Sinus Drug Delivery Before and After Treatment for Chronic Rhinosinusitis

Amanda Balash, BS[1,2]; Dennis Frank-Ito, PhD[1]

[1]Department of Head and Neck Surgery & Communication Sciences, Duke University Medical Center, [2]Charles E. Schmidt College of Medicine, Florida Atlantic University

Department of Head and Neck Surgery & Communication Sciences
Duke University School of Medicine

FAU SCHMIDT COLLEGE OF MEDICINE
Florida Atlantic University

Introduction

- Chronic Rhinosinusitis (CRS) is defined as the symptomatic inflammation of the sinonasal tract for more than 12 weeks[1].
- Intranasal steroids are often used as first-line treatment of CRS but some patients experience ongoing symptoms despite medical management and may require surgical intervention[2].
- By determining optimal drug delivery parameters, CRS outcomes can improve[3].

Methods and Materials

- CT scans of an adult male patient with CRS who was under medical management for 6 years before undergoing FESS were obtained at 3 timepoints: initial diagnosis (PRE1), 31 months after initial diagnosis (PRE2), and 6 months post FESS (POST; 77 months after initial diagnosis).

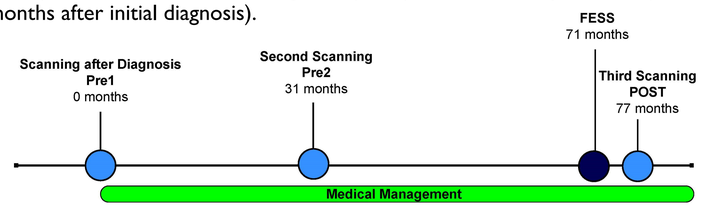

Figure 1. Timeline for patient's CT scan and surgical intervention

- CT scans were used to create anatomically realistic and patient-specific 3D models to quantify sinonasal airway volume and surface area (Figure 2) [3].

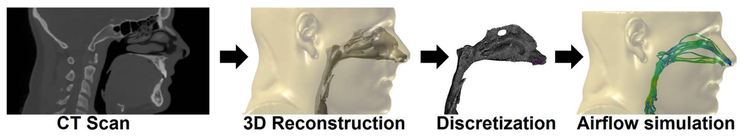

Figure 2. Patient- specific 3D model generation[3]

- Airflow simulations and spray drug particle transport were performed using computational fluid dynamics (CFD) modeling at 15 L/min inhalation flow
- Spray particles of 1-100 microns with release speeds of 1, 5, 10 m/s were simulated in 5 head positions: Mygind, Tilted-Back, Tilted-Forward, Upright, and Supine (Figure 3).

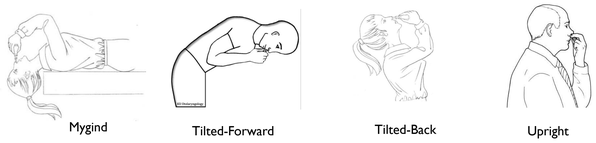

Figure 3. Head Positions Assessed (missing supine head position)

- 5 release locations were simulated: Top, Medial, Center, Lateral, Bottom (Figure 4).
- Nozzle insertion depth of 15 mm.
- Particle deposition was quantified for each paranasal sinus.

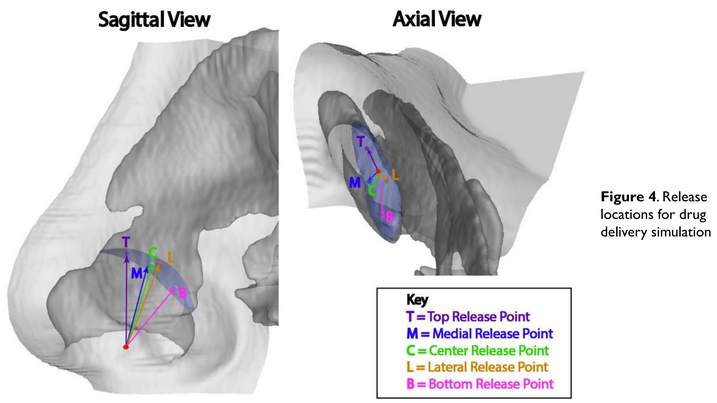

Figure 4. Release locations for drug delivery simulation

Results

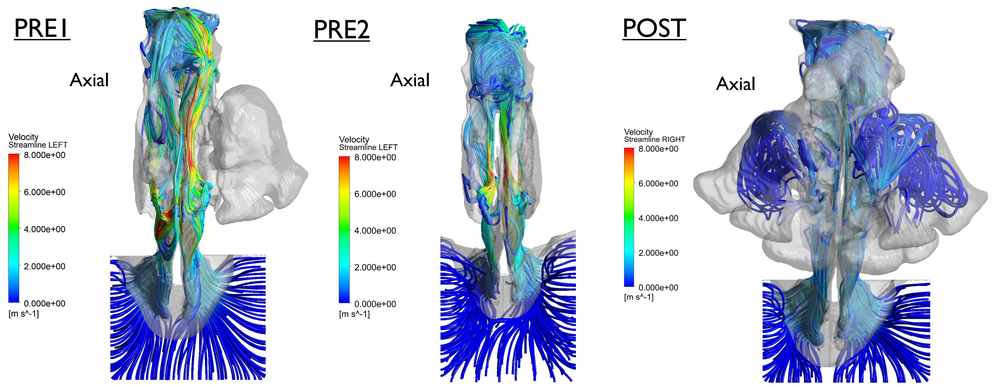

Figure 5. PRE1, PRE2, and POST Airflow Streamlines at 15 L/min inhalation flow

Subject	Region	Head Position	Release Location	Velocity (m/s)	Particle Size Group (μm)	Max % Deposition
Pre1	Right ES	**Mygind**	**Top**	**5 m/s**	**1-5 μm**	**0.005714286**
	No other sinuses	-	-	-	-	-
Pre2	No sinuses	-	-	-	-	-
Post	Left ES	Mygind	Central	5 m/s	6-10 μm	7.765714286
		Supine	**Central**	**5 m/s**	**6-10 μm**	**7.954285714**
		Tilted Back	Central	1 m/s	11-20 μm	6.571428571
		Tilted Forward	Top	5 m/s	6-10 μm	2.691428571
		Upright	Top	5 m/s	6-10 μm	2.702857143
	Left FS	Mygind	Top	5 m/s	11-20 μm	0.182857143
		Supine	**Top**	**1 m/s**	**21-30 μm**	**0.505714286**
		Tilted Back	Top	5 m/s	11-20 μm	0.18
		Tilted Forward	Top	5 m/s	11-20 μm	0.222857143
		Upright	Top	5 m/s	11-20 μm	0.191428571
	Left MS	Mygind	Top	1 m/s	6-10 μm	4.017142857
		Supine	Lateral	5 m/s	11-20 μm	5.925714286
		Tilted Back	Lateral	5 m/s	11-20 μm	6.277142857
		Tilted Forward	Top	1 m/s	6-10 μm	6.142857143
		Upright	**Top**	**1 m/s**	**6-10 μm**	**6.994285714**
	Left SS	**Mygind**	**Top**	**1 m/s**	**11-20 μm**	**0.065714286**
		Supine	Top	10 m/s	6-10 μm	0.022857143
		Tilted Back	-	-	-	-
		Tilted Forward	Top	10 m/s	1-5 μm	0.051428571
		Upright	Top	10 m/s	1-5 μm	0.011428571
	Right ES	Mygind	Medial	1 m/s	6-10 μm	4
		Supine	Medial	1 m/s	51-60 μm	9.848571429
		Tilted Back	Medial	1 m/s	51-60 μm	7.851428571
		Tilted Forward	**Medial**	**1 m/s**	**51-60 μm**	**10.25142857**
		Upright	Medial	1 m/s	51-60 μm	8.165714286
	Right FS	**Mygind**	**Top**	**1 m/s**	**11-20 μm**	**0.148571429**
		Supine	-	-	-	-
		Tilted Back	-	-	-	-
		Tilted Forward	-	-	-	-
		Upright	-	-	-	-
	Right MS	Mygind	Central	5 m/s	11-20 μm	16.54571429
		Supine	**Top**	**5 m/s**	**11-20 μm**	**17.68**
		Tilted Back	Top	5 m/s	11-20 μm	16.92
		Tilted Forward	Central	1 m/s	31-40 μm	7.505714286
		Upright	Central	5 m/s	11-20 μm	10.52285714
	Right SS	Mygind	Central	1 m/s	11-20 μm	4.545714286
		Supine	**Central**	**1 m/s**	**6-10 μm**	**45.29142857**
		Tilted Back	Central	1 m/s	6-10 μm	37.44
		Tilted Forward	Central	1 m/s	6-10 μm	43.33142857
		Upright	Central	1 m/s	6-10 μm	35.04

Table 1. Maximal drug deposition for each sinus in each head position. Bolded head position represents the parameters with maximum deposition for each sinus.

Results

- PRE1 had one patent sinus (right ES) with maximum deposition of 0.0006% in the Mygind head position and top release location at 5m/s with particle sizes ranging from 1-5μm.
- PRE2 had no patent sinuses.
- Maximum depositions for POST sinuses were: Left: ES=7.954%, FS=0.506%, MS=6.994%, SS=0.06575; Right: ES=10.251%, FS=0.148%, MS=17.680%, SS=45.291%.
- Particles between 1-30 μm had the most sinus deposition at 1 m/s (except for the left ES) for the left sinuses with varied head positions.
- For the left sinuses, Supine was best for ES and FS, Upright was best for MS, and Mygind for SS.
- Right sinuses, particles sized 1-20μm (except ES at 51-60μm), had best deposition at 1 m/s (except MS at 5 m/s) at varied head positions.
- For the right sinuses, Tilted-Forward was best for ES, Mygind for FS, and Supine for MS and SS.
- Top was the most common release location for maximum deposition in each sinus.
- Supine was the most common head position.

Subject	Region	Head Position	Release Location	Velocity (m/s)	Particle Size Group (μm)	Max % Deposition
Pre1	Right ES	Mygind	Top	5 m/s	1-5 μm	0.005714286
Pre2	No sinuses	-	-	-	-	-
Post	Left ES	Supine	Central	5 m/s	6-10 μm	7.954285714
	Left FS	Supine	Top	1 m/s	21-30 μm	0.505714286
	Left MS	Upright	Top	1 m/s	6-10 μm	6.994285714
	Left SS	Mygind	Top	1 m/s	11-20 μm	0.065714286
	Right ES	Tilted Forward	Medial	1 m/s	51-60 μm	10.25142857
	Right FS	Mygind	Top	1 m/s	11-20 μm	0.148571429
	Right MS	Supine	Top	5 m/s	11-20 μm	17.68
	Right SS	Supine	Central	1 m/s	6-10 μm	45.29142857

Table 2. Optimal parameters for maximum drug deposition in each sinus

Discussion/Conclusions

- FESS was very effective in improving the patient's outcome compared to medical management.
- Optimal head position and release location vary depending on the desired deposition location.
- Current-use indications are head Tilted-Forward and a lateral release location. Findings suggest that intranasal spray administration to target delivery of drugs into the paranasal sinuses may not provide maximum benefit under manufacturer's current recommended instructions
- Limitation: small sample size due to rare CRS treatment timeline and contraindications to post-operative CT scans plus extremely high computational time and demands of this work.

References

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[3]Patki A, Frank-Ito DO. Characterizing human nasal airflow physiologic variables by nasal index. Respir Physiol Neurobiol. 2016 Oct;232:66-74. doi: 10.1016/j.resp.2016.07.004. Epub 2016 Jul 16. PMID: 27431449.