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A theoretical approach to the deposition and clearance of fibers with variable size in the human respiratory tract

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ABSTRACT

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Keywords: Fiber Monte Carlo model Aerodynamic diameter Lung clearance Multicompartment model In the study presented here, a mathematical approach for the deposition and clearance of rigid and chemically stable fibers in the human respiratory tract (HRT) is described in detail. For the simulation of fiber transport and deposition in lung airways an advanced concept of the aerodynamic diameter is applied to a stochastic lung model with individual particle trajectories computed according to a random walk algorithm. Interception of fibrous material at airway bifurcations is considered by implementation of correction factors obtained from previously published numerical approaches to fiber deposition in short bronchial sequences. Fiber clearance is simulated on the basis of a multicompartment model, within which separate clearance scenarios are assumed for the alveolar, bronchiolar, and bronchial lung region and evacuation of fibrous material commonly takes place via the airway and extrathoracic path to the gastrointestinal tract (GIT) or via the transepithelial path to the lymph nodes and blood vessels.

Deposition of fibrous particles in the HRT is controlled by the fiber aspect ratio β in as much as particles with diameters <0.1 µm deposit less effectively with increasing β , while larger particles exhibit a positive correlation between their deposition efficiencies and β . A change from sitting to light-work breathing conditions causes only insignificant modifications of total fiber deposition in the HRT, whereas alveolar and, above all, tubular deposition of fibrous particles with a diameter ≥ 0.1 µm are affected remarkably. For these particles enhancement of the inhalative flow rate results in an increase of the extrathoracic and bronchial deposition fractions. Concerning the clearance of fibers from the HRT, 24-h retention is noticeably influenced by β and, not less important, by the preferential deposition sites of the simulated particles. The significance of β with respect to particle size may be regarded as similar to that determined for the deposition scenarios, while breathing conditions do not have a valuable effect on clearance.

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1. Introduction

1.1. General aspects

In the past decades deposition of aerosol particles in the human respiratory tract (HRT) has attracted considerable scientific attention due to its significance in occupational health. Numerous studies on the behaviour of spherical particles in bronchial airways could find an unequivocal evidence for the dependence of health effects on the site of preferential particle deposition as well as the physical properties of the inhaled particulate matter [1–3]. A highly important role concerning the particle-induced generation of lung diseases has been attributed to fibers which per definition are elongated particles with approximately cylindrical shape, a length exceeding 5 μ m, and an aspect ratio (i.e. the ratio of the

length to the diameter) greater than 3 [4,5]. As exhibited by a limited number of experiments dealing with the deposition of fibrous material in bronchial airway casts [6-8], principal factors affecting the deposition patterns and efficiencies of fibers include the aerodynamic properties of these particles, expressed by the aerodynamic diameter, and the nature of convective flow in single airway bifurcations. Studies already carried out in the 1970s have underlined the important fact that the aerodynamic diameter of a fiber chiefly depends on its cylindrical diameter but is only slightly influenced by its length [9]. Contrary to spheres there are four main mechanisms controlling the deposition of fibers in the HRT, namely inertial impaction, interception, sedimentation, and diffusion (Fig. 1). By some authors also a mechanism called electrostatic precipitation is associated with fiber deposition [10], but due to the non-availability of experimental data the role of this deposition force is not quite clear hitherto. Inertial impaction and interception mainly occur in the larger bronchial airways, where flow velocities are enhanced and fibers are propelled out of bending flow streamlines due to their momentum. While impaction commonly increases with the aerodynamic diameter, interception is dependent upon local Stokes

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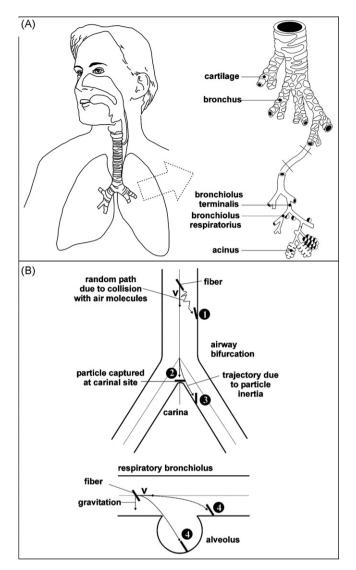


Fig. 1. (A) Architecture of the tracheobronchial tree and the pulmonary region responsible for the O_2 - CO_2 gas exchange. (B) Mechanisms of fiber deposition in proximal and terminal (alveolated) airways of the HRT: (1) Brownian diffusion, (2) interception, (3) inertial impaction, (4) gravitational settling (sedimentation). Abbreviation: v – particle velocity vector.

number as well as fiber length, i.e. the longer a fiber, the higher its deposition by interception. Sedimentation, on the other side, is favoured by low flow velocity, therefore preferentially occurring in small airways. Diffusion describes the collisions between air molecules and airborne fibers and becomes highly important for particles smaller than 0.5 µm. Experiments, where rats were exposed to an atmosphere including variably sized glass fibers for several hours, indicated that fibers exceeding a length of 10 µm are mostly deposited in the extrathoracic region and penetrability of fibrous material into the rat lung drops sharply with aerodynamic diameter above 2 µm [11,12]. More current experiments using replica of the extrathoracic region and the proximal airways of the HRT mainly confirmed these previous findings in rats, but also considered the possibility of a penetration of long fibers into deeper regions of the lung in the case of low flow velocities and aerodynamic diameters around $1 \mu m [1,5,13]$.

The clearance of fibrous particles deposited in the HRT depends on both the site of deposition and the physical properties of the fibers. Fibrous material accumulated in the tracheobronchial airways is mainly transported on the surface of the mucus layer towards the larynx, where it is swallowed and passes into the gastrointestinal tract (GIT) [10]. Besides this mucociliary clearance taking place within the first 24h after exposure to the fibrous aerosol, a part of the material deposited in the airway tubes is also subject to slow clearance mechanisms including the uptake of fibers by airway macrophages, epithelial transcytosis, as well as the temporary storage of the particles in the periciliary liquid layer and subsequent recapture by the mucus layer (Fig. 2) [14,15]. According to several inhalation experiments [16] the half-time of this slow bronchial clearance may vary between several days and weeks. Fibers deposited in small nonciliated airways and alveoli are affected by a strongly increased retention, and clearance from these distal deposition sites mainly takes place by translocation and disintegration [10]. Translocation represents the movement of an intact fiber either along the epithelial surface towards the terminal bronchioles or into and through the epithelium towards the interstitial tissue. The transport of the fibrous material is usually realized due to its ingestion by alveolar macrophages but smaller fibers may be also dislocated on the surfactant layer [10]. Disintegration, on the other hand, refers to the subdivision of a fiber into smaller segments and the dissolution of specific fiber components, whereby both phenomena are highly dependent upon the biodegradability of the material. Asbestos and man-made mineral fibers are practically not clearable by disintegration, whereas glass fibers exhibit a measurable clearance by this mechanism which negatively correlates with the length of the particles [17,18]. In general, alveolar clearance half-times of fibers smaller than 5 µm in length range from 100 to 150 days [10,16].

1.2. Modelling fiber deposition and clearance in the HRT – state of the art

Deposition models are highly appropriate for the detailed prediction of particle concentrations in specific regions of the HRT, where the experimental measurement is not feasible. Due to this advantage, mathematical approaches describing the behaviour of particles in the lung have become essential tools in medical science meanwhile. Concerning the deposition of fibers (expressed by spheres with respective aerodynamic diameters) in the HRT, preliminary theoretical models date back to the 1970s and subdivide the respiratory compartment into three distinct parts (head, tracheobronchial, and pulmonary region) [19,20]. Later approaches assume a single-path, dichotomous lung geometry, where inhaled particles are transported along an average airway trajectory [21–23]. These deposition models are limited to the prediction of regional fiber deposition in the HRT but are not able to generate reliable information regarding the distribution of particulate matter within a selected lung lobe or a single airway generation. This significant drawback was solved by the development of multiplepath deposition models considering a nonsymmetric, more realistic structure of the lung and thus allowing more site-specific predictions [24]. Currently, results of theoretical approaches to fiber deposition in single airway bifurcations were implemented in stochastic deposition models of the entire lung, thereby enabling the computation of rather precise generation-by-generation deposition plots [25]. Precise predictions of fiber deposition in the lungs are to a high extent based on respective numerical simulations investigating the behaviour of nonspherical particles in single airway bifurcations or small bifurcation sequences [6,7,37,38,41–43].

Mathematical models dealing with the clearance of inhaled particulate matter deposited in the HRT are so far limited to spherical insoluble particles, whereby various approaches to mucociliary clearance as well as slow bronchial and alveolar clearance mechanisms have been introduced [16,26–29]. Regarding the clearance of fibrous material, the human respiratory tract model (HRTM) introduced by the International Commission on Radiation Protection Download English Version:

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