Effect of microgravity and hypergravity on deposition of 0.5- to 3-µm-diameter aerosol in the human lung

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Darquenne, Chantal, Manuel Paiva, John B. West, and G. Kim Prisk. Effect of microgravity and hypergravity on deposition of 0.5- to 3-µm-diameter aerosol in the human lung. J. Appl. Physiol. 83(6): 2029–2036, 1997.—We measured intrapulmonary deposition of 0.5-, 1-, 2-, and 3-µm-diameter particles in four subjects on the ground (1 G) and during parabolic flights both in microgravity (µG) and at ~1.6 G. Subjects breathed aerosols at a constant flow rate (0.4 l/s) and tidal volume (0.75 liter). At 1 G and ~1.6 G, deposition increased with increasing particle size. In µG, differences in deposition as a function of particle size were almost abolished. Deposition was a nearly linear function of the G level for 2- and 3-µm-diameter particles, whereas for 0.5- and 1.0-µm-diameter particles, deposition increased less between µG and 1 G than between 1 G and ~1.6 G. Comparison with numerical predictions showed good agreement for 1-, 2-, and 3-µm-diameter particles at 1 and ~1.6 G, whereas the model consistently underestimated deposition in µG. The higher deposition observed in µG compared with model predictions might be explained by a larger deposition by diffusion because of a higher alveolar concentration of aerosol in µG and to the nonreversibility of the flow, causing additional mixing of the aerosols.

aerosol deposition; gravity; human lung

The deposition of aerosols in the human lung is primarily due to the mechanisms of inertial impaction, sedimentation, and Brownian diffusion. Inertial impaction causes most of the particles ~>5 µm to deposit in the upper airways. Brownian diffusion affects smaller particles (<0.5 µm), which deposit mainly in the alveolar region. Sedimentation is the gravitational settling of particles and mainly affects particles in the size range 1–5 µm. Of these three mechanisms, sedimentation is a gravity-dependent process and is therefore expected to be changed in altered gravity (G) environments. Besides affecting sedimentation, G is also responsible for regional differences in ventilation. Because the lung distorts under its own weight, the alveoli at the base of the lung are relatively compressed compared with the apical alveoli, and, because poorly expanded alveoli are more compliant, ventilation is greatest near the bottom of the lung and becomes progressively reduced near the top. Changes in the G level (i.e., in lung weight) will affect the distribution of ventilation and are therefore expected to affect the distribution and deposition of aerosols.

In a theoretical analysis in 1967, Muir (15) examined the influence of G on aerosol deposition in the lungs of subjects on the surface of the moon (1/6 G) for particle sizes up to 8 µm. On the basis of knowledge of such deposition on Earth, he predicted a reduction in the overall deposition but an increase in deposition in the alveolar region. He suggested, therefore, that astronauts might be more susceptible to infection by bacteria penetrating more deeply into the lung. Beeckmans (2) developed a computer program based on experimental data available at 1 G to predict deposition within the respiratory tract. He computed deposition for particle size ranging from 0.2 to 15 µm at decreased G levels, and his computations suggested a lower alveolar deposition than that suggested by Muir (15) at 1/6 G. Hoffman and Billingham (13) conducted the only experimental study to date to obtain deposition data at various G levels on a National Aeronautics and Space Administration (NASA) Learjet. They measured the deposition of only 2-µm-diameter particles in three different subjects. They found an almost linear increase in deposition, with increasing G in the range 0–2 G. However, at 0 G, deposition was lower than that predicted by Beeckmans (2). Thus the amount of deposition of aerosol particles of different sizes in the absence of G is largely unknown.

In a spacecraft environment, the potential for significant airborne particle concentrations is high because the environment is closed and no sedimentation occurs. Measurements in the US Space Shuttle air environment have shown a substantial increase in microbial counts during missions (9, 14), and a large variety of airborne particles, including hair, food, paint chips, and synthetic fibers, has been found. It is therefore of considerable interest to determine the fate of inhaled aerosols in an environment that has altered gravitational levels, and hence altered deposition, and a potentially large airborne particulate load. Furthermore, many drugs are now administered by aerosolized drug-delivery systems, and a further understanding of how gravity affects aerosol deposition is clearly desirable in the terrestrial environment.

In the present study, we measured total deposition in normal subjects of aerosols having a diameter spanning the range from 0.5 to 3 µm. Data were collected on the ground (in 1 G) and aboard the NASA Microgravity Research Aircraft during parabolic flights in both the weightless phase (microgravity; µG) and the ~1.6-G pullout phase. The data are compared with the previous studies (2, 13, 15) and with predicted numerical values from Darquenne and Paiva’s model (3). The comparison of data obtained in µG and ~1.6 G with deposition at 1 G helps to elucidate the impact of gravitational sedimentation on deposition processes. For convenience, the ~1.6 G condition will be referred to as 1.6 G in the text.
Methods

Equipment. Deposition data were collected by using the equipment shown in Fig. 1. The subject breathed aerosol from a reservoir at constant inspiratory and expiratory flow rates (~0.4 l/s) and tidal volume (~0.75 liter). A two-way nonrebreathing valve (NRV) allowed the subject to inhale from the reservoir and to exhale into the room through a filter. An additional three-way valve was connected to the inhalation port of the NRV, allowing the subject to breathe pure air through a filter before the start of the experiment. The measurement of the aerosol concentration and the flow rate was provided by a photometer (model 993000, Pari) (24) and a Validyne M-45 differential pressure transducer connected via short tubes to the two ports of a pneumotachograph (Fleisch no. 1, OEM Medical, Richmond, VA), respectively. The photometer, the pneumotachograph, and the NRV were heated to body temperature to prevent water condensation. A diffusion dryer was located between the photometer and the mouthpiece. It removed the water vapor from the exhaled air to avoid condensation on the lenses of the photometer.

Aerosol generator. The reservoir was filled with aerosol containing monodisperse polystyrene latex particles (Duke Scientific). The particles were supplied in suspension (water), and the concentrate was diluted and dispensed via two Acorn II nebulizers (Marquest Medical Products). Before entering the reservoir, the aerosol flowed through a heated hose and a diffusion dryer to remove water droplets. The following particle sizes, as provided by the manufacturer, were used in the study: 0.497 ± 0.0094, 1.07 ± 0.014, 2.04 ± 0.044, and 2.92 ± 0.081 (SD) µm. For convenience, these are hereafter referred to as 0.5-, 1-, 2-, and 3-µm-diameter particles, respectively. The aerosol concentrations were ~10^6 particles/ml of air for 0.5- and 1-µm particles, ~5 × 10^2 particles/ml of air for 2-µm particles, and ~10^3 particles/ml of air for 3-µm particles.

Data recording and analysis. A PC (IBM ThinkPad 360 CSE) equipped with a 12-bit analog-to-digital card (National Instruments, DAQ700) was used for data acquisition. Signals from the photometer, a G sensor, a barometric pressure transducer, and the pneumotachograph were sampled at 100 Hz. Custom software was developed for the data acquisition by using National Instruments Lab Windows CVI.

Data were collected on the ground and aboard the NASA Microgravity Research Aircraft. A typical flight consisted of a climb to an altitude of ~10,000 m with the cabin pressurized to ~600 Torr. A "roller-coaster" flight profile was then performed. The aircraft was pitched up at 1.6 G, to a 45° nose-high attitude. Then, the nose was lowered to abolish wing lift, and thrust was reduced to balance drag (thus maintaining µG). A ballistic flight profile resulted and was maintained until the aircraft's nose was 45° below the horizon. In this manner, µG was maintained for ~27 s. An averaging 1.6G-G, pullout maintained for ~40 s caused the nose to pitch up to a 45° nose-high attitude and allowed the cycle to be repeated.

Subjects and protocol. Four healthy subjects participated in the study. Their relevant anthropometric data are listed in Table 1. They were asked to breathe through the mouthpiece at a constant flow rate (~0.4 l/s) and tidal volume (~0.75 liter) over a period covering the duration of four parabolas including the hyper-G phase between maneuvers. A flowmeter provided visual feedback to the subject, and an audible metronome was used to maintain a constant breathing frequency. This protocol was repeated twice with each particle size. Before the flight, a set of data was also collected on the ground (1 G) with the same protocol. The protocol was approved by both the Committee on Investigations Involving Human Subjects at the University of California, San Diego, and by the Human Research Policy and Procedures Committee at the Johnson Space Center, Houston, TX.

Data analysis. For each breath, total deposition (DE) was calculated by using the following equation

\[
DE = 1 - \frac{N_{ex}}{N_{in}} \times \frac{V_{in}}{V_{ex}} \tag{1}
\]

where \(N_{in}\) and \(N_{ex}\) are the number of inspired and expired particles, and \(V_{in}\) and \(V_{ex}\) are the inspired and expired volumes, respectively. Only the breaths where \(V_{in}\) and \(V_{ex}\) differed by < 3% were considered in the analysis. For the data acquired during the flights, we excluded from the analysis the breaths occurring during the transition from µG to 1.6 G and from 1.6 G to µG as well as the first breath after each transition because these breaths were considered likely to contain data from different and unknown gravitational loadings.

Statistical analysis was performed by using Systat V5.0 (Systat, Evanston, IL). Data were grouped in three categorical variables: G level (µG, 1 G, and 1.6 G), particle size (0.5-, 1-, 2-, and 3 µm), and subject (subjects 1–4). A two-way analysis of variance was then performed to test for differences between the chosen categorical variables. Post hoc testing by using Bonferroni adjustment was performed for tests showing
RESULTS

The effect of G level and particle size on deposition is displayed in Fig. 2. In Fig. 2A, total deposition averaged over the four subjects (mean ± SD) is plotted as a function of the particle size for each G level. In Fig. 2B, deposition values are plotted as a function of the particle size for each G level. The open symbols refer to our data, and the closed circles refer to data obtained by Hoffman and Billingham (13) by using 2-µm particles. At 1 and 1.6 G, deposition is strongly size dependent, with the greatest deposition occurring for the largest particle sizes. Deposition ranged from 16.5 to 44.0% at 1 G and from 20.0 to 60.7% at 1.6 G. In µG, differences in deposition between particle sizes are almost abolished, with deposition ranging from 12.9 to 14.9%.

For a given particle size, significant (P < 0.01) variations from one G level to the other were found, with lower deposition being present at lower G levels. Significant (P < 0.03) differences in deposition were also present between different particle sizes at each G level, except for the deposition of 2- and 3-µm particles in µG, which was not different. Although differences are smaller in µG, deposition of 0.5-µm particles was found to be significantly larger than deposition of 1-µm particles. Intrasubject variability is illustrated in Fig. 3, where total deposition in each subject is plotted as a function of particle size for each G level. Intrasubject variability was sufficiently low so that clear differences in deposition were visible among G levels.

Our data were compared with numerical results obtained by using a one-dimensional (1D) model developed by Darquenne and Paiva (3). In that model, a 1D equation describing the transport and deposition of aerosols is solved in a lung structure based on data of Haeefi-Bleuer and Weibel (8). The main equations used in the simulations are summarized in the Appendix. The comparison between the numerical and experimental results is shown on Fig. 4 for each G level. For the experimental data, the mean values averaged over the four subjects are displayed as well as the standard deviation (SD; left bar of each pair), whereas the numerical results (right bar of each pair) are shown with the contribution of each mechanism of deposition considered in the numerical simulations: impaction is represented by the open segment, sedimentation by the hatched segment, and diffusion by the solid segment. In 1 and 1.6 G, the experiments agree with the numerical data within 1.5 SD, except in the case of 0.5-µm particles in 1.6 G, for which the simulations predict a lower deposition than we measured. In µG, the numerical data significantly underestimate measured deposition for each particle size except 3 µm. Although the model underestimates deposition in µG, it should be noted that the model predicts a minimum deposition for 1.0-µm-diameter particles, and this is consistent with the experimental observations.

Figure 5 shows the total deposition values obtained on the ground. In Fig. 5A, deposition data are shown for each subject separately. They are represented by their mean and SD, the SD being an indication of the intrasubject variability. In Fig. 5B, our data averaged over the four subjects (●) are compared with experimental data of Heyder et al. (11, 12): data obtained for a tidal volume of 0.5 liter and a flow rate of 0.25 l/s (∆) and data obtained for a 1-liter tidal volume and a flow rate of 0.5 l/s (○). Note that these protocols do not exactly match ours in either flow rate or tidal volume. The last set of data (○) in Fig. 5B refers to data obtained in 20 subjects for a flow rate of 0.4 l/s and a tidal volume of 0.8 liter (12), a protocol very similar to ours, although these data are only available for 1- and 3-µm particles. For the purpose of clarity, this last set of data has been slightly shifted to the right. Note that in Fig. 5B, the SD in our data reflects both the intersubject and intrasubject variability.

Figure 2. Total deposition of aerosol particles (DE; mean ± SD) averaged over 4 subjects. A: total deposition as a function of particle size. G, gravity. ●, microgravity (µG); ▲, 1 G; □, 1.6 G. B: total deposition as a function of G level. ○, 0.5 µm particle diameter (dp); □, dp = 1 µm; ▲, dp = 2 µm; △, dp = 3 µm; ●, data from Hoffman and Billingham obtained with 2-µm-diameter particles (13).
DISCUSSION

Effect of gravity. Figure 2A shows the strong size dependence of total deposition at 1 G and 1.6 G and the virtual absence of such effect in μG. The analysis of variance shows, however, that there is a small but significant difference in deposition in μG for different particle sizes, except for particles between 2 and 3 µm in diameter. Although the deposition differences are small, the much smaller data variability in μG makes this difference significant. For 0.5- and 1-µm particles, deposition increases less between μG and 1 G than between 1 and 1.6 G, whereas deposition is an approximately linear function of G level for 2- and 3-µm particles (Fig. 2B). This is in agreement with the work of Hoffman and Billingham (13), who also found an essentially linear increase in total deposition with increasing G levels between 0 and 2 G for 2-µm particles. They measured a deposition of 19.74, 33.47, and 46.25% in μG, 1 G, and 2 G, respectively, compared with 15.5 ± 1.5, 37.1 ± 8.5, and 52.4 ± 7.2% in μG, 1 G, and 1.6 G, respectively, in our experiments. For purposes of comparison, their data are plotted (●) in Fig. 2B. Although both sets of data show an almost linear increase of deposition with increasing G level, the increasing rate is higher in our study than in Hoffman and Billingham’s study.

If the different mechanisms of deposition were independent, the change in G level would only affect deposition by sedimentation, which is a gravitational process. According to Stokes’ law, particles sediment with a velocity ($v_s$)

$$v_s = \frac{\rho_p d_p^2}{18 \mu} G$$

where $\rho_p$ is particle density, $d_p$ is particle diameter, and $\mu$ is gas viscosity. With the assumption of an unlimited source of aerosols, deposition by sedimentation should increase linearly with G and in a quadratic way with $d_p$. For the biggest particles (2 and 3 µm), diffusion may be neglected and deposition is mainly due to sedimentation in the distal airways and impaction in the upper airways. Impaction is gravity independent and increases also in a quadratic way with $d_p$ (see Eq. A4). For a given particle size, deposition by sedimentation should increase linearly and deposition by impaction should be constant. Therefore, total deposition should increase linearly with G.

On the other hand, for a given G level, both deposition by sedimentation and impaction should vary in a quadratic way with the particle size. Deposition by impaction occurs in the upper airways and affects the...
number of particles available for deposition by sedimentation in the smaller airways. Thus the number of particles available to deposit by sedimentation decreases with increasing particle size, and the use of Eq. 2 to describe total deposition is no longer as straightforward as it was for a given particle size at different G levels.

As we would expect, deposition of 2- and 3-µm particles varies almost linearly with altered G level (Fig. 2). For 0.5- and 1-µm particles, however, if we assume that the relationship between 1 and 1.6 G defines the gravitational influence, then the extrapolation to µG predicts a deposition less than that measured, especially for 1.0-µm-diameter particles, where deposition in µG would be expected to approach zero. Because the deposition by impaction is negligible for these small particles, a plausible explanation for the results in µG might be a larger deposition by diffusion because sedimentation is absent in µG. The absence of deposition by sedimentation increases the aerosol concentration in the small airways, leaving a larger number of particles available for deposition by diffusion and/or for being transported more deeply in the lung, where deposition by diffusion may also occur. This is reflected in the results of the simulation, which show a much increased deposition component because of diffusion in µG compared with 1 and 1.6 G (Fig. 4). Deposition by diffusion decreases from 8.4% in µG to 7.3% at 1.6 G for 0.5-µm particles, from 5.6 to 3.6% for 1-µm particles, from 3.8 to 1.4% for 2-µm particles, and from 3.0 to 0.6% for 3-µm particles. Despite this, deposition
is still underestimated by the model. A possible effect is the nonreversibility of flows in the airways of the human lung (19). During reciprocal tidal breathing, unequal time constants in different parts of the lung and other perturbations, such as the mechanical pulsations of the heart, all serve to make flow reversals within the lung asymmetric. Thus an additional mixing effect is introduced that will serve to move the particles in the direction of the alveoli. This would have the effect of increasing the apparent contribution of diffusional loss of particles in the lung. In the absence of gravity, with the reduction in losses due to sedimentation, this effect will become more prominent than in 1 G.

Another factor that may explain that deposition in µG is larger than we expected is the reduction in the functional residual capacity (FRC) that occurs in the weightless environment (6, 7, 16, 17). Elliot et al. (7) found that during sustained periods of µG, FRC decreased significantly by 15% (500 ml) compared with 1 G standing FRC. Paiva et al. (16) and Eddyvean et al. (6) also demonstrated a 200- to 500-ml decrease in FRC during short periods of µG. Davies et al. (5) and Heyder et al. (10) showed that deposition increased as the resting expiratory reserve volume was decreased. For 0.5-µm-diameter particles, Davies et al. (5) found an ~2.5% increase in deposition when the tests were performed from (FRC – 500 ml) instead of FRC. Therefore, the reduction in FRC observed in µG likely contributes to the higher deposition than would be expected if the tests were performed from the same FRC as in 1 G. However, this increase remains lower than what we observed in our measurements. Thus, even if we correct for the reduction in FRC in µG by using a controlled protocol, deposition will still be higher than that predicted by the model.

An interesting observation shown in Fig. 3 is the very small intrasubject variability of the µG data. This result seems surprising, in view of the more difficult experimental conditions during a parabolic trajectory than on the ground. A potential explanation may be the sensitivity of deposition by gravitational sedimentation to the conditions of the test, such as flow or tidal volume. This observation is very promising in the sense that experiments in µG will help in studying the different mechanisms (except gravitational sedimentation) that affect aerosol behavior in the lung without the disturbing influence of gravity. In particular, the use of aerosol bolus in µG will allow the determination of deposition at different depths within the lung. Performing the bolus tests with small or large particles will allow better estimates of deposition by diffusion or impaction, respectively. These experimental data could also be used to improve present 1D models, and, more particularly, the deposition functions used in the 1D equation describing aerosol transport and deposition in the bronchial tree. These improvements, in conjunction with further developments of the 1D models suggested by multidimensional studies on aerosol transport in the alveolar zone of the lung (4, 21, 22), will allow more accurate predictions of deposition in the respiratory tract.

Figure 3 shows that in subjects 2, 3, and 4, the largest difference between 1 G and µG occurs for the largest (3-µm) particles, whereas in subject 1 the difference seems to plateau between 2- and 3-µm-diameter particles. This difference is consistent with the results of the simulation (Fig. 4), which show that deposition due to sedimentation is greatest for the largest particles at the highest G level. It is predictable, also on the basis of Fig. 4, that in µG, for particles larger than 3 µm, deposition would increase due to impaction. Comparisons between simulations and experiments in 1 G (Fig. 4B) show an almost linear increase of deposition with particle diameter for the simulated results, whereas the experimental observations show higher deposition for the smallest particles than predicted, and lower deposition for the largest particles. The higher deposition for the smallest particles might be explained by the additional diffusional losses because of the nonreversibility of the flows, as already discussed above.

Figure 4 shows the contribution of each mechanism of deposition as computed by the numerical model. In µG, there is, by definition, no deposition by sedimentation. Small particles (0.5 and 1.0 µm) deposit almost only by diffusion, whereas deposition by impaction becomes more and more predominant with increasing particle size. For each particle size, the fraction of particles that deposit by impaction (open segment of right bar of each pair) is independent of the G level, whereas deposition by diffusion decreases with increasing G level, i.e., when deposition by sedimentation increases. The interdependence of deposition by diffusion and deposition by sedimentation might be explained by the fact that they both take place in the same region of the lung (the distal airways), whereas deposition by impaction occurs in the first generations of the respiratory tract.

Comparison with previous studies. Particle deposition at 1 G was compared with data previously obtained by Heyder et al. (11, 12) for slightly different breathing patterns (Fig. 5). The first of the three protocols has higher tidal volume and flow rate than ours, the second one has lower tidal volume and flow rate, and the last one is similar to ours. In all their protocols, however, the residence time, defined as the duration of one breath, is the same and is equal to 4 s. In our protocol, the residence time of 3.75 s is similar. We found particle deposition similar to the data of Heyder et al., with the exception of 0.5-µm particles, whereby our results show a slightly higher deposition: 16.2 ± 3.0% compared with 12%. However, given the intersubject and intrasubject variability, there are no significant differences between our results and those of Heyder et al. The large dispersion of aerosol deposition in different subjects is one of the reasons for the difficulties in the interpretation of aerosol data. Comparing the first two breathing protocols, Heyder et al. found the same average deposition for 0.5- and 1-µm particles. For 2- and 3-µm-diameter particles, deposition is higher for the larger tidal volume, higher flow rate protocol because these particles deposit mainly by inertial impaction and gravitational sedimentation. Deposition by inertial im-
paction increases with the flow. Sedimentation is a time-dependent process that mainly occurs in the distal generations of the lung, where the airway dimensions are smaller. Because the residence time in both protocols is the same, the increase in deposition in the larger tidal volume, higher flow rate protocol could be attributed in the higher tidal volume, allowing particles to reach more distal airways than in the smaller tidal volume, lower flow rate protocol. In the third protocol, which closely approximates our protocol of a 0.4 l/s flow rate and 0.75-liter tidal volume, Heyder et al. (12) measured a total deposition of 15 ± 4% for 1.0-μm-diameter particles and 45 ± 6% for 3.0-μm-diameter particles. Our data show a deposition of 17.0 ± 5.8 and 44.4 ± 11% for 1.0- and 3.0-μm-diameter particles, respectively, suggesting that our results may safely be compared with those of previous terrestrial studies of total intrapulmonary deposition.

Effect of altitude. Four flights (1/particle size) were performed to collect all the data. During each flight, before the start of the first parabola, we were able to collect data at 1 G with one subject and compare the deposition with that obtained on the ground with the same subject. These values are shown in Table 2. The data obtained in the aircraft refer to 6–10 breaths, whereas the data on the ground refer to over 50 breaths. Because the order in which the subjects performed the tests differed on each flight, the data do not necessarily correspond to a single subject. Data for the subject in whom these measurements were made are shown in Table 2. The comparison shows that analogous results are obtained in both environments, with no statistical differences between aircraft and ground data. This means that there were no systematic differences in our data introduced by the lower barometric pressure in the aircraft cabin and that we may therefore valuable compare aircraft and ground data.

In summary, aerosol deposition was measured in four subjects on the ground and aboard the KC-135 aircraft during both the weightlessness and the hyper-G phases, with particles having diameters ranging from 0.5 to 3 μm. Deposition was an almost linear function of the G level for 2- and 3-μm-diameter particles. For 0.5- and 1.0-μm particles, however, deposition increased less between μG and 1 G than between 1 and 1.6 G. The higher deposition observed in μG might be explained by a larger deposition by diffusion because of both the absence of sedimentation and the nonreversibility of the flow, producing an apparent mixing effect, and by a smaller FRC. Comparison with model predictions showed good agreement for 1-, 2-, and 3-μm-diameter particles at 1 and 1.6 G, whereas the numerical model consistently underestimates deposition in μG. This difference arises probably from the fact that the model does not incorporate the effect of the apparent diffusion because of the nonreversibility of the flow.

APPENDIX

The Numerical Model

A 1D equation of aerosol transport and deposition is solved in a human lung model (3). The lung model is a trumpet because of the nonreversibility of the flow. The functions describing deposition by gravitational sedimentation (Ls) and Brownian diffusion (Ld) are described in the study by Darquenne and Paiva (3). The function describing deposition by inertial impaction is based on experimental data measured in a cast of the upper airways (18) and is expressed by

\[
L_s = 13 \frac{CQ}{I} (St - 0.0001) \quad \text{St} \geq 0.0001
\]

\[
L_s = 0 \quad \text{St} < 0.0001
\]

where St is Stokes' number ( = ρp \( d^2 \)) / 18μd; u is the mean gas velocity in the airway, and d is the airway diameter. The higher the value of the Stokes' number, the more readily particles will diverge from the airflow streamlines and the more likely they are, therefore, to deposit by impaction on the airway walls.
by

$$L_s = \frac{CQ}{l(1-\alpha) \left[ 1 - \exp \left(-2\frac{N(z) v_s l_s}{Q} \right) \right]} + \frac{N_s(z)}{l} \tag{A5}$$

for gravitational sedimentation and by

$$L_d = \frac{CQ}{l(1-\alpha) \left[ 1 - \exp \left(-\frac{36D_d l N(z)}{Q} \right) \right]} + \frac{N_s(z)}{l} \tag{A6}$$

for diffusion, where \(\alpha\) is fraction of alveolated surface of airway, \(N(z)\) is the number of airways in generation \(z\), \(v_s\) is gravitational settling velocity, \(N_s(z)\) is deposition rate by sedimentation, \(N_s(z)\) is number of alveoli in generation \(z\), \(\phi_d\) is deposition rate by diffusion, and \(s_a\) is inner surface area of alveolus.

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