

Investigation of Ultrafine Particle Deposition in Human Airway to the 9th Generation of Bronchial Tubes Using Computational Fluid and Particle Dynamics

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Abstract. The behavior of airborne particles in the human respiratory system is closely related to local tissue dosimetry and its associated health risks. The inhalation of these particles is known to be the origin of lung diseases, such as lung cancer, chronic obstructive pulmonary disease, and cardiovascular disease. To compensate for the difficulty of experiments involving volunteers, *in silico* studies using numerical models have been adopted as promising alternatives. Therefore, this study applied the computational fluid and particle dynamics technique to investigate the deposition of ultrafine particles in the human respiratory tract from the nostrils to the ninth generation of bronchi. A computational model was created using computed tomography images. The airflow patterns were simulated under steady and incompressible conditions at breathing flow rates of 7.5 and 15 L/min, respectively. The discrete phase was simulated for ultrafine particles with aerodynamic diameters of 2–100 nm. Consequently, the validation work confirmed the simulation accuracy for particle sizes > 25 nm. In the lower respiratory system, the total deposition fraction decreased as the particle size increased. In addition, the eighth generation is a focal point of the deposited particles, elucidated by the local deposition fraction. The results of this study will benefit further studies involving health risk assessments and drug delivery.

1 Introduction

One of the current concerns of public health is air pollution by respirable airborne particles, which are jointly responsible for premature death globally [1]. Ultrafine particles (UFPs, aerodynamic diameter < 100 nm) are released into the environment by several sources, including fossil fuel combustion, condensation of volatile compounds, industrial emissions, and cooking-heating activities [2,3]. The number of on-road vehicles using diesel engines is still increasing worldwide, which is responsible for the large concentration of emitted UFPs in the environment [4]. Inhalation of UFPs is closely linked to detrimental effects on the respiratory, cardiovascular, central nervous systems, and other organs owing to their translocated characteristics [5]. The front line between the UFPs and other organs is the pulmonary system, which filters particles from inhaled air during inhalation/exhalation processes. However, regarding their small size, the UFPs can pass straight through the extra-thoracic region and penetrate deeper into the lungs, which is identified as a critical public health problem causing mortality in all ages. Therefore, investigating the fate of UFPs in the human thoracic region can establish an understanding of their potential health risks.

In this respect, efforts involving volunteers have been experimentally executed in the past decades [6–8]. These early studies constituted the first step in quantitatively reporting the deposition pattern in the human extra-thoracic and thoracic regions using radioactive particles for measurement. Although ethical issues have been strictly addressed, these experimental efforts have followed the simulation technique, which utilizes computer resources and a numerical model of the human respiratory tract. Currently, the computational fluid dynamics (CFD) method has provided reliable results for fluid flow characteristics in enclosed spaces, especially in animal/human respiratory systems. Further, the computational fluid and particle dynamics (CFPD) technique has been applied to predict the deposition of UFPs and has been previously analyzed in the extra-thoracic [9–11] and thoracic regions [12,13]. Nonetheless, the complex structure of the thoracic region restricted the realistic generation of the numerical model; instead, tube-like models mimicking the morphometry of this region were mostly used in previous studies, which may have affected the deposition results because the structural features are one of the critical factors of airway deposition analysis.

Against this background, the present study applies the CFD method to investigate the deposition of UFPs in a human lower airway model up to the ninth generation of bronchi. Realistic features of the lower airway were

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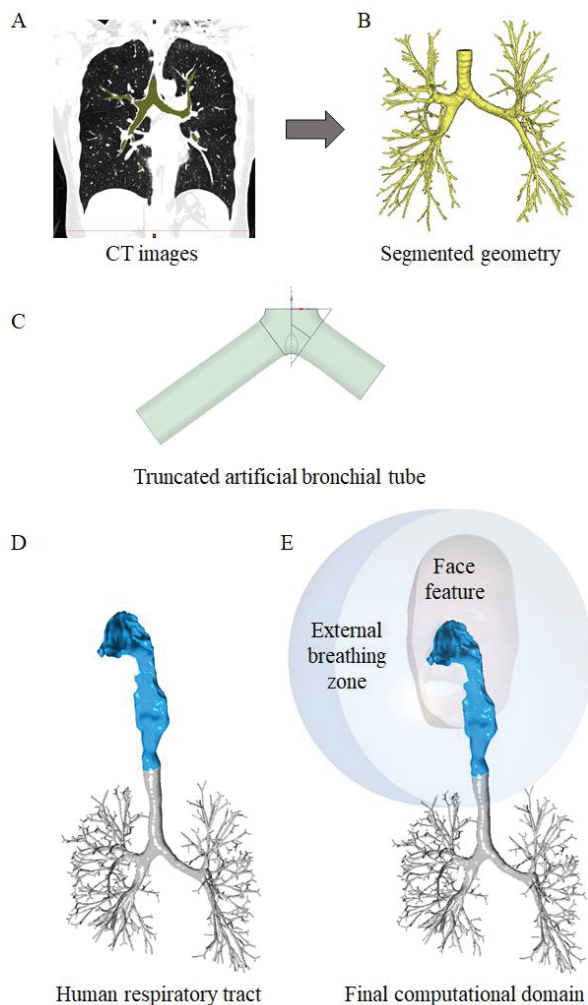


Fig. 1. Generation workflow of the human respiratory tract and outline of the computational domain.

strictly preserved in the computed tomography (CT) images. Nonetheless, the resolution of CT images partially hampers the segmentation of the desired lung model, reaching the ninth generation; thus, the tube-like bronchial is adopted to close the gap. The fluid flow was simulated under steady conditions for two breathing flow rates of 7.5 and 15 L/min. Then, particle analysis was conducted for UFPs with aerodynamic diameters ranging from 2 to 100 nm.

2 Methodology

2.1 Model generation

A realistic lower airway was segmented from the CT data of a healthy adult male. A representative coronal plane denoting the CT data used in this study is shown in Fig. 1a, where the black color denotes the air-filled region and the white color indicates the bony structure as a function of X-ray adsorption. The raw solid geometry of the human lower airway was extracted and segmented semi-automatically and manually based on the grayscale level (Fig. 1b). However, the resolution of CT data limits the detailed geometric information of the lower airway, especially after the eighth generation of bronchi. Hence, a truncated artificial bronchial trachea

tube was created following Tena et al. 2017 [14], as shown in Fig. 1c, and was connected to a realistic model to achieve a more comprehensive model reaching the ninth generation. The human respiratory tract was obtained by combining the upper airway (blue) and lower airway (gray), as shown in Fig. 1d. To create proper simulation conditions, the external breathing zone and face features were integrated into the respiratory tract, finally forming a complete computational model, as depicted in Fig. 1e. The information about the lower airway geometry is listed in Table 1.

Table 1. Geometric information of the human lower airway

Generation order	Number of branches	Total surface area (mm ²)
1 st	1	34.4
2 nd	2	16.8
3 rd	4	17.7
4 th	9	22.8
5 th	19	39.1
6 th	39	74.6
7 th	77	114.8
8 th	127	119.5
9 th	173	104.5

2.2 Mesh design in computational model

This study adopted poly hex-core elements for meshing, a combination of Hexa cells in the bulk region, and polyhedral cells adjacent to the boundary wall, which were shown to balance the accuracy and computational cost [15]. Moreover, 10 prism layers were created adjacent to the boundary wall of the upper airway, which optimized the accuracy of the flow profile in the vicinity of the wall. For the lower airway, five prism layers were applied because of the small diameter of the bronchial tubes.

2.3 Continuous phase simulation

We assumed and simulated a steady-state, isothermal, and incompressible fluid flow in the respiratory tract using the Eulerian method, in which the set of Reynolds-averaged Navier-Stokes (RANS) equations (Eqs. 1 and 2) was solved computationally for each control volume, as shown in Eqs. 1 and 2:

$$\frac{\partial \bar{U}_i}{\partial x_i} = 0 \quad (1)$$

$$\frac{\partial \bar{U}_i}{\partial t} + \frac{\partial \bar{U}_i \bar{U}_j}{\partial x_j} = -\frac{1}{\rho_g} \frac{\partial \bar{p}_g}{\partial x_i} + \frac{\partial}{\partial x_j} \left[(\nu + \nu_t) \left(\frac{\partial \bar{U}_i}{\partial x_j} + \frac{\partial \bar{U}_j}{\partial x_i} \right) \right] \quad (2)$$

where $\bar{U}$ represents the ensemble mean velocity, and p_g , ρ , ν , and ν_t denote the pressure, density, viscosity of the fluid, and turbulent viscosity, respectively. This study applied the low-Reynolds-type $k-\epsilon$ (Abe-Kondoh-Nagano) turbulent model, which has been shown to provide a reliable prediction of airflow in the respiratory model [16,17]. Different breathing flow rates of 7.5 and 15 L/min were selected to cover resting and normal human activities. The numerical boundary conditions are listed in Table 2.

The human lower airway is geometrically divided into five main regions: the right upper, right middle, right lower, left upper and left lower lobes [18]. Therefore, outflow weighting was set differently for each lobe, as performed in a previous study [19] (Table 3).

Table 2. Formatting sections, subsections, and subsubsections

Parameters	Information
Turbulent model	Low Reynolds type k-e model (Abe–Kondoh–Nagano)
Algorithm	SIMPLE
Convection scheme	Second order upwind
Inflow boundary	$Q_{in} = 7.5$ and 15 L/min Turbulent intensity (TI)=10%
Outflow boundary	Gradient zero with outflow weighting (Table 3)

Table 3. Outflow weighting boundary condition for each lung lobe

Lobes	Flow weighting
Right upper lobe (RUL)	0.1194
Right middle lobe (RML)	0.1089
Right lower lobe (RLL)	0.3001
Left upper lobe (LUL)	0.2376
Left lower lobe (LLL)	0.2349

2.4 Discrete phase simulation

Particle trajectories were predicted using the Lagrangian equation, as shown in Eqs. 3.

$$\frac{d\vec{u}_p}{dt} = \vec{F}_D + \vec{F}_G + \vec{F}_S + \vec{F}_B \quad (3)$$

where the subscript p refers to the particle phase, F_G and F_S refer to the gravitational and Saffman lift forces, respectively, F_D indicates the drag force per particle mass unit, and F_B denotes Brownian diffusion. A total of 50,000 monodispersed particles were introduced into the flow field in front of the nose, with an initial velocity equal to the fluid velocity at the released position. The aerodynamic diameter of the particles is assigned in the range of 2–100 nm, with a density of 1,000 kg/m³. In the Lagrangian tracking process, a perfect trap condition was assumed for the respiratory walls, which meant that the particles could not rebound into the flow after hitting the walls.

The total deposition fraction of particles in the respiratory tract is defined as the ratio between the number of particles deposited, “ C_{dep} ” and that of particles entering the respiratory tract, “ C_{in} ” (Eq. 4). In addition, the total deposition in the lower airway region, ignoring the filtration effects of the upper airway, is defined by the ratio of the number of particles deposited “ C_{dep} ” and that of particles entering the lower airway “ $C_{in-lower\ airway}$ ” (Eq. 5). Accordingly, the local deposition fraction in a specific region i , the specific bronchial tube generation, is defined as the number deposited in the region i divided by the total number entering the respiratory tract (Eq. 6).

$$\eta_a = \frac{C_{dep}}{C_{in}} \times 100\% \quad (4)$$

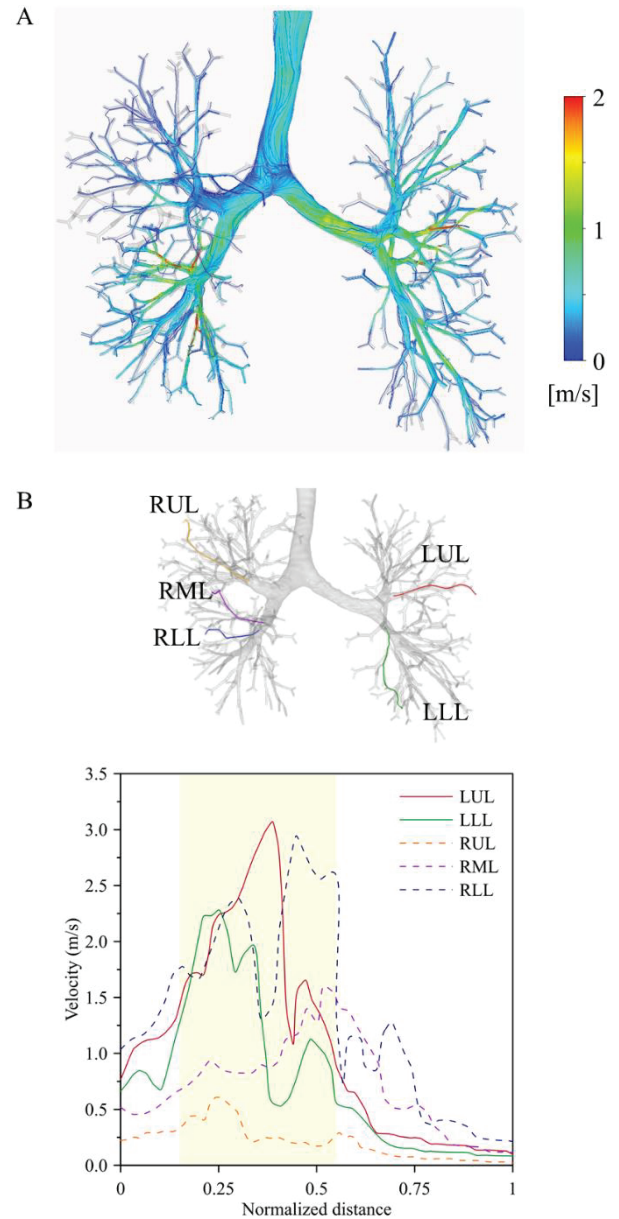


Fig. 2. Streamlines distribution in the lower airway (A), and representative velocity profile in the five different lobes (B). The highlighted region denotes the 5th-7th generation.

$$\eta_b = \frac{C_{dep}}{C_{in-lower\ airway}} \times 100\% \quad (5)$$

$$\eta_i = \frac{C_{dep-i}}{C_{in}} \times 100\% \quad (6)$$

3 Results and Discussion

3.1 Airflow characteristics at the resting condition (7.5 L/min)

The 1,000 streamlines describe the distribution of fluid flow in the human respiratory tract, as shown in Fig. 2a. The high velocity of the airstream is denoted by the red color, whereas the blue color represents the low velocity. The airflow characteristics of the upper airway have been extensively discussed in previous studies [20,21];

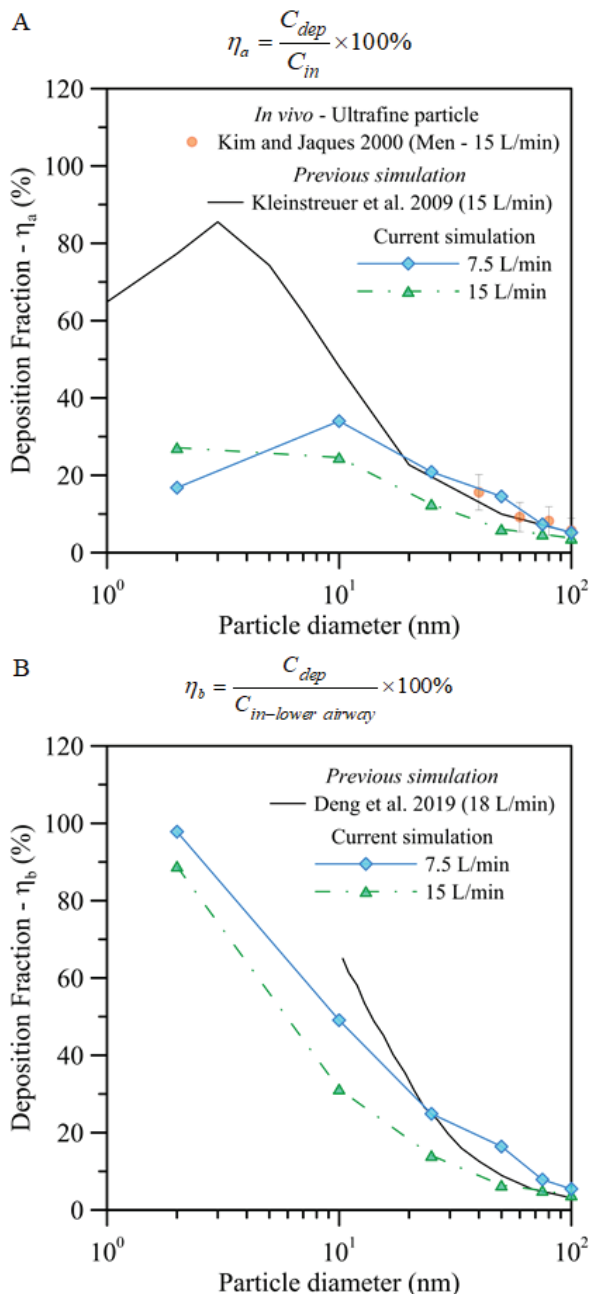


Fig. 3. Comparison of the current simulation results with the experimental data and previous simulation results.

therefore, only the fluid physics in the lower region is discussed herein. The results showed that the airstream smoothly passed through the tracheal region and reached the first generation, where the stream was branched and tilted to the left and right lungs. In the first and second generations, the skewed velocity profile toward the bottom was evidenced in our previous research [22], among others [23,24]. In this region, the flow was continuously split into branches flowing through the branching system of human lung geometry from the third to the ninth generation, which might hamper the detailed analysis of the flow features. Nonetheless, from the colored streamlines, acceleration can be observed in some specific regions. These phenomena can be attributed to subject-related individual structures. More explicitly, the centered polylines were created intentionally toward these peak velocity regions to deliver the quantitative velocity

profile (Fig. 2b). The results showed that the peak velocity occurred in the LUL region at 3 m/s, followed by the second peak in the RLL region. Excluding the RML, the velocity profiles in the other positions (RUL and LLL) capture the specific acceleration of the fluid. Additionally, accelerated and fluctuating airflow can be observed mostly in the 5th–7th generation of all the lobes. Leaving the 5th–7th generation, the fluid velocity rapidly reduced in the posterior generation. Despite the significant impacts of individual structures, these results indicate that the realistic geometry of the lung region would benefit the precise physics of fluid flow, which might not be captured in the tube-like model.

3.2 Validation of total particle deposition simulation data

The results of the particle deposition data are shown and compared with the experimental data set [25] and previous simulation data [26,27] for the lower airway region (Fig. 3). The previous simulation results were conducted in the representative tracheobronchial units (TBUs) separately in “series and parallel”; then, the total lung deposition was calculated based on the averaged results [26]. Another method is to simplify and treat the human lung region as the 1D lumped “trumpet” model relies on the parameters of the airway cross-sectional area and volume [27]. The total deposition fraction in the lower airway, shown in Fig. 3a, is calculated using Eq. 4, and that shown in Fig. 3b was obtained using Eq. 5. The results emphasize the consistency between the simulation and experimental data sets for particle sizes > 25 nm. Nevertheless, for particle sizes < 25 nm, a significant gap between the datasets can be observed. The discrepancies derived from the data indicate that the current model only reaches the ninth generation of the human lung region.

The integration of the upper airway in analyzing the total deposition in its lower partner exerted a marked phenomenon in the case of 2 nm for 7.5 L/min (Fig 3a). Specifically, the high deposition fraction in the upper region reduces the number of particles penetrating the lower region, consequently decreasing deposition in this region. This phenomenon was also observed in the previous simulation results (Fig. 3a). By eliminating the effects of the upper airway, the deposition fraction of the lower airway reduced as the particle size increased at both investigated flow rates. These results indicate that the lower airway compensates for particles that can escape the filter mechanisms of the upper region. In addition, as the particle size approached 100 nm, they had a high possibility of penetrating deeper into the lungs, thereby posing higher health hazards.

3.3 Deposition per generation and lobe in the lower airway region

The deposition in each generation is shown in Fig. 4, which was calculated using Eq. 6. The most captured region of particles was observed at the eighth generation for particle sizes >10 nm. This can be attributed to the effect of Brownian motion, in which the deposited

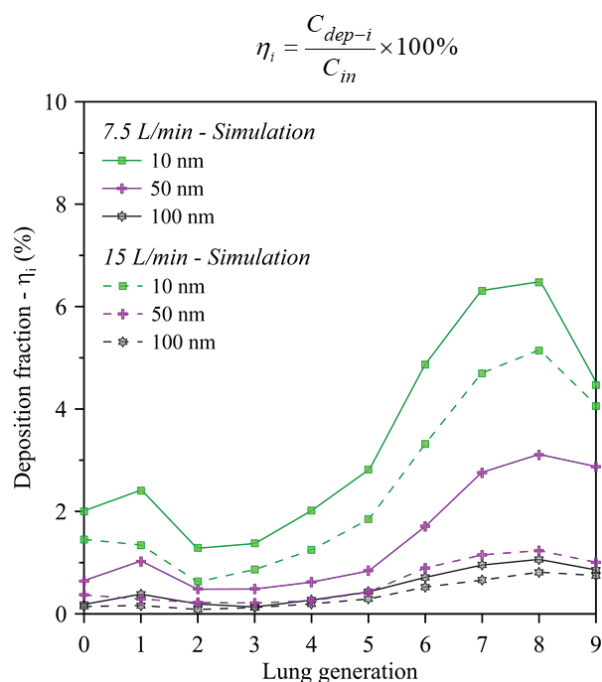


Fig. 4. Deposition per generation in the human lower airway at the breathing flow rate of 7.5 and 15 L/min.

particles within this effect tend to be evenly distributed on the inner surface. Therefore, the higher the inner surface area, the higher the possibility of trapping particles. As expected, the eighth generation possessed the highest surface area (Table 1); hence, the focal point of ultrafine particle deposition can be observed in this generation. Under the effect of the increment flow rate, the hot spot of the deposited particles remained almost constant, which indicated less dependence of the highly diffusive particles on the flow rates. The focal point of the particles deposited in the current study is strongly related to the individual structure of the lung model rather than the universal findings. This individual discrepancy may not be observed in studies involving tube-like generations. Therefore, the investigation of lung deposition is more challenging than that of the upper airway region because of the significant impacts of realistic morphometry and comprehensive models.

Despite the morphometry-related insufficiency in predicting the deposition of small particles, the CFPD method has the advantage of providing 3D visualization of deposited particles (Fig. 5). The results showed a uniform distribution of deposited particles on the inner surface of the lower airway. Moreover, the deposition in each lobe can be calculated using the CFPD method, which reveals the higher deposition in the RLL, LUL, and LLL. These results can be explained by the difference in flow weighting in each lobe (Table 3); the higher the flow weighting, the greater the flow portion, and the more particles can enter the corresponding region. As can be observed, the utilization of the CFPD method can mimic humans' more realistic breathing patterns, which might be absent in other methods.

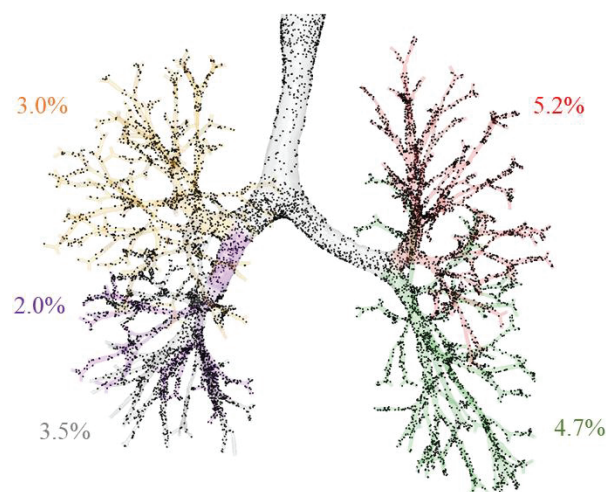


Fig. 5. Visualization of deposited particles (25 nm) in the lower airway region at breathing flow rate of 7.5 L/min. The percentage number denotes the deposition fraction in each lung lobe calculated by Eq. 6

4 Conclusions

This study aimed to investigate ultrafine particle deposition in the human respiratory tract up to the ninth generation of the bronchi. The CFPD method successfully predicted the transportation and deposition of ultrafine particles in a complex human respiratory tract. The individual morphometric features of bronchial airways exerted the acceleration of the fluid in specific regions, at 5th–7th generation in this case. Although a complex geometry of the lower airway was employed, the prediction accuracy was successfully confirmed for particle sizes > 25 nm; meanwhile, the lack of several bronchi reduced the accuracy of the particle size < 25 nm. As a detailed analysis of the deposition in each generation, the focal point was confirmed at the eighth generation reflecting the individual structure of the model. Three-dimensional visualization revealed the deposition characteristics of ultrafine particles, which showed a uniform distribution on the inner surface of the airway. These results indicate the importance of realistic and comprehensive airway generation to precisely capture the total and local deposition fractions in the lung region, particularly for particle sizes < 25 nm. In addition, we propose a promising direction for the CT image-based CFPD method in simulating deposited particles in the human lung region.

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