Human exposure to hydrogen sulfide (H₂S) gas can occur from a variety of natural and industrial sources and results in dose-related neurological, respiratory, and cardiovascular effects. Olfactory neuronal loss in H₂S-exposed rats has been used to develop occupational and environmental exposure limits based on exposure concentration. Anatomically accurate computational fluid dynamics (CFD) models have shown a correlation between tissue flux and olfactory pathology in rodents, suggesting an influence of airflow patterns on lesion locations that may affect extrapolation of tissue dose levels to humans. Human nasal anatomy varies considerably among individuals, affecting patterns of airflow and gas absorption. In this study, inter-human variability of H₂S nasal dosimetry was investigated using CFD models of the nasal passages of five adults and two children generated from MRI or CT data. Approximations of olfactory epithelia were mapped in each model to compare olfactory dosimetry predictions among individuals. Steady-state inspiratory airflow and H₂S uptake were simulated using Fluent™ CFD software with differences in the 99th percentile and average flux values being < predictions among individuals. Steady-state inspiratory airflow and children have little effect on H₂S olfactory dosimetry patterns. Neurological, respiratory, and cardiovascular effects. Olfactory regions in some subjects. Differences in maximum flux values were < 3-fold among different subjects. Differences in maximum flux values were < 3-fold and differences in the 99% percentile and average flux values were < 1.2-fold at an inhaled concentration of 1 ppm (additional concentrations will be considered in future studies). These results suggest that differences in nasal anatomy and ventilation among adults and children have little effect on H₂S olfactory dosimetry patterns.

**ABSTRACT**

Human exposure to hydrogen sulfide (H₂S) gas can occur from a variety of natural and industrial sources and results in dose-related neurological, respiratory, and cardiovascular effects. Olfactory neuronal loss in H₂S-exposed rats has been used to develop occupational and environmental exposure limits based on exposure concentration. Anatomically accurate computational fluid dynamics (CFD) models have shown a correlation between tissue flux and olfactory pathology in rodents, suggesting an influence of airflow patterns on lesion locations that may affect extrapolation of tissue dose levels to humans. Human nasal anatomy varies considerably among individuals, affecting patterns of airflow and gas absorption. In this study, inter-human variability of H₂S nasal dosimetry was investigated using CFD models of the nasal passages of five adults and two children generated from MRI or CT data. Approximations of olfactory epithelia were mapped in each model to compare olfactory dosimetry predictions among individuals. Steady-state inspiratory airflow and H₂S uptake were simulated using Fluent™ CFD software with differences in the 99th percentile and average flux values being < predictions among individuals. Steady-state inspiratory airflow and children have little effect on H₂S olfactory dosimetry patterns. Neurological, respiratory, and cardiovascular effects. Olfactory regions in some subjects. Differences in maximum flux values were < 3-fold among different subjects. Differences in maximum flux values were < 3-fold and differences in the 99% percentile and average flux values were < 1.2-fold at an inhaled concentration of 1 ppm (additional concentrations will be considered in future studies). These results suggest that differences in nasal anatomy and ventilation among adults and children have little effect on H₂S olfactory dosimetry patterns.

**RESULTS**

- There was a wide range in nasal surface areas, yet the gross morphological features remained consistent among subjects (Table 1, Figure 1).
- Olfactory surface areas ranged from 9-14 cm², slightly larger than what has been reported in the literature (< 10 cm²).
- The bulk of inhaled airflow passed through the middle and ventral regions, consistent with results from previous studies on other human subjects. Olfactory airflow allocations ranged from 1.6 to 16.2%. Repairing the occlusion in the olfactory region of Adult 5 resulted in increased olfactory airflow allocation from 2.2 to 4.9%.
- The olfactory region of Adult 1A was defined to be consistent with previous studies (Schroeter et al., 2006), the olfactory regions of the other models are defined to be more anatomically precise and consistent across individuals.
- The 99th percentile flux values will be used to estimate inter-individual variability in NOAEL(TED) estimates based on tissue dose.
- Additional simulations with inhalation concentrations of 5 and 10 ppm will be conducted in future studies.
- Future work will involve binning flux values in the olfactory regions of all individuals to examine how dosimetry patterns vary between subjects.

**APPROACH**

- Nasal geometries of five adults and two children were reconstructed from MRI or CT data (Fig. 1) [1]. Artificial nasopharynx were constructed in Adults 2, 3, 4, and Child 2.
- Approximate locations of olfactory epithelium were mapped into each model. Olfactory regions in some subjects were manually repaired due to scan errors or natural airflow obstructions (Fig. 2).
- Unstructured tetrahedral meshes were generated in each model using Icem-CFD (ANSYS, Inc.). Each model contained 3-4 million elements.
- Steady-state inspiratory airflow was simulated in Fluent using allometrically equivalent breathing rates = 2*minute volume (Table 1): 13.6 – 18.0 L/min in adults, 11.0 – 11.6 L/min in children (Fig. 3).
- Transport and dosimetry of inhaled H₂S was simulated in Fluent at an inhalation concentration of 1 ppm.
- Olfactory dosimetry patterns (maximum, 99th percentile, and average flux values) were compared to examine inter-individual variability (Table 2).
- There were a wide range in nasal surface areas, yet the gross morphological features remained consistent among subjects (Table 1, Figure 1).
- Olfactory surface areas ranged from 9-14 cm², slightly larger than what has been reported in the literature (< 10 cm²).
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**CONCLUSIONS**

- Using allometrically equivalent breathing rates, differences in nasal anatomy and ventilation had little effect (< 1.2-fold in 99th percentile and average flux values) on H₂S olfactory dosimetry among five adults and two children.
- Rats exposed to H₂S develop olfactory neuronal loss. This lesion has been used to develop exposure standards based on exposure concentration. Schroeter et al. (2006) used quantitative tissue dose estimates to extrapolate results from rats to humans to develop tissue-dose based exposure levels, but results were based on one adult. These simulations suggest there would be little variation among adults and children, based on the limited number of subjects used in this study.
- The 99th percentile flux values will be used to evaluate inter-individual variability in NOAEL(TED) estimates based on tissue dose.
- Additional simulations with inhalation concentrations of 5 and 10 ppm will be conducted in future studies.
- Future work will involve binning flux values in the olfactory regions of all individuals to examine how dosimetry patterns vary between subjects.

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**REFERENCES**