

Comparing asynchrony in two noninvasive ventilators

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Abstract

Objectives: Noninvasive ventilation (NIV) is commonly used in respiratory failure as an alternative to more invasive tracheal intubation. A major challenge of NIV is synchronization between the patient's spontaneous breathing efforts and the support of the ventilator.

Design: We compared simulator-ventilator synchrony characteristics of two ventilators during noninvasive ventilation, using an adult lung simulator under three leak configurations.

Setting: Bench test with lung simulator.

Patients and participants: Active Servo Lung with the bellavista 1000 NIV (bellavista NIV) and Respironics V60 (V60).

Interventions: Three configurations simulating different levels of unintended leak were tested for each ventilator: No Leak, Continuous Leak, and Inspiratory Leak. The recorded pressure and volume waveforms were analyzed to quantify trigger delay, triggering pressure-time product (PTP_{trig}), pressure-time product at 300 ms (PTP_{300}), insufflation time excess ($T_{L,excess}$), and time required to reach 63.2% ($T_{exp,63}$) and 95.0%

($T_{exp,95}$) of expired tidal volume (VT_{exp}) for each ventilator in all three leak scenarios.

Measurements and results: Trigger delays for the bellavista NIV were significantly lower for all three leak conditions ($p < 0.0001$) and it responded faster to simulated muscle activity compared to the V60. Both the bellavista NIV and V60 experienced no auto-trigger or missed trigger events. The bellavista NIV reached target pressure values more quickly as indicated by significantly higher PTP_{300} for all three leak conditions ($p < 0.0001$) and had significantly shorter $T_{L,excess}$ ($p < 0.0001$). The bellavista NIV experienced no delayed cycling breaths while more than 25% of V60 breaths showed delayed cycling during inspiratory leak tests.

Conclusions: The bellavista NIV showed significantly lower trigger delays for all three leak conditions, reached target pressure values more quickly (i.e., higher PTP_{300}), and showed superior cycling performance (i.e., lower trigger delay) compared to the V60, which may improve patient-ventilator synchrony and patient comfort.

Key words: Ventilator, critical care, noninvasive ventilation, weaning, ventilator-associated conditions.

Introduction

Noninvasive ventilation (NIV) has become a standard of care to support patients with various etiologies of acute respiratory failure. (1) It has been shown to help prevent intubation and mechanical

ventilation as well as to prevent re-intubation after extubation. (2-6) Although NIV has been shown to improve clinical outcomes, the incidence of failure remains problematic, mainly due to patient discomfort and non-adherence with treatment. (7)

A significant factor that contributes to non-compliance and patient discomfort with NIV is asynchrony between the spontaneous breathing effort of the patient and the support by the ventilator. This occurs either when the ventilator and the patient's spontaneous breathing effort are not coordinated or when there is increased or variable leak at the interface between the mask and patient's face. Studies have shown that asynchronies not only lead to patient discomfort, (7) but also increased work of breathing, (8,9) weaning failure, and increased mortality. (3,9,10)

To improve patient ventilator asynchrony, ventila-

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tor manufacturers have implemented sophisticated adjustable algorithms to sense the spontaneous effort by the patient and to trigger ventilation support. Studies have shown that dedicated noninvasive ventilators, specifically the Respironics V60 (Respironics, Philips, Carlsbad, California), have lower levels of auto triggering and increased overall patient-ventilator synchrony compared to ICU ventilators with NIV modes. (8) Additionally, dedicated noninvasive ventilators eliminate most of the trigger delays, reduce workload, decrease pressurization, and reduce delayed cycling seen with increasing leaks. (11) Although these sophisticated algorithms have improved patient ventilator synchrony, asynchronies remain as one of the major challenges in NIV. (9) Further improvements with these controllers and control algorithms are needed to reduce asynchrony and improve compliance and patient discomfort.

The objective of this study was to compare asynchrony between two ventilators, the bellavista 1000 NIV (bellavista NIV, Vyair Medical, United States) and the Respironics V60, in a bench study using an adult lung simulator.

Methods

Experimental methods

A series of bench experiments were conducted to compare patient-ventilator asynchrony during noninvasive ventilation using the bellavista NIV and V60 ventilators. The lung and ventilator settings used in this study were adapted from those described in Carteaux et al. (11) A lung simulator (Active Servo Lung [ASL] 5000, Ingmar Medical, United States) was used to simulate patient inspiratory effort. Specifically, the simulator's inspiratory muscle pressure (P_{muscle}) was set to 5 cmH₂O at a spontaneous breath rate of 15 breaths per minute (bpm). The simulator's inspiratory effort lasted for a total simulated inspiratory time ($T_{i,\text{sim}}$) of 0.8 s. Inspiration included a 0.4 s period of increasing P_{muscle} , followed by a 0.4 s period of decreasing P_{muscle} . Lung compliance was set to 80 ml/cmH₂O, and a 10 cmH₂O/l/s mixed resistor response model was used. Inspiratory positive airway pressure (IPAP) was 15 cmH₂O consisting of a pressure support (P_{support}) setting of 10 cmH₂O and positive end-expiratory pressure (PEEP) of 5 cmH₂O. Fraction of inspired oxygen (FiO₂) was set to 21%. Equivalent ventilator settings were used for the bellavista 1000 NIV and V60. The maximum inspiratory time before expiration was set to 1.5 s and apnea backup rate was set to 5 bpm. The bellavista NIV was set to Pressure Support Ventilation, Spontaneous (PSV) mode while the V60 was set to spontaneous/timed (S/T)

mode. Both ventilators were set to their fastest pressure rise rates of 0 ms (bellavista NIV) and a setting of 1 (V60).

Three configurations simulating different levels of unintended leak were tested for each ventilator (**Figure 1**): No Leak, Continuous Leak, and Inspiratory Leak. In the No Leak condition, a single limb noninvasive ventilation patient circuit was connected directly to the lung simulator. In Continuous Leak, a T-piece was placed between the lung simulator and single limb patient circuit. The patient circuits used for bellavista NIV and V60 tests were functionally equivalent with similar levels of intentional leak. A 4 mm hole was created using a Rp30 resistor, which resulted in a 16 l/min leak at 5 cmH₂O. In Inspiratory Leak tests, the 4 mm opening was connected to a tube immersed in a 7 cmH₂O water column. That arrangement enabled leaks during inspiration after the pressure in circuit reached higher than 7 cmH₂O and approximately 22 l/min of leak at 15 cmH₂O. Continuous Leak tests were intended to assess triggering asynchronies, while Inspiratory Leak tests examined cycling-off asynchronies.

Each test was run for one minute to establish steady state conditions. After reaching steady state, airway pressure (P_{airway}), muscle pressure (P_{muscle}), and volume (V) waveforms from the lung simulator were recorded at 512 Hz for three minutes (i.e., 45 breaths).

Asynchrony measurements

The recorded pressure and volume waveforms were analyzed to quantify several simulator-ventilator asynchrony parameters using MATLAB (MathWorks, United States) on a breath-by-breath basis based on the metrics defined in Carteaux et al. (11) Auto-triggering events were identified as ventilator breaths delivered without simulator effort while missed triggering effects were identified as an inspiratory muscle effort not followed by a ventilator breath.

The sensitivity of the ventilators to respond following a simulator effort was characterized using trigger delay and the triggering pressure-time product (PTP_{trig}). Trigger delay was quantified as the time between physiological inhalation and the rise in airway pressure (**Figure 2**), providing a measure of how quickly the ventilator detects simulator inspiratory effort. PTP_{trig} was defined as the area between the PEEP baseline and P_{airway} waveform during this trigger delay and quantifies the degree to which airway pressure is affected during expiration while the simulator starts to inhale. PTP_{trig} is expressed as a negative value by convention. The start of physiological inhalation was defined as the moment that

P_{muscle} started decreasing.

The pressure-time product at 300 ms (PTP_{300}) was quantified as the area above the PEEP baseline for 300 ms after the start of physiological inhalation (**Figure 3**). Pressures below PEEP represent negative area. PTP_{300} is a measure of how quickly the ventilator reaches its target pressure value.

Next, the insufflation time excess ($T_{I,\text{excess}}$) was calculated as the time between physiological muscular relaxation and the start of expiration (**Figure 4**). Muscular relaxation was defined as the time at which P_{muscle} starts increasing and the start of expiration was defined the start of negative simulator flow (i.e., decreasing volume). $T_{I,\text{excess}}$ is correlated to simulator synchrony. Specifically, negative $T_{I,\text{excess}}$ results in premature cycling and positive $T_{I,\text{excess}}$ results in delayed cycling. Premature cycling was defined as an inspiratory time less than 2/3 of the simulated inspiratory time (i.e., $T_{I,\text{excess}} < -267$ ms) and delayed cycling was defined as an inspiratory time greater than two times the simulated inspiratory time (i.e., $T_{I,\text{excess}} > 800$ ms). (11)

Finally, the exhalation performance of the ventilators was quantified by calculating exhalation times (**Figure 5**). Total exhalation time was defined as the time from when the simulator flow becomes negative to the time at which the entire expired tidal volume (VT_{exp}) was exhaled. We calculated the time it took to reach 63.2% ($T_{\text{exp},63}$) and 95.0% ($T_{\text{exp},95}$) of VT_{exp} (**Figure 5**). Assuming an exponentially decreasing function, these values correspond to 1- and 3- time constants, respectively. Exhalation times are correlated to the expiratory resistance felt by the simulator.

Data and statistical analysis

We calculated trigger delay, PTP_{trig} , PTP_{300} , $T_{I,\text{excess}}$, $T_{\text{exp},63}$, and $T_{\text{exp},95}$ for each breath of each 3-minute trial. All data processing and statistical analyses were conducted using MATLAB (MathWorks, United States). Lilliefors tests for normality were used to assess the breath data for calculated parameters. Non-normal population data are presented as medians and boxplots. The boxplots have a box extending from the 25th to the 75th percentile with the median as a thicker horizontal line within this box. The whiskers extend to the minimum and maximum data points with a dashed line. Wilcoxon signed-rank tests were conducted to compare the performance of the bellavista NIV and V60 devices for each of the calculated parameters under each of the three leak conditions. A Bonferroni correction was applied to account for multiple comparison and the level of significance was set at a conservative value of $\alpha=0.001$.

Results

The performance of the ventilator to trigger in response to muscle activity was quantified using trigger delay and PTP_{trig} (**Figure 6**). The bellavista NIV's trigger delays were significantly lower than the trigger delay of the V60 for all three leak conditions ($p<0.0001$). Specifically, median trigger delays for the bellavista NIV were 84, 92, and 100 ms for the No Leak, Continuous Leak, and Inspiratory Leak conditions, respectively, compared to 131, 131, and 123 ms for the V60. In other words, the bellavista NIV responses were between 23 and 47 ms faster in response to the simulator's muscle activity compared to the V60. The two devices had similar metrics for PTP_{trig} with median values ranging between -0.027 and -0.032 cmH₂O·s for both devices and leak conditions. The PTP_{trig} was significantly higher for the bellavista NIV compared to the V60 for the Continuous Leak condition (-0.028 vs -0.032 cmH₂O·s, $p<0.0001$). Both the bellavista NIV and V60 experienced no auto-trigger or missed trigger events during all trials and leak configurations.

The bellavista NIV reached target pressure values more quickly compared to the V60 as indicated by significantly higher PTP_{300} for all three leak conditions ($p<0.0001$). Specifically, bellavista NIV had median PTP_{300} values of 1.50, 1.13, and 1.25 cmH₂O·s for the No Leak, Continuous Leak, and Inspiratory Leak conditions, respectively, compared to 0.88, 0.74, and 0.81 cmH₂O·s for the V60 (**Figure 6**).

The bellavista NIV also had significantly shorter $T_{I,\text{excess}}$ compared to the V60 (**Figure 7**). For the No Leak and Continuous Leak conditions, $T_{I,\text{excess}}$ was significantly shorter for the bellavista NIV compared to the V60 ($p<0.0001$). Specifically, the bellavista NIV median $T_{I,\text{excess}}$ was 404 ms and 465 ms shorter for No Leak and Continuous Leak conditions, respectively. For the Inspiratory Leak tests, the bellavista NIV had similar performance as during the No Leak and Continuous Leak tests. Median $T_{I,\text{excess}}$ did not differ between the bellavista NIV and V60 during Inspiratory Leak test ($p=0.20$), but the V60 had noticeably higher breath-to-breath variance with values ranging from -117 to 998 ms and interquartile range (IQR) of 870 ms. In contrast, bellavista NIV had high reproducibility for the detection of inspiratory cycling for all conditions with IQRs of 3.9, 7.8, and 9.8 ms for the No Leak, Continuous Leak, and Inspiratory Leak conditions, respectively.

Delayed cycling was defined as inspiratory times greater than twice the simulated inspiratory time of 800 ms. Therefore, breaths with a $T_{I,\text{excess}}$ greater

than 800 ms (purple dashed horizontal line) were classified as delayed cycling breaths (purple circles). The bellavista NIV experienced no delayed cycling breaths under all leak conditions. The V60 had no delayed cycling breaths for the No Leak and Continuous Leak, but 25.6% of breaths during the Inspiratory Leak condition were classified as delayed cycling breaths. No breaths for either ventilator met the criterion for premature cycling.

Figure 8 compares the pressure and volume waveforms for three representative breaths of the bellavista NIV and V60 under Inspiratory Leak conditions. The first breath of the V60 shows a significant delay between the end of the simulated muscle pressure and the start of expiration (i.e., high insufflation time excess [$T_{I,excess}$]), which results in a larger delivered volume. The next two V60 breaths have better agreement between the end of active inspiration and start of expiration. This breath-to-breath variability in $T_{I,excess}$ during Inspiratory Leak was observed in the data presented in **Figure 8**. The three bellavista NIV breaths had low $T_{I,excess}$ and consistent delivered volumes.

The bellavista NIV and V60 had similar exhalation times as indicated by the time to reach 63.2% ($T_{exp,63}$) and 95.0% ($T_{exp,95}$) of the total VT_{exp} . Specifically, median $T_{exp,63}$ for the bellavista NIV were 0.93, 0.96, and 0.95 s for the No Leak, Continuous Leak, and Inspiratory Leak conditions, respectively, compared to 0.91, 0.89, and 0.90 s for the V60. $T_{exp,95}$ for the bellavista NIV were 2.29, 2.31, and 2.30 s for the No Leak, Continuous Leak, and Inspiratory Leak conditions, respectively, compared to 2.17, 2.11, and 2.30 s for the V60. The exhalation times were shorter for the V60 compared to bellavista NIV for the No Leak and Continuous Leak conditions ($p < 0.0001$).

Discussion

In this bench test study, we compared the bellavista 1000 NIV and the Philips V60 ventilators. The bellavista NIV showed significantly shorter trigger delays compared to the V60 for all three leak conditions. Both ventilators worked as expected and the increased leak did not increase trigger delay time. Trigger delays for the bellavista NIV during our study were lower than those reported by Delgado et al. in their evaluations of seven mid-level turbine critical care ventilators. (12)

The bellavista NIV reached target pressure values more quickly compared to the V60 (i.e., higher PTP_{300}) and showed improved cycling performance (i.e., lower trigger delay). A more rapid rise time in airway pressure (correlates with PTP_{300}) has been shown to reduce inspiratory work of breathing. (13)

A shorter $T_{I,excess}$ translates to better patient-ventilator synchrony and improved patient comfort. (14) Taking these benchmark results into account, the bellavista NIV shows favorable behavior in all the metrics which are seen as important for patient-ventilator interaction. Compared to the prolonged time delays and variability shown by the Philips V60 in $T_{I,excess}$ with Inspiratory Leak conditions, the bellavista NIV showed stable behavior under all three leak conditions. In clinical practice, intubation is not always successful (15) and noninvasive ventilation driven by an optimized ventilator may be beneficial. The clinical implications of millisecond improvements in trigger delays or small changes in flow are often unclear. (16) When the interaction between the patient and the ventilator are optimized (i.e., lower trigger delay, lower PTP_{300}), patient-ventilator asynchrony is reduced. (17) According to recent studies, patient-ventilator asynchrony is associated with adverse clinical effects and with unwanted patient events including discomfort, dyspnea, poor oxygenation, increased respiratory effort, damage to respiratory muscles, poor sleep, need for sedation or pharmacologic paralysis, longer time on ventilator, and higher mortality rates. (10,18) Air hunger is very common while on mechanical ventilation, particularly volume-controlled modes, often requiring sedation. Asynchrony can lead to decreased oxygenation. In a study by Yonis et al., (19) the use of neurally adjusted ventilatory assist (NAVA) led to an improvement in oxygenation and the PaO_2/FiO_2 ratio, although NAVA has been susceptible to double triggering depending on its sensitivity settings and diaphragmatic activity. (20) Excessive pressures can cause respiratory muscle damage, and inadequate pressures lead to muscle fatigue due to the increased work of breathing. These effects may delay the time to extubation and increase ventilator-associated events. Interestingly, despite several studies supporting the idea that asynchrony increases mortality, a direct causal relationship has not been established. (10) Studies have confirmed that poor ventilator responsiveness increases the work of breathing and may masquerade as weaning intolerance, delaying extubation. (21,22) While the literature is scarce regarding the isolated impact of any one of the measured parameters noted in our study (other than trigger delay), taken together they translate to poor quality patient-ventilator interactions, asynchrony, and adverse clinical outcomes. (2,23)

Our results are consistent with the bench data reported by Carreaux et al. who performed equivalent testing using the V60, but not on the bellavista NIV. (11) Specifically, the median trigger delay, PTP_{trig} ,

PTP₃₀₀, and T_{I,excess} values in the Inspiratory Leak test with the V60 in the Carteaux study were 91 ms, -0.030 cmH₂O·s, 1.37 cmH₂O·s, and 15 ms, respectively. The median trigger delay, PTP_{trig}, PTP₃₀₀, and T_{I,excess} values for the equivalent tests in this study were 123 ms, -0.029 cmH₂O·s, 0.81 cmH₂O·s, and -2 ms, respectively. This consistency in results obtained by two independent investigators supports the reliability of the data presented in this study. While the median T_{I,excess} during Inspiratory Leak tests reported by Carteaux et al. and this study were similar (15 ms vs -2 ms), the current study found large intra-breath variability (**Figures 4 and 5**) in the V60, which was not explicitly reported by Carteaux et al. (10)

Our study has certain limitations. This was an experimental model using standardized measures with a lung model and did not involve actual patients. The lung model was set to simulate an adult patient with mild chronic obstructive pulmonary disease (COPD), and results may be different for pediatric or neonatal settings or for a diseased lung model. Additional testing may be helpful using settings for compliance and resistance seen in COPD, restrictive lung disease, or acute respiratory distress syndrome (ARDS) as described in other studies, (8) although Carlucci et al. found no correlation between asyn-

chronies and altered lung mechanics. (7)

Conclusions

We found that even one of the most frequently-used noninvasive ventilators currently available has a level of asynchrony that can be largely corrected with improved technology. NIV is prone to failure in some patients and some conditions, often due to intolerance by the patient. (7) Intolerance can stem from mask issues (claustrophobia, skin irritation) and the urge to “fight the vent”. Asynchrony is known to contribute to intolerance and NIV failure. (23) It will be interesting to see if more contemporary noninvasive ventilators like the bellavista NIV impact outcomes and indications for noninvasive ventilation.

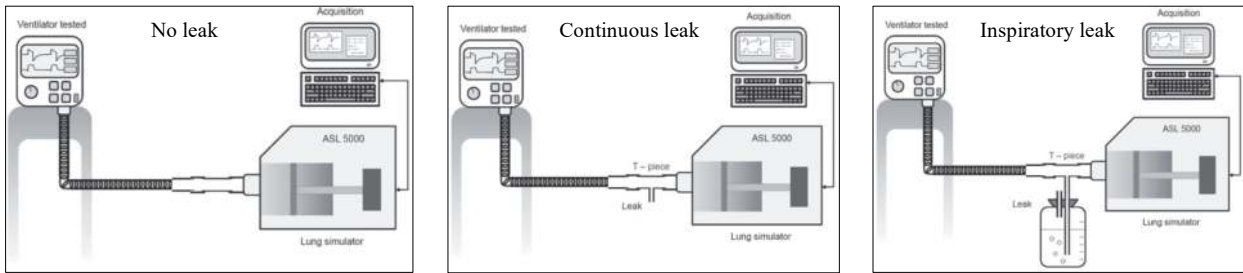
Acknowledgements

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Conflicts of interest

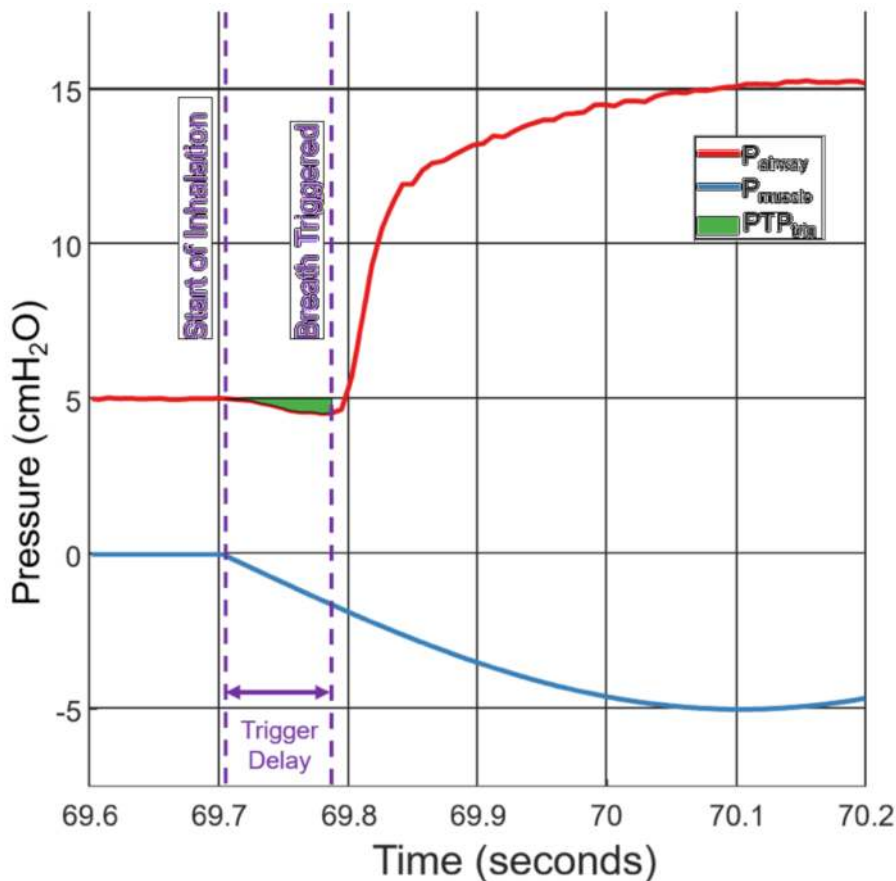
Dr. Pedro, Mr. Remus, and Mr. Waldmann are employees of Vyaire Medical. Vyaire Medical provided support for the bench testing and for the writing of this manuscript.

Figure 1. Bench testing schematics for the three leak conditions



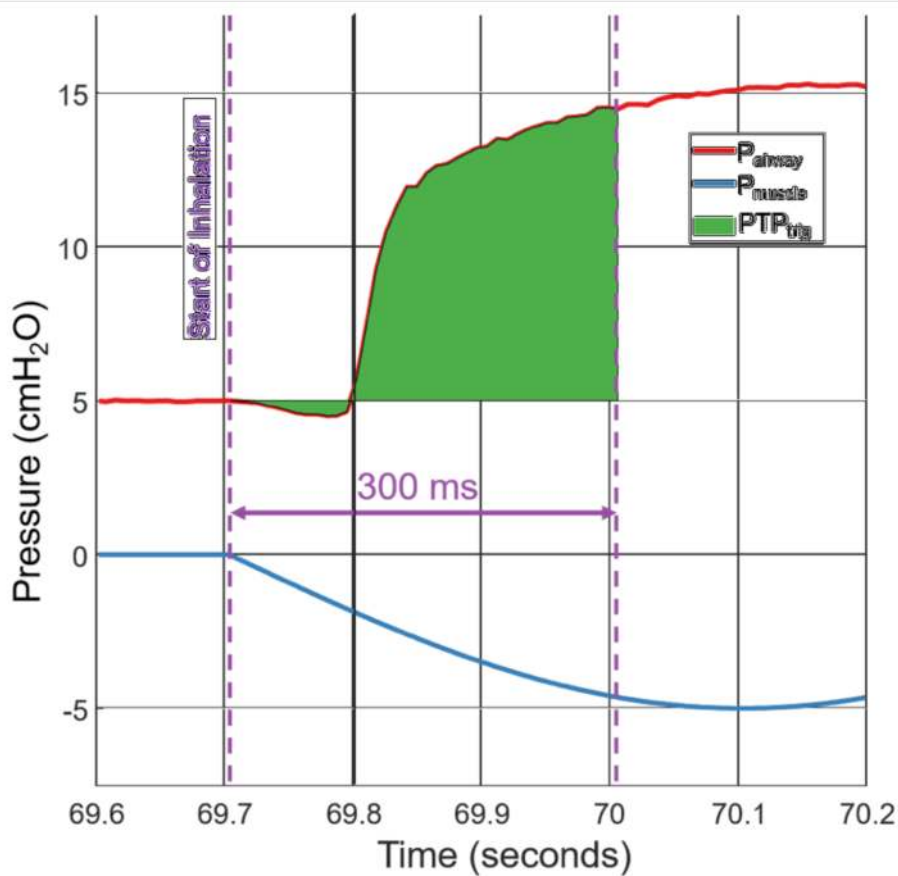
Legend: In all tests, the ventilators (bellavista 1000 NIV or Respironics V60) were connected to a lung simulator (Active Servo Lung [ASL] 5000) with a single limb simulator circuit. In No Leak tests, the simulator circuit was connected directly the lung simulator. In Continuous Leak, a T-piece was placed between the lung simulator and simulator circuit and 16 l/min leak at 5 cmH₂O was created with a 4 mm hole. In Inspiratory Leak tests, this hole was connected to a tube immersed in a 7 cmH₂O water column. Therefore, there were no leaks below 7 cmH₂O and leaks of 22 l/min at 15 cmH₂O.

Figure 2. Example of trigger delay and trigger pressure-time product (PTP_{trig}) calculation



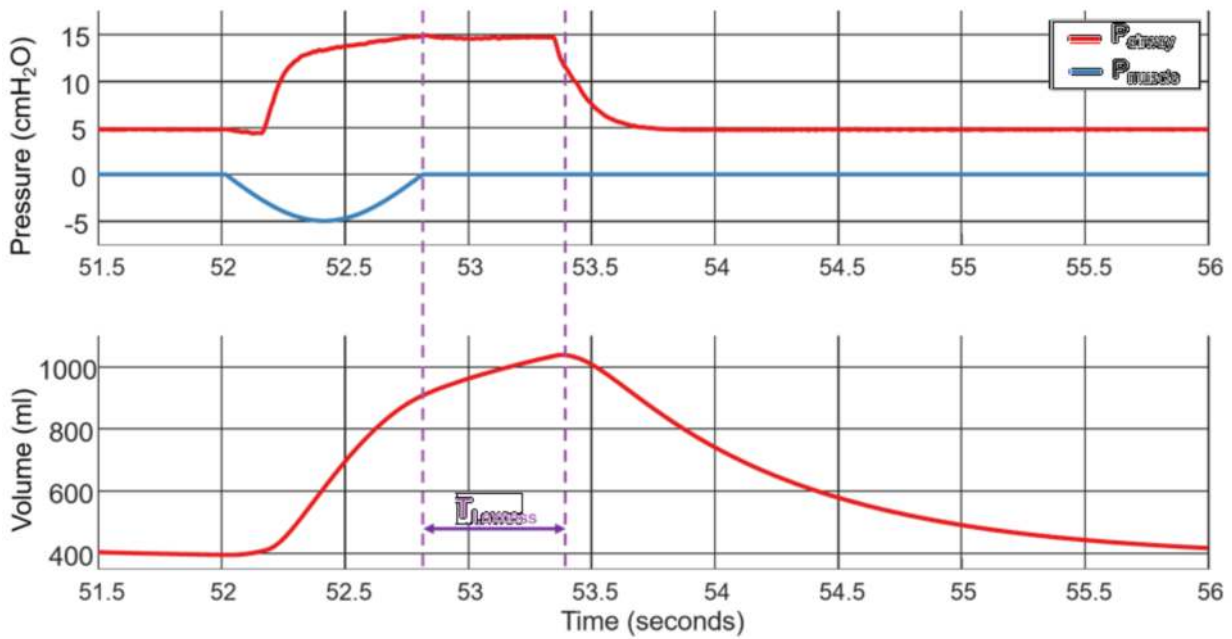
Legend: A decrease in muscular pressure (P_{muscle} , blue line) defines the start of inhalation (left purple dashed line). Airway pressure (P_{airway} , red line) initially decreases and then increases once a breath is triggered (right purple dashed line). trigger delay was quantified as the time between the purple dashed lines, and PTP_{trig} was calculated as the area between the positive end-expiratory pressure (PEEP) baseline (5 cmH₂O) and P_{airway} waveform during this trigger delay.

Figure 3. Example of pressure-time product at 300 ms (PTP_{300}) calculation during inhalation with a positive end-expiratory pressure (PEEP) setting to 5 cmH₂O



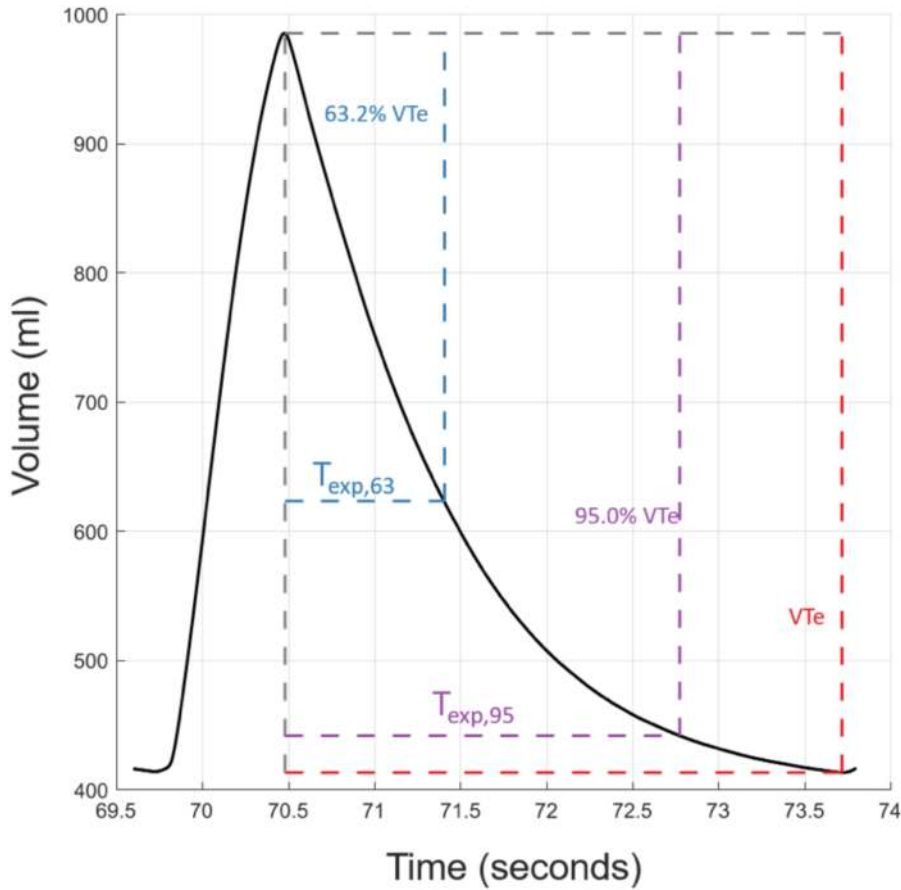
Legend: A decrease in muscular pressure (P_{muscle} , blue line) defines the start of inhalation (left purple dashed line). Airway pressure (P_{airway} , red line) initially decreases and then increases once a breath is triggered. PTP_{300} (green shaded area) is calculated as the area above PEEP from the start of physiological inhalation until 300 ms after (right purple dashed line).

Figure 4. Example of the calculation of the insufflation time excess ($T_{I,excess}$) under the Continuous Leak condition



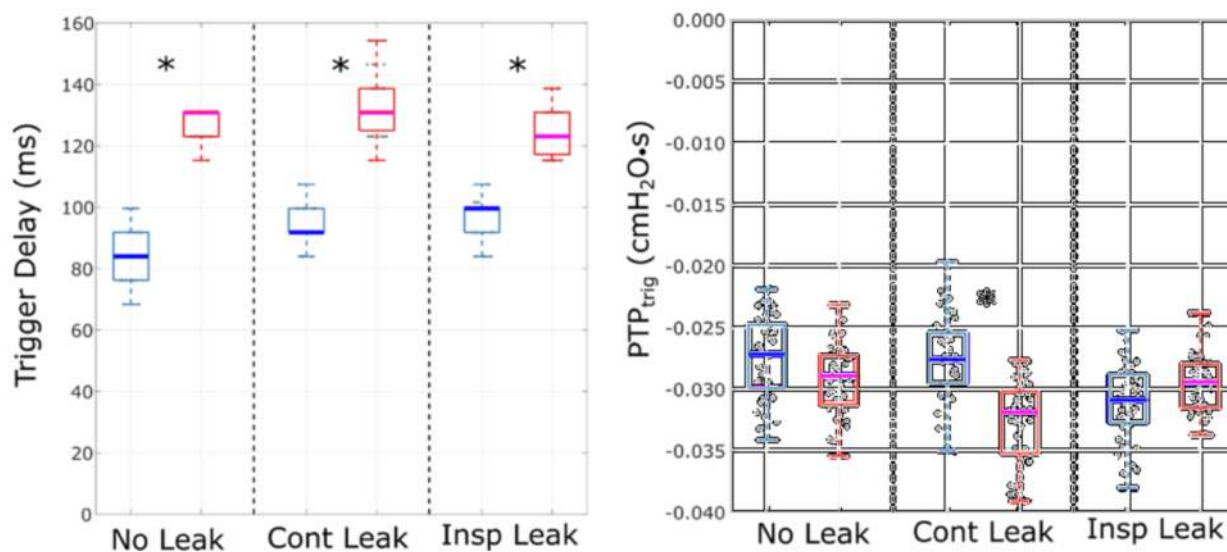
Legend: The top graphs show airway pressure (P_{airway} , red) and simulator muscular pressure (P_{muscle} , blue) while the bottom plot shows volume (red). $T_{I,excess}$ was calculated as the time between physiological muscular relaxation (left purple dashed line) and the start of expiration (right purple dashed line). Note that the approximately 400 ml of volume at the start of inspiration represents the lung simulator's equivalent of functional residual capacity at a positive end-expiratory pressure (PEEP) of 5 cmH₂O.

Figure 5. Example of the exhalation time calculation



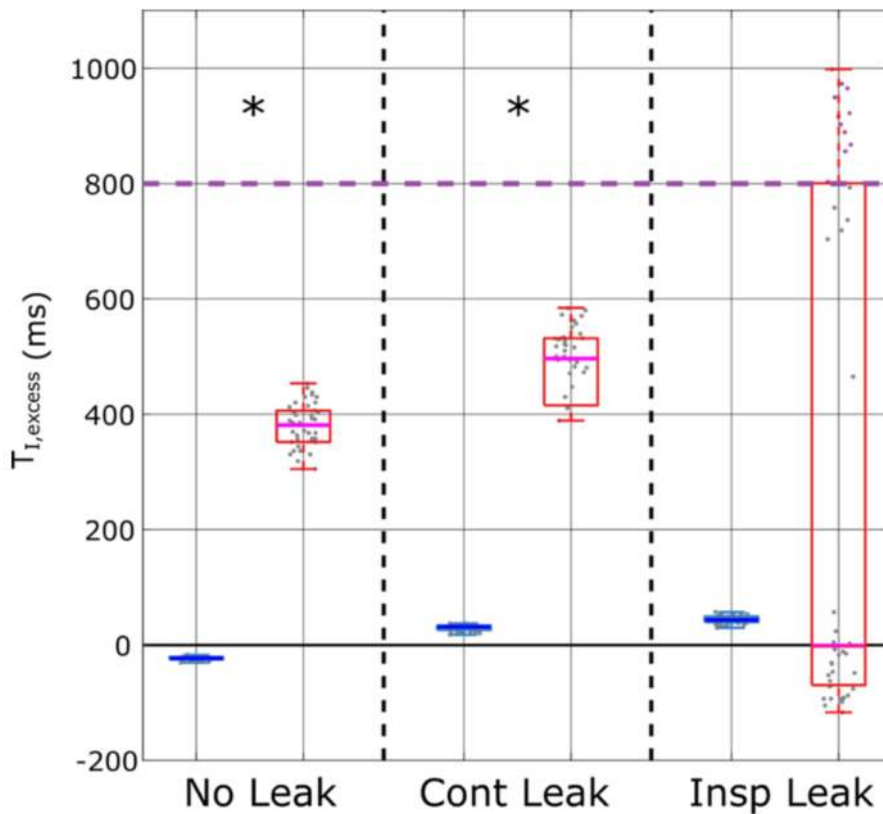
Legend: The volume waveform is shown as a solid black line. Exhalation times to reach 63.2% (blue dashed line, $T_{exp,63}$) and 95.0% (purple dashed line, $T_{exp,95}$) of the total expired tidal volume (V_{Te} , red dashed line) were calculated. Note that the approximately 400 ml of volume at the start of inspiration represents the lung simulator's equivalent of functional residual capacity at a positive end-expiratory pressure (PEEP) of 5 cmH₂O.

Figure 6. Trigger performance comparison of bellavista 1000 NIV (blue) and Respiroics V60 (red) for No Leak, Continuous Leak (Cont Leak), and Inspiratory leak (Insp Leak) test conditions



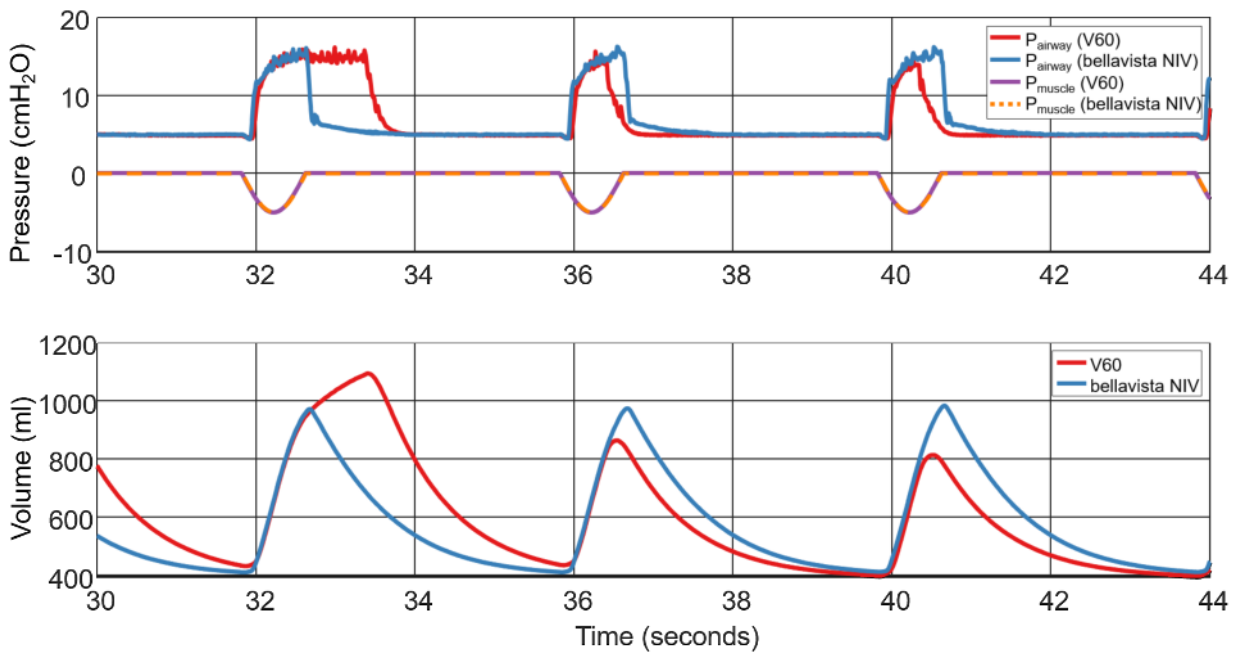
Legend: Left: The bellavista NIV had significantly lower trigger delays for all conditions compared to the V60. Right: Trigger pressure-time products (PTP_{trig}) were similar for the bellavista NIV and V60. Median values are represented by thick darker blue (bellavista NIV) and magenta (V60) lines. Individual breaths are shown as gray circles. * $p < 0.0001$.

Figure 7. Insufflation time excess ($T_{I,excess}$) performance comparison of bellavista NIV (blue) and Respironics V60 (red) for No Leak, Continuous Leak (Cont Leak), Inspiratory leak (Insp Leak) test conditions



Legend: bellavista NIV had shorter $T_{I,excess}$ for No Leak and Continuous Leak conditions compared to the V60. For Inspiratory Leak tests, V60 had noticeably higher variance in $T_{I,excess}$ compared to the bellavista NIV. Delayed cycling was defined as an inspiratory time greater than twice the simulated inspiratory time (i.e., $T_{I,excess} > 800$ ms, purple horizontal dashed line). The bellavista NIV had no delayed cycling breaths under all leak conditions. The V60 had no delayed cycling breaths for the No Leak and Continuous Leak, while 25.6% of breaths during the Inspiratory Leak condition were classified as delayed cycling breaths (purple circles). Median values are represented by thick darker blue (bellavista NIV) and magenta (V60) lines. Individual breaths which were not delayed cycling are shown as gray circles. * $p < 0.0001$.

Figure 8. Comparison of bellavista 1000 NIV (blue) and Respironics V60 (red) pressure (top) and volume waveforms of three representative breaths under Inspiratory Leak conditions



Legend: Waveforms are aligned in time using the simulated muscle pressure, which were identical for the V60 (purple) and bellavista NIV (orange). The first breath of the V60 shows a significant delay between the end of the simulated muscle pressure and the start of expiration (i.e., high insufflation time excess [$T_{I,excess}$]), which results in a higher delivered volume. The next two V60 breaths have better agreement between the end of active inspiration and start of expiration. This breath-to-breath variability in $T_{I,excess}$ during Inspiratory Leak is observed in the data presented in **Figure 7**. The three bellavista NIV breaths had low $T_{I,excess}$ and consistent delivered volumes.

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