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Negative Lung Elastance in Mechanically Ventilated Spontaneously Breathing Patient

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Abstract: Mathematical modelling of respiratory system can guide clinicians in better monitoring and decision making for mechanically ventilated (MV) patients in intensive care unit (ICU). However, most mathematical models are develop for fully sedated patients and not particularly reliable to be applied for spontaneous breathing (SB) patients. Monitoring respiratory mechanics of SB patients requires invasive clinical protocols and equipment that are clinically too intensive to carry out. Previous study hypothesized that negative elastance occurred in SB patients due to the SB effort produced by the patient. Thus, this paper aims to further investigate the distribution of negative elastance in SB patients by extending the non-invasive time-varying elastance model. By capturing and reviewing the distribution of the negative elastance in SB patient, it can provide more consistent monitoring and decision making particularly for SB patients. Clinical data from 5 MV patients from Christchurch Hospital were used in this study. The area under the curve (AUC) for the time-varying elastance, E_{drs}, is estimated and analysed in each SB patient. The results are reported as median and interquartile range (IQR) for continuous data with a total of 82 hours. From the result, it was found that all patients have distribution of negative elastance with Patients 1 and 3 have higher distribution of negative elastance due to the SB effort. The median vaue for the negative elastance for all patients' ranges from -0.66 cmH_2O.s/l to -2.27 cmH_2O.s/l. Negative elastance occurs when negative pressure is generated in the patient's pleural space causing air volume to enter the lung. Thus, by capturing and reviewing the distribution of the negative elastance in SB patient, it can provide more consistent monitoring and decision making particularly for SB patients.

1. INTRODUCTION

Mechanical ventilation (MV) is one of the most difficult, costly and variably delivered therapies for Acute Respiratory Distress Syndrome (ARDS) and respiratory failure patients in the intensive care unit (ICU). These patients experience severe widespread breathing problems and require MV for breathing support. Since conventional MV does not provide enough real-time information to guide or individualize therapy that could increase the risk of further lung injury and complications, respiratory mathematical models are developed to provide unique insight to patient-specific condition and response to treatment.

However, most of the lung models that have been developed are only effective for fully sedated patients (Brochard *et al.*, 2012; Hickling, 1998; Sundaresan *et al.*, 2009). They cannot be applied directly to the spontaneously breathing (SB) patients due who intermittently modify pressure and flow due to their own inspiratory effort without added invasive measurements or manoeuvres (Damanhuri *et al.*, 2016). However, because there are a significant number of patients on mechanical ventilation (MV) who have some level of SB effort, it will be valuable to develop and integrate a metric that allows analysis of the true respiratory mechanics in SB patients (Kallet & Branson, 2007).

SB patients have individual breathing efforts aside from the ventilator support (Grinnan & Truwit, 2005). These efforts modify the measurable airway pressure and/or flow waveforms, which can significantly alter the identified lung mechanics. The main obstacle is to be able to find a metric that able to detect the presence of the SB effort and to then identify or estimate the level of SB effort exerted by the patient. A suitable method might thus quantify the effort from sudden or unnatural changes in the pressure or flow waveforms, or may require direct measurement of the SB patient's muscular movement, as seen in invasive measurements in the NAVA system (Chiew *et al.*, 2013).

There are some techniques that have been applied to directly measure or attempt to monitor the breathing effort made by

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SB patients. One of the most well-known methods is the balloon-catheter technique used to measure the oesophageal pressure, which is the surrogate of the pleural pressure (P_{pl}) (Khirani *et al.*, 2010; Talmor *et al.,* 2008). However, this technique is not suitable for clinical practise as it requires the balloon to be inserted into the patient and used to interrupt breathing. It is thus a very intrusive measurement and not feasible for regular clinical use despite its potential to accurately measure SB effort and thus potentially optimise and guide MV for SB patients with ARDS (Guérin & Richard, 2012).

Another approach to measure the SB effort is by monitoring the electrical activity of the diaphragm (E_{adi}) of the ventilated patient. This measure captures muscle activity as a surrogate for this SB input. It can thus provide a better monitoring of patient-ventilator synchrony in SB patients (Moorhead *et al*., 2013; Piquilloud *et al.,* 2011). However, there is a potential of tidal volume leak in this, also invasive, measurement that can affect the measurement of the SB effort (Moorhead *et al.,* 2013). In addition, this measurement requires an additional expensive sensor that must be very accurately positioned.

Study by Chiew *et. al* (2015) found that there is a negative elastance occurred when patients were breathing spontaneously eventhough on MV mode. This negative elastance is hypothesised to be due to a positive lung volume intake through the SB effort induced negative pressure in the lung compartment (Chiew *et al*., 2015). Thus, in this paper, a non-invasive model-based method, based on time varying respiratory system elastance, (Chiew *et al*., 2011) is implemented to extend the investigation on the distribution of negative elastance in SB patients from Christchurch Hospital, to quantify its potential level and impact.

2. METHODOLOGY

2.1 Patients Data

In this research, data was obtained from 5 mechanically ventilated patients with respiratory failure in the Intensive Care Unit (ICU) of Christchurch Hospital between April 2014 and November 2014 with respiratory failure (Davidson *et al.,* 2014; Szlavecz *et al.,* 2014). All patients were ventilated using a Puritan Bennet PB840 ventilator (Covidien, Boulder, CO, USA). The airway pressure and flow for each patient were recorded at 50 Hz and analysed using a time-varying elastance model proven on sedated MV patients (Davidson *et al.,* 2014; Szlavecz *et al.,* 2014). The New Zealand South Regional Ethics Committee approved the trial and the use of the data.

In this study, patients were enrolled if they were over the age 16 and were on MV therapy. Patients were only included if they were diagnosed with an ARDS severity defined by a ratio of partial pressure of arterial oxygen to the fraction of inspired oxygen (PF) of less than 300 mmHg (Force 2012). Patients were excluded if they were deemed likely to be discontinued from MV within 24 hours by the attending clinician, were moribund and/or not expected to survive for more than 72 hours. The detailed clinical protocol can be found online in the Australian New Zealand Clinical Trial Registry Website (http://www.anzctr.or.au/). The trial number is ACTRN12613001006730. Table 1 shows the patient demographics.

Table 1. Characteristics of the patients

Patient No.	Gender	Age	Clinical Diagnostic
1	Female	53	Faecal peritonitis
2	Male	71	Cardiac surgery
3	Male	60	Pneumonia
4	Male	36	Pneumonia
5	Male	61	Pneumonia

2.2 Time Varying Elastance Model

Time varying elastance (E_{drs}), as proposed by Chiew et. al (Chiew *et al*., 2011), is an extension of respiratory system elastance (E_{rs}) with the aim of providing a higher resolution metric for use in guiding optimal PEEP selection. It is an in-breath-specific respiratory elastance over an inspiratory time period that can potentially provide further unique insight into patient-specific lung condition and response to MV settings (Carvalho *et al*., 2006; Chiew *et al*., 2011;)

A single compartment lung model is used as a reference in deriving the equation of time varying elastance model.

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

The single compartment lung model in Equation 7.1 consists of resistive and elastic components of the respiratory system for a fully sedated patient (Bates 2009). Respiratory elastance (E_{rs}) is substituted with a time-varying elastance (E_{drs}) that comprises of 3 subcomponents which are the cage elastance (E_{cage}), the demand elastance (E_{demand}) and the lung elastance (E_{lung}) as defined:

$$E_{drs}(t) = E_{cw}(t) + E_{demand}(t) + E_{lung}(t) \quad (2)$$

E_{lung} is a measure of the elastic properties of the lung or the collection of alveoli. E_{lung} decreases if overall alveoli recruitment outweighs the pressure build-up. E_{lung} will increase if the overall alveoli are stretched with lesser or no further recruitment (Chiew *et al.,* 2011). Thus, E_{lung} is the representation of true mechanics that captures the patient-specific response to MV in each breathing cycle and thus provides an indication of the patient disease state. The elastic properties of the chest wall (E_{cw}) is consists of rib cage and the intercostal muscles. This elastance subcomponent can be assumed not vary with disease-state and is thus a patient-specific constant (Chiumello *et al.,* 2008). Finally, E_{demand} represents the patient-specific inspiratory demand, which varies depending on patient-specific and breath-specific effort. This elastance is negative ($E_{demand} < 0$) as it represents the reduced apparent elastance due to the patient's inspiratory effort creating a pressure reduction by opening the lung.

In fully sedated patient, E_{drs} values were always found positive ($E_{drs} > 0$) and had similar elastance to ARDS patients (Carvalho *et al.,* 2008; Chiew *et al.,* 2011; Suarez-Sipmann *et al.,* 2007). However, if the patient exhibits an inspiratory effort, this will result with a negative value of E_{demand} ($E_{demand} < 0$). The negative value of E_{demand} will decrease the overall values of E_{drs} and resulting with variability in overall respiratory elastance. As patient demand aids breathing effort, the effective overall airway pressure is therefore reduced (Damanhuri *et al.,* 2016). In any given breathing cycle, the time-varying E_{drs} of Equation 7.2 captures all three elastance components together.

2.4 Analysis

In this study, the area under the curve (AUC) for the time-varying elastance, E_{drs}, is estimated and analysed in each SB patient. The results are reported as median and interquartile range (IQR) for continuous data with a total of 82 hours. The changes in AUC E_{drs} across all PEEP levels indicate the patient's lung condition.

$$AUC\ E_{drs} = AUC\ E_{drspositive} + AUC\ E_{drsnegative} \qquad (3)$$

3. RESULTS

Figs. 1 and 3 present the distribution of positive and negative AUC E_{drs} for all 5 patients. For the same patients, the 5th, 50th, and 95th percentiles of the negative and positive AUC E_{drs} data are also tabulated in Table 2. Separating the positive and negative values into two plots allows easier quantification at these elastance values. A negative AUC indicates the entire elastance E_{drs} profile was less than 0. This behaviour occurs when as seen in Fig 2. The vast majority have AUC $E_{drs} > 0$ as expected.

Figs. 4 and 5 show the airway pressure and AUC E_{drs} for Patients 1 and 3, where asynchrony events occurred during MV that resulted in a sudden change of AUC E_{drs}.

Table 2. Negative and positive AUC E_{drs} (5th, 25th, 59th, 75th, 95th percentile) for all 5 patients

Patient	Negative AUC E_{drs} ($cmH_2O.s/l$)			Positive AUC E_{drs} ($cmH_2O.s/l$)		
	5th	50th	95th	25th	50th	95th
1	-7.76	-1.65	-0.18	2.51	18.94	31.63
2	-16.81	-2.08	-0.23	2.91	4.67	16.70
3	-11.52	-0.66	-0.03	2.40	14.99	21.15
4	-6.08	-2.27	-0.16	14.87	18.36	21.43
5	-6.02	-0.98	-0.19	14.50	19.73	24.57

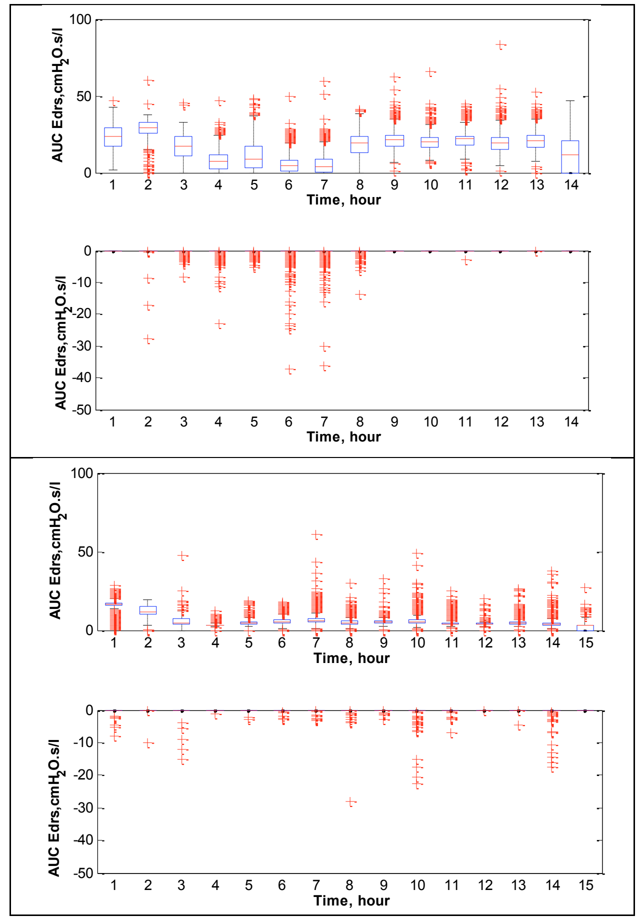

Fig. 1. The distribution of positive (upper) and negative (lower) values of AUC E_{drs} by hour for (***Top***) Patient 1 and (***Bottom***) Patient 2. The positive and negative values are combined for the entire distribution.

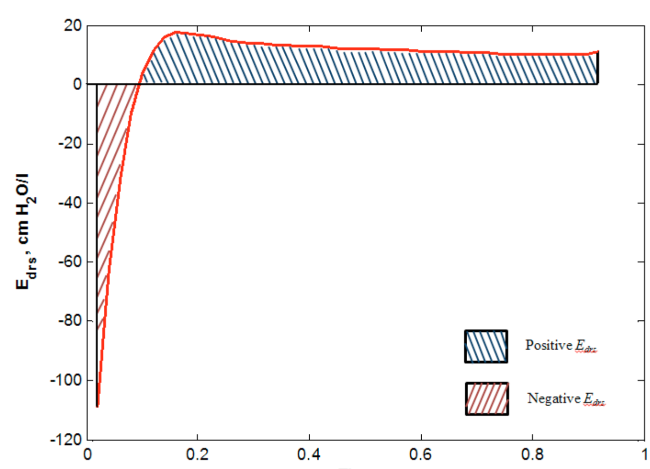

Fig. 2. The E_{drs} for a single breathe for Patient 3 that shows the negative and positive values of *Edrs*.

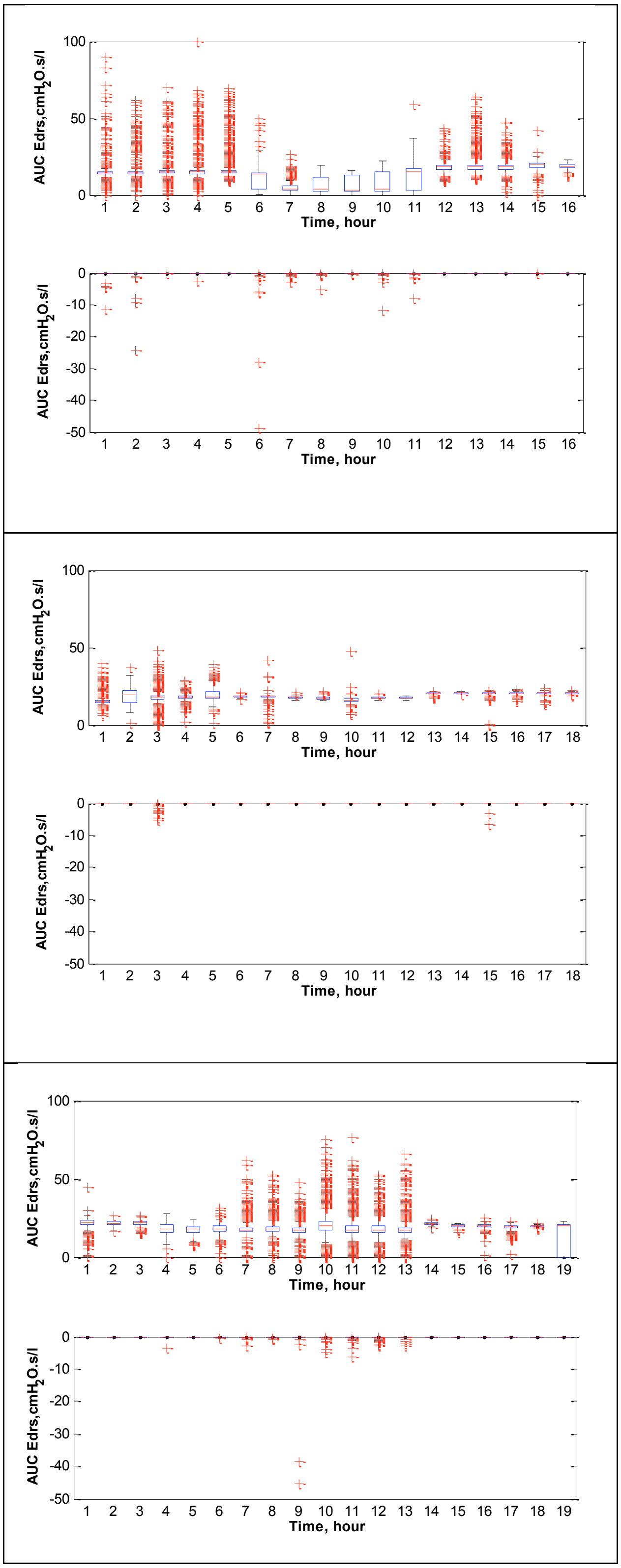

Fig. 3. The distribution of positive (upper) and negative (lower) values of AUC E_{drs} by hour for (*Top*) Patient 3 (*Middle*) Patient 4 and (*Bottom*) Patient 5. The positive and negative values are combined for the entire distribution.

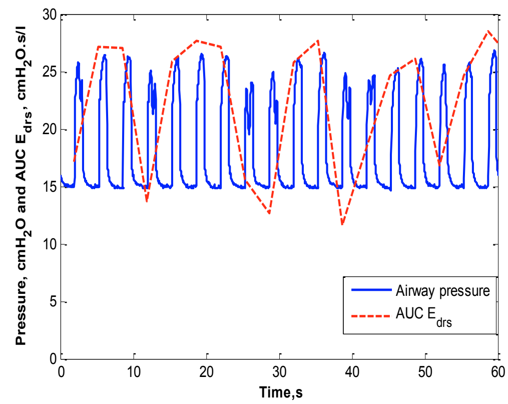

Fig. 4 Airway pressure and AUC E_{drs} plots for Patient 1 containing asynchrony events which resulting with a sudden change of AUC E_{drs} indicating an asynchrony event has occurred

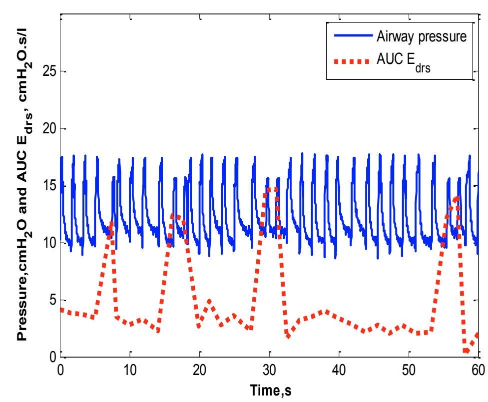

Fig. 5 Airway pressure and AUC E_{drs} plots for Patient 3 containing asynchrony events which resulting with a sudden change of AUC E_{drs} indicating an asynchrony event has occurred.

4. DISCUSSION

In this research, based on the results as shown in Figs. 1 and 3, all 5 patients had some negative AUC E_{drs}. Negative elastance occurs when negative pressure is generated in the patient's pleural space causing air volume to enter the lung. As pleural pressure decreases due to patient's inspiratory demand, the airway pressure or flow changes. More specifically, E_{drs} will be less than zero when patient-breathing demand is high at the beginning of inspiration, and will gradually decrease in magnitude as patient demand decreases during the breath.

A negative AUC E_{drs} occurs when this negative area outweighs the positive area when $E_{drs} < 0$, as seen in Fig. 2. The increasing of negative elastance (AUC $E_{drsnegative}$) leads to a decreasing in overall value of AUC E_{drs} of the lung. The negative elastance value corresponds to bigger patient effort.

From Table 2, it can be seen that the 95th percentile of the positive AUC E_{drs} was above 23 cmH_2O.s/l for Patient 1, although this patient exhibits a negative elastance due to SB efforts. ARDS patients have been shown to have higher respiratory elastance with E_{drs} > 25 cmH_2O/l (The ARDS

Definition Task Force, 2012). These results show that, the proposed AUC E_{drs} metric is able to capture mechanics similar to those observed in ARDS patients when fully sedated in MV, giving confidence of the clinical relevance of the AUC E_{drs} value used here. For the other patients, the 95th percentile of AUC E_{drs} were below than 25 cmH_2O/l, which suggests that the patients in this SB study were more compliant than that of fully sedated ARDS patients lungs, as might be expected for SB patients with less intrusive ventilation (Chiew *et al.,* 2014).

The AUC E_{drs} for SB patient is dependent on the initial pleural pressure or the magnitude of negative $E_{demand.}$ Thus, a lower AUC E_{drs} may indicate that a patient has comparatively higher individual breathing effort than others, and obviously more than a sedated patient. Thus, the AUC E_{drs} metric is able to uniquely capture the information of SB patients without the use of invasive protocols.

Specifically, for Patient 4, the negative AUC E_{drs} occurred only at 3 and 15 hours. The existence of the negative elastance might be due to the ventilator setting of the patient during this time when the ventilation mode was switched to an assisted spontaneous breathing (ASB) mode. As expected, Patients 1 and 3 have the largest distribution of negative AUC E_{drs} values due to the larger number of asynchrony events they experienced as shown in Figs 4 and 5. Asynchrony happens when the patient's breathing effort is not synchronised with mechanical ventilation's breathing support which resulting with a sudden change of AUC E_{drs}. However, it happens more frequently during non-invasive ventilation or partially assisted modes, where the patient is breathing spontaneously and the ventilator support is triggered by patient respiratory effort (Epstein, 2011; Tobin *et al.*, 2001; Vignaux *et al.*, 2009). Thus, the higher distribution of negative elastance in Patients 1 and 3 are due to the SB effort.

This model can thus be generalised over the SB and sedated MV patients based on the E_{drs} value, where negative E_{drs} relates to SB effort and reduced AUC E_{drs} can also indicate SB efforts. Thus, the E_{drs} value and trajectory can be used as a simple, real-time indicator to assess patient-specific disease state and response to MV specifically for SB patients monitoring.

5. CONCLUSIONS

This proposed spontaneous breathing model monitoring is able to capture unique dynamic respiratory mechanics specifically for spontaneously breathing patient without additional measuring equipment or interruption of care. Thus, with this metric, it is able to guide clinicians in setting the optimal mode of the ventilation that meet the patient's demand.

6. CONFLICT OF INTEREST

The authors declared that they have no conflict of interest.

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