WHITE PAPER

BiWaze® Clear System – evaluation of aerosol delivery in vitro

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Introduction

An issue when caring for patients with a respiratory condition is when excess mucus production surpasses the normal capacity of the body to clear it from the airways, it leads to blockage, collapsed lungs and impaired respiratory function.[1] To address this issue, oscillating lung expansion (OLE) therapy is used to mobilize and remove mucus, helping to reinflate partially or fully collapsed lungs.[2,3] OLE therapy can be administered noninvasively using a face mask, mouthpiece, or trach adapter. It combines various treatments for airway clearance, including positive expiratory pressure, high-frequency oscillations, and therapeutic aerosol delivery.

Positive expiratory pressure increases airflow to the collapsed lung regions and increases functional residual capacity.[4] High-frequency oscillations generate small pressure bursts, known as "micro coughs," which increase airflow velocity, shear mucus, and facilitate its mobilization from the peripheral airways.[2,3] During OLE therapy, aerosol medication is also delivered to reduce inflammation, bronchoconstriction, and thin secretions.

In the past, there were concerns about the effectiveness of OLE therapy due to low aerosol deposition caused by limitations in older device designs. The aim of this in vitro study was to compare the aerosol medication delivery efficiency of the two newest OLE systems during simulated therapy.

New Technology

The BiWaze® Clear System (ABM Respiratory Care, USA) is an innovative OLE system that has recently obtained FDA 510k Clearance. BiWaze Clear has a unique two-blower design precisely engineered to drive and separate the inhaled and exhaled airflow. BiWaze Clear has a proprietary Dual Lumen Breathing Circuit which includes a coaxial bacterial/viral filter, coaxial breathing tube, handset, Aerogen® Solo nebulizer (Aerogen, Ireland), and a patient interface. The Aerogen Solo nebulizer is electronically powered and controlled by the BiWaze Clear through the Aerogen power cable provided with the BiWaze Clear system.

Figure 1: BiWaze Clear Control Unit and BiWaze Clear Dual Lumen Breathing Circuit

Aerosol delivery with BiWaze Clear was compared to the Volara (Baxter-Hillrom, USA), which received FDA clearance in 2020. The Volara uses a single-limb breathing circuit which includes a standard filter, standard breathing tube, handset with an integrated expiratory leak valve, and a Sidestream jet nebulizer (Philips Respironics, USA) which is driven from an internal motor generating compressed air through the nebulizer and into the handset for therapy.

While both systems provide OLE therapy, they use different abbreviations for the treatment phase names. BiWaze Clear calls positive expiratory pressure PEP, while Volara calls it CPEP. BiWaze Clear calls high-frequency oscillations OSC, while Volara calls it CHFO.

Study Method

Scintigraphy (gamma) imaging was used to quantify inhaled aerosol deposition to the upper airways and lungs as well as residual losses to the OLE systems' components, nebulizer, and fugitive aerosol transmission to the

atmosphere. The OLE systems were programmed with the same settings to complete a typical 10 minute therapy. The PEP/CPEP phase was set to a typical setting of 10 cm H_2O and the nebulizer was set to run throughout the therapy. The OSC/CHFO phase was set to a typical setting of 20 cm H_2O with a frequency of 4 Hz and the nebulizer was set to run throughout the therapy.

A spontaneous breathing adult lung model, ALS 5000 (Ingmar Medical, USA,) was configured with 12 breaths/min frequency, tidal volume of 700 mL, compliance of 100 mL/cm H_2O and resistance of 10 cm H_2O/L/s. A 3D-printed adult upper airway nasotracheal (NT) cast was attached to a simulated trachea and lung model. Each OLE system's proprietary handset was attached to the mouthpiece and inserted into the oral opening of the upper airway model, and the nostrils were covered to minimize the leak from the nose (see Figure 2). A filter was attached between the tracheal outlet and the lung model to capture inhaled aerosol at the distal trachea and quantify the inhaled lung dose. The handset, nebulizer, mouthpiece, nasal airway, and trachea were placed into a sealed plethysmograph box (see Figure 2). A filter was attached to a vacuum toward the top of the plethysmograph box to capture fugitive aerosols that leaked out of the OLE system during therapy.

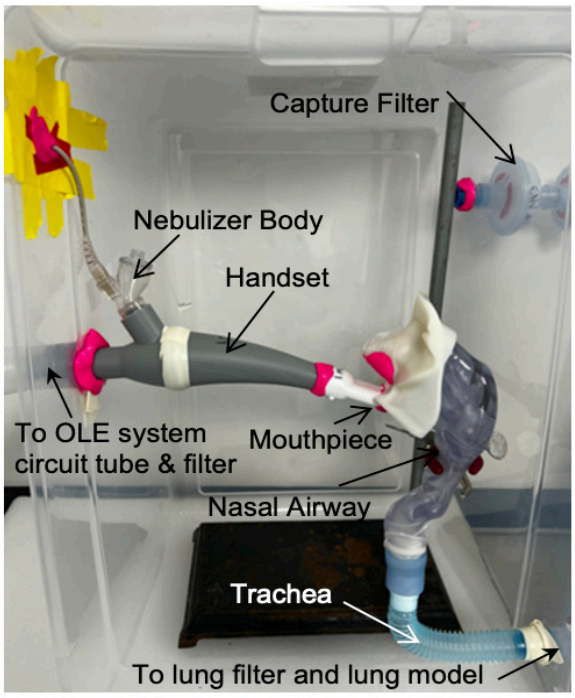

Figure 2: Experiment setup

Technetium (99mTc) pertechnetate (RLS Bio, USA), a nonabsorbable radiopharmaceutical particulate, was mixed with 2.5 mL normal saline and nebulized as a radio-tagged aerosol to be a surrogate for inhaled medication. The deposited aerosols were quantified with a SPECT gamma camera, GE Starcam XCT (GE Healthcare, USA) by scanning the following regions of interest (ROI):

1) OLE system components (i.e., bacterial/viral filter, breathing circuit, nebulizer, handset, mouthpiece)
2) Nasopharyngeal and tracheal airways
3) Lung (filter)
4) Plethysmograph and filter (fugitive aerosol)

A 20 µCi dose of 99mTc was confirmed with a dosimeter. The radioaerosol solution was placed into the nebulizer, then scanned with the dosimeter and gamma camera to correlate the loading dose (µCi) to gamma camera counts (µCi/ct.). A timer was started to correct for radio decay over time. The 99mTc loaded nebulizer was inserted into the handset within the sealed plethysmograph box. The radioaerosol solution (2.5 mL) was nebulized to completion with BiWaze Clear using the Aerogen Solo. The Volara with the Sidestream was noted to have a volume of liquid remaining in the nebulizer reservoir after the typical 10 minute therapy, so the therapy was continued for 5 more minutes for a total therapy time of 15 minutes and no liquid remained in the reservoir.

After the completion of therapy, the experimental set-up was kept enclosed within the sealed plethysmograph box for five minutes, enabling the capture of fugitive aerosols within the chamber filter. Each component was carefully disconnected in series, and individual ROIs were scanned with the gamma camera to quantify deposited radioaerosol. The fugitive aerosols were calculated as the sum of radiation counts deposited within the plethysmograph box and outlet vacuum filter. The radiation counts at each ROI was converted to dose (µCi) based on the calibration conversion factor and adjusted for radioactive decay. A mass balance was calculated, and activity counts detected in each ROI were expressed as a percentage (%) of the total sum of the counts. Also, images were acquired to illustrate the spatial distribution of radioaerosol deposited within the respective ROIs using low energy, high-resolution function with a 256x256 pixel/count matrix. The digital color spectrum was selected, with red showing the highest pixel/count activity (aka hotspots) and green, blue, and black illustrating progressively lower activity levels, respectively.

Test Results

The mass balance of deposited radioaerosol droplets within the different ROIs of both BiWaze Clear and Volara after OLE therapy, are shown in Tables 1 and 2, respectively.

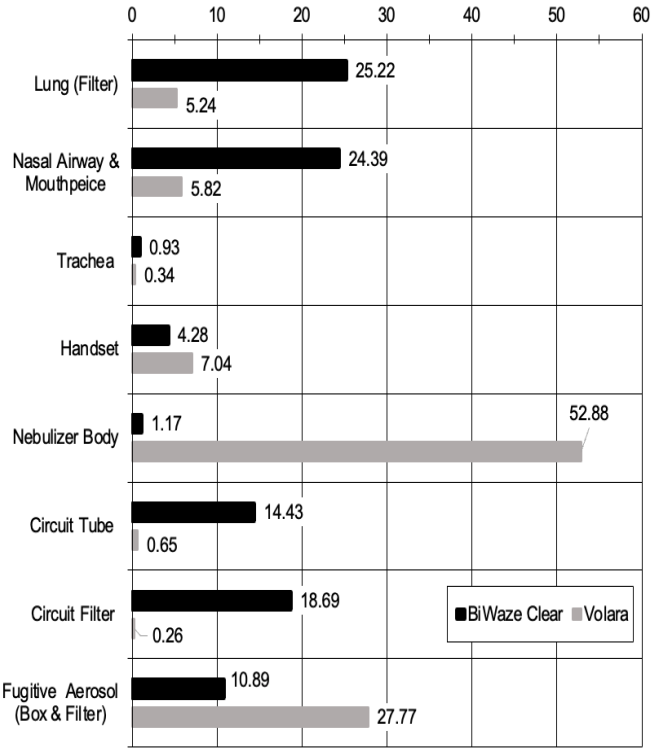

Table 1: Percent of Regional Aerosol Deposition for BiWaze Clear and Volara with the setting of PEP/CPEP 10 cm H_2O

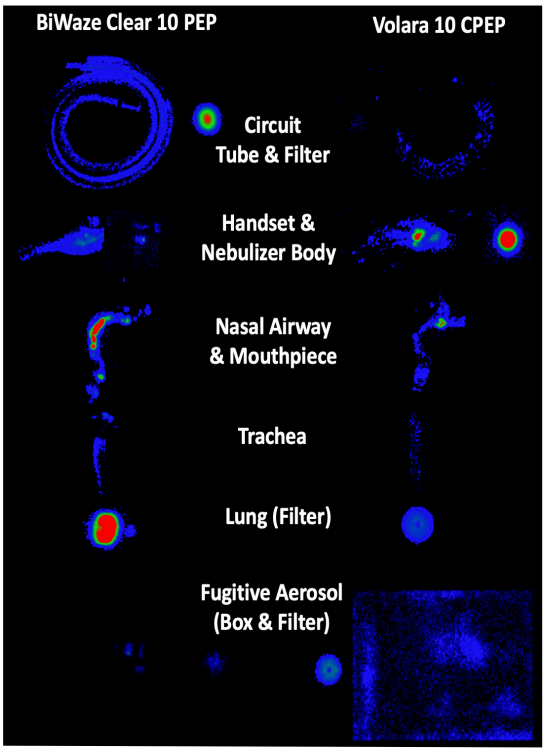

Figure 3: Gamma camera images showing aerosol deposition at different regions of interest for BiWaze Clear and Volara with the setting of PEP/CPEP 10 cm H_2O

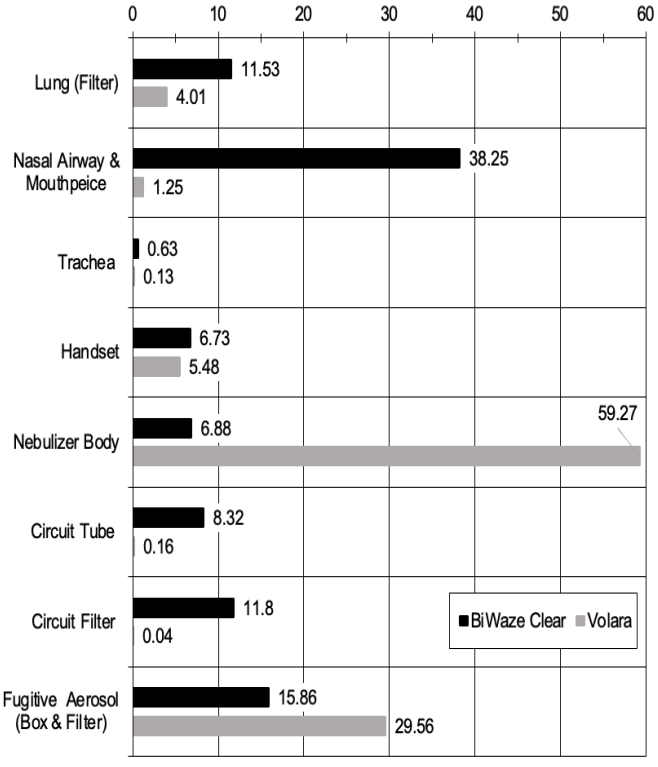

Table 2: Percent of Regional Aerosol Deposition for BiWaze Clear and Volara with the setting of OSC/CHFO 20 cm H_2O at 4 Hz

The corresponding gamma camera images illustrating the aerosol deposition with different regions of interest for both BiWaze Clear and Volara are shown in Figures 3 and 4, respectively.

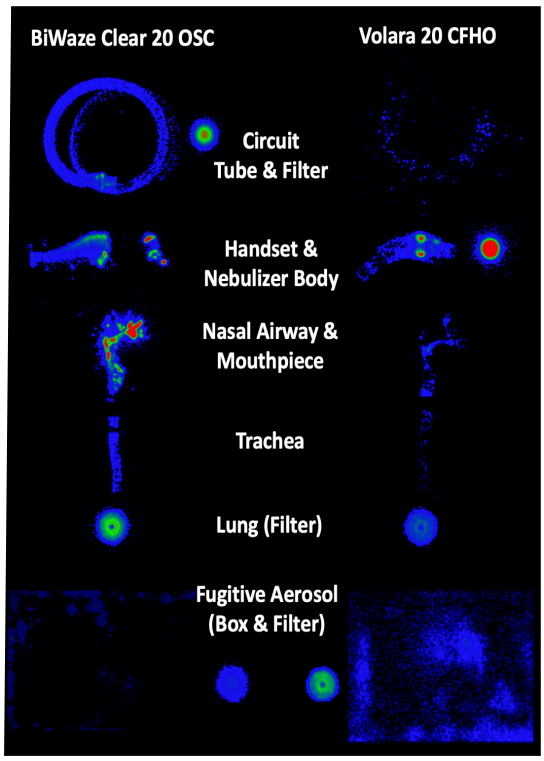

Figure 4: Gamma camera images showing aerosol deposition at different regions of interest for BiWaze Clear and Volara with the setting of OSC/CHFO 20 cm H_2O at 4 Hz

BiWaze Clear and Volara had greater inhaled lung deposition with PEP/CPEP than OSC/CHFO therapy phases. The BiWaze Clear showed a 5-fold greater lung deposition

with PEP and a 3-fold greater lung deposition with OSC therapy than Volara. Increased nasal airway deposition naturally led to an increase in lung delivery efficiency with BiWaze Clear. The residual nebulizer losses were high (>50%) with the Volara and low with BiWaze Clear (<7%) for both therapy phases of OLE therapy. The depositional losses within the BiWaze Clear Dual Lumen Breathing Circuit (closed circuit design) coincided with a lower concentration of fugitive aerosol released to the atmosphere than Volara. The Volara had low deposition in the lung filter and single-limb breathing circuit (open circuit design), with about 1/3 of the aerosol dispersed through their proprietary handset's expiratory leak valve as fugitive aerosols.

Discussion

The administration of aerosols during OLE therapy remains prevalent in patients receiving airway clearance in both the hospital and home healthcare settings. This is the first in vitro study to evaluate aerosol delivery with the BiWaze Clear and Volara systems. The major finding of these experiments demonstrates that BiWaze Clear has a higher medication delivery efficiency of inhaled aerosol than Volara.

We attribute these findings to multiple factors which include the use of the Aerogen Solo's vibrating mesh nebulizer which has an aerosol output 2 to 3 times greater than a jet nebulizer, with a documented low residual medication volume in the nebulizer following therapy (<0.2 mL).[5] BiWaze Clear's Dual Lumen Breathing Circuit is a coaxial, closed circuit and has been optimized to prevent aerosol retention, minimize expiratory medication losses, and increase the availability of small particles for inhalation. It has been suggested that bi-directional (transitional) flows through a valveless handset could result in high impactive losses and reduced aerosol delivery with an OLE system. However, this was not the case with BiWaze Clear, which had only 4 - 6% loss of radio-tagged aerosol. The BiWaze Clear's handset may prevent aerosol waste to the circuit by holding some of the small, exhaled particles and those continuously generated by the nebulizer on exhalation to remain within the handset chamber, serving as a reservoir to increase the concentration of inhaled particles during subsequent breaths. Furthermore, the BiWaze Clear Dual Lumen Breathing Circuit's bacterial/viral coaxial filter sufficiently captured exhaled aerosols and prevented high fugitive aerosol losses.

In a previous study, Li et al. showed that an inhaled dose with a gas-powered jet nebulizer and aerosol mask alone was as high as 10%, but when the same nebulizer was placed into a predicate OLE system, the MetaNeb (Baxter-Hillrom, USA) proprietary circuit, consisting of a venturi and entrainment port, the inhaled dose was reduced to 2% during the high-frequency oscillation (CHFO) therapy phase.[6] They speculated that MetaNeb's handset design increases the impact-related loss of larger aerosol particles. The Volara showed a similar low inhaled dose (4%) as the MetaNeb study when applying CHFO. The MetaNeb and Volara OLE systems share several common features: they use jet nebulizers, apply aerosol through a single-limb circuit, and apply a manifold leak (aka exhalation valve) into the handset to eliminate carbon dioxide.

We identified a leak manifold in the Volara handset that produced fugitive aerosols, resulting in a 2-fold increase compared to the closed breathing circuit of the BiWaze Clear system. The fugitive losses in Volara significantly impacted medication delivery. Even after extending the nebulizer's runtime by 5 minutes beyond the manufacturer's recommended treatment time, the residual losses within Volara's nebulizer (50-60%) remained the primary factor affecting delivery efficiency.

Conclusion

In conclusion, our study found that BiWaze Clear's aerosol efficiency was superior to Volara. BiWaze Clear delivered a 5-fold greater aerosol deposition with PEP therapy and a 3-fold greater aerosol deposition with OSC therapy to the patient's lungs compared to Volara. Additionally, the fugitive aerosols generated by Volara were 2-fold greater than those produced by BiWaze Clear.

Short-term physiologic studies designed to evaluate the effectiveness of aerosol therapy on secretion removal with BiWaze Clear and other forms of airway clearance are underway.

References

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