Unsteady Aerosol Output Rate Measurements: Assessing the eFlow Nebulizer Aerosol Bolus

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Background and Objectives

- For the measurement of delivered dose (DD) or aerosol output (AO) standardized procedures are used.
- Aerosol output rate (AOR) is determined by dividing AO by the measurement duration.
- Due to the defined test setup, only the integral values of AO or AOR can be determined.

→ How AO or AOR develops over time is not covered. This is suitable for most nebulizers (triggered or continuously operated, no storage) but less for nebulizers using an aerosol storage chamber.

PARI's eFlow nebulizer (Fig. 1) is such a nebulizer using an aerosol storage chamber, a continuously operated aerosol head, and inhalation and exhalation valves [1,2]:

Figure 1: Investigational PARI eFlow nebulizer during exhalation (left) and inhalation (right)

Exhalation:
Inhalation valve is closed, exhalated air escapes through exhalation valve. Aerosol is stored in aerosol storage chamber.

Inhalation:
Inhalation valve open: Stored aerosol first leaves the device followed by the continuously generated aerosol, leading to an unsteady aerosol output rate (uAOR) especially at the beginning of the inhalation phase. Excess aerosol is called "aerosol bolus".

Problem: No measurement system available to quantify bolus → New method had to be developed

Materials and Methods

Approach: Addition of a fast-switching valve and a secondary aerosol filter to the standard setup for AO-measurements (Fig. 2):

- Using the fast-switching valve, aerosol can be diverted from the measurement filter to a secondary filter after a given delay relative to the start of inhalation.
- Increasing the delay between measurements, cumulated AO can be determined as a function of time.
- The first derivative of cumulated AO is the uAOR which is used to quantify the bolus.

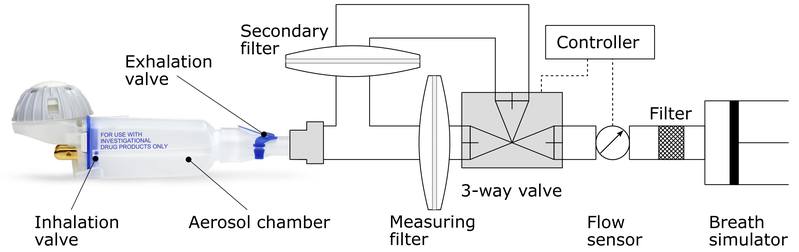

Figure 2: Experimental setup to measure cumulated AO as a function of time

- Test solution: Isotonic saline + 1000 µg/ml tartrazine (0.1 %).
- Concentration of tartrazine assessed using ultraviolet-visible (UV-Vis) photometry.
- Cumulated AO determined from tartrazine concentration (Fig. 3).

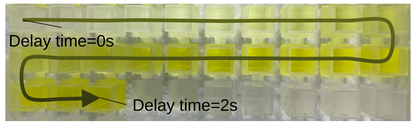

Figure 3: Samples taken at increasing delay times for cumulated AO measurement (Fig. 4), showing increasing tartrazine concentrations

Results

Results of the cumulated AO measurement for an investigational eFlow nebulizer (TOR*: ~650 mg/min, MMD: ~3µm) and the subsequently derived AOR as a function of time are presented in Figure 4:

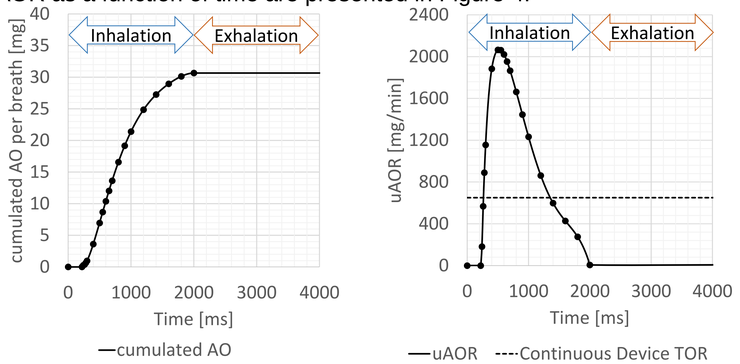

Figure 4: Cumulated AO over time for single breath (left), unsteady AOR for single breath (right)
Each data point represents a measured time segment

- Beginning of the inhalation phase: The aerosol bolus is transported from the aerosol chamber to the patient/filter.
  → During the first ~240 ms no deposition is measured on the filter.
- The steepest gradient in the cumulated AO results in a peak of 2070 mg/min in uAOR at 500 ms. → Increase of more than 300 % compared to the TOR of the continuously operated aerosol head.
- At 1350 ms the uAOR meets the value of the constant aerosol head TOR: → The newly produced aerosol is directly transported away from the aerosol head.
- After 1350 ms: uAOR drops below the aerosol head's output rate, indicating limited transport capabilities and that aerosol is stored again in the chamber.

*TOR: Total Output Rate of aerosol head only

Summary and Conclusions

A new method to measure the unsteady aerosol output of nebulizers was developed. This method was used to quantify the aerosol bolus of the PARI eFlow nebulizer showing the advantages of an aerosol storage chamber:

- A large amount of aerosol is delivered to the patient right at the beginning of the inhalation, leading to higher peripheral deposition [4].
- More aerosol can be delivered during inhalation, leading to reduced treatment times (Fig. 5, [3]).
- Higher drug efficiency as aerosol is stored during exhalation.

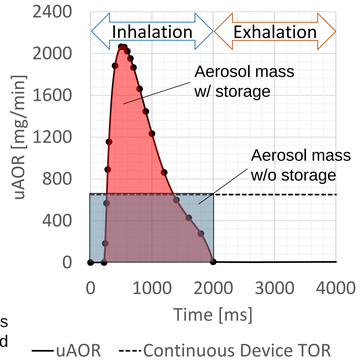

Figure 5: Comparison of delivered aerosol mass during inhalation for system with (idealized) and without aerosol storage

References

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[3] Bitterle E, Denk O, Luithlen A, Reul K, Hoyer K, Uhlig M, Tservistas M, Keller M: Comparison of aerosol delivery efficiency nebulising Colistin by electronic and jet nebulisers. DDL 2008, 19.

[4] Martin A: Regional Deposition: Targeting. Journal of Aerosol Medicine and Pulmonary Drug Delivery 2021, 34:1-10.