Estimating the Dose of Dry Powder Inhalers Delivered to the Larynx Using Computational Fluid Dynamics

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MOTIVATION

- Dry Powder Inhalers (DPIs) have been a mainstay in the treatment of chronic reactive airway diseases such as asthma.
- The upstream location of the larynx leads to premature deposition of drug particles in these locations where they evoke local side effects, including dysphonia (hoarse voice).
- Dysphonia has been documented to occur in 8% to 58% of DPI users.
- Discontinuation of DPI is a solution, but it is not effective for patients, whose symptoms are difficult to control.

RESEARCH QUESTION

- The goal of this study is to estimate the corticosteroid dose that deposits in the larynx of patients using DPIs and to investigate possible strategies to reduce dysphonia associated with DPI use.

METHODS

- **Computational Fluid Dynamics (CFD)** is an effective technique to **simulate airflow and particle transport** by solving the motion equations numerically.
- A 3D computational model of the respiratory tract of a healthy adult was constructed based on magnetic resonance imaging **(Fig. 1A).** Poly-hexcore meshes of 2.9 million (coarse), 5.6 million (medium) and 9.2 million (fine) cells and 5 prism layers were created in ANSYS Fluent Meshing. **Fig. 1B** shows a Poly-hexcore Mesh of 5.6 million cells with 5 prism layers.
- **Transient CFD simulations** were performed in ANSYS Fluent. Respiratory airflow and particle transport were simulated for constant oral inhalation rates (Q) of 30, 45, and 60 L/min.
- **k-omega and Large Eddy Simulation (LES) turbulence models have been compared to predict laryngeal doses. LES modelling is more accurate but computationally intensive.**
- Log-normal particle size distribution with X_{50} = $2\mu m$ and σ_g=1.99. X_{50} represents half the mass is in particles smaller than X_{50}. σ_g represents the width of distribution **(Fig. 2).**

RESULTS

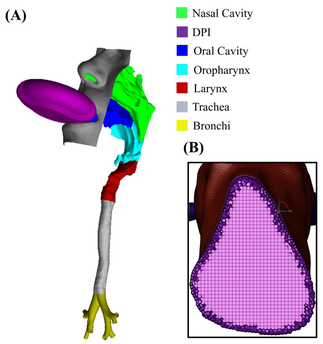


Figure 1 – (A) Geometry of a 3-dimensional computational model showing different upper-airway region of the respiratory tract. (B) Poly-hexcore mesh with 5.6 million cells with 5 prism layers.

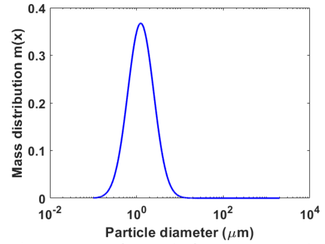


Figure 2 – Log-normal particle size distribution of a hypothetical DPI with X_{50}= 2 microns and σ_g = 1.99.

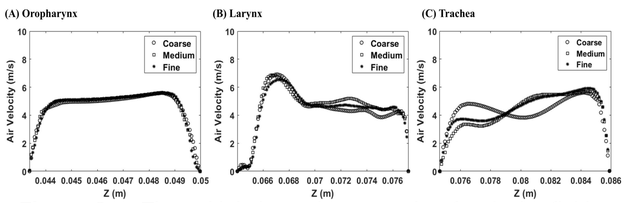


Figure 3 – The grid independence study of velocity field showed good agreement for air velocity calculated along z-direction on (A) Oropharynx, (B) Larynx and (C) Trachea.

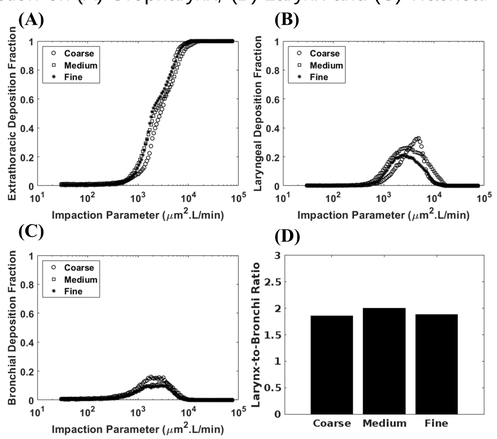
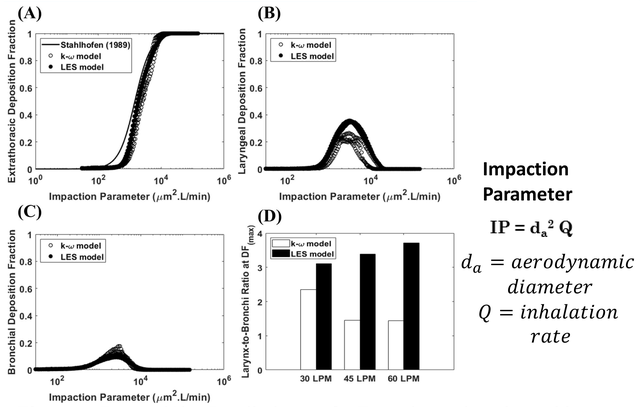


Figure 4 – The grid independence study of particle deposition showed good agreement for (A) Extrathoracic, (B) Laryngeal, (C) Bronchial Deposition and (D) Larynx-to-Bronchi Ratio.



Impaction Parameter

$$IP = d_a^2\, Q$$

$d_a = aerodynamic\ diameter$

$Q = inhalation\ rate$

Figure 5 – (A) Prediction of Extrathoracic deposition compared to the experimental data of Stahlhofen et al. (1989). (B) $k-\omega$ model predicted higher laryngeal deposition fraction (DF) compared to the LES model. (C) Bronchial deposition is similar for both models. (D) LES model predicted higher Larynx-to-Bronchi Ratio at max DF with increasing flowrates.

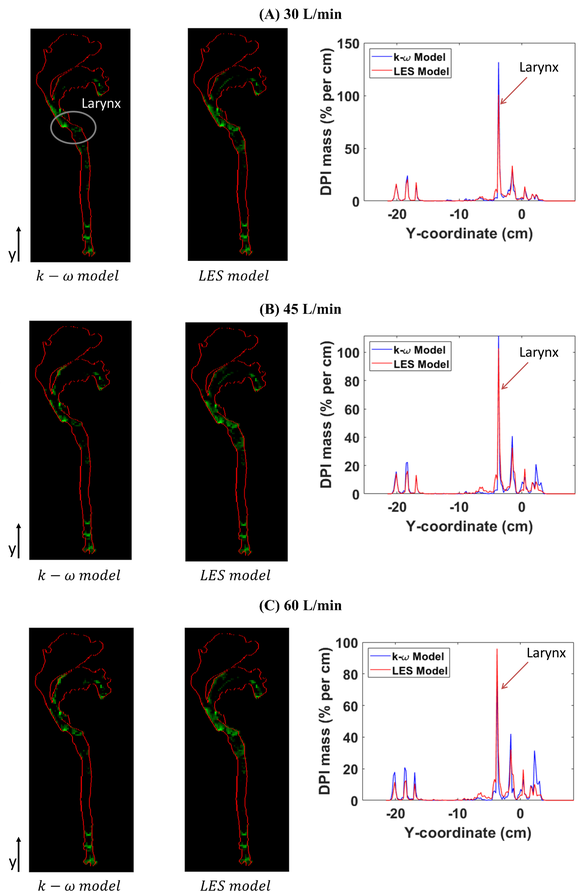


Figure 6 – LES model predicted higher overall laryngeal deposition compared to the k-omega model with increasing flowrate of (A) 30 LPM, (B) 45 LPM and (C) 60 LPM.

DISCUSSION

- A **grid independence study** revealed that a mesh with **5.6 million elements** provided an air velocity field nearly mesh independent for both air velocity field and particle deposition **(Fig. 3 and Fig. 4).**
- **Validation:** Our CFD simulations are in good agreement with experimental data of Stahlhofen et al. (1989) **(Fig. 5A).**
- The dose of inhaled corticosteroids depositing in the larynx was predicted to be 3- to 4-fold higher than the dose delivered to the primary bronchi for all inhalation rates using the LES model **(Fig. 5D).**
- **LES model predicted proportional relationship between Larynx-to-Bronchi Ratio (LBR) and oral inhalation rate.** k-omega model predicted inverse relationship between oral inhalation rate and LBR.
- Regional doses show a **hotspot of deposition in the larynx** compared to other region predicted by LES model **(Fig.6).**

CONCLUSIONS

- The CFD simulations suggested a reduced laryngeal dose can be achieved by using DPIs with smaller particles.
- In future, we will investigate the effect of sinusoidal breathing profile and different breathing techniques (e.g.: short vs long breath, deep vs shallow breath) to estimate the dose of DPIs delivered to the larynx.

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