Using Functional Respiratory Imaging (FRI) to Compare Predicted Airway Deposition Between Pressurized Metered Dose Inhaler (pMDI) with *AeroChamber Plus** *Flow-Vu** Valved Holding Chamber (VHC) and Two Dry Powder Inhalers (DPIs) in a COPD patient

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BACKGROUND

- Both pMDI/VHC and DPI routes are prescribed to deliver inhaled aerosol-based medications to the lungs for the treatment of COPD. A slow and long inhalation often accompanied by a breath-hold is preferred when using a pMDI/VHC, whereas a forceful inhalation of short duration is advocated for passive DPI use.

OBJECTIVE

- Use Functional Respiratory Imaging acquired from a model adult patient with COPD to compare predicted airway deposition between pMDI with ***AeroChamber Plus**** ***Flow-Vu**** Valved Holding Chamber and two Dry Powder Inhalers at optimal and sub-optimal inhalation profiles.

MATERIALS & METHODS

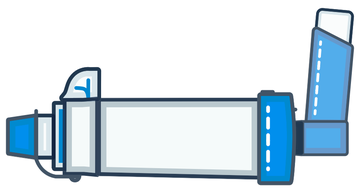
Patient:

- The model adult patient was based on the CT scan of a male subject aged 67 years having height of 170 cm, with moderate COPD (GOLD stage III[2]) accompanied by moderate emphysema (emphysema score = 0.9% lung volume)

Inhalers:

Symbicort† Turbuhaler†
(formoterol fumarate/ budesonide; AstraZeneca)

Trelegy† Ellipta† DPI
(fluticasone/umeclednium/vilanterol; GSK)



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

- Modelled optimal and sub-optimal inhalation conditions were assessed as part of the FRI technology for each inhaler class based on breathing profile data in an ERS/ATS task force consensus statement[1] in accordance with the parameters specified in TABLE 1
- It is important to note that peak inspiratory flows for the DPIs were higher (approx. 90 and 45 L/min for optimal and sub-optimal) than the reported mean flow rates

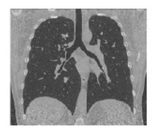
Inhaler Class	Condition	Duration(s)	Mean Flow Rate (L/min)
pMDI/VHC	Optimal	5	30
	Sub-Optimal	2.5	60
DPI (Turbhaler†)	Optimal	2.5	60
	Sub-Optimal	1.5	30
DPI (Trelegy† Ellipta†)	Optimal	2.5	60
	Sub-Optimal	1.5	30

Table 1: Modelled Optimal and Sub-Optimal Inhalation Conditions

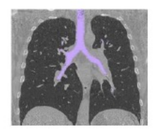
Note: APSD values for Trelegy† Ellipta† sub-optimal were gerated at 40L/min

FUNCTIONAL RESPIRATORY IMAGING (FRI)

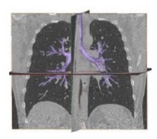
1. **HRCT**
   Patient data obtained by taking low dose CT scans



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



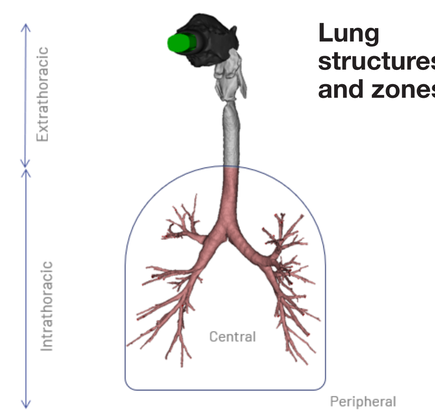
3. **Patient-specific 3D Model**
   3D model generated based on segmentation



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

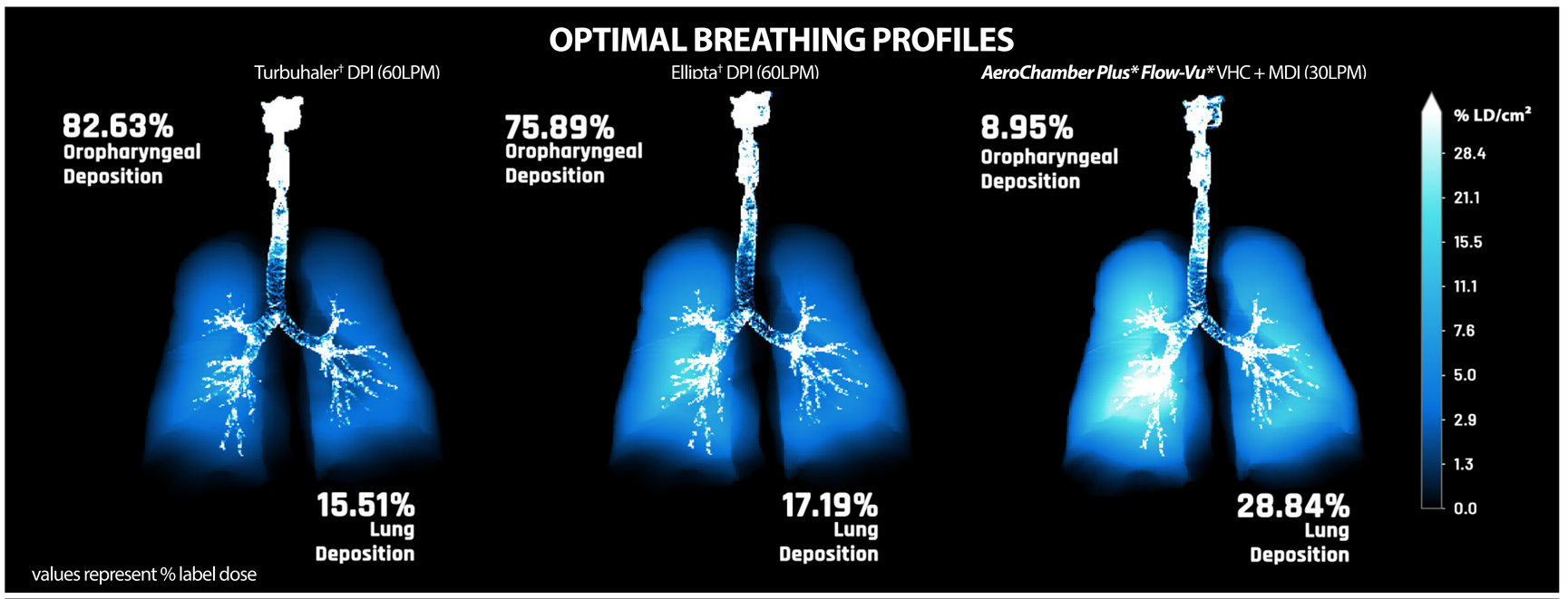
FRI INTERPRETATION METHODOLOGY

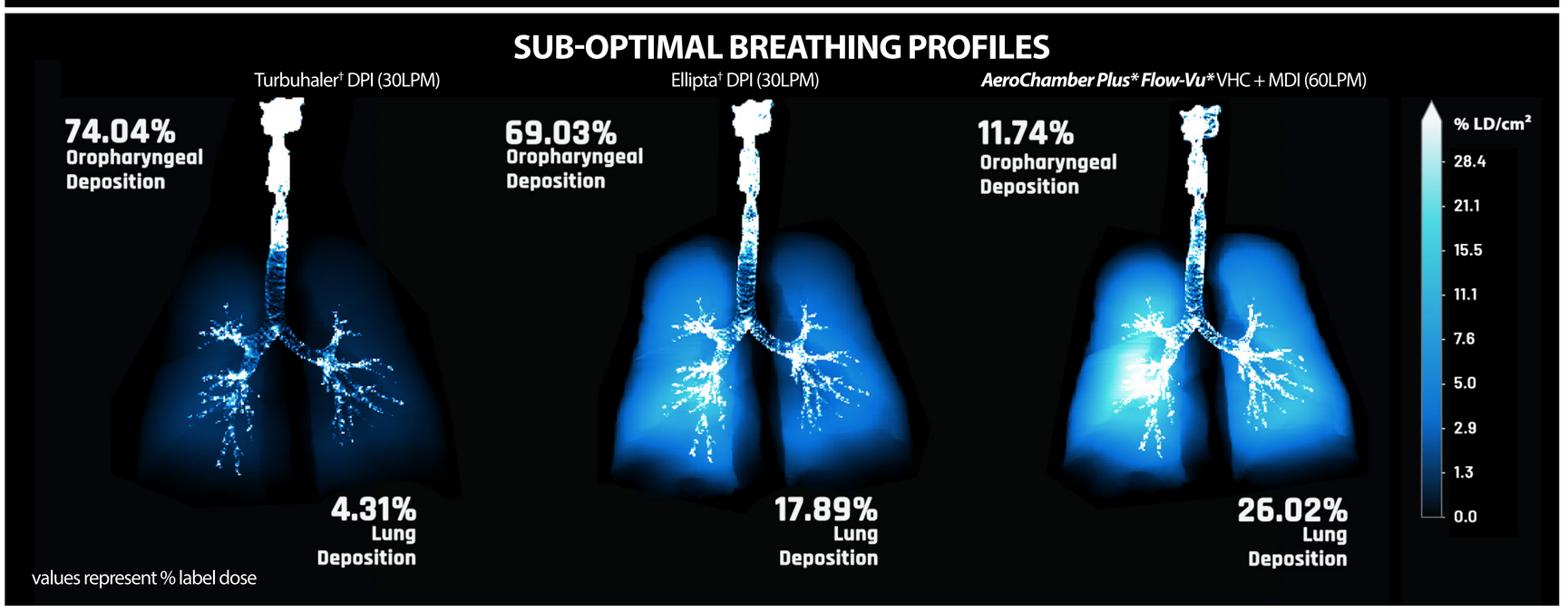
- Aerodynamic particle size distribution (APSD) profiles and corresponding delivered doses (DDs) were obtained from published data



RESULTS

- Expressed as a percentage of labelled metered doses (average values used when more than one drug in combination)





Delivery Device	Flow Rate (L/min)	API (label claim dose)(µg)	Extrathoracic (% label claim dose)	Intrathoracic (% label claim dose)	Central (% label claim dose)	Peripheral (% label claim dose)	Central/Peripheral Deposition Ratio
pMDI/VHC	30	100	8.95	28.84	13.05	15.79	0.83
	60		11.74	26.02	13.40	12.63	1.06
Turbhaler† Ellipta† DPI	30	100	82.07	14.10	7.54	6.56	1.15
		62.5	64.03	17.83	8.57	9.27	0.92
		25	60.98	21.73	10.82	10.92	0.99
	60	100	86.34	13.19	7.34	5.85	1.25
		62.5	71.92	17.66	8.94	8.72	1.03
		25	69.40	20.72	10.89	9.84	1.11
Symbicort† Turbhaler† DPI	30	200	73.89	4.80	2.50	2.30	1.09
		6	74.19	3.81	1.98	1.82	1.09
	60	200	81.22	16.67	8.55	8.12	1.05
		6	84.04	14.34	7.37	6.97	1.06

Table 2: FRI predicted airway deposition profiles for pMDI + VHC compared with those from the two passive DPIs for optimal and sub-optimal inhalations
Data are reported in terms of percentage label claim dose to allow for the widely differing values of absolute mass of the active pharmaceutical ingredients (APIs) involved

CONCLUSION

- Predictions from FRI, mimicking inhalation by an adult patient with moderate-to-severe lung function impairment defined by GOLD stage III COPD provide support for the claim that efficiency of inhaled medication delivery to the lungs by pMDI with the tested VHC when inhaling either optimally or sub-optimally is likely to be greater than that for the two widely prescribed passive DPIs evaluated.
- Regional lung deposition based on C/P ratio is predicted to be only slightly influenced by deviations in inhalation flow rate from optimal to sub-optimal within the flow rate ranges studied, with the greatest peripheral deposition observed for the pMDI/VHC system at optimal inhalation flow

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December 7-9, 2022

[1] 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.