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Note: Device names previously referencing ‘Aeroneb’ are now referencing ‘Aerogen’. The Aerogen Ultra was also previously known as Aeroneb Solo Adapter.
Aerogen’s vibrating mesh nebulizer technology, available within the Aerogen® Solo, Pro and also the NIVO, has been adopted for use across many areas of the hospital during a variety of ventilatory support including conventional mechanical ventilation, high frequency oscillatory ventilation, non-invasive ventilation and nasal high flow. This technology is becoming the standard of care in many hospitals and clinical researchers have established its superior performance and potential for cost savings in comparison to other nebulizer offerings.

Aerogen nebulizers can provide the patient with up to 9 fold higher drug dose than a standard small volume (jet) nebulizer (SVN) during mechanical ventilation.\cite{1} It is also cost effective, as shown by multiple hospitals switching to Aerogen and observing significant savings.\cite{2}-\cite{4} The Aerogen technology is not only available for use during both invasive and non-invasive ventilation but can be used with spontaneously breathing patients with mouthpieces and masks throughout the acute care setting. The Aerogen Ultra enables effective aerosol therapy of over 30% inhaled dose available to the patient.\cite{5}
2. High Efficiency Nebulization During Ventilation

The Aerogen nebulizers are highly efficient vibrating mesh nebulizers which can be used inline during any type of respiratory support including mechanical ventilation, high frequency oscillatory ventilation (HFOV), non-invasive ventilation (NIV), continuous positive airway pressure (CPAP) and Nasal High Flow (NHF).\textsuperscript{[1,6]-[10]} The nebulizer utilizes active vibrating mesh technology, where energy applied to the vibrational element, causes vibration of each of the 1000 funnel shaped apertures within the mesh. The mesh acts as a micropump drawing liquid through the holes producing a low velocity aerosol optimized for targeted drug delivery to the lungs. The Aerogen nebulizers can deliver up to 9 times more aerosol dose compared to standard SVNs during mechanical ventilation,\textsuperscript{[1,6]} and outperforms standard SVNs when positioned at both the wye (proximal to the patients in the inspiratory limb) and before the humidifier.\textsuperscript{[1]} (Figure 1). This difference in aerosol deposition related to positioning was originally studied by Ari et al. and demonstrated improved deposition when the Aerogen Solo was placed before the humidifier compared to at the wye with both adult and pediatric settings when utilizing a bias flow;\textsuperscript{[6]} without bias flow improved aerosol deposition was noted when the nebulizer was positioned closer to the patient.\textsuperscript{[11]}

![Figure 1](image-url)

**Figure 1.** Comparison of drug deposition after aerosol therapy through a ventilation circuit with standard SVNs and the Aerogen Solo. The position of the nebulizer tested included: at the wye and before the humidifier (closer to the ventilator). The Aerogen Solo outperforms both SVNs in both positions in the ventilator circuit. Adapted from [1].
Physiological lung dose was studied in a neonatal animal model, where quantification of 99mTc-DTPA was measured after aerosol inhalation through a ventilator circuit, tested with both a SVN and the Aerogen Pro. The Aerogen Pro demonstrated a 25 fold higher deposition of aerosol in the lungs compared to a standard SVN.[12] The Aerogen Pro achieved a lung dose of 13% and the difference in aerosol deposition between the two nebulizers can be clearly observed in the scintigraphy pictures below (Figure 2).[12]

![SVN vs Aerogen Pro](image)

Figure 2. Lung Scintigraphy images of a ventilated neonate animal model after inhalation of 99mTc-DTPA using either a SVN or the Aerogen Pro nebulizer. The Aerogen Pro delivered a significantly greater lung dose than the SVN. Adapted from [12].

The superior drug deposition available with Aerogen nebulizers is associated with the minimal residual volume left in the device after nebulization. Standard SVNs on average leave up to half of the drug behind which can be quite costly when using more expensive drugs.[13] Dubus et al. observed that the standard SVN has a residual volume of 1.1 mL after nebulization of 3-mL of 99mTc-DTPA. In contrast the Aerogen Pro had a residual volume of 0.1 mL after nebulization of 0.5-mL.[12]
Although drug delivery efficiency has been shown to be similar between a pressurized metered dose inhaler (pMDI) and the Aerogen nebulizer, the actual dose emitted from the pMDIs (e.g., 100 ug per actuation with salbutamol) are much lower than the typical 2.5 mg dose used with a nebulizer. In addition, pMDIs aren’t without difficulties as failure to synchronize actuations with inspiration has been shown to reduce the aerosol drug delivery. It is also important to ensure canisters are shaken before use as the dose may vary due to separation from the propellant. There are several studies which provide evidence that the cost savings achieved by switching from combivent MDI to the Aerogen Solo are significant. Blake et al. discussed substantial cost savings in conjunction with staff satisfaction after switching. They also discussed a potential system wide annual saving of up to $1.74 million across 105 hospitals.
3. Optimal Drug Delivery During NIV & NHF

The Aerogen nebulizer can also be connected to a NIV circuit and can deliver aerosol during NIV and CPAP. Studies have shown that aerosol deposition with the Aerogen Pro connected into the circuit, patient side of the leak valve, provided 2-3 fold more inhaled drug than a standard SVN in the same position. The importance of positioning of the nebulizer is observed in this study as the Aerogen Pro efficiency of 51% is reduced to 19% if connected before the leak valve (Figure 3).[7]

![Diagram of in vitro aerosol testing during NIV. Positioning of the Aerogen Pro during NIV is optimal in position A, patient side of the leak valve. Adapted from [7].](image)

Additional studies have confirmed these data with the Aerogen NIVO which fits directly into an NIV mask.[8][17] In an in vitro comparison of a vibrating mesh (NIVO) nebulizer vs a SVN during NIV, a similar difference in inhaled drug was noted (Figure 4).[17] It’s also important to note that the efficiency of the Aerogen Solo and NIVO has been directly compared and similar aerosol deposition has been reported.[18]
Figure 4. Aerosol deposition during NIV using the Aerogen NIVO and a SVN. During both BIPAP and CPAP aerosol deposition was higher with the Aerogen NIVO compared to the SVN. Adapted from [17].

Lung dose correlates directly to these in vitro studies. Dornelas et al. completed a scintigraphy study with healthy patients using the Aerogen NIVO during NIV and quantified the inhaled dose to be 18.3% for the vibrating mesh nebulizer and 7.85% with the SVN. A lung dose of 5.9% was measured with the vibrating mesh nebulizer which was 3-4 fold greater than the 1.6% measured with a standard SVN (Figure 5).[19]
Figure 5. Distribution of aerosol in the lungs of healthy patients after nebulization with a SVN and Aerogen NIVO. Lung deposition is significantly greater with the Aerogen NIVO. Adapted from [19].

Aerosol therapy during the use of Nasal High Flow can be provided by the Aerogen Solo inline with a variety of NHF systems, delivering aerosol directly through the nasal cannula. This technique allows aerosol delivery without interruption of oxygen flow and pressure and is more effective than placement of an aerosol mask over the nasal cannula. Preliminary studies have demonstrated sub-optimal delivery of aerosol with the placement of aerosol masks over the cannula compared to taking the cannula off to administer aerosol therapy.[20] Initial studies have demonstrated that the Aerogen Solo can provide effective aerosol therapy through the cannula of a NHF system.[9],[21],[22] Ari et al. studied aerosol delivery in pediatric patients and showed that an inhaled dose of 11% was achievable at a gas flow rate of 3L/min. The effect of flow and gas type does modify the aerosol deposition where heliox and lower flow rates have a favorable effect on aerosol dose.[9] More recent research into adult NHF showed that even at flow rates of 30L/min it is still possible to achieve a lung dose of 14%.[22]
4. Aerogen Nebulizer Technology For Patients “Off-Ventilation”

Aerogen has now developed the Aerogen Ultra, which can be used with their existing vibrating mesh nebulizer (Aerogen Solo) for spontaneously breathing patients with mouthpiece and mask for use across the entire acute care setting. This new Aerogen Ultra will provide a connection to low flow oxygen and can be used for both intermittent and continuous treatments in both pediatric and adult patients (Figure 6). The device is composed of a valved collection chamber which connects the Aerogen Solo nebulizer and a mouthpiece or facemask (Figure 6).

The innovative design of the device’s valved system controls the flow of air through the aerosol chamber. On inhalation, the air is drawn through the inlet valve on the base of the device creating a flow of air or oxygen through the device. This purges the aerosol chamber of aerosol and delivers drug to the patient via the mouthpiece. When the patient breathes out, the inlet valve closes and the exhalation valve on the mouthpiece opens. This allows the patient to exhale through the port on the mouthpiece while the aerosol chamber is refilled by the Aerogen Solo nebulizer.

Figure 6. Aerogen Ultra
Initial bench testing has demonstrated the aerosol drug deposition of this new offering compared with SVN is highly efficient providing an inhaled dose available at the end of the trachea of up to 35% with no added flow\textsuperscript{[5]} (Figure 7). In addition, as the Aerogen nebulizers have minimal residual volume remaining in the nebulizer after aerosol treatments, more drug will therefore be available to the patient compared to a standard SVN.\textsuperscript{[13]} Even with the addition of 2 liter per minute of flow through the device, 15% inhaled dose is still achievable with the Aerogen Ultra with a mouthpiece or valved face mask (Figure 7).\textsuperscript{[5]}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{chart.png}
\caption{Inhaled dose of the Aerogen Ultra compared to a standard jet nebulizer with 2 liters per minute of flow through the device. The mouthpiece, a valved and open mask were tested where an enhanced efficiency was noted with mouth piece or valved mask. When no flow is utilized, 35% inhaled dose can be achieved with the mouthpiece. Adapted from [5].}
\end{figure}
The Aerogen Ultra also provides a more efficient delivery of medication in a shorter period of time as observed by Hickin et al. (Figure 8): “Our lab-based study has shown that a mesh nebuliser is quicker and more effective than a jet nebuliser, delivering more salbutamol over a shorter period of time.” Dr Hickin was interested in obtaining data on the Aerogen Ultra before using the device in a clinical study where it would be compared to a small volume nebulizer for use in COPD patients in the Emergency Department. Initial data on the device performance has supported their hypothesis “that a mesh nebuliser is a more effective method of delivering inhaled bronchodilators to patients with respiratory disease” as the study demonstrated that in a COPD model the device provides more than 8 times the medication in half the time (Figure 8).[23]

![Figure 8. The dose rate of the Aerogen Ultra compared to a SVN along with the nebulization time, respirable dose and residual volume. The Aerogen Ultra provides a superior dose in a shorter period time with minimal residual volume left in the nebulizer. Adapted from [23]](image-url)
5. Summary

The Aerogen nebulizers provide superior aerosol therapy within the intensive care environment during ventilation, NIV and NHF. In addition to the nebulizer’s optimal performance, substantial cost savings have also been acknowledged when hospitals make the transition to the device. This high class nebulization therapy is now available across the acute care setting so that optimal aerosol treatments can be delivered to all respiratory patients including those that do not require mechanical ventilatory assistance.
6. References


4. Streepy KS, Dawson AM, Grigonis AM, Hammerman SI, Snyder LK. Conversion from metered dose inhalers to a vibrating mesh nebulizer in long term acute care hospitals: Cost effectiveness and respiratory staff perception Poster presentation at American Society of Health-System Pharmacists 2013

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