LES Study on the Poly-disperse Particle Deposition in the Human Upper Airway

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Abstract

Aerosol particle application of therapeutic agents into the deep lung represents an essential treatment of asthma and other lung diseases. The advantage of pulmonary drug delivery through inhalation is the topical treatment of specific lung conditions with limited whole-body effects. Aerosol particle deposition in this region has important implications in drug delivery efficiency. Thus, it is highly desirable to study particle deposition in the human upper airway.

Although significant investigations have been performed in this field, little research has focused on the study of poly-disperse particle deposition in the human respiratory system, considering a realistic drug dose. In the present study, a poly-disperse particle distribution from a dry powder inhaler is adopted using a realistic drug dose of 200 μg, which is introduced into the human upper respiratory system through the mouth. The mouth-throat configuration is constructed based on cast. Ansys ICEM-CFD 11.0 is used to generate the numerical grid. Both one-way and two-way coupling are implemented to model the two phase flow. Large eddy simulation (LES) with the Smagorinsky sub-grid model is used to simulate the transitional laminar–turbulent gas flow, and the method is combined with Lagrangian particle motion. The open source software of OpenFOAM 1.5 is adopted to solve the governing equations, where new solvers have been constructed to account for the particle motion using a Lagrangian tracking method within the LES formulation for the flow field.

The numerical results show that the particle deposition in the human mouth-throat is dominated by the particle size distribution pattern. The contribution of particle deposition in the human mouth-throat is related to both the initial particle size and the geometric region. The particle deposition efficiency of the poly-disperse particles is much higher than the mono-disperse particle deposition efficiency, where two different mono-disperse particle distributions were used: the Sauter diameter and the mass medium diameter of the reference poly-disperse particle size distribution. The numerical results display that particles in the size range of 1–5 μm are most likely to reach the deep lung. It is found that the poly-disperse particle deposition in the trachea is mainly caused by particles less than 1 μm, in the pharynx and larynx by particles larger than 5 μm, whereas in the mouth cavity, contributions of both particle size ranges deposit.

Introduction

Aerosol drug therapy, which mainly delivers the drug through the nasal or oral airway to the lung or other location of the respiratory tract, has become a popular way to treat different diseases such as asthma and chronic obstructive pulmonary disease, due to the advantage of smaller dose, minimal systematic adverse effects and rapid response [1]. It is desired that the drug would penetrate deep into the lung, which is the location where the disease is active. Nowadays, the drug delivery efficiency is very low: the maximum drug delivery efficiency is typically less than 30% [2]. It is well-known that the upper airway is the first barrier for the drug [1], therefore it is very important to study the particle deposition, in particular, the poly-disperse particle deposition, in the upper human respiratory system.

The particle deposition in the human upper airway has been investigated intensively during the past decades, in particular, the mono-disperse particle deposition has been studied intensely. Mono-disperse particle deposition has been simulated in a cast-based mouth-throat using Reynolds-averaged Navier–Stokes (RANS) equations coupled with the low Reynolds number $k-\omega$ model by [3]. In this study, the total particle deposition is shown to increase with the impact parameter. The particles mainly deposit in the mouth cavity and the constriction location such as the soft plate and glottis. As discussed by Jayaraju et al. [4], the RANS simulation only represents the mean flow variables and neglects the turbulent fluctuations, which may be inaccurate when predicting the particle deposition. Recently LES is more and more employed in the modeling of particle deposition in the upper human airway, and it has proved [4] that LES improves the prediction of particle deposition compared to RANS. Therefore, LES coupling with Lagrangian equations is adopted in the present paper.

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Even though many numerical studies concern mono-disperse particle distribution, the aerosol drug, which is used in the medical treatment, is usually poly-disperse. Thus, researchers also started to investigate poly-disperse particle deposition. Longest et al. [5, 6] adopted a poly-disperse particle distribution in an upper airway model, the particle distribution has been obtained from a laser fraction system (Spraytec, Malvern Instruments Inc.). In their research, particles have been injected with the same particle number in each class and the final mass deposition efficiency was scaled to match the experimental initial poly-disperse size distribution [6]. However, they did not consider the realistic drug dose in their research as well as the mass fraction was not considered when the particles are injected.

In the present paper, poly-disperse particle deposition is studied using both one-way and two-way coupling. Mono-disperse particle size distributions are simulated considering the Sauter mean diameter (SMD), the mass medium diameter (MMD) as well as the Sauter mean diameter of the poly-disperse spray using the realistic drug dose. When the realistic drug dose are injected, two-coupling way is used, otherwise one-way coupling is adopted. The results show that it is very important to use a realistic poly-disperse particle size distribution, and use of two-way coupling is suggested for the simulation of the poly-disperse particle size distribution.

Numerical Methods and Computational Conditions

The study concerns an idealized mouth-throat configuration based on human cast as shown in Fig. 1. Details can be found in Refs. [7, 8]. Depending on the injected particle mass, one-way or two-way coupling is used. LES is applied to treat the turbulence, and the sub-grid scale (SGS) Smagorinsky model ([9]) is adopted. Lagrangian equations are used to track the particle motion. With negligance of particle interaction, only the drag force and the gravitational force are considered ([10]). The Brownian force is considered when the particle size is in the range of submicron meters [12]. It is a common practice to neglect the sub-grid scale flow variables when LES is adopted [13], because the long-time particle dispersion is governed by the resolved flow [14]. Only recently, the influence of the sub-grid scale flow turbulence on the particle motion has been considered [13]. However, it is found that the particle dynamics is much more influenced by the sub-grid fluid turbulence if particle segregation or inter-particle collisions are considered [15]. In the present work, the interaction between particles is neglected, an therefore, it is reasonable to neglect the influence of sub-grid flow variables.

The software platform OpenFOAM 1.5 is adopted to solve the governing equations. New solvers for the flow field (using LES) and the particle motion with the Lagrangian tracking method were constructed based on the solvers oodles and icolagrangianFoam using either one-way or two-way coupling. More details on one-way coupling are given in Ref. [11], whereas two-way coupling is discussed in [17, 18]. The computational grids are generated with Ansys ICEM-CFD 11.0. The mesh number is increased until flow field independence of the solution on the number of grid nodes is guaranteed, and the final number of grid nodes is 1,276,500. The flow field was carried out at a steady inspiration flow rate of 30 L/min with 2% initial velocity fluctuation.

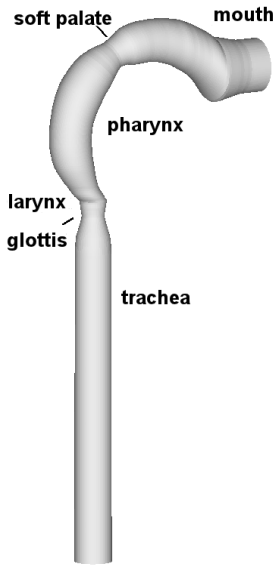

Figure 1. Three-dimensional view of the circular idealized mouth-throat geometry [8].

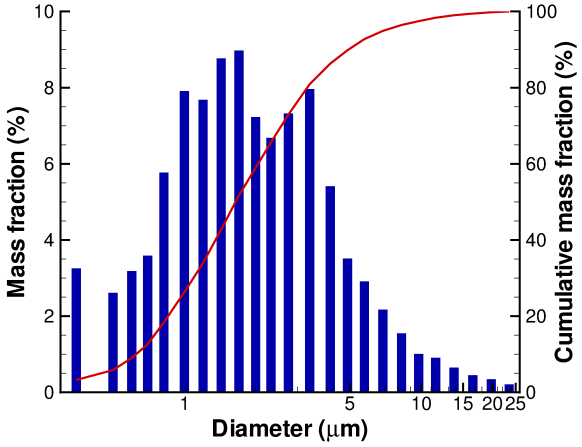

Figure 2. Relationship between the initial poly-disperse particle diameter distribution and mass fraction [16].

The poly-disperse particle distribution has been studied experimentally by the group of Prof. Urbanetz (Research Center Pharmaceutical Engineering GmbH, Graz, Austria) from DPI (dry powder inhaler). The relationship between the particle mass fraction and the particle diameter is shown in Fig. 2 [16]. The particle diameter ranges from 0.35 to 23.5 μm. The mass medium diameter is 1.79 μm, and the Sauter mean diameter is 1.38 μm. The particle density is 1,000 $\mathrm{kg/m^3}$ and the initial particle velocity is assumed to be same as the air inspiration flow velocity of 1.592 m/s. Particles are distributed randomly but uniformly at the inlet plane. Initial conditions for the different situations studied in the present paper are presented in Tab. 1.

In the present study, the injection for one actuation injection is considered, which is 200 μg for the drug "Salbutamolsulfat" from MDI [2]. 10,000 parcels are injected at the same time at the inlet plane. Each parcel has the same mass, and the parcel number distribution for each class is proportional to the experimental mass fraction. The parcel velocity is the same as the inspiration flow velocity, and parcles distribute randomly but uniformly at the inlet plane. The particle position is controlled by a Gaussian distribution. The particle density is 1,000 $\mathrm{kg/m^3}$. The injection process can be described through the following equations:

$$m_{\mathrm{parcel}} = \frac{m_{\mathrm{in}}}{N_p} \tag{1}$$

$$N_{pi} = \frac{m_{\mathrm{in}} f_i}{m_p} = N_p f_i, \tag{2}$$

where N_p is the total parcel number, N_{pi} is the parcel number corresponding to the i^{th} class , m_{in} is the injection mass of one actuation, m_p is the mass of one parcel, and f_i is the mass fraction of the i^{th} size class. In the computation, the injection mass is set to $m_{\mathrm{in}} = 200$ μg, and the injection parcel number is taken to be $N_p = 10{,}000$.

For comparison with the results of the poly-disperse particle distribution, a computation with a mono-disperse distribution of 1.38 μ, which is the Sauter mean diameter of the poly-disperse distribution, is performed, where two-way coupling is used. The injection conditions are fixed.

Results and Discussion

Table 1 provides an overview over the cases studied and the models used. Moreover, the particle deposition efficiency is shown. It is striking that the mono-disperse particle deposition efficiency is considerably lower than the poly-disperse particle deposition efficiency. In the mono-disperse situation, large particles size are neglected, which contribute dominantly to particle deposition. Particle deposition pattern will be discussed in more detail below. Considering the realistic drug dose, it appears that the deposition efficiency for the two-way coupling situation is more that a factor of ten larger for the poly-disperse distribution compared to the mono-disperse with corresponding Sauter mean diameter, which shows that the widely assumed assumption that the characteristics of a poly-disperse distribution may be represented by the characteristics of the mono-disperse distribution with appropriate Sauter mean diameter is a poor assumption.

The major reason for this deviation is the fact, that, in contrast to mono-disperse particle simulation, the poly-disperse particle computation considers the large particles, which dominantly deposit in the upper airway. The total

particle deposition efficiency is 7.6% using one-way coupling for the poly-disperse particle distribution, whereas it is 6.47% using two-way coupling for the same particle distribution. Both of these results are much higher than the particle deposition efficiency for all mono-disperse situations as shown in Tab. 1. This result may be compared to the values of 14.7% and 20.8% of deposition efficiency in an induction port and a simplified mouth-throat model obtained by Longest et al. [5]. The higher values may result from differences in the geometric model and the numerical methods. However, the most important reason is the difference in initial particle size distribution. The mass fraction of particles larger than 5 µm in the particle size distribution used by Longest et al. [5] is about 0.2, whereas in the present study, it is only 0.1. Since the particles in this size range contribute greatly to the particle deposition (see discussion below), particle deposition efficiency in the present study is much lower than the values published by Longest et al. [5].

The poly-disperse particle deposition on the surface is shown in Fig. 3 using one-way (left) and two-way (right) coupling. These patterns may be compared to the computation of Longest et al. [5] using one-way coupling only, where the deposition pattern in a CT-based geometry is studied using a poly-disperse particle distribution with larger droplets as discussed above. For large particles, the region of particle deposition is similar, whereas for smaller particles, it deviates. The gas-phase model in their work, however, is a RANS simulation with one-way coupling combined with Lagrangian particle tracking. Figure 3 shows that large particles deposit in the mouth cavity, in the posterior side of the pharynx, and in the glottis. The smaller particles appear to deposit in the mouth cavity, the anterior side of the pharynx, and the trachea. A comparison of particle deposition obtained with one-

Table 1. Particle deposition in the cast-based mouth-throat for different initial conditions.

Particle distribution	mono-disperse SMD	mono-disperse MMD	mono-disperse SMD	poly-disperse	poly-disperse
Particle size	1.38 µm	1.79 µm	1.38 µm	see Fig. 2	see Fig. 2
Injection drug dose	0.014 µg	0.03 µg	200 µg	16.5 µg	200 µg
Coupling method	one-way	one-way	two-way	one-way	two-way
Particle/parcel number	10,000	10,000	10,000	24,000	10,000
Particle deposition	0.45%	0.49%	0.51%	7.6%	6.37%

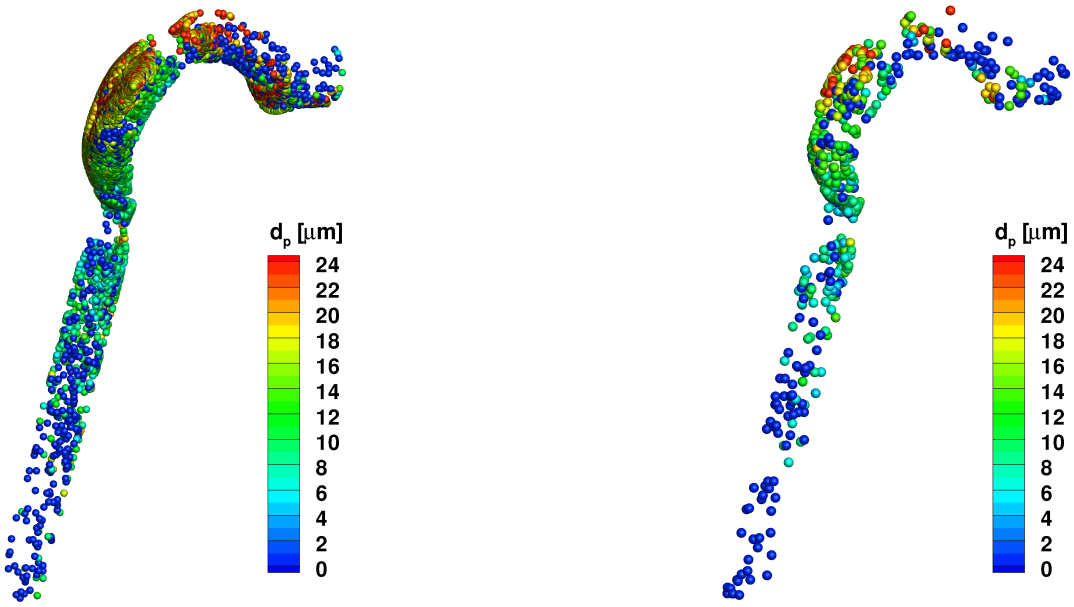

Figure 3. Poly-disperse particle deposition on the surface of the cast-based mouth-throat using one-way (left) and two-way (right) coupling.

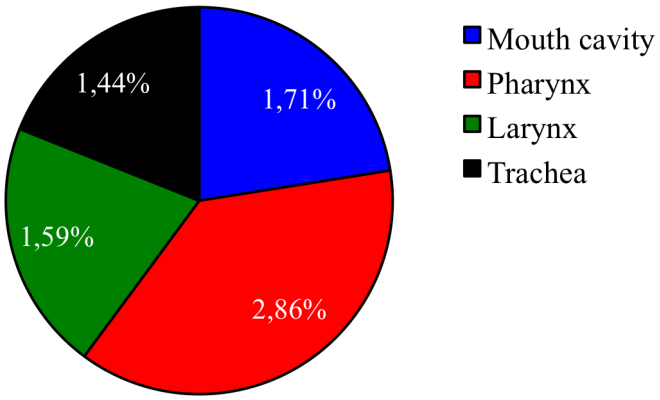

Figure 4. Poly-disperse particle deposition in different regions of the cast-based mouth-throat using one-way coupling.

way and two-way coupling reveals that the principal pattern is similar, and the deposition efficiency is smaller if two-way coupling is used as shown in Fig. 3. The particle deposition efficiencies in different regions are shown in Fig. 4, which shows that almost 50% of the particles deposit in the pharynx, whereas trachea, larynx and mouth cavity share the remainder of the particle deposition rate almost equally. To identify the contribution of each particle class to the geometric particle deposition rate in different regions, the relationship between the particle deposition efficiency and particle diameter in the mouth cavity, pharynx, larynx and trachea is shown in Fig. 5.

It is found that particles in the initial size range of 1–5 μm contribute only little to the particle deposition displayed in Fig. 5, although the major part of injected mass consists of these particles, c.f. Fig. 2. The total mass fractions of particles in the size ranges of 0.35–1 μm, 1–5 μm, and 5–23.5 μm are 26.3%, 63.5%, and 10.2%, respectively, whereas the corresponding particle deposition efficiencies are 3.1%, 0.4%, and 4.1%. It is found that the particles larger than 5 μm mainly deposit in the pharynx and larynx, whereas the particles less than 1 μm may deposit in different regions of the mouth throat other than the larynx.

The results of the poly-disperse particle deposition presented so far were obtained using one-way coupling. A comparison of these results with computations using two-way coupling is shown in Fig. 6, which shows that the main difference between the coupling methods arises in the size range of sub-micron particles. The sub-micron particle deposition is considerably reduced if two-way coupling is used compared to one-way coupling, whereas

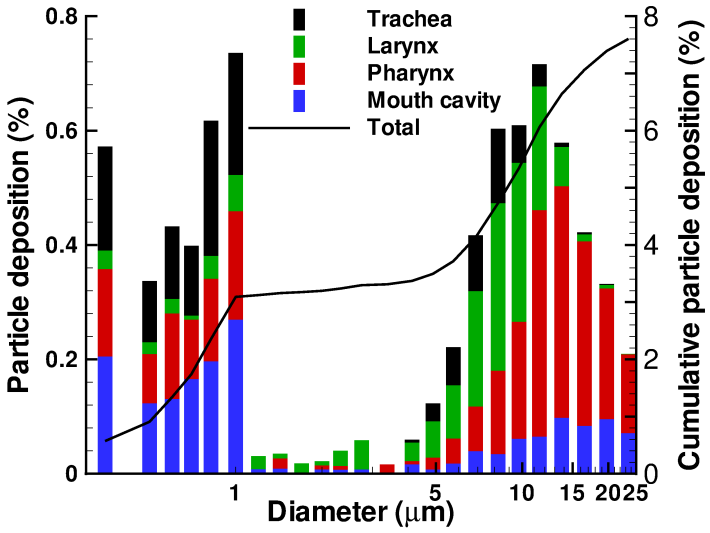

Figure 5. Contribution of each class to particle deposition in different regions of the cast-based mouth-throat using one-way coupling.

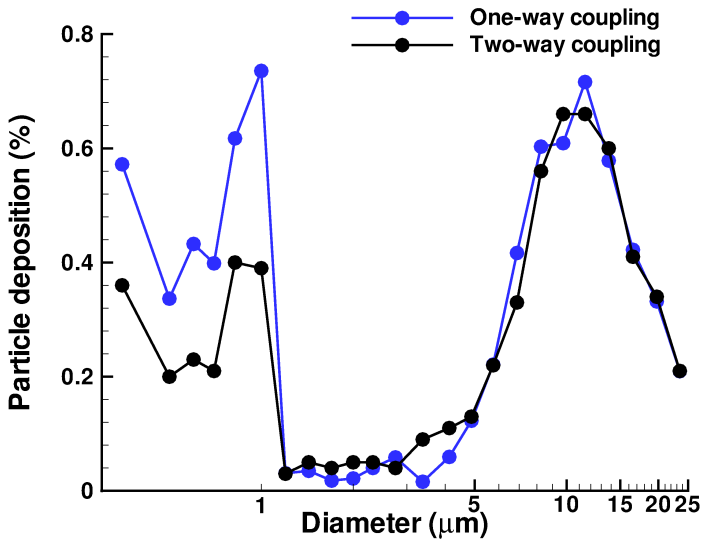

Figure 6. The comparison of contribution of each class on the total particle deposition efficiency in the cast-based mouth-throat using two different coupling methods.

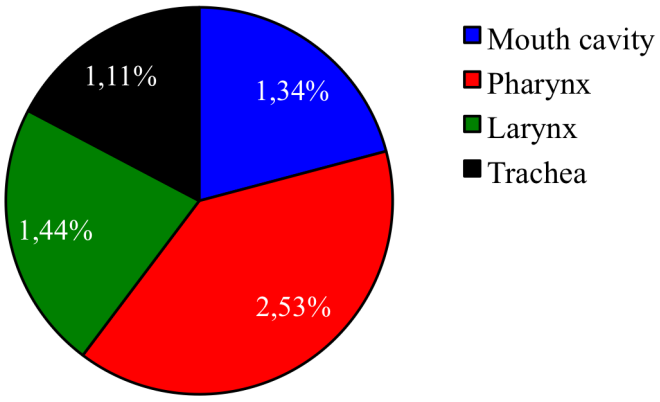

Figure 7. Poly-disperse particle deposition deposition in different regions of the cast-based mouth-throat using two-way coupling.

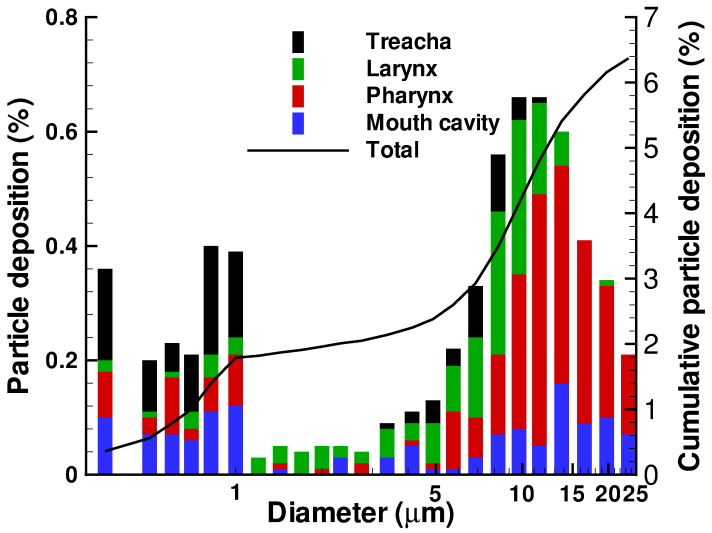

Figure 8. Contribution of each class to particle deposition in different regions of the cast-based mouth-throat using two-way coupling.

larger particles are not much affected. Corresponding contributions of particles in the ranges of 0.35–1 μm, 1–5 μm, and 5–23.5 μm are 1.79%, 0.59%, and 3.99%. Using one-way coupling, the particle deposition in different regions of the mouth-throat is higher than for two-way coupling as can be seen when comparing Figs. 4 and 7. This may mainly result from the negligence of particle momentum to the gas, when one-way coupling is adopted. Thus, it is recommended that two-way coupling is used when the poly-disperse particle pattern is considered.

The contribution to poly-disperse particle deposition in different regions of the mouth-throat using two-way coupling is shown in Fig. 8. It can be seen that few particles in the sub-micron range deposit in the larynx compared to particles depositing in the mouth cavity, pharynx and trachea. However, in the range between 1 and 5 μm, the deposition in the larynx contributes most to the deposition efficiency. No particles in this size range deposit in the trachea. When the particle diameter is larger than 5 μm, the particles are filtered gradually from the mouth cavity. For instance, the maximum particle deposition appears in the mouth cavity and pharynx for particle size larger than 15 μm, and no particles deposit in the larynx and trachea, when the particle diameter is larger than 15 μm. Particle deposition in the larynx and trachea mainly consists of particles ranging from 5 to 15 μm. From Fig. 8 it can also be seen that particle sizes of 13.75, 11.5, 9.75, and 0.82 μm contribute the most to the deposition in the mouth cavity, pharynx, larynx, and trachea, respectively.

In summary, the particle size distribution greatly influences particle deposition in the human upper airway, and it is very important to use the poly-disperse particle pattern in the numerical study. From the comparison of the one-way and two-way coupling, it is found that the difference is mainly caused by the sub-micron sized particles. It is necessary to use two-way coupling for the numeral modeling of poly-disperse particle distribution as shown for the situation with realistic drug dose. It is also suggested to generate particle distributions in the size range of 1 to 5 μm for the drug formation, since the particles in other size ranges considerably contribute to particle deposition in the upper human airway even though they attain a low mass fraction.

Summary and Conclusions

In this study, both mono-disperse and poly-disperse particle deposition have been simulated in a cast-based human mouth-throat. One-way and two-way coupling have been implemented without or with considering the realistic injection drug dose. LES coupled with a Lagrangian tracking method has been developed to describe the entire process.

From the comparison of the mono-disperse and poly-disperse particle distribution, it has found that the poly-disperse particle distribution pattern has great influence on the particle deposition efficiency, and it is absolutely necessary to adopt the poly-disperse particle distribution in the numerical simulations. The particle deposition efficiency is higher using one-way coupling, and mainly particles in the sub-micron size range contribute to the difference, since the sub-micron particles are more affected by gas diffusion than large particles. Therefore, two-way coupling should be used in future numerical simulations. It is also found that the particles less than 1 μm and

larger than 5 μm have main contributions to the particle deposition, whereas particles between 1 and 5 μm reach the deep lung. Particles in the sub-micron size range mainly deposit in the trachea and the mouth cavity, whereas particles larger than 5 μm mainly deposit in the larynx and pharynx.

Thus, poly-disperse particle size distribution greatly influences particle deposition in the human upper airway, and particles in the size range of 1–5 μm are most likely to reach the deep lung. The present method is suitable to study ploy-disperse particle deposition, and it will be used in more realistic mouth-throat models based on computed tomography (CT) scans in the near future.

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