**Online Supplemental Material 1 – Respiratory Parameters**

During the development phase of the project an algorithm was created. The algorithm was developed to estimate the perceived patient-ventilator asynchrony and the suggested need for clinical intervention as a trained clinician. Based on previous experience with leak flow during NIV[1] we did not attempt to measure patient-ventilator asynchrony as is commonly done with the Asynchrony Index[2]. Our hypothesis was to determine if the effects of patient-ventilator asynchrony can be recognized in patient airway pressure and flow waveforms. With frequent interaction between clinical scientists, engineers, and clinicians it became apparent that to detect the effects of patient-ventilator asynchrony new parameters to explore this relationship needed to be developed. Listed here in this online supplemental material (table 1) are the tested parameters.

During development of the Breathing Variability Detection Tool process we desired to understand the relationship between the expert panel’s collective asynchrony scores and each respiratory parameter. To evaluate this relationship, linear regression was performed between the expert panel’s asynchrony scores and each respiratory parameter. All parameter calculations were done on data segments spanning 45 seconds of waveform and breath data. The correlation coefficient for each parameter is included in table 1. For comparative purposes the respiratory parameters are organized by correlation coefficient in table 2.

Discussion on Online Supplement Material 1 Results

 The respiratory parameters were divided into three groups based on their correlation coefficient with the expert panel’s asynchrony scores [<0.3, 0.3-0.6, >0.6]. This comparison is an indirect evaluation on which parameter is closest to the expert panel’s interpretation of asynchrony. The respiratory parameters which measured variability of breathing had higher correlation coefficients while the parameters which measured averages had low correlation coefficients. We interpret this result to imply that patient ventilator asynchrony is perceived to cause breathing variability. Since patient-ventilator asynchrony is difficult to detect non-invasively, one might be able to detect its effects on the breathing pattern because of the increased breathing variability.

**Table 1:** Respiratory parameters used in the development phase to develop the breathing variability detection algorithm. All parameters were calculated on data during the 45 second period.

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| --- | --- | --- |
| Parameter Name | Parameter Calculation | Correlation Coefficient |
| Average Breath Length (s) | Mean of the breath lengths for all breaths in the 45 second segment. | 0.17 |
| Average Inspiratory Time (s) | Mean of the inspiratory times for all breaths in the 45 second segment. | 0.20 |
| Average Expiratory Time (s) | Mean of the expiratory times for all breaths in the 45 second segment. | 0.13 |
| Average Breathing Frequency (1/s) | Mean of $\frac{1}{Breath Length}$ for all breaths in the 45 second segment. | 0.17 |
| Average Ti/Ttot (%) | Mean of $\frac{Inspiratory Time}{Total Breath Time }$ for all breaths in the 45 second segment. | 0.03 |
| Average Rapid Shallow Breathing Index (f/vt, br/L\*s)  | Mean of $\frac{f}{Vt}$ for all breaths in the 45 second segment. | 0.12 |
| Average Tidal Volume (L) | Mean of the tidal volumes for all breaths in the 45 second segment. | 0.49 |
| Average Minute Ventilation (L/min) | Mean of the minute ventilations for all breaths in the 45 second segment. | 0.43 |
| Average Peak Flow (L/sec) | Mean of the peak flow rates for all breaths in the 45 second segment. | 0.49 |
| Average P(0.1) (cmH20) | Mean of the pressure changes during the first 0.1 seconds of inspiration for all breaths in the 45 second segment. | 0.25 |
| Average Resistance (cmH20/L/s) | Mean of the airway resistance calculations for all breaths in the 45 second segment. The airway resistance was calculated using an exhalation time constant method.[3] | 0.25 |
| Average Compliance (L/cmH20) | Mean of the lung compliance calculations for all breaths in the 45 second segment. The lung compliance was calculated using an exhalation time constant method.[3] | 0.25 |
| Average Leak (L/min) | Mean of the leak flows for all breaths in the 45 second segment. | 0.43 |
| Average Residual Volume (mL) | Mean of the residual volumes for all breaths in the 45 second segment. Residual Volume was calculated with the integral of the leak corrected flow per breath. | 0.45 |
| Average Ineffective Triggers (#) | Mean of the ineffective efforts for all breaths in the 45 second segment. The Ineffective efforts were calculated by waveform analysis.[4] This calculation was an estimation of the ineffective triggers since no measurement of patient effort was made.  | 0.55 |
| Average Flow Reversal L/sec) | Mean of the flow reversal rates for all breaths in the 45 second segment. Flow reversal was calculated as the flow at the end of exhalation. | 0.60 |
| Average Flow Limitation (%) | Mean of the estimated flow limitation for all breaths in the 45 second segment. Flow limitation was estimated by $\frac{Max exhale flow rate}{Exhale flow rate at quarter volume}$  | 0.04 |
| Average PEEPi (cmH20) | Mean of the estimated intrinsic positive end expiratory pressure (PEEPi) for all breaths in the 45 second segment. The PEEPi was estimated with $\frac{V\_{t}}{C\*\left(e^{-\frac{E Time}{R\*C}}-1\right)}$. Where C and R are estimated with the exhalation tau method.[3] | 0.60 |
| Average WOB (J/min) | Mean of the estimated work of breathing (WOB) by the patient per minute (J/min) for all breaths in the 45 second segment. The WOB is estimated with the noninvasive neural network method.[1] | 0.23 |
| Breath Length Variability (s) | Standard deviation of the breath length for all breaths in the 45 second segment. | 0.78 |
| Exhalation Time Variability\* (s) | Standard deviation of the exhalation times for all breaths in the 45 second segment. | 0.75 |
| Inspiratory Time Variability (s) | Standard deviation of the inhalation times for all breaths in the 45 second segment. | 0.62 |
| Tidal Volume Variability (L) | Standard deviation of the tidal volumes for all breaths in the 45 second segment. | 0.72 |
| Peak Flow Variability (L/sec) | Standard deviation of the peak flow rate for all breaths in the 45 second segment. | 0.63 |
| Leak Flow Variability (L/sec) | Standard deviation of the leak flow rate for all breaths in the 45 second segment. | 0.48 |
| Average Waveform Error  | The average waveform error is calculated by averaging the flow correlation and the pressure waveform error. The flow error was calculated as the root mean squared error of the flow from one breath (current breath) to the flow of the average breath. The average flow was calculated by combining all the flow waveforms in the 45 second data segment into one average breath. First a phase shift was applied between the breaths to align all inhalations. Outliers were excluded by discarding the maximum and minimum flow value at each time interval. (Our data collection was at 100 Hz, so the time interval was 0.01 seconds) The flow waveform of the average breath is the average of the remaining flows at each time interval. The pressure correlation calculation is similar; except the phase shift of the pressure waveforms was the same phase shift from the flow waveforms.  | 0.56 |
| Average Waveform Correlation\* | The average waveform correlation is calculated by averaging the flow correlation and the pressure waveform correlation. The flow correlation was calculated as the correlation of the flow from one breath (current breath) to the flow of the average breath. The average flow was calculated by combining all the flow waveforms in the 45 second data segment into one average breath. First a phase shift was applied between the breaths to align all inhalations. Outliers were excluded by discarding the maximum and minimum flow value at each time interval. (Our data collection was at 100 Hz, so the time interval was 0.01 seconds) The flow waveform of the average breath is the average of the remaining flows at each time interval. The pressure correlation calculation is similar; except the phase shift of the pressure waveforms was the same phase shift from the flow waveforms.  | 0.80 |

\*-Parameter used in the breathing variability algorithm; exhalation time variability and average waveform correlation

**Table 2:** Respiratory parameters organized by correlation coefficient.

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| Parameter Name | Correlation Coefficient |
| Average Waveform Correlation\* | 0.80 |
| Breath Length Variability (s) | 0.78 |
| Exhalation Time Variability\* (s) | 0.75 |
| Tidal Volume Variability (L) | 0.72 |
| Peak Flow Variability (L/sec) | 0.63 |
| Inspiratory Time Variability (s) | 0.62 |
| Average PEEPi (cmH20) | 0.60 |
| Average Flow Reversal L/sec) | 0.60 |
| Average Waveform Error  | 0.56 |
| Average Ineffective Triggers (#) | 0.55 |
| Average Tidal Volume (L) | 0.49 |
| Average Peak Flow (L/sec) | 0.49 |
| Leak Flow Variability (L/sec) | 0.48 |
| Average Residual Volume (mL) | 0.45 |
| Average Minute Ventilation (L/min) | 0.43 |
| Average Leak (L/min) | 0.43 |
| Average Compliance (L/cmH20) | 0.25 |
| Average P(0.1) (cmH20) | 0.25 |
| Average Resistance (cmH20/L/s) | 0.25 |
| Average WOB (J/min) | 0.23 |
| Average Inspiratory Time (s) | 0.20 |
| Average Breath Length (s) | 0.17 |
| Average Breathing Frequency (1/s) | 0.17 |
| Average Expiratory Time (s) | 0.13 |
| Average Rapid Shallow Breathing Index (f/vt, br/L\*s)  | 0.12 |
| Average Flow Limitation (%) | 0.04 |
| Average Ti/Ttot (%) | 0.03 |

**References**

1. Banner MJ, Tams CG, Euliano NR, Stephan PJ, Leavitt TJ, Martin AD, Al-Rawas N, Gabrielli A. Real time noninvasive estimation of work of breathing using facemask leak-corrected tidal volume during noninvasive pressure support: validation study. Journal of clinical monitoring and computing. 2016 Jun 1;30(3):285-94.
2. Thille AW, Rodriguez P, Cabello B, Lellouche F, Brochard L. Patient-ventilator asynchrony during assisted mechanical ventilation. Intensive care medicine. 2006 Oct 1;32(10):1515-22.
3. Al-Rawas N, Banner MJ, Euliano NR, Tams CG, Brown J, Martin AD, Gabrielli A. Expiratory time constant for determinations of plateau pressure, respiratory system compliance, and total resistance. Critical Care. 2013 Feb;17(1):R23.
4. Chen CW, Lin WC, Hsu CH, Cheng KS, Lo CS. Detecting ineffective triggering in the expiratory phase in mechanically ventilated patients based on airway flow and pressure deflection: feasibility of using a computer algorithm. Critical care medicine. 2008 Feb 1;36(2):455-61.