Aerosol flows in a human respiratory tract: experimental studies and modelling

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Introduction

The delivery of a drug into the human respiratory tract is one of the important tasks of inhalation therapy. Despite considerable progress achieved in the development of various delivery devices, inhalation is still one of the most complex types of drug therapy. A wide range of factors affecting the delivery to certain areas of the respiratory tract include the patient's application of the inhalation technique, variability of pulmonary function, and properties of the respiratory tract [8, 10]. Also, the drug properties, characteristics of delivery devices and individual characteristics of the human tracheobronchial tree affect the deposition of drugs in the respiratory tract [9].

The deposition fraction of inhaled drugs ranges from 2 to 67% of the nominal dose for the intrathoracic lungs (without the upper airway) [5]. The selection of the most appropriate inhaler depends not only on the type of drug and its dosage, but also on specific physical parameters of the delivery vehicle, and on the patient's inspiratory manoeuvre [11]. In the previously used approaches to modelling the heat and mass transfer processes in drug aerosol flows for delivery to the respiratory tract either the hydroscopic growth of aerosols due to the high humidity of ambient air in the respiratory tract was the dominant process modelled [6] or evaporation/condensation processes in these flows were ignored altogether [18]. Several studies focused on the evaporation processes in the respiratory tract were not related to the problem of drug delivery there (e.g. [13]). At the same time, aerosol evaporation during the delivery of a drug into the respiratory tract can have important effects on aerosol deposition at low ambient air moisture (less than 90%). This condition can be observed during breathing in dry ambient air, dehydration, respiratory diseases (for example, bronchial asthma, chronic obstructive pulmonary disease (COPD), and SARS) [15, 16, 17], and hyperventilation following a known mechanism of exercise-induced bronchoconstriction [7, 2].

Thus, the analysis of evaporating aerosol drug delivery in respiratory tract is important for practical medical applications, although this process has not been investigated so far to the best of our knowledge. Our investigation is specifically focused on the analysis of this case.

Materials and Methods

In-house experimental data were obtained in the form of averaged distributions of aerosol droplets by radii at the exit from the lower respiratory tract, printed on the Elegoo Saturn 3 Ultra 3D printer using Anycubic High Clear Resin as print material. A general view of the model prepared following this procedure is shown in Figure 1.

In order to make the inner surface of the model of the respiratory tract as close as possible to its real-life tissues, which have hydrophilic properties [14], the model was immersed in TWEEN 80 solution before the experiment, following the approach described by Salmanipour et al. [12]. The medicine approximated by water was sprayed using a constant flow jet nebulizer (Omron CompAir NE-C20 Basic Nebulizer (Omron Healthcare Inc)). A typical image of this spray (Spiriva® Respimat®) at 0.07 ms after the start of spray injection is shown in Figure 2.

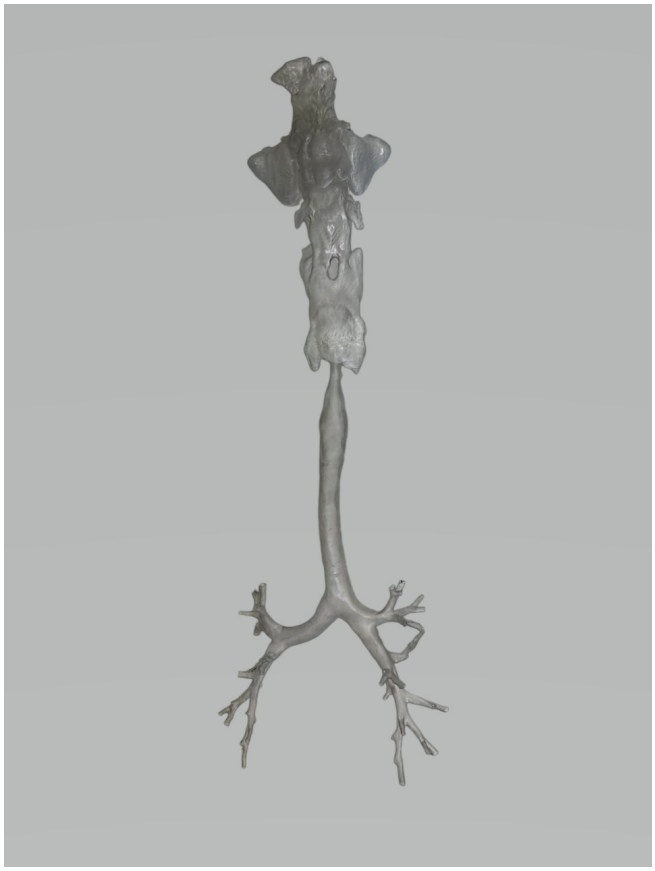

Figure 1. A general view of the respiratory tract used in the experiments.

The initial lognormal distribution of aerosols by sizes was assumed (the average aerosol radius was 4.0 ± 0.1 μm, their dispersion (geometric standard deviation (GSD)) was equal to 13.6 ± 0.1 μm, aerosol velocity was 0.22 ± 0.02 m/s. The flow of medical aerosols, generated by the nebulizer, was fed into the three-dimensional structure approximating the respiratory tract. Inhalation at a constant rate of 0.5 ± 0.1 m/s was simulated using a DSZH WK-115N vacuum pump. The initial temperature was the room temperature (300 ± 5 K).
Three-dimensional simulations, using COMSOL Multiphysics with the Heat Transfer, Fluid Flow, and Particle Tracing, were performed using the geometry shown in Figure 3. Model predictions were validated using experimental data presented in [1, 4] and in-house ones.

Results and Discussion

It was shown that the effects of aerosol heating and evaporation on their dynamics cannot be ignored when modelling the process of drug delivery in the human respiratory tract. This effect was shown to be particularly strong for patients with high body temperatures (higher than 310.15 K). It affected aerosol deposition in various regions of the respiratory tract taking into account the respiratory tract geometries for individual patients.
High human body (ambient) temperature is shown to increase the predicted rate of evaporation of aerosols leading to a decrease in their diameters. The latter was shown to affect the depth of penetration of aerosols into the respiratory tract and their deposition within it. When a certain threshold of this temperature (310.15 K) was reached, the aerosol deposition in the bronchi increased by 60% compared to the case when the process took place at normal human body temperature (309.75 K), assuming that aerosol velocity was 8 m/s, air flow velocity was 0.5 m/s, average aerosol diameter was 4.5 μm, and the number of aerosols was 10^5. It was demonstrated that most aerosols can deposit in the upper respiratory tract and least in the trachea. The asymmetry of bronchi location was shown to lead to asymmetry of deposition in the bronchi with deposition in the left bronchus up to about 80% higher than that in the right.

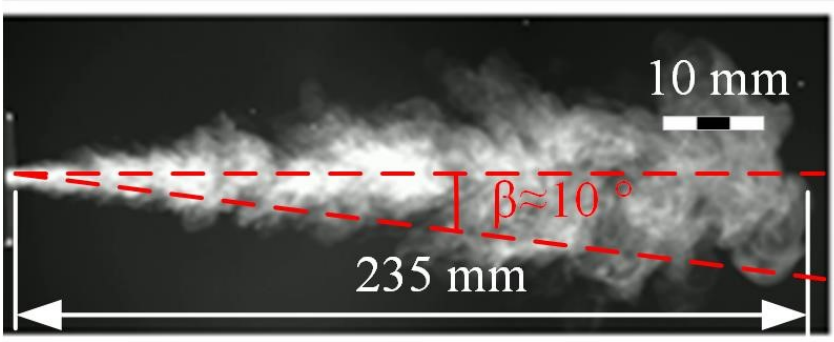

Figure 2. A typical image of medical aerosol spray (Spiriva® Respimat®) at 0.07 ms after spray injection.

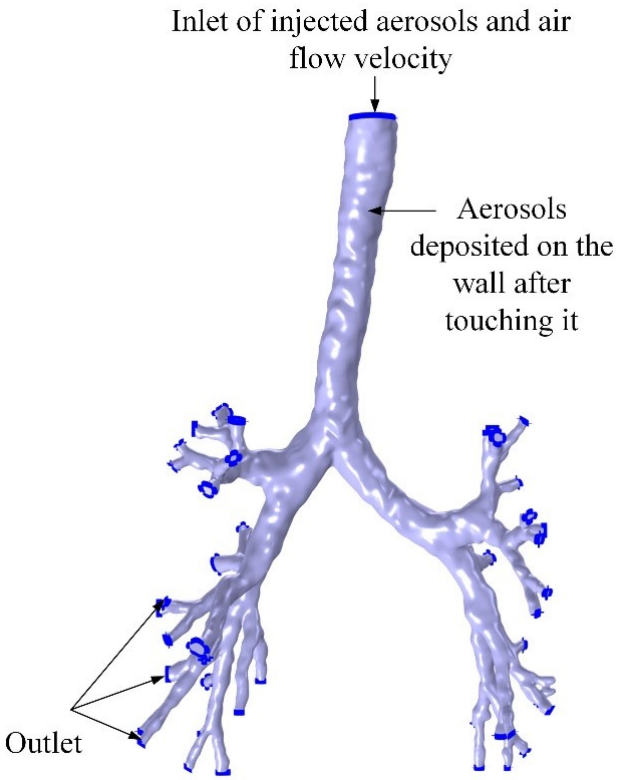

Figure 3. A geometry used in calculations of the flow, heat and mass transfer processes in drug aerosol streams for delivery to the respiratory tract. The image was prepared using the geometry provided by Bartol et al. [3].

The predicted deposition fractions of aerosols in three zones (trachea, left bronchus, and right bronchus) and for three ambient temperatures are compared in Figure 4. As can be seen in this figure, the deposition fractions strongly depend on both the temperature and the location (Zones 1, 2, and 3).

Conclusion

A thermophysical approach to controlling aerosol flows in a human airway was proposed to achieve maximum drug deposition, considering patients' individual characteristics (physiology of the airways and the architecture of the human tracheobronchial tree). The problem was addressed based on three-dimensional simulations using COMSOL Multiphysics with the Heat Transfer, Fluid Flow, and Particle Tracing modules. It was demonstrated that it is essential to take into account the processes of heat and mass transfer when simulating the flows of aerosols for targeted delivery to human airways at elevated temperatures (above 310.15 K). Using the database obtained from our study, conditions were formulated to increase the deposition rate of drugs in the respiratory tract. Hydrodynamic properties of aerosol fluxes were obtained

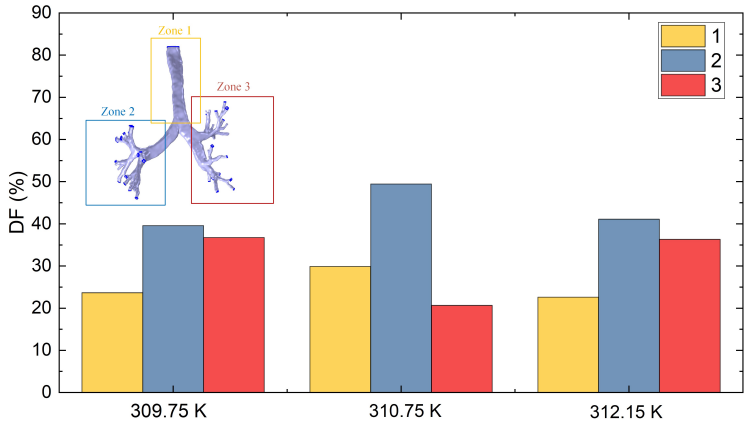

Figure 4. Aerosol deposition fractions (DF) in three respiratory tracts in the trachea (Zone 1), left bronchus (Zone 2) and right bronchus (Zone 3). Numbers in the figure show the number of the zone. Three temperature were used in calculations, as shown in the figure.

experimentally based on phase Doppler anemometry, shadow photography and tracer imaging. Three different inhalation drug delivery devices were used: Jet Nebulizer with Permanent Flow Metered Dose, Pressurized Aerosol Inhaler, and Soft Mist Type Inhaler (Respimat).

Acknowledgments

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