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Evaluation of Bio-Relevant Mouth-Throat (MT) Models to Determine the Aerosol Deposition and Particle Size Distribution of QVAR® Using Cascade Impactor

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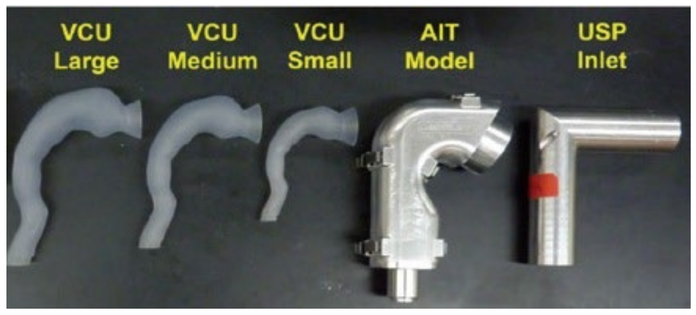
PURPOSE

- The objective of this work was to evaluate various bio-relevant MT models designed for the assessment of total lung dose and aerodynamic particle size distribution (APSD) of the drug-aerosol delivered to the lungs from orally inhaled drug products (OIDPs).
- The methodology developed in this study could improve the *in vitro-in vivo* correlations (IVIVCs) for OIDPs and help innovator and generic sponsors during development of their products.

METHOD

- Five MT models: the USP Induction Port, the Alberta Idealized Throat (AIT), and the large, medium, and small models developed by Virginia Commonwealth University (VCU).
- The MT models were connected to Andersen cascade impactor (ACI, USP apparatus 1) and APSD was determined at a flow rate of 28.3 LPM.
- Both USP Induction Port (has a uniform right-angled bend) and AIT (has a human-like geometry) are commercially available in metal.
- The MT models developed by VCU are based on realistic mouth-throat geometry[6-8].
- QVAR® (Beclomethasone Dipropionate HFA) Inhalation Aerosol was used as a model drug product.
- Same canister was used to perform experiments with each MT model. Five replicate experiments were performed with each MT model (n=5).
- Five actuations were delivered per experiment. The beginning, middle, and end of the life-stage of the canister was studied.



FUNDING

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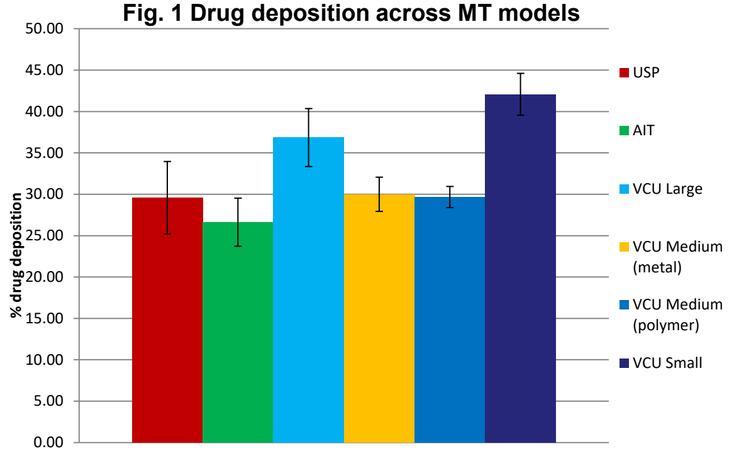
RESULTS

Fig. 1 Drug deposition across MT models



- The charge measured on the VCU medium (metal or polymer) model was found to be negligible (nearly 0).
- No statistically significant differences were observed in MT deposition for USP throat (29.6±4.4%), AIT (26.6±2.9%), or VCU medium models (29.7±1.3%).
- However, compared to the MT deposition in the VCU medium model, a 24% increase was observed in the VCU large model (36.9±3.5%) and a 42% increase was observed in VCU small model (42.1±2.5%).
- MT deposition was influenced by the geometry and/or the internal space volume of the throat models.
- The MT deposition values (Fig. 1) obtained in this study closely matched or were similar to those reported in the literature clinical data[1-5].

- A statistically significant difference ($p<0.05$) observed in the MMAD obtained from USP throat and AIT against VCU Small model. The MMAD (0.88-0.95 µm) values (Fig. 2) obtained in this study matched with the values reported in the literature[1].

Fig. 2 MMAD across MT models

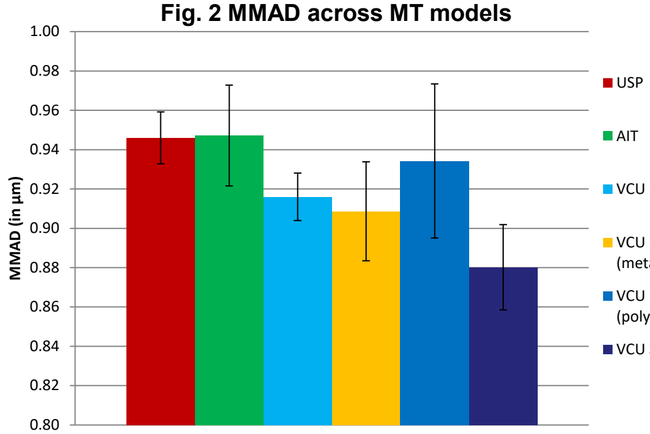
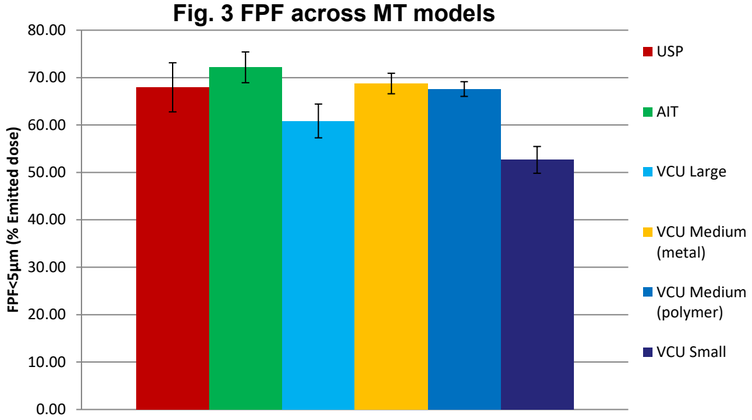


Fig. 3 FPF across MT models



- Fine particle fraction (FPF<5µm) values (Fig. 3) of the MT models showed a similar trend to that observed for TLD values. The similar trend is consistent with majority of QVAR® aerosols entering the cascade impactor being fine particles.

QVAR HFA 40 mcg	USP Throat		AIT		VCU Large		VCU Medium (metal)		VCU Medium (polymer)		VCU Small	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Total Emitted dose (µg)	39.3	1.4	42.2	1.4	40.5	1.5	41.8	1.1	41.1	2.4	38.4	2.2
EDA	0.75	0.05	0.78	0.08	0.69	0.04	0.67	0.04	0.67	0.05	0.48	0.01
MMAD (in µm)	0.95	0.01	0.95	0.03	0.92	0.01	0.91	0.03	0.93	0.04	0.88	0.02
FPF<5µm (% Emitted dose)	68.0	5.2	72.2	3.2	60.9	3.6	68.7	2.2	67.6	1.6	52.6	2.8
FPF<5µm (% Total dose)	52.3	5.7	56.0	4.1	45.5	3.5	51.8	2.9	51.9	2.2	38.1	2.9
Throat (%)	29.6	4.4	26.6	2.9	36.9	3.5	30.0	2.1	29.7	1.3	42.1	2.5
Total Lung Dose (% ED)	67.8	5.1	72.6	3.0	61.9	3.3	69.2	2.2	69.6	1.3	56.5	2.2
%LC	98.3	3.5	105.5	3.6	101.2	3.7	104.5	2.7	102.8	5.9	95.9	5.5

CONCLUSION

- The mouth-throat and total lung deposition of QVAR® were influenced by the geometry and internal space volume of MT models.
- By contrast, the measured particle size distributions were similar across all models.
- The deposition of QVAR® measured across the MT models closely matched with the clinical data reported in the literature further suggesting a strong *in-vitro in-vivo* correlation (IVIVC).

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