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Intranasal Deposition of Dry Particles in Anatomically Correct Physical Models of Children and Adults during Inspiratory Flow Rates Representing Sitting Awake, Light Activity, and Light and Heavy Exercise

Jana Kesavan
RESEARCH AND TECHNOLOGY DIRECTORATE

Valerie Alstadt
OAK RIDGE INSTITUTE FOR SCIENCE AND EDUCATION
Oak Ridge, TN 37831-0117

Jerold Bottiger
EXCET, INC.
Springfield, VA 22150-2110

Keith Sedberry
CFD RESEARCH CORPORATION
Huntsville, AL 35806-2900

Beth Laube
THE JOHNS HOPKINS MEDICAL INSTITUTIONS
Baltimore, MD 21287-0011

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Excet, Inc.; 6225 Brandon Avenue, No. 360, Springfield, VA 22150-2110
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Physical models of the respiratory system provide a method for quantifying particle deposition in humans without exposing them to toxic agents. Although particles may be liquid or dry, little is known about intranasal deposition of dry particles within models. We compared intranasal deposition of 0.58–10 µm particles of test dust in models of 2-, 5-, and 18-year-old humans at flow rates representing sitting awake (SA), light activity (LA), light exercise (LE), and heavy exercise (HE). Intranasal deposition increased with particle size and airflow rate, and deposition for the 18-year-old model agreed with published in vivo results in adults. For SA conditions, intranasal deposition was significantly greater in the 2- and 5-year-old models than in the 18-year-old model for particles $\leq$3.52 µm. Under LA, LE, and HE breathing conditions, intranasal deposition of most particles $\geq$2.46 µm was significantly greater in the 18-year-old model as compared to the 5-year-old model. This study is the first to show that intranasal deposition of dry particles between 0.58 and 3.52 µm may be greater in children $\leq$5 years old during SA, as compared to adults. Information from this study could inform future policies designed to protect children from exposure to inhaled toxic particles.

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PREFACE

The work was started in October 2017 and completed in May 2021. At the time this work was performed, the U.S. Army Combat Capabilities Development Command Chemical Biological Center (DEVCOM CBC; Aberdeen Proving Ground, MD) was known as the U.S. Army Edgewood Chemical Biological Center (ECBC).

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CONTENTS

FIGURES

TABLES

INTRANASAL DEPOSITION OF DRY PARTICLES IN ANATOMICALLY CORRECT PHYSICAL MODELS OF CHILDREN AND ADULTS DURING INSPIRATORY FLOW RATES REPRESENTING SITTING AWAKE, LIGHT ACTIVITY, AND LIGHT AND HEAVY EXERCISE

1. INTRODUCTION

Particulate matter released into the ambient air from pollution sources in urban and industrial environments likely poses a significant health risk for local inhabitants (Calderón-Garcidueñas et al., 1998). Studies in adults provide strong evidence for the carcinogenic effects of occupational inhalants in the nasal cavity and sinuses (Calderón-Garcidueñas et al., 1998) and the development of olfactory dysfunction with long-term exposure to environmental pollutants (Ajmani et al., 2016). Other airborne particulates composed of biologics, including bacteria and viruses, lead to infections in the intranasal and lower airways in the general population. Most people, including young children, breathe through the nose when sitting awake or performing light exercise (Cheng, 2014). Thus, the intranasal region (nasal airways and nasopharynx) is the first line of defense against inhaled particles during nose-breathing, providing protection to the lower respiratory tract from toxic agents by filtering out a large majority of inhaled particles before they can damage the lungs (Proctor and Andersen, 1982). Understanding particle deposition within human intranasal airways is important to the study of airborne hazards because the location and quantity of particle deposition affects the body's response to hazardous aerosol exposures.

A few in vivo studies have been conducted in older children and adults to assess liquid particle deposition in intranasal airways (ICRP, 1994; Becquemin et al., 1991; Kesavanathan et al., 1998; Kesavanathan and Swift, 1998; Kesavan et al., 2000; Bennett et al., 2008). However, quantification of particle deposition in vivo is a significant undertaking. Conduct of such tests requires approval from ethical and scientific review boards to be sure the exposure is safe. These tests are also expensive and may be inaccurate because human subjects may not perform the necessary breathing maneuvers correctly. In addition, these studies are not feasible in infants and young children. Nevertheless, the potential for negative effects from toxic particle deposition in the intranasal airways of children makes quantification of deposition in this region essential.

Anatomically correct physical models created using stereolithography (SL) and 3D printing technologies provide a way to quantify particle deposition in humans without exposing them to potentially toxic agents or relying on correct breathing maneuvers. Several investigators have quantified the deposition of liquid particles in physical models representing the intranasal airways of healthy infants and children (Javaheri et al., 2013; Janssens et al., 2001; Storey-Bishoff et al., 2008; Golshahi et al., 2011; Xi et al., 2011; Xi et al., 2012; Zhou et al., 2013, 2014). However, toxic particles may be liquid or dry, and little is known about intranasal deposition of dry particles within models of children performing different levels of activity. In addition, the geometry and size of the extrathoracic airways continue to change during infancy and childhood (Xi et al., 2012), and such changes could affect particle deposition. To begin to address this information gap, we used computed tomography (CT) scans to create anatomically correct SL models of the intranasal airways of 2-, 5-, and 18-year-old humans. We systematically compared intranasal deposition of 0.58–10 µm particles of Arizona test dust (ATD) in these models, during inspiration only, at flow rates that represented four breathing conditions: sitting awake, light activity, light exercise, and heavy exercise. To validate the use of the models, deposition of dry particles in the 18-year-old model was compared to in vivo aerosol deposition data that was obtained previously in human adults (Kesavanathan et al., 1998; ICRP, 1994).

2. METHODS

2.1 Physical Model Production

Anatomically correct physical models of the head and intranasal airways were produced after transforming CT scans of the head (obtained in the supine position) into the SL format. For details regarding the selection of CT scans and the production of the models, see Laube and colleagues (2015). Each of the completed models consisted of a soft, flexible face with closed lips and a nose with patent nostrils, nasal vestibule, nasal valve area, main nasal airway, and nasopharynx. Photographs of the three models are shown in Figure 1. To simulate the mucus coating of the airways, the inside surfaces of the models were pre-coated with nebulized corn oil droplets.

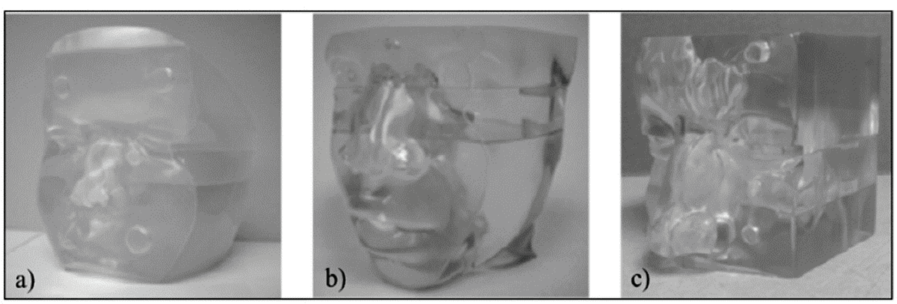

Figure 1. Anatomically correct models of (a) 2-year-old, (b) 5-year-old, and (c) 18-year-old humans.

2.2 Breathing Conditions

Each of the three models was tested under four breathing conditions: sitting awake, light activity, light exercise, and heavy exercise. Table 1 lists representative inspiratory flow rates for these four breathing conditions for 2- and 5-year-old children and an 18-year-old adult. The sitting awake and light exercise flow rates were based on inspiratory flow rates reported by the International Commission on Radiological Protection (ICRP, 1994) for humans of these ages.

Flow rates for light activity and heavy exercise for the 18-year-old adult model match the flow rates previously reported by Kesavanathan and colleagues (1998) for adults during nasal breathing. Flow rates for the 18-year-old adult did not exceed 35 L/min for any breathing condition because higher values would have surpassed the pump capability. Flow rates for light activity and heavy exercise for the 2- and 5-year-old models represent similar increments from the sitting-awake test conditions that were used for the adult model.

Table 1. Inspiratory Flow Rates for 2- and 5-Year-Old Children and an 18-Year-Old Adult

Age of Human Model (years)	Inspiratory Flow Rate (L/min)			
	Sitting Awake	Light Activity	Light Exercise	Heavy Exercise
2	2.5	5	7.3	10.2
5	4	8	9.5	13.3
18	10	15	25	35

2.3 Dry Particle Exposure

Dry particle exposure was conducted in a large Plexiglas chamber (60 × 36 × 48 in.) as shown in Figure 2. The setup was designed so that an Aerodynamic Particle Sizer spectrometer (APS; TSI, Inc.; Shoreview, MN) could sample either from the upstream side, representing the reference, or from the model on the downstream side. A solenoid switch enabled the operator to switch APS sampling between upstream and downstream channels. An external pump was used to generate flow through the model at preselected inspiratory rates for the model under study. Lines and fittings were identical for the upstream and downstream sides and were carefully constructed to minimize losses in the airflow path. A sonic nozzle aerosol generator was used to aerosolize the ATD (60.0 ± 3.8 mg) as a dry powder into the chamber. A fan mixed the chamber air for 45 s after the ATD was introduced.

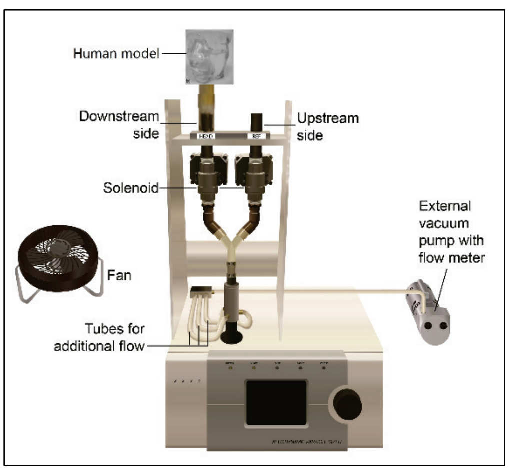

Figure 2. Experimental setup.

2.4 APS Sampling

APS sampling began 65 s after aerosol generation was started. Each of the upstream and downstream APS measurements was 20 s in duration, and the number of particles for each size bin was recorded. There was a 10 s interval between measurements to accommodate the solenoid switching between upstream and downstream channels. A total of 10 pairs of measurements (upstream and downstream) were obtained for each aerosol release into the chamber. After 10 pairs of runs, the aerosol concentration in the chamber was very low, so the chamber air was cleared, and a new aerosol release was conducted. Three aerosol releases were conducted, and 10 pairs of upstream and downstream measurements were made after each release for a total of 30 pairs of upstream and downstream measurements.

2.5 Quantification of Deposition

Deposition for each size bin was calculated as a percentage (η_i) by dividing the downstream measurement by the average upstream measurements before and after the downstream measurement was obtained (eq 1). Reported averages and standard deviations were determined to support calculation of the deposition percentage (η) for the 30 pairs of measurements:

$$\eta_i = [1 - \frac{\text{Downstream measurement}}{\text{Average upstream measurement before and after downstream measurement}}] \times 100 \qquad (1)$$

Average deposition was quantified for the following particle size bins in all three models at the inspiratory flow rates shown in Table 1: 0.58, 0.6 , 0.67, 0.72, 0.78, 0.84, 0.90, 0.97, 1.04, 1.11, 1.20, 1.29, 1.38, 1.49, 1.60, 1.72, 1.84, 1.98, 2.13, 2.29, 2.46, 2.64, 2.84, 3.05, 3.28, 3.52, 3.79, 4.07, 4.37, 4.70, 5.05, 5.43, 5.83, 6.26, 6.73, 7.23, 7.77, 8.35, 8.98, and 9.64 µm.

Average deposition was compared in the three models for the following selected size bins at the inspiratory flow rates shown in Table 1: 0.58, 1.60, 2.46, 3.5, 4.70, 5.83, 6.73, 7.77, 8.98, and 9.64 µm. These size bins were selected because they were approximately 1 µm apart in size. Deposition was quantified and compared as a function of impaction parameter (d^2Q) for all size bins, where d is the aerodynamic diameter and Q is the flow rate.

Deposition was also quantified and compared as a function of impaction parameter for all size bins combined with the anatomical parameters of $A_{\min}$ (the minimum cross-sectional area of either the right or the left nostril) and ellipticity (the nostril length-to-width ratio), using eq 2 (derived by Kesavanathan and Swift, 1998; and Kesavanathan et al., 1998).

$$\text{PDE} = [1 - \exp^{\left(-0.1\times d^{1.78}\times\left(\frac{Q}{100}\right)^{1.12}\times A_{\min}^{-1.33}\times E^{1.26}\right)}] \times 100 \qquad (2)$$

where PDE is the particle deposition efficiency, d is the aerodynamic diameter (µm), Q is the flow rate (L/min), $A_{\min}$ is the intranasal cross-sectional area of the left or right nostril (cm^2), and E is the ellipticity (unitless).

2.6 Best-Fit Curve for Deposition Data

We chose three well-described equations to determine the best-fit curve for the deposition data:

- the equation by Kelly and colleagues (2004), where α and β were determined constants:

$$\eta = \left[1 - \exp^{-(\alpha d^2 Q)^{\beta}}\right] \times 100 \qquad (3)$$

- the equation from ICRP (1994):

$$\eta = [1 - \frac{1}{(\alpha d^2 Q + 1)}] \times 100 \qquad (4)$$

- the equation from the Task Group of the National Council on Radiation Protection and Measurement (NCRP, 1997), where ρ is particle density:

$$\eta = [\frac{1}{1+\left(\frac{\rho d^2 Q}{\alpha}\right)^{-\beta}}] \times 100 \qquad (5)$$

2.7 Data Analysis

For each model, the mean percent deposition and standard deviation were quantified for each size bin between 0.58 and 10 µm at the inspiratory flow rates shown in Table 1. Analysis of variance (ANOVA) and Tukey honestly significant difference (HSD) tests were used to determine whether the mean deposition for each size bin and the inspiratory flow rate were statistically significantly different between models. *P* values of <0.05 were considered to be statistically significant.

To validate the use of the SL models as representative of in vivo deposition, data for the 18-year-old model were expressed as a function of impaction parameter combined with the anatomical parameters of A_{min} and ellipticity. The constants determined by Kesavanathan and colleagues (1998) in eq 2 were used for particles between 2.12 and 6.26 µm at inspiratory flow rates of 15, 25, and 35 L/min. These particle sizes and flow rates were selected for comparison because they were studied in both the model and the in vivo experiments. These deposition data were then visually compared with in vivo data obtained in adult subjects by Kesavanathan and colleagues (1998). In addition, deposition data for the 18-year-old model were calculated as a function of impaction parameter using units of micrometers for d and cubic centimeters per second for Q. These data were then visually compared with in vivo deposition data that had been calculated in the same way and reported by the ICRP (1994) for nasal deposition efficiency in adult Caucasian males.

Deposition was also quantified and compared as a function of impaction parameter for each model as described above. Equations 3–5 were then fit to the model data, using Igor Pro software (version 6.37; WaveMetrics; Portland, OR). The equation that best fit the model data was used to visually compare deposition for the three models. The α and β constants were determined for each age model and were compared by ANOVA and Tukey HSD tests.

Deposition data for the three models for each size bin and inspiratory flow rate were also calculated as a function of impaction parameter combined with the anatomical parameters of A_{min} and ellipticity The constants determined by Kesavanathan and colleagues (1998; shown in eq 2) were used, and the data were visually compared.

3. RESULTS

Table 2 provides demographics for the human subjects upon which the models were based as well as the A_{min} and the ellipticity measured in each model.

Figure 3 shows the percentage of intranasal deposition in the 18-year-old SL model in the current study compared with intranasal deposition measured in vivo for 10 human subjects, ages 18–58, who participated in a previous study reported by Kesavanathan and colleagues (1998). Equation 2 was used to calculate the percentage of deposition in both studies as a function of impaction parameter combined with A_{min} and ellipticity values. Intranasal deposition data for the 18-year-old SL model clearly overlaps with the in vivo data. In addition, deposition comparisons between the model and the human subjects revealed similar values for specific particle sizes and flow rates. For example, for 4.06 µm particles at 25 L/min, deposition in the model was calculated to be 62.4%, which was well within the range of 45.5–89.5% that was calculated for the human subjects. In a second comparison with in vivo data, in the 18-year-old model, intranasal deposition was calculated as a function of impaction parameter (using units of micrometers for particle size and cubic centimeters per second for airflow rate) to be 13 and 76% for impaction parameters of 1,000 and 10,000, respectively. These were similar to values reported by the ICRP (1994) for adult Caucasian males and the same impaction parameters (22 and 76%, respectively).

Table 2. Demographics for Humans and Intranasal Anatomical Information for Each Model

Age of Human (years)	Sex	Ethnicity	A_{min}: Left, Right (cm^2)	Ellipticity: Length/Width
2	F	AA	(0.517, 0.181)	1.25
5	M	AA	(1.127, 0.682)	1.93
18	M	Unk	(0.606, 0.530)	1.63

AA, African American; Unk, unknown.

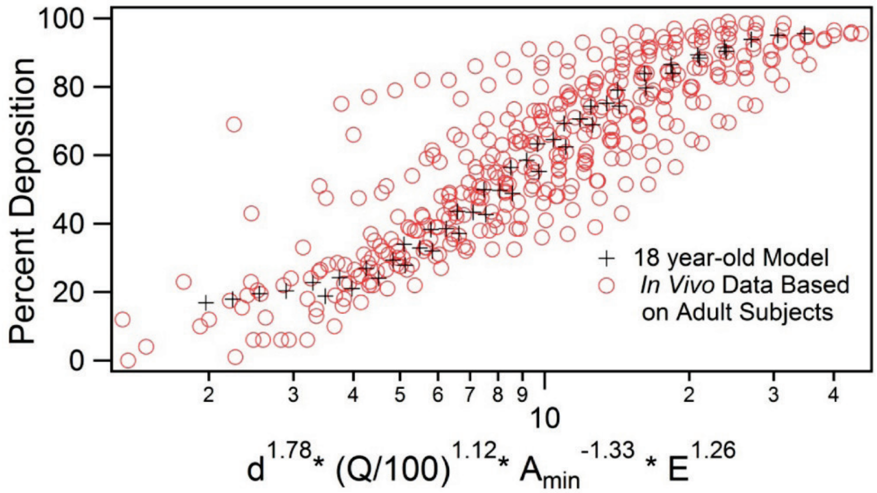

Figure 3. Percentage of particle deposition in the 18-year-old model and in 10 human subjects.

Figure 4 shows the percentage of intranasal deposition as a function of all size bins for each age model at the inspiratory flow rates shown in Table 1. For all three models, deposition increased with increasing particle size and inspiratory flow-rate conditions.

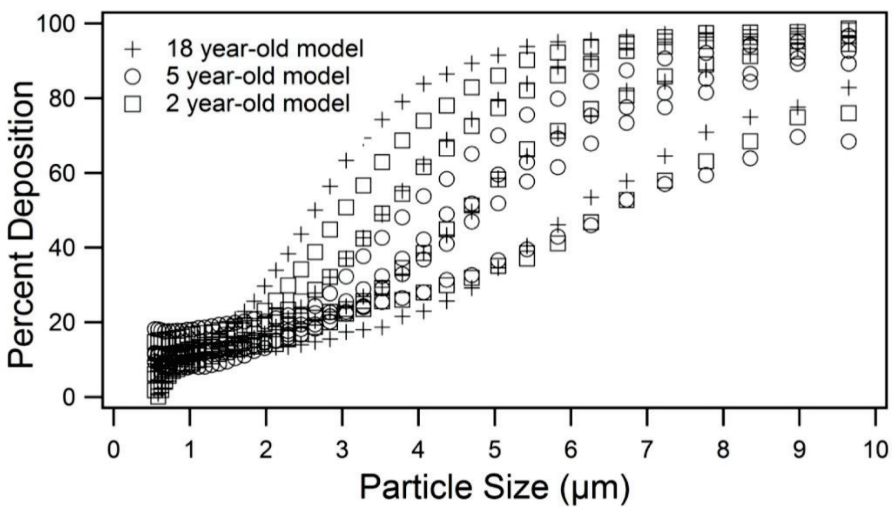

Figure 4. Percentage of particle deposition as a function of particle size for each model at the tested flow rates.

Figure 5 shows the percentage of intranasal deposition, based on the particle size for each model, in the selected size bins for the four breathing conditions (sitting awake, light activity, light exercise, and heavy exercise). For the sitting awake breathing condition, intranasal deposition was significantly greater in the 2- and 5-year-old models as compared with the 18-year-old model for particles ≤3.52 µm. For particles >3.52 µm, intranasal deposition increased in all models, but the increase was more significant in the 18-year-old model.

For the light-activity breathing condition, intranasal deposition was similar for all models for 3.52 µm particles. Deposition was significantly less in the 2- and 5 year-old models than in the 18-year-old model for 1.60 and 2.46 µm particles. For particles ≥5.83 µm, intranasal deposition in the 5-year-old model was significantly less than in the 2- and 18-year-old models.

For the light-exercise breathing condition, intranasal deposition in the 5-year-old model was significantly less than in the 2- and 18-year-old models for particles ≥2.46 µm. Deposition in the 2-year-old model was significantly greater than in the 5- and 18-year-old models for 1.60 µm particles.

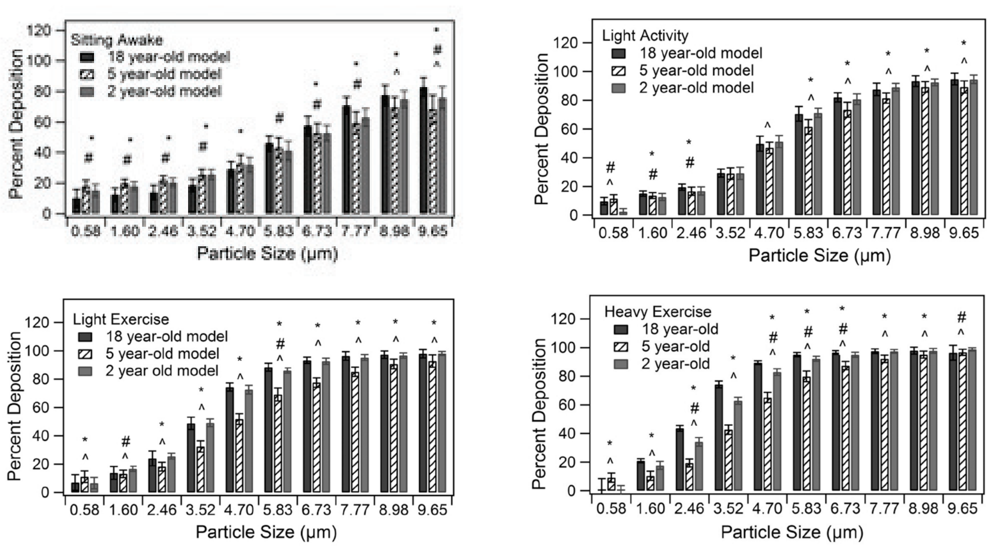

Figure 5. Percent deposition as a function of particle size for four breathing conditions: sitting awake (top left), light activity (top right), light exercise (bottom left), and heavy exercise (bottom right).*Depositions in the 18- and 5-year-old models are statistically significantly different. ^Depositions in the 2- and 5-year-old models are statistically significantly different. #Depositions in the 18- and 2-year-old models are statistically significantly different.

For the heavy-exercise breathing condition, intranasal deposition in the 5-year-old model was significantly less than in the 2- and 18-year-old models for particles ≥1.60 µm and ≤8.98 µm. Intranasal deposition in the 2-year-old model was significantly less than in the 18-year-old model for 2.46, 4.70, 5.83, 6.73, and 9.65 µm particles.

Figure 6 shows the percentage of intranasal deposition for each model, for all size bins and inspiratory flow rates (shown in Table 1), plotted as a function of impaction parameter. Data that appeared as disparate points for each model in Figure 4 appear more closely associated, and data for each model fell on its own discrete best-fit curve. Although there was still a large degree of variability between models, Figure 6 also shows that for a given impaction parameter, intranasal deposition in the 2- and 5-year-old models was higher than in the adults.

Of the equations that were tested (i.e., eqs 3–5), eq 3 provided the best fit to the data. This equation incorporates the flow rate, particle size, and α and β constants that were calculated for each model. The α and β constants associated with eq 3 for each of the three models are shown in Table 3. ANOVA and Tukey HSD tests showed that both α and β constants were statistically significantly different between models. This indicates that the equation that predicts deposition is specific for each model.

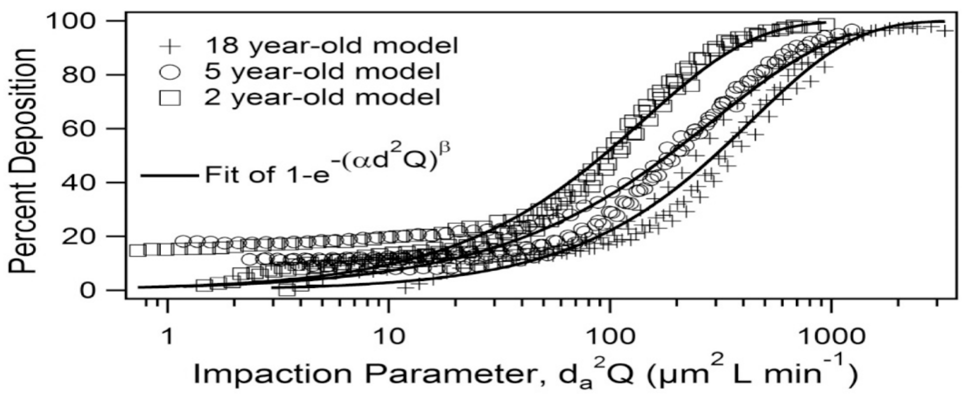

Figure 6. Particle deposition as a function of impaction parameter for 2-, 5-, and 18-year-old models.

Table 3. α and β Constants for Three Models Based on Eq 3, Using $\eta = \left(1 - e^{-(\alpha d^2 Q)^\beta}\right) \times 100$

Age of Human Model (years)	α*	β†
2	7.06E-3 ± 1.87E-4	8.66E-1 ± 2.38E-2
5	3.40E-3 ± 1.21E-4	7.69E-1 ± 2.52E-2
18	2.28E-3 ± 5.48E-5	9.36E-1 ± 2.53E-2

*ANOVA and Tukey HSD tests showed that α was statistically significantly different between all three models.

†ANOVA and Tukey HSD tests showed that β was statistically significantly different between all three models.

Figure 7 shows the percentage of intranasal deposition for the three models, calculated as a combination of inspiratory flow rates for all size bins in the form of impaction parameter, the anatomical parameters of A_{min} and ellipticity, and the constants determined by Kesavanathan and colleagues (1998; in eq 2). As compared to Figure 6, variability in deposition between the three models was reduced using this combination of parameters. In addition, deposition values for the 2- and 18-year-old models, but not for the 5-year-old model, appear to collapse into one curve.

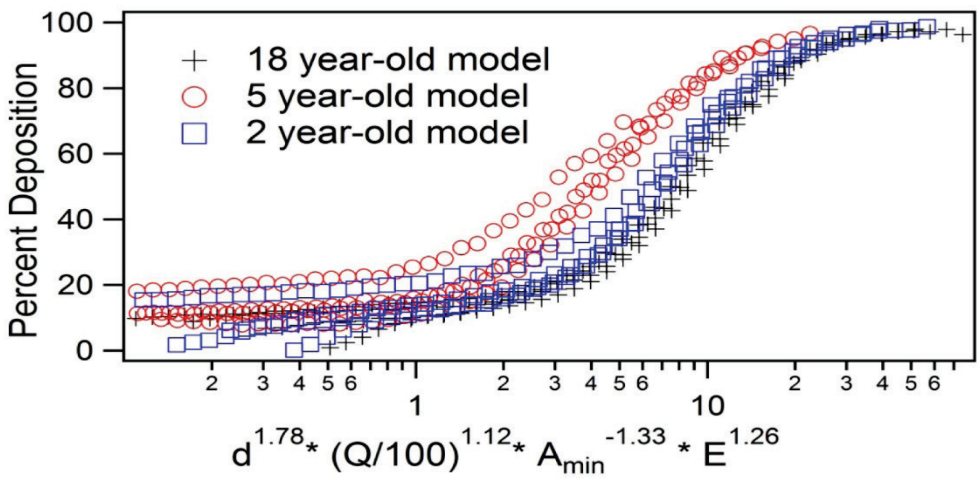

Figure 7. Percent intranasal deposition for the three models, calculated as a combination of inspiratory flow rates for all size bins in the form of impaction parameter, $A_{\min}$ and ellipticity, and the constants determined by Kesavanathan and colleagues (1998; eq 2).

4. DISCUSSION

This is the first study to systematically compare intranasal deposition of dry particles ranging in size from 0.58 to 10 µm in anatomically correct SL models that are based on CT scans of a 2-, 5-, and 18-year-old human, during inspiration only, at flow rates representing sitting-awake, light-activity, light-exercise, and heavy-exercise breathing conditions. Intranasal deposition of ATD for all three models increased with increasing particle size and inspiratory flow rate, which indicates impaction as the dominant deposition mechanism for these particles. Similar results have been reported using liquid particles in studies with different age models (Swift, 1991; Cheng, 2003; Golshahi et al., 2011).

We validated the use of the models by comparing intranasal deposition of the dry particles in the 18-year-old model to deposition of liquid particles previously quantified in vivo in human adults (Kesavanathan et al., 1998; ICRP 1994). Deposition in the 18-year-old SL model was similar to deposition reported in both of the in vivo studies, which indicates that in terms of intranasal deposition, this model provides similar information as in vivo studies in adults. It is reasonable to assume that deposition data obtained using the 2- and 5-year-old models would be similar to in vivo data obtained in age-matched children, given that these younger-age models were constructed using the same techniques and with the same inclusionary criteria as the 18-year-old model. Similar methods have been used to validate models based on CT and magnetic resonance imaging scans using 3D printing technology (Golshahi et al., 2011; Zhou et al., 2013).

No in vivo studies have quantified aerosol deposition of 0.58–10 µm particles in the intranasal airways of children ≤5 years of age at flow rates similar to those used in this study for the sitting-awake breathing condition. Two studies investigated nasal deposition of 1–2.8 µm particles in children ≥5.5 years of age and in adults under higher flow-rate conditions (Becquemin et al., 1991; Bennett et al., 2008). Bennett and colleagues (2008) reported statistically greater intranasal deposition in adults for 2 μm particles during their light-exercise breathing condition as compared to children 6–10 years of age. Similarly, Bequemin and colleagues (1991) reported statistically greater intranasal deposition in adults for 2.05 and 2.8 μm particles during their resting breathing condition and for 1.0, 2.05, and 2.8 μm particles during their moderate-exercise breathing condition as compared to children 5–12 years of age. Based on these findings, the authors concluded that for these particle sizes and breathing conditions, the intranasal airways of adults appear to be a target for greater particle exposure as compared to children ≥5.5 years of age.

As best we can determine, the flow rates used by Bennett and colleagues (2008) and Bequemin and colleagues (1991) were similar to the flow rates we selected for light activity, light exercise, or heavy exercise in our model study. At those flow rates, we also found that intranasal deposition was significantly higher in the 18-year-old (adult) model as compared to the 5-year-old model for 1.60 and 2.46 μm particles and light activity (Figure 5, top right), for particles ≥2.46 μm for light exercise (Figure 5, bottom left), and for particles ≥1.60 μm for heavy exercise (Figure 5, bottom right). These model findings are therefore similar to what Bennett and colleagues (2008) and Bequemin and colleagues (1991) showed in their in vivo studies.

Importantly, during much slower breathing conditions (i.e., sitting awake) in the present model study, we found that intranasal deposition was statistically significantly higher in the models of the young children compared to the model of the adult, for particles ≤3.52 μm (Figure 5).This indicates that for these particle sizes and the sitting-awake breathing condition, the intranasal airways of children ≤5 years of age appear to be a target for greater particle exposure as compared to adults.

When impaction parameter was used, results from the present study with dry particles (Figure 6) were similar to model data reported by Swift (1991) and Zhou and colleagues (2014) with liquid particles. In all of these studies, for a given impaction parameter, intranasal deposition was greater in models of very young children than in models of adults.

Variability between deposition in the three models was reduced significantly when eq 2 was used to combine the anatomical parameters of $A_{\min}$ and ellipticity with the impaction parameter. These results confirm the importance of including these two anatomical parameters in any comparison of intranasal deposition between individuals, as mentioned by other investigators (Kesavanathan et al., 1998; Kesavan et al., 2000; Cheng, 2003; Storey-Bishoff et al., 2008; Golshahi et al., 2011; Zhou et al, 2014). Nevertheless, after the impaction parameter was combined with $A_{\min}$ and ellipticity, deposition for the 5-year-old model did not collapse onto the same curve as that for the 2- and 18-year-old models. This suggests that other parameters may also affect deposition. Another parameter that may contribute to intranasal deposition is the pressure drop within the intranasal airways during inhalation. The effect of this parameter was explored previously by others (Hounam et al., 1971; Garcia et al., 2009; Golshahi et al., 2011; Xi et al., 2012; Zhou et al., 2013). However, measurement of this parameter was beyond the scope of this study.

Interestingly, $A_{\min}$ and ellipticity are associated with the anterior region of the nasal cavity, specifically, the area nearest the nasal valve, where the probability of deposition by impaction is high. Variability in deposition among the different-aged models could also involve anatomical characteristics associated with other areas of the nasal passage. For example, Fry and Black (1973) showed that a significant amount of particle deposition also occurs in the middle and posterior nasal passage. Therefore, including middle and posterior nasal passage characteristics might further reduce the variability.

It is not known why intranasal deposition in the 2-year-old model so closely resembled that of the 18-year-old model while deposition in the 5-year-old model was different for particles ≥5.83 µm for light activity and for particles ≥2.46 µm for light exercise (except for 5.83 µm). However, one of the limitations of the present study was that deposition measurements were based on a model of a single human for each age group. Additional studies are needed to confirm the current findings and to identify variability between similarly aged models.

Another limitation was the previously observed drop-off in detection efficiency for the APS used in these experiments for particles <2 µm; this could have affected our deposition calculations. However, Kesavan and colleagues (2014) found that the drop-off in efficiency was less than ~2%. An additional limitation was that the 2- and 5-year-old models were based solely on CT scans of African American children. Kesavanathan and colleagues (1998) have shown that African American adult subjects have significantly different nostril widths, ellipticity, and angles compared to European American adults. In addition, Bennett and Zeman (2005) reported reduced intranasal deposition of 1 and 2 µm particles in African American adults versus Caucasian adults for light-exercise conditions. However, possible variances in deposition that result from differences in ethnicity have not been evaluated in vivo or in models of young children.

The deposition fraction within the intranasal airways versus the lungs is clearly an important factor to consider in assessing exposure from an inhaled agent. In the case of the 2- and 5-year-old models, higher intranasal deposition of an inhaled dose during the sitting-awake breathing condition could lead to less exposure in the lungs, thereby protecting the lungs. Conversely, reduced intranasal deposition during light activity and light and heavy exercise conditions could lead to increased lung exposure. However, determinants of deposition within the lung compartment are also important for exposure assessments, and several investigators report that changes with age in both lung growth and breathing pattern could affect the deposition fraction within the lungs (Bennett and Smaldone, 1987; Bennett, 1988; Heyder et al., 1988). The effects of these factors could be addressed in models that include the tracheobronchial and pulmonary regions of the lungs.

5. CONCLUSIONS

To our knowledge, this is the first study to compare deposition of dry particles in anatomically correct SL models (based on the intranasal airways of 2-, 5-, and 18-year-old humans) at activity levels ranging from sitting awake to heavy exercise. Similar to the results reported for liquid particles, data from this study indicate that impaction is the predominant deposition mechanism for dry particles. In addition, results obtained for the 18-year-old model were similar to those obtained in vivo for liquid particles in nose-breathing adults. This validates the use of the models and indicates that dry particles and liquid particles deposit similarly in the intranasal airways of adults for a given flow rate and particle size.

We believe our in vitro findings for the 5-year-old model at inspiratory flow rates representing light activity and light and heavy exercise are similar to results reported for in vivo studies of children ≥5 years of age (Bennett et al., 2008; Bequemin et al., 1991). This suggests that at those flow rates, the lungs of children ≥5 years of age may sustain greater exposure from particles between 1 and 3 µm, as compared to adults.

Findings from this in vitro study extend the in vivo findings of Bennett and colleagues (2008) and Bequemin and colleagues (1991) by providing information about intranasal deposition for younger children exposed to a wider range of particle sizes at lower activity levels. New information from this study suggests that intranasal deposition of dry particles sized between 0.58 and 3.52 µm may be greater in children ≤5 years of age during sitting-awake breathing, as compared to adults. This new information could inform future policies designed to protect the intranasal airways of children from exposure to inhaled toxic dry particles. Importantly, differences in deposition between the models were small, and the effects of these small differences in terms of exposure are unknown. Studies in additional models based on children of similar age are needed to confirm these findings.

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ACRONYMS AND ABBREVIATIONS

ANOVA	analysis of variance
APS	Aerodynamic Particle Sizer
ATD	Arizona test dust
CT	computed tomography
HSD	honestly significant difference
ICRP	International Commission on Radiological Protection
PDE	particle deposition efficiency
SL	stereolithography

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