EFFECT OF ACTUATION FORCE ON SIMULATED REGIONAL NASAL SPRAY DEPOSITION IN A HEALTHY NASAL CAVITY

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INTRODUCTION

- Nasal steroid sprays are often prescribed to help treat inflammatory nasal conditions
  - Rhinitis, rhinosinusitis, nasal polyposis
- Nasal sprays are often delivered by hand-actuated pumps
  - Manual actuation may introduce variability in actuation force
- Both droplet size and speed may get affected by actuation force
- Droplet size and speed may impact deposition patterns
- Measurements of nasal spray duration and droplet size distribution (DSD) were made for three commercial nasal sprays using three different actuation forces (see poster by Schroeter et al. in this session)
- Can use this information to predict how actuation force affects spray deposition
  - Results for one product (fluticasone propionate suspension nasal spray, FP) are presented here

OBJECTIVES

- **Construct computational fluid dynamics (CFD) simulation of nasal spray droplet deposition**
- **Test the hypothesis that regional droplet deposition is affected by actuation force**

METHODS

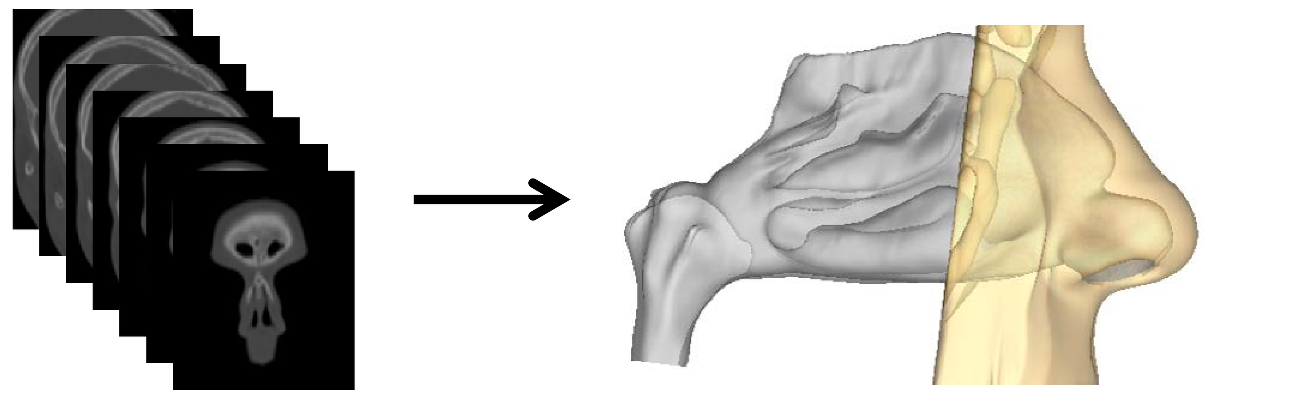
- Use three-dimensional (3D) nasal reconstruction based on a healthy CT scan
- Position a nasal spray nozzle inside nasal vestibule and subtract it from airspace
  - Using 3D reconstruction of nasal spray bottle from CT scan
  - Head and bottle positioned according to instructions from package insert
- Create regions of interest for post-processing
- Create a computational mesh of nasal airspace
  - Base mesh = approx. 4 million unstructured tetrahedral mesh elements
  - Prism layers = 4 0.1-mm layers extruded from surface mesh
- Conduct steady-state inspiratory airflow simulation (according to package insert)
  - Right nostril closed, pressure at left nostril and outlet set to 0 and -16.3 Pa, respectively, air velocity set to 0 at airway walls ("no-slip" condition)
- Conduct droplet transport simulations and compute regional deposited spray mass
  - Actuation forces: 34.3 N, 56.9 N, and 84.3 N (N, Newton)
  - Spray velocities: 15.6, 21.9, and 22.7 m/sec using nasal spray duration measurements with spray orifice diameter estimated to be 0.3 mm
  - Droplet sizes: Using actuation force-specific DSD and shot weight measurements
  - Spray cone angle: 70° (Cheng et al., 2001)

ACKNOWLEDGEMENTS

The authors would like to thank the Division of Rhinology at the University of North Carolina at Chapel Hill for advice on target sites for treatment of rhinitis by nasal sprays. Funding was provided by Grant U01FD005201, from the Food and Drug Administration. Views expressed here do not necessarily reflect the official policies of the DHHS; nor does any mention of trade names, commercial practices or organizations imply endorsement by the United States Government.

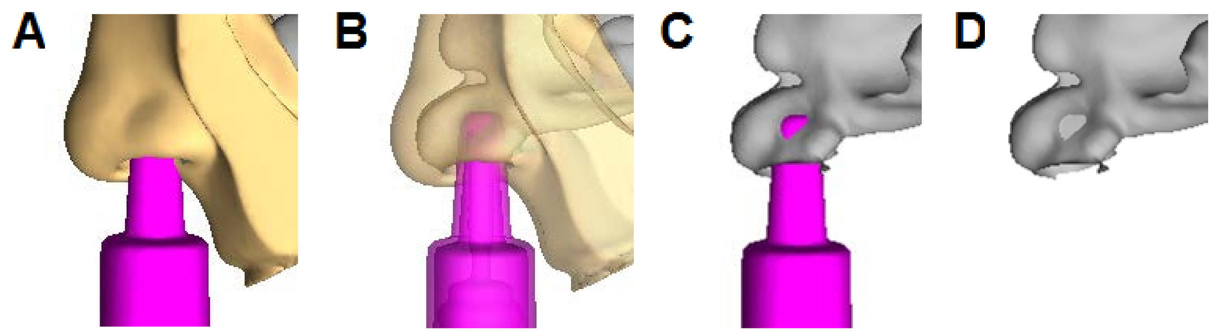
METHODS

CT scan **3D Reconstruction of Main Nasal Cavity**



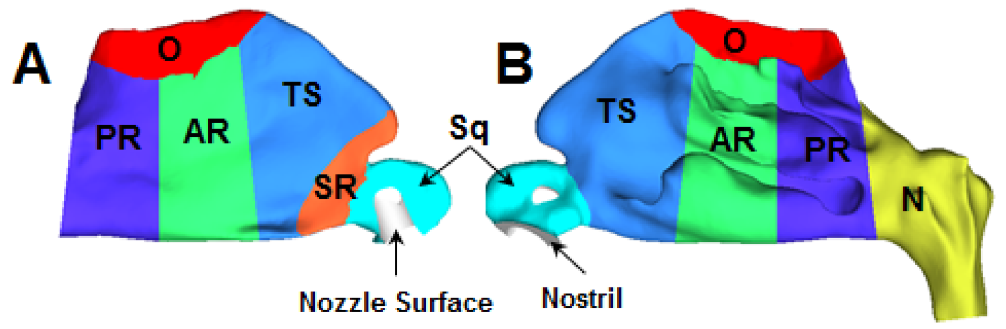
A 3D nasal reconstruction was previously created using Mimics™ software (Materialise, Inc., Plymouth, MI) based on a CT scan of a healthy individual (37 year-old female, 56.7 kg)

Nozzle Positioning and Subtraction from Airspace



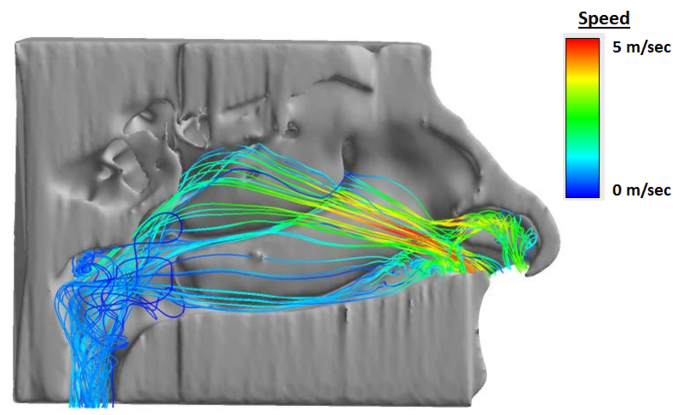
A 3D nasal spray bottle reconstruction was created from a CT scan and inserted into the left nasal vestibule of the nasal cavity reconstruction (A, B) with bottle upright, head tilted slightly forward. Insertion depth was 1 cm (not specified in package insert). The nasal cavity walls were slightly distended around the nozzle (C) and the nozzle was then subtracted from the nasal airspace (D).

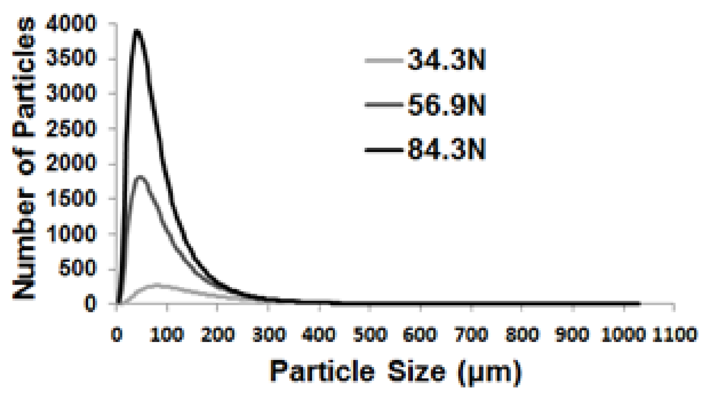
Creation of Regions of Interest for Post-Processing



A surface rendering of the airspace above was exported from Mimics™ in STL format and imported into ICEM-CFD™ (ANSYS, Inc., Canonsburg, PA) where regions of interest were created: O, olfactory; PR, posterior respiratory; AR, anterior respiratory; TS, target site for allergic rhinitis treatment; SR, septal respiratory; Sq, squamous; N, nasopharynx.

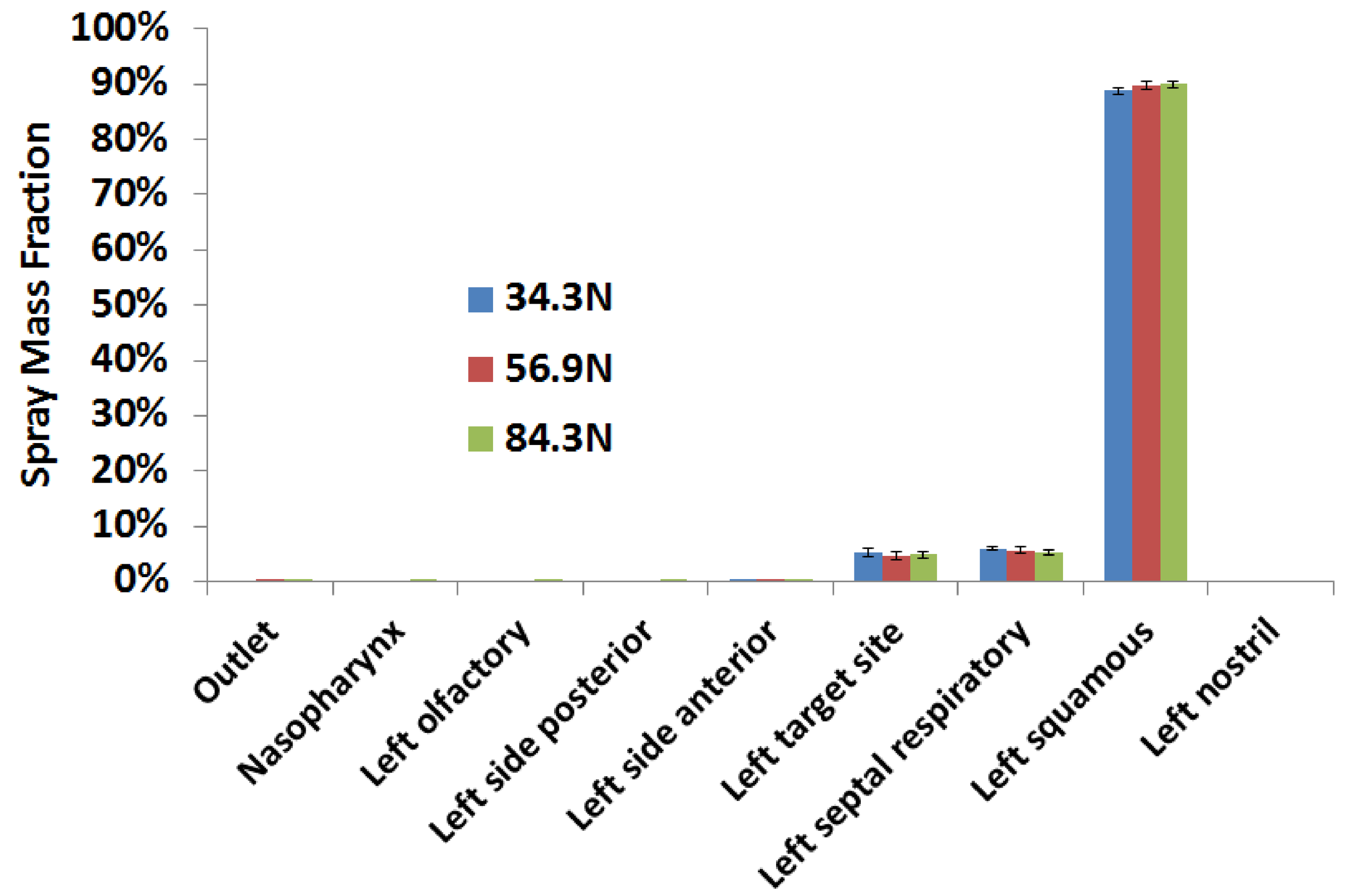
Simulation of Inspiration and Spray Droplet Transport





RESULTS

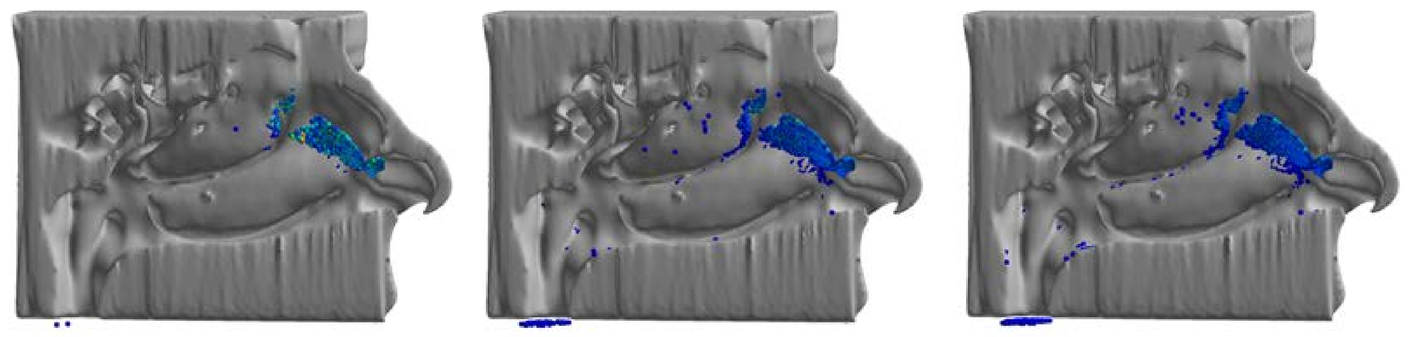
Deposition Fraction by Region of Interest



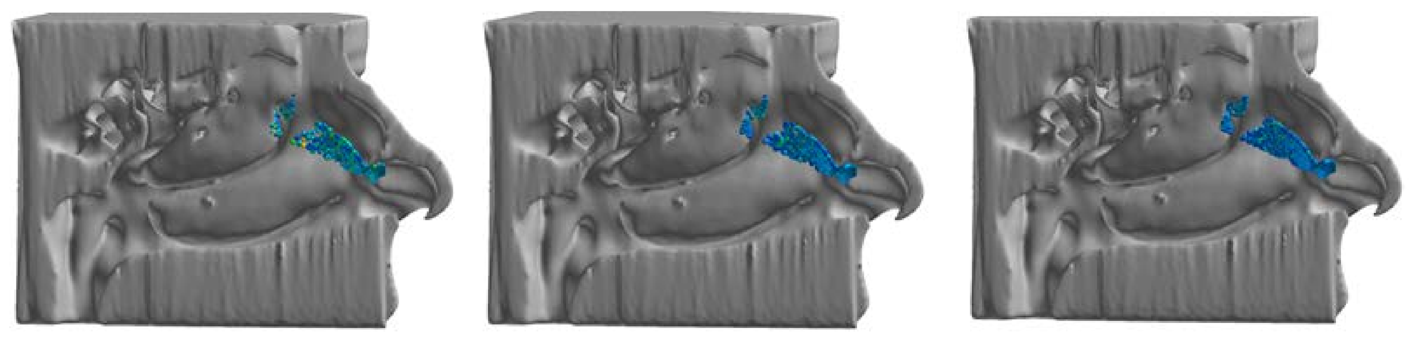
Simulated Droplet Deposition Patterns

All droplets:

34.3 N **56.9 N** **84.3 N**



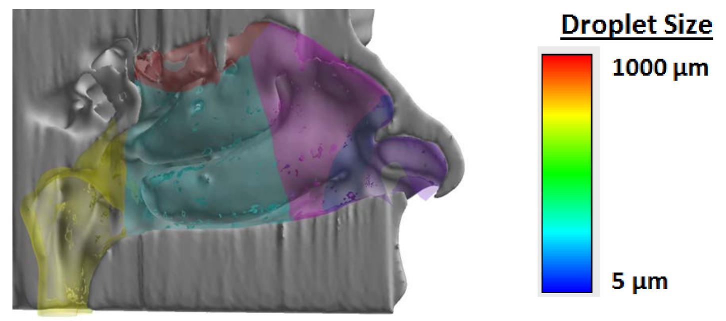
Droplets greater than 100 μm in mass-median aerodynamic diameter:



	FP Nasal Spray		
	34.3N	56.9N	84.3N
Shot weight (mg)	96.5 ± 0.3%	108 ± 19.2%	100.96 ± 0.9%
Spray duration (ms)	87.6 ± 1.3	69.6 ± 1.3	63.0 ± 2.1
Spray speed (m/s)	15.6 ± 0.2	21.9 ± 4.4	22.7 ± 0.7
x50 (μm)	79.45 ± 2.5%	46.4 ± 4.6%	41.31 ± 8.6%
GSD (μm)	2.06 ± 1.4%	2.09 ± 2.4%	2.02 ± 2.3
est. no. of particles	9701	40,552	72,640
est. orifice diam. (mm)	0.3	0.3	0.3

$$f(x) = \frac{1}{\sqrt{2\pi}\ \ln \sigma_g}\ exp\left[-\frac{(\ln x - \ln x_0)^2}{2\ (\ln \sigma_g)^2}\right]$$

x_0 is the volume median diameter (x50)
σ_g is geometric diameter (GSD)



CONCLUSIONS

- Differing actuation forces may not affect the regional deposition of droplets generated by the FP suspension nasal spray in the anterior nasal cavity
- Spray speeds and DSDs changed with actuation force in agreement with other reports (Cheng et al, 2001; Kimbell et al., 2007)
  - Formulation and nasal sprayer used here were not the same as used by Cheng and colleagues (2001)
  - Speeds and sizes of most droplets were larger in this study than previously used by Kimbell and colleagues (2007)
  - These large speeds and sizes caused most droplet deposition to occur in the anterior nose regardless of actuation force
- This study suggests that variability in hand-actuation of spray pumps may not significantly affect anterior nose target site deposition
- Anterior deposition would also be likely in the rhinitic case
  - Due to complexity of particle deposition and disease processes in the nasal cavity, a rhinitic study is warranted

FUTURE DIRECTIONS

- Conduct study in nasal model based on patient with rhinitis
- Incorporate spray-airflow interaction
- Incorporate DSD evolution over spray lifetime
- Incorporate time-dependent airflow, turbulence modeling

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