

In Vitro Evaluation of Regional Drug Deposition in Nasal Airways of Children Using Realistic Anatomical Replicas

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Overview and Objectives

- To study the effect of intersubject variability due to age on drug delivery efficiency of nasal spray drug products
- To address the complexity in controlling administration parameters in children using in vitro methods in lieu of clinical studies
- This study describes an in vitro investigation of the regional drug deposition in children from 2 to 11 years old (20 nasal airway replicas, half male and half under 6 years old) with a commercially available nasal spray product (FLONASE[®] SENSIMIST[™] ALLERGY RELIEF)

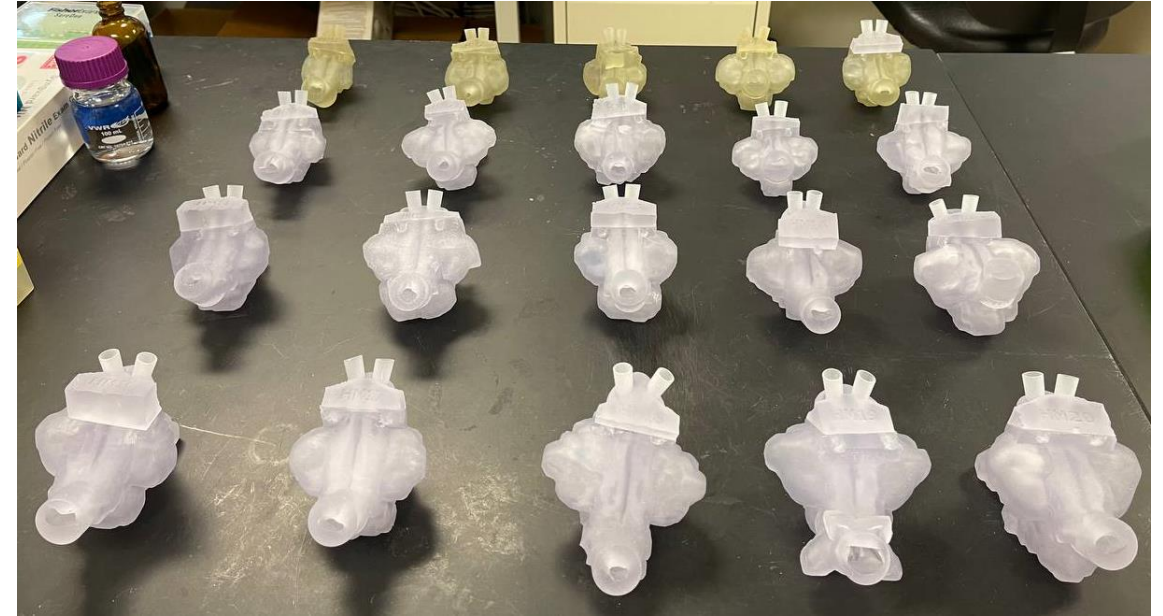
Methodology

➤ Nasal Sprays In Vitro Characterization

- ✓ Dv50 (droplet diameter below which 50% of the sample volume exists), Plume Angle, Plume Width, Ovality and Area

➤ Nasal Airway Models Development

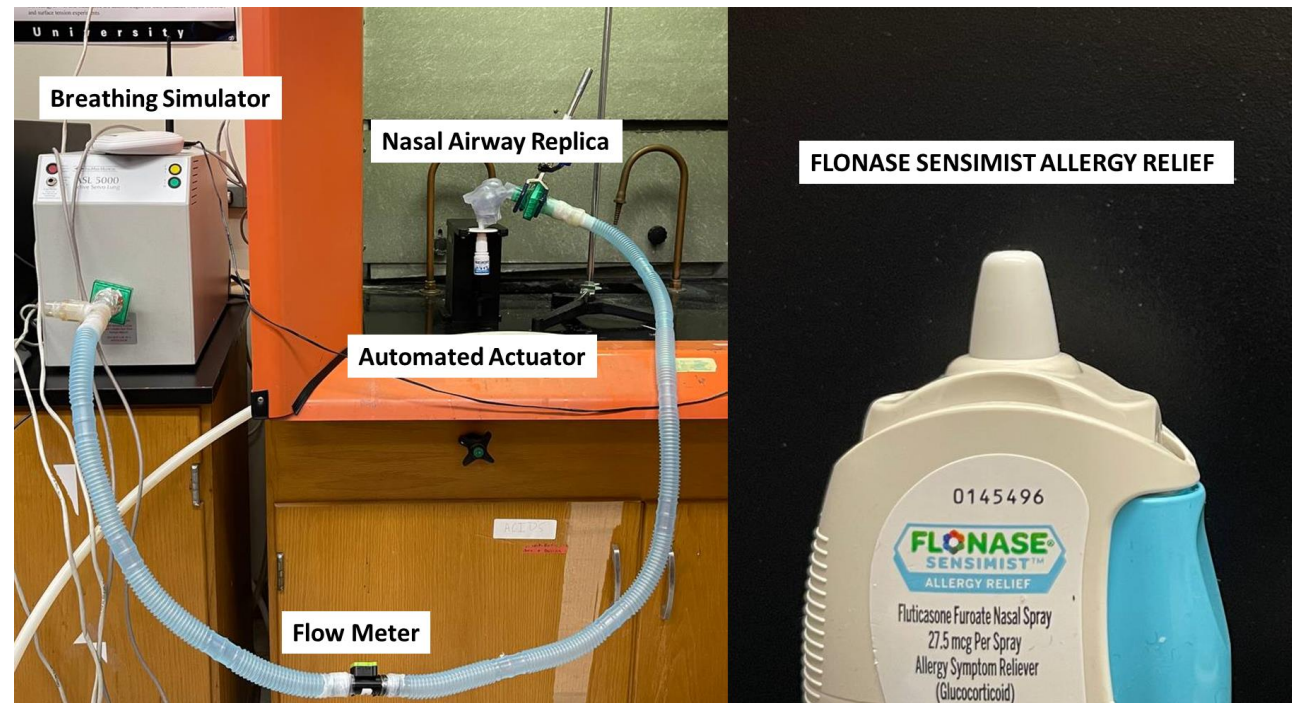
- ✓ Reviewed the CT scans based on Lund MacKay Score
- ✓ Generated the 3-D models using Mimics Innovation Suite 21.0
- ✓ Segmented the final models in 3-Matics 13.0
- ✓ Rapid prototyped the final pieces in high clarity rigid plastic with nozzle tip positioner



Methodology

➤ In Vitro Drug Deposition Study

- ✓ The gentle breathing pattern was generated using an ASL 5000 breathing simulator.
- ✓ While one nostril was blocked, one shot of FLONASE SENSIMIST ALLERGY RELIEF nasal spray was sprayed in the other nostril at the beginning of the inhalation.
- ✓ Drug content in each piece was quantified with a Shimadzu HPLC instrument.



Experimental setup of the deposition study (Left) and the FLONASE SENSIMIST ALLERGY RELIEF (Right)

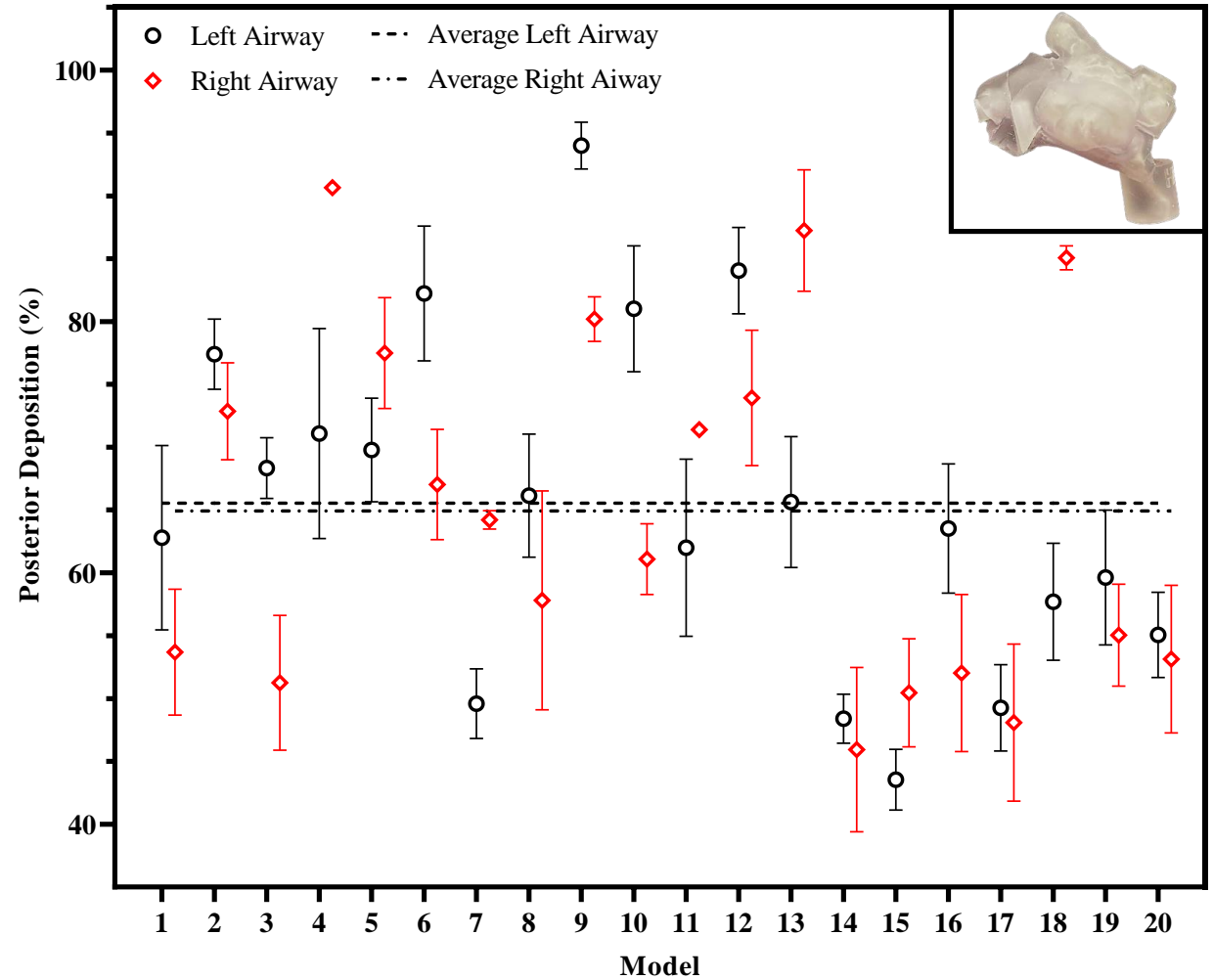
Results

- DSD and plume characteristics of FLONASE SENSIMIST ALLERGY RELIEF nasal spray at 30 and 60 mm from the spray tip.

Actuation Distance (mm)	30	60
$D_{v50} \pm SD$ (μm)	66.1 ± 0.8	54.1 ± 1.2
Plume Angle ($^\circ$)	N/A	36.9 ± 2.1
Plume Width (mm)	N/A	39.7 ± 2.2
Ovality	1.2 ± 0	1.2 ± 0.1
Area (mm^2)	398.3 ± 39.5	1115 ± 86.2

Results

- Posterior deposition of FLONASE SENSIMIST ALLERGY RELIEF in the left and right sides of the nasal airway models of 20 children.
- We observed a wide range of deposition (44 – 94%) from the 20 models.
- There was no significant difference in posterior drug deposition in the left and right nasal cavities of children.



Error bars show the SD of each case. Inset: an anatomically correct nasal airway replica of one of the 20 subjects.

Results

- ANOVA test revealed significant differences in drug deposition values in children vs. adults ($p = 0.0265$) with the same nasal spray [1].
- For adults, the experimental range was 42 – 92% and 29 – 92% in the left and right sides of the nasal airways [1]. However, for children, the observed range of deposition was narrower (left side: 44 – 94%, right side: 46 – 91%), showing more consistent intranasal drug delivery in children.

[1] Manniello, M. D., Hosseini, S., Alfaifi, A., Esmaeili, A. R., Kolanjiyil, A. V., Walenga, R., ... & Golshahi, L. (2021). In vitro evaluation of regional nasal drug delivery using multiple anatomical nasal replicas of adult human subjects and two nasal sprays. *International Journal of Pharmaceutics*, 593, 120103.



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Thanks for your attention!

Please feel free to contact if you have any questions

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