Automated Logging of Inspiratory and Expiratory Non-Synchronized Breathing (ALIEN) for Mechanical Ventilation*

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Abstract—**Asynchronous Events (AEs) during mechanical ventilation (MV) result in increased work of breathing and potential poor patient outcomes. Thus, it is important to automate AE detection. In this study, an AE detection method, Automated Logging of Inspiratory and Expiratory Non-synchronized breathing (ALIEN) was developed and compared between standard manual detection in 11 MV patients. A total of 5701 breaths were analyzed (median [IQR]: 500 [469-573] per patient). The Asynchrony Index (AI) was 51% [28-78]%. The AE detection yielded sensitivity of 90.3% and specificity of 88.3%. Automated AE detection methods can potentially provide clinicians with real-time information on patient-ventilator interaction.**

I. Introduction

Asynchronous events (AEs) occur when a patient's breathing on mechanical ventilation (MV) is not synchronized with ventilator support. Frequent occurrence of AEs result in poor patient-ventilator interaction, leading to an increase in work-of-breathing and potentially other adverse effects [1, 2]. These adverse effects include patient discomfort, increased need for sedation, increased length of MV, and higher mortality [3]. Thus, AE detection in real-time may be useful as a clinical marker for assessment of patient-ventilator interaction, and used as an indication for the need to modify ventilation settings, or adjust sedation level for better patient-ventilator interaction [4, 5].

AEs can occur anytime during partially- or fully-controlled ventilation. However, it is more frequent during partially assisted modes where the patient is breathing spontaneously and the ventilator support is triggered by patient respiratory effort [3, 6]. Currently, patient-ventilator interaction is assessed using the Asynchrony Index (AI), a measure of the AEs as a percentage of the total number of breaths (AI = 100% × Number of AE/ total breaths) [6]. However, this metric is normally calculated retrospectively where clinicians detect AEs by manually inspecting patient airway pressure and flow waveforms [2, 3, 6]. This process is onerous and not practical for assessing patient-ventilator interaction in real-time.

Several studies have investigated methods to automate AE detection. Gutierrez et al. [7] used spectral analysis of the airway flow waveform, but this method focused only on the airway flow and not the pressure changes, neglecting the mismatching of pressure and flow that defines an AE [8]. Sinderby et al. [9] investigated ventilation asynchrony using electrical diaphragmatic signals (Eadi). This method has shown promising results to detect and minimize AEs, but it requires the Eadi signal and thus added invasive sensors and cost. Blanch et al. [10] reported a system that detects Ineffective Efforts (IEs) with high specificity and sensitivity. However, IEs make up only a small portion of all AEs [10] and only expiration was considered in this study. Cuvelier et al. [11] showed that correlating flow and pressure waveforms has the potential to identify IEs at both inspiration and expiration. However, it was only verified on a very small sample with 56 asynchronous breaths. More testing needs to be conducted to verify the findings. Thus, there is a need for robust, real-time AE detection method without additional invasive measuring tools. In addition, it should be efficient, consistent, and objective compared to manual detection.

This research presents a method to automate AE detection and AI estimation. This method is known as the Automated Logging of Inspiratory and Expiratory Non-synchronized breathing (ALIEN). ALIEN monitors the shape of the patient's airway pressure and flow waveform, with independent algorithms to classify AEs during inspiration and expiration. ALIEN was developed using retrospective airway pressure and flow data from MV patients. The ALIEN method was compared with conventional manual inspection to assess its performance.

II. Methods

A. Patients and Ventilator Settings

Retrospective data from 11 MV patients admitted to the Christchurch Hospital, Intensive Care Unit (ICU) were used in this study. Patients were ventilated using Puritan Bennett 840 ventilators (Covidien, Boulder, CO, USA) with different ventilation modes as determined by attending clinicians. Ventilation modes included: 1) Bi-Level pressure ventilation (BL); 2) Synchronized Intermittent Mandatory Ventilation (SIMV); and 3) Assisted Spontaneous Breathing (ASB). For each patient, 30 minutes of pressure and flow data were analyzed. The use and publication of the data was approved by the New Zealand Upper South Regional Ethics Committee.

*Research is supported by New Zealand Health Research Council.

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B. Automated Asynchrony Event Detection

ALIEN uses a combination of methods to detect asynchronous breathing using the observed airway pressure and flow data. An algorithm-based method detects anomalous deflections in the flow and pressure waveforms compared to typical waveforms. The statistical method detects deviations of breath-specific parameters from a patient-specific model. Inspiratory AE detection relies on an algorithm-based method, while expiratory AE detection combines the algorithmic and statistical methods. Results were collated to calculate overall per-patient AI values.

C. Inspiratory Asynchrony Event Detection

An algorithm is used to detect AEs via gradient sign changes in airway pressure and flow waveforms. For each breath, the pressure and flow are segmented based on the sign of their gradient, showing whether the waveform is increasing or decreasing. In a synchronized breath, there are typically two breath segments during inspiration, consisting of a sharp initial increase in flow and pressure, followed by a steady decrease as shown in Fig. 1(a) 1st breath. A breath with more than 2 segments in either pressure or flow is labelled as an AE (Fig. 1(a) Breaths 2 and 3). Fig 1(b) shows a graphical representation of the gradient-based segmentation method.

a)

b)

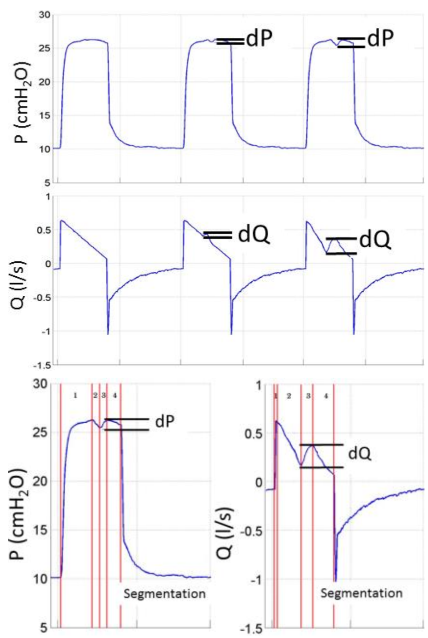


Figure 1. (a) Top is the airway pressure, *P* and bottom is the airway flow, *Q*. The 1st breath from the left is synchronized breath but 2nd and 3rd are asynchronous, (b) Gradient-based segmentation method.

To reduce the effect of noise, segments are discarded if their net change in flow (dQ) or pressure (dP) is less than a corresponding breath-specific threshold. For deflections in flow, the threshold is proportional to the maximum inspiratory flow ($Q_{max,insp}$) in the breath cycle being evaluated. For deflections in pressure, the threshold is proportional to the difference between the maximum inspiratory pressure and the Positive End-Expiratory Pressure (PEEP) ($P_{max,insp}$ – PEEP). The resulting inspiratory flow and pressure proportionality fractions, $K_{Q,insp}$ and $K_{p,insp}$, were optimized using Receiver Operator Characteristic (ROC) analysis. Equations (1) and (2) define the conditions for classifying asynchrony:

$$|\,dQ\,| \geq K_{Q,insp}\; Q_{max,insp}(n) \qquad (1)$$

$$|\,dP\,| \geq K_{P,insp}\; (P_{max,insp}(n) - PEEP(n)) \qquad (2)$$

where n is the breath number. If a dQ or dP value within a breath satisfies either Equation (1) or (2), it is considered as a segment. A breath is labelled as an AE, if it consists of more than 2 segments. This method detects double triggering, auto triggering, delayed cycling at inspiration, periodic breathing, and other types of variance and discontinuity, which all are classified as AEs [3].

D. Expiratory Asynchrony Event Detection

During expiration, AEs are detected through a combination of algorithmic and statistical methods. As for inspiration, an algorithm detects AEs via unexpected gradient sign changes in the flow waveform (dQ) as defined by Equation (3), with $K_{Q,exp}$ optimized using ROC. An expiratory AE is defined when a breath consists of more than 2 segments, as calculated using Equation (3).

$$|\,dQ\,| \geq K_{Q,exp}\; Q_{max,exp}(n) \qquad (3)$$

In addition, an exponential model is fitted to the expiratory flow waveform and 2 metrics associated with this curve fit are used to classify AE. The metrics are i) the exponential decay time-constant, τ, and ii) the area between the model fit curve and the actual expiratory flow, A_{Diff} as shown in Fig. 2.

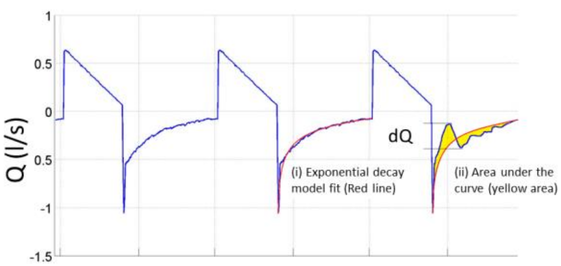


Figure 2. Expiratory AE detection criteria, i) Exponential decay model fit (τ) and ii) difference in area under the curve (A_{Diff}).

For an asynchronous breath, one or both of these metrics (τ or A_{Diff}) will deviate significantly from those obtained for a synchronous breath [8]. To calculate the breath-specific exponential τ and A_{Diff}, a single compartment lung model was used [12]:

$$P(t) = E_{rs}\textstyle\int Q(t) + R_{rs}Q(t) + P_0 \qquad (4)$$

where P is the airway pressure, t is time, E_{rs} is the respiratory system elastance, $\int Q(t)$ is the air leaving the lung, R_{rs} is the respiratory system resistance, $Q(t)$ is the airway flow and P_0 is the offset pressure. During expiration phase, P is approximately equal to the P_0 yielding:

$$E_{rs}\textstyle\int Q(t) + R_{rs}Q(t) = 0 \qquad (5)$$

Solving differential equation for $Q(t)$ yielded:

$$Q(t) = Q_0 e \wedge (-\tau/t) \qquad (6)$$

where Q_0 is the initial flow, $\tau = R_{rs}/E_{rs}$, is the time constant.

For each breath, τ and A_{Diff} are calculated and compared with the median (*med*) of that metric calculated over 500 breaths. If either metric deviates significantly from its median, the breath is labelled as an AE. A significant deviation is defined with a proportional term ($K_{\tau,exp}$ for τ, and $K_{A,exp}$ for A_{Diff}) that were optimized using ROC. Thus, a breath is also labelled as an AE if it satisfy any of Equations (7) or (8).

For the metric τ, an expiratory breath is asynchronous if

$$\tau(n) > med(\tau) + K_{\tau,exp} med(\tau) \quad \text{or}$$
$$\tau(n) < med(\tau) - K_{\tau,exp} med(\tau) \quad (7)$$

For the metric A_{Diff}, an expiratory breath is asynchronous if

$$A_{Diff}(n) > med(A_{Diff}) + K_{A,exp} med(A_{Diff}) \quad \text{or}$$
$$A_{Diff}(n) < med(A_{Diff}) - K_{A,exp} med(A_{Diff}) \quad (8)$$

E. Manual Asynchrony Event Detection

To validate the automated AE detection methods, comparisons were made with manually identified AEs. Researchers were guided by clinicians in the classification of synchronous and non-synchronous breaths. For each breath, researchers manually logged AEs, separating inspiratory and expiratory AEs. Exactly 30 minutes of data were manually classified for each patient, providing a total of 5701 classified breaths over the 11 patients.

III. Results

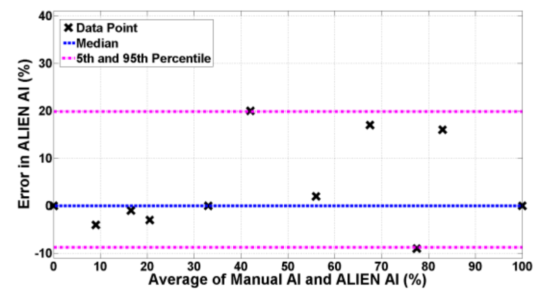
ALIEN inspiratory detection had sensitivity = 90.7% and specificity = 94.8%, measured across all 5701 breaths. ALIEN expiratory detection had sensitivity = 77.0% and specificity = 77.7%. Combining both inspiratory and expiratory detection, the ALIEN algorithm yielded a total sensitivity = 91.2% and a total specificity = 81.7%. Table I shows a summary of the optimal AE detection proportional constants selected by ROC analysis. The summary of AI and AE detection for all 11 patients is shown in Table II.

TABLE I. Summary of AE Detection Proportion Constant

	Proportional Constant	Optimal Value
Inspiratory	$K_{Q,insp}$	0.0012
	$K_{P,insp}$	0.0009
Expiratory	$K_{Q,exp}$	0.0022
	$K_{\tau,exp}$	0.8
	$K_{A,exp}$	1.0

Fig. 3 shows the agreement between AI determined using ALIEN and manual methods during inspiration (Fig. 3(a)) and expiration (Fig. 3(b)). There is no significant bias in Fig. 3(a), indicating that the ALIEN method does not tend to over- or under- estimate AI during inspiration. Fig. 3(b) shows equivalent data for expiration. The expiratory results are not as reliable as during inspiration, with a positive bias of 0.12, indicating that ALIEN tends to overestimate AI compared to manual detection during expiration.

a)



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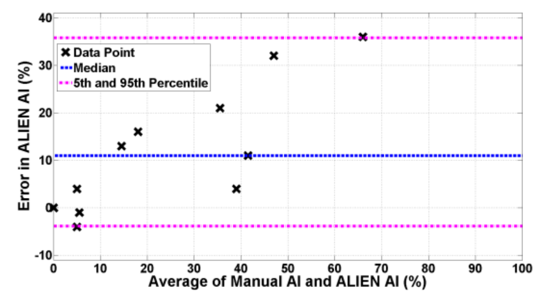

Figure 3. Bland-Altman plot for manual AI versus ALIEN AI calculation. (a) Inspiratory phase, (b) expiratory phase.

IV. Discussion

Studies on AE detection to date have mostly been carried out through manual visual inspection of airway pressure and flow waveforms by clinicians. However, this method is manual, onerous, and cannot provide real time information in guiding better patient-ventilator interaction. Furthermore, Columbo et al. [14] showed that manual AE identification via inspection of waveforms is inherently limited and error-prone, whether carried out by first-year ICU residents or expert senior intensive care physicians [13]. Thus, it is clear that there is a need of an automated method that can quantify these AEs in a consistent fashion.

TABLE II. The Summary of ALIEN AE detection

Patient Number	Ventilation Mode	Breaths	Number of AE (Manual)	Number of AE (ALIEN)	Manual AI (%)	ALIEN AI (%)	ALIEN Sensitivity (%)	ALIEN Specificity (%)
1	BL	613	211	385	34	63	92.4	52.7
2	SIMV	533	115	112	22	21	72.2	93.1
3	ASB	264	93	97	35	37	88.2	91.2
4	BL	468	316	342	68	73	94.0	70.4
5	SIMV	478	1	1	0	0	-	99.8
6	BL	750	616	566	82	75	89.1	87.3
7	SIMV	469	69	131	15	28	78.3	80.8
8	ASB	446	341	424	76	95	95.0	4.8
9	SIMV	523	267	289	51	55	83.1	73.8
10	SIMV	657	657	656	100	100	99.8	100.0
11	BL	500	402	488	80	98	99.5	10.2

As shown in Fig. 3, ALIEN is able to detect inspiratory AI with a high degree of accuracy, but it consistently over-estimates expiratory AI. However, automated expiratory AI detection is still strongly correlated with manually detected AI, and the bias towards overestimation could be eliminated via post-processing. The ALIEN inspiratory algorithm only provides accurate inspiratory detection, defined by both high sensitivity and high specificity, under pressure controlled or pressure support ventilation. In these modes, both airway pressure and flow waveform can be used for AE detection. Comparatively, during volume controlled mode, the flow-based inspiratory AE detection is less reliable. Hence, inspiratory volume controlled detection is forced to rely only on the pressure waveform to detect asynchrony, and is less accurate due to the decrease in available information. Expiratory detection can be used in all modes, but has an overall lower sensitivity and specificity. Both pressure and flow also exhibit much greater variability in the expiratory portion of their waveforms compared to the inspiratory portion, making it more difficult to clearly detect asynchrony. Advanced signal filtering could be one possible solution to this issue.

The subjectivity and potential for error in manual detection during accuracy assessment must be noted [13]. Such error can be large and, depending on definitions used or operator error, a large number of AEs may not be classified. In particular, all breaths have some variability. Thus, the objective methods presented here may be a better standard than the limited "gold standard" of manual detection. This lack of a true, objective gold standard makes assessment and validation of the methods difficult [14]. In defense of the methods presented, approximately half of the patients have very similar identified AE levels. In addition, Patient 5 has only 1 asynchrony in 478 breaths, a null or zero test case. Hence, the methods presented and their results may, in fact, be a more true representation of patient response, and should be validated against clinical outcomes.

The ALIEN algorithm was able to capture AE, but does not capture the magnitude or effect of each AE. Thus, further research is warranted to investigate methods for quantifying the magnitude of AEs. The ALIEN AE expiratory detection also warrants further investigation to improve its overall sensitivity and specificity. Finally, the method does enable clinical studies that could link size or severity of AEs or AI to clinical outcomes and to better refine the clinical use of these metrics.

V. Conclusion

The proposed ALIEN algorithm, combining inspiratory and expiratory AE classifiers can be used as a method to measure AI for mechanically ventilated patients. Monitoring the AI trends over time could provide a clinical marker to assess patient-specific patient-ventilator interaction at different ventilation settings, ensuring that the ventilator settings can be optimized for the patient. Furthermore, ALIEN's ability to automate asynchrony logging could enable investigation of the impact of patient-ventilator asynchrony on patient condition.

Acknowledgment

The authors would like to thank the New Zealand Health Research Council and the EU-Sponsorship - "eTime" - ID: "FP7-PEOPLE-2012-IRSES" for supporting the research. We would also like to thank Mr. Bastien Andreu (bastien.andreu@enise.fr) from Ecole Nationale d'Ingénieurs de Saint Etienne (ENISE) for his work in manual asynchrony detection.

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