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THE EFFECT OF MOUTH-THROAT GEOMETRY ON REGIONAL DEPOSITION IN THE TRACHEOBRONCHIAL TREE

Pantelis G. Koullapis[1], Laura Nicolaou[2], and Stavros C. Kassinos[1]

[1]Department of Mechanical and Manufacturing Engineering, University of Cyprus, Kallipoleos Avenue 75, Nicosia 1678, Cyprus, {koullapis.g.pantelis,kassinos}@ucy.ac.cy

[2]Department of Mechanical Engineering, Imperial College London, Exhibition Road, London SW7 2AZ, UK, laura.nicolaou@imperial.ac.uk

SUMMARY

In silico methods offer a valuable approach to predict localized deposition in the tracheobronchial tree, important in the topical treatment of respiratory diseases and the systemic administration of drugs with limited lung bioavailability. In this study, we examine the effect of extrathoracic airway variation on regional deposition in order to assess whether standard mouth-throat models can be adopted for more efficient predictions. Despite large qualitative differences in the extrathoracic airways, deposition patterns and efficiencies in the tracheobronchial region remain largely unaffected for particles smaller than 6 microns. The findings suggest that for drug delivery applications, standard mouth-throat models could be adopted to predict deposition in the central airways.

Key words: *inhaled drug delivery, regional deposition, conducting airways*

1 INTRODUCTION

Pulmonary drug delivery is widely used for the topical treatment of pulmonary infections and respiratory diseases such as asthma, COPD and cystic fibrosis. More recently, the inhaled route has also been adopted for the systemic administration of drugs, due to the favourable absorption characteristics of the lungs. The efficacy of drug delivery depends, in part, on the site of deposition within the airways. Therefore, quantifying regional deposition is important in assessing and optimising topical treatments as well as systemic delivery of drugs with limited lung bioavailability.

In recent years, there have been significant advancements in pulmonary imaging techniques for *in vivo* measurement of aerosol deposition [1]. However, spatial resolution remains insufficient for visualisation of localized deposition. For inhalation product development, the current industry standard is the use of standardised throat models mounted on cascade impactors, which provide estimates of total lung deposition but cannot determine regional deposition.

In silico models can complement *in vivo*/*in vitro* testing and provide detailed information on regional deposition. However, high-fidelity simulations in realistic geometries of the respiratory airways are computationally demanding [2]. The aim of this study is to examine the effect of the extrathoracic airways on localized deposition in the tracheobronchial tree, in order to assess whether standard mouth-throat models can be used to predict deposition in the central airways. By adopting precomputed flowfields in these standard models, simulations can then be restricted to the tracheobronchial tree resulting in significant savings in computational cost.

2 METHODOLOGY

Three extrathoracic airways geometries, with different geometric and deposition characteristics, are merged onto the same tracheobronchial tree in order to examine the effect of the mouth-throat on the flow dynamics and deposition patterns in the central airways. The full geometries are shown in figure 1.

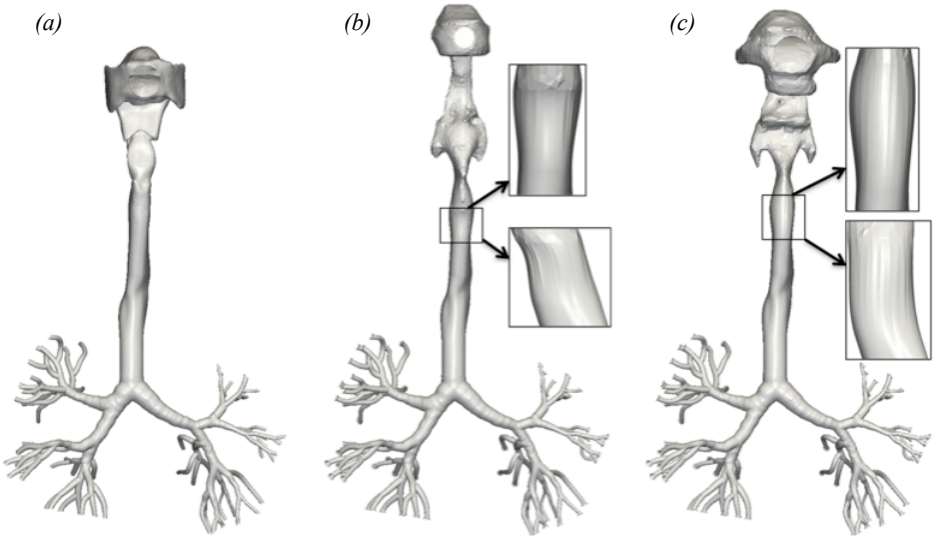

Figure 1: Geometries adopted in the study: (a) R1; (b) S1a; and (c) S2.

Large eddy simulations (LES) with a dynamic Smagorinsky sub-grid scale model are performed at a steady flow rate of 30 L/min [3]. For geometries R1 and S2, the inlet Reynolds number is in the laminar regime, therefore a parabolic velocity profile is prescribed at the inlet. For S1a, turbulent inflow conditions are obtained from a precursor simulation in a pipe. At the outlets, flow rates are prescribed to match *in vitro* measurements [4]. The ventilation distribution to the left and right lungs is non-uniform, with 71% of the inhaled volume entering the right lung.

To model the aerosol transport and deposition, a Lagrangian particle-tracking scheme is adopted. The equations of motion solved for the particle velocity and position are given by

$$m_p \frac{d\mathbf{u}_p}{dt} = \mathbf{F}_D + \mathbf{F}_G + \mathbf{F}_B, \qquad \frac{d\mathbf{x}_p}{dt} = \mathbf{u}_p, \tag{1}$$

where m_p, $\mathbf{u}_p$ and $\mathbf{x}_p$ are the mass, velocity and position of the particle respectively. The forces acting on the particles are the drag, $\mathbf{F}_D$, gravity, $\mathbf{F}_G$, and Brownian forces, $\mathbf{F}_B$. One-way coupling is adopted, and deposition is assumed once a particle comes into contact with the airway wall, due to the presence of sticky mucus gel. At each time step, 10 particles are released at random locations on the inlet plane, and 100,000 particles in total are tracked for each size.

3 RESULTS AND CONCLUSIONS

3.1 Flow field

Figure 2 shows contours of mean velocity magnitude in the mouth-throat region and the trachea across the three geometries. Large qualitative differences in the flow characteristics can be observed in the extrathoracic airways. In the trachea however, the flow has time to develop and these differences are significantly diminished at the exit (figure 2b). Mean velocity fields in the main bronchi and smaller airways in generations 3 and 4 are shown in figure 3. Minor differences exist across geometries in the first bifurcation and the left main bronchus (figure 3a). A slightly larger variation is observed in the right bronchus, which can be attributed to the higher ventilation of the right lung. Further down the tracheobronchial tree, we continue to observe a similar trend. Variations in the flow are more prominent in the right lung, as shown in figure 3c. Overall however, despite significant differences in the extrathoracic flow dynamics, the mean velocity in the tracheobronchial tree remains qualitatively similar across the three geometries. Inspection of the secondary flow motion and turbulent kinetic energy reveals similar results.

3.2 Aerosol deposition

The deposition fractions as a function of particle size, in the mouth-throat region and tracheobronchial tree, are shown in figure 4. In the extrathoracic airways, the large effect of geometric variation on

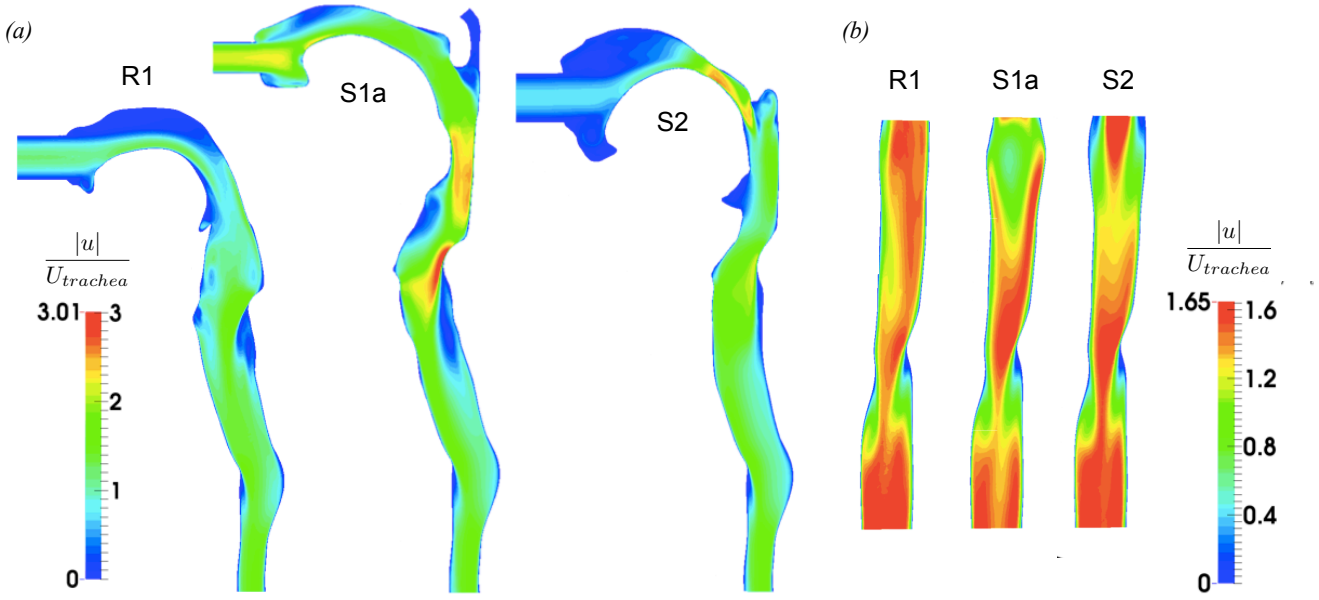

Figure 2: Contours of mean velocity magnitude in (a) the mouth-throat region, and (b) trachea.

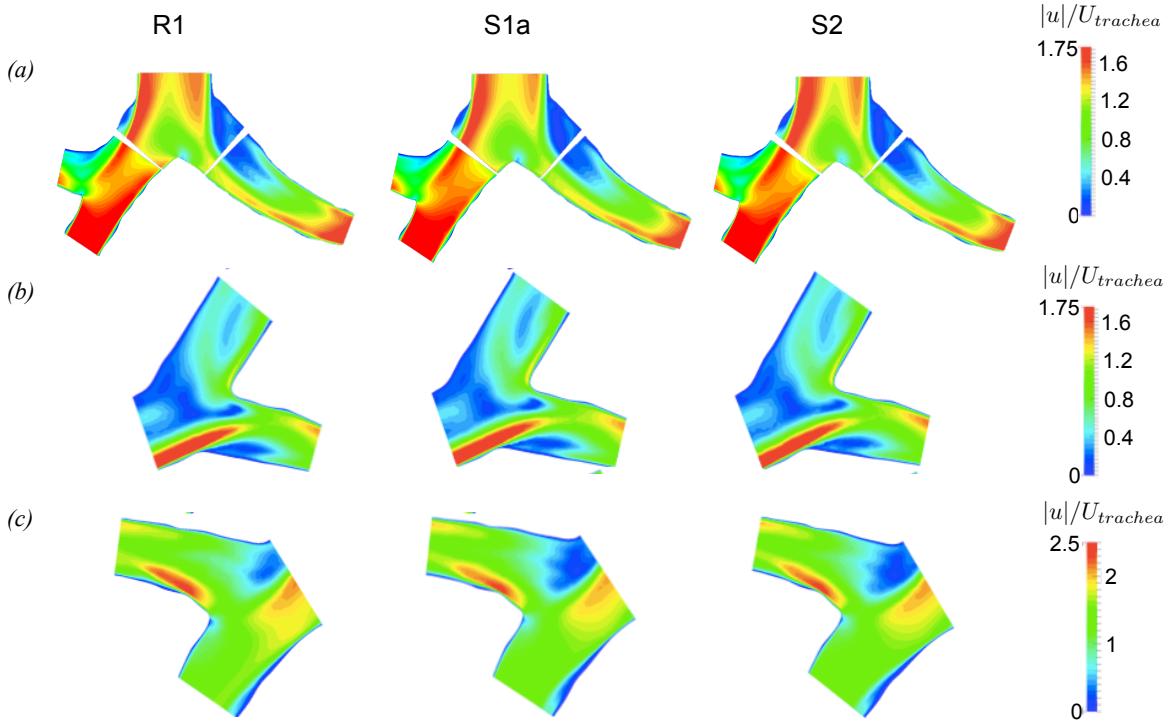

Figure 3: Contours of mean velocity magnitude in the tracheobronchial tree: (a) first bifurcation and main bronchi; (b) third generation bifurcation in the left lung; and (c) third generation bifurcation in the right lung.

deposition efficiency is evident. In the tracheobronchial tree however, for particles smaller than 6 microns, total deposition is largely unaffected by the mouth-throat geometry. The deposition of 6 micron particles is shown in more detail in figure 5. Beyond the trachea, similar deposition patterns are observed across all three geometries, and deposition fractions show similar values even at a localized level (figure 5b).

For particle sizes typically used in drug delivery applications, i.e. 1-5 microns, localized deposition in the central conducting airways is largely unaffected by the mouth-throat geometry and could therefore be predicted using a standard extrathoracic model. Future work will verify these findings in different tracheobronchial geometries and at higher flowrates, which are relevant to more specific drug delivery applications in the upper tracheobronchial region.

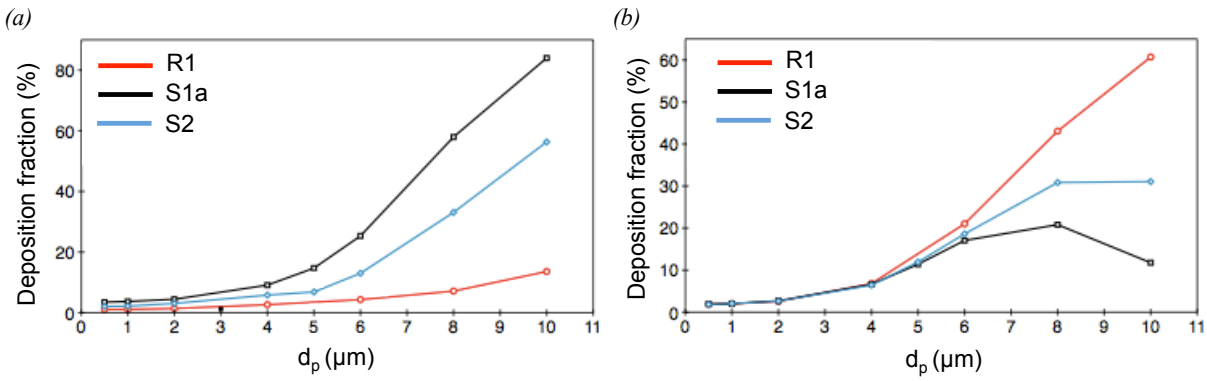

Figure 4: Total deposition: Deposition fraction versus particle size in (a) the extrathoracic airways; and (b) the tracheobronchial tree.

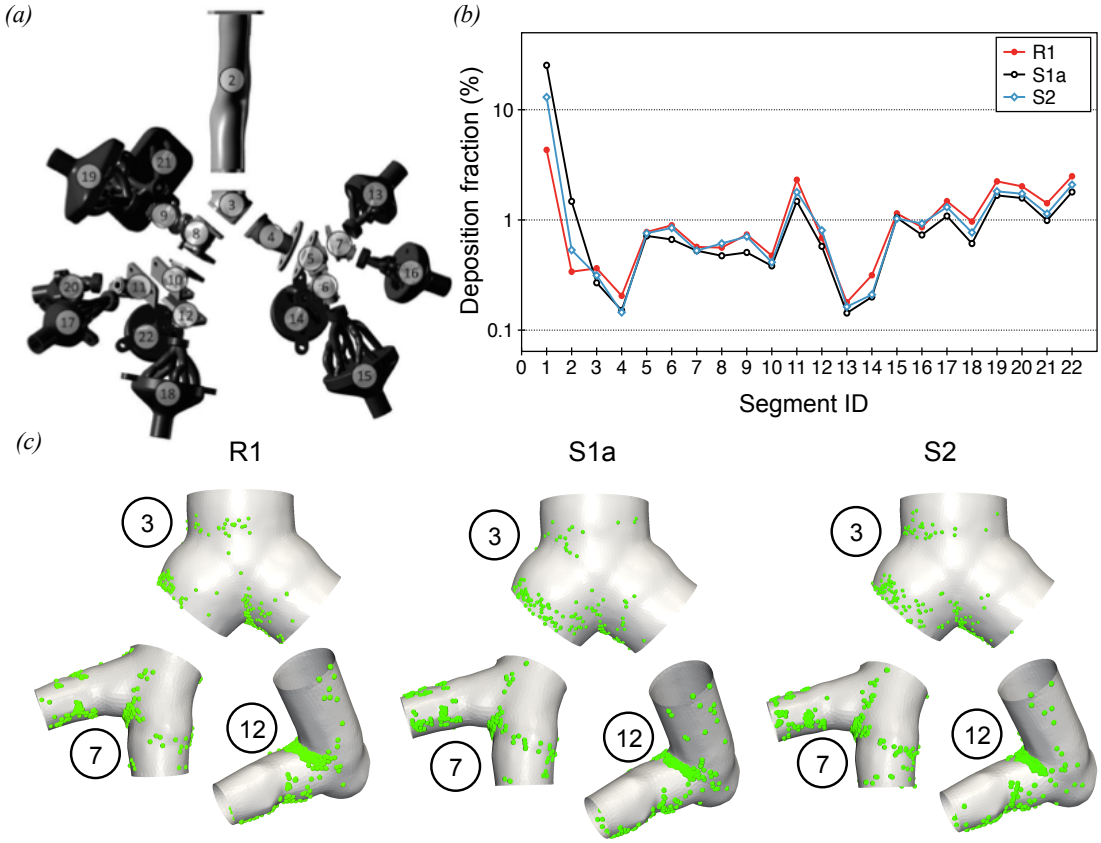

Figure 5: Localized deposition for $6\mu m$ particles: (a) segment numbering on tracheobronchial tree [4]; (b) deposition fraction versus segment ID; and (c) deposition patterns.

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