal to the total pressure supplied by the ventilator. The supplied pressure supports both the pressure driving airflow and the pressure needed to prevent lung collapse at the end of expiration, PEEP. Thus the pressure driving airflow, P_d, can be defined:

$$P_d(t) = R_{rs}Q(t) + E_{rs}V(t) \tag{2}$$

Any airflow into or out of the lung will create a change in lung pressure. The relationship between airflow and lung pressure is defined:

$$Q(t) = \frac{1}{E_{rs}}\frac{dP_{lung}(t)}{dt} \tag{3}$$

Substituting, Eq. (3) into Eq. (2) results in a non-homogeneous ordinary differential equation (ODE) relating the driving pressure supplied by the ventilator and lung pressure:

$$P_d(t) = \frac{R_{rs}}{E_{rs}}\frac{dP_{lung}(t)}{dt} + P_{lung}(t) \tag{4}$$

During passive expiration no driving pressure is supplied by the ventilator, $P_d = 0$. Solving Eq. (4) for no external driving pressure, the modeled lung pressure during expiration becomes:

$$P_{lung}(t) = (P_{lung}(0))e^{\frac{-tE_{rs}}{R_{rs}}} \tag{5}$$

The expected flow measured in expiration can now be found by substituting P_{lung} from Eq. (5), into Eq. (3) yielding:

$$Q = \frac{-P_{lung}(0)}{R_{rs}}e^{\frac{-tE_{rs}}{R_{rs}}} \tag{6}$$

Eq. (6) shows that during passive expiration, the expected air flow out of the lung would be exponentially decaying. This response is observed in expiration for MV patients, confirming that this model is appropriate for both inspiration and expiration. Additionally, this response shows that the model becomes structurally non-identifiable for passive expiration because E_{rs} and R_{rs} have a combined affect on the exponential decay rate.

2.2. Model identification

It has previously been shown that the single compartment model becomes structurally non-identifiable when analysing passive expiratory data [23,24]. This stems from E_{rs} and R_{rs} being lumped together in an exponential decay term, so the relative effects of resistance and elastance cannot be separated. The following is a proposed method to modify expiratory pressure data to allow a direct least-squares estimation of expiratory respiratory mechanics from just the expiration data alone.

The pressure supplied by the ventilator during expiration may be viewed as a large negative pressure applied to P_i. This negative driving pressure causes air to flow out of the lung, decreasing volume from its initial end-inspiratory value. This can be expressed by shifting expiratory pressure and volume to have initial values of zero. This data shift allows for estimation of lung elastance from the new end expiratory pressure and volume measures, letting the effects of elastance and resistance be separated from the exponential decay term.

Fig. 1a shows expiratory lung and resistive pressures identified with a least squares fit to expiratory airflow, unaltered expiratory pressure and unaltered expiratory volume data. The estimated respiratory mechanics are not physiologically possible. The lung pressure is clearly incorrect, P_{lung} should start at the same pressure as maintained by the ventilator at the end of inspiration, P_i. Fig. 1b shows pressure estimates for the same breath after shifting pressure and volume to have initial values of zero. P_{lung} now decays exponentially from the pressure measured at the start of expiration. Further support for this method of calculating expiratory lung mechanics is provided by the positive, physiologically reasonable estimates of respiratory mechanics. Hence, all expiratory respiratory mechanics presented in this study were estimated using shifted pressure and volume data.

SB efforts occurring at the end of inspiration will alter P_i. The method used in this study to calculate expiratory respiratory mechanics are highly dependent on this value, hence any error in P_i reduces estimation accuracy. To identify breaths likely to have unreliable estimates, a simple reconstruction method developed by Damanhuri et al. [25] was used to quantify the magnitude of SB effort. Respiratory mechanics were not calculated for a breath if the area after peak pressure changed by more than 12.5% post-reconstruction. This was the level at which researchers trained to identify dissynchrony in waveforms were no longer able to confirm a reduction in pressure was due to breathing effort.

2.3. Data

This study analysed retrospective Datasets from 8 patients, where patients 1A-D were fully sedated and Patients 2A-2D contained transitions from partial to full sedation allowing validation of the mechanics properties obtained in SB when compared to full sedation. They are thus a selected representative set of patients useful for this analysis. All patients were ventilated with a volume controlled ramp flow profile on synchronous intermittent mandatory ventilation (SIMV) mode. The ventilators used were PB-840 ventilators (Coviden-Puritan Bennet, Boulder, CO). Patient ventilation details are presented in Table 1. Approval for this study and the use of the clinical data collected, were provided by the NZ Upper South Island Regional Ethics Committee.

Patients 1A–1D were fully sedated, with all breaths free from SB effort. This data was used to identify any relationships between inspiratory and expiratory respiratory mechanics. The data contains 1013 breaths with 12 recruitment manoeuvres (RM).

Each dataset from patients 2A–2D contained 60 breaths, 30 breaths each from before and shortly after sedation. All patients exhibited varying levels of SB effort pre-sedation, and were then sedated without any changes to ventilation settings. Sedation was given for clinical reasons. This data was used to validate whether the relationships identified provided clinically useful information. Fig. 2 shows the first 10 breaths, pre- and post- sedation, where sedation eliminated SB efforts, as expected.

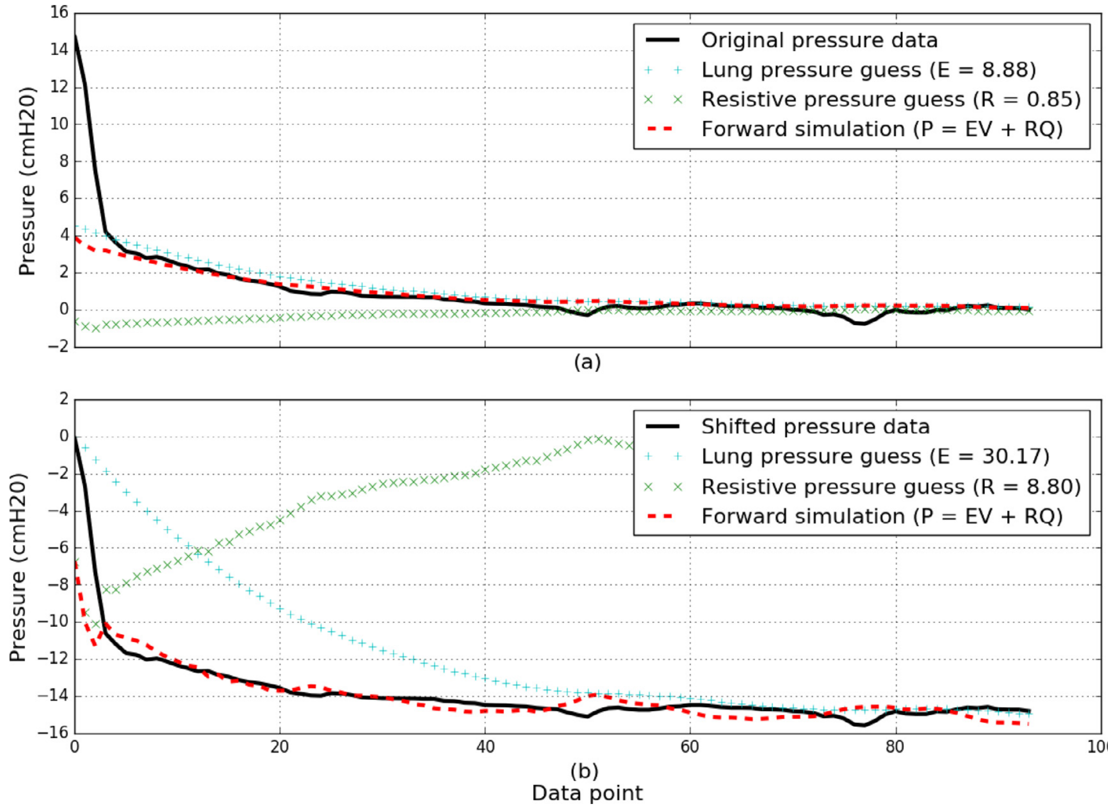

Fig. 1. Pressure profile and forward simulation of driving, lung, and resistive pressure for expiration. Respiratory mechanics used in simulations obtained from two approaches (a) Direct linear single compartment model fit to unchanged ventilator data. (b) Linear single compartment model fit to data, with pressure and volume data adjusted to have initial values of 0.

Table 1
Patient information, including ventilation details.

Patient	Primary diagnosis	Tidal volume (ml)	Respiratory rate (/minute)	PEEP (cmH_2O)
1A	Peritonitis	510	20	16–25
		520	20	14–22
		315	20	18–26
		320	20	19–27
1B	Pneumonia	465	18	11–19
		465	18	12–20
1C	Pneumonia	385	20	12–32
1D	Ischaemic gut	470	18	20–36
		460	18	20–36
		420	20	24
		420	20	22–30
		420	20	22–30
2A	Peritonitis	365	18	15
2B	Peritonitis	370	19	17
2C	Cardiac surgery	480	14	11
2D	Pneumonia	540	18	13

2.4. Validation

For patients 1A to 1D, The inspiratory and expiratory respiratory mechanics of each breath were calculated for patients 1A to 1D. If a cohort-wide trend was identified, a 95% confidence interval and 95% prediction interval were calculated using bootstrapping of 1000 random subsets of breaths generated with replacement.

To assess whether trends between inspiratory and expiratory mechanics provided clinically useful information, this study looked at whether expiratory mechanics could be used to estimate inspiratory mechanics in SB patients. For these patients, expiratory mechanics estimates are expected to be reliable because expiration is hypothesised to be a primarily or completely passive process [19,20]. Data from patients 2A to 2D has examples of both SB and full sedation. Within the roughly 10 min period recorded, it is assumed respiratory mechanics would show only minimal variation [26]. Hence, the median mechanics and Median Absolute Deviation (MAD) or mechanics were calculated to indicate the accuracy of inspiratory mechanics estimates.

3. Results

Fig. 3 compares expiratory and inspiratory elastance for patients 1A to 1D. A linear relationship was identified between inspiratory and expiratory elastance. This linear relationship was very

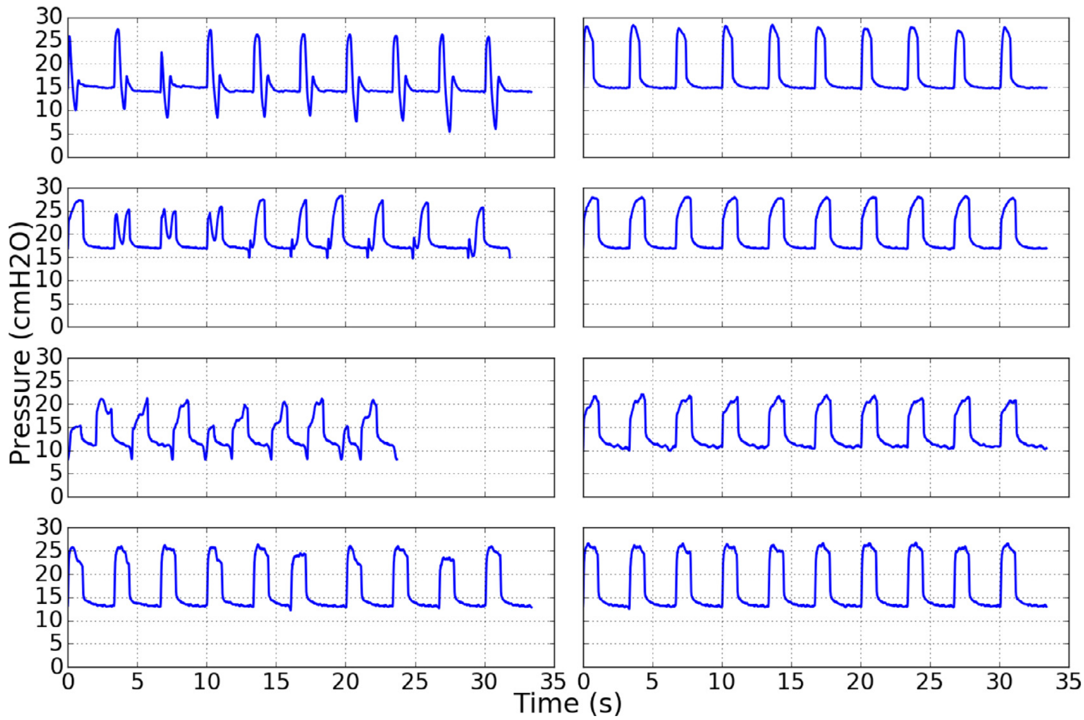

Fig. 2. Pressure waveform of first 10 breaths pre- and post-sedation for datasets 2A (Top) through to 2D (Bottom).

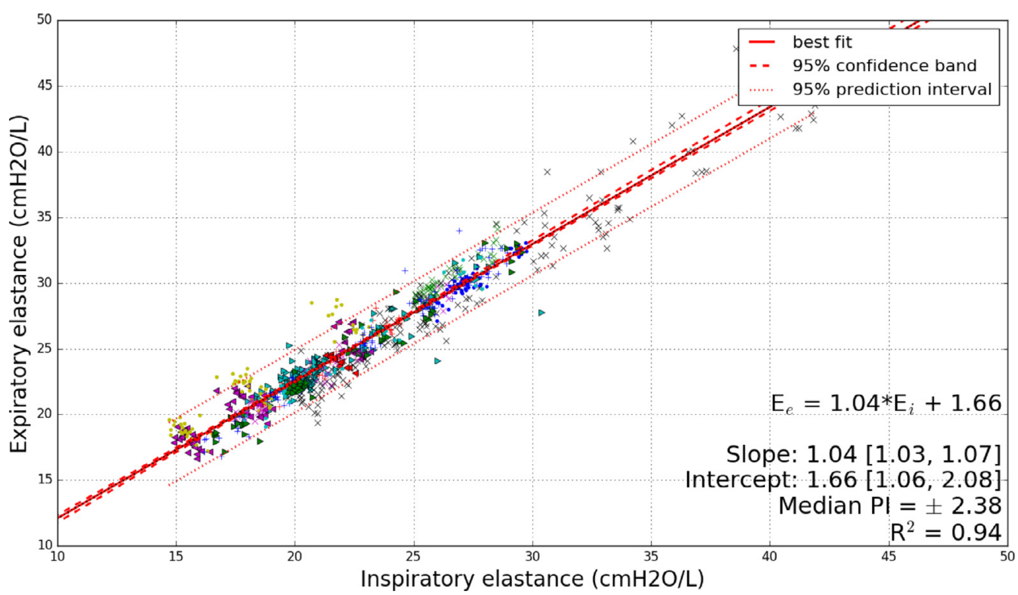

Fig. 3. The linear regression of inspiratory and expiratory elastance (cmH_2O/L) for patients 1A to 1D. Also shown are 95% confidence interval and 95% prediction interval. A different marker is used for each of the 12 datasets. The regression was calculated from expiratory elastance to inspiratory elastance, as is reflected by the equation presenting the line-of-best-fit. The inverse of this equation, $Ei = Ee/1.04–1.60$, was used to calculate inspiratory elastance from expiratory data.

strong ($R^2 = 0.94$) and cohort-wide. The identified confidence intervals are very narrow, with 95% confidence the gradient falls within in the range 1.04 to 1.07. The offset shows a larger range, from 1.04 to 2.05. 95% of the data was shown to be within ± 2.38 cmH_2O/L of the identified mean.

No cohort-wide trend could be identified for respiratory resistance. Respiratory resistance for all breaths for patients 1A to 1D and a 1:1 trend line are shown in Fig. 4.

3.1. Using elastance trend to estimate elastance under SB

In this section, elastance estimated only from inspiratory data is referred to as “true inspiratory elastance”, and elastance estimated using the trendline in Fig. 3 is referred to as “estimated inspiratory elastance”. Fig. 5 shows a sample forward simulation for each dataset.

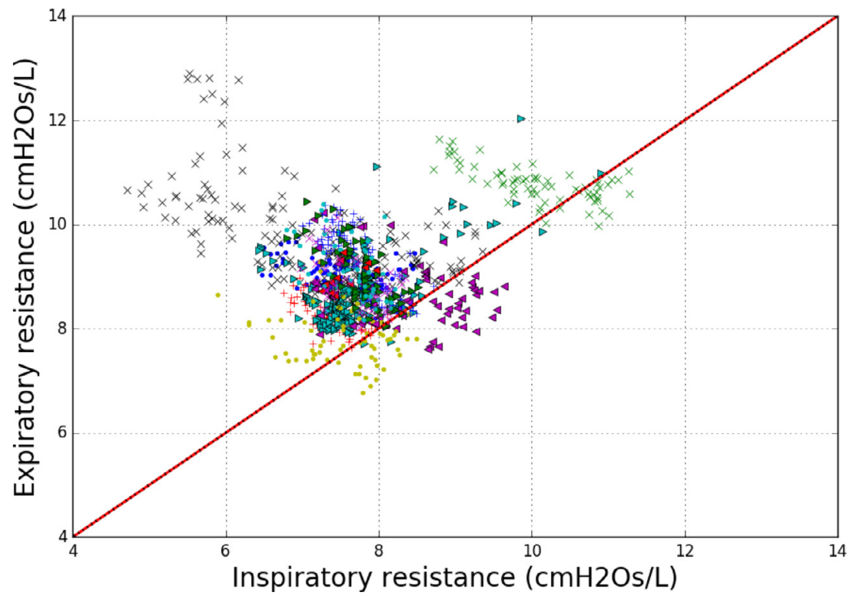

Fig. 4. Inspiratory and expiratory resistance ($cmH_2O/L/s$) for patients 1A to 1D. Also shown is a 1:1 line. A different marker is used for each of the 12 datasets.

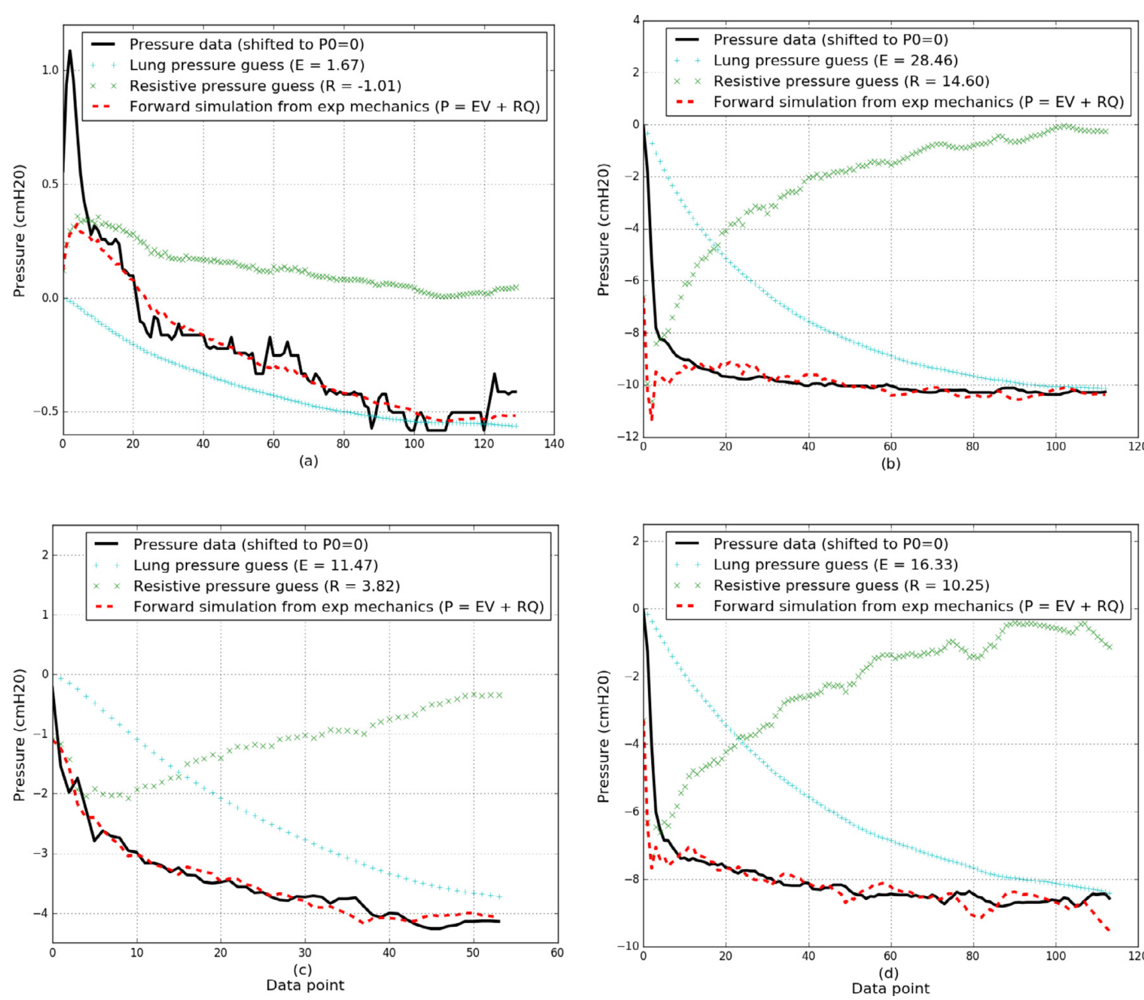

Fig. 5. Pressure profile and forward simulation of driving, lung, and resistive pressure for expiration for patients 2A to 2D, respectively. Note the poor fit for patient 2A where the true end-expiratory pressure is obfuscated by breathing effort.

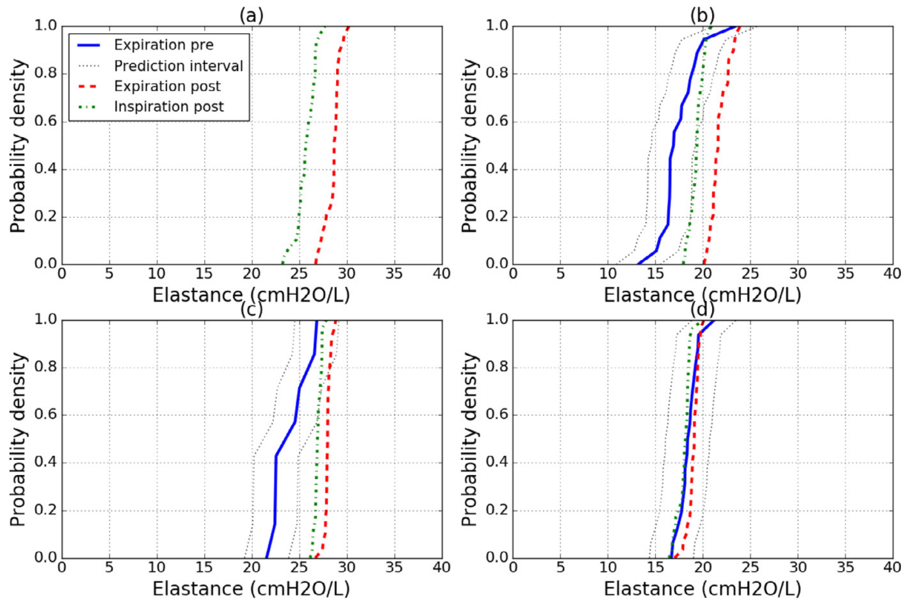

Fig. 6. The cumulative distributions of elastance (cmH_2O/L) for patients 2A to 2D: Estimated pre-sedation (solid) with prediction interval (dotted), estimated post-sedation (dashed), and true post-sedation (dash-dot). For prefect estimation, pre-sedation estimate would exactly match true post-sedation elastance.

Table 2
Results for SB patients 2A to 2D. Median [interquartile range] and median absolute distribution (MAD) identified for true (left) and estimated (right) inspiratory elastance (cmH_2O/L).

		Inspiration (true)		Inspiration (estimated)	
		Median [IQR]	MAD	Median [IQR]	MAD
1	pre	−20.51 [−27.98:−18.70]	2.91	NA [NA:NA]	NA
	post	25.69 [25.11:26.52]	0.72	28.68 [28.33:29.01]	0.35
2	pre	10.46 [2.25:26.48]	9.74	23.57 [22.49:25.42]	1.29
	post	26.92 [26.76:27.26]	0.24	27.99 [27.88:28.12]	0.12
3	pre	15.66 [12.99:17.65]	2.60	16.91 [16.45:18.55]	0.86
	post	19.38 [18.87:19.83]	0.51	21.59 [21.09:22.49]	0.51
4	pre	16.75 [13.84:17.32]	0.99	18.38 [17.92:19.05]	0.66
	post	18.17 [17.83:18.42]	0.30	19.10 [18.75:19.42]	0.33

Fig. 6 shows the post-sedation cumulative distribution of true and estimated inspiratory elastance values. The mechanics identified for sedated patients represents the minimum level or breath-to-breath variation. As variation increases, the slope of the distribution becomes less vertical. Hence, for an ideal case, the pre-sedation variation would exactly overlap post-sedation measurements.

The results are shown in Table 2. Expiratory mechanics were not able to be calculated for patient 2A because all breaths were significantly affected by end-inspiratory SB effort. In contrast, elastance prediction for patient 2D were almost ideal. Post-sedation MAD for all patients was low, with similar values for true and estimated elastance. Median estimated elastance was larger than median true elastance for every patient, where the maximum difference was identified for patient 2A at 2.99 cmH_2O/L.

4. Discussion

For patients 1A to 1D, a strong, linear, patient independent trend was observed between inspiratory and expiratory elastance. Inspiratory elastance was found to be lower than expiratory elastance. This matches the findings of previous studies [27,28]. However, no cohort-wide trend was found for resistance between ins- and expiration. In general, expiratory resistance was higher than inspiratory resistance. This relationship was expected, as airways are compressed by expiratory effort and expanded by inspiratory effort. Overall, the relationships found between inspiratory and expiratory mechanics provide validation for the methods and underlying model used in this study.

4.1. Estimating inspiratory elastance with SB effort

The overall analysis is set to determine whether expiratory mechanics could be used to estimate inspiratory mechanics in SB patients. The comparison to sedated patients after a transition from partial to full sedation allows a clear test case of how inspiratory and expiratory mechanics are related without interference from the asynchrony seen in SB. This transition eliminates asynchrony as the patient is fully paralysed by sedation and the ventilator takes over the complete work of breathing. The transition was implemented clinically for clinical reasons and was not an intervention made for this study. More importantly, for this research, the model is well validated in both SB and fully sedated patients in prior work [5,18], so there is no error introduced by assessing or comparing mechanics across this clinical transition.

Despite all patients being sedated and ventilated in volume control mode, different severity and rates of SB efforts were observed. These datasets represent a wide range of SB effort, from mild to very severe, where mild means infrequent and/or small changes in pressure waveform and severe means the pressure waveform was almost completely destroyed by breathing effort, a worst case scenario. Patient 2A represents the worst case result for measuring expiratory lung mechanics. Every breath pre-sedation showed a very high level of SB effort in the approximately 1.5 min recorded, preventing any reliable lung mechanics measurements. However, lung mechanics are not expected to change significantly over small time periods. In practice a good elastance estimate does not need to be calculated for every breath, or perhaps for several minutes. However the frequency of measurements needed is not assessed by this study.

Expiratory elastance measurement were generally stable, showing moderate breath-to-breath variation. The change in median estimated elastance from pre- to post-sedation is small, with a maximum change of 4.7 cmH_2O/L for patient 2C. The estimated elastance pre-sedation showed significantly less variation than true inspiratory elastance measurements for all patients. However, the variability of estimated elastance is larger than may be acceptable clinically.

In contrast to other methods, using expiratory data does not alter the pressure waveform in an attempt to remove the effect of SB efforts [29–31]. Altering pressure data can only give a proxy for the true waveform. The final result would also be strongly affected by the assumed lung behaviour. Identifying lung mechanics directly from expiratory pressure is expected to give a better reflection of lung condition.

4.2. Limitations

All patients in this proof of concept study were ventilated in volume control mode. Hence, the relationships identified by this study may not apply beyond this ventilation mode. Additionally, the relationship may not extrapolate beyond the elastance range 15–45 cmH_2O/L.

At low inspiratory elastance values, close to 0 cmH_2O/L, the possible expiratory elastance values given by the CI ranges from -1.63 to 3.98 cmH_2O/L. Although negative elastance has been measured in SB patients, this may not be physiologically reasonable in fully sedated patients [18]. A larger study is required to verify whether the linear relationship is valid over a wider range of elastance values and larger cohort.

5. Conclusions

A method capable of measuring expiratory respiratory mechanics was presented in this proof of concept study. The method provided reasonable estimates of expiratory respiratory mechanics of SB patients, when no large end-inspiratory SB efforts were present. This method is capable of real-time, breath-to-breath mechanics estimation without additional invasive manoeuvres or measures. This study shows that when conventional methods fail, expiratory data may provide clinicians with the lung mechanics measurements needed guide MV therapy.

Declaration of Competing Interest

Authors declare that they have no conflict of interest.

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