TRUDELL MEDICAL INTERNATIONAL

Helping people
breathe better
and live fuller lives.

in collaboration with

FLUIDDA

Jason A. Suggett[1],
Cedric Van Honsbeke[2], Stien Van Steen[2],
Benjamin Mignot[2] & Jolyon P. Mitchell[3]

[1]Trudell Medical International, London, Canada.
[2]FLUIDDA Inc., Kontich, Belgium.
[3]Jolyon Mitchell Inhaler Consulting Services Inc., London, Canada.

A Comparison, Using Functional Respiratory Imaging (FRI), of Adult Airway Deposition Profiles from a Pressurized Metered Dose Inhaler with Valved Holding Chamber (pMDI/VHC) and Two Dry Powder Inhalers (DPI)

Respiratory Drug Delivery (RDD) 2021
Virtual Conference

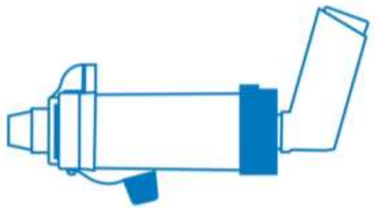
INTRODUCTION

Purpose:

Use Functional Respiratory Imaging (FRI) to compare the predicted delivery of medication from a pMDI/VHC combination and two commonly prescribed mid-resistance DPIs using optimal and sub-optimal inhalation flow rates

MATERIALS & METHODS

- The model adult patient was based on CT scans collected from a male subject aged 21 years with moderate asthma
- Devices tested:



AeroChamber Plus* Flow-Vu* ((AC+) valved holding chamber (VHC), Trudell Medical International) delivering salbutamol from a **Ventolin† EvoHaler† pMDI** (100 µg; GSK)

Symbicort† Turbuhaler† (6 µg formoterol fumarate/200 µg budesonide; AstraZeneca)

Seretide† Diskus† (50 µg salmeterol xinafoate/250 µg fluticasone propionate; GSK)

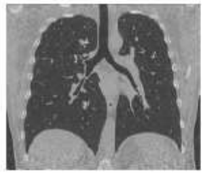
- The aerodynamic particle size distribution (APSD) profiles and delivered doses were obtained from published data [1,2]

1. Johal B, Howald M, Fischer M, Marshall J, Venthoye G: Fine Particle profile of fluticasone propionate/formoterol fumarate versus other combination products: The DIFFUSE Study. *Comb Prod Ther* 2013, 3: 39–51.
2. Buttini F, Brambilla G, Copelli D, Sisti V, Balducci AG, Bettini R, Pasquali I: Effect of flow rate on *in-vitro* aerodynamic performance of NEXThaler in comparison with Diskus and turbohaler dry powder inhalers. *J Aerosol Med Pulmon Drug Deliv* 2016, 29(2): 167–178.

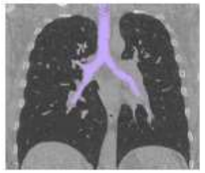
MATERIALS & METHODS

Functional Respiratory Imaging

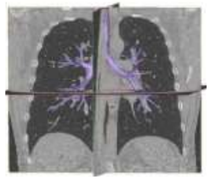
1. HRCT
Patient data obtained by taking dose CT scans



2. Structure Segmentation
Patient-specific airway and lung structures are extracted

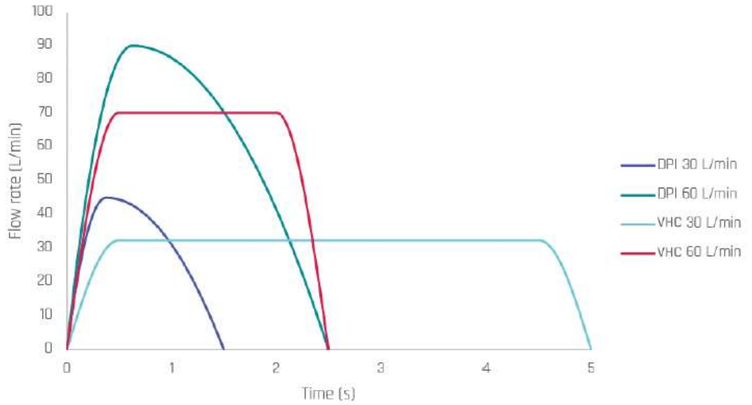


3. Patient-specific 3D Model
3D model generated based on segmentation



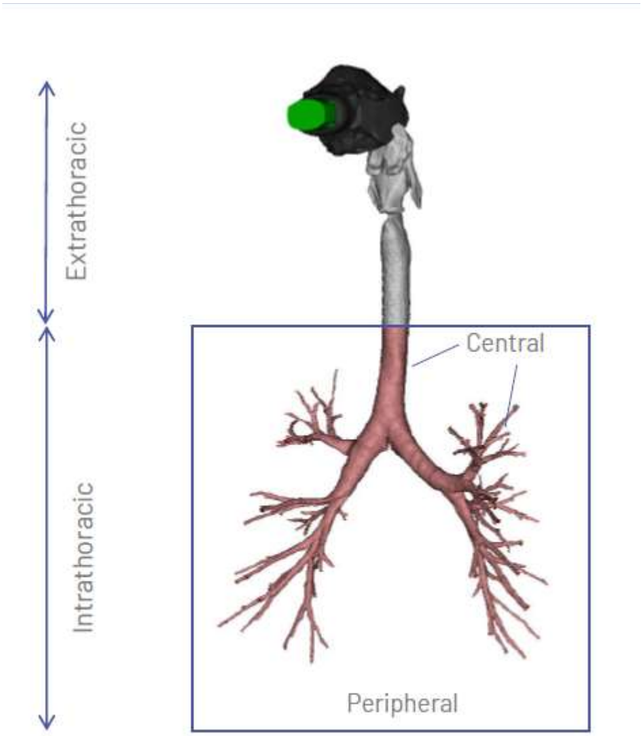
4. Flow Simulation (CFD):
Flow and particle simulations applied to the 3D model

Flow Profiles[3]



	OPTIMAL	SUB-OPTIMAL
MDI+ VHC	Mean flow rate = 30 L/min for 5 seconds	Mean flow rate = 60 L/min for 2.5 seconds
DPIs	Mean flow rate = 60 L/min for 2.5 seconds	Mean flow rate = 30L/min for 1.5 seconds

Lung Structure and Zones[3]



3. Laube BL, Janssens HM, de Jongh FHC, Devadason SG, Dhand R, Diot P, Everard ML, Horvath IL, Navalesi P, Voshaar T, Chrystyn H: ERS/ISAM task force consensus statement: What the pulmonary specialist should know about the new inhalation therapies. *ERJ Express* 2011, 37(6): 1308–1331.

RESULTS

Optimal Inhalation Profile Deposition (Percent of Label Dose)

Zone	Turbuhaler† DPI			Diskus† DPI			pMDI/AC + VHC
	FF	BUD	Average	SX	FP	Average	SAL
Extrathoracic	77.64	80.94	**79.29**	81.59	87.05	**84.32**	**5.56**
Intrathoracic	20.25	17.45	**18.85**	10.88	9.14	**10.01**	**32.22**
Central	7.11	6.14	6.63	4.33	3.69	4.01	9.54
Peripheral	13.14	11.30	12.22	6.55	5.46	6.01	22.67

Table 1. Predicted active pharmaceutical ingredient (API) deposition profiles using optimal inhalation flow rates
(Mean flow rate = 30 L/min pMDI + VHC; 60 L/min DPI)

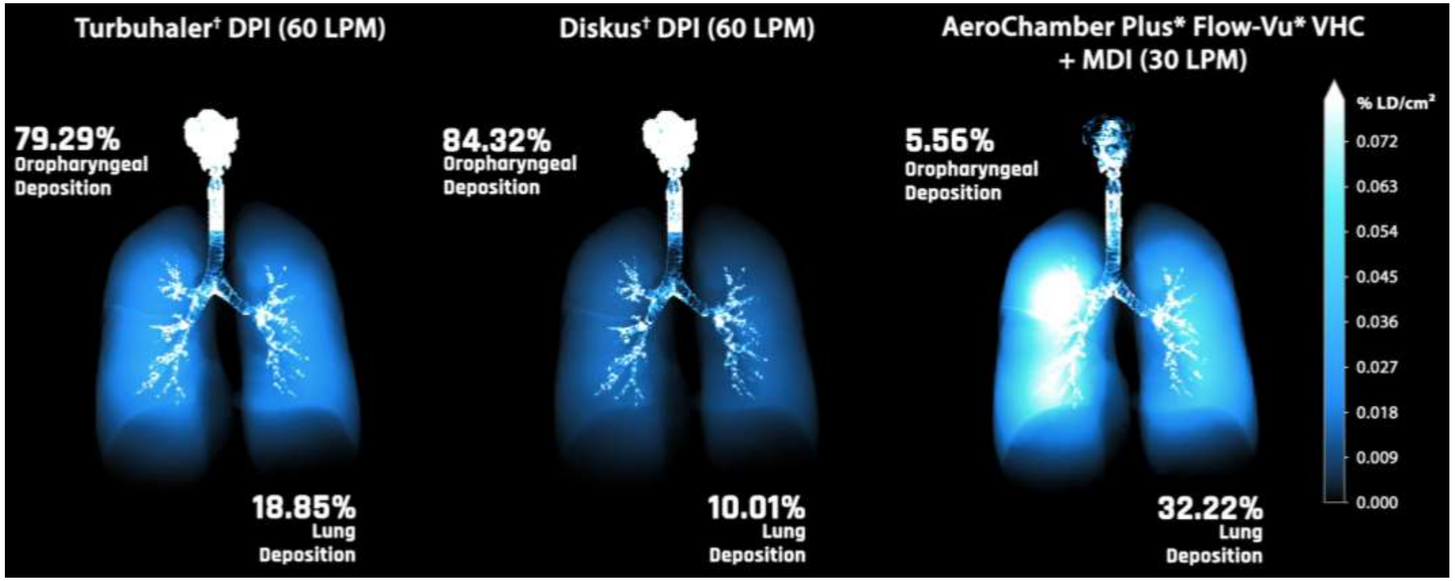


Figure 1. Visual representation of the API deposition profiles using optimal inhalation flow rates

RESULTS

Sub-Optimal Inhalation Profile Deposition (Percent of Label Dose)

Zone	Turbuhaler† DPI			Diskus† DPI			pMDI/AC + VHC
	FF	BUD	Average	SX	FP	Average	SAL
Extrathoracic	73.64	73.99	**73.82**	80.32	83.38	**81.85**	**7.49**
Intrathoracic	5.06	4.01	**4.54**	8.03	7.41	**7.72**	**30.29**
Central	1.80	1.42	1.61	3.15	2.89	3.02	10.50
Peripheral	3.26	2.58	2.92	4.88	4.53	4.705	19.79

Table 2. Predicted active pharmaceutical ingredient (API) deposition profiles using sub-optimal inhalation flow rates
(Mean flow rate = 60 L/min pMDI + VHC; 30 L/min DPI)

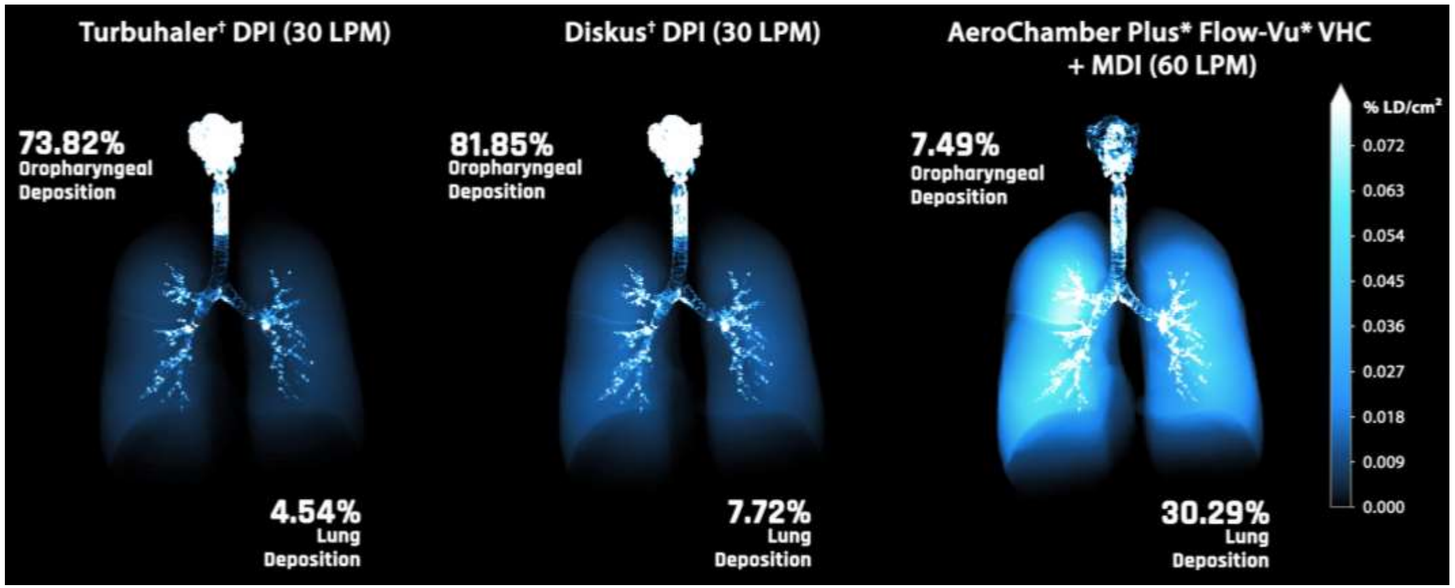


Figure 2. Visual representation of the API deposition profiles using sub-optimal inhalation flow rates

DISCUSSION

Intrathoracic component (dose to the lungs) with the pMDI/VHC combination was greater than either DPIs

- Corresponding much lower extrathoracic values were expected, given VHC's role in removing the ballistic component emitted by the pMDI - much of which would deposit in the oropharynx and contribute to the extrathoracic content had the VHC been absent
- Minimal change in the deposition profile for the pMDI/VHC system at the suboptimal compared with optimal inhalation

Predicted intrathoracic deposition for either API of the combination delivered with the Turbuhaler† DPI was greater than the corresponding data for the Diskus† DPI at the optimal inhalation flow rate

- Turbuhaler† DPI appeared to be more sensitive to change in flow rate, as at suboptimal flow rates the intrathoracic deposition values were lower than those for the Diskus† DPI

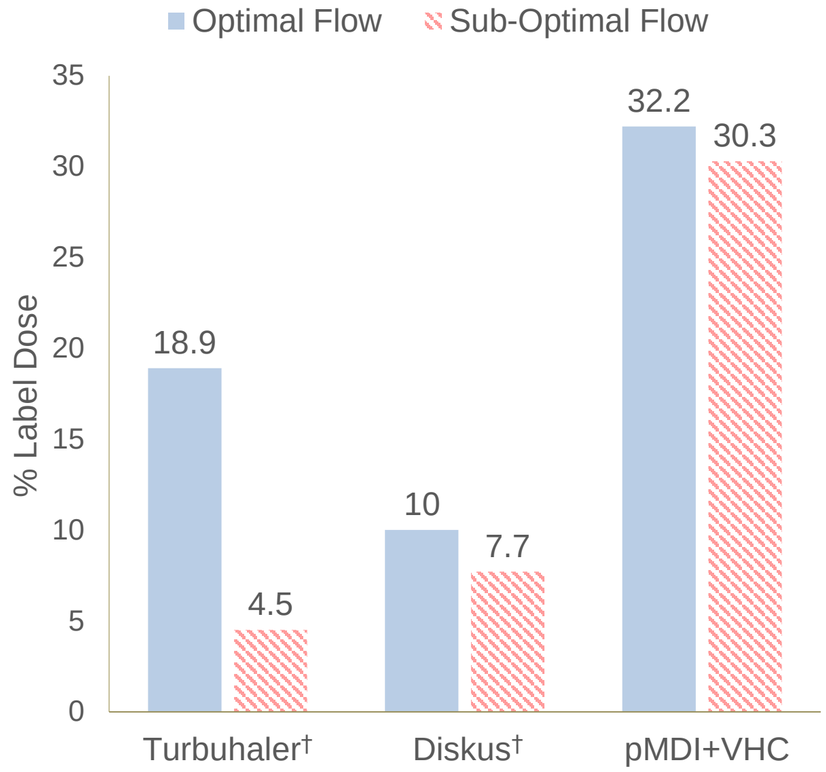


Figure 3. Intrathoracic (lung) delivery at optimal and sub-optimal inhalation flow rates

CONCLUSION

- FRI-based modelling study predicted that pMDI/VHC combination would likely deliver a greater proportion of medication to the lungs and be less sensitive to changes in inhalation profiles from optimal to selected sub-optimal
- Study results highlight important considerations for healthcare professionals when patients are not adherent to inhalation technique instructions indicated for optimal use
- Differences were observed between the two DPIs, indicating that even within devices of similar resistance, device and formulation may cause variability in the powder dispersion and resultant airway deposition
- Further work is desirable to examine a wider range of suboptimal conditions using FRI in order to understand in more detail robustness of these inhalers to non-ideal use