Numerical Modeling of Deposition of Inhaled Particles in Central Human Airways

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The objective of our research is to model physical and biological processes related to the development of adverse health effects, especially initiation of lung cancer in the central human airways following inhalation of aerosol particles. There is experimental evidence that bronchogenic carcinomas originate mainly at the dividing zone of large central airway bifurcations where primary hotspots of deposition have been found. However, current lung deposition models do not take into consideration the inhomogeneity of deposition within bronchial airways. The flow field within three-dimensional morphologically realistic geometries of airway generations 3–6 of the human tracheobronchial tree is computed by the FLUENT CFD (computational fluid dynamics) code for a wide range of flow rates during both inhalation and exhalation. A large number of particle trajectories has been simulated to determine the resulting deposition patterns, which were finally quantified by local deposition enhancement factors. Both the local airflow fields and deposition patterns strongly depend on the shape of the geometry, especially on the form of the carinal ridge. The computed enhancement factors indicate that local deposition densities may be two orders of magnitude higher than the average values for scanning on the surface by a 100 x 100 µm surface element, i.e. at approximately cellular dimensions.

Keywords: particle deposition; airway bifurcation; numerical modeling

INTRODUCTION

In clinical studies, local distributions of inhaled particulate matter have been implicated in causal relationships with lung carcinomas. Histological studies have noted highly localized pre-neoplastic and neoplastic lesions at the carinal regions of large bronchial airway bifurcations, especially at airway generations 3–5, indicating the preferential sites of tumor development caused by the inhalation of airborne particles. Despite the evidence, current lung deposition models do not take into consideration the inhomogeneity of deposition within the airways.

Pathogenic processes begin when the local quantity of deposited particles at the cellular level exceeds the normal protective capacity of the lung. The regional pattern of deposition of inhaled particles is often related to the topographical distribution of certain occupational lung diseases. Because the distribution of deposition is highly non-uniform, local doses at the cellular level may be much higher than the upper limit of the protective capacity even at low doses of air pollution.

In the present study, computed local deposition distributions of inhaled particles in idealized and morphologically realistic human airway bifurcation models are analyzed for different flow rates and particle sizes in airway generations 3–6. Then, for the quantification of the distribution of deposition, local deposition enhancement factors, defined as the ratio of local to average deposition densities, are computed by scanning along the surface of the bifurcation with pre-specified surface area elements.

COMPUTATION OF GEOMETRY AND AIRFLOW

In our simulations, we apply the three-dimensional idealized ‘narrow’ geometric models introduced by Balásházy and Hofmann (1993) and a mathematically developed version of the physiologically realistic bifurcation model of Heistracher and Hofmann (1995), which assures smooth transitions between the airways and may have a curved carina. Here, the
surface is described mathematically, and a computer program provides input data for the GAMBIT code, which is a geometry creator and mesh generator program of the FLUENT CFD (computational fluid dynamic) software package.

The described geometry must be meshed for the numerical solution of the fluid flow and particle trajectory equations. The structure and resolution of the mesh may strongly influence the results; therefore the construction of a well-structured computational grid is highly important. Here, an inhomogeneous mesh is generated which is denser where the velocity gradient is enhanced (near to the walls) and where relatively high local deposition density values can be expected (central region, inner part of daughter branches, upper and lower sides of the parent branch). Figure 1 shows the main characteristics of this mesh.

**FLOW FIELD CALCULATIONS**

Applying the above-described computational method, inspiratory and expiratory flow patterns were computed at idealized ('narrow') and physiologically realistic bifurcation geometries for a wide range of flow rates (10–120 l/min). The results show significant dependency on the shape of the geometry and on the flow rate during both inspiration and expiration. In the case of a wide curved carina, reverse flows may occur at the dividing spur which strongly effect the local distribution of deposition.

The local flow fields within a bifurcation are very sensitive to the entrance flow profile and, as a conse-

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**Fig. 1.** Structure of the constructed numerical mesh. The idealized 'narrow' bifurcation contains 160000 numerical cells.
Model of inhaled particle deposition in human airways

Sequence, local deposition patterns depend greatly on the entrance flow and particle profile. Therefore, flow fields were simulated in double and triple bifurcations. Velocity isolines in symmetric physiologically realistic triple bifurcations, which are in one plane configuration, are presented in Fig. 2. The figure demonstrates that the flow fields are quite different in the second and third bifurcations compared with those of the first branching.

DEPOSITION PATTERNS OF INHALED PARTICLES IN LARGE CENTRAL HUMAN AIRWAYS

Deposition experiments in bronchial airway models and lung casts are restricted to large bronchial airways. This region, for which only limited experimental data are available, coincides with the region in which the majority of bronchial carcinomas has been detected (Spencer, 1977). Furthermore, Martin and Jacobi (1972) observed enhanced deposition at airway branching sites only in the first six bronchial airway generations. Based on these experimental and pathological observations, the bronchial airway bifurcation models used in the present study correspond to airway generations 3–4 (segmental bronchi) in Weibel’s Model-A (Weibel, 1963). Analytical lung deposition models cannot describe the local inhomogeneities of deposition within airway bifurcations. In the present study, local deposition patterns in airway bifurcations are computed by a recently developed numerical particle deposition model (Balásházy and Hofmann, 2000). To quantify the inhomogeneity of predicted deposition patterns, the whole surface of the bifurcation is scanned by a pre-specified surface element. Local deposition enhancement factors are then determined as the ratio of local to average deposition densities. Distributions of enhancement factors and their corresponding maximum values are computed for physiologically realistic bifurcation geometries. Simulations are performed for the whole range of respirable particle sizes (1 nm–20 µm).

In the present study, inhaled particles are selected randomly by Monte Carlo techniques at the inlet of the parent branch in accordance with the assumed parabolic inlet air velocity profile. Aerosol particle trajectories are then simulated by considering the concomitant effects of Brownian motion, inertial impaction, gravitational settling and interception. Having simulated a large number of particle trajectories, deposition patterns and related deposition efficiencies are determined.

Fig. 2. Velocity isolines in a set of symmetric physiologically realistic triple bifurcations, in one-plane configuration. Linear dimensions correspond to airway generations 3–6 (Weibel Mode-A), 30 l/min minute volume.
Deposition patterns of 0.01, 1 and 10 µm diameter unit density particles are presented in Fig. 3 for a 30 l/min minute volume breathing condition. For the ultrafine and 1 µm particles, the deposition mechanisms are not strong enough against the reverse flows at the curved carina. This is why there is no deposition exactly at the carinal ridge in these cases. However, for the 10 µm particles, the impaction is strong enough to cause deposition at the carinal ridge. Deposition patterns are distinctly inhomogeneous in all the three cases, forming hotspots in the central zone or in the inner sides of the daughter branches downstream of the carina.

For the quantification of inhomogeneities of deposition patterns, local deposition enhancement factors are computed by scanning along the surface of the bifurcation with a pre-specified surface element (patch). Details of this method are presented in Balásházy and Hofmann (2000).

From a microdosimetric point of view, the patch should have a reasonable size. Since the presence of several neighboring biological cells seems to be necessary for the development of a tumor (Crawford-Brown and Hofmann, 1996), a scanning patch size of ~100 x 100 µm (i.e. ~10 x 10 epithelial cells) has been selected here.

Figure 4 displays the maximum local deposition enhancement factors as a function of particle size over the whole range of respirable particle sizes at a high flow rate (60 l/min), airway generations 3–4 (Weibel Model-A), 0.1 x 0.1 mm scanning patch size.

**SUMMARY AND CONCLUSIONS**

Computed air velocity fields and particle deposition patterns demonstrate the significant role of well-constructed meshes, realistic geometry and flow calculations for particle deposition computations. In the case of inspiration, areas of enhanced deposition are formed primarily in the vicinity of the carinal ridge or at the inner sides of the daughter branches. The sizes of these deposition hotspots depend on bifurcation geometry, flow rate and particle size. The computed local deposition enhancement factors exhibit strong local inhomogeneities for all respirable particle sizes. The computed maximum enhancement factors are as high as several hundreds, suggesting that epithelial cells located at these sites will receive massive doses relative to the assumption of a uniform nuclide distribution. Since the prevalent philosophy of inhalation risk assessment is based upon the assumption of a uniform particle deposition pattern, the incorporation of deposition enhancement factors within airway bifurcations will provide more realistic estimates of computed carcinogenic risk. The significance of the inhomogeneity of deposition increases further if we consider the impaired clearance at the carinal ridges of the branchings.
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REFERENCES


