Preprints of the 19th World Congress
The International Federation of Automatic Control
Cape Town, South Africa. August 24-29, 2014

Managing Patient-Specific Mechanical Ventilation: Clinical Utilisation of Respiratory Elastance (CURE) – Model and Software Development

Daniel P. Redmond*, Shaun M. Davidson*, Hamish A. Laing*, Richard H. White*, Faizi Radzi*, Yeong Shiong Chiew*, Sarah F. Poole*, Nor Salwa Damanhuri*, Thomas Desaive, Geoffrey M. Shaw, J. Geoffrey Chase*

**Department of Mechanical Engineering, University of Canterbury, Christchurch, New Zealand (e-mail: daniel.redmond@pg.canterbury.ac.nz.com).*
***GIGA Cardiovascular Science, University of Liege, Liege, Belgium (email: tdesaive@ulg.ac.be)*
**** Intensive Care Unit, Christchurch Hospital, Christchurch, New Zealand, (e-mail: geoff.shaw@cdhb.govt.nz)*

Abstract: Mechanical ventilation (MV) is one of the most common, but difficult, costly and variably delivered therapies in intensive care. Model-based estimated patient-specific respiratory elastance can be used to guide clinical staff in selecting positive end-expiratory pressure (PEEP) for MV patients. The Clinical Utilisation of Respiratory Elastance (CURE) trial investigates the potential to optimise PEEP in MV patients. A software system, CURE Soft, capable of providing real-time patient-specific respiratory elastance was developed for the purpose of CURE clinical trial. CURE Soft uses airway pressure and flow data from the ventilator to calculate respiratory elastance using a time-varying elastance model. The CURE Soft graphical user interface (GUI) was developed to provide patient-specific respiratory elastance in real time, history and response during a recruitment manoeuvre both of which offer significant clinical insight. CURE Soft was extensively tested on a mechanical test lung to verify the model-based elastance estimation and its robustness. Model fitting errors are low across a range of ventilation modes, showing it can successfully identify respiratory elastance. Real-time monitoring of respiratory elastance enables new insights into patient-specific lung condition, with no added patient burden. The additional insight available to clinicians will provide the information necessary for improved decision-making and patient outcomes.

1. INTRODUCTION

Patients in the intensive care unit (ICU) often require Mechanical Ventilation (MV) for breathing support. In particular, MV supports patients breathing to reduce their work of breathing and aid their recovery (Mercat et al., 2008, Kallet and Branson, 2007, The Acute Respiratory Distress Syndrome Network, 2000). Positive end-expiratory pressure (PEEP) is one of the important settings during MV, to recruit collapsed lung and maintain oxygenation. However, setting an optimal patient-specific PEEP is a difficult task and there is limited consensus on this issue (Meade et al., 2008, Sundaresan and Chase, 2011).

One method in optimising PEEP that has been suggested is based on minimal respiratory elastance (Chiew et al., 2011, Chiew et al., 2012). Setting PEEP at minimal respiratory elastance has been found in experimental trials to maximise recruitment, improve oxygenation and prevent lung injury (Carvalho et al., 2007, Lambermont et al., 2008, Suarez-Sipmann et al., 2007). However, there are limited clinical studies to investigate the clinical benefit. In particular, one reason is that information on patient respiratory elastance is not readily available at the patient bedside without specific clinical protocol (Lindahl, 1979, Allen et al., 1985). Thus, to provide this information at patient bedside and allow PEEP optimisation, a software system is developed to calculate patient-specific respiratory elastance for each breath in real time.

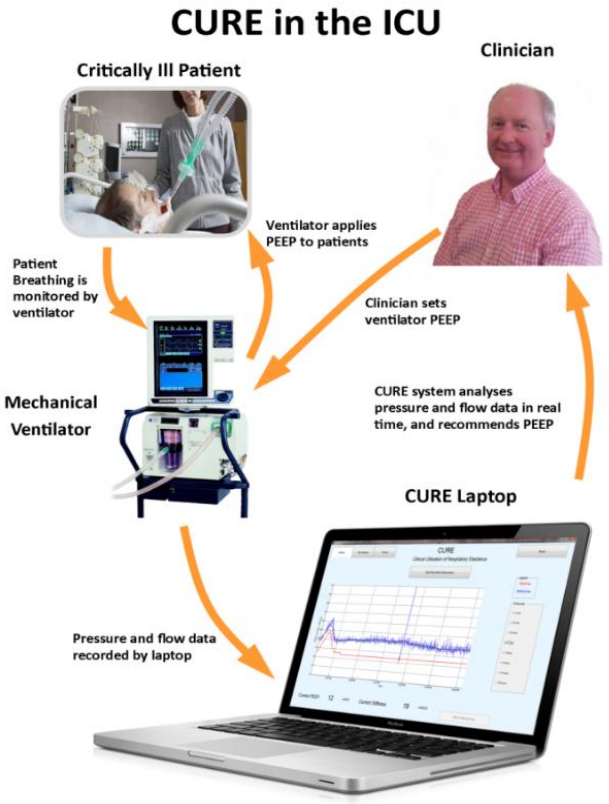

Fig. 1. Flowchart showing CURE Soft implementation in the ICU

A clinical trial, Clinical Utilisation of Respiratory Elastance (CURE), is being carried out to investigate the potential of using respiratory mechanics to optimise PEEP in MV in Christchurch Hospital, New Zealand (Australian New Zealand Trial Registry Number: ACTRN12613001006730). This paper focuses on the development of a software system used for this trial. This system (CURE Soft) is designed to offer additional information about patient-specific respiratory mechanics to aid selecting optimal PEEP. In particular, CURE Soft is a non-invasive software tool that uses readily available patient breath-to-breath airway pressure and flow data to calculate patient-specific respiratory mechanics. A flow chart showing the application of CURE Soft in the ICU is as shown in Fig. 1.

2. SOFTWARE DEVELOPMENT

CURE Soft was developed using Matlab 2013a (MathWorks, Natick, MA), and tested using Puritan Bennett PB840 ventilators (Covidien, Boulder, CO, USA).

2.1. Data Acquisition

Airway pressure and flow data is obtained from the ventilator through the ventilator's Waveforms output function. The RS-232 serial port on the rear of the ventilator display is connected to a laptop through an external USB adapter and a USB cable. A schematic is shown in Fig. 2. A serial data stream design pattern was used to enable simultaneous data acquisition and processing. A serial port object was set up in Matlab with a baud rate of 38400, to match the ventilator output. When the input buffer has 2^{11} bytes available, a callback function is executed. This callback function reads all the available data and stores it in vectors. The data is read line by line and the airway pressure and flow information is stored in vectors. In addition to numerical data, the ventilator also outputs characters "BS" and "BE" to signify breathing start and end respectively. "BS" appears when the ventilator starts to provide breathing support and "BE" appears immediately prior to this point. The index values of the "BS" characters are recorded for breath identification process.

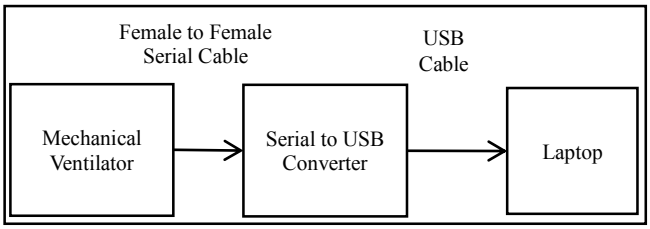

Fig. 2. Schematic of Data acquisition set-up

2.2. Data processing

Patient-specific respiratory elastance is calculated from the single compartment lung model using only the inspiratory portion of breathing (Chiew et al., 2011, van Drunen et al., 2013). Therefore, to enable the automated calculation of real-time elastance, the breathing data must be split into inspiration sections. The occurrence of the "BS" character signifies the beginning of inspiration, and the next occurrence of these characters is the end of expiration. The end of inspiration is determined by searching for the first point where air flow changes from being positive to negative. In addition to identifying the end of inspiration, a volume threshold of 50 mL is used to filter artefacts of the pressure and flow measurements (Moorhead et al., 2013). Flow is integrated over time through the inspiration section to find the index of this threshold volume. If the breath does not satisfy the characteristics of an inspiration and expiration section, and having a sufficiently large tidal volume, it is discarded and not used for elastance calculations.

2.3. Time-varying Elastance Model

CURE Soft uses a time-varying elastance model (van Drunen et al., 2013, Chiew et al., 2011). The inspiratory sections of pressure and flow are used to calculate elastance for each breath.

$$P_{aw}(t) = E_{rs}\,V(t) + R_{rs}\,Q(t) + P0 \tag{1}$$

Eq. (1) defines the single compartment lung model used in the CURE system. P_{aw} is the airway pressure throughout the breath (cmH_2O) , E_{rs} is the respiratory system elastance (cmH_2O/L), V is the volume inspired during the breath (L), R_{rs} is the airway resistance (cmH_2Os/L, Q is the airway flow (L/s), and *P0* is the offset pressure (cmH_2O). *V(t)* is calculated by integrating the flow (*Q(t)*). E_{rs} and R_{rs} can be determined through the integral based method (Chiew et al., 2011).

The time-varying respiratory system elastance is calculated using Eq. (2).

$$E_{drs}(\mathrm{t}) = \frac{P_{aw}(t) - P0 - R_{rs}\,Q(t)}{V(t)} \tag{2}$$

Each breathing cycles' E_{drs} is normalised to its maximum time and the area under the E_{drs} curve is used as the metric of lung elastance in CURE Soft.

2.4. CURE Soft Graphical User Interface

In CURE Soft, the user interface, is designed with 3 different tabs for information display, as shown in Fig. 3. The tabs are 1) History Tab; 2) Recruitment; and 3) Events. A "Reset" button is present in all tabs, for the purpose of stopping the timer, data processing, closes the data acquisition port, clears the figures, and saves all processed and raw data.

2.4.1 History Tab

CURE Soft is initiated using "Start Collecting Data" command in the History Tab as shown in Fig. 3. In this Tab, the horizontal axis of Fig. 3 represents time. The axis can be adjusted from 3 min to 48 hours using the Timescale box to allow Patient elastance monitoring. The red line in the history tab is PEEP (cmH_2O). The blue and black lines are both elastance. Elastance has been labelled as stiffness. This nomenclature is due to the conceptual understanding of the clinical staff who do not have an engineering background. If the label "elastance" is used, clinical staff tend to interpret an increase in elastance as something becoming more elastic and stretchy, when this understanding engineering is contrary to the true meaning of increased elastance. Using the label "stiffness" lessens the misunderstanding. The blue line is elastance measured breath by breath, this has been overlaid with a black line which is a moving average of elastance.

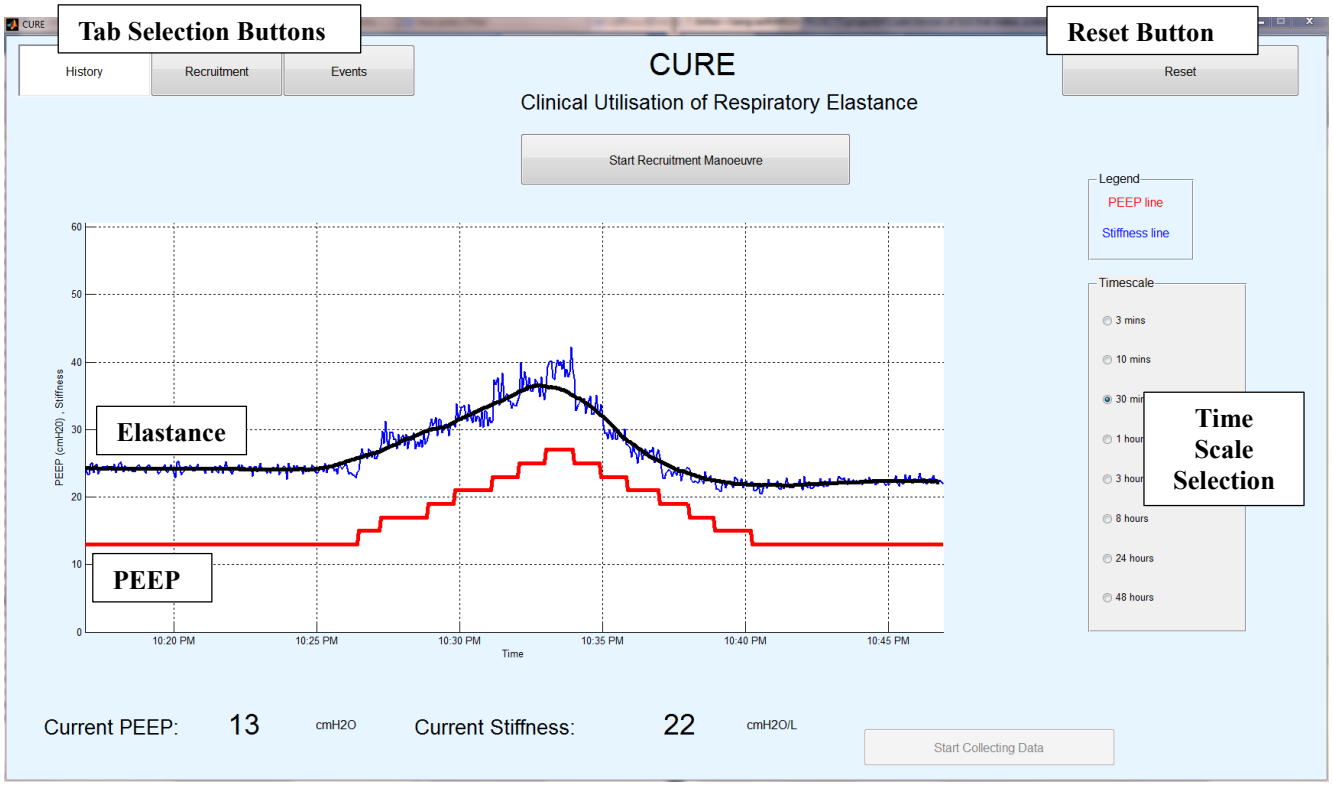

Fig. 3. CURE Soft Graphical user interface: History Tab

2.4.2 Recruitment Tab

The Recruitment Tab shown in Fig. 4 is used when the patient undergoes a recruitment manoeuvre (RM). The recruitment tab provides information on patient-specific respiratory elastance corresponding to PEEP changes during a RM. The horizontal axis is PEEP (cmH_2O) and the vertical axis is elastance (cmH_2O/L). The blue line shows elastance changes with incremental PEEP, and the red line is decremental PEEP. Each point on the curve is an average of the elastance of all the breaths that occur at a single PEEP during the RM.

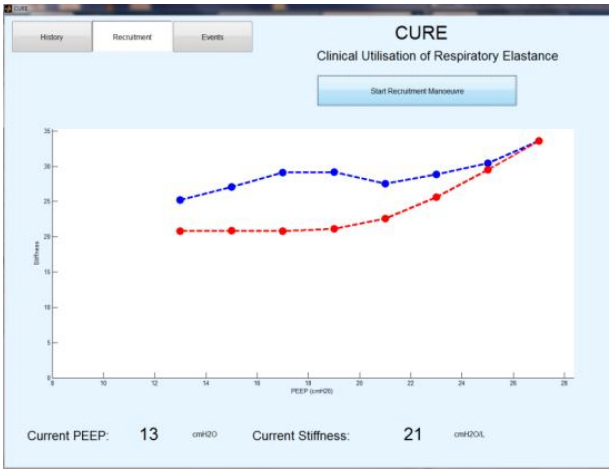

Fig. 4. Recruitment Tab of CURE Soft.

2.4.3 Events Tab

The Events Tab (Fig. 5) records the RM details, or clinical events that may interrupt MV delivery throughout the trial. This Tab features a manual events input that allows the user to store clinical events that occur, such as adjustment of the endotracheal tube, moving the patient or perform airway suctioning.

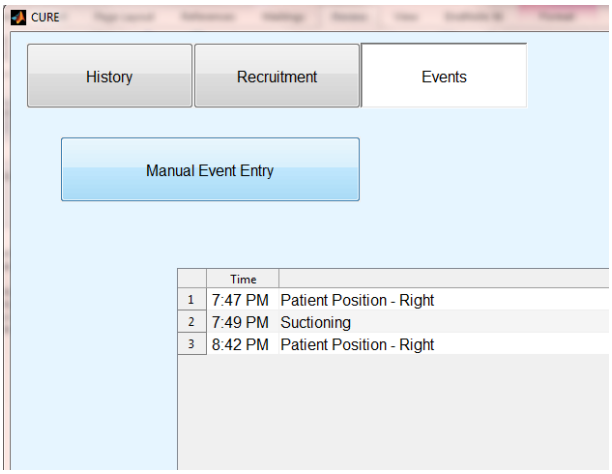

Fig. 5. Events Tab of CURE Soft.

2.5 Simulation and CURE Soft testing

Software development and testing was carried out using a mechanical lung (Michigan Instruments Dual Adult Test Lung) connected to the PB840 ventilator. The software was extensively tested on the mechanical lung to ensure it was robust. MV patients are highly variable breath-to-breath (Kallet et al., 2007). Thus, the airway pressure and flow profile are subject to noise and significant artefacts that are not considered as breathing. To simulate this condition, external disturbances were applied to a mechanical lung in the form of

manual rapid compressions of the mechanical lung bellow, which causes significant pressure and flow mismatch. These disturbances were used to ensure the software can continue operation with non-uniform breathing data, such as can occur with coughing, suctioning or other ventilation asynchronies.

To verify the model-based time varying elastance estimation, a series of test were performed using a mechanical lung. Curve fitting error calculations were made for each breath at a range of ventilator settings and MV modes. The mechanical lung was set to two different elastance levels for the testing (Level 1 = 6 cmH_2O/L and Level 2 = 20 cmH_2O/L). Of note, the mechanical lung uses compliance (C) as a measure of lung stiffness (Elastance = 1/ Compliance). Using these set of elastances, the ventilator was set to three different ventilation modes: Bi-Level, Synchronous Intermittent Mandatory Ventilation Pressure Control (SIMV-PC) and Synchronous Intermittent Mandatory Ventilation Volume Control (SIMV-VC). The two pressure control modes (SIMV-PC and Bi-Level) were tested at a range of different high and low pressures, while the volume control mode (SIMV-VC) was tested with both square and ramp flow profiles, with two PEEP levels, and two different tidal volumes. At each of these settings approximately 30 breaths were recorded and processed through CURE Soft.

3. RESULTS

Tables 1 and 2 showed the ventilator settings during the mechanical lung testing and the model fitting error to the airway pressure curve. The model fitting errors are presented as absolute percentage error (median and Interquartile Range (IQR)). The median elastance measured at elastance Level 1 (Table 1) is 6.44 cmH_2O/L (IQR: 5.60-8.38). The median elastance at elastance Level 2 (Table 2) is 22.22 cmH_2O/L (IQR: 21.82-24.98). Tables 1 and 2 show the median curve fitting errors are generally lower in pressure control modes (Bi-Level and SIMV pressure control), which is likely due to changes in shapes of the pressure and flow curve profile, that make the parameter identification more susceptible to noise. In general curve fitting errors are low, and elastance can be estimated accurately with low model fitting error.

Table 1. Model fitting error for Elastance Level 1 (6 cmH_2O/L)

Ventilator Settings					Curve fitting error for each breath	
Mode	**PEEP (cmH_2O)**	**PIP* (cmH_2O)**	**Vt* (mL)**	**Flow profile**	**Median [IQR]**	**No. of Breathing Cycle**
Bi-Level	10	15	-	-	0.44 [0.40 – 0.49]	38
Bi-Level	10	20	-	-	0.47 [0.44 – 0.51]	38
Bi-Level	15	20	-	-	0.35 [0.31 – 0.38]	26
SIMV PC	10	20	-	-	0.47 [0.45 – 0.51]	31
SIMV-PC	15	25	-	-	0.38 [0.34 – 0.40]	29
SIMV-PC	20	30	-	-	0.31 [0.29 – 0.34]	27
SIMV-VC	10	-	300	Ramp	1.85 [1.70 – 1.93]	35
SIMV-VC	10	-	300	Square	2.33 [2.22 – 2.42]	22
SIMV-VC	10	-	600	Ramp	1.30 [1.24 – 1.36]	33
SIMV-VC	10	-	600	Square	0.95 [0.65 – 1.08]	26
SIMV-VC	20	-	300	Ramp	1.06 [0.99 – 1.10]	23
SIMV-VC	20	-	300	Square	1.49 [0.72 – 1.85]	35
SIMV-VC	20	-	600	Ramp	0.83 [0.79 – 0.87]	28
SIMV-VC	20	-	600	Square	0.27 [0.22 – 0.36]	29

***PIP –** Peak inspiratory pressure; Vt – Tidal Volume

Table 2. Model fitting error for Elastance Level 2 (20 cmH_2O/L)

Ventilator Settings					Curve fitting error for each breath	
Mode	**PEEP (cmH_2O)**	**PIP (cmH_2O)**	**Vt (mL)**	**Flow profile**	**Median [IQR]**	**No. of Breathing Cycle**
Bi-Level	10	15	-	-	0.70 [0.62 – 0.73]	23
Bi-Level	10	20	-	-	1.01 [0.93 – 1.22]	22
Bi-Level	15	20	-	-	0.48 [0.43 – 0.54]	24
SIMV-PC	10	25	-	-	1.65 [1.38 – 1.78]	24
SIMV-PC	15	30	-	-	1.27 [1.09 – 1.49]	21
SIMV-PC	20	35	-	-	1.13 [0.97 – 1.29]	22
SIMV VC	10	-	300	Ramp	1.13 [1.05 – 1.31]	27
SIMV VC	10	-	300	Square	4.34 [3.83 – 4.56]	22
SIMV VC	10	-	600	Square	0.67 [0.47 – 0.83]	26
SIMV VC	20	-	300	Ramp	0.83 [0.75 – 0.92]	25
SIMV VC	20	-	300	Square	1.33 [1.21 – 1.46]	25
SIMV VC	20	-	600	Ramp	0.60 [0.57 – 0.68]	27
SIMV VC	20	-	600	Square	0.44 [0.32 – 0.51]	21

Fig. 6 shows an example of the processing and filtering carried out on one breath. The pressure curve shows the pressure calculated from the identified parameters (E_{rs} and R_{rs}), and the pressure measured from the ventilator. There is good agreement between the calculated and measured pressures, indicating the time–varying elastance model can successfully capture the respiratory dynamics. The performance of the breath identification algorithms is shown on the flow profile. The square shows where the start of inspiration is detected, the circle is the volume threshold point, and the diamond is the end of inspiration. Fig. 6 also shows the E_{drs} trajectory for this breath, and the calculation of the area under the E_{drs} curve, which is used as the metric for lung elastance in CURE Soft.

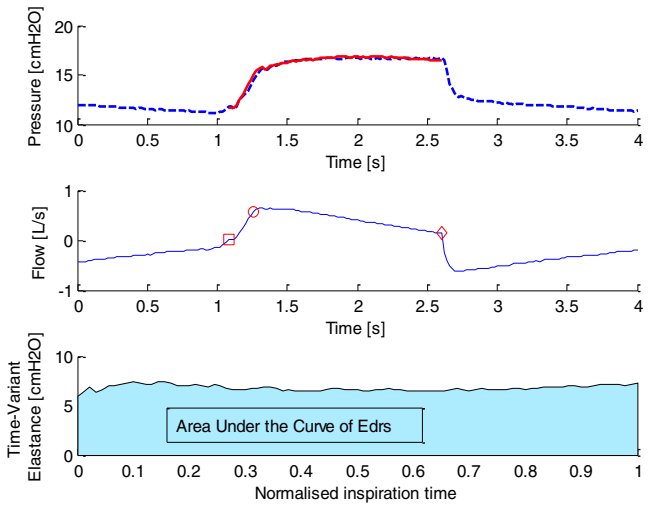

Fig. 6. Top graph shows pressure during a breathing cycle, the solid red line is the pressure calculated according to Equation 1. The middle graph shows flow during a breath, the symbols represent the identified inspiration start, threshold and end points. The bottom graph shows E_{drs} varying through the inspiration, and the calculation of are under the curve of E_{drs}.

4. DISCUSSION

CURE Soft successfully identifies respiratory elastance in real-time as evidenced by the low curve fitting error when testing on a mechanical lung. True respiratory system elastance can be determined from breathing data.

Calculations of respiratory elastance were previously only available by performing an inspiratory pause (Barberis et al., 2003) or specific clinical protocols (Albaiceta et al., 2003, Allen et al., 1985). The existing methods of respiratory elastance monitoring are invasive or require additional monitoring equipment, which makes clinical application difficult. In comparison to CURE Soft the model based approach using readily available airway pressure and flow profile adds no additional burden to patients and provides more information than was previously available.

CURE Soft can work on any mode of ventilation, with any settings, as only pressure and flow waveforms are required. CURE Soft. uses multiple linear regression rather than a two point pressure/volume calculation, this provides advantages in the accuracy of the calculation. This provides advantages in the accuracy of the calculation.

Clinically, the CURE system allows continuous tracking of patient disease state across time. Information about changing patient condition over time is very useful to clinical staff, as they can use more information to evaluate the efficacy of previous treatments.

CURE Soft also provides real-time feedback on the effect of a RM, and allows clinical staff to determine whether a patient is recruitable or not, and what PEEP level is optimal for that particular patient at that time. Monitoring elastance continuously can also provide information about patient-ventilator interactions and how the patients breathing synchronises with the ventilators breathing support. Monitoring patient-ventilator interactions can provide suggestions to clinical staff as to whether they need to modify the ventilator settings or the amount of sedation.

The history and recruitment tabs of CURE Soft are easy to use, and provide quick information to clinical staff about how the patients' lung condition is changing over time, or during a recruitment manoeuvre.

CURE Soft was developed specifically to enable a clinical proof of concept trial, the CURE trial, to run. The CURE trial is testing using real-time model-based respiratory elastance to provide clinical decision making support to optimise PEEP selections. Hence, it is a unique and new capability.

5. LIMITATIONS

There are some limitations on CURE Soft in its present form. Like any new software, errors may occur, and CURE Soft has not yet had sufficient testing on real patients to identify or fine-tuned all of these. Extensive testing has occurred with a mechanical lung, but real patients have significant differences and this testing is not yet complete. As more patients are recruited, the software robustness can be demonstrated and improved.

CURE Soft was developed in Matlab, which is not the ideal platform, but was adequate for the development phase. In future, CURE Soft could be rewritten in a more suitable programming language and run on a tablet, rather than a laptop, or other more user friendly device, incorporating added features like a touch screen.

In the future, further use of CURE Soft will mean there is more feedback from users that can be incorporated into future versions to improve usability, and the display of information. In addition, as more data is collected and analysed from the clinical trial, better methods of optimum PEEP selection can be incorporated.

6. CONCLUSIONS

CURE Soft enables the calculation in real-time of model-based respiratory elastance for patients undergoing mechanical ventilation. The use of CURE Soft in clinical trials enables new insights into patient-specific lung condition, with no added patient burden, that were not previously available. The additional insight available to clinicians will provide the potential for improved decision-making and improved patient outcomes.

7. CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

REFERENCES

Albaiceta, G. M., Piacentini, E., Villagrã¡, A., Lopez-Aguilar, J., Taboada, F. and Blanch, L. (2003). Application of continuous positive airway pressure to trace static pressure-volume curves of the respiratory system. *Crit Care Med,* volume 31**,** 2514-2519.

Allen, J. L., Frantz, I. D. and Fredberg, J. J. (1985). Regional alveolar pressure during periodic flow. Dual manifestations of gas inertia. *The Journal of Clinical Investigation,* volume 76**,** 620-629.

Barberis, L., Manno, E. and Guérin, C. (2003). Effect of end-inspiratory pause duration on plateau pressure in mechanically ventilated patients. *Intensive Care Medicine,* volume 29**,** 130-134.

Carvalho, A., Jandre, F., Pino, A., Bozza, F., Salluh, J., Rodrigues, R., Ascoli, F. and Giannella-Neto, A. (2007). Positive end-expiratory pressure at minimal respiratory elastance represents the best compromise between mechanical stress and lung aeration in oleic acid induced lung injury. *Critical Care,* volume 11**,** R86.

Chiew, Y. S., Chase, J. G., Shaw, G., Sundaresan, A. and Desaive, T. (2011). Model-based PEEP Optimisation in Mechanical Ventilation. *BioMedical Engineering OnLine,* volume 10**,** 111.

Chiew, Y. S., Chase, J. G., Shaw, G. M. and Desaive, T. (2012). Respiratory system elastance monitoring during PEEP titration. *Critical Care,* volume 16**,** P103.

Kallet, R. H. and Branson, R. D. (2007). Do the NIH ARDS Clinical Trials Network PEEP/FIO2 Tables Provide the Best Evidence-Based Guide to Balancing PEEP and FIO2 Settings in Adults? *Respiratory Care,* volume 52**,** 461-477.

Kallet, R. H., Hemphill, J. C., Dicker, R. A., Alonso, J. A., Campbell, A. R., Mackersie, R. C. and Katz, J. A. (2007). The Spontaneous Breathing Pattern and Work of Breathing of Patients With Acute Respiratory Distress Syndrome and Acute Lung Injury. *Respiratory Care,* volume 52**,** 989-995.

Lambermont, B., Ghuysen, A., Janssen, N., Morimont, P., Hartstein, G., Gerard, P. and D'orio, V. (2008). Comparison of functional residual capacity and static compliance of the respiratory system during a positive end-expiratory pressure (PEEP) ramp procedure in an experimental model of acute respiratory distress syndrome. *Critical Care,* volume 12**,** R91.

Lindahl, S. (1979). Influence of an end inspiratory pause on pulmonary ventilation, gas distribution, and lung perfusion during artificial ventilation. *Critical Care Medicine,* volume 7(12)**,** 540-546.

Meade, M. O., Cook, D. J., Guyatt, G. H., Slutsky, A. S., Arabi, Y. M., Cooper, D. J., Davies, A. R., Hand, L. E., Zhou, Q., Thabane, L., Austin, P., Lapinsky, S., Baxter, A., Russell, J., Skrobik, Y., Ronco, J. J., Stewart, T. E. and For the Lung Open Ventilation Study, I. (2008). Ventilation Strategy Using Low Tidal Volumes, Recruitment Maneuvers, and High Positive End-Expiratory Pressure for Acute Lung Injury and Acute Respiratory Distress Syndrome: A Randomized Controlled Trial. *JAMA,* volume 299**,** 637-645.

Mercat, A., Richard, J.-C. M., Vielle, B., Jaber, S., Osman, D., Diehl, J.-L., Lefrant, J.-Y., Prat, G., Richecoeur, J., Nieszkowska, A., Gervais, C., Baudot, J., Bouadma, L., Brochard, L. and For the Expiratory Pressure Study, G. (2008). Positive End-Expiratory Pressure Setting in Adults With Acute Lung Injury and Acute Respiratory Distress Syndrome: A Randomized Controlled Trial. *JAMA,* volume 299**,** 646-655.

Moorhead, K., Piquilloud, L., Lambermont, B., Roeseler, J., Chiew, Y., Chase, J. G., Revelly, J.-P., Bialais, E., Tassaux, D., Laterre, P.-F., Jolliet, P., Sottiaux, T. and Desaive, T. (2013). NAVA enhances tidal volume and diaphragmatic electro-myographic activity matching: a Range90 analysis of supply and demand. *Journal of Clinical Monitoring and Computing,* volume 27**,** 61-70.

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

Sundaresan, A. and Chase, J. G. (2011). Positive end expiratory pressure in patients with acute respiratory distress syndrome - The past, present and future. *Biomedical Signal Processing and Control,* volume 7**,** 93-103.

The Acute Respiratory Distress Syndrome Network (2000). Ventilation with Lower Tidal Volumes as Compared with Traditional Tidal Volumes for Acute Lung Injury and the Acute Respiratory Distress Syndrome. *N Engl J Med,* volume 342**,** 1301-1308.

Van Drunen, E., Chiew, Y., Zhao, Z., Lambermont, B., Janssen, N., Pretty, C., Desaive, T., Moeller, K. and Chase, J. (2013). Visualisation of Time-Variant Respiratory System Elastance in ARDS Models. *Biomedical Engineering/Biomedizinische Technik,* volume.