In Vitro Inter-subject Comparison of Inhaled Aerosol Deposition in Realistic Human Upper Respiratory Models

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Abstract – The purpose of this study was to investigate the effects of inhaled particle size and inhalation flow rate on particle deposition patterns within two different subject-specific airway models using experimental analyses. The three-dimensional subject-specific airway models were created from a series of CT scanned images and constructed using a 3D printer (ProJet^{TM} HD3000). Liquid aerosols with 0.1% fluorescent and 0.4% oleic acid were generated with a vibrating orifice aerosol generator (VOAG, TSI Inc.). The aerosol size from the vibrating orifice was calculated and verified by Wide-range Particle Spectrometer (WPS) simultaneously during each experiment. The particle sizes were ranged from sub-micron size to micron size. The airflow rates through each model were varied from 30 to 60 LPM, which represent normal to heavy exercise breathing conditions. The overall deposition trend of micron size particles was varied, increasing as the Stokes number increases. The total deposition fraction data for the two different models, A and B, were found to be very similar to each other in spite of their difference in three-dimensional geometries. However, at higher flow rate, the total deposition within the model B was observed to be significantly increased compared to the model A, with greater regional differences. Although more accurate modeling techniques are required, this experimental study showed that the effect of subject-specific geometry on aerosol particle deposition was minimal in total deposition. However, the regional (i.e., local) deposition fractions were not the same. As the flow rate increased, the larger differences in regional deposition data between the two models were observed due to their difference in three-dimensional geometry.

Keywords: experiment, mono-dispersed aerosol, inhaled aerosol, respiratory system, subject variability

INTRODUCTION

Inhaled aerosol deposition studies with an accurate model of the human respiratory system allow health professionals to gain insight into the interactions between particulate matter and the exposed surfaces of the lung airways. Pharmaceutical companies and pulmonologists find aerosol deposition studies of the human airway to be vitally important in developing drug delivery systems for pharmaceutical aerosols and assessing the effective dosage necessary to combat chronic airway diseases [Lambert, 3]. Employing extensive experimental approaches, a realistic and accurate model can be created to predict inhaled particle depositions within the upper respiratory regions including oral and upper tracheobronchial airways. Subject-specific in vitro particle deposition experiments provided new physical insights into complex fluid-particle-wall interaction mechanisms.

Extensive research has been conducted to provide a better understanding of human respiratory system. This research has been occurring on many fronts, both in vivo and in vitro using experimental or computational analysis with realistic settings [Stapleton, 6]. Cheng et al. [Cheng, 2] performed an in vitro experiment with a subject-specific model, while Longest et al. [Longest, 4] studied computational fluid dynamic predictions of respiratory aerosol

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deposition with more complicated settings. However, because of the complexity of the human respiratory system, the need for further research on specific characteristics of human respiratory systems has become more significant.

Due to the asymmetry of the airway tree and the heterogeneous airflow characteristics experienced in the airway, it is essential to understand regional differences in aerosol deposition including left and right lung differences [Ryans, 5]. Lambert [Lambert, 3] used the geometry of the human airway including an oral cavity from the first bifurcation through the sixth, as well as the five lobes. He then performed a computational analysis using Large-Eddy simulation with in-house Lagrangian particle tracking code. Asgharian et al. [Asgharian, 1] studied theoretical aerosol deposition in the human lung with a lobe- specific flow rate model and compared deposition of different aerosol sizes and their locations. They found that the majority of aerosols were deposited in the inferior right and left lobes regardless of the particle size. Subramaniam et al. [Subramaniam, 7] then studied these lobular differences; they investigated the lobular differences of aerosol deposition in a symmetric lung model that had structurally different lobes. As a result, it was found that the deposition in the inferior lobes was approximately twice that of the upper lobes, and that the right middle lobe had the smaller deposition fraction of the group. This was because of the differences between lobular air flow rates: about 31% of the air flow to each lower lobe, 15% of the air to each upper lobe, and the last 8% to the right middle lobe.

As discussed, numerous studies on the various characteristics of inhaled aerosols have been conducted. Only a few have been done experimentally with inter-subject variability of the human upper respiratory geometry, one of the most important subject to study for devising a universal inhaler or universal aerosol delivery system. The study conducted by Zhang et al. [Zhang, 8] focused on creating an idealized model that could accurately represent particle deposition in human patients. The geometry of the human mouth-throat region is highly irregular, and so the possession of a simpler model that retained the deposition characteristics of live patients would be invaluable to subsequent deposition studies. They devised a simple model that consisted of a long, horizontal cylinder that represented the human mouth, a gently curved nozzle that represented the back of the throat, and a 90˚ bend to represent the oropharyngeal transition to the larynx and trachea. From the results of the previous study, it was found that the simple model with a 90˚ bend was not a valid representation of a real human upper respiratory system.

EXPERIMENTAL FACILITY

Nomenclature

C Solution concentration (%)
D aerosol diameter (m)
f frequency (s^{-1})
St Stokes Number
v velocity (m s^{-1})
P pressure (Nm^{-2})
Q flow rate (cc min^{-1})

Greek letters

ρ density (kg m^{-3})
μ viscosity (Pas)

Subscripts

p aerosol particle
t throat

Two different three-dimensional (3D) subject-specific models were created from a series of CT scanned images using an image processing software, ScanIP (Simpleware). The completed models were then constructed using a 3D printer (ProJet™ HD3000) and used for the experimental measurement of regional aerosol depositions. Both models were printed with the same plastic material (VisiJet EX200); therefore the material property of each model was the same including the surface property. Since a hard acrylic plastic material is used, the effect of moist and temperature

or the flexibility of real human airways have been excluded for this study. Based on our previous studies, the effect of moist and temperature generally increased the overall deposition within the models. Figure 1 shows the two different subject-specific models used for the experiments.

Figure 1. Two Subject-specific Models Used for the Experiments: Left-Model A and Right-Model B

The liquid micron-sized aerosols with florescent (i.e., liquid droplets) were generated with a vibrating orifice aerosol generator (VOAG, TSI Inc.), which fed into a steady airflow. Particles of 0.1% fluorescent and 0.4% oleic acid were suspended in a solution composed of 400 cc alcohol and 100 cc deionized water. The aerosol size (Dp) from the vibrating orifice was calculated by Eq. 1, where Q is the flow rate [cc/min] of the solution, C is the concentration [%] of the solution, and f is the frequency [1/sec] of the vibrating orifice.

$$Dp = (6CQ/(\pi f))1/3 \qquad (1)$$

The average droplet diameter varied for each experiment from 8.33 to 9.23 microns. For quality control purposes, the particle size distributions were evaluated by an aerodynamic particle sizer (Model 3310, TSI Inc., St. Paul, MN). The airflow rates through the MT airway models were 30, 45, and 60 liters per minute (LPM), which represent from rest to heavy exercise breathing conditions for an average human. Figure 2 shows the experimental measurement set-up for the study.

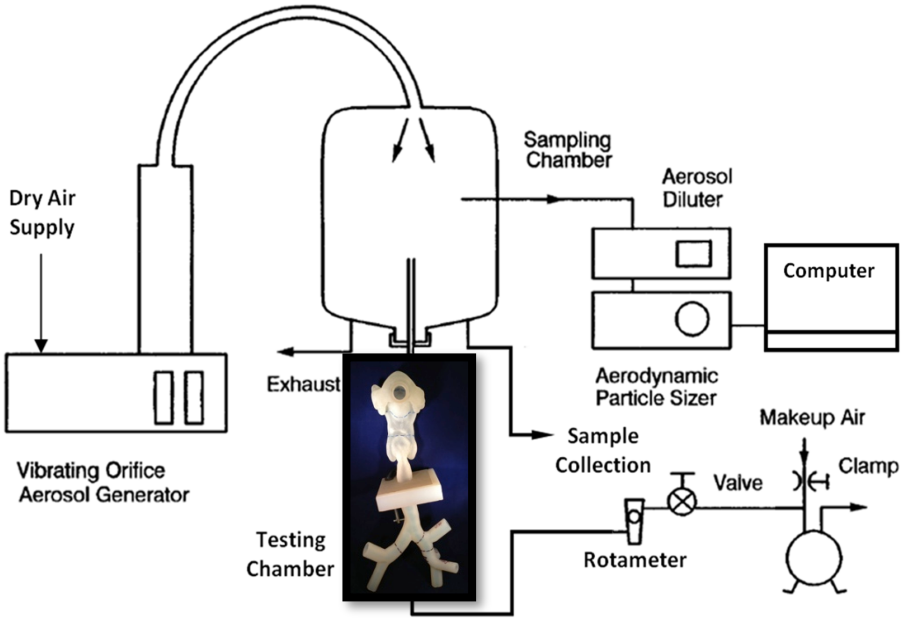

Figure 2. Setup of the Apparatus used for Studying Aerosol Deposition

After aerosol deposition/collection experiment, each section of the model was individually dipped into the deionized water to dissolve the deposited florescent. This process was repeated 4 to 5 times to ensure the complete removal of droplets deposited in the region. A Fluorometer (Model 110, Turner Associates or GloMax-Multi Jr., Promega Corp.) was utilized to evaluate a sample of the suspended florescent solution five times to determine the florescent concentration in the DI water solution. Regional aerosol deposition was calculated by regional florescent deposition concentration, Eq. 2.

$$DF = (\text{Amount Deposited in the Region}) / (\text{Amount Entering the System}) \times 100 \qquad (2)$$

where the Amount Entering the System is total aerosol delivered to the system. The Stokes number (St) for each case was calculated using Eq. 3.

$$St = (\rho_p \cdot D_p^2 \cdot V)/(18 \cdot \mu \cdot D_t) \qquad (3)$$

Estimating the importance of inertial impaction during flow can be calculated by finding the Stokes number (Stk).

RESULTS AND DISCUSSION

All data were plotted as shown on Figure 3 to analyze the correlation between the experimental data from Model A & B and Cheng 1999 data. The deposition fraction data for the dry model were found to be similar to the data obtained from Cheng 1999. Also Both Model A & B showed a very similar deposition fraction vs. Stokes number trend. This indicates that the total deposition within the model does not significantly vary between the two models.

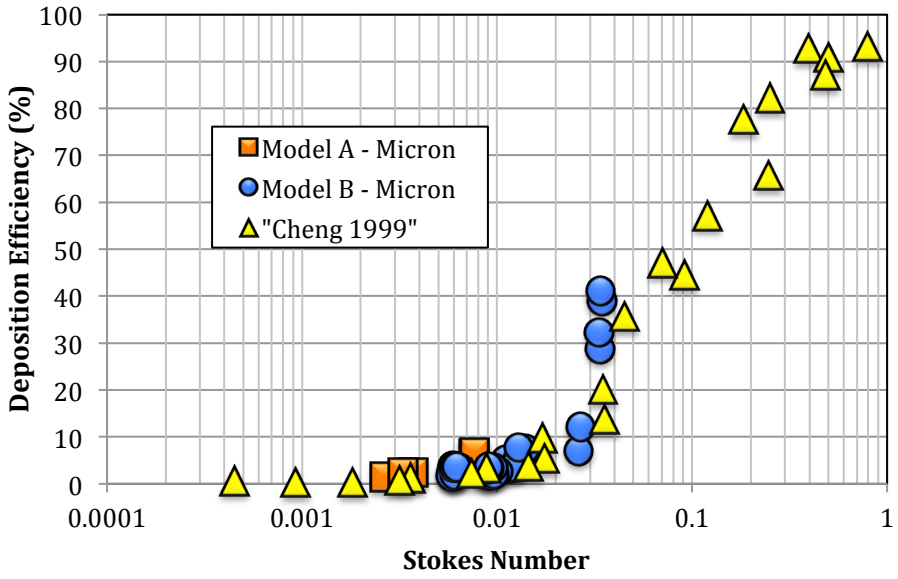

Figure 3. Deposition Fraction vs. Stokes Number

The comparison of regional deposition fraction between the two models at the highest flow rate, 60 LPM, shows a significant difference at each location within the geometry. The overall deposition trend of micron size particles was varied, increasing as the Stokes number increases. The total deposition fraction data for the two different models, A and B, were found to be very similar to each other in spite of their difference in three-dimensional geometries. However, at higher flow rate, the total deposition within the model B was observed to be significantly increased compared to the model A, with greater regional (i.e., local) differences as shown in Figures 4 through 6.

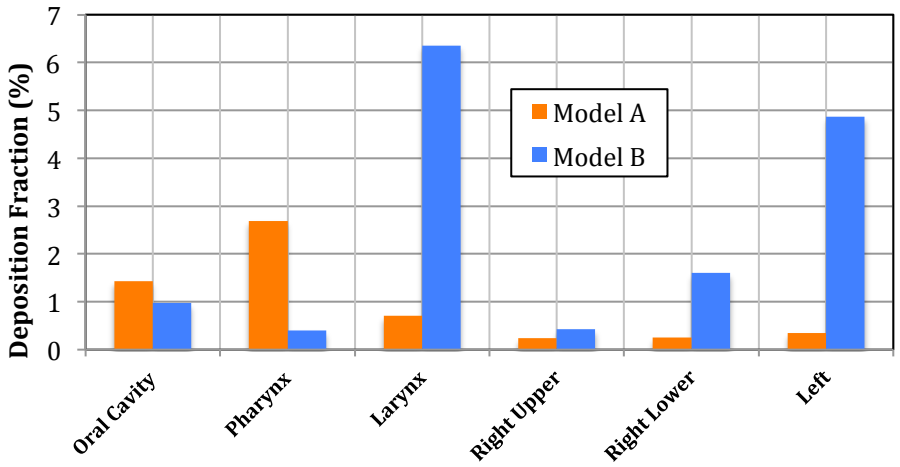

Figure 4. Regional Deposition at 60 LPM

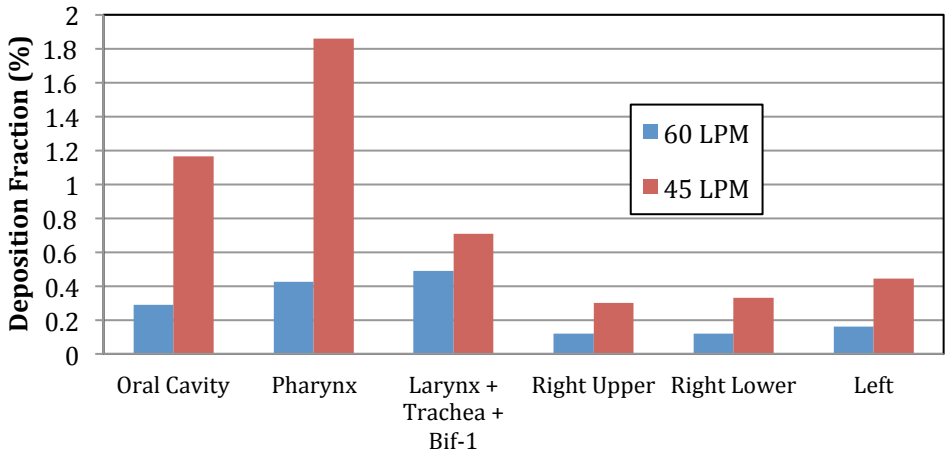

Figure 5. Regional Deposition within Model A

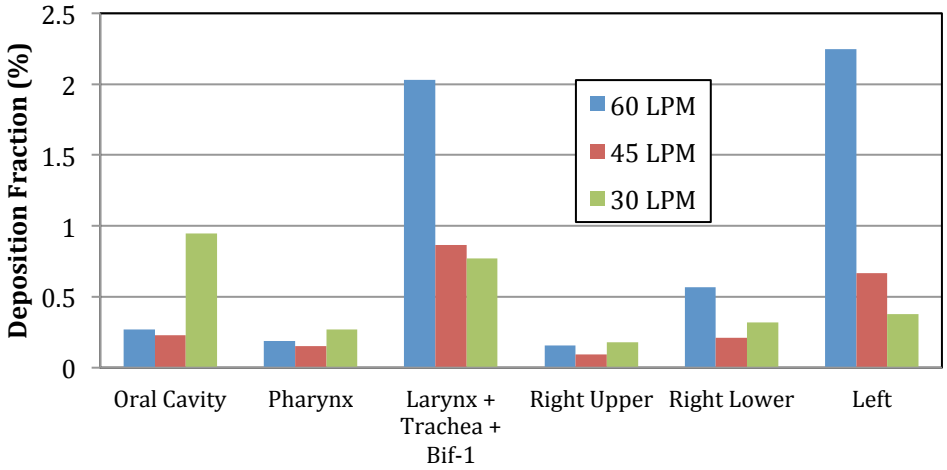

Figure 6. Regional Deposition within Model B

The following graphs provide additional evidences by presenting regional and lobular deposition at various flow rates. As shown in Figures 7 and 8, there was no significant difference in deposition fraction with the five different lobes between the two models at 45 LPM. However, the difference increased as the flow rate was increased to 60 LPM, Model B showing overall less deposition fraction especially within the Left Upper and Left Lower lobes.

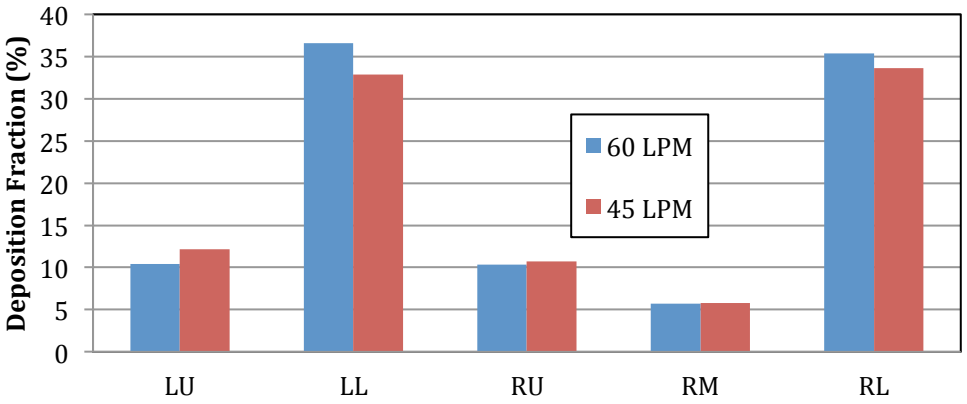

Figure 7. Lobular Deposition within Model A

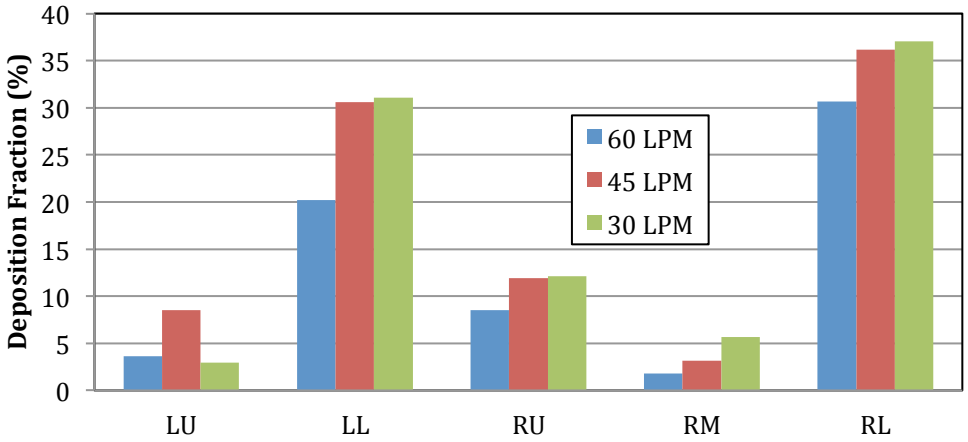

Figure 8. Lobular Deposition within Model B

CONCLUSION

Although more accurate modeling techniques are required, this experimental study showed that the effect of subject-specific geometry on aerosol particle deposition was minimal in total deposition. However, the regional (i.e., local) deposition fractions were not the same. As the flow rate increased, larger differences in regional deposition data between the two models were observed due to their difference in three-dimensional geometry.

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