Aerogen®

Pioneering Aerosol Drug Delivery

Clinical White Paper

Table of Contents

1 Abstract

Aerogen's vibrating mesh technology, available within the Aerogen® Solo, Aerogen® Pro and 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 high flow nasal cannula. Clinical researchers have established its superior performance in bench and imaging studies[1-13]. Aerogen devices can provide the patient with up to 9 fold higher drug dose than a standard small volume nebuliser (SVN) during mechanical ventilation[2]. In paediatric patients in respiratory failure Aerogen aerosolised Salbutamol resulted in improved lung recruitment[14]. It is also cost effective, as shown by multiple hospitals in the US switching to Aerogen and observing significant savings compared to MDIs[15-18]. 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 where Aerogen® Ultra enables effective aerosol therapy of up to 35% inhaled dose available to the patient[19]. Recent clinical data have shown significant improvements in clinical outcomes and reduced drug dose in the ED for all patients requiring Salbutamol via the Aerogen Ultra [37].

Key Take Away Points

- Aerogen's vibrating mesh technology has been adopted across the hospital and used during MV, HFOV, NIV, HFNC and with spontaneous breathing patients.
- Aerogen technology enables optimal aerosol therapy across all ventilatory support.
- Bench, imaging and case studies all provide evidence of the superior performance of the Aerogen aerosol drug delivery devices.
- Substantial cost savings have been observed in comparison to MDIs in the US.
- Improved lung recruitment compared to baseline can be achieved with Aerogen aerosolised Salbutamol in paediatric respiratory failure patients.
- Improved clinical outcomes observed with use of the Aerogen Ultra in the ED.

2 High Efficiency Aerosol Drug Delivery During Ventilation

Aerogen devices are highly efficient vibrating mesh aerosol drug delivery systems 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 High Flow Nasal Cannula (HFNC)[1-4, 7, 20, 23]. The Aerogen Solo utilises 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 optimised for targeted drug delivery to the lungs. The Aerogen device can deliver 9 times more aerosol dose compared to standard small volume nebuliser during mechanical ventilation[2], and outperforms all standard small volume nebulisers when positioned at both the wye (proximal to the patients in the inspiratory limb) and before the humidifier[2] (Figure 1). While the Ultrasonic nebuliser efficiency is comparable to the Aerogen Solo at the Y, there are many limitations with the device which include an inability to aerosolise viscous solutions, heat generation which can degrade some solutions and large residual volumes[21]. Furthermore the use of ultrasonic nebulisers is now minimal in the hospitals.

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 paediatric settings when utilising a bias flow[1]; without bias flow improved aerosol deposition was noted when the nebuliser was positioned closer to the patient[22].

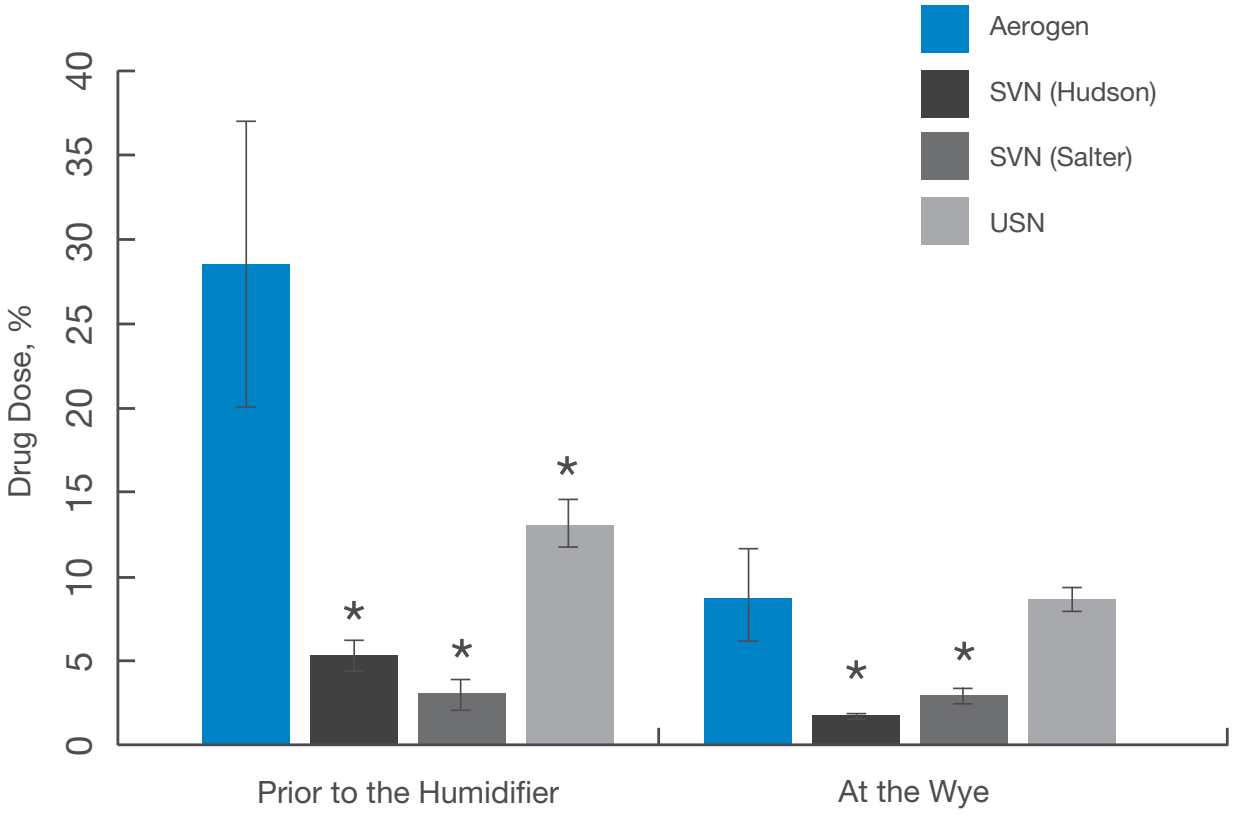


Figure 1

Comparison of drug deposition after aerosol therapy through a ventilation circuit with standard small volume nebulisers, ultrasonic and the Aerogen Solo. The position of the nebuliser tested included: at the wye and before the humidifier (closer to the ventilator). In this paediatric model of mechanical ventilation with bias flow the Aerogen Solo outperforms both small volume nebulisers in both positions in the ventilator circuit. *p<0.001. Adapted from [2].

Physiological lung dose was studied in an infant animal model, where quantification of radiolabelled aerosol was measured after inhalation through a ventilator circuit, tested with both a small volume nebuliser and the Aerogen Pro. The Aerogen Pro demonstrated a 25 fold higher deposition of aerosol in the lungs compared to a standard small volume nebuliser[13]. The Aerogen Pro achieved a lung dose of 13% and the difference in aerosol deposition between the two systems can be clearly observed in the scintigraphy pictures below (Figure 2)[13].

The superior drug deposition available with Aerogen is associated with the minimal residual volume left in the device after nebulisation. Standard small volume nebulisers on average leave up to half of the drug behind which can be quite costly when using more expensive drugs[24]. Dubus et al. observed that the standard small volume nebuliser has a residual volume of 1.1 mL after nebulisation of 3-mL of solution. In contrast the Aerogen Pro had a residual volume of 0.1 mL after 0.5-mL[13].

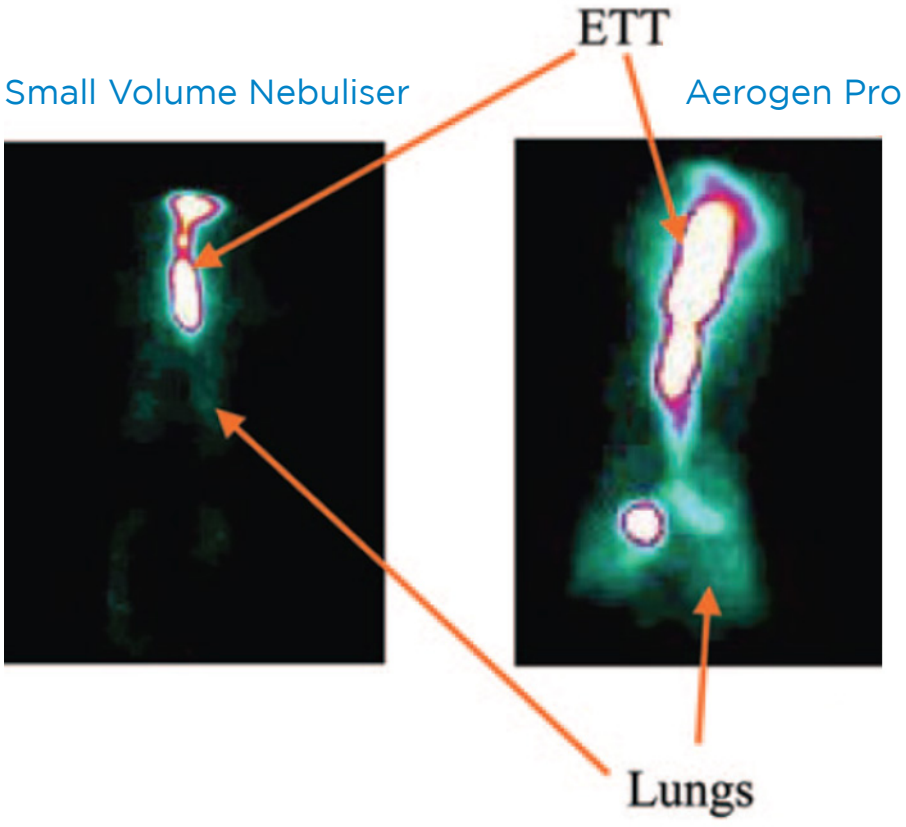


Figure 2

Lung Scintigraphy images of a ventilated infant animal model after inhalation of radiolabelled aerosol using either a small volume nebuliser or the Aerogen Pro . The Aerogen Pro delivered a significantly greater lung dose than the small volume nebuliser. Adapted from [13].

3 Lung Recruitment Strategy for Patients with Respiratory Failure utilising Aerogen

Strategies to improve lung recruitment in patients with acute respiratory distress syndrome (ARDS) and respiratory failure can include the use of B-agonists. These drugs are used extensively to treat hypoxemic ventilated patients even without a confirmed clinical benefit. A recent study has investigated whether providing inhaled Salbutamol delivered by Aerogen technology can improve the lung function of paediatric patients[14]. Compared to baseline, aerosolised Salbutamol improved the functional residual capacity of critically ill children with respiratory failure. This study provides new evidence for the use of aerosolised B-agonists as another strategy to improve lung recruitment with ARDS[14].

4 Comparison of Aerogen with MDIs

Although drug delivery efficiency has been shown to be similar between a pressurised metered dose inhaler (pMDI) and Aerogen[22], the actual dose emitted from the pMDIs (e.g, 100µg per actuation with Salbutamol) is much lower than the typical 2.5mg dose used with Aerogen. In addition, pMDIs aren't without difficulties as failure to synchronise actuations with inspiration has been shown to reduce the aerosol drug delivery[25]. It is also important to ensure canisters are shaken before use as the dose may vary due to separation from the propellant[26]. There are several studies, which provide evidence that the cost savings of switching from combivent MDI to the Aerogen Solo is significant[15-18, 27]. Blake et al. discussed substantial cost savings in conjunction with staff satisfaction after switching and a potential system wide annual saving of up to $1.74 million across 105 hospitals[15]. Loborec et al. investigated the financial impact of replacing ipratropium-albuterol MDIs for Aerogen and calculated a three month cost saving of $99,359 and projected yearly saving of $397,436.[18]

5 Superior Drug Deposition during HFOV

HFOV has historically been a challenge for aerosol administration. It represents another ventilation mode where aerosol can be delivered during the therapy with Aerogen technology. In an in vitro model of adult, paediatric and infant ventilation, Fang et al. compared drug deposition during HFOV with the Aerogen Solo in comparison to a standard small volume nebuliser[3]. Drug deposition was minimal with both devices during HFOV when the nebuliser was placed back at the humidifier. Conversely, the deposition of aerosol in all simulated lung models was significantly higher with the Aerogen Solo compared to standard ventilation when the Aerogen Solo was placed proximal to the patient (Figure 3)[3].

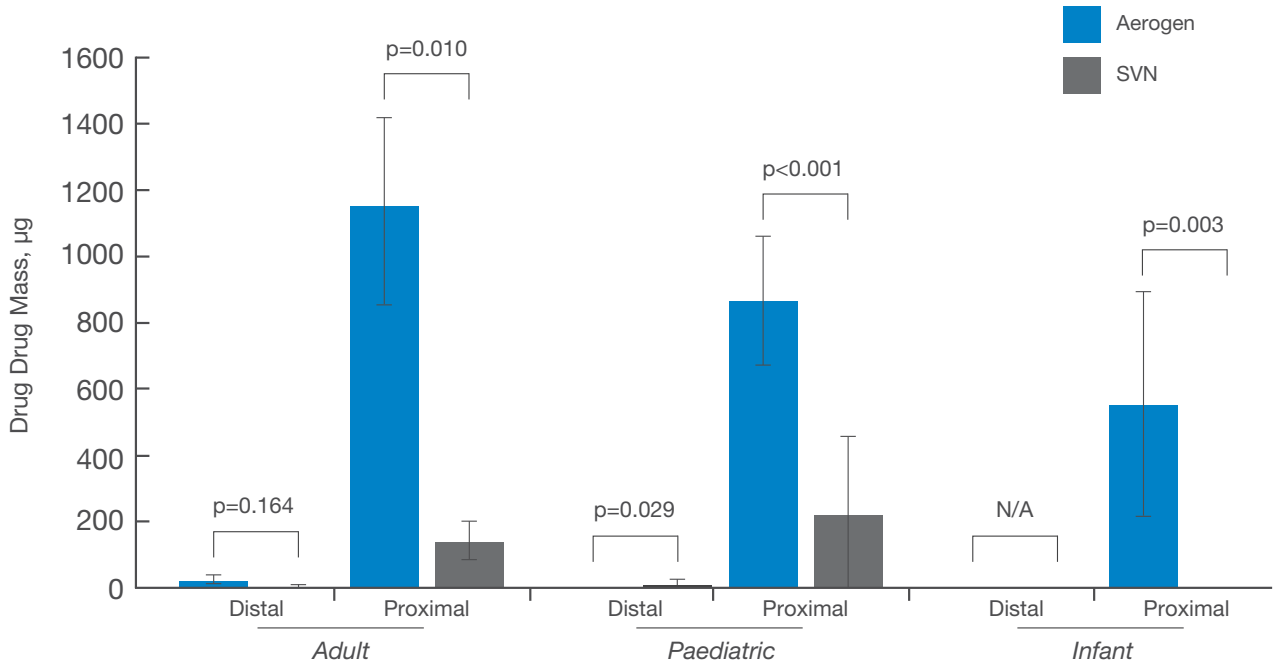


Figure 3

Aerosol delivery during HFOV using the Aerogen Solo compared to a standard small volume nebuliser. Positioning of the Aerogen Solo closer to the patient provided a higher drug deposition. Adapted from [3].

6 Optimal Drug Delivery During NIV & HFNC

The Aerogen device 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 small volume nebuliser in the same position. The importance of positioning of the nebuliser is observed in this study as the Aerogen Pro efficiency of 51% is reduced to 19% if connected before the leak valve (Figure 4)[4].

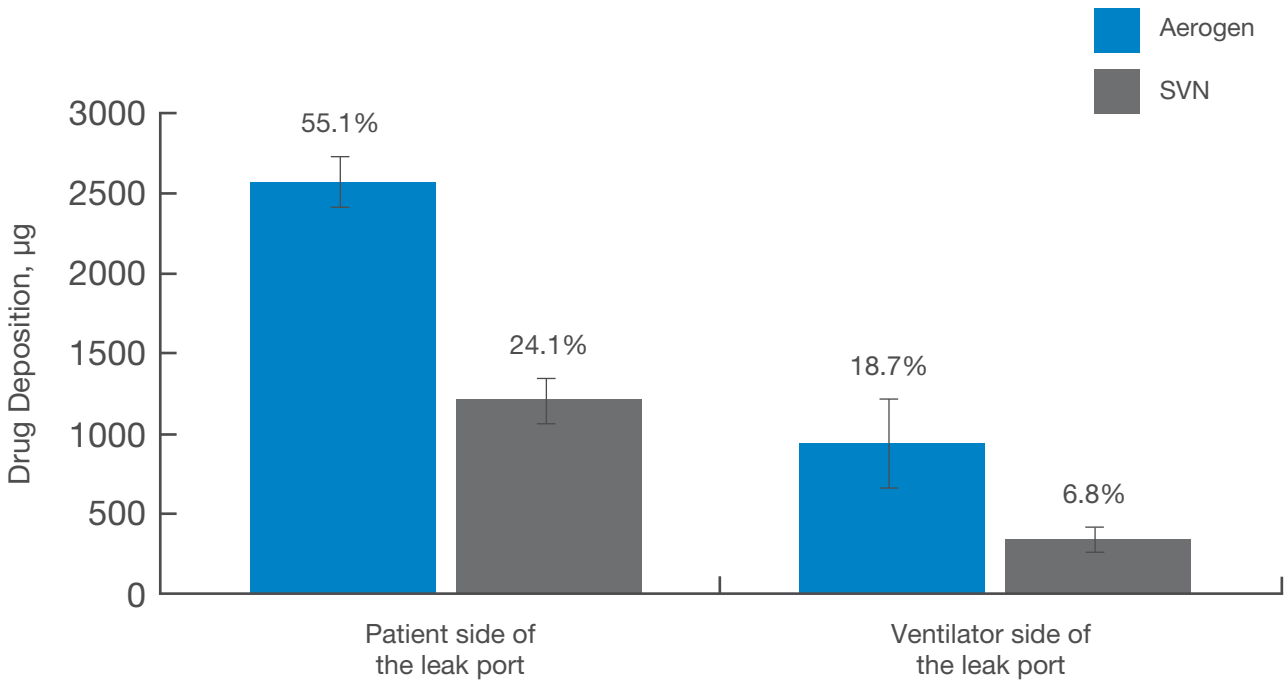


Figure 4

Aerosol dose at the patient side and ventilator side of the leak port during NIV. The Aerogen Pro provided increased dose both at the patient and ventilator side of the leak port in comparison to the SVN. Aerosol dose is higher when either nebuliser is positioned patient side of the leak port. Adapted from [4].

Additional studies have confirmed these data with the NIVO, which fits directly into an NIV mask[6, 28]. In an in vitro comparison of a vibrating mesh (NIVO) vs a small volume nebuliser during NIV, a similar difference in inhaled drug was noted (Figure 5)[6]. It is also important to note that the efficiency of the Aerogen Solo and NIVO has been directly compared and similar aerosol deposition has been reported[29].

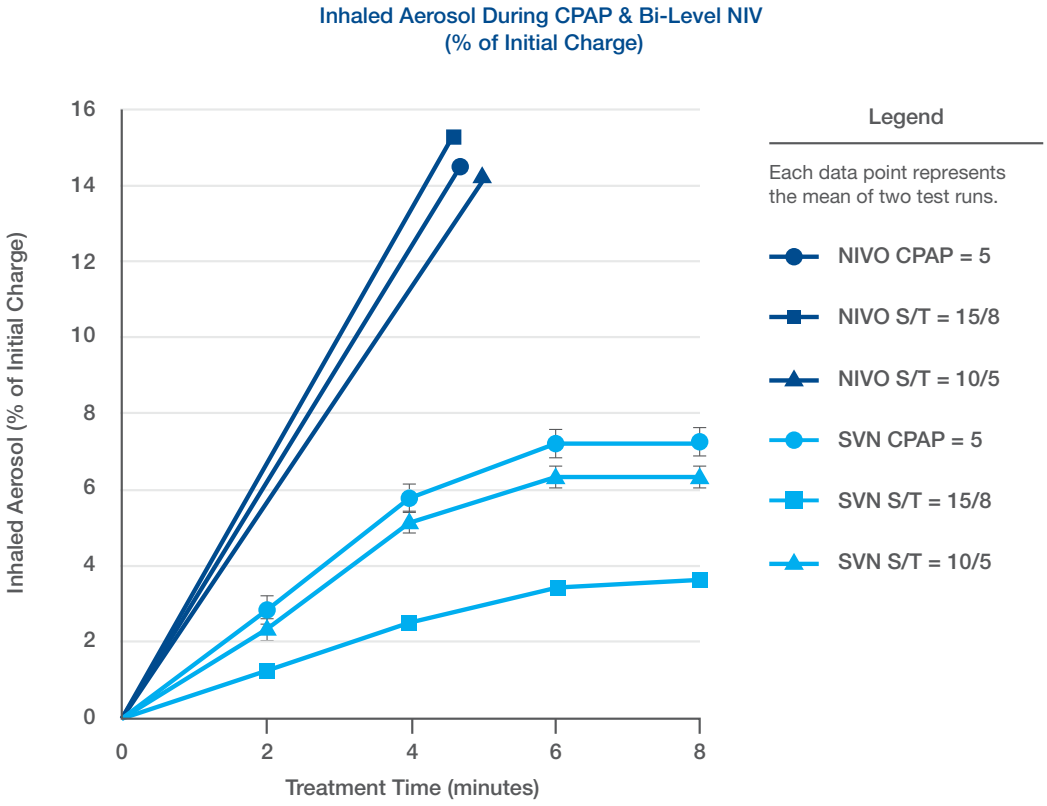


Figure 5

Aerosol deposition during NIV using the NIVO and a small volume nebuliser. During both BIPAP and CPAP aerosol deposition was higher with the NIVO compared to the small volume nebuliser. Adapted from [6].

Lung dose correlates directly to these in vitro studies. Galindo-Filho et al. completed a scintigraphy study with healthy patients using the NIVO during NIV and quantified the inhaled dose to be 23.1% for the vibrating mesh and 6.1% with the small volume nebuliser. A lung dose of 5.5% was measured with the vibrating mesh, which was 3-4 fold greater than the 1.5% measured with a standard small volume nebuliser (Figure 6)[5].

NIVO

SVN

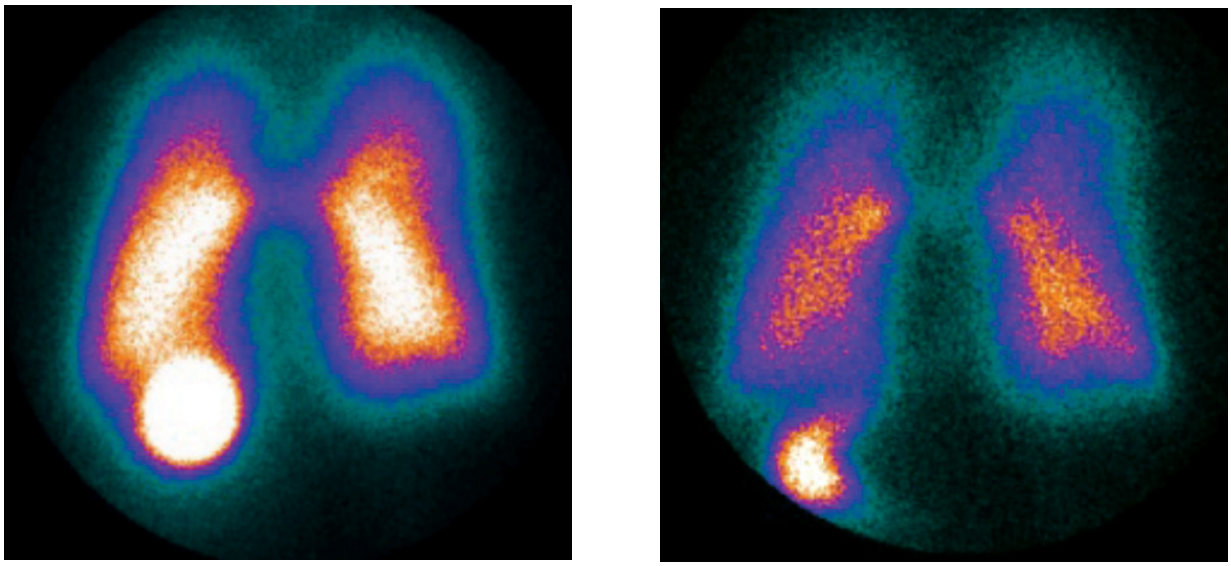


Figure 6

Distribution of aerosol in the lungs of healthy patients after nebulisation with a SVN and NIVO. Lung deposition is significantly greater with the NIVO. Adapted from [5].

Aerosol therapy during the use of High Flow Nasal Cannula (HFNC) can be provided by the Aerogen Solo inline with a variety of HFNC 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[30]. Initial studies have demonstrated that the Aerogen Solo can provide effective aerosol therapy through the cannula of a HFNC system[7, 31, 32]. Ari et al. studied aerosol delivery in paediatric 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 favourable effect on aerosol dose[7]. More recent research into adult HFNC showed that placing the Aerogen Solo before the humidifier provided optimal aerosol therapy in comparison to two small volume nebulisers[8]. Reminiac at al. commented that the Aerogen Solo "was associated with high nebulisation efficiency, a high fraction of aerosol made of particle with a diameter of 0.4 to 4.4 µm, a shorter nebulisation duration, and the absence of added gas flow" which could potentially influencing the inspired oxygen fraction[8]. A lung dose of between 2-10% were achieved at flows rates 30, 45, and 60 L/min and aerosol delivered was greater with distressed breathing than with normal breathing. This may be due to the higher inspiratory flow and volumes, allowing more of the aerosol to be inhaled (Figure 7)[8].

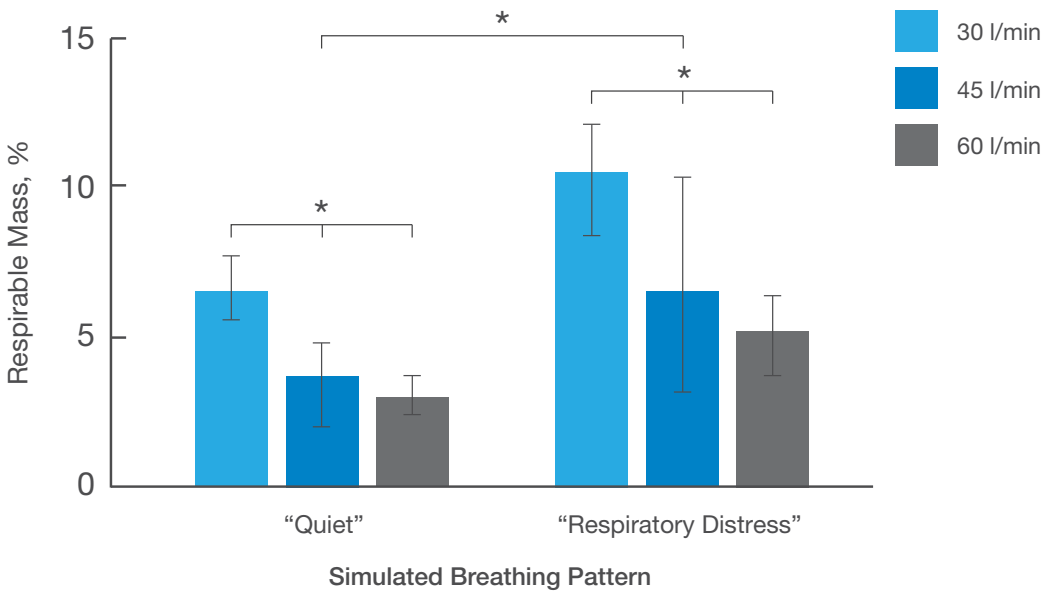
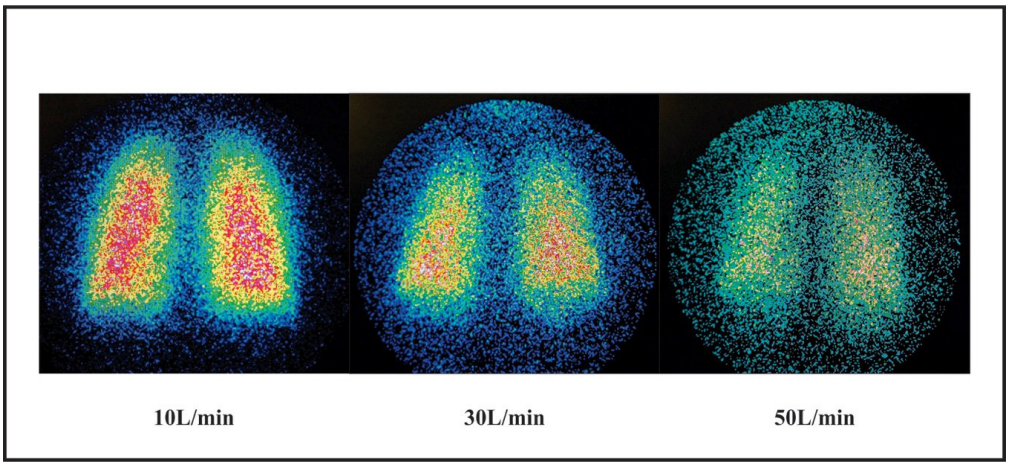


Figure 7

Respirable dose measured at three flow rates of 30, 45 and 60 L/min and with two different breathing patterns; "quiet" and "respiratory distress". Increasing flow rate results in a decrease in respirable mass. Elevated aerosol was delivered with distressed breathing than with normal breathing. Adapted from [8].

Alcoforado et al. have recently studied the effect of flow rate on aerosol deposition during adult HFNC in healthy patients[33]. The study results correlated with previous in vitro data demonstrating higher aerosol deposition is achieved at lower flow rates (Figure 8).



	10L/min	30L/min	50L/min
Lung Dose (%)	10.6 ± 5	3.3 ± 1.3	1.9 ± 0.8

Figure 8

Actual lung deposition in health patients during HFNC at flow rates of 10, 30 and 50 L/min. A lung dose of 10.6% is achievable at a flow rate of 10L/min. Lower flow rates correlate with higher drug deposition. Adapted from [33].

7 Aerogen Aerosol Drug Delivery Technology For Non-Vented Patients

The Aerogen Ultra, which can be used with the Aerogen Solo provides a platform to deliver aerosolised drugs to spontaneously breathing patients with mouthpiece and mask for use across the entire acute care setting. The Aerogen Ultra connects to low flow oxygen and can be used for both intermittent and continuous treatments in both paediatric and adult patients (Figure 9). The device is composed of a valved collection chamber, which connects the Aerogen Solo and a mouthpiece or facemask (Figure 9).

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 breaths 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.

Figure 9
Aerogen Ultra

Initial bench testing has demonstrated the aerosol drug deposition of this new offering compared with small volume nebulisers is highly efficient providing an inhaled dose available to the patient of up to 35% with no added flow[19] (Figure 10). In addition, as the Aerogen Solo has minimal residual volume remaining after aerosol treatments, more drug will therefore be available to the patient compared to a standard small volume nebuliser[12, 24]. Even with the addition of 2 litre 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 10)[19].

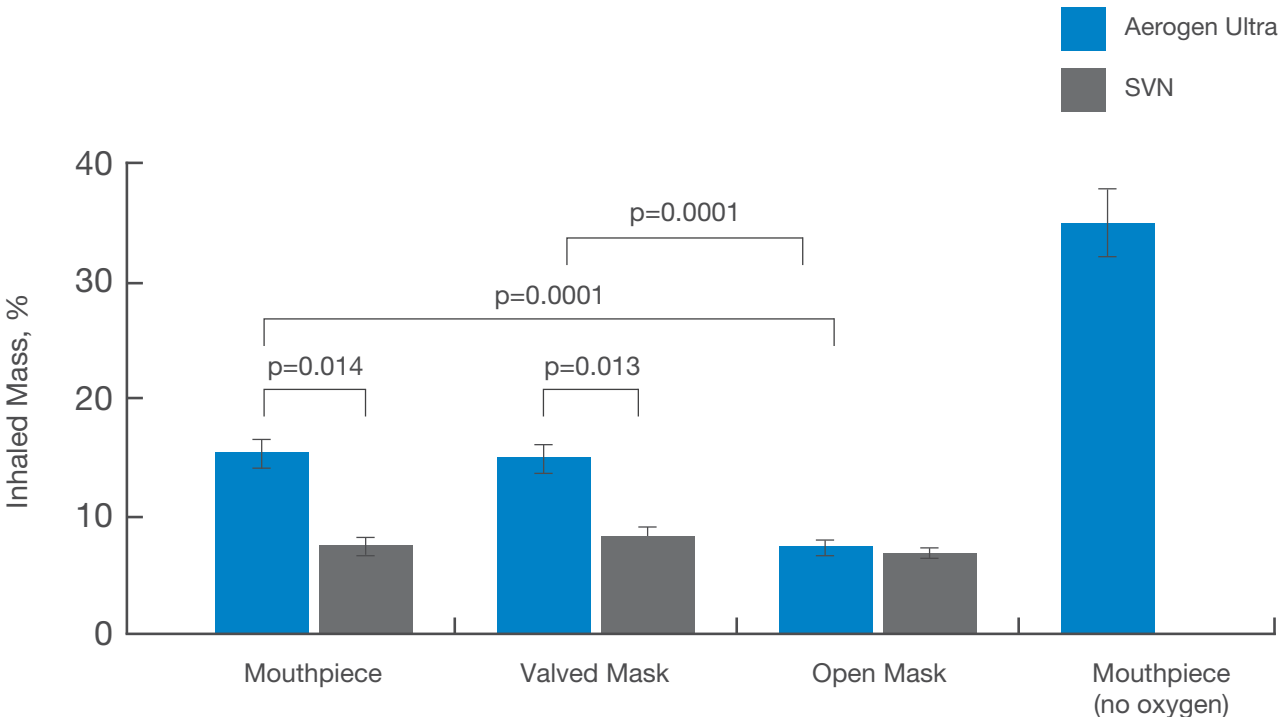
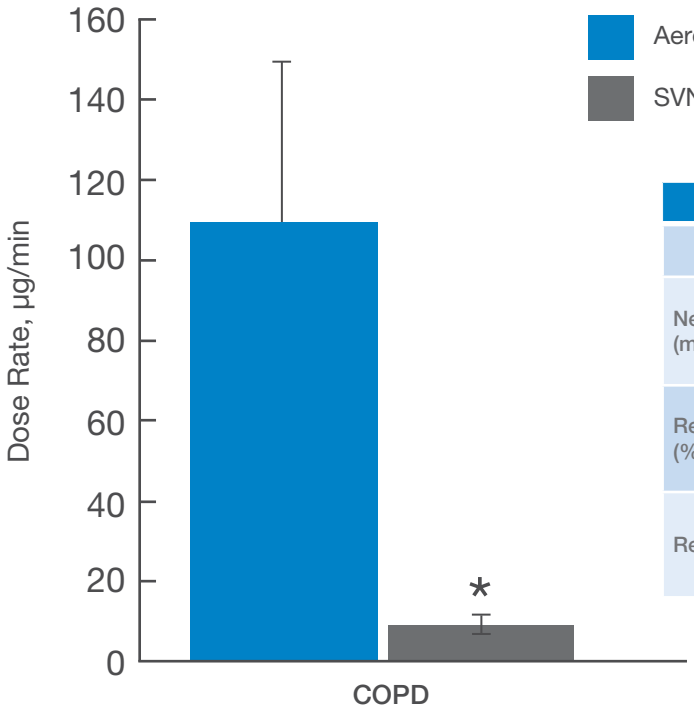


Figure 10

Inhaled dose of the Aerogen Ultra compared to a standard small volume nebuliser with 2 litres 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 utilised, 35% inhaled dose can be achieved with the mouthpiece. Adapted from [19].

The Aerogen Ultra also provides a more efficient delivery of medication in a shorter period of time as observed by Hickin et al. (Figure 11): "Our lab-based study has shown that a vibrating mesh system is quicker and more effective than a small volume nebuliser, delivering more Salbutamol over a shorter period of time." 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 nearly half the time (Figure 11)[12].



COPD Breathing Pattern		
	Aerogen Ultra	Jet Nebuliser
Nebulisation Time (mins: secs)	4.38	8.50
Respirable Dose (% of total dose)	12.6%	1.6%
Residual Volume (%)	0.9%	42.9%

Figure 11

The dose rate of the Aerogen Ultra compared to a small volume nebuliser and the nebulisation time, respirable dose and residual volume. The Aerogen Ultra provides a superior dose in a shorter period of time with minimal residual volume left in the nebuliser. Adapted from [12].

Multiple scintigraphy studies have determined the pulmonary aerosol deposition in healthy adults and demonstrated a 4-6 fold significant rise in drug entering the lungs using the Aerogen Ultra with a mouth piece compared to a standard small volume nebuliser (Figure 12)[9, 11]. In addition to this, experience of using Aerogen in the Emergency department by Baystate hospital both with spontaneously breathing patients and with HFNC led to a performance improvement plan for paediatric patient in respiratory distress[34]. The goal was to improve the clinical outcome of these patients with the least invasive methods. The improvements included use of Aerogen and HFNC. The plan resulted in a positive impact on clinical outcomes and staff and patient satisfaction. The same hospital has already noted in two case studies describing their experience with the Aerogen Ultra, that the use of the device with a mouthpiece or valved mask improved clinical response in paediatric patients with asthma exacerbations and potentially prevented escalation of care [35, 36].

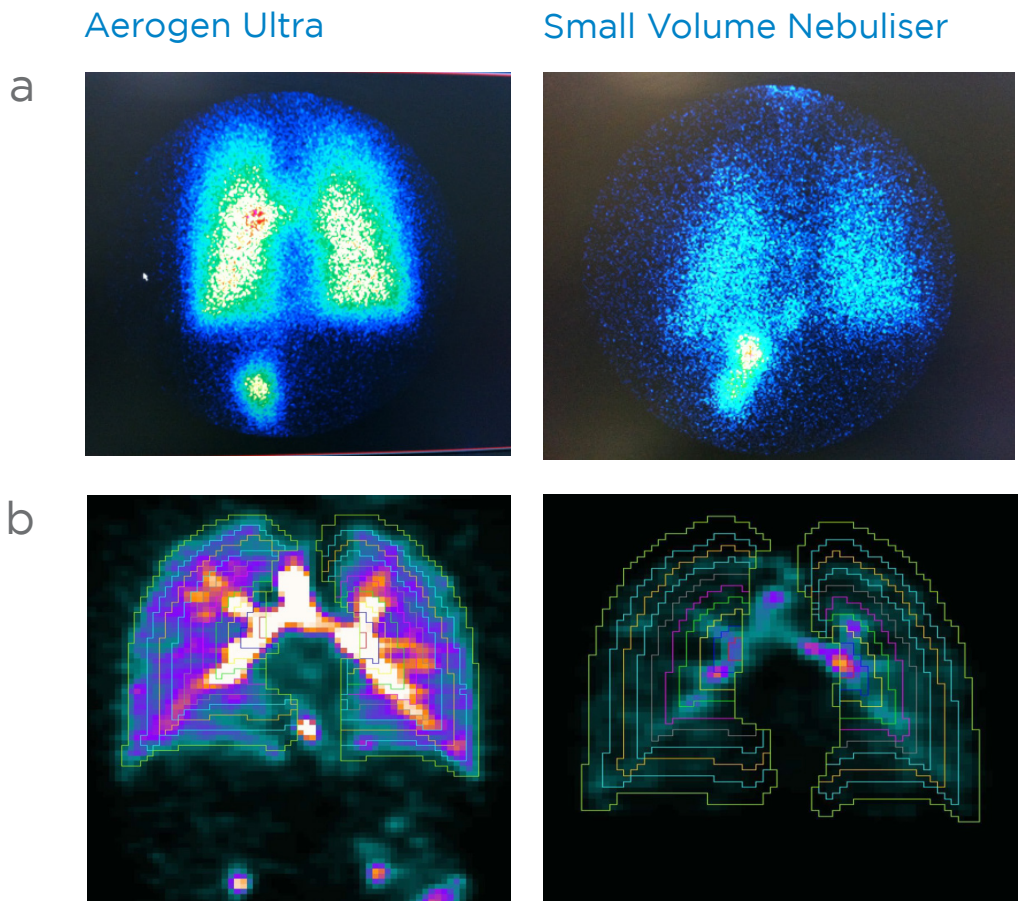


Figure 12

Scintigraphic images of the lung deposition of aerosol using the Aerogen Ultra or a small volume nebuliser. (a) Alcoforado et al.[9] and (b) Dugernier et al.[11] In both studies the lung deposition was significantly higher with the use of the Aerogen Ultra (left images) compared to the small volume nebuliser (right images).

8 Aerogen Improves Clinical Outcomes in the Emergency Department

The Aerogen Ultra has demonstrated improved inhaled dose and superior lung deposition compared to standard SVNs in multiple bench and imaging studies. Although it's important to note the improved efficiency of the Aerogen Ultra, clinical outcome data in patients is essential to support healthcare and economic arguments for use of this device.

A retrospective chart review was recently completed comparing emergency department (ED) patients who received aerosolised bronchodilator treatments. The review compared the hospital standard practice with an SVN to implementation of the Aerogen Ultra. A total of 1594 patients were included in the study. When compared to the standard SVN treatment the admission rate of patients into the hospital was 32% lower with the Aerogen Ultra. Discharges home from the ED were 30% higher with the Aerogen Ultra and the median length of stay in the ED was 37 minutes less per patient[37]. Furthermore, the Salbutamol dose required to alleviate symptoms was significantly lower when the Aerogen Ultra was used (Figure 13). This retrospective study has shown significant improvements in clinical outcomes and reduced drug dose for all patients requiring Salbutamol in the ED when delivery was via the Aerogen Ultra[37]. These data confirm the health and economic impact of using Aerogen technology in the ED.

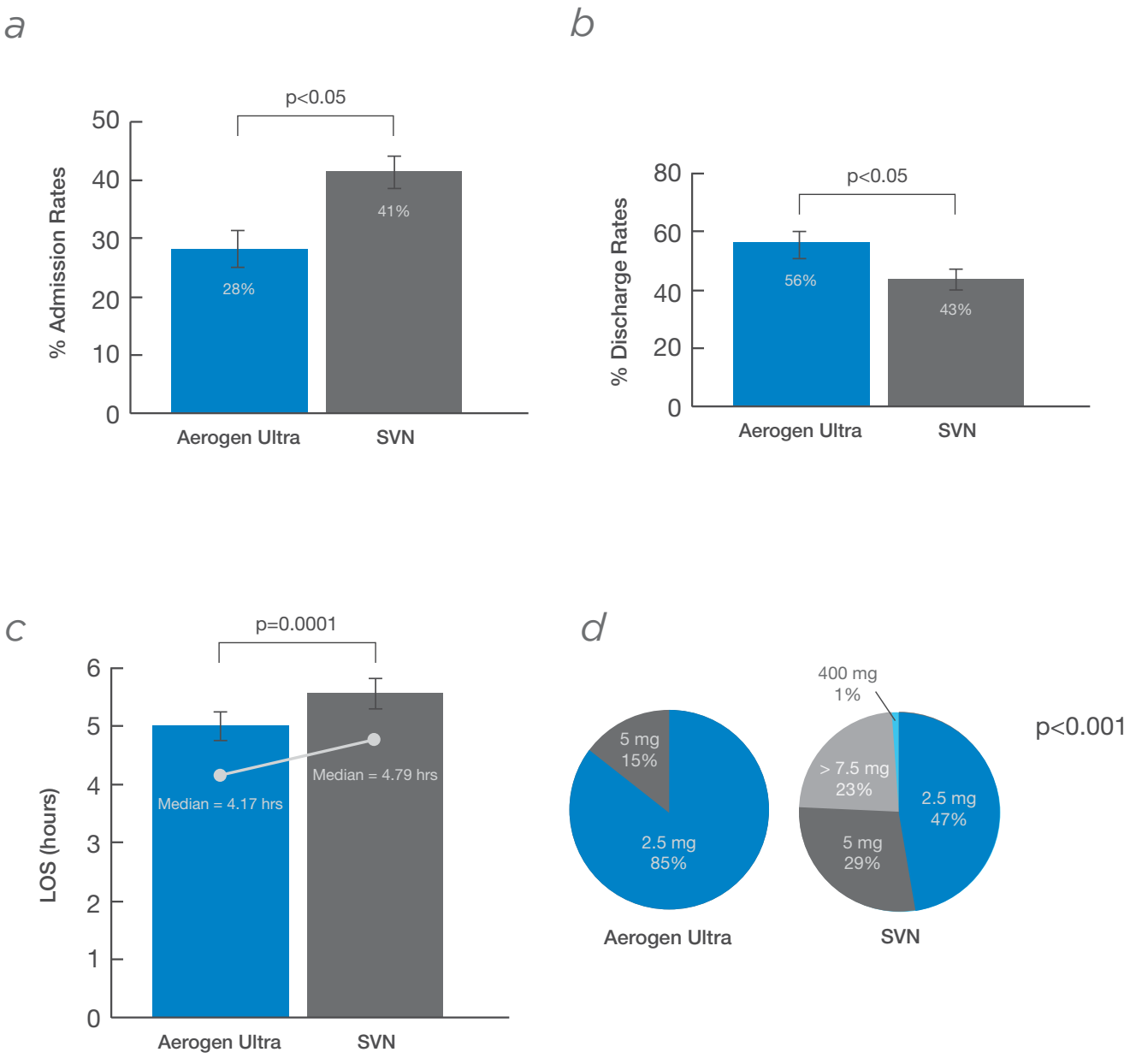


Figure 13

Retrospective chart review of patients in the ED requiring bronchodilator treatment.
(a) Admission rate into the hospital was 32% lower when compared to the standard SVN treatment. (b) Discharges home from the ED were 30% higher with the Aerogen Ultra when compared to the standard SVN treatment. (c) Median length of stay in the ED was 37 minutes less per patient with Aerogen Ultra when compared to the standard SVN treatment. (d) Salbutamol dose was significantly lower with the Aerogen Ultra when compared to the standard SVN treatment [37].

9 Aerogen in the OR

The Aerogen Solo can also be used during surgery in the presence of general anaesthesia in line with the limits outlined in the instructions for use. A case study published in 2012 described an intraoperative bronchospasm of a 3 year old asthmatic patient admitted for dental restorations under general anaesthetic[38]. The bronchospasm was relieved with the use of the Aerogen Pro “after MDI, small volume nebuliser and other pharmacologic interventions failed”[38].

10 Summary

Aerogen provides superior aerosol therapy within the intensive care environment during ventilation, NIV, HFNC and with spontaneously breathing patients. In addition to the optimal performance, substantial cost savings have also been acknowledged when hospitals make the transition to the device. This advanced aerosol delivery is now available across the acute care setting delivering optimal aerosol treatments to all respiratory patients.

11 References

1 Ari A, Atalay OT, Harwood R, Sheard MM, Aljamhan EA and Fink JB. Influence of nebulizer type, position, and bias flow on aerosol drug delivery in simulated pediatric and adult lung models during mechanical ventilation. *Respiratory care*. 2010;55:845-51.

2 Berlinski A and Willis JR. Albuterol delivery by 4 different nebulizers placed in 4 different positions in a pediatric ventilator in vitro model. *Respiratory care*. 2013;58:1124-33.

3 Fang TP, Lin HL, Chiu SH, Wang SH, DiBlasi RM, Tsai YH and Fink JB. Aerosol Delivery Using Jet Nebulizer and Vibrating Mesh Nebulizer During High Frequency Oscillatory Ventilation: An In Vitro Comparison. *Journal of aerosol medicine and pulmonary drug delivery*. 2016.

4 Abdelrahim ME, Plant P and Chrystyn H. In-vitro characterisation of the nebulised dose during non-invasive ventilation. *The Journal of pharmacy and pharmacology*. 2010;62:966-72.

5 Galindo-Filho VC, Ramos ME, Rattes CS, Barbosa AK, Brandao DC, Brandao SC, Fink JB and de Andrade AD. Radioaerosol Pulmonary Deposition Using Mesh and Jet Nebulizers During Noninvasive Ventilation in Healthy Subjects. *Respiratory care*. 2015;60:1238-46.

6 McPeck M. Improved Aerosol Drug Delivery with an Electronic Mesh Nebulizer during Non-invasive Ventilation *AARC poster*. 2012

7 Ari A, Harwood R, Sheard M, Dailey P and Fink JB. In vitro comparison of heliox and oxygen in aerosol delivery using pediatric high flow nasal cannula. *Pediatric pulmonology*. 2011;46:795-801.

8 Reminiac F, Vecellio L, Heuze-Vourc'h N, Petitcollin A, Respaud R, Cabrera M, Le Pennec D, Diot P and Ehrmann S. Aerosol Therapy in Adults Receiving High Flow Nasal Cannula Oxygen Therapy. *Journal of aerosol medicine and pulmonary drug delivery*. 2015.

9 Alcoforado L, de Melo Barcelar J, Castor Galindo V, Cristina S. Brandão S, Fink J, B. and Dornelas de Andrade A. Analysis of Deposition Radioaerosol Nebulizers Membrane in Healthy Subjects. *ISAM poster presentation* 2015.

10 Ari A, de Andrade A, Sheard M, AlHamad B and Fink JB. Performance Comparisons of Jet and Mesh Nebulizers Using Different Interfaces in Simulated Spontaneously Breathing Adults and Children. *Journal of aerosol medicine and pulmonary drug delivery*. 2014.

11 Dugernier J, Reychler G, Depoortere V, Roeseler J, Michotte JB, Laterre PF, Jamar F and Hesse M. Tomoscintigraphiccomparison of lung deposition with a vibrating-mesh and a jet nebulizer. *ERS conference poster* 2015.

12 Hickin S, Mac Loughlin R, Sweeney L, Tatham A and Gidwani S. Comparison of mesh nebuliser versus jet nebuliser in simulated adults with chronic obstructive pulmonary disease. *Poster at the College of Emergency Medicine Clinical Excellence Conference*. 2014

13 Dubus JC, Vecellio L, De Monte M, Fink JB, Grimbert D, Montharu J, Valat C, Behan N and Diot P. Aerosol deposition in neonatal ventilation. *Pediatric research*. 2005;58:10-4.

14 Ramsi MA, Henry M, Milla CE and Cornfield DN. Inhaled beta2-Agonist Therapy Increases Functional Residual Capacity in Mechanically Ventilated Children With Respiratory Failure. *Pediatric critical care medicine : a journal of the Society of Critical Care Medicine and the World Federation of Pediatric Intensive and Critical Care Societies*. 2015;16:e189-93.

15 Blake G, Yaklic J and Cobb J. Transition from ipratropium/albuterol inhaler to nebulizer on quality and cost savings in ventilated patients. *Poster presentation at American Society of Health-System Pharmacists*. 2013.

16 McDaniel C, Glynn G, Gudowski S, Pezzano T and Weibel S. Conversion of pressurized Metered-Dose Inhaler to Vibrating Mesh Nebulizer Administered Medications. *Poster presentation at the Society of Critical Care Medicine*. 2013.

17 Streepy KS, Dawson AM, Grigonis AM, Hammerman SI and 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.

18 Loborec SM, Johnson SE and Keating EA. Financial effect of converting ipratropium-albuterol therapy from inhalers to nebulizer treatments at an academic health system. *American journal of health-system pharmacy : AJHP : official journal of the American Society of Health-System Pharmacists*. 2016;73:121-5.

19 Ari A, de Andrade AD, Sheard M, AlHamad B and Fink JB. Performance Comparisons of Jet and Mesh Nebulizers Using Different Interfaces in Simulated Spontaneously Breathing Adults and Children. *Journal of aerosol medicine and pulmonary drug delivery*. 2015;28:281-9.

20 Reminiac F, Vecellio L, Heuze-Vourc'h N, Petitcollin A, Respaud R, Cabrera M, Pennec DL, Diot P and Ehrmann S. Aerosol Therapy in Adults Receiving High Flow Nasal Cannula Oxygen Therapy. *Journal of aerosol medicine and pulmonary drug delivery*. 2016;29:134-41.

21 Ari A and Fink JB. Guidelines for aerosol devices in infants, children and adults: which to choose, why and how to achieve effective aerosol therapy. *Expert review of respiratory medicine*. 2011;5:561-72.

22 Ari A, Areabi H and Fink JB. Evaluation of aerosol generator devices at 3 locations in humidified and non-humidified circuits during adult mechanical ventilation. *Respiratory care*. 2010;55:837-44.

23 Sidler-Moix AL, Di Paolo ER, Dolci U, Berger-Gryllaki M, Cotting J and Pannatier A. *Physicochemical aspects and efficiency of albuterol nebulization: comparison of three aerosol types in an in vitro pediatric model.* Respiratory care. 2015;60:38-46.

24 Ari A, Fink JB and Dhand R. Inhalation Therapy in Patients Receiving Mechanical Ventilation: An Update. *Journal of aerosol medicine and pulmonary drug delivery.* 2012.

25 Diot P, Morra L and Smaldone GC. Albuterol delivery in a model of mechanical ventilation. Comparison of metered-dose inhaler and nebulizer efficiency. *American journal of respiratory and critical care medicine.* 1995;152:1391-4.

26 Everard ML, Devadason SG, Summers QA and Le Souef PN. Factors affecting total and “respirable” dose delivered by a salbutamol metered dose inhaler. *Thorax.* 1995;50:746-9.

27 Emberger J. Cost Reduction using Aeroneb Solo in a Medical ICU Ventilator Population. . *Respiratory Care, Christiana Care Health System, Newark, 2011 OPEN FORUM Abstracts*. 2011.

28 White CC, Crotwell DN, Shen S, Salyer J, Yung D, Zheng J and DiBlasi RM. Bronchodilator delivery during simulated pediatric noninvasive ventilation. *Respiratory care.* 2013;58:1459-66.

29 AlQuaimi M, Fink JB, Harwood R, Sheard M, Bryant L and Ari A. The effect of nebulizer type and mask design on aerosol delivery during noninvasive positive pressure ventilation of an adult lung model. *AARC poster* 2012.

30 Alalwan M, Ari A, Fink J, Harwood R, Bryant L and Sheard M. Delivery of albuterol by pressurized metered-dose inhaler and jet nebulizer via mask with high flow nasal cannula in place reduces aerosol delivery. *AARC Open Forum Abstract.* 2012.

31 Bhashyam AR, Wolf MT, Marcinkowski AL, Saville A, Thomas K, Carcillo JA and Corcoran TE. Aerosol delivery through nasal cannulas: an in vitro study. *Journal of aerosol medicine and pulmonary drug delivery*. 2008;21:181-8.

32 MacLoughlin R, Power P, Wolny M and Duffy C. Evaluation of vibrating mesh nebulizer performance during nasal high flow therapy. *Poster Presentation at International Society of Aerosols in Medicine* 2013.

33 Alcoforado L, Ari A, De Melo Barcelar J, Brandao SS, Fink JB and Dornelas De Andrade A. Comparison of Aerosol Deposition with Heated and Unheated High Flow Nasal Cannula (HFNC) in Healthy Adults. *Poster presentation at ATS*. 2016.

34 Dailey P, Tina T, Santos J and Gurung P. Performance Improvement Plan for Pediatric Patients in Respiratory Distress: Clinical Experience. *Respiratory Therapy.* 2015;10:27-29.

35 Newsome T, Thayer T and Lieberman S. Pediatric Patient with Severe Asthma Treated with a Vibrating Mesh with Valved Adapter. *Respiratory Therapy Case Study*. 2015;10:28-29.

36 Thayer T, Hodgens E and Lieberman S. A Case Study: Use of Vibrating Mesh with a Valved Adapter in a Pediatric Patient with a Severe Asthma Exacerbation. *Respiratory Therapy Case Study*. 2016;11:52.

37 Dunne R, Shortt SA and Dailey PA. Comparison of bronchodilator administration with vibrating mesh with adapter and jet nebulizer in the emergency department *AARC Open Forum Abstract.* 2016.

38 Golden LR, Desimone HA, Yeroshalmi F, Pranevicius M and Saraghi M. Severe intraoperative bronchospasm treated with a vibrating-mesh nebulizer. *Anesthesia progress*. 2012;59:123-6.

Aerogen®

Pioneering Aerosol Drug Delivery

Aerogen Ltd.
Galway Business Park,
Dangan, Galway,
Ireland.

INTL. +353 91 540 400
US. (886) 423-7643

www.aerogen.com

PM349