Evaluating Lung Function Changes with Environmental Exposures

Integrated Cardiovascular and Pulmonary Team (ICAP)

Northeastern University Center for STEM Education

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NSF · Young Scholars Program · Northeastern University College of Engineering

Abstract

Motive

- Investigate the biological underpaintings of the respiratory system following aerosol exposure + its effect on pulmonary health
- Understand how e-cigarette exposure remodels lungs over time

Methods

- High-resolution computed tomography (CT) imaging data employed , generating comprehensive 3D models through SimVascular
- Image-J analysis software utilized to quantify mean intensities of alpha smooth muscle actin (aSMA) and epithelial cell mass in the airways of mice exposed to JUUL e-cigarettes for 8, 16, and 24 weeks

Results

- Examination of 3D models revealed undamaged nasal cavities and unobstructed airflow pathways
- Constriction examinations highlighted an increased response to methacholine leading up to 24 weeks of e-cigarette exposure, at which point there was no response to the drug at the highest exposure period

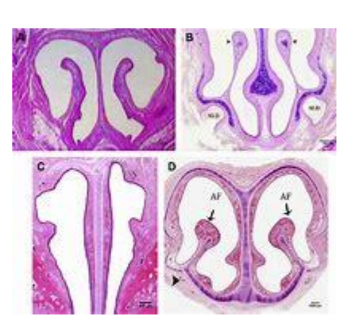
Background

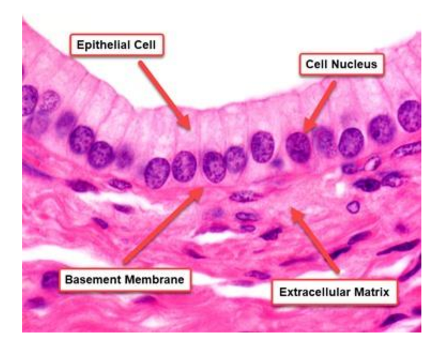
SimVascular Modeling

- 3D modeling technology utilized to create detailed maps of the nasal cavity in mice.
- Enhanced understanding of airflow through nasal passages and particle filtration.
- Research aims to develop new respiratory treatments, including for asthma and allergies.

Analytical Assessment of Methacholine and aSMA

- Lung sections stained for smooth muscle actin to measure muscle content in airways, specifically epithelial cell nucelli and smooth muscle tissue
- Methacholine used to quantify constrictions of airways
- Hypothesized transient abnormalities in smooth muscle cells



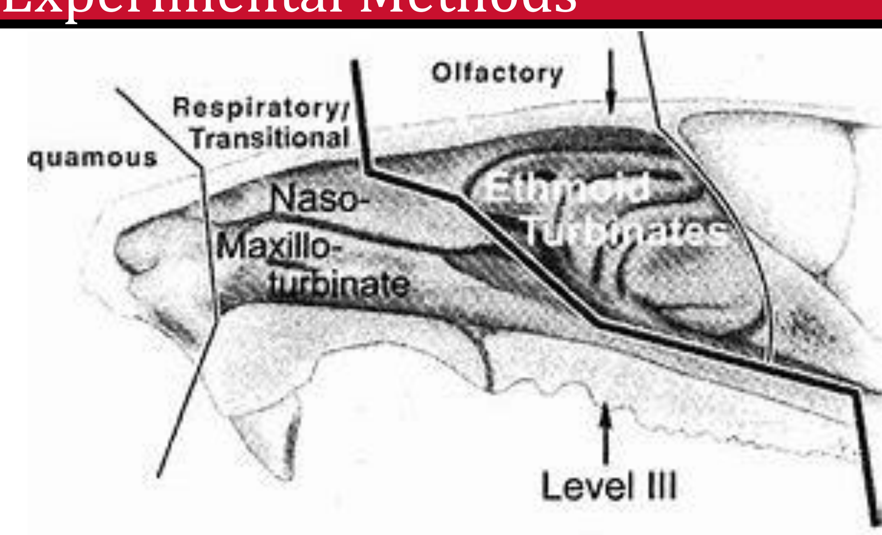


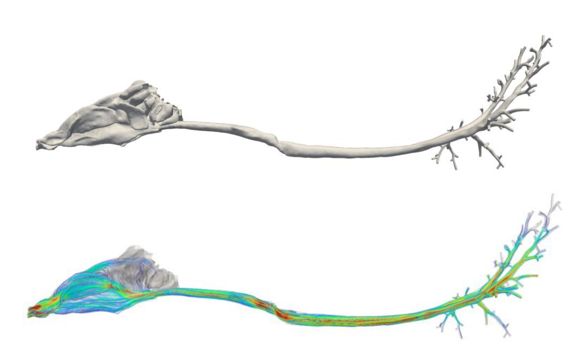
InExpose (Scireq)

Experimental Methods

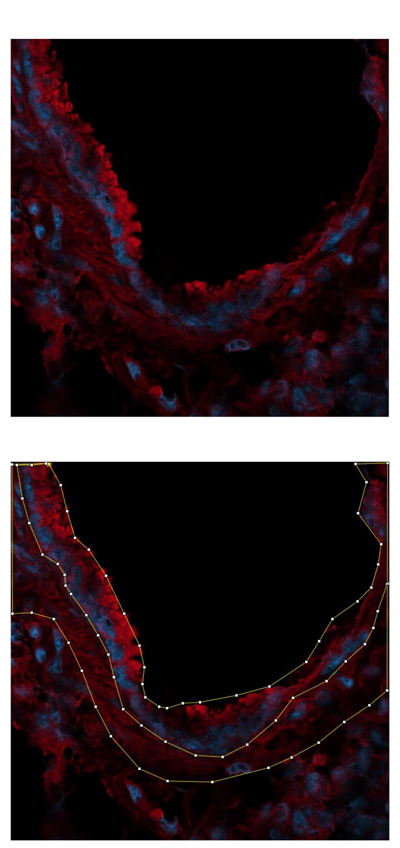
Model Construction

- 3D model created using SimVascular
- Allowed for a detailed visualization of mice nasal cavity
- Key anatomical structures observed and analyzed turbinates, olfactory epithelium
- Cross-sectional views + virtual tours used to enhance understanding

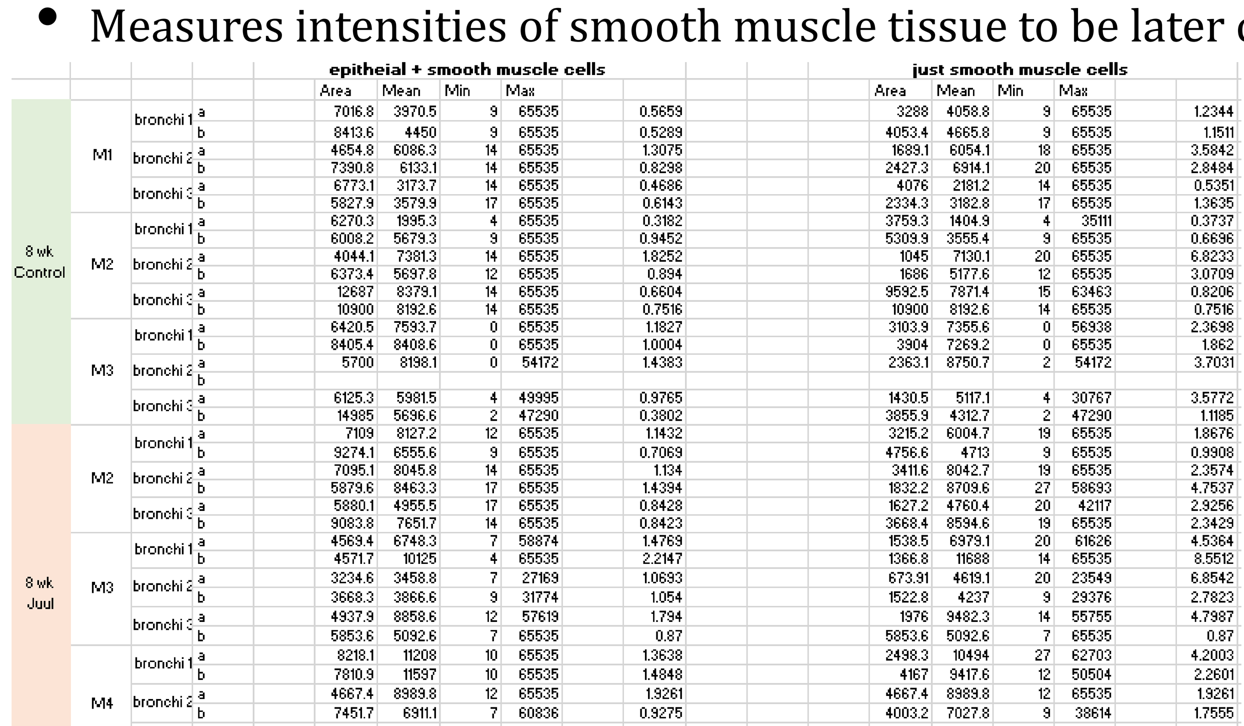




Data and Graphical Analysis



- Brightfield fluorescent microscope
- Image-J FIJI Analysis Software; measure intensity of smooth muscle tissue
- Cross sections analyzed ranging from 8 weeks, 16 weeks, and 24 weeks of exposure
- Measures intensities of smooth muscle tissue to be later compiled in an excel sheet

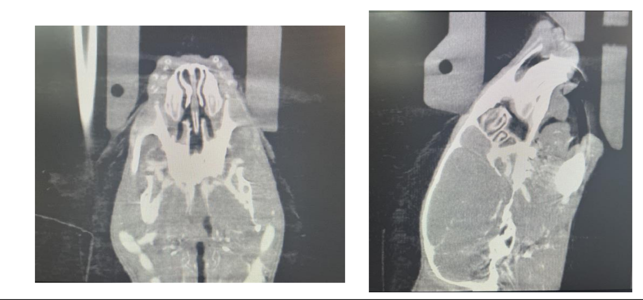


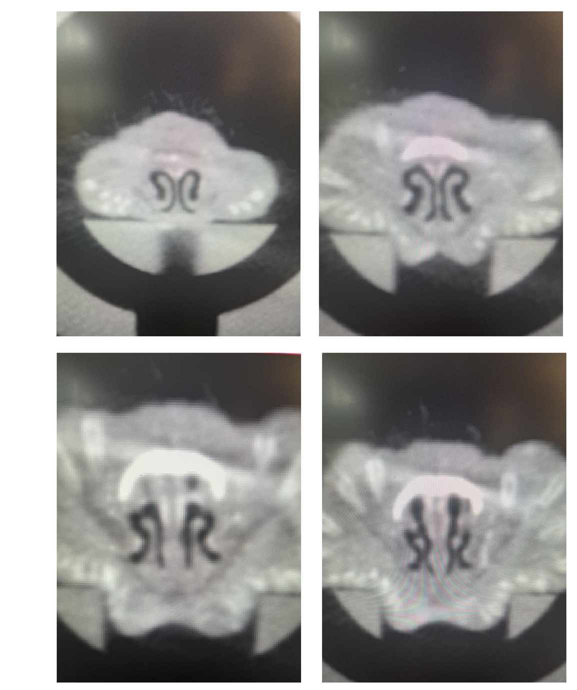
- Find differences that are meaningful with exposure to pollutants
- Brightfield and Polarized images taken to analyze Picrosirius red collagen stains

Results

Modeling Conclusions

•Using 3D modeling technology, researchers created detailed models of the mice nasal cavity, providing clear visualizations of its internal structures. They carefully included key features of the nasal cavity in the models, enabling a comprehensive examination.
•3D models revealed all components of nasal cavity were in their expected positions, suggesting that the mice had healthy and normal nasal structures, essential characteristics for proper respiratory function



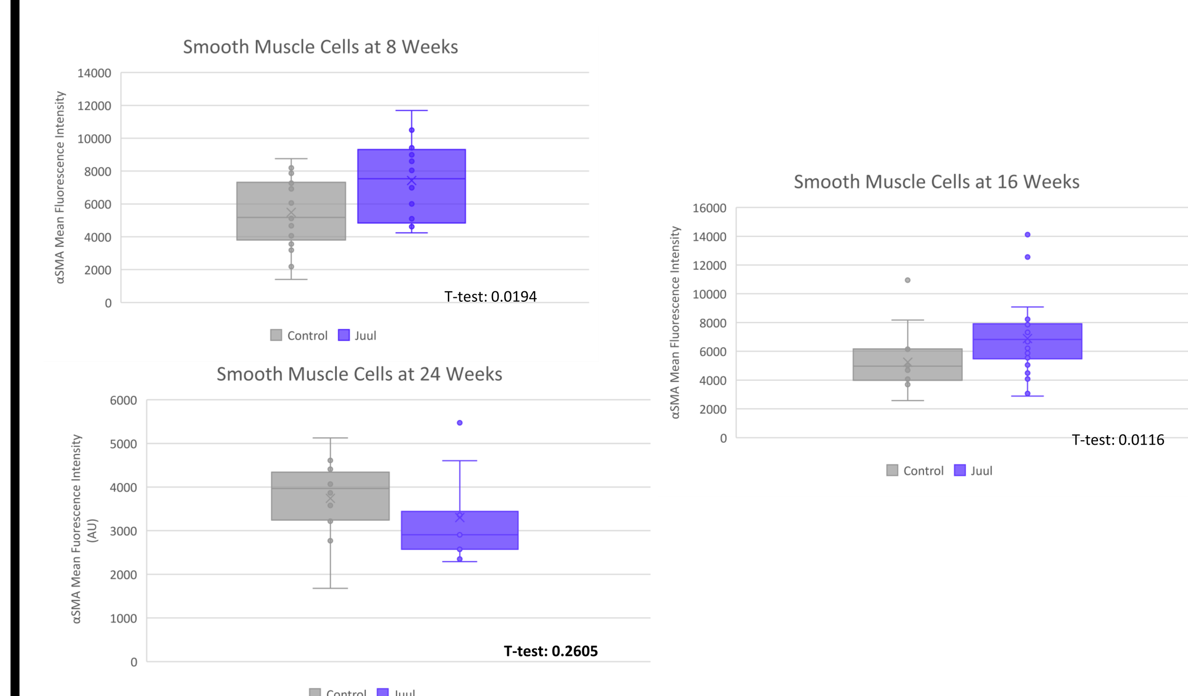


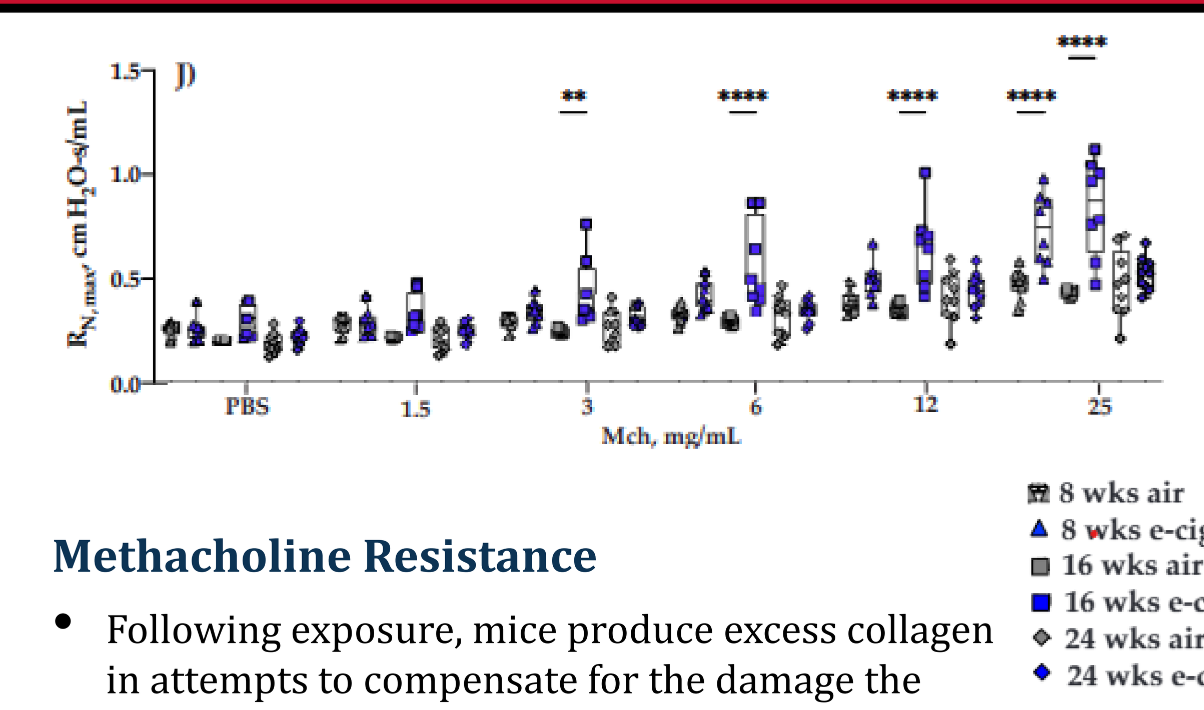
- Notable presence of clear, unobstructed pathways for airflow within nasal cavities; unhindered airflow is crucial for efficient breathing and ensures the effective exchange of oxygen in the respiratory system

Results

Epithelial and Smooth Muscle Cell Data

- T-tests employed to analyze statistical differences
- **Hypertrophic muscle, indicated by increased aSMA, is associated with airway reactivity**
- 8 and 16 weeks showcased statistical differences between the exposed and control groups, 24 weeks showed none





Methacholine Resistance

- Following exposure, mice produce excess collagen in attempts to compensate for the damage the smoke causes, consequently constricting the airways and making it more difficult for them to expand
- Imaging revealed mice exposed for 8 weeks responded to the drug at highest dose, 16 weeks responded much lower dose, 24 weeks didn't have a change in their response (resistance same as control)
- Demonstrates hyperreactivity across 8 weeks and 16 weeks, none at 24 weeks

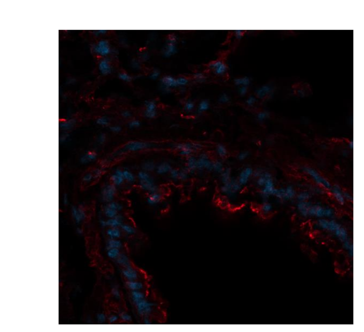
Conclusion + Moving Forward

Modeling in the Future

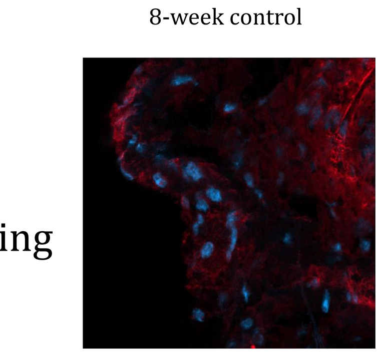
- Studies to be conducted on the mice nasal cavities post-aerosol exposure, making this a long-term project utilizing different researchers to build upon each other
- Our final project helps researchers understand how smoke inhalation affects the mice nasal cavities
- Sketches of nasal cavities drawn before and after exposure, giving researchers a visual means of comparing the discontinuities to better understand the effects of smoke exposure on the respiratory system
- Essential for understanding how smoke might impact the respiratory health of both mice and humans

Data Continued

- Continuing investigation on the 24-week exposure group, to be studied to develop deeper understandings of the long-terms effects of aerosol exposure
- These findings suggest that regulating airway muscle hypertrophy could be a potential therapeutic target in asthma
- Study emphasizes the importance of understanding the mechanisms underlying ASM remodeling in asthma



8-week control



8-week Juul

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