Assessment of Oscillatory Pressure and Flow Waveforms with the Biwaze® Clear System

Robert DiBlasi RRT-NPS, FAARC Niko Kontoudios RRT Hattie KenKnight, BS
Seattle Children's Hospital and Research Institute, Seattle, Washington, USA

Introduction

Airway clearance is critical in maintaining respiratory health, especially for chronic and acute lung diseases. Common conditions associated with mucostasis include cystic fibrosis, bronchiectasis, bronchitis, and pneumonia, where ineffective cough or mucociliary dysfunction prevents the removal of airway secretions.[1] Left unresolved, mucostasis can result in the accumulation, impaction, and obstruction of mucus in the bronchioles, which can partially or fully collapse the lungs, impair lung function, promote morbidity, and prolong hospitalization.[1]

Oscillating lung expansion (OLE) therapy airway clearance systems, like the BiWaze Clear, combine lung expansion, secretion clearance, aerosol, and oxygen into a single therapy. High-frequency oscillation (HFO) applies distending pressure during the respiratory cycle to maintain airway patency, recruit collapsed airways and alveoli and improve lung volumes and gas exchange. The rapid pulses of oscillating flow shear the mucus from the airway lining and assist in mobilizing secretions from peripheral airways to larger conducting airways, which can then be removed via airway suctioning or coughing.[2] A critical aspect of effective mucus mobilization is the expiratory flow bias (EFB), which occurs when peak expiratory flow (PEF) exceeds peak inspiratory flow (PIF). This dynamic, reflected in the PIF/PEF ratio, ensures that airflow directs secretions out of the lungs rather than deeper into the airways. A PIF/PEF ratio below 0.9 is considered optimal for airway clearance therapy.[2,6,9,10,11,12,20]

The therapeutic benefits and clinical efficacy of high-frequency oscillation are not well known with existing OLE airway clearance systems. However, several mechanisms are thought to contribute to secretion clearance and lung expansion, which include:

1. Applying higher inspiratory and expiratory flow in the airways increases the transairway pressure gradient, gas flow velocity, turbulence, mechanical stress, and differential shear forces. These factors contribute to a reduction in the stability of mucus viscosity at the air-mucus interface, thereby preventing the adhesion of secretions on the mucus layer of the airway lining.[3]
2. Changes in the kinetic energy between the expiratory and inspiratory flows create differences in airflow velocities during the oscillatory phases. During the expiratory phase of the oscillation, the higher airflow velocities can induce a reduction in airway diameter, which, combined with the velocity differences between expiratory and inspiratory phases, may help prevent mucus from moving deeper into the lung periphery and instead facilitate its clearance toward the central airways.[4]
3. The pressure gradient within the airway needs to be high enough to dilate the airway, get the air behind (distal to) the mucus, and accelerate the expiratory flow leading to the expulsion of mucus from deep within the peripheral airways (aka "mini coughs").[5]
4. The effectiveness of endobronchial secretion mobilization from the bronchioles to the central airways is optimized by the airway pressure oscillations that produce an EFB.[2,6,9,10,11,12,20]

The overall effectiveness of HFO on secretion mobilization may be highly dependent on the expiratory flow bias but also the frequency and magnitude of the airway pressure oscillations and the attenuation through the airways, as well as the impact of pressure and flow related to the underlying lung mechanics (pulmonary pathophysiology) and mucus viscosity.

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Moreover, the effects of superimposed airway pressure oscillations on flow, tidal volume (V_T), mean airway pressure ($P\overline{aw}$), and end-expiratory lung pressure (PEEP) during spontaneous breathing with HFO are important factors to consider for maintaining airway patency, expansion, recruitment, and lung protection during airway clearance therapy.

We conducted descriptive studies in vitro to characterize the pressure-flow relationship during HFO produced with the BiWaze® Clear system. We analyzed the effect of HFO in spontaneously breathing pediatric and adult patients having normal, obstructed, and restricted lung mechanics. HFO pressure and waveforms were also analyzed to quantify the mechanical forces and flow bias that could promote secretion clearance and lung expansion during HFO. The findings from these experiments will be used to corroborate the outcomes related to the efficiency of mucus transport and compare it with another OLE airway clearance therapy device, the Volara® System (Baxter Hillrom, Deerfield, IL).

Table 1: Study Model Parameters

	Lung Condition	Respiratory Rate *(breaths/min)*	Ti *(s)*	~I:E	Tidal Volume *(mL)*	Compliance *(mL/cm H_2O)*	Resistance *(cm H_2O/L/s)*	Pleural Pressure *(cm H_2O)*
ADULT (70 kg)	Normal	15	1.3	1:2	520	100	4	8
	Obstructed	14	0.85	1:4	600	100	20	31
	Restricted	25	0.8	1:2	420	35	9	17
PEDIATRIC (25 kg)	Normal	25	0.8	1:2	145	55	25	12
	Obstructed	22	0.68	1:3	140	42	50	21
	Restricted	38	0.52	1:2	100	30	15	7

Study Method

Device Descriptions

The BiWaze® Clear features a dual-blower design with each blower dedicated to inhaled and exhaled airflows and oscillatory pressures independently. The filtered coaxial breathing circuit has separated inspiratory and expiratory gas flow pathways and a sealed (aka 'closed') handset. In contrast, the Volara® System features a single-blower design and utilizes a filtered single-limb breathing circuit. The Volara breathing circuit includes an integrated fixed-leakage port, referred to as the "expiratory valve," on the open handset to flush out exhaled carbon dioxide. In both systems, internal oscillations are delivered directly to the patient airway.

Experimental Setup

A digitally controlled, high-fidelity lung simulator (ASL 5000; Ingmar Medical, Pittsburgh, PA) was used to replicate realistic breathing patterns for both pediatric (25 kg) and adult (70 kg) subjects. The simulator was configured to model normal, obstructive, and resistive lung mechanics and breathing parameters. Utilizing a screw-drive-controlled piston and advanced mathematical modeling, the system enabled precise simulation of tidal breathing while measuring flow, pressure, and volume with high accuracy. *The model parameters are shown in Table 1.*[13,14,15,16,17,18,19]

A realistic 3D-printed pediatric[7] and adult[8] anatomic upper airway model was attached to the simulator during spontaneous breathing. Baseline spontaneous breathing measurements (without HFO) were obtained for each patient model and disease state to determine the effects of HFO on the flow bias, tidal volume, and pressure. Following baseline measurements, HFO was applied via a sealed mouthpiece attached to the oral opening of the 3D printed anatomic airway model, using HFO setting of 20 and 30 cm H_2O with medium frequency (4 Hz).

The raw airway pressure and flow signals from the internal lung chamber of the simulator were recorded at 500 Hz using the ASL software and later used to reconstruct waveforms and calculate different breathing parameters. In addition, the raw pressure and flow recording data were acquired with a low-resistance flow pneumotachometer and pressure transducer placed in series with the distal trachea of each airway model. The voltage signals were acquired and processed in real-time (1000 Hz) with an analog-to-digital converter (PowerLab, ADInstruments, Colorado Springs, CO) and later used to characterize the tracheal oscillations in pressure and flow across all the different experimental conditions. Each test lasted 2 minutes.

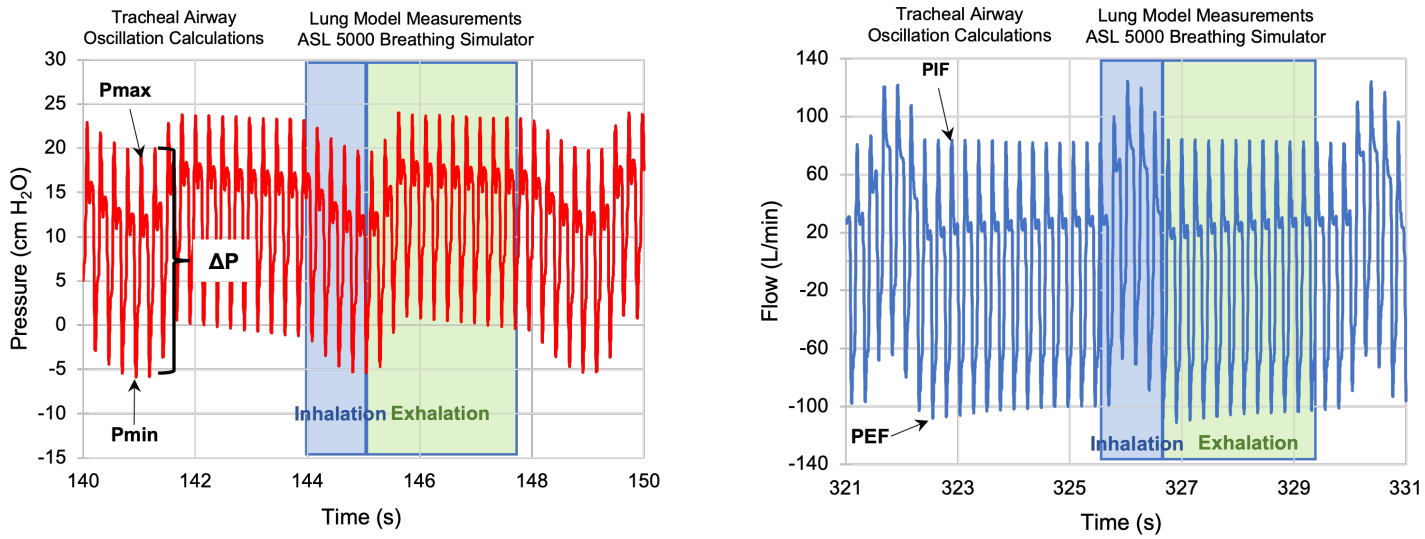
Measured Parameters-Data Analysis and Results

After completing the experimental runs, the tracheal measurement data recorded for each condition was analyzed to calculate the change in airway pressure (ΔP) between the minimum (Pmin) and maximum (Pmax) values. The resulting peak inspiratory flow (PIF) and peak expiratory flow (PEF) generated by the therapy pressure oscillations were also determined. As previously noted, sufficient driving pressure (ΔP or trans airway pressure gradient) is required to transport gas past the mucus obstructions, generating enough kinetic force to shear secretions from the airway lining and accelerating expiratory flow to effectively mobilize secretions from the lungs.

Oscillatory flow values were used to calculate the expiratory flow bias (EFB) by subtracting the peak inspiratory flow (PIF) from the peak expiratory flow (PEF). A negative EFB indicates a tendency to drive secretions further into the distal airways, while a positive EFB supports improved mucus mobilization toward the proximal airways. The PIF/PEF ratio was also calculated to compare the relative differences between baseline spontaneous breathing and HFO therapy conditions, evaluating whether the therapy improved or hindered secretion mobilization.

PIF/PEF ratio changes were categorized based on their impact on flow bias. Ratios decreasing from baseline (e.g., PIF/PEF decreasing from 1.0 to 0.6) were associated with a positive EFB, improving mucus mobilization. Conversely, ratios increasing from baseline (e.g., PIF/PEF increasing from 1.0 to 1.5) were associated with a negative EFB, which is unfavorable to mucus mobilization (aka inspiratory flow bias).[20] Additional calculations were performed using the breath-by-breath data acquired from within the ASL 5000 to evaluate the cumulative effect of superimposed airway pressure oscillations on the peak inspiratory pressure (PIP), PEEP, ($P\overline{aw}$), and V_T during spontaneous breathing **(see Figure 1)**.

Figure 1: Tracheal and Lung Simulator Model Measurements



Results

ADULT MODEL

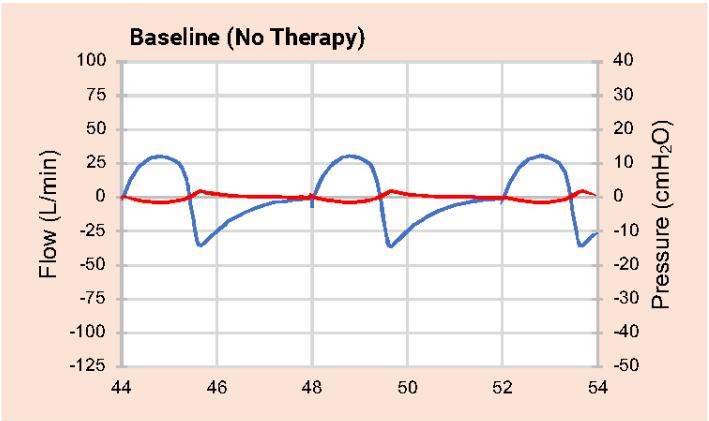
In the spontaneously breathing adult model with normal lung mechanics, the tracheal oscillatory ΔP increased from baseline (no therapy) with both systems **(Table 2A)**. The BiWaze Clear generated nearly two-fold higher ΔP pressures than Volara, resulting in higher PEF during HFO. The PEF was 2 to 3-fold greater with BiWaze Clear compared to the baseline, whereas the PEF measured with Volara was less than the baseline. This resulted in a significantly improved EFB and PIF/PEF ratio (0.67) with BiWaze Clear. Conversely, Volara demonstrated a 7 to 9-fold reduction in the EFB compared to baseline, resulting in an inspiratory flow bias, which is an unfavorable flow pattern that may drive mucus deeper into the lungs **(see Table 2A)**.

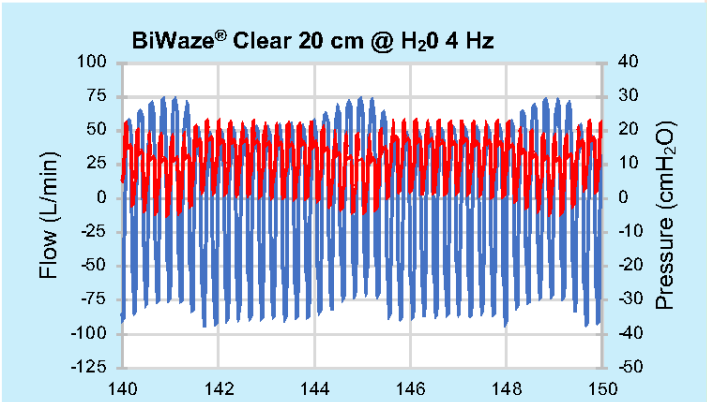
Overall, the measured tracheal oscillatory pressures with BiWaze Clear were more consistent with the set pressure and exhibited lower variability (SD) than Volara, which underdelivered oscillatory pressure by approximately 50% of the set pressure during HFO. The additive effects of superimposed oscillations on spontaneous breaths resulted in intrinsic reductions in the delivered V_T (~50%) to the lung model with both systems **(Table 2B)**. However, V_T increased as the set pressure was raised from 20 to 30 cmH_2O in BiWaze Clear but decreased in Volara under the same conditions. Additionally, higher PIP, PEEP, ($P\overline{aw}$) and flows were observed in the lung model with BiWaze Clear compared to Volara, attributed to the relatively higher oscillatory ΔP generated by BiWaze Clear **(Table 2A).**

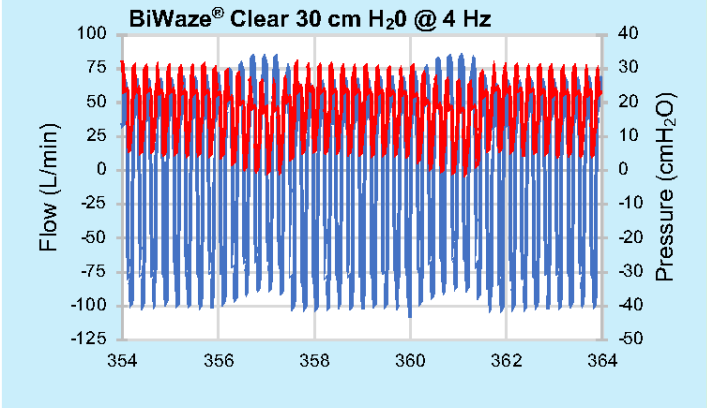
Normal Adult Model

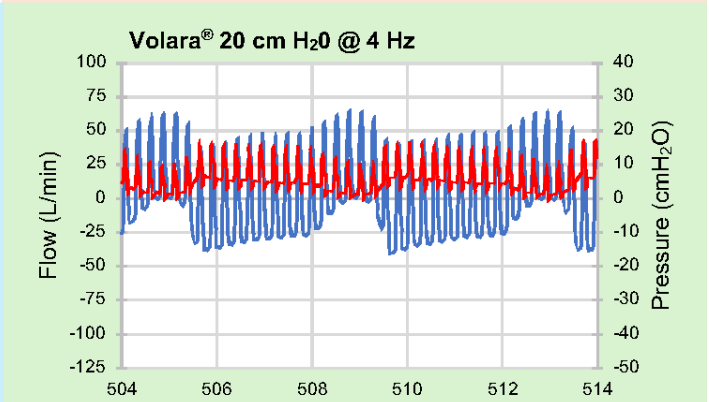
Figure 2: Pressure and Flow Waveforms - Normal Adult Model

In the Normal Adult Model, Oscillatory pressure and flow waveforms show that BiWaze® Clear consistently delivered higher tracheal oscillatory pressures (ΔP) that were closer to the set pressures, demonstrated lower variability, and achieved lower Pmin values compared to Volara. The peak expiratory flow (PEF) generated with BiWaze Clear was 2-3 times greater than baseline, resulting in a significantly improved expiratory flow bias (EFB) and an optimal PIF/PEF ratio below 1. In contrast, Volara exhibited lower PEF than baseline, leading to a negative EFB and unfavorable PIF/PEF ratios.









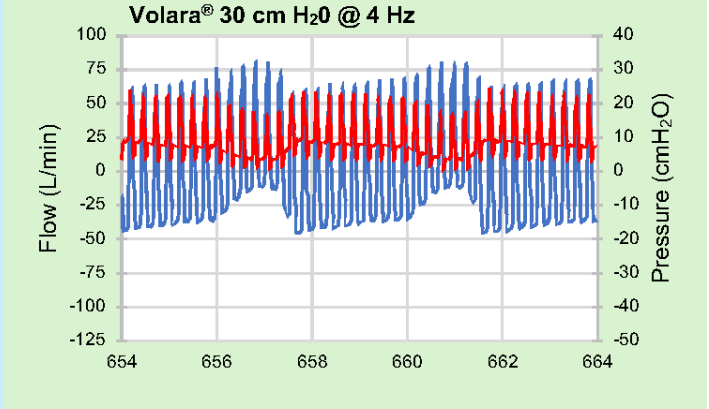


Table 2A: Tracheal Measurements - Spontaneously Breathing Normal Adult Model

	Baseline	20 cm H_20 @ 4 Hz		30 cm H_20 @ 4 Hz	
Measurements	**No Therapy**	**BiWaze® Clear**	**Volara®**	**BiWaze® Clear**	**Volara®**
ΔP (cm H_2O)	3.34 (0.14)	21.00 (0.57)	11.64 (1.00)	26.08 (0.71)	16.41 (1.17)
PIF (L/min)	29.64 (0.27)	65.82 (8.92)	61.65 (8.27)	80.48 (8.92)	83.17 (7.68)
PEF (L/min)	35.24 (0.56)	98.24 (7.53)	29.47 (12.19)	117.94 (6.21)	35.15 (13.23)
EFB (L/min)	5.60 (0.62)	32.42 (11.67)	-32.84 (14.73)	37.46 (10.82)	-48.02 (15.03)
PIF/PEF (L/min)	0.84 (0.02)	0.67 (0.10)	2.09 (0.91)	0.68 (0.08)	2.37 (0.92)

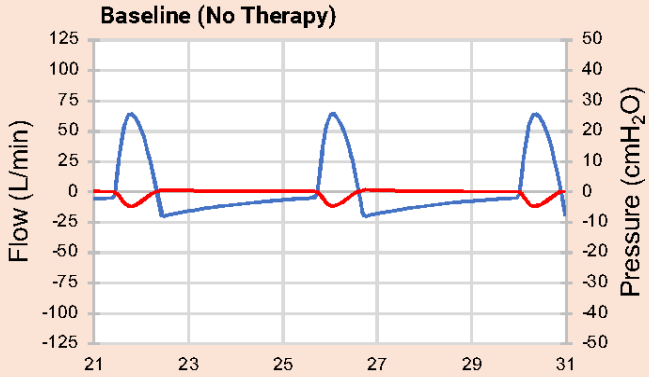
Table 2B: Lung Simulator Measurements - Spontaneously Breathing Normal Adult Model

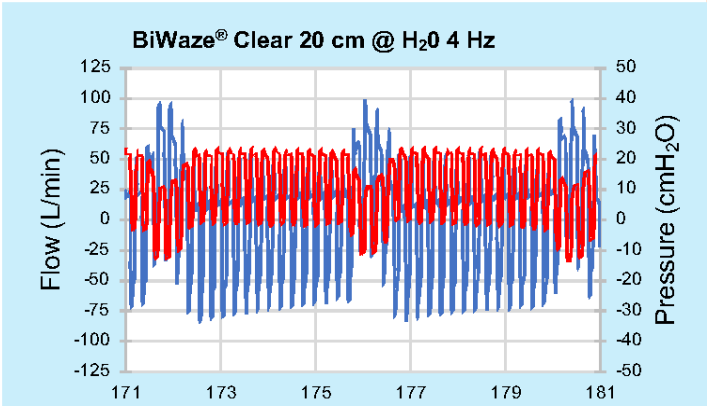
	Baseline	20 cm H_20 @ 4 Hz		30 cm H_20 @ 4 Hz	
Measurements	**No Therapy**	**BiWaze® Clear**	**Volara®**	**BiWaze® Clear**	**Volara®**
Tidal Volume (mL)	525.04 (2.15)	250.79 (16.52)	232.76 (24.44)	273.30 (17.35)	228.64 (20.89)
PIP (cm H_2O)	0.13 (0.01)	24.75 (0.14)	19.46 (0.32)	33.32 (0.68)	26.24 (0.31)
PEEP (cm H_2O)	0.05 (0.04)	12.90 (0.31)	6.67 (0.21)	18.85 (0.64)	10.11 (0.28)
Pmean (cm H_2O)	0.01 (0.02)	11.79 (0.17)	6.02 (0.14)	17.43 (0.53)	9.29 (0.15)
PIF (L/min)	30.60 (0.21)	77.34 (0.45)	68.68 (1.00)	88.72 (0.96)	87.19 (0.96)
PEF (L/min)	36.38 (0.40)	93.47 (1.26)	36.96 (1.10)	108.52 (3.34)	45.83 (0.92)

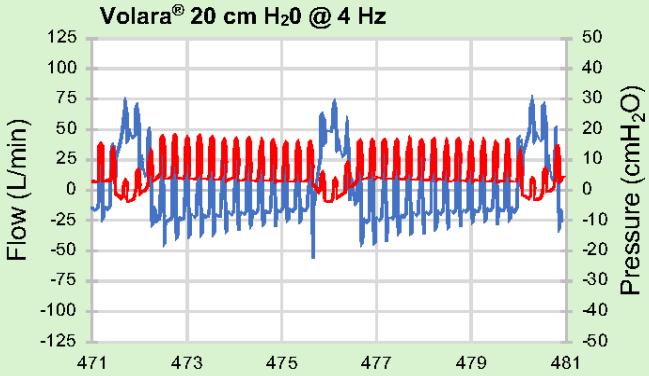
Obstructed Adult Model

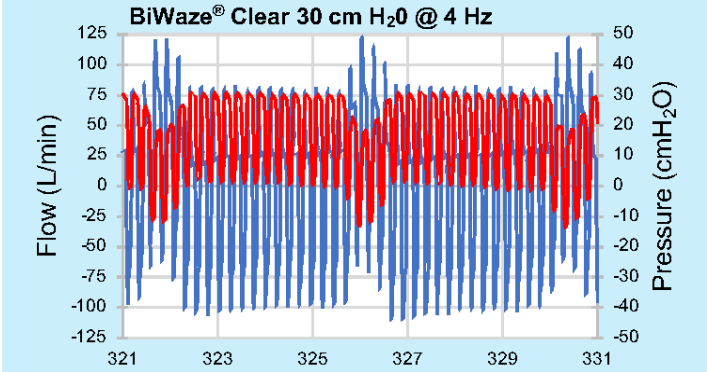
Figure 3: Pressure and Flow Waveforms – Obstructed Adult Model

In the Obstructed Adult Model, the BiWaze® Clear achieved higher tracheal oscillatory pressures (ΔP), closer to set pressures, with lower variability compared to Volara. BiWaze Clear also demonstrated higher peak expiratory flow (PEF) and a notable improvement in expiratory flow bias (EFB) compared to baseline, while Volara showed lower EFB than baseline. Increasing the pressure to 30 cm H_2O did not have any further positive impact on both the parameters in both systems.









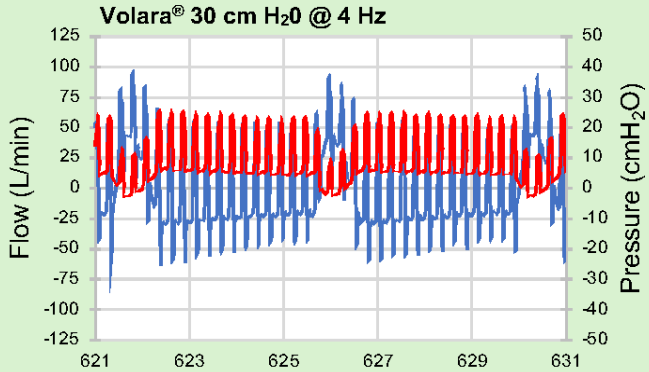


Table 3A: Tracheal Measurements - Spontaneously Breathing Obstructive Adult Model

	Baseline	20 cm H20 @ 4 Hz		30 cm H20 @ 4 Hz	
Measurements	No Therapy	BiWaze® Clear	Volara®	BiWaze® Clear	Volara®
ΔP (cm H2O)	6.10 (0.01)	23.48 (2.27)	17.09 (3.32)	33.95 (2.09)	22.88 (2.35)
PIF (L/min)	63.41 (0.03)	44.65 (13.9)	45.99 (20.74)	61.74 (14.60)	59.42 (15.38)
PEF (L/min)	19.48 (0.08)	59.34 (9.40)	32.34 (5.35)	74.69 (10.73)	39.23 (13.43)
EFB (L/min)	-43.93 (0.08)	14.69 (16.78)	-13.65 (21.42)	12.95 (18.12)	-20.19 (20.42)
PIF/PEF (L/min)	3.25 (0.01)	0.75 (0.26)	1.42 (0.68)	0.83 (0.23)	1.52 (0.65)

Table 3B: Lung Simulator Measurements - Spontaneously Breathing Obstructive Adult Model

	Baseline	20 cm H20 @ 4 Hz		30 cm H20 @ 4 Hz	
Measurements	No Therapy	BiWaze® Clear	Volara®	BiWaze® Clear	Volara®
Tidal Volume (mL)	610.02 (11.93)	388.33 (51.70)	533.22 (18.13)	419.24 (41.70)	471.32 (43.59)
PIP (cm H2O)	0.12 (0.01)	24.54 (0.08)	18.27 (0.36)	31.31 (0.62)	26.24 (0.40)
PEEP (cm H2O)	0.12 (0.11)	13.97 (0.27)	8.37 (0.12)	19.47 (1.54)	11.95 (0.21)
Pmean (cm H2O)	0.0 (0.01)	11.15 (0.19)	6.03 (0.12)	16.50 (1.11)	9.45 (0.20)
PIF (L/min)	64.61 (12.61)	106.19 (1.22)	82.65 (1.60)	131.01 (2.71)	103.64 (1.82)
PEF (L/min)	19.77 (12.17)	89.29 (3.18)	50.24 (2.28)	117.00 (4.62)	74.07 (4.41)

Restrictive Adult Model

Figure 4: Pressure and Flow Waveforms – Restrictive Adult Model

In the Restrictive Adult Model, BiWaze® Clear achieved higher tracheal oscillatory pressures (ΔP) that were closer to set pressures with lower variability compared to Volara. BiWaze Clear improved expiratory flow bias (EFB) and PIF/PEF ratio over baseline, while Volara reduced the EFB and PIF/PEF ratio from baseline. Increasing the pressure to 30 cm H_2O had marginal positive impact with BiWaze Clear while impact was negative with Volara.

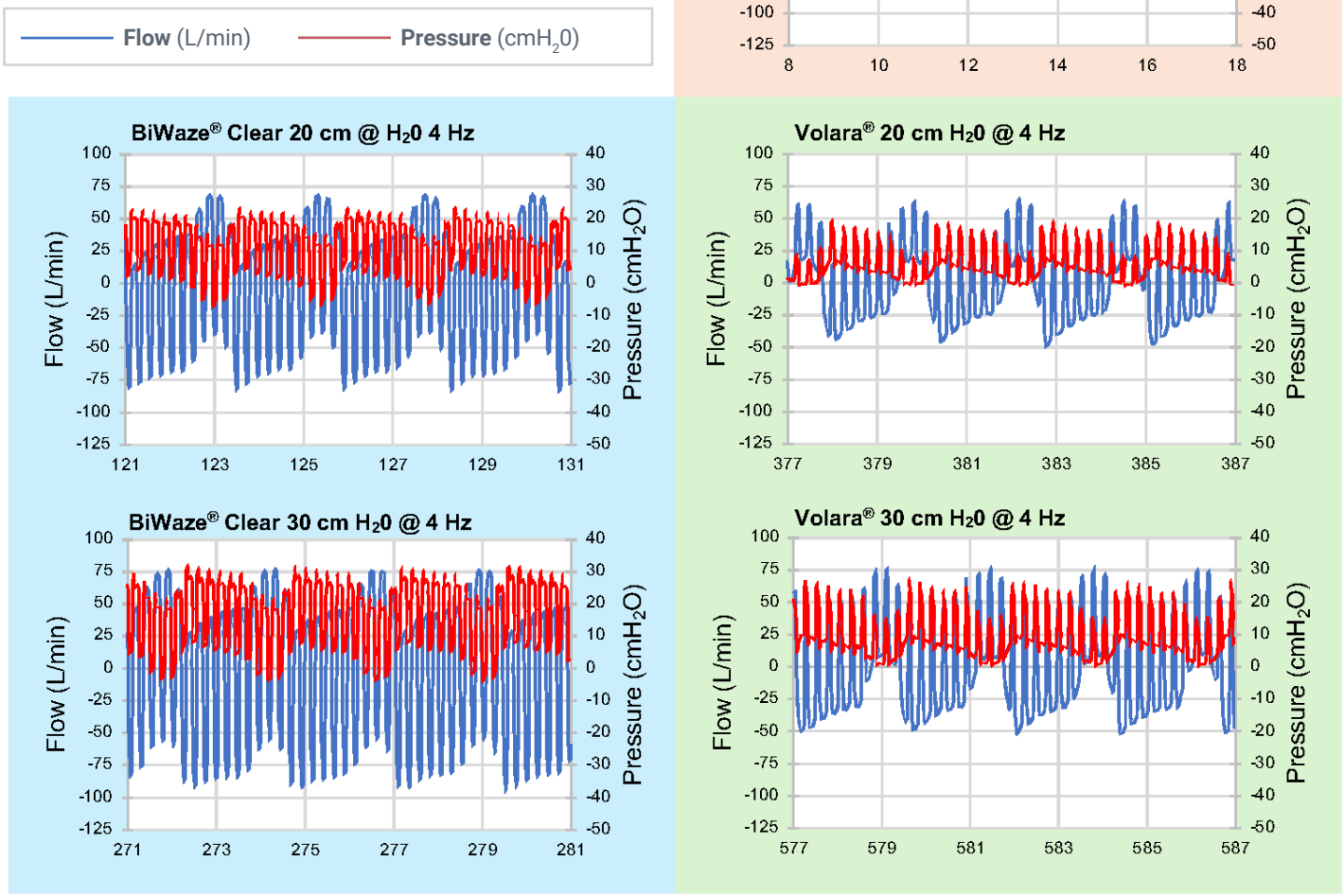


Table 4A: Tracheal Measurements - Spontaneously Breathing Restrictive Adult Model

	Baseline	20 cm H_20 @ 4 Hz		30 cm H_20 @ 4 Hz	
Measurements	**No Therapy**	**BiWaze® Clear**	**Volara®**	**BiWaze® Clear**	**Volara®**
ΔP (cm H_2O)	4.98 (0.02)	22.27 (2.76)	15.16 (3.28)	26.92 (2.42)	18.31 (2.17)
PIF (L/min)	38.80 (0.07)	54.36 (16.60)	56.24 (15.31)	64.08 (15.13)	71.32 (12.52)
PEF (L/min)	45.20 (0.16)	71.10 (14.28)	41.60(12.40)	88.92 (13.15)	33.51 (19.16)
EFB (L/min)	6.40 (0.17)	16.74 (21.9)	-14.64 (19.7)	24.84 (20.05)	-37.81 (22.89)
PIF/PEF (L/min)	0.86 (0.00)	0.77 (0.28)	1.36 (0.56)	0.72 (0.20)	2.13 (1.27)

Table 4B: Lung Simulator Measurements - Spontaneously Breathing Restrictive Adult Model

	Baseline	20 cm H_20 @ 4 Hz		30 cm H_20 @ 4 Hz	
Measurements	**No Therapy**	**BiWaze® Clear**	**Volara®**	**BiWaze® Clear**	**Volara®**
Tidal Volume (mL)	421.20 (0.08)	244.27 (27.36)	351.64 (21.29)	266.35 (27.38)	315.59 (21.63)
PIP (cm H_2O)	0.15 (0.01)	24.48 (0.18)	21.81 (0.47)	33.14 (0.33)	29.43 (0.70)
PEEP (cm H_2O)	0.03 (0.01)	12.91 (0.74)	7.22 (0.45)	18.93 (0.85)	10.85 (0.61)
Pmean (cm H_2O)	0.10 (0.01)	10.92 (0.17)	6.09 (0.12)	16.56 (0.26)	9.41 (0.13)
PIF (L/min)	39.66 (0.03)	70.71 (0.64)	64.39 (0.86)	79.59 (0.58)	79.34 (0.80)
PEF (L/min)	46.06 (0.04)	77.05 (1.69)	41.35 (2.61)	92.55 (1.36)	47.84 (2.13)

In the spontaneously breathing adult model with obstructive lung mechanics, the ΔP increased from baseline at both pressure settings, exhibiting trends in the transtracheal pressure delivery similar to those observed in the normal model. However, ΔP was comparatively higher in the obstructive model due to the higher lung resistance and turbulence in the central airways **(Table 3A)**. The oscillatory PIF decreased from baseline while the PEF was improved with both systems, with BiWaze Clear showing the greatest improvement in EFB and P/F from baseline. While BiWaze Clear showed a PIF/PEF ratio of less than 0.9 in both settings, the ratio did not improve significantly, though it increased slightly with a pressure increase to 30 cm H_2O. Volara, on the other hand, showed a higher PIF/PEF ratio greater than 1 across the settings. Overall, BiWaze Clear delivered tracheal oscillatory pressures *(Pmax,* **Figure 3***)* closer to set pressures and with less variability (SD) compared to Volara, which underdelivered oscillatory pressure by up to 25% of the set pressure during HFO **(Table 3A)**.

The addition of superimposed oscillations on spontaneous breaths resulted in lower V_T in the lung model with both systems when compared to baseline, with the lowest V_T observed with BiWaze Clear **(Table 3B**). While V_T increased when the pressure setting was increased from 20 to 30 cm H_2O with BiWaze Clear, it decreased with the Volara. Additionally, BiWaze Clear demonstrated higher PIP, PEEP, ($P\overline{aw}$) and flows in the lung model compared to Volara due to the relatively higher oscillatory pressures generated with the BiWaze Clear **(Table 3A)**.

The waveforms shown in **Figure 3** illustrate the oscillatory pressure and flow profiles generated at baseline and HFO at various pressure settings in the obstructive adult model during spontaneous breathing with both systems. Increasing the HFO pressure setting resulted in a notable increase in Pmax and ΔP and significant improvements in the PEF and EFB with BiWaze Clear. In contrast, Volara showed only marginal improvements in PEF and EFB compared to the baseline.

In the spontaneously breathing adult model with restrictive lung mechanics, intratracheal oscillatory ΔP and PIF increased from baseline, with both HFO settings for BiWaze Clear and Volara **(Table 4A)**. While BiWaze Clear at the HFO pressure of 20 improved PEF and EBF compared to baseline, the PIF/PEF ratio improved slightly from 0.86 to 0.77. In contrast, Volara at HFO of 20 demonstrated reduced PEF and EFB, leading to a worsened PIF/PEF ratio from baseline (0.86 to 1.36). Increasing the HFO pressure to 30 cm H_2O resulted in nearly double the PIF and PEF and a four-fold greater EFB compared to baseline, while optimizing the PIF/PEF ratio (0.72) with BiWaze Clear.

The tidal breathing parameters in the restrictive adult model showed similar trends between baseline and HFO settings as observed in the normal and obstructive lung models, though with reduced V_T and flows, due to the lower compliance used in this model **(see Table 4B and Figure 4)**.

PEDIATRIC MODEL

The intratracheal pressure, flow oscillation measurements, and tidal breathing parameters for the normal, obstructive, and restrictive pediatric models are shown in **Tables 5, 6, and 7**, with corresponding waveforms in **Figures 5, 6, and 7**, respectively.

In all pediatric lung models, both BiWaze Clear and Volara demonstrated increased ΔP compared to baseline breathing, with BiWaze Clear consistently delivering the highest pressures and significant improvements in PEF and EFB. Notably, BiWaze Clear was the only HFO system to consistently achieve substantially lower PIF/PEF ratios than baseline or HFO settings with Volara. Across all testing conditions, BiWaze Clear maintained PIF/PEF ratios below 1 in the pediatric models, indicating optimized expiratory flow dynamics. Additionally, BiWaze Clear demonstrated higher V_T, PIP, PEEP, and ($P\overline{aw}$) than Volara. These factors highlight BiWaze Clear's ability to maintain effective ventilation, improve secretion clearance, and provide consistent and predictable therapy outcomes, making it a more favorable option for pediatric respiratory therapy.

Normal Pediatric Model

Figure 5: Pressure and Flow Waveforms – Normal Pediatric Model

In the Normal Pediatric Model, BiWaze® Clear consistently delivered higher tracheal oscillatory pressures (ΔP) closer to set pressures and achieved significantly higher peak expiratory flow (PEF) and expiratory flow bias (EFB) compared to Volara. BiWaze Clear maintained optimal PIF/PEF ratios below 1 across all pressure settings, indicating superior mucus mobilization. In contrast, Volara exhibited lower PEF and higher PIF/PEF ratios, reflecting less effective expiratory flow dynamics.

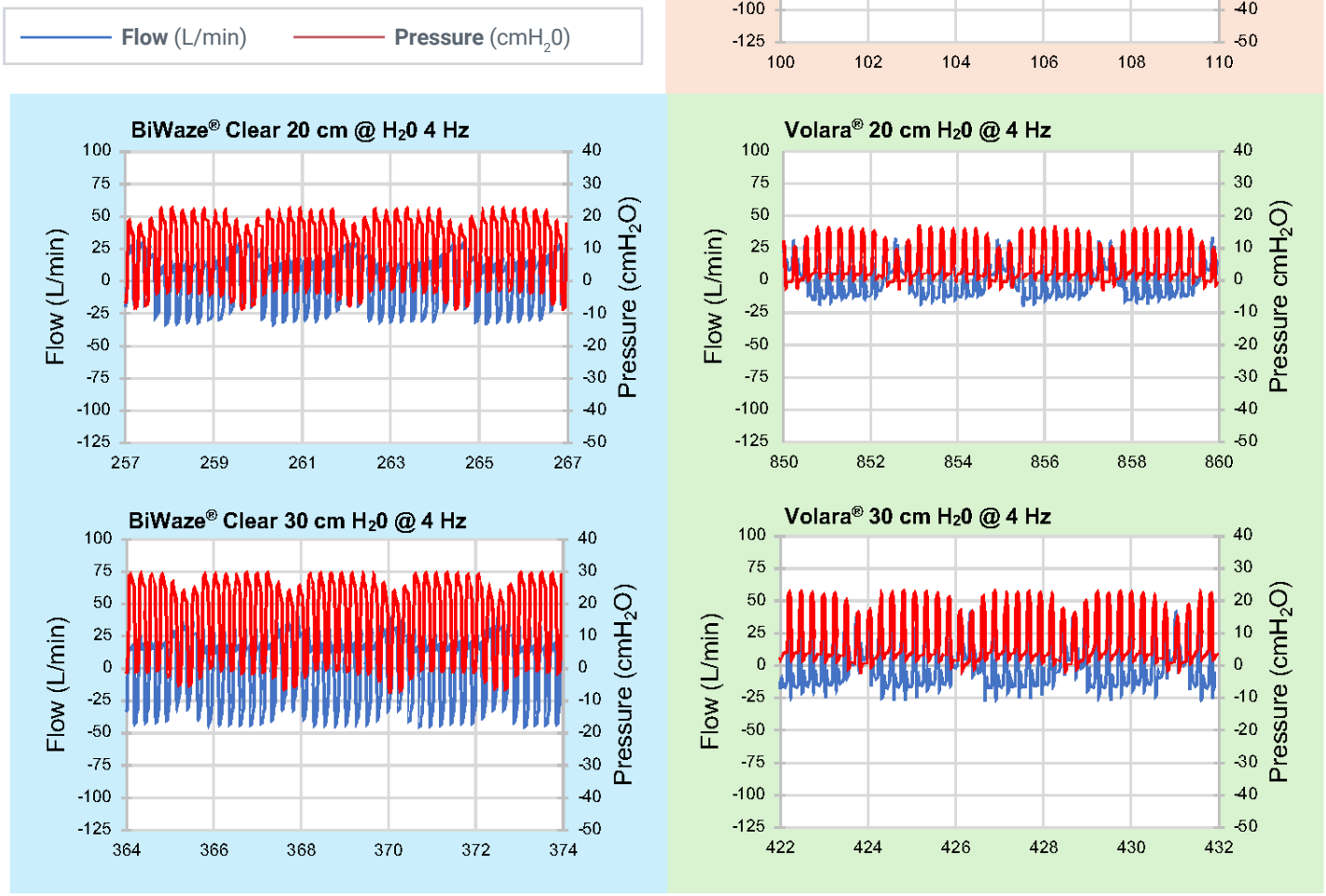


Table 5A: Tracheal Measurements - Spontaneously Breathing Normal Pediatric Model

	Baseline	20 cm H_20 @ 4 Hz		30 cm H_20 @ 4 Hz	
Measurements	**No Therapy**	**BiWaze® Clear**	**Volara®**	**BiWaze® Clear**	**Volara®**
ΔP (cm H_2O)	2.36 (0.00)	24.69 (1.00)	15.17 (4.32)	33.91 (1.03)	22.65 (1.01)
PIF (L/min)	17.58 (0.06)	28.17 (4.79)	29.05 (4.91)	35.70 (4.24)	39.49 (4.15)
PEF (L/min)	8.50 (0.12)	34.99 (4.49)	18.78 (7.27)	44.23 (4.00)	27.77 (6.25)
EFB (L/min)	-9.08 (0.12)	6.82 (6.57)	-10.27 (8.77)	8.53 (5.83)	-11.71 (7.5)
PIF/PEF (L/min)	2.07 (0.03)	0.80 (0.17)	1.55 (0.65)	0.81 (0.12)	1.42 (0.35)

Table 5B: Lung Simulator Measurements - Spontaneously Breathing Normal Pediatric Model

	Baseline	20 cm H_20 @ 4 Hz		30 cm H_20 @ 4 Hz	
Measurements	**No Therapy**	**BiWaze® Clear**	**Volara®**	**BiWaze® Clear**	**Volara®**
Tidal Volume (mL)	149.02 (6.24)	82.90 (15.06)	107.28 (26.06)	104.85 (12.07)	72.87 (18.64)
PIP (cm H_2O)	0.08 (0.01)	23.50 (0.68)	17.15 (0.12)	30.62 (0.60)	24.32 (0.22)
PEEP (cm H_2O)	0.17 (0.08)	12.06 (0.67)	6.97 (0.13)	17.44 (0.66)	9.77 (0.16)
Pmean (cm H_2O)	0.14 (0.12)	9.84 (0.54)	5.02 (0.20)	15.05 (0.52)	7.72 (0.14)
PIF (L/min)	17.34 (6.79)	36.86 (1.07)	32.31 (1.28)	47.36 (1.22)	41.89 (1.43)
PEF (L/min)	8.19 (5.91)	36.50 (2.19)	17.12 (1.33)	49.16 (2.11)	25.90 (1.03)

Obstructive Pediatric Model

Figure 6: Pressure and Flow Waveforms – Obstructive Pediatric Model

In the Pediatric Obstructive Model, BiWaze® Clear achieved higher tracheal oscillatory pressures (ΔP) and demonstrated significantly higher peak expiratory flow (PEF) and expiratory flow bias (EFB) compared to Volara. Increasing pressure settings further to 30 cm H_2O enhanced EFB and PIF/PEF ratio with BiWaze Clear, while Volara showed reduction in both parameters.

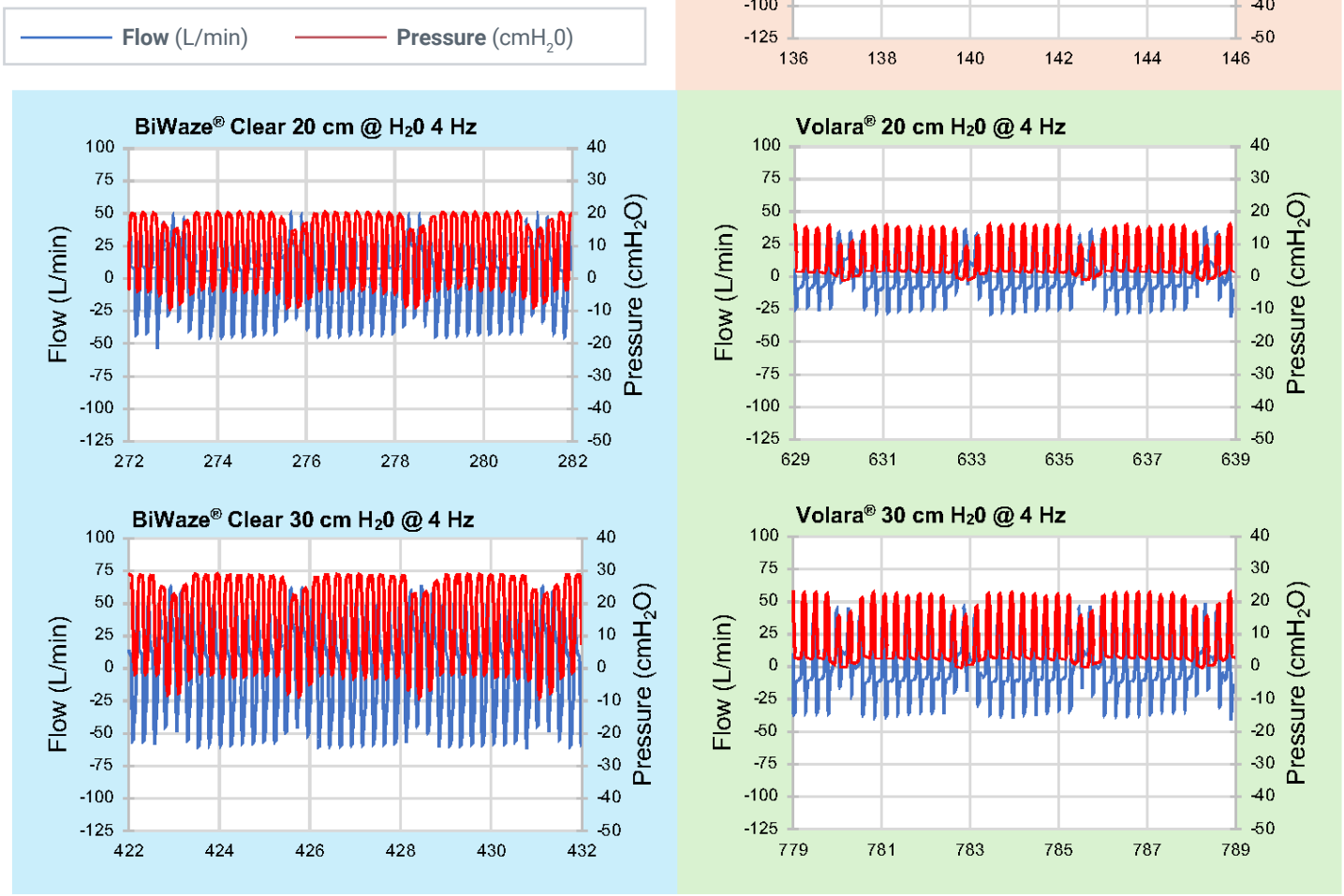


Table 6A: Tracheal Measurements - Spontaneously Breathing Obstructive Pediatric Model

	Baseline	20 cm H_2O @ 4 Hz		30 cm H_2O @ 4 Hz	
Measurements	**No Therapy**	**BiWaze® Clear**	**Volara®**	**BiWaze® Clear**	**Volara®**
ΔP (cm H_2O)	2.38 (0.03)	24.20 (1.10)	15.90 (0.78)	33.93 (1.25)	22.06 (0.93)
PIF (L/min)	18.46 (0.06)	34.67 (4.95)	30.71 (4.67)	41.88 (4.48)	40.90 (3.93)
PEF (L/min)	6.38 (0.06)	38.06 (4.36)	25.18 (6.75)	48.29 (3.83)	34.56 (6.08)
EFB (L/min)	-12.08 (0.08)	3.39 (6.6)	-5.53 (8.2)	6.41 (5.89)	-6.34 (7.24)
PIF/PEF (L/min)	2.89 (0.03)	0.91 (0.17)	1.22 (0.38)	0.87 (0.12)	1.18 (0.24)

Table 6B: Lung Simulator Measurements - Spontaneously Breathing Obstructive Pediatric Model

	Baseline	20 cm H_2O @ 4 Hz		30 cm H_2O @ 4 Hz	
Measurements	**No Therapy**	**BiWaze® Clear**	**Volara®**	**BiWaze® Clear**	**Volara®**
Tidal Volume (mL)	140.27 (5.04)	106.49 (15.95)	85.67 (22.74)	133.67 (14.53)	99.96 (20.14)
PIP (cm H_2O)	0.05 (0.01)	21.10 (0.08)	16.61 (0.16)	29.35 (0.36)	23.95 (0.31)
PEEP (cm H_2O)	0.08 (0.01)	12.45 (0.34)	7.66 (0.19)	18.19 (0.52)	10.42 (0.23)
Pmean (cm H_2O)	0.15 (0.03)	9.59 (0.23)	5.02 (0.18)	15.13 (0.33)	7.72 (0.18)
PIF (L/min)	18.60 (6.77)	55.87 (0.73)	40.40 (1.57)	67.27 (0.79)	52.74 (1.49)
PEF (L/min)	6.06 (5.84)	50.20 (1.05)	34.30 (2.37)	65.09 (3.03)	46.88 (2.94)

Restrictive Pediatric Model

Figure 7: Pressure and Flow Waveforms – Restrictive Pediatric Model

In the Pediatric Restrictive Model, BiWaze® Clear delivered higher tracheal oscillatory pressures (ΔP) closer to set pressures and achieved significantly higher peak expiratory flow (PEF) and expiratory flow bias (EFB) compared to Volara. BiWaze Clear consistently maintained optimal PIF/PEF ratios below 1, while Volara exhibited higher PIF/PEF ratios, reflecting less effective expiratory flow bias.

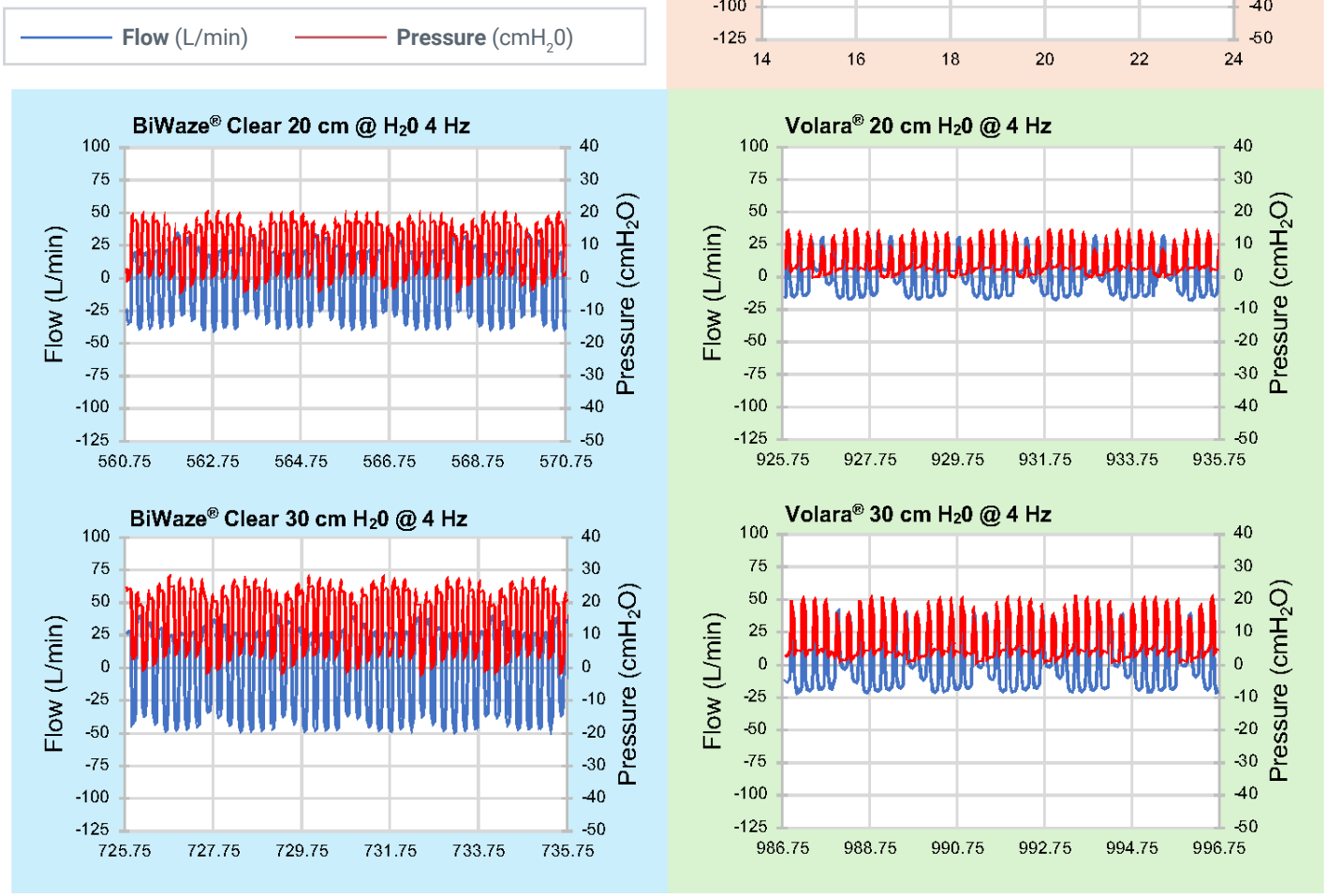


Table 7A: Tracheal Measurements - Spontaneously Breathing Restrictive Pediatric Model

	Baseline	20 cm H_20 @ 4 Hz		30 cm H_20 @ 4 Hz	
Measurements	**No Therapy**	**BiWaze® Clear**	**Volara®**	**BiWaze® Clear**	**Volara®**
ΔP (cm H_2O)	2.78 (0.03)	20.48 (1.22)	12.20 (0.7)	25.17 (1.28)	16.55 (0.74)
PIF (L/min)	18.65 (0.09)	32.68 (5.50)	32.15 (5.12)	39.03 (4.92)	43.88 (4.41)
PEF (L/min)	10.10 (0.14)	42.38 (4.67)	14.23 (6.29)	52.45 (4.41)	19.50 (6.24)
EFB (L/min)	-8.55 (0.17)	9.70 (7.22)	-17.92 (8.11)	13.42 (6.61)	-24.38 (7.64)
PIF/PEF (L/min)	1.85 (0.03)	0.77 (0.16)	2.26 (1.06)	0.74 (0.11)	2.25 (0.75)

Table 7B: Lung Simulator Measurements - Spontaneously Breathing Restrictive Pediatric Model

	Baseline	20 cm H_20 @ 4 Hz		30 cm H_20 @ 4 Hz	
Measurements	**No Therapy**	**BiWaze® Clear**	**Volara®**	**BiWaze® Clear**	**Volara®**
Tidal Volume (mL)	98.13 (2.01)	78.07 (10.69)	69.69 (34.60)	104.44 (8.70)	58.05 (11.09)
PIP (cm H_2O)	0.06 (0.01)	21.81 (0.14)	16.45 (0.26)	28.73 (0.67)	22.38 (0.22)
PEEP (cm H_2O)	0.11 (0.01)	11.59 (0.48)	5.98 (0.26)	17.13 (0.85)	8.55 (0.38)
Pmean (cm H_2O)	0.10 (0.01)	9.98 (0.26)	4.75 (0.16)	15.32 (0.61)	7.19 (0.11)
PIF (L/min)	18.03 (3.80)	32.76 (1.49)	31.25 (3.00)	36.93 (1.02)	40.08 (1.30)
PEF (L/min)	10.06 (1.20)	40.58 (0.58)	16.35 (0.87)	49.71 (1.54)	20.94 (0.78)

Discussion

The findings from our in vitro study highlight the superior performance of BiWaze® Clear in generating HFO waveforms that could be useful for lung expansion and secretion mobilization during OLE therapy. BiWaze Clear consistently delivered higher tracheal airway pressures that were closely aligned with the set pressures, outperforming Volara, which underdelivered pressure relative to the set pressure. These findings suggest that BiWaze Clear's ability to maintain higher PEEP and improved EFB can enhance alveolar recruitment, reduce atelectasis, and promote better mucus mobilization.

Decreasing atelectasis through improved alveolar recruitment and enhanced collateral channel ventilation can lead to a reduction in recurrent lower respiratory tract infections, airway wall destruction, and the development of bronchiectasis. This may translate into fewer respiratory complications, reduced need for mechanical ventilation, and improved patient comfort. Additionally, optimized PIF/PEF ratios (<0.9) indicate more effective secretion clearance, which could lead to shorter hospital stays and faster recovery times for patients with chronic respiratory conditions such as cystic fibrosis or bronchiectasis. The higher driving pressures and ($P\overline{aw}$), enhance the ability of BiWaze Clear to distribute gas flow effectively through mucus-impacted airways or collateral channels, assisting with alveolar and distal airway expansion and reducing the risk of atelectasis.

BiWaze Clear's dual blower design delivers HFO pressures with an active pressure release mechanism to maintain an expiratory flow bias, which is critical for effective mucus mobilization and to avoid airway collapse, especially for distal airways. Additionally, the closed breathing circuit and sealed handset prevent flow leakage, ensuring that pressures are preserved within in the system. These features optimize the beneficial effects of HFO, optimizing mucus mobilization.

In contrast, Volara's single-blower and single-limb circuit designs appear to contribute to pressure attenuation and variability. These limitations may reduce the therapy's effectiveness and inhibit Volara's ability to achieve EFB and PEF, both of which are critical for effective secretion clearance. Clinically, this could result in suboptimal mucus mobilization, increased risk of airway obstruction, and potentially longer recovery times for patients.

Our findings suggest that BiWaze Clear could provide superior pressure delivery and lung recruitment, which are essential for enhancing airway clearance, preventing atelectasis, and supporting efficient gas exchange.

The oscillatory pressure and flow profiles at baseline and during HFO highlight differences between the two systems under various pressure settings during spontaneous breathing in the normal adult model. BiWaze Clear consistently delivered higher Pmax values closer to the set pressures and achieved lower Pmin values than Volara.

Mobilization of mucus requires asymmetric airway oscillations with a positive EFB. Symmetric flow profiles when PIF equals PEF or when the PIF exceeds the PEF, creating an inspiratory flow bias or negative EFB, impede mucus mobilization, causing secretions to pool in the lung or are propelled further down into the peripheral airways. BiWaze Clear reliably delivered greater intratracheal flow oscillations, greater PEF, improved EFB, and optimal PIF/PEF ratios (<0.9) across the lung models.[2,6,9,10,11,12,20] Conversely, Volara showed suboptimal PIF/PEF ratios (>1), which could result in less effective mucus mobilization than baseline spontaneous breathing.

The observed limitations with Volara, lower driving pressure compared to set and inspiratory flow bias, may be attributed to the compressor design, single-limb circuit turbulence, or leakage through its integrated valve. These factors likely attenuate the pressure transmission and reduce oscillator flow performance, particularly under high-resistance or low-compliance conditions.

This study highlights the utility of using of multiple lung models to reveal distinct differences in EFB and pressure dynamics, providing insights into the conditions needed for optimal lung recruitment and mucus mobilization. While promising, the results should be interpreted cautiously, as in vitro findings may not fully predict in vivo outcomes. Future studies have been planned to evaluate the clinical efficacy of HFO on physiologic improvements related to this form of airway clearance. Additionally, the HFO delivered by BiWaze Clear warrants further investigation to understand the potential impact on gas trapping, secretion mobilization, and overall patient outcomes.

Conclusion

This study provides a comprehensive evaluation of the performance of BiWaze Clear and Volara systems during high-frequency oscillation (HFO) therapy with different pressure settings using multiple in vitro lung models, including normal, obstructive, and restrictive adult and pediatric conditions. The findings demonstrate that BiWaze Clear consistently outperforms Volara in delivering precise and effective mechanical high-frequency oscillations, which is crucial for airway clearance therapy. By improving key parameters such as PEEP, EFB, and PIF/PEF ratios, BiWaze Clear has the potential to significantly enhance patient outcomes. These improvements could lead to better secretion clearance, reduced lung inflammation, and faster recovery, ultimately improving quality of life and reducing the burden on healthcare resources.

BiWaze Clear exhibited higher intratracheal pressures and flow oscillations that closely aligned with set pressures, achieving superior peak expiratory flow (PEF), expiratory flow bias (EFB), and optimal PIF/PEF ratios (<0.9). These results indicate that BiWaze Clear could enhance mucus mobilization and airway stability, supporting effective secretion clearance and reducing the risk of atelectasis. By contrast, Volara frequently underdelivered pressure showed suboptimal EFB and often displayed PIF/PEF ratios exceeding 1, which could impair secretion mobilization and clearance.

Key design features of BiWaze Clear, such as its dual-blower system, active pressure release mechanism, and sealed breathing circuit, were instrumental in maintaining reliable pressure delivery and optimizing airflow dynamics. These features provide significant advantages in maintaining expiratory flow bias and minimizing leakage, particularly under high-resistance or low-compliance conditions.

The study also highlights the challenges of achieving EFB and flow performance with Volara, potentially due to pressure attenuation caused by its single-limb circuit and integrated leak valve. These limitations were more pronounced in restrictive and obstructive lung models, emphasizing the need for precise pressure control in airway clearance therapy.

While the results suggest that BiWaze Clear may provide superior therapeutic benefits, further clinical studies are needed to evaluate its impact on physiologic outcomes, including secretion clearance and lung expansion. This in vitro study is a foundational step in understanding the mechanisms and potential clinical advantages of HFO, particularly with systems like BiWaze Clear that deliver consistent and effective oscillatory pressures.

These findings underscore the importance of advanced design and precise pressure control in optimizing airway clearance therapy, offering valuable insights for respiratory therapists and healthcare professionals seeking effective solutions for managing mucus mobilization and airway stability in diverse patient populations.

KEY FINDINGS SUMMARY

- **Enhanced Mucus Mobilization:**
  BiWaze® Clear demonstrated consistent positive expiratory flow bias (EFB) and optimal PIF/PEF ratios (<0.9), critical for effective secretion clearance.
- **Superior Pressure Delivery:**
  BiWaze® Clear delivered higher and more consistent tracheal pressures (ΔP) which closely aligned with set values while maintaining precision and reducing variability.
- **Effective Airway Clearance Across Models:**
  Waveform analysis shows potential for high clinical efficacy of BiWaze® Clear in normal, obstructive, and restrictive lung conditions for adult and pediatric models.
- **Dual-Blower Design Advantages:**
  BiWaze Clear's dual-blower system provided superior control of inspiratory and expiratory flows, reducing leakage and optimizing pressure dynamics.
- **Potential for Improved Clinical Outcomes:**
  BiWaze® Clear showed a potential to reduce atelectasis, enhance lung recruitment and secretion mobilization through precise and reliable airway clearance therapy.

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