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Comparison of Computer Simulations of Total Lung Deposition to Human Subject Data in Healthy Test Subjects

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Comparison of Computer Simulations of Total Lung Deposition to Human Subject Data in Healthy Test Subjects

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ABSTRACT

A mathematical model was used to predict the deposition fractions (DF) of PM within human lungs. Simulations using this computer model were previously validated with human subject data and were used as a control case. Human intersubject variation was accounted for by scaling the base lung morphology dimensions based on measured functional residual capacity (FRC) values. Simulations were performed for both controlled breathing (tidal volumes [V_T] of 500 and 1000 mL, respiratory times [T] from 2 to 8 sec) and spontaneous breathing conditions. Particle sizes ranged from 1 to 5 µm. The deposition predicted from the computer model compared favorably with the experimental data. For example, when V_T = 1000 mL and T = 2 sec, the error was 1.5%. The errors were slightly higher for smaller tidal volumes. Because the computer model is deterministic (i.e., derived from first principles of physics), the model can be used to predict deposition fractions for a range of situations (i.e., for different ventilatory parameters and particle sizes) for which data are not available. Now that the model has been validated, it may be applied to risk assessment efforts to estimate the inhalation hazards of airborne pollutants.

IMPLICATIONS

This work describes a mathematical computer model that can be used to predict particle deposition fractions in human lungs. Used in conjunction with measurement data on PM contained in an ambient air sample, this model can be employed to estimate human exposures for dosimetry analyses by an inhalation toxicologist. The computer model therefore provides an important link between air pollution data and the potential threat to the health of a population.

INTRODUCTION

To estimate the threat to human health presented by inhaled PM, it is valuable to know the spatial distribution of the inhaled particles. Therefore, an ongoing goal of our work is to effectively model deposition, beginning with healthy subjects, so that we can predict deposition for a large range of particle types and ventilatory parameters. In subsequent efforts, we shall address the effects of airway diseases (e.g., chronic obstructive pulmonary disease [COPD]).

Determining where airborne PM is deposited in the lung is a complicated problem. The site of deposition is affected by many variables. These variables include particle characteristics, ventilatory parameters, and lung morphology. In this work, we improved upon our existing, previously validated model[1-3] by using a more physiologically realistic lung morphology. We then used the model to calculate deposition patterns for particle sizes other than those used in the reported human subject experiments.

METHODS

The primary mechanisms for particle deposition in the lung are sedimentation, diffusion, and inertial impaction. The mechanism by which an individual particle is deposited depends on the size and velocity of the particle. In turn, a particle's velocity depends on ventilatory parameters and lung morphology.

Our computer program[4] calculates particle deposition in each generation and organizes the data by deposition mechanism. The parameters that must be specified for the code are particle characteristics (i.e., hydroscopic

nature, shape, density [ρ], and geometric diameter [D_s]), ventilatory parameters (i.e., tidal volume, time of inhalation, time of pause, and time of expiration), morphology (i.e., a file consisting of a morphological definition by lengths and volumes of generations), and simulation parameters (i.e., mouth or nose breathing). Because we were simulating human subject experiments, the parameters were defined based on the experiments conducted.

Human Subject Experiments

Our experimental data came from two sources. The experiments were headed by Bennett[5] and Kim.[6-7] The details can be found in the literature, but a short summary is given below.

Bennett used 2-µm monodisperse carnauba wax particles with salt nuclei. These particles were generated using a condensation aerosol generator. Each subject was instructed to mouth breath at a normal sedentary rate, and this breathing pattern was recorded for use by that subject in the experiments. The breathing parameters for the spontaneous breathing simulations ranged from tidal volume (V_T) = 195 to 656 mL and flow volume (Q) = 124 to 383 mL/sec (see Table 1).

Kim's experiments also used monodisperse particles. The particles were di-2-ethylhexyl sebacate oil aerosols generated by an evaporation-condensation aerosol generator in 1-, 3- and 5-µm sizes. The test subjects were instructed to mouth breath in a controlled, predefined manner. The breathing conditions were defined by flow volume and flow rate. For our simulations, the breathing parameters ranged from V_T = 500 and Q = 150 mL/sec to V_T = 1000 and Q = 500 mL/sec (see Table 2).

Computer Model

The computer code contains additional options that do not depend on the nature of the human subject experiments. We have control over the air velocity profile used in the simulations, and we can use either a fully developed parabolic profile or a uniform (or plug) profile. The actual profile lies somewhere between these two curves.[8] Determining the actual velocity profile requires significant computation time,[9] so it is necessary to use an approximation. If we calculate the deposition fractions twice, once with each profile, we get an envelope that contains the actual value.

We made two main modifications to our existing morphology model for this study. We used a more physiologically realistic lung model that was also customized to each individual test subject. The more physiologically realistic lung model, developed by Martonen et al.,[10,11] is an improvement over the previous model.[12,13] The old model allowed the two lobes of the lung to grow in such a way that they overlapped each other. The new model overcomes this by having the lung separated into two distinct lobes.

Table 1. Breathing parameters for test subjects in spontaneous breathing experiments.

Subject	V_T (mL)	Q (mL/sec)
1	488	383
2	195	150
3	545	270
4	656	325
5	306	124
6	491	318
7	293	169
8	478	182
9	620	348
10	341	175
11	386	275

Table 2. List of controlled breathing experiments performed.

D_g (µm)	V_T (mL)	Q (mL/sec)
1, 3, 5	500	150
		250
		500
1, 3, 5	1,000	500
		1,000
2	spontaneous breathing	

We also took into account each individual subject's lung volume. The functional residual capacity (FRC) measurement defines the amount of air left in the lung after the subject exhales. We added this value to half of the tidal volume to get the average lung size during a breathing cycle. Our base model uses the length and diameter measurements from the Weibel lung,[14] which Martonen[15] determined to be preferable to other lung models for conducting computer simulations. However, these dimensions define a lung with a volume of 4800 mL. Since the subjects we were simulating had FRC values ranging from 1850 to 6820 mL, we wanted to take into account individual variation. To do this, we modified the airway diameters (and hence the airway volumes) by a uniform scaling factor, based on the research of Hughes, Hoppin, and Mead,[16] who determined that airway diameters scale proportionally to the cube root of the lung volume.

Other groups, such as the International Commission on Radiological Protection (ICRP) and the National Council on Radiation Protection (NCRP), have developed lung deposition models. It is beyond the scope of this paper to compare our model with the other inhaled particle deposition models, but references are included for the reader's

edification. Details regarding the ICRP model can be found in the literature.[17,18] Further information pertaining to the NCRP model is also available.[19,20]

RESULTS

Total aerosol deposition fractions for the parameters described above have been calculated and recorded in Figures 1–6. The graphs compare total lung deposition fraction (DF) values calculated by the computer code with the experimental DF data. We plotted simulation results for runs made with parabolic and plug (i.e., uniform) velocity profiles. Each figure contains the experimental data points as well as the computer-generated points for each individual subject. In most cases, we had additional FRC measurements for test subjects who did not participate in these deposition experiments; this allowed us to run extra computer simulations, so that we had more theoretical data points than experimental data points. As seen in the graphs, the theoretical predictions of the code compare very well to the outcomes of the laboratory experiments. For comparison, we also plotted the DF value for the unmodified morphology. The solid line indicates the DF for a plug flow simulation, and the dashed line indicates the DF for a parabolic velocity profile simulation.

Figure 7 shows computer-calculated deposition of submicron particles. Here, V_T = 500 mL and Q = 250 mL/sec. The lung morphologies were based on the human subjects from the controlled breathing experiments.

DISCUSSION

Several conclusions can be drawn from the results presented above. When the controlled breathing experiments are examined as a group, we see that the deposition increased as the particle size increased from 1 to 3 to 5 µm. This trend was the same for each of the five breathing conditions. These figures also demonstrate the value of customizing the lung morphology for each subject. Qualitatively, the DF values varied as the FRC changed. This is what we would expect, since deposition fractions depend on airway diameters, which depend on lung size. Quantitatively, we saw a decrease in percent error when we compared predicted values to experimental values. For example, when V_T = 1000 mL and Q = 500 mL, the average deposition fraction for 3-µm particles was 0.61 according to the experimental data. Our average predicted value was 0.54 with morphology modifications and 0.53 without the modifications. The percent error dropped from 13.1 to 11.5% when the lung morphology was individualized. Similar results were seen in most of the simulations.

Because we were not able to scale the lung to fit the subjects in the spontaneous breathing experiments (no FRC value was available from the literature), we found

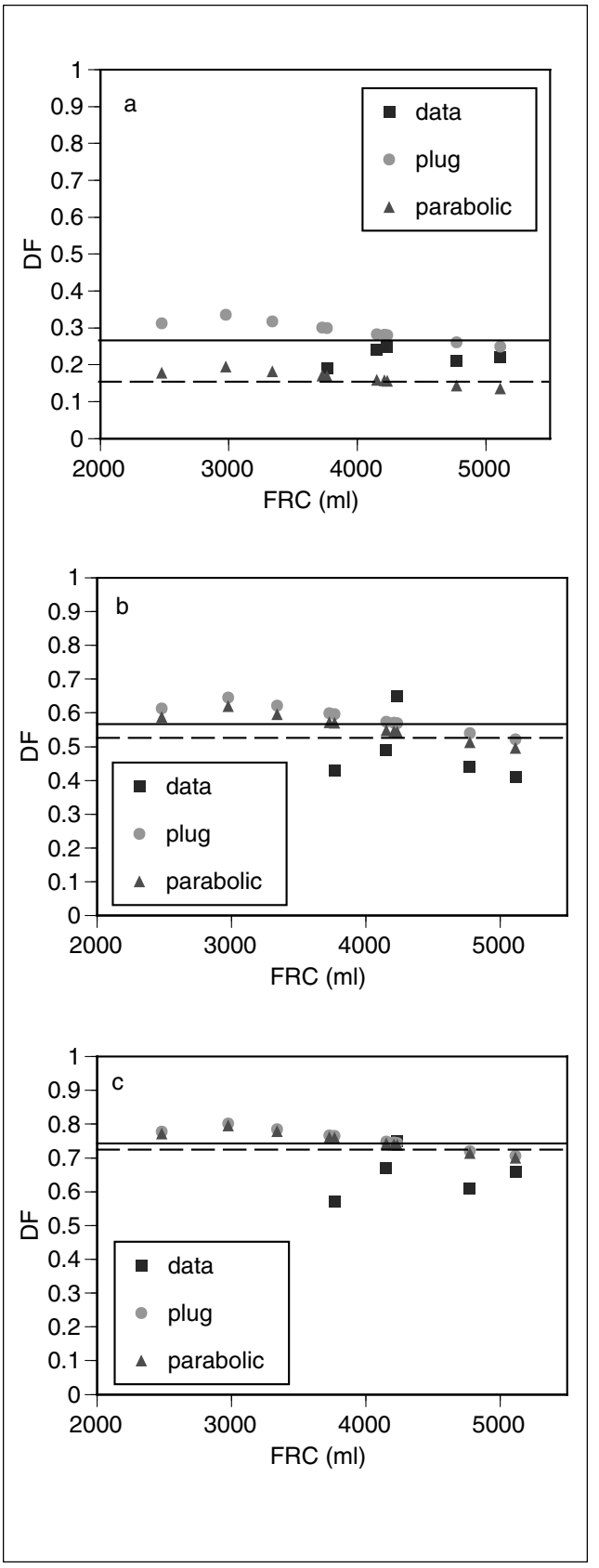

Figure 1. Particle deposition fractions for flow conditions with V_T = 500 mL and Q = 150 mL/sec. Figures 1a, 1b, and 1c contain data for 1-, 3- and 5-µm particles, respectively. The solid and dashed lines indicate the DF in the unmodified morphology, using the plug flow and parabolic velocity profiles, respectively.

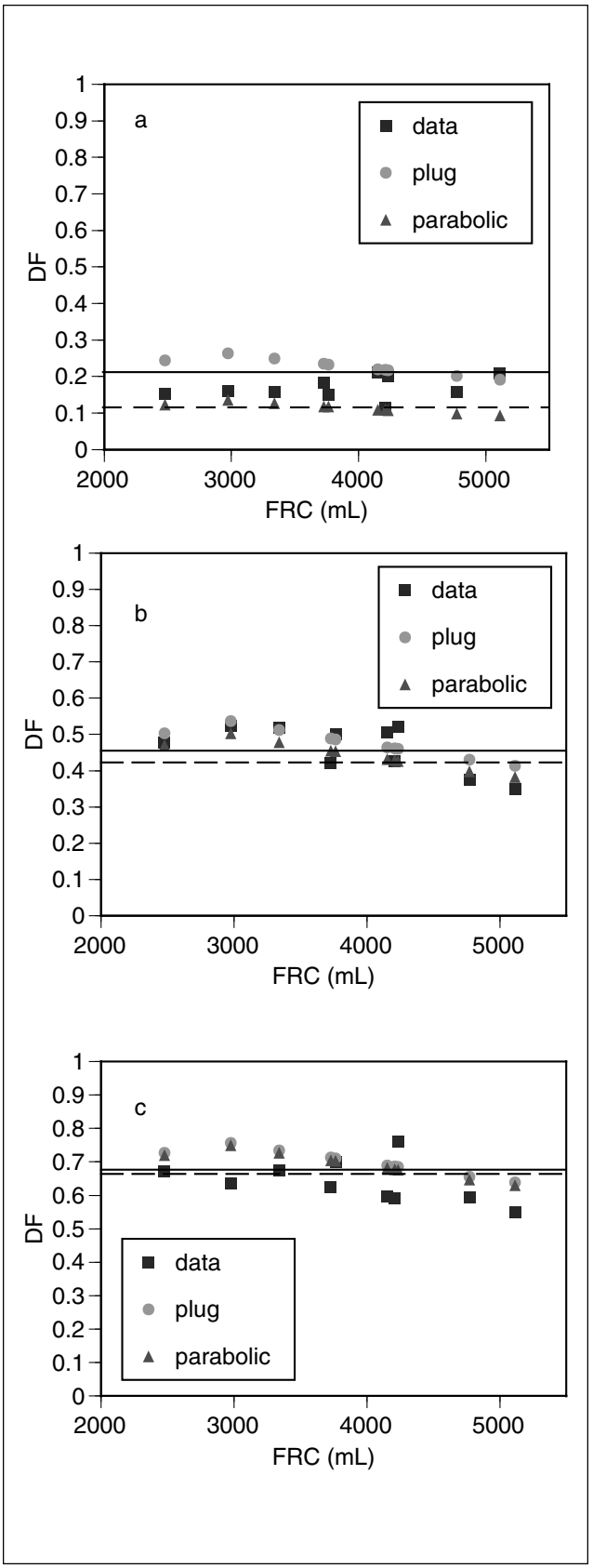

Figure 2. Particle deposition fractions for flow conditions with V_T = 500 mL and Q = 250 mL/sec. Figures 2a, 2b, and 2c contain data for 1-, 3- and 5-μm particles, respectively. The solid and dashed lines indicate the DF in the unmodified morphology, using the plug flow and parabolic velocity profiles, respectively.

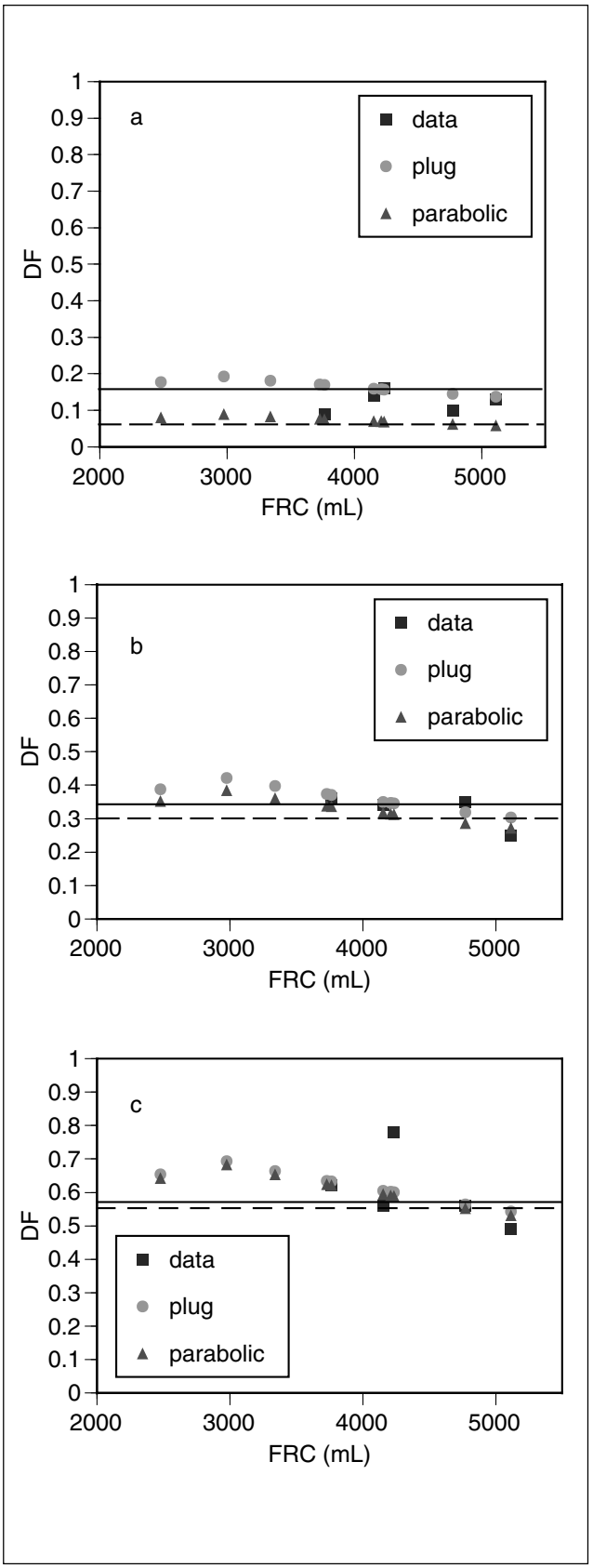

Figure 3. Particle deposition fractions for flow conditions with V_T = 500 mL and Q = 500 mL/sec. Figures 3a, 3b, and 3c contain data for 1-, 3- and 5-μm particles, respectively. The solid and dashed lines indicate the DF in the unmodified morphology, using the plug flow and parabolic velocity profiles, respectively.

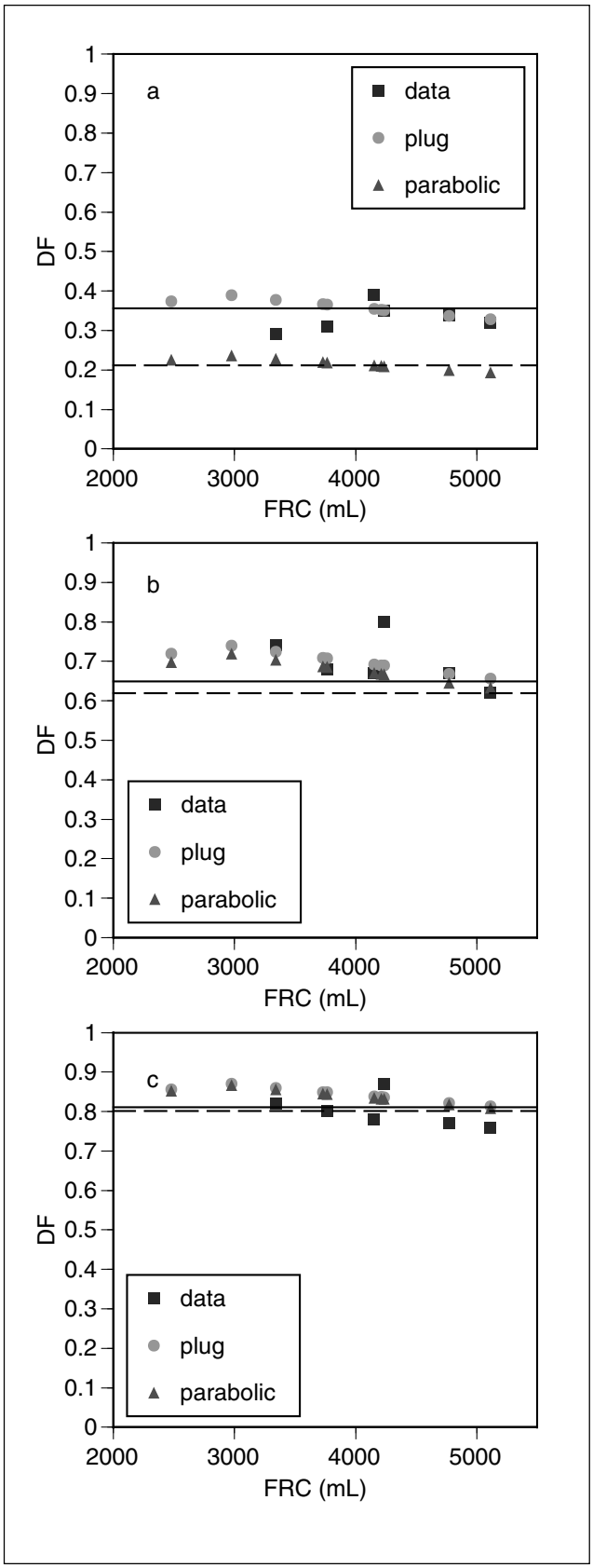

Figure 4. Particle deposition fractions for flow conditions with V_T = 1000 mL and Q = 250 mL/sec. Figures 4a, 4b, and 4c contain data for 1-, 3- and 5-μm particles, respectively. The solid and dashed lines indicate the DF in the unmodified morphology, using the plug flow and parabolic velocity profiles, respectively.

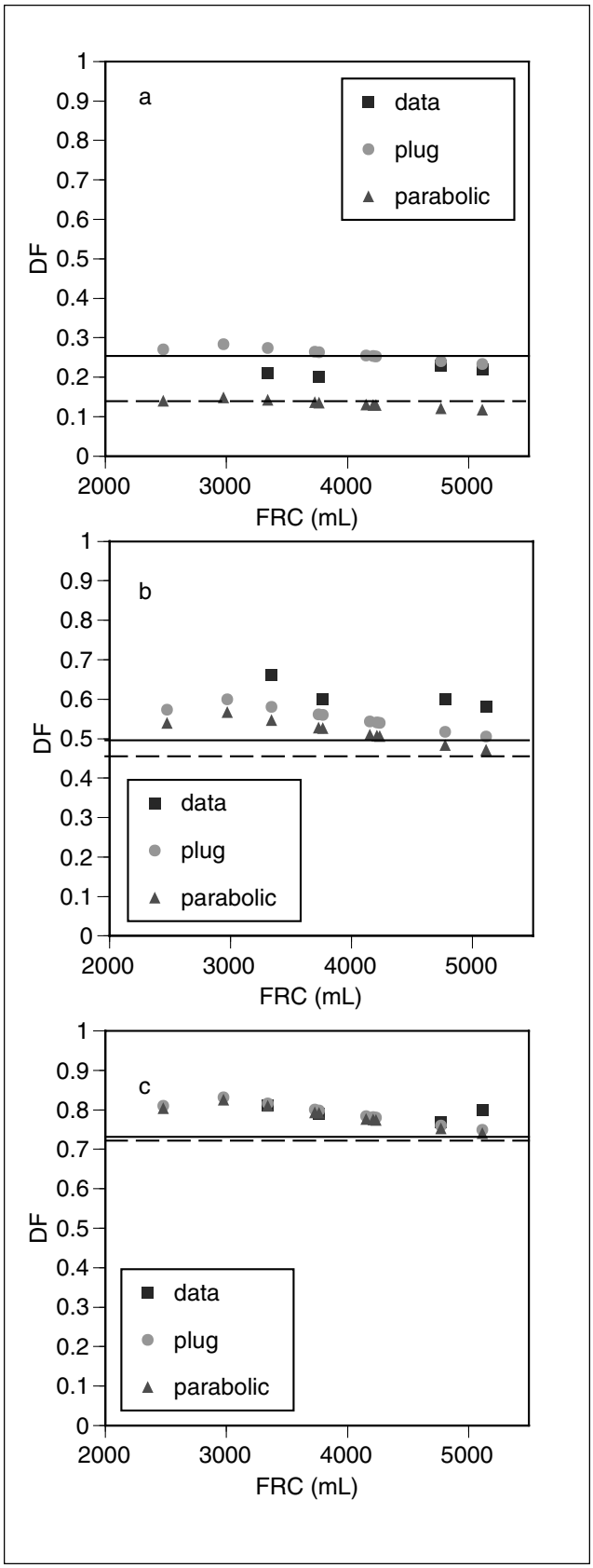

Figure 5. Particle deposition fractions for flow conditions with V_T = 1000 mL and Q = 500 mL/sec. Figures 5a, 5b, and 5c contain data for 1-, 3- and 5-μm particles, respectively. The solid and dashed lines indicate the DF in the unmodified morphology, using the plug flow and parabolic velocity profiles, respectively.

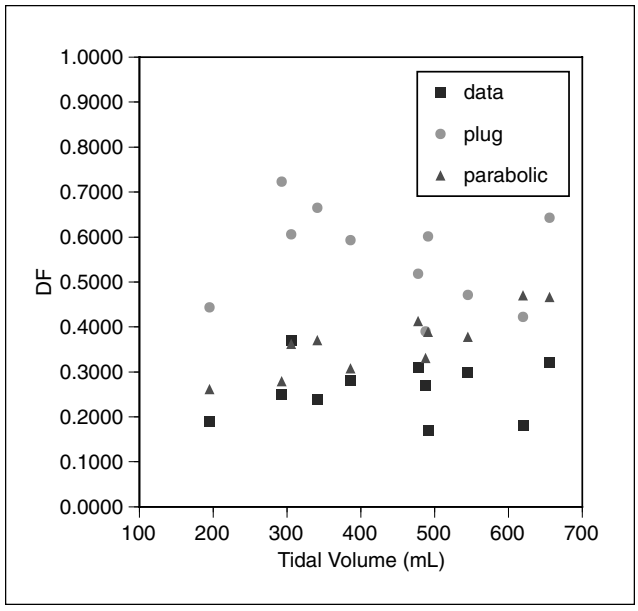

Figure 6. Particle deposition fractions for 2-μm particles. Flow conditions are based on the spontaneous breathing patterns used by patients as described in Table 1.

the deposition code to be less effective for this data set. We still obtained reasonable agreement, but for the subjects with higher tidal volumes the match is not as good. Scaling for each individual's lungs should reduce the error in our predictive values.

The DF simulations for the submicron particles provide some interesting information. The DF for the 0.01-μm particles was very high, due to the high rate of deposition by diffusion. It is interesting to note that while the parabolic profile and the plug profile provide different DFs for the other submicron particles, the difference between the two values for the 0.01-μm particle was small, because diffusion was very efficient for the small particles. In the other cases, the diffusion was not as efficient, and the difference in the velocity profile resulted in different deposition efficiencies. Assuming uniform particle distribution in the inhaled air, particles transported in flow with a parabolic profile are less likely to be close to the airway wall than particles in a uniform flow field. Therefore, particle deposition due to diffusion will be lower

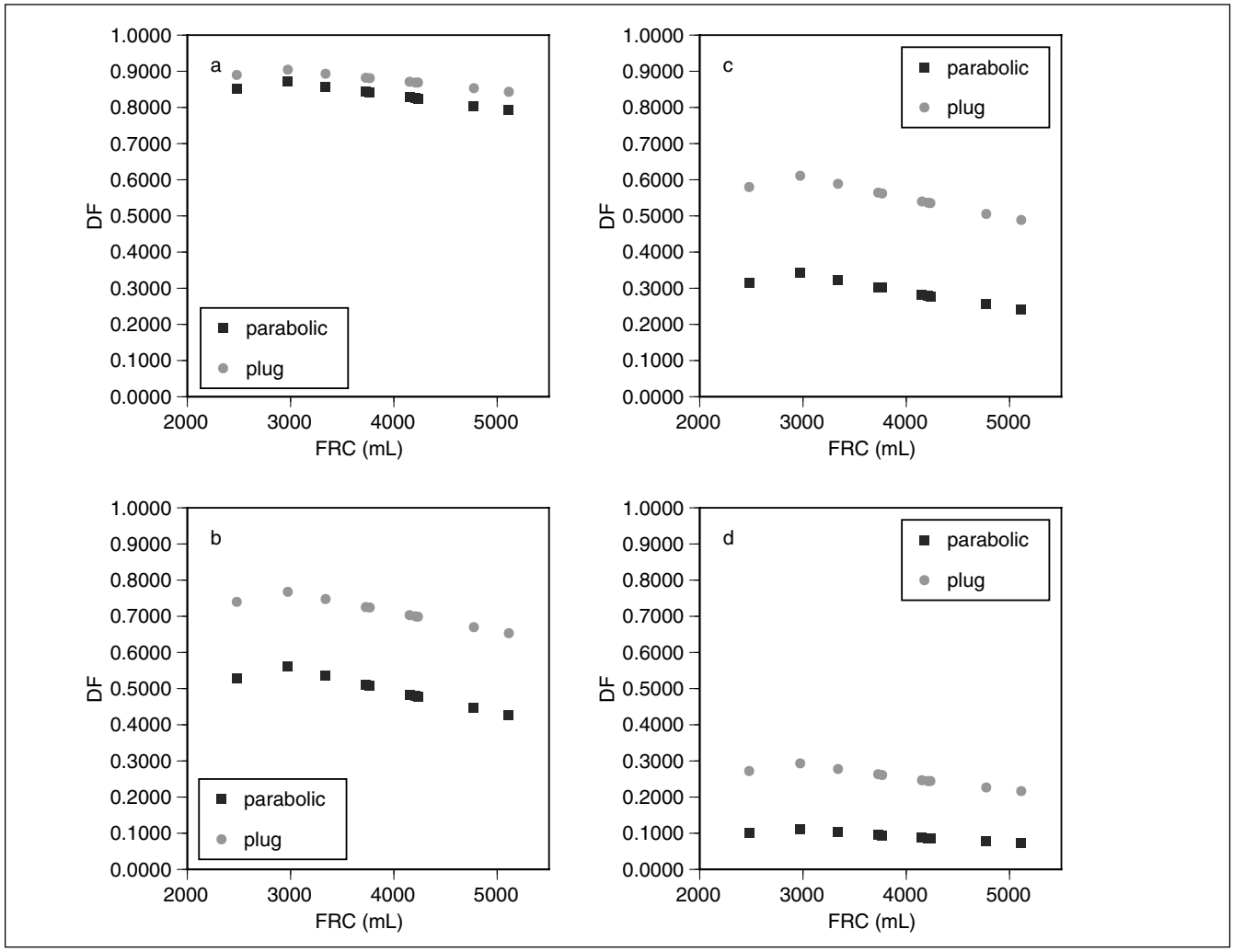

Figure 7. Particle deposition fractions for flow conditions of V_T = 500 mL and Q = 250 mL/sec. Figures 7a, 7b, 7c, and 7d contain data for 0.01-, 0.05-, 0.1- and 0.5-μm particles, respectively.

when using a parabolic flow profile. We would like to expand our analysis of submicron particle deposition to determine whether adjusting the model lung to each individual test subject improves our prediction capabilities.

In summary, good agreement was found between theory and experiment. These results support the use of our computer model for studying factors affecting PM deposition. The findings indicate that scaling the lung based on an FRC measurement provides a basis for a more accurate prediction of deposition.

Because the computer model is deterministic (i.e., derived from first principles of physics), the model can be used to predict deposition fractions for a range of conditions (i.e., different ventilatory parameters and particle sizes) for which data is not readily available. The model may, therefore, be extended in future efforts to simulate effects of airway disease (e.g., COPD) in risk assessment efforts to estimate the inhalation hazards of airborne pollutants for a sensitive subpopulation.

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DISCLAIMER

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