Effect of Spray Momentum on Nasal Spray Droplet Transport and Deposition

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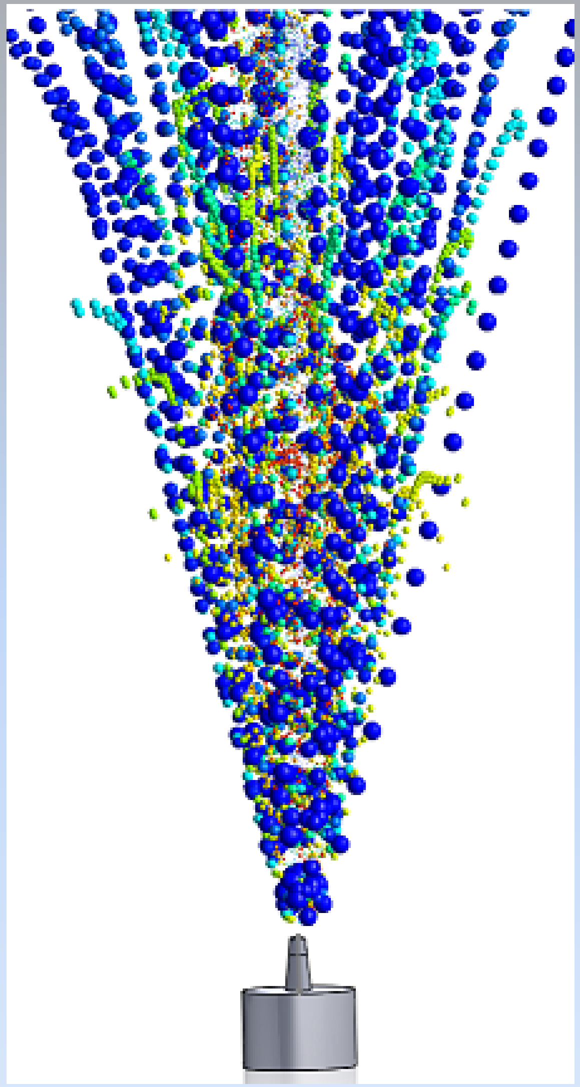
Nasal Drug Delivery using Sprays

- Popular choice for intranasal delivery of locally-acting drugs such as corticosteroids, antihistamines, and anticholinergic drugs
- Advantages include non-invasive administration, fast onset of action, avoidance of first-pass metabolism and good patient compliance
- A spray is formed when the device is actuated, which forces a liquid formulation through an orifice [1]

[1] FDA, Nasal Spray and Inhalation Solution, Suspension, and Spray Drug Products—Chemistry, Manufacturing, and Controls Documentation, 2002.

Nasal Sprays Carry High Momentum

- Nasal sprays produce relatively larger droplets with sizes mostly higher than 10 μm [1]
- Due to the large spray droplet size and high spray velocity, these droplets carry significant momentum
- This momentum from the droplets influences the gas phase in the region surrounding the spray nozzle tip
  - Two-way coupled momentum transfer



[1] Hosseini S, Wei X, Wilkins Jr JV, Fergusson CP, Mohammadi R, Vorona G, and Golshahi L: In Vitro Measurement of Regional Nasal Drug Delivery with Flonase,® Flonase® Sensimist,™ and MAD Nasal™ in Anatomically Correct Nasal Airway Replicas of Pediatric and Adult Human Subjects. Journal of aerosol medicine and pulmonary drug delivery 2019,32:374-385.

CFD Modeling of Nasal Sprays

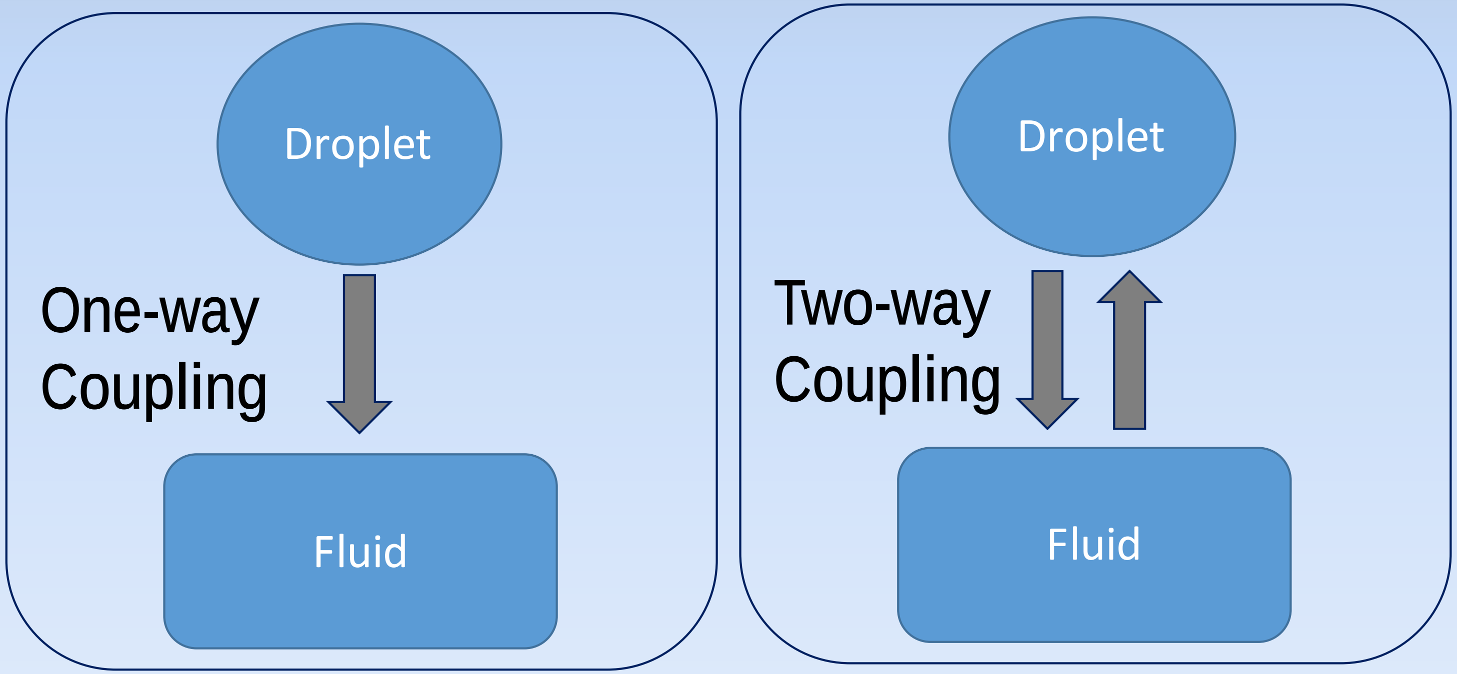
- Previous CFD spray studies use one-way coupled discrete phase particle transport modeling and do not account for two-way momentum coupling
  - In one-way coupling the effect of the droplets on the gas phase is ignored
- An exception is Rygg and Longest[1]
  - This study approximated two-way coupled momentum transfer by applying an air-jet that captured the injected droplet momentum
- As a more direct approach, a Lagrangian discrete phases particle transport model can be used to simulate two-way coupled momentum exchange through an iterative process

[1] Rygg A, and Longest PW: Absorption and clearance of pharmaceutical aerosols in the human nose: development of a CFD model. *Journal of aerosol medicine and pulmonary drug delivery* 2016,29:416-431

Objective

- Analyze effects of two-way momentum exchange between the nasal spray droplets and the surrounding air on a first principles basis using CFD simulations of Flonase® Sensimist™ in simplified and realistic nasal cavity models

- Compare nasal spray transport using two-way coupled vs. one-way coupled discrete phase Lagrangian particle transport model



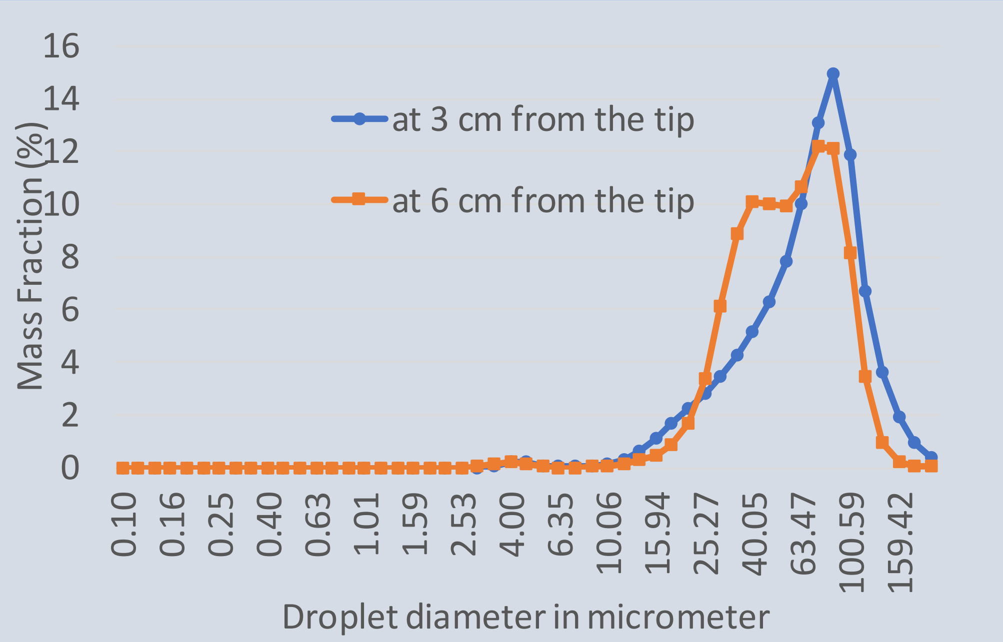
Methods

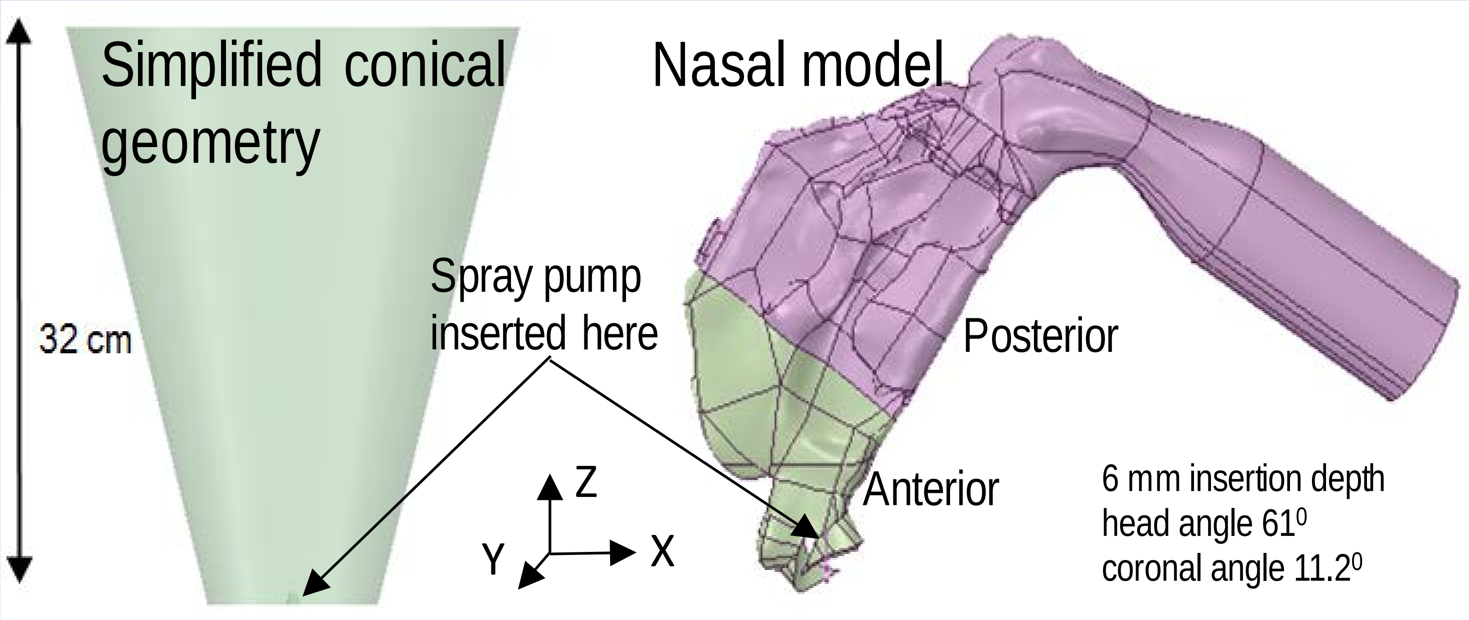
- CFD simulations were run using Ansys Fluent 19.0
- Mesh and solver settings followed our best practices and recommendations [1]
- Initial and boundary conditions for the CFD model were based on measurements from in-house *in vitro* experiments
- Spray droplets were injected with polydisperse droplet size distributions, cone angle of 35^0 and a turbulent velocity profile with an average velocity of 14.4 m/s
- Spray transport was simulated in a simplified conical geometry and in a nasal airway geometry with no inhalation flow

[1] Rygg A, and Longest PW: Absorption and clearance of pharmaceutical aerosols in the human nose: development of a CFD model. *Journal of aerosol medicine and pulmonary drug delivery* 2016,29:416-431

Flonase® Sensimist™ spray droplet size distribution measured 3 cm and 6 cm from the spray tip using laser diffraction and hand actuation

Two geometries for simulating spray droplet transport: Simplified conical geometry starting with the spray tip and a realistic nasal model of an adult with healthy nasal airway

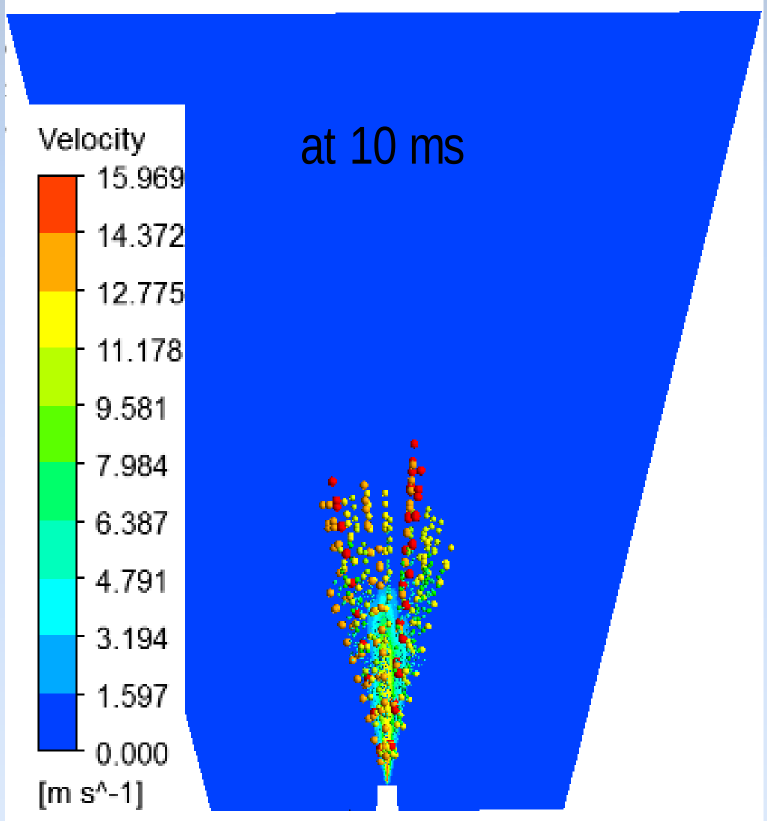


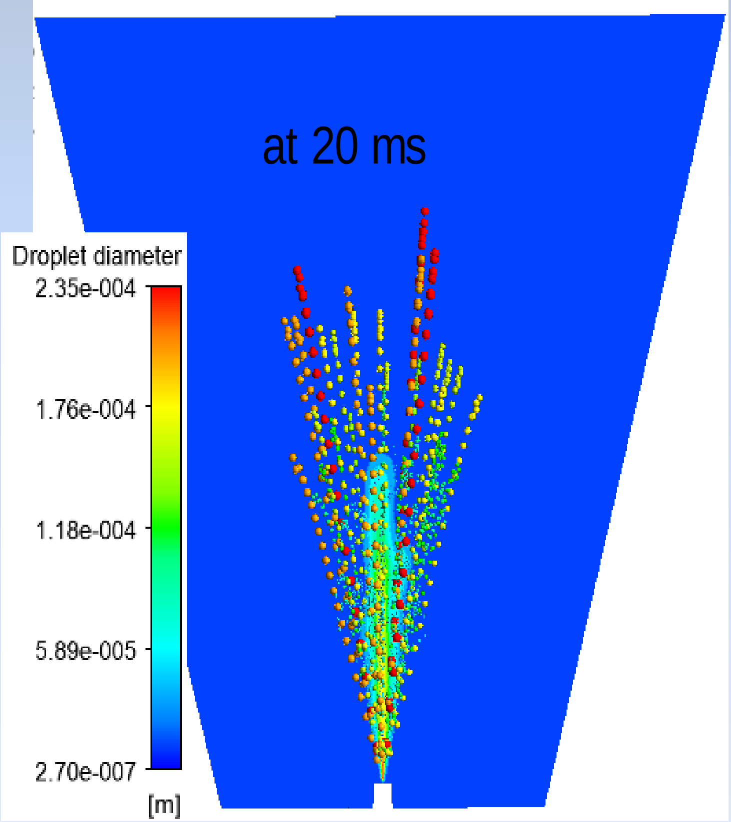


Spray Transport in Simplified Conical Geometry

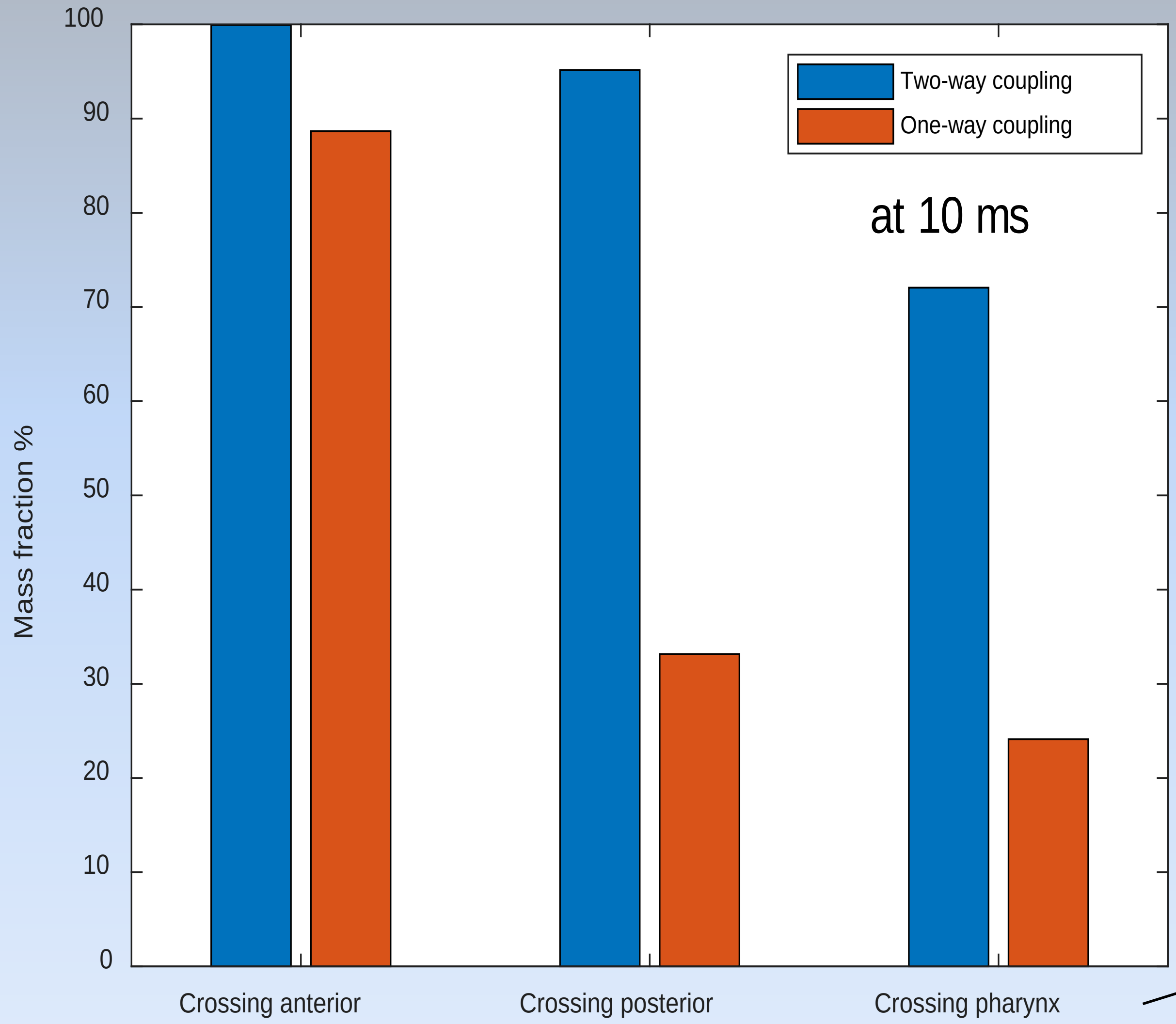
- Momentum exchange from the injected spray droplets to the surrounding air results in an air-jet like velocity profile, with velocity magnitude comparable to the spray droplet velocity

- Gas phase velocity is displayed as colored contours
- This induced gas phases velocity imparted additional momentum on the smaller droplets

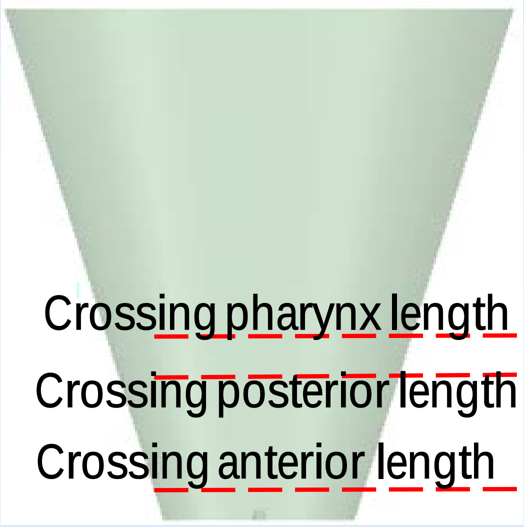




Comparison of Distance Traveled by the Liquid Mass in Simplified Conical Geometry

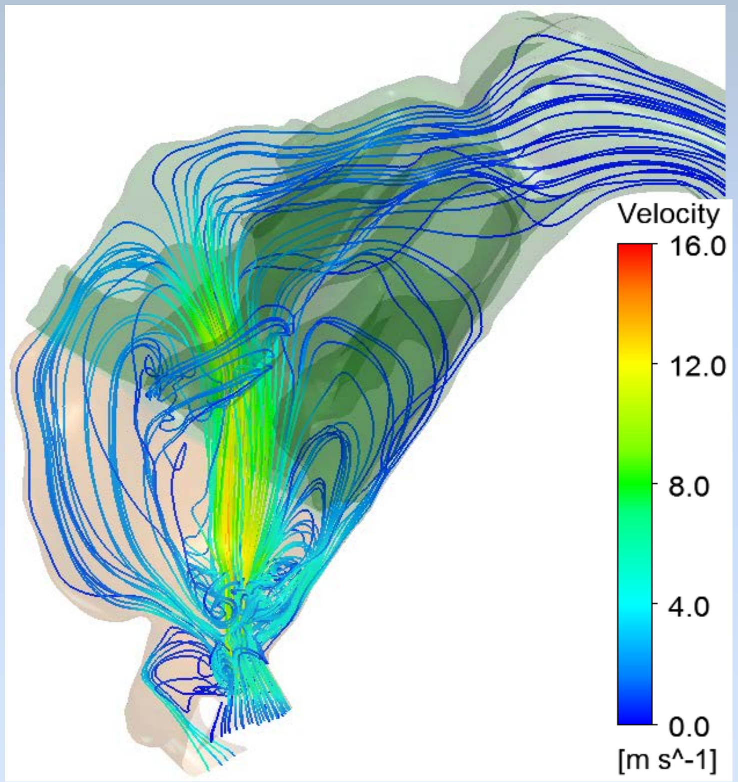


- Plot shows the percentage of spray mass fraction that has crossed each boundary at a time of 10 ms after actuation
- Two-way coupling imparts higher momentum causing the droplets to travel further at a set time

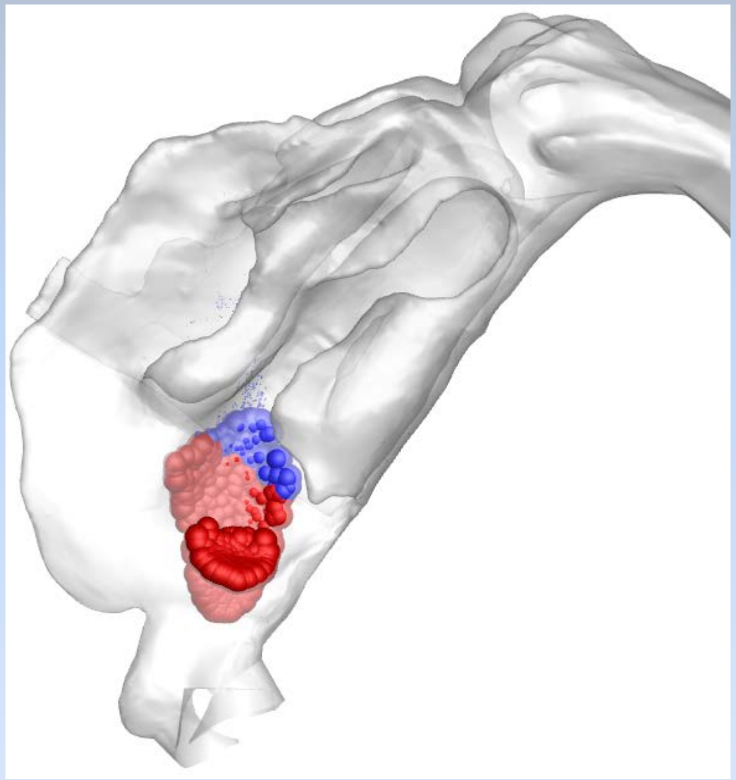


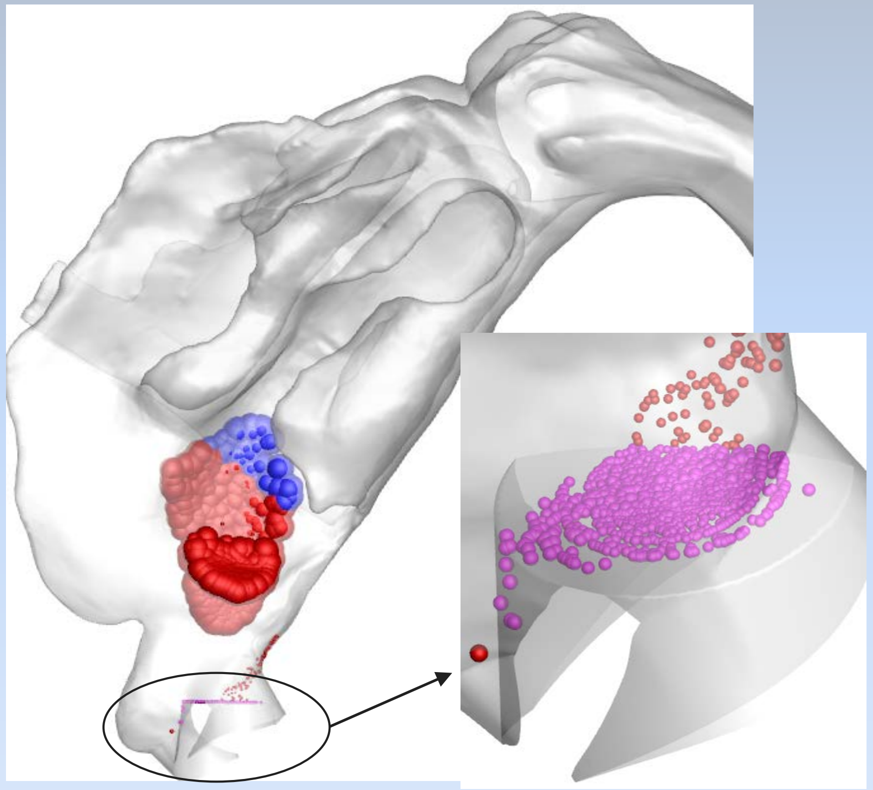
Spray Transport and Deposition in a Nasal Model

With the one-way coupling approach, smaller droplets have lower momentum and fall back to deposit on the spray nozzle



Streamlines with two-way coupling


Two-way coupling approach


One-way coupling approach

Comparison of Deposition Results

- Anterior region was defined as approximately front 1/3 of the geometry

	Anterior region (%)	Spray nozzle + drip (%)	Posterior region (%)	Relative error (anterior region + nozzle + drip) (%)	Relative error (posterior region) (%)
CFD two-way coupling	92.5	0.0006	6.9	0.2	9.8
CFD one-way coupling	89.0	6.6	4.0	3.6	47.2
In vitro	92.4±0.5		7.7±0.5		

Compared to the *in vitro* data, the one-way coupled solution produced a 47.2% relative error in predicting the posterior nasal deposition, which was reduced to <10% with the two-way coupled solution

Conclusions and Future Works

- Effects of two-way momentum exchange between the nasal spray droplets and the surrounding air is significant and influences the spray droplet deposition in the nasal cavity
  - A direct two-way coupled Lagrangian model was shown to capture this effect, but was computationally expensive
  - Future studies will compare this method with the more computationally efficient approach of injecting an equivalent momentum gas velocity
  - Future CFD advancements are also required to capture high momentum droplet splash and post-deposition droplet spread

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