Improved Estimation of E-Vapor Product Aerosol Delivery Using Standard Puff Machine Data and Human Puff Topography Profiles

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Background

TOPOGRAPHY STUDY

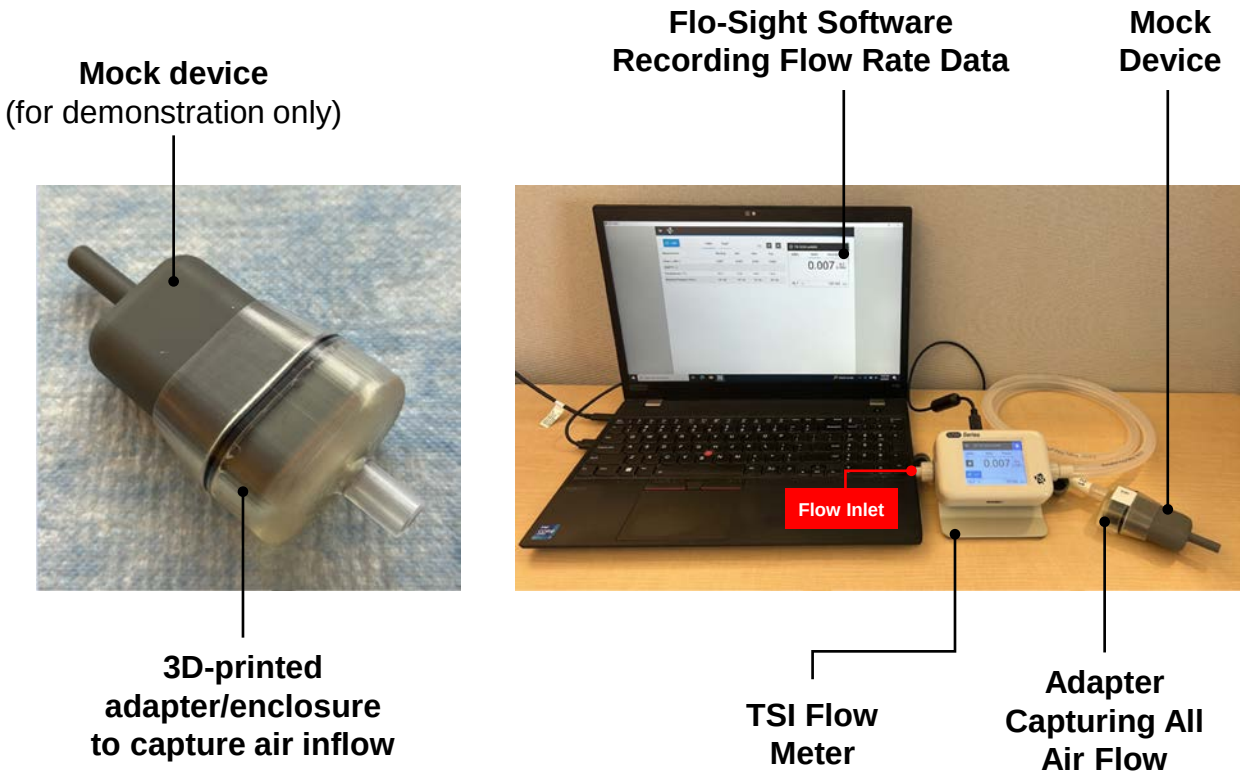
45
NUMBER OF PARTICIPANTS

ENDS Prototypes

- Five e-liquid formulations
- Same device and product configuration

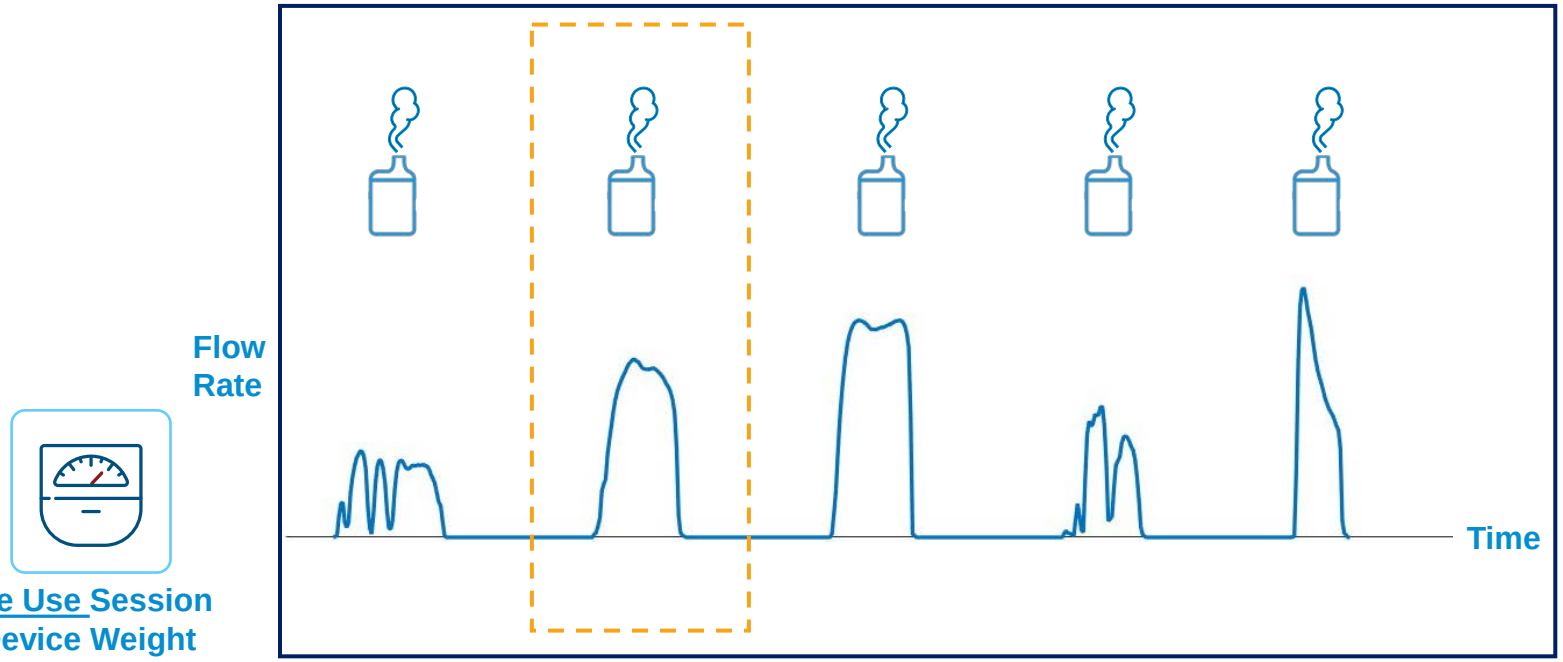
Flow rate and duration of 8000+ individual puffs recorded

Product weights pre- and post-use measured



Background (Cont'd)

Example of Product Use Session in Topography Study



Total Aerosol Mass Delivered to User

=

Device Weight Change

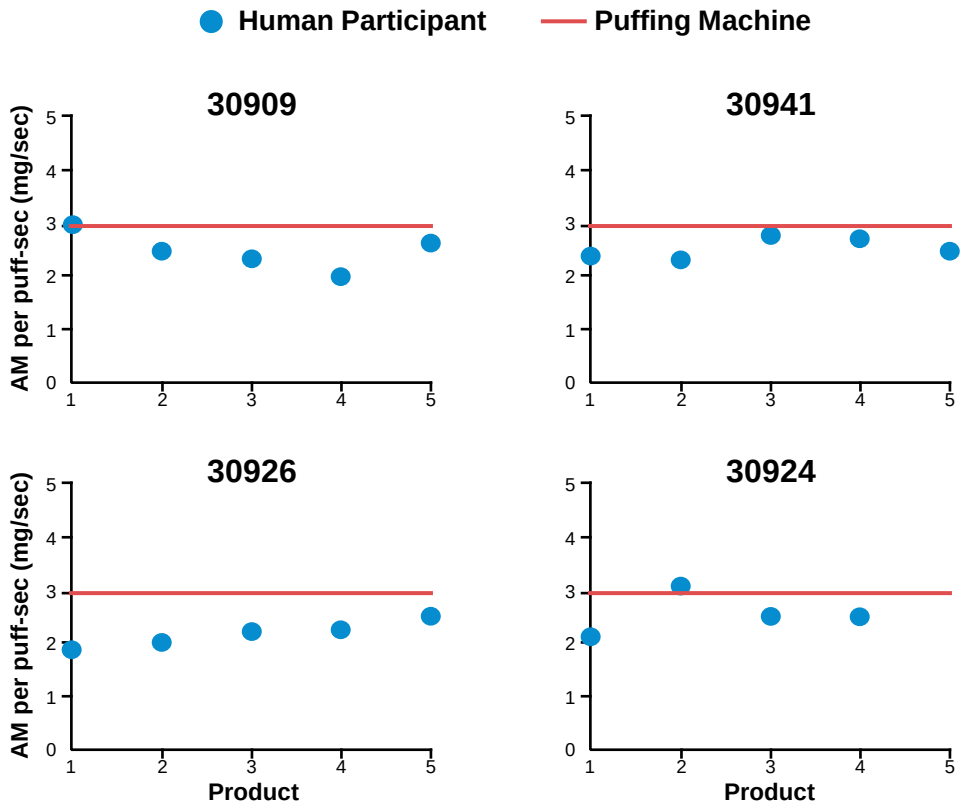
- Product weight change over use session = Total aerosol delivered to a user over the use session (in mgs)
- **Research Question:** Can we more accurately estimate AM delivered to the user for each individual puffs?
  - *Benefits:* (1) Better estimate of exposure per puff (2) More robust inputs for PBPK modeling and other assessments

PBPK = Physiologically Based Pharmacokinetics Modeling

Aerosol Mass (AM) per Puff Second - Machine Data Compared to Human Topography Data

AM per puff-second = 2.93 mg/s

- Machine generated AM: 8.8 mg
- Puff profile: 55 ml, 3 second puff, square wave

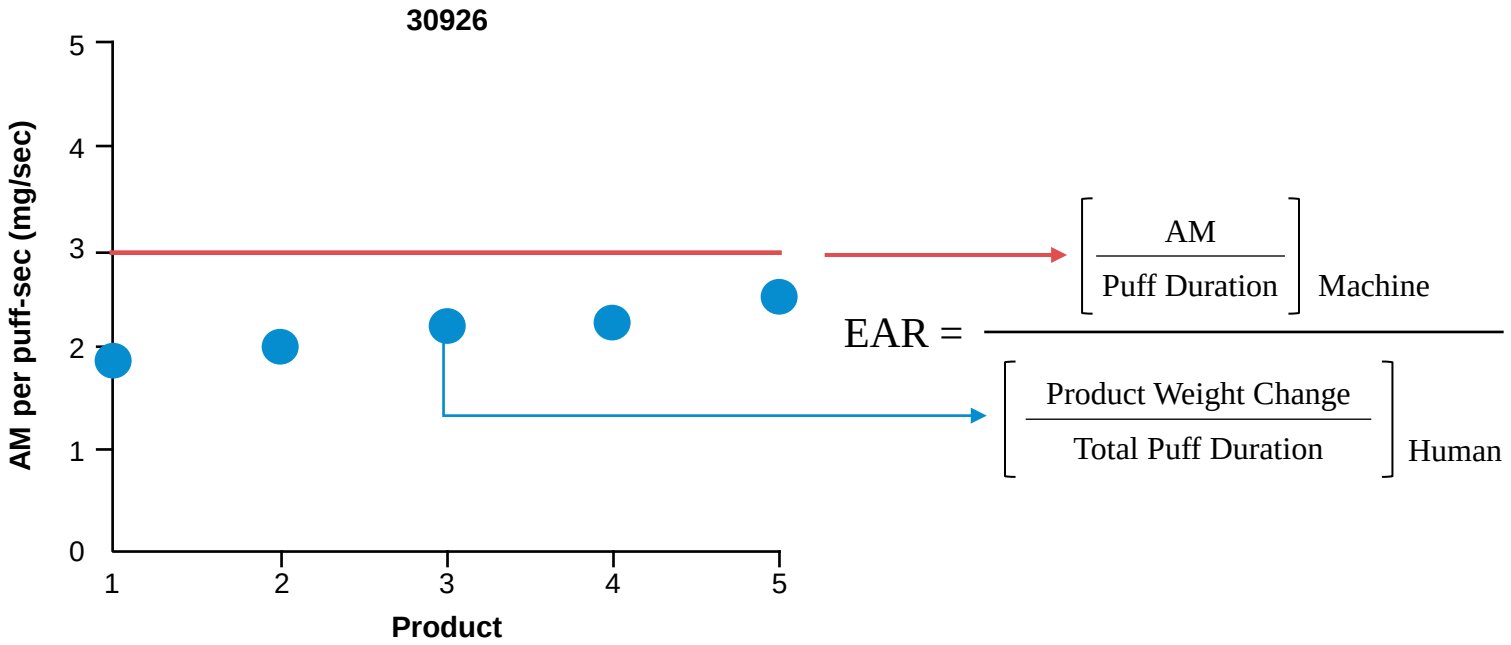


- AM per puff-sec estimated from puffing machine-generated data is typically higher than AM per puff-sec estimated using data from human topography studies (product weight change/total puff duration)
  - Observation was consistent across all five e-liquids prototypes

Machine Puffing Generated AM/Puff-sec Overestimates Average Delivery

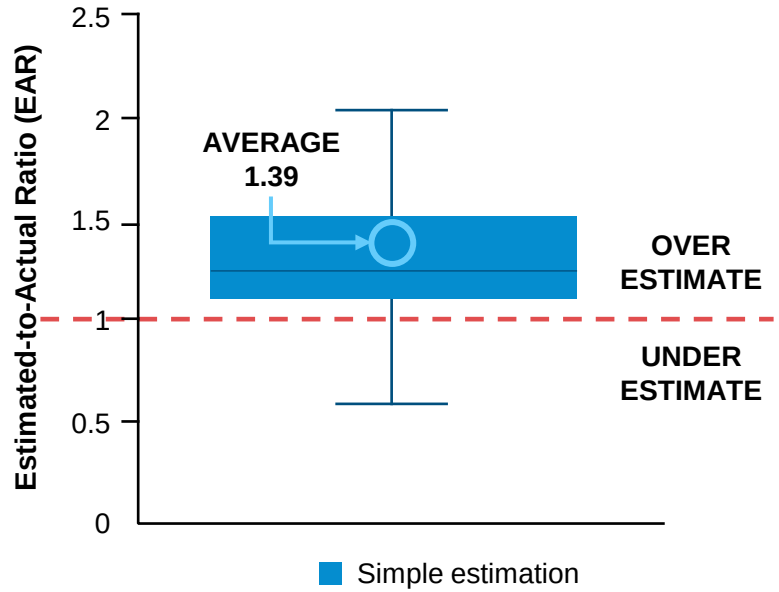
Estimate-to-Actual Ratio (EAR):

- **Calculated** for each participant-product session
- **Collection** of ~200 one-hour sessions



$$EAR = \frac{\left[\frac{AM}{\text{Puff Duration}}\right]_{\text{Machine}}}{\left[\frac{\text{Product Weight Change}}{\text{Total Puff Duration}}\right]_{\text{Human}}}$$

Each dot represents a use session within the topography study



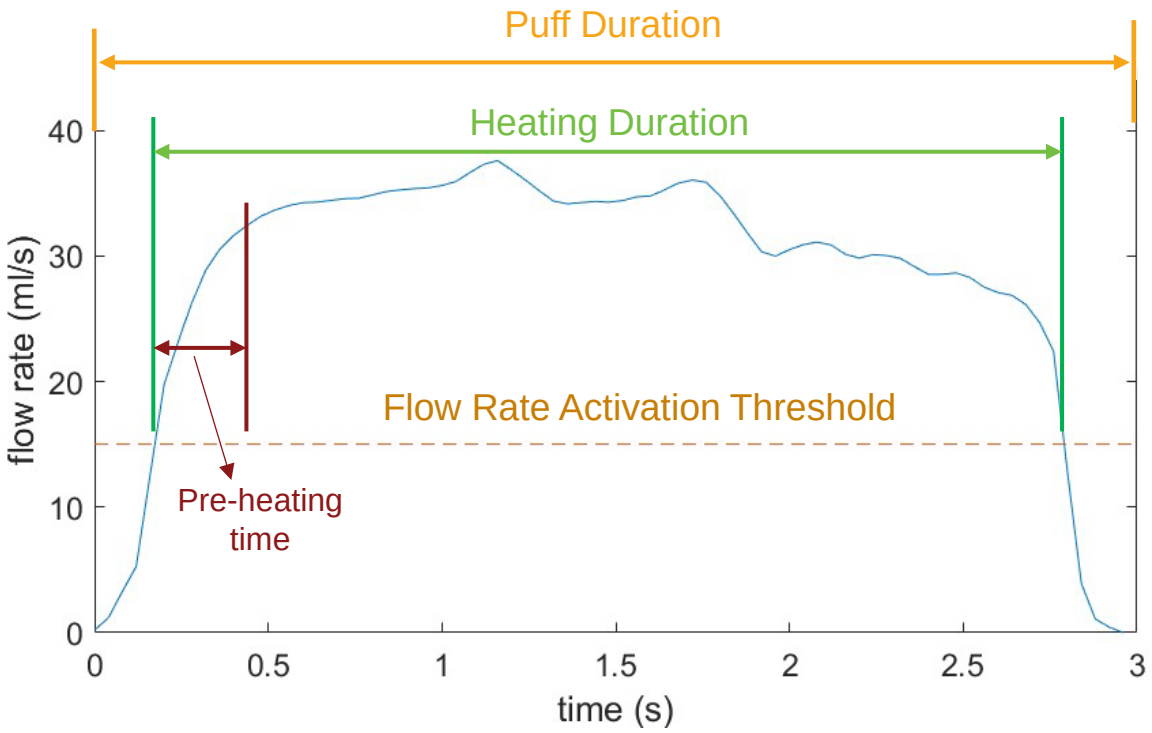
AM=Aerosol Mass

Why Using Machine Data May Lead to Overestimation of Aerosol Delivered to the User

1. **Heating durations (i.e., time the heater is on) are shorter than puff duration**
   - Driver: Atomizer is not activated until a flow rate activation threshold is met

2. **Pre-heating time:** After activation, there will be a pre-heating time before the atomizer gets to aerosol-generating temperatures

Example of a Puff Profile Measured in the Topography Study



Estimating Per Puff AM Deliveries From Topography Data

PROPOSED APPROACH

Correcting Topography Data Using Parameters Estimated from Machine Puffing Experiments to Generate More Accurate Estimates of the Amount of AM/puff Potentially Inhaled by the User

Using **Machine puffing**-based experiments

Individual Puff Profile from Topography Study

1

DETERMINE DEVICE SPECIFIC FLOW-BASED ACTIVATION THRESHOLD

Truncate each individual puff by applying the activation threshold

REPLACED "Puff Duration" with "Heating Duration"

2

DEVELOP A RELATIONSHIP Between AM Generated and Heating Duration to Estimate "Pre-Heating Time"

Apply the relationship to correct AM delivery for pre-heating time

Generate a More Accurate Estimate of Aerosol Mass delivered per puff-sec that incorporates corrections for:

- **Activation** threshold
- **Pre-heating** time

Device Activation Threshold

Determination of Activation Flow Rate Threshold

Gradually increased the puffing machine's flow rate to identify the activation threshold

Flow Rate (ml/s)	Percent of Puffs where LED light Remained ON
11	0%
12	0%
13	37%
14	26%
15	100%
16	100%
18	100%

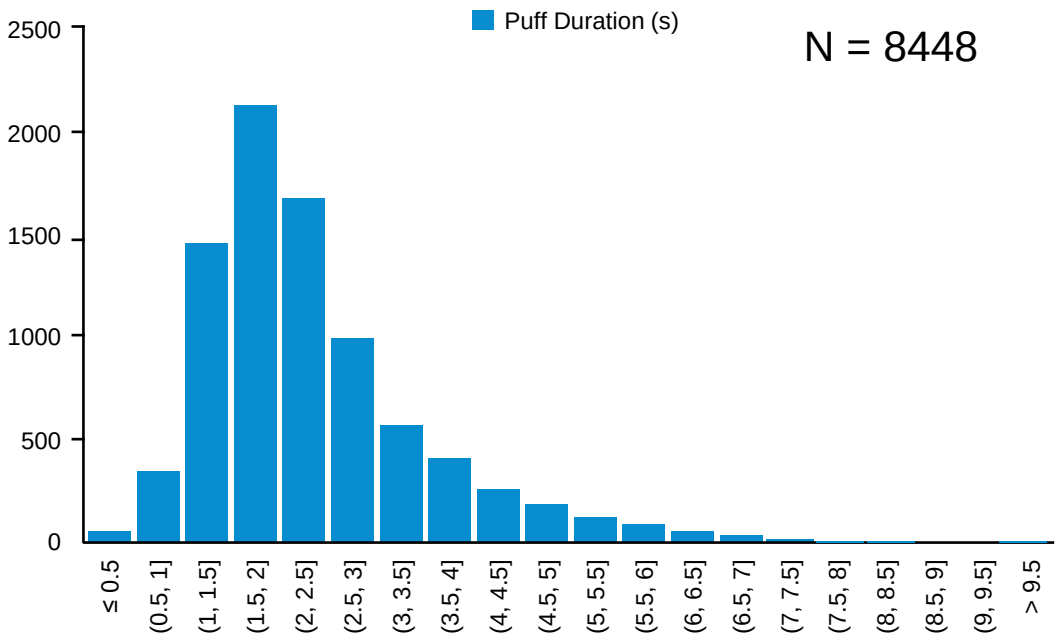
- Flow rates ranging from 11 to 18 ml/s and at various puff durations using a rectangular puff profile.
- LED On ⇒ Heating activated
- The prototype product consistently activated at flow rates of **≥15 ml/s**

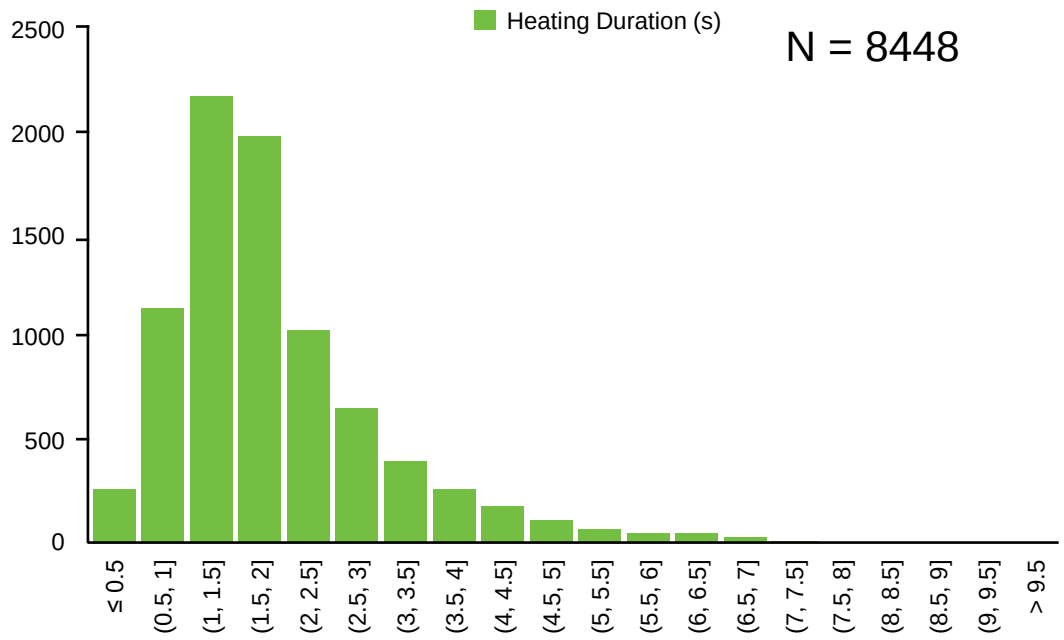
The 15 ml/s activation threshold was used to truncate each of the 8000+ puff profiles collected in the topography study to ***determine actual heating durations***

Heating Duration Correction Results

Each puff is individually processed to obtain the actual heating time (by truncation)

	Puff Duration	Heating Duration	Truncated Time	Truncated Fraction
Mean ± SD	2.37 ± 1.23	1.92 ± 1.16	0.45	19%

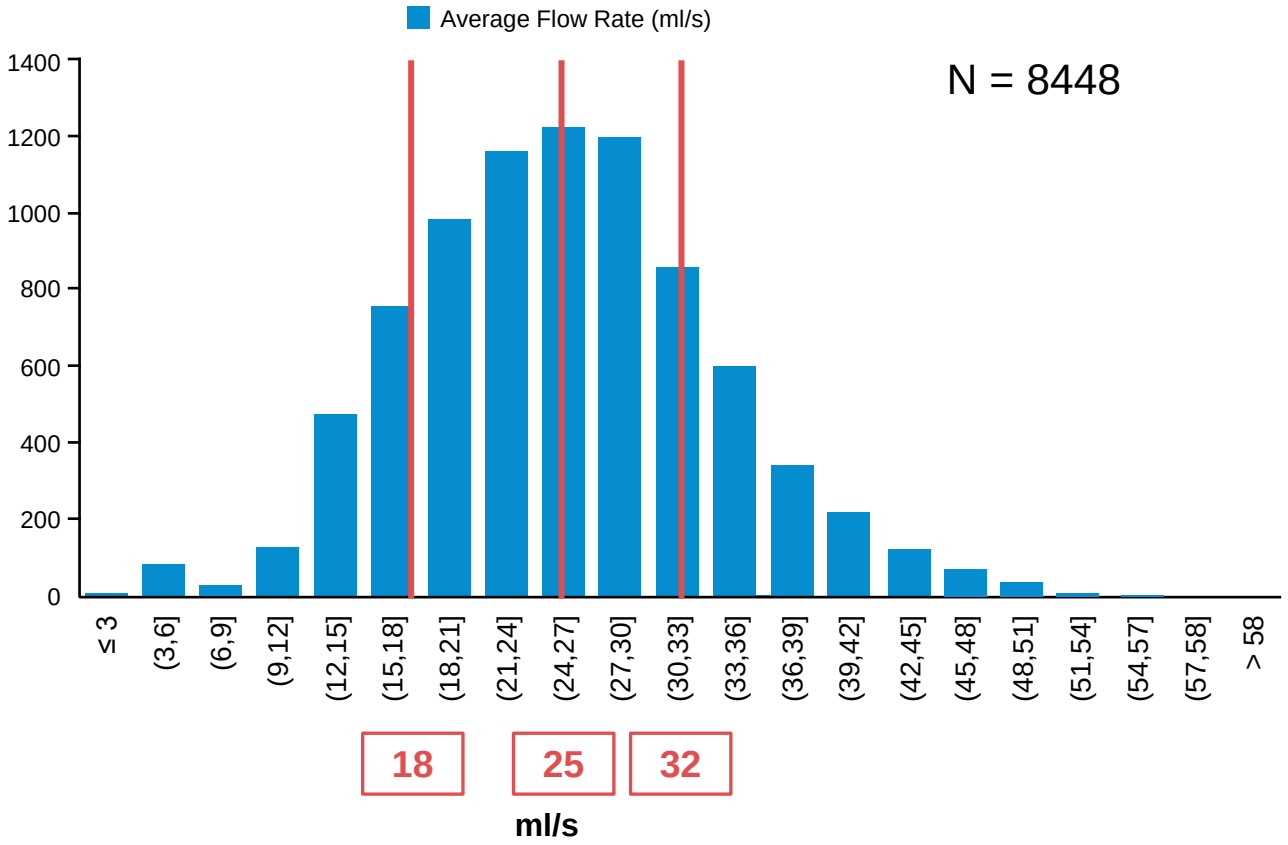




Estimate “Pre-Heating Time”

Three Representative Flow Rates Were Chosen for Machine Puffing

Statistics of the User Average Flow Rate From the Topography Study



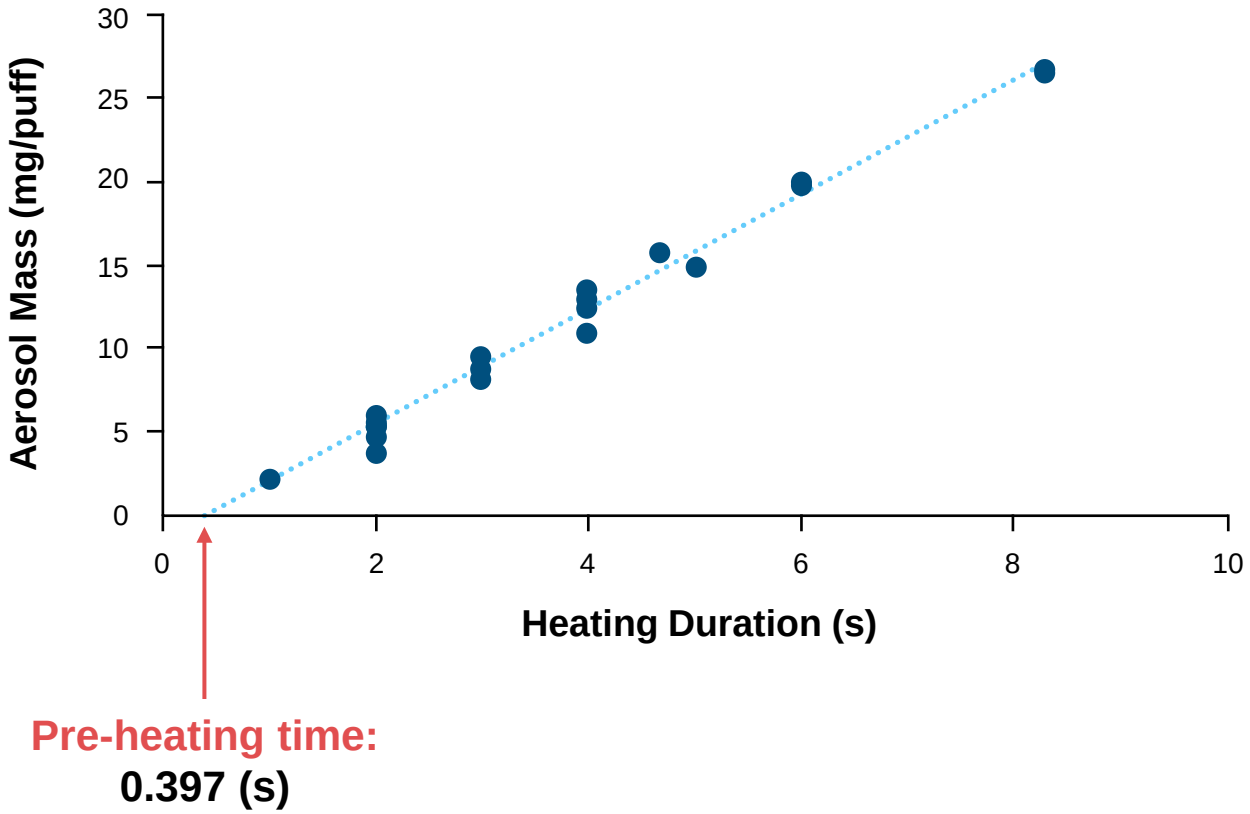
Statistics	Average Flow Rate (ml/s)
Mean	25.60
SD	8.34
Minimum	1.80
25th percentile	19.79
Median	25.36
75th percentile	30.64
Maximum	66.61

Machine Puffing Experimental Design

- Three flow rates (18, 25, and 32 ml/sec)
  - Informed by data from topography study
- Multiple heating durations
- Square Wave
- N = 3 replicates

Develop a Relationship Between AM Generated and Heating Duration to Estimate “Pre-Heating Time”

Linear Regression with Heating Duration



AM = m*(Heating Duration – Pre-heating Time)		
m	Pre-heating Time	R^2
3.421	0.397	0.992

AM is linearly correlated with heating duration

Positive x-intercept represents the pre-heating time before the atomizer reaches aerosol-generating temperatures.

AM (mg) = 3.421 (mg/s)*(Heating Dur. (s) – 0.397 (s))

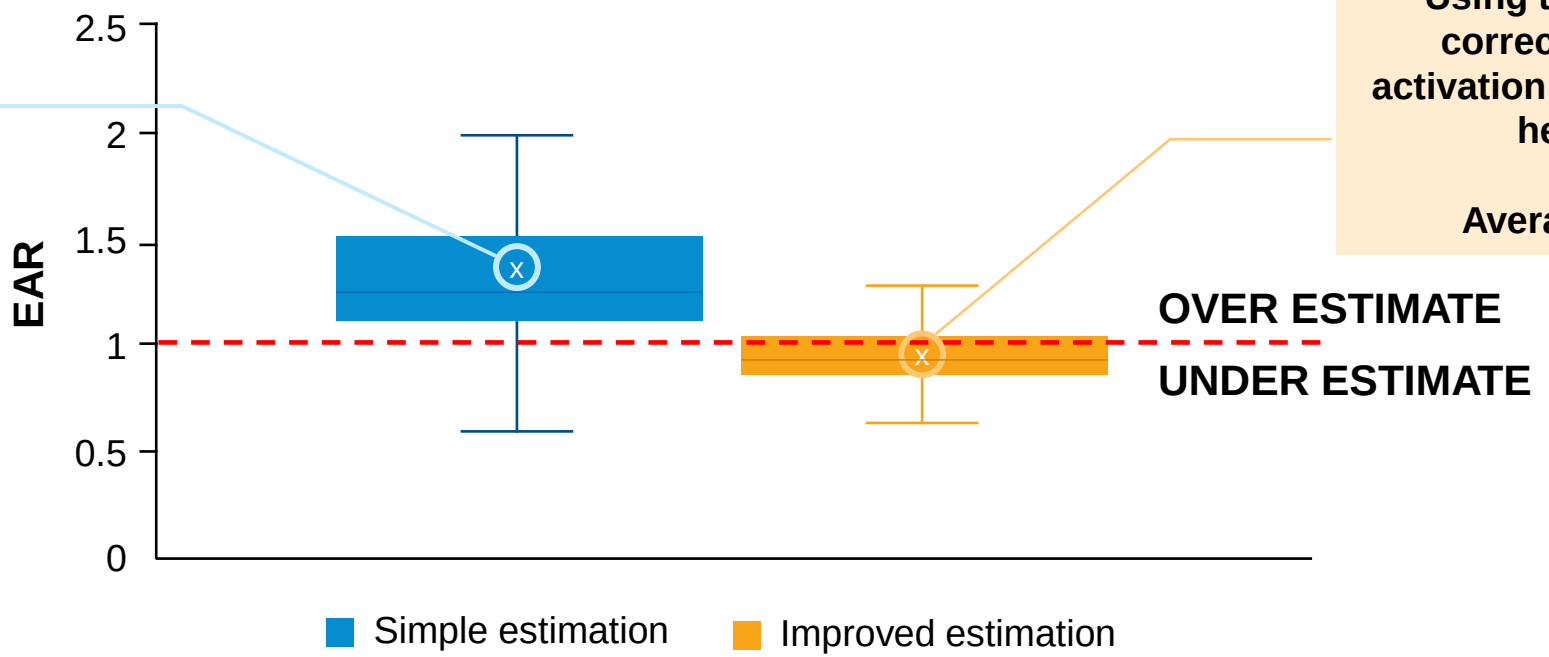
Proposed Estimation Method Provides Better EAR Between Aerosol Mass and Product Weight Change

New Correlation: **AM (mg) = 3.421 (mg/s)*(Heating Dur. (s) – 0.397 (s))**

Estimated AM to Product Weight Change Ratio (Closer to 1 the better)

Using topography data as-is

Average EAR: 1.39



Using topography data corrected for heating activation threshold and pre-heating time

Average EAR: 0.98

Conclusions

- A new protocol was successfully developed for translating aerosol mass data measured on a per-session basis in the topography studies to aerosol mass delivered on a per puff basis
- Machine puffing-based experiments need to be conducted to measure device-specific (a) Flow activation thresholds and (b) Pre-heating time
- 8000+ individual puff profiles from the topography study were truncated to reflect “heating durations” instead of “puff durations”
- Using topography data corrected for heating activation threshold and pre-heating time led to a stronger correlation (i.e., EAR of 0.98) between aerosol mass per puff-sec estimated from topography data and its corresponding machine-measured values.

Thank you