Optimization of a Combination Device for High Efficiency Aerosol Delivery and High Flow Nasal Cannula Therapy

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Introduction

- High flow nasal cannula (HFNC) therapy is becoming increasingly popular for patients with respiratory insufficiency or failure caused by underlying lung conditions which are also possibly treatable through inhaled pharmaceutical aerosols [1,2].
- A convenient method to deliver aerosol to the lungs in these patients is to add medication directly to the inspired gas stream, but lung delivery efficiencies of current systems are especially low during HFNC therapy due in part to the relatively large droplet size generated by commercial nebulizers [2].
- A new system is proposed that is capable of providing HFNC and an on-demand aerosol at a high lung delivery efficiency. The novel device is designed to efficiently mix and heat the nebulized aerosol to produce a submicrometer aerosol delivered with minimal device deposition losses.
- Separate identical mesh nebulizers are used to deliver humidified air and drug aerosols, respectively, overcoming the challenges of past HFNC system designs [3] and providing either a heated and humidified ventilation gas or a pharmaceutical aerosol.

Objective

Develop a new device based on commercially available vibrating mesh nebulizers capable of providing continuously heated and humidified HFNC gas therapy as well as an on-demand pharmaceutical aerosol delivered with high delivery efficiency using the nose-to-lung route.

Methods

Analyze system performance using multiple "visualization" methods focusing on three designs

a) Initial-12-cm b) Optimized-16-cm c) Vertical-Optimized-16cm

- Unique device components of Air Inlet Unifier, Mixing Section, and Heating Section
- Shared device components of Tubing, Cannula Interface, Control Module, and Commercial Nebulizers
- Aerosols generated from a 0.5% albuterol sulfate + 0.5% sodium chloride solution in Aerogen Solo

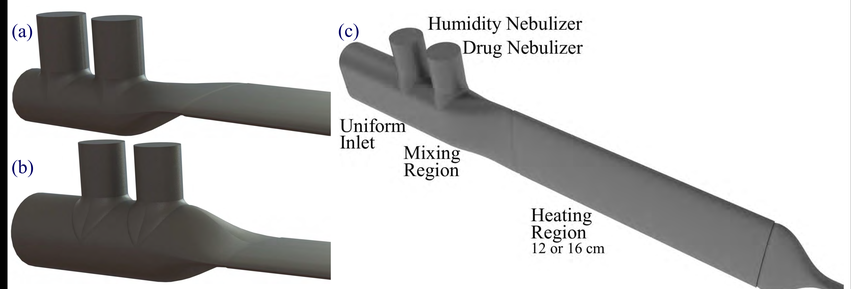

***Figure 1**. Air flow pathway of a) Initial-12-cm, b) Optimized-16-cm, and c) Vertical-Optimized-16cm designs intended to provide aerosol depositional losses <5%, submicrometer outlet particles, and an airstream comfortable for continuous direct nasal inhalation.*

Pharmaceutical Aerosol Characterization and Deposition Profile

- Aerosol size determined at heating section outlet with Andersen Cascade Impactor.
- Drug deposition on device components were quantified using validated HPLC.

High Speed Video using Photron FASTCAM PCI R2

- Captured aerosol plume within 3D printed clear models of each design.
- Captured aerosol plume leaving Aeroneb Solo into still air.
- Gained insight into the dynamics of system.

Inlet Flow Unifier Design using Pitot Tube Traverse Measurements

- The Sensirion pressure sensor (SDP600-500Pa) employed to detect pressure at a point in flow which can be related to flow velocity.
- Measurements were made along the vertical plane just before nebulizers to identify airflow uniformity.
- Screened additional inlet configurations before implementation.

Infrared Thermal Imaging using Fluke Ti25 and Smartview 4.3 Software

- Photographed and monitored temperature on outer surface of heating region consisting of wrapped double layer aluminum sheets sandwiching two 25W polymide film heaters (each 1" x 5").
- Control Module regulated temperature to preset value via thermocouple sandwiched near outlet end.
- Provided heating plate temperature distribution and ensured Control Module function.

Results

High Speed Video using Photron FASTCAM PCI R2

- Initial-12cm design pulled aerosol from both humidity and drug nebulizers back to perforated plate inlet.
- Optimized-16cm design eliminated reverse flow in the mixing region but develops long term recirculation in commercial nebulizer skirt section causing poor spreading of aerosol.
- Vertical-Optimized-16cm design eliminates mixing region flow reversal and the nebulized aerosol jet distributes particles throughout the heating region.

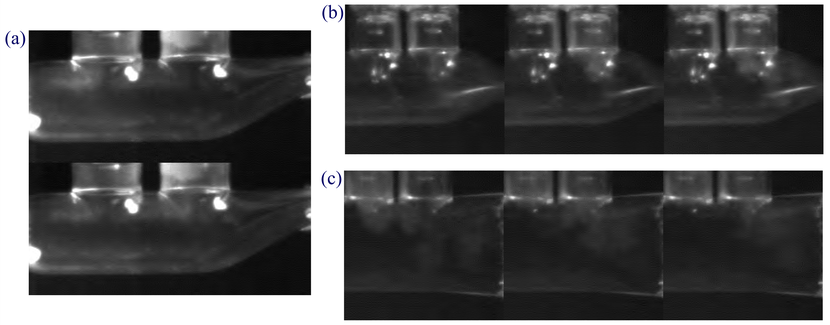

***Figure 2**. Frame montage of aerosol production and movement in clear prototyped devices a) Initial device, b) Optimized device, and c) Vertical-Optimized device*

Pitot Tube Flow Measurements to Develop Inlet Flow Unifier

- Figure 3a shows that the optimized-16cm design with the flow unifier achieved substantially higher uniformity of the inlet air.
- Findings of reversed flow in the initial-12cm design agrees with high speed video images.
- Flow unifier consists of an array of alternating rods ending in filter media from a *Pulmo*GUARD II (Figure 3b).
- Implementation of the grids decreased variations in space and the filter decreased variations in time (Figure 3c).

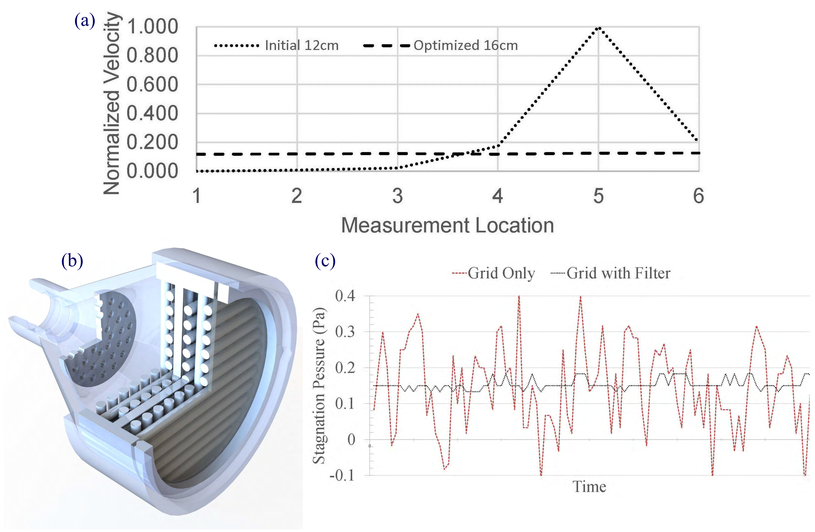

***Figure 3a**. Normalized inlet velocity profile of Initial-12cm and Optimized-16cm designs at locations based on a 6 point log-tchebycheff method pitot tube traverse*
***Figure 3b**. Inlet flow unifier for Optimized-16cm design with main features of rod array grid and filter*
***Figure 3c**. Sample plot of pitot tube readings at a single point through time with and without a filter*

Infrared Thermal Imaging

- The heating region of aluminum (inner surface) and outer 3D printed shells (outer surface) transfers energy into aerosol flow to (i) evaporate the aerosol from the humidity nebulizer for humidification, (ii) dry aerosol from the drug nebulizer to produce a submicrometer aerosol, and (iii) to align air with rest of flow path. Figure 4 shows the temperature profile for the optimized-16cm heater.

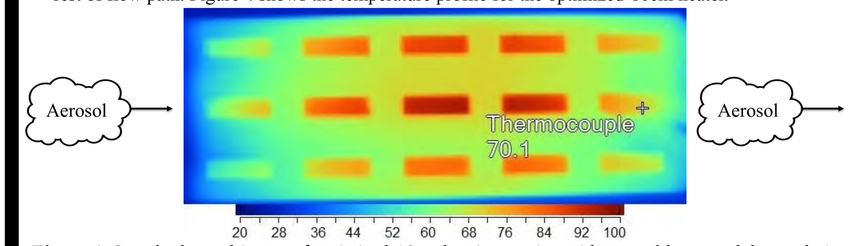

***Figure 4**. Sample thermal image of optimized-16cm heating section with control base module regulating thermo-couple temperature to 70ºC under high flow nasal cannula therapy conditions*

Pharmaceutical Aerosol Characterization and Deposition Profile

- The device drug depositional losses were > 10% in Initial-12cm mixer and heater regions.
- The optimized-16cm design reduced drug depositional loss to just below 5%.
- 90% of the nominal dose was delivered from the vertical-optimized-16cm design.

***Table 1**. Mean (SD) drug deposition reported as percent nebulized dose at 30 liters per minute device flow rate with device operated at 60º C plate regulation temperature*

Unit	Neb	Device	Filter	MMAD (μm)
Initial-12cm	6.1 (0.8) %	11.2 (1.5) %	76.6 (0.4) %	1.6 (0.0)
Optimized-16cm	6.9 (1.3) %	4.6 (0.3) %	83.0 (0.5) %	1.7 (0.2)
Vertical-Optimized-16cm	6.7 (0.4) %	3.6 (0.2) %	90.1 (4.1) %	1.6 (0.1)

CFD Analysis

- Outlet temperature and relative humidity (RH) in target range for patient comfort appeared feasible and were estimated to be 32º C ±2º C and RH > 40%.
- The CFD projected plate temperature for the heating region was 60º C.
- Incomplete droplet evaporation was observed for some trajectories resulting in a micrometer rather than submicrometer aerosol, and was in agreement with the experimental observations.
- Initial CFD predictions under-estimated depositional loss in the device and nebulizer (data not shown).

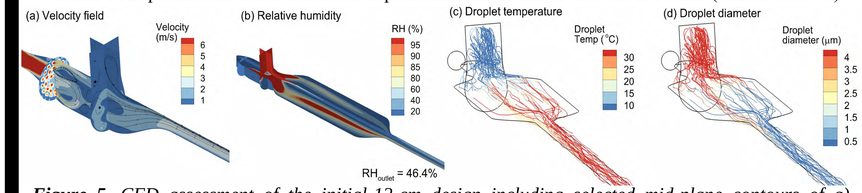

***Figure 5**. CFD assessment of the initial-12-cm design including selected mid-plane contours of a) velocity magnitude and b) relative humidity (RH), as well as droplet trajectories contoured based on c) droplet temperature and d) droplet/particle diameter*

Conclusions

- Design modifications achieved high delivery efficiency (~90%) with proposed combination HFNC & pharmaceutical aerosol device.
- Lead designs are Optimized and Vertical-Optimized units with 16 cm heating regions.
- Air stream unification serves a complex and important role in reducing drug aerosol depositional losses.

Acknowledgements

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References

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3 *Respiratory Care* 2014; 59:1476-86