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Research article

ASSESSING SPATIAL DISTRIBUTION OF SITES WITH A RISK OF DEVELOPING BRONCHOPULMONARY PATHOLOGY BASED ON MATHEMATICAL MODELING OF AIR-DUST FLOWS IN THE HUMAN AIRWAYS AND LUNGS

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The article continues the series of studies that describe a mathematical model of the respiratory system developed by the authors and dwell on its use in practice to assess and predict risks for human health caused by negative effects of airborne environmental factors. The mathematical model includes several submodels that describe how an air mixture flows in the air-conducting zone (it includes the nasal cavity, pharynx, larynx, trachea and five generations of bronchi) and the lungs approximated with a continuous two-phase elastically deformed porous medium. The mathematical model is described by using continuum mechanics relationships. It is realized numerically by using engineering software (to investigate processes in the airways) and a self-developed set of programs (to simulate processes in the lungs). Numeric modeling of a non-stationary flow of an air-dust mixture is performed for a personalized three-dimensional geometry of the human respiratory system based on CT-scans.

The study provides calculated lines of velocity for a flow of particles in inhaled air in the airways. We have quantified shares of deposited articles with their diameters being 10 µm, 2.5 µm, and 1 µm (PM_{10}, $PM_{2,5}$, PM_1) in the airways; the study also provides trajectories of particulate matter. As particles become smaller and lighter, the share of deposited ones goes down in the airways and grows in the lungs. According to numeric modeling, most (more than 95 %) large particles (PM_{10}) are deposited in the nasal cavity, pharynx and larynx; small particles are able to reach the lower airways and bronchi (most particles that reach the lungs penetrate lobar bronchi predominantly in the right lung). Sites with maximum health risks in the human lungs have been identified relying on assessing changes in an air phase mass within the respiration cycle; they are located in lower lobes of the lungs. When contacting airway walls, particles are able to be deposited and accumulate over time producing irritating, toxic and fibrogenic effects; they can thus cause and / or exacerbate pathological states.

Keywords: *mathematical model, respiratory system, air-dust mixture, particle sedimentation, risk sites, human health, numeric modeling, personalized model.*

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Contemporary Russian and foreign studies provide abundant evidence of negative effects produced on human health by ambient air pollutants such as chemicals and particulate matter with various disperse and component structure[1] [1]. Chemicals introduced by inhalation have toxic effects on the systems and organs in the human body [2, 3], the respiratory system included [4, 5].

Particulate matter, depending on a size, composure, shape and a deposition site can cause and / or exacerbate bronchopulmonary pathology at different sites [6, 7]. Chemicals that are present on particle surfaces are able to enhance their aggressive, toxic and irritating properties [8–13].

Most large particles (PM_{10} and larger) are deposited in the upper airway mucosa whereas $PM_{2.5}$ and nano-sized particles are able to reach alveoli in the lungs[2] [14–19]. Fine solid particles are able to penetrate through the blood-gas barrier and enter the circulatory system [20, 21], translocate to lymph nodes [22, 23]; carried by blood and lymph, such particles can translocate to various organs and tissues [24].

Long-term accumulation of solid dust particles in the human lungs can cause pneumoconiosis[2]. The disease has a particular feature; namely, it typically involves developing pneumosclerosis when the non-elastic connective tissue grows in the lungs and replaces the lung parenchyma. As a result, proper respiration is disrupted, the lung tissue permeability is reduced, the alveolar-capillary membranes become thicker and flatter, and an effective gas exchange area decreases.

The existing laboratory and instrumental methods[3] make it possible to perform a complex medical check-up of a patient, obtain an objective picture of the current health status, put a correct diagnosis and select a treatment scheme. Despite high informative value of medical diagnostic techniques and their invaluable utility for solving a wide range of tasks, they are not eligible for predicting a future health status and cannot be used to assess influence of harmful health risk factors.

At present, development of three-dimensional personalized models seems a promising technique. Such models allow detailed description of heterogeneous spatial processes occurring in the human body [25–30]. The authors have been developing a mathematical model that describes the human respiratory system as a tool for quantifying introduction of airborne chemical pollutants into the body and predicting their subsequent effects on health (the respiratory organs included) as well as for describing respiration in a healthy body and in a case a disease is already present in it [31].

The present study focuses on numeric modeling of spatial distribution of air-dust flows and sites with maximum risks of adverse effects on the human respiratory organs.

Materials and methods. The mathematical model that is being developed by the authors depicts the respiratory system as a complex of the rigid air-conducting zone (airways; colored blue in Figure 1) and elastically deformed respiratory zone (the lungs that contain small airways and alveoli, colored green in Figure 1). The airways include the nasal cavity, pharynx, larynx, trachea, and five generations of bronchi (Figure 1). The three-dimensional geometry of the airways

[1] WHO global air quality guidelines: Particulate matter ($PM_{2.5}$ and PM_{10}), ozone, nitrogen dioxide, sulfur dioxide and carbon monoxide; approved by the Guidelines Review Committee. Geneva, World Health Organization, 2021.

[2] Katsnel'son B.A., Alekseeva O.G., Privalova L.I., Polzik E.V. Pnevmokoniozy: patogenez i biologicheskaya profilaktika [Pneumoconiosis: pathogenesis and biological prevention]. In: V.N. Chukanov ed. Ekaterinburg, RAS Urals Branch Publ., 1995, 324 p. (in Russian).

[3] Grebenev A.L. Propedevtika vnutrennikh boleznei [Propedeutics of internal diseases]: manual, 5th ed., reviewed and expanded. Moscow, Meditsina Publ., 2001, 592 p. (in Russian).

and lungs was built based on CT-scans; the building technology was described in detail in [18, 19]. Exits from the bronchi are entries to the lungs; data exchange between the submodels is performed by using boundary conditions.

Generally, air is a multi-phase and multicomponent mixture of gases and dust particles with various disperse structure. The walls of the upper (and large lower) airways contain rigid cartilaginous tissue that prevents them from getting narrow (and expanding) easily; therefore, they are assumed to be rigid. Airflow in the rigid airways is described with fluid and gas mechanics equations; the task statement for airflow was described in detail in [18, 19]. Based on this statement, we investigated airflows and deposition of dust particles with various sizes in the nasal cavity [18] and lower airways (from the trachea to the fifth generation of bronchi) [19].

The human lungs go through cyclic elastic deformations during respiration. Typical lungs of an adult person contain approximately 600–700 million alveoli as well as connecting channels between them[4]. It is very difficult to model each individual channel and alveolus in the lungs. The developed mathematical model of the respiratory system describes the upper and large lower airways in detail whereas the human lungs that are formed from smaller airways and alveoli with air inside them are modeled as a continuous two-phase cyclically elastically deformed saturated porous medium [31]. Lung tissue is the first phase, which is described with a model of a deformed solid body; a gas that fills in the porous space is the second phase. Relative motion of the air phase in the lung porous medium is described using the filtration theory[5].

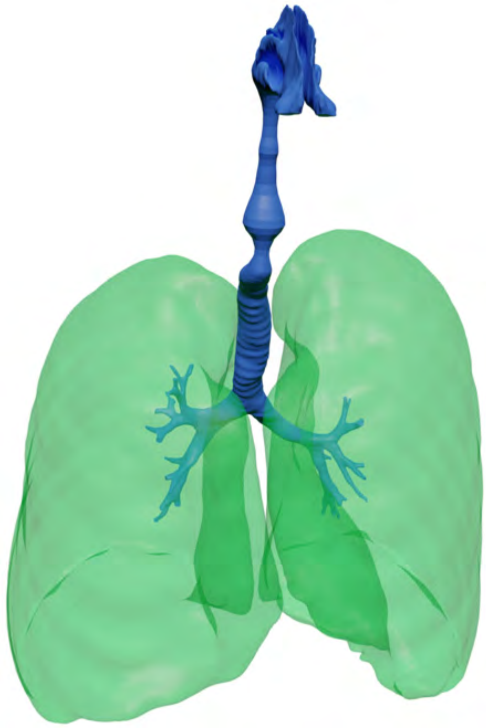

Figure 1. The model of the respiratory system including the air-conducting zone (blue color) and lungs (green color)

An algorithm for implementing the mathematical model of the respiratory system made of submodels that describe airflow in the human airways and lungs, considering data exchange between these submodels, involves sequential performance of the following stages.

The submodel of the lungs (that involves setting boundary conditions – the law for the lung wall motion) identifies changes in a shape of the lungs, pressure distribution in the lungs, air mixture flows, as well as determines the law of changes in pressure at the exits from the bronchi during the respiratory cycle. Air mixture flows in the airways from the nasal cavity to the 5th generation of bronchi are investigated by using boundary conditions (parameters, component and disperse structure of an inhaled air mixture at the entry

[4] Borzyak E.I., Volkova L.I., Dobrovol'skaya E.A., Revazov V.S., Sapin M.R. Anatomiya cheloveka [Human anatomy]: in 2 volumes. In: M.R. Sapin ed. Moscow, Meditsina Publ., 1993, vol. 1, 544 p. (in Russian).

[5] Leibenzon L.S. Dvizhenie prirodnykh zhidkostei i gazov v poristoi srede [Motion of natural fluids and gases in a porous medium]. Moscow; Leningrad, Gostechizdat Publ., 1947, 244 p. (in Russian); Barenblatt G.I., Entov V.M., Ryzhik V.M. Teoriya nestatsionarnoi fil'tratsii zhidkosti i gaza [The theory of non-stationary fluid and gas filtration]. Moscow, Nedra Publ., 1972, 288 p. (in Russian).

as well as the law of changes in pressure at the exits from the bronchi) and the submodel describing airflows in the airways. This study also involved assessing deposition of dust particles with various disperse structure in the airways, establishing primary sites for particle deposition, estimating shares of particles able to reach the lower airways and alveoli in the lungs, and determining an air mixture composition at the entry to the lungs.

Preliminary calculations revealed that large particles able to influence airflow tended to be deposited in the upper airways; finest particles that moved along with airflow were able to reach the lungs. Sites with the highest risks in the human lungs were identified relying on the lung submodel and information about a composition of an air phase that reached the lungs. The greatest changes in a mass of an air mixture during the respiratory cycle occur in such zones.

The mathematical statement of the task of an air mixture flow in the respiratory system is described by using continuum mechanics relationships. Ansys CFX, a computational fluid dynamics (CFD) software program, was applied to investigate processes in the airways; processes in the lungs were investigated using a self-developed software package. Data exchange between the submodels of the airways and lungs was performed by using boundary conditions.

Results and discussion. Numeric modeling of a non-stationary flow of an air-dust mixture in the human respiratory system was performed using a personalized three-dimensional geometry of the human airways and lungs based on CT-scans (see Figure 1) of an adult person without any respiratory pathology and conforming to the physiological norms.

We considered the periodical (sinusoidal) law of the wall with a respiratory period of four seconds[6] typical for calm respiration. The moment 'the end of exhalation – transition to inhalation' is considered the initial state of the respiratory cycle. At this moment, particle velocity in inhaled air is assumed to be equal to 0; there is no pressure difference in the lungs and airways (at the entry to the lungs); air pressure in the lungs is equal to atmospheric pressure.

Inhaled air volume (the breath volume) is 0.79 l during the respiratory cycle within the considered scenario; respiratory excursion (the difference between the chest circumference during inhalation and exhalation) is 1.9 %; the highest shift of the base along the vertical coordinate is 0.0155 m for the left lung and 0.0146 m for the right lung. These parameters correspond to conventional physiological data typical for calm respiration of an adult person.

Preliminary calculations established that a share of particles (with a specific size) deposited in the airways was constant and did not depend on an input concentration. A share of deposited particles depended on their size and mass (density). We considered motion and deposition of particles sized 10 μm, 2.5 μm, and 1 μm and density equal to 2700 kg/m^3.

The respiratory cycle lasts for 4 seconds; the interval (0; 2) sec corresponds to inhalation; (2; 4) sec, exhalation. Figures 2 and 3 show the velocity vectors for motion of particles in the two-phase porous lung medium in the middle of inhalation (t = 1 sec) (Figure 2) and in the middle of exhalation (t = 3 sec) (Figure 3) in axonometry. Figures 4 and 5 show movements of particles in the two-phase porous lung medium at the inhalation maximum (t = 2 sec) in axonometry (Figure 4) and in frontal plane (Figure 5).

The lungs are located in the thoracic cavity (each in its own pleura) and are separated from each other by the mediastinum. The lungs contact the diaphragm, the main respiratory muscle, at the bottom and the thoracic walls at their sides.

[6] West J.B. Respiratory Physiology – the Essentials. In: N.N. Alipov translation; A.M. Genin ed. Moscow, Mir Publ., 1988, 200 p. (in Russian).

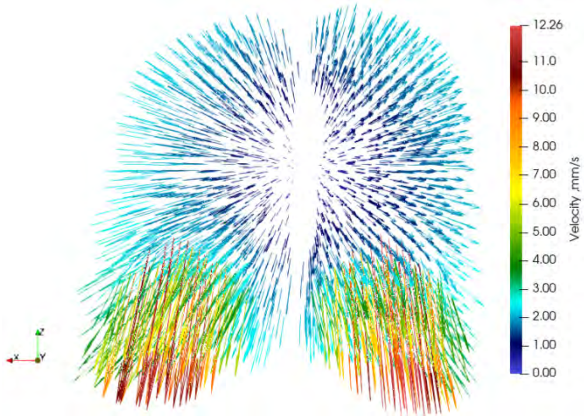

Figure 2. The velocity vectors for motion of particles in the two-phase porous lung medium in the middle of inhalation (frontal view)

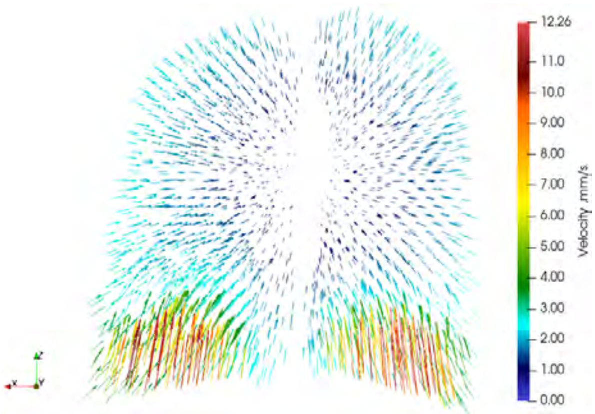

Figure 3. The velocity vectors for motion of particles in the two-phase porous lung medium in the middle of exhalation (frontal view)

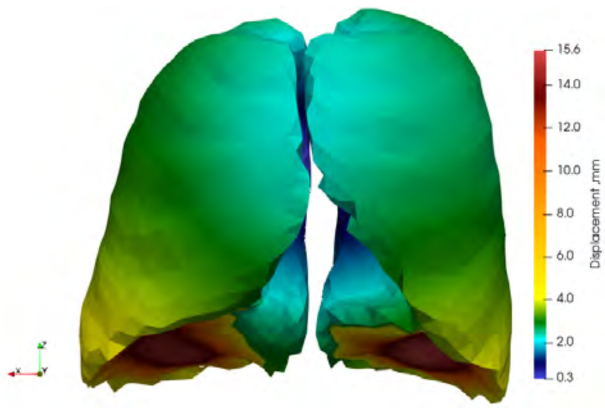

Figure 4. Movements of particles in the two-phase porous lung medium at the inhalation maximum (frontal view)

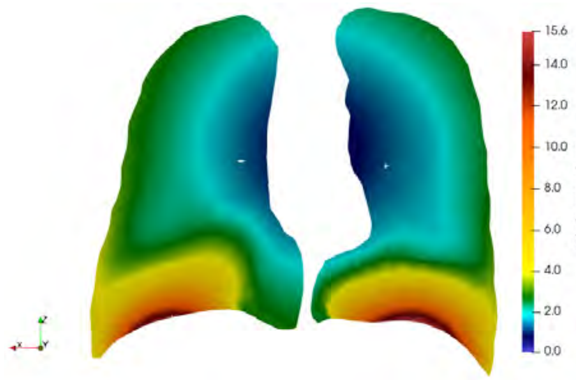

Figure 5. Movements of particles in the two-phase porous lung medium at the inhalation maximum (in frontal plane, frontal view)

The highest velocity of particles in the two-phase lung medium (see Figures 2 and 3) as well as the longest movements (Figures 4 and 5) are observed along the vertical coordinate at the points located at the base of lung above the diaphragm. The bases (lower boundaries) of lung that contact the diaphragm are cupola-shaped. During respiration, the diaphragm (as well as the base of lung) move downwards and the greatest shift appears at the cupola top. The bases of lungs flatten out at the end of inhalation.

The areas where the main bronchi enter the lungs (*'the lung hilum'*), which are attached to the rigid main bronchi, have the smallest shift. The lung walls that contact the thorax expand / shrink during the respiratory cycle. The size of lung wall expansion is uneven depending on the vertical coordinate; the smallest expansion occurs at the top of lung and the expansion size grows closer to the base of lung.

Uneven change in the volume of lungs approximated by the two-phase porous medium leads to uneven changes in pressure in the lung volume (Figures 6 and 7). Figure 6 shows the field of gas phase pressure in the human lungs during inhalation (at the moment t = 1.5 sec after the respiratory cycle starts); Figure 7, during exhalation (at the moment t = 2.5 sec after the respiratory cycle starts). The lung areas with the greatest changes in the volume tend to have the greatest pressure

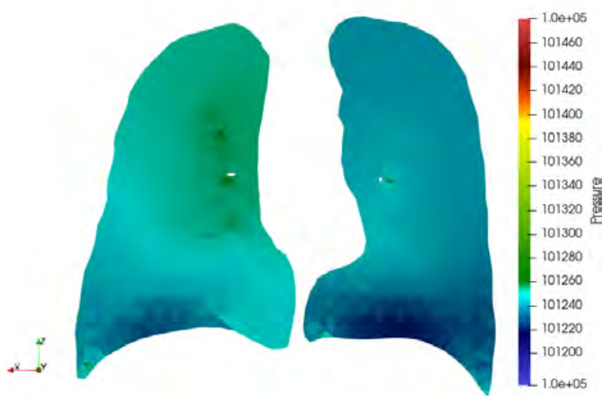

Figure 6. The field of gas phase pressure in the human lungs during inhalation (at the moment *t* = 1.5 sec after the respiratory cycle starts) (in frontal plane, frontal view)

Figure 7. The field of gas phase pressure in the human lungs during exhalation (at the moment *t* = 2.5 sec after the respiratory cycle starts) (in frontal plane, frontal view)

gradients (colored dark blue in Figure 6 and dark red in Figure 7). Changes in pressure make the air mixture move (from an area with high pressure to an area with low pressure).

The laws of changes in pressure at the exits from the bronchi during the respiratory cycle were determined based on numeric modeling of spatial distribution of air phase parameters. These laws were then used as boundary conditions in the submodel that describes airflows in the airways.

Use of the submodel that describes an air mixture flow in the air-conducting zone made it possible to establish velocities of the carrier air phase flow and motion paths for particles (with various sizes) in the dust phase; to quantify deposition of particles with various sizes in the airways and identify particles able to reach the lower airways and lung alveoli.

Figure 8 provides the calculated velocity lines and field for particles in inhaled air in the airway section from the nasal cavity to the 5th generation of bronchi in the middle of inhalation. The greatest airflow velocities are observed in the oral pharynx and larynx (the glottis), which is due to the channels becoming narrower in this section of the airways. Airflows are turbulent in the nasal cavity and laryngopharynx due to their anatomical complexity. An airflow is transitional turbulent in its essence; the *k*-ω model was used to describe airflow turbulence.

Figures 9–11 show the motion paths of solid particles PM_{10}, $PM_{2.5}$ and PM_1 in the airways during inhalation. Ability to be deposited in the airways differs depending on particle sizes and mass. As a size and mass go down, a share of deposited particles also declines. Particles sized 10 μm and bigger are deposited effectively in the first sections of the airways (the nasal cavity, pharynx and larynx) due to inertia (Figure 9). Particles sized 2.5 μm and smaller are able to reach the human lungs (Figures 10 and 11). Particles are deposited effectively in the nasal cavity due to its anatomic complexity; in areas where the airways become narrower (the oral pharynx and larynx); in areas where the airways bifurcate.

According to numeric modeling, most particles that reach the lungs penetrate lobar bronchi predominantly in the right lung. When dust particles penetrate the airways, they are able to stimulate development of various bronchopulmonary diseases, pneumoconiosis included. When silicosis is diagnosed, x-ray images show enhancement and deformations of a lung pattern at its initial stage; as a rule, these changes are symmetrical but sometimes more

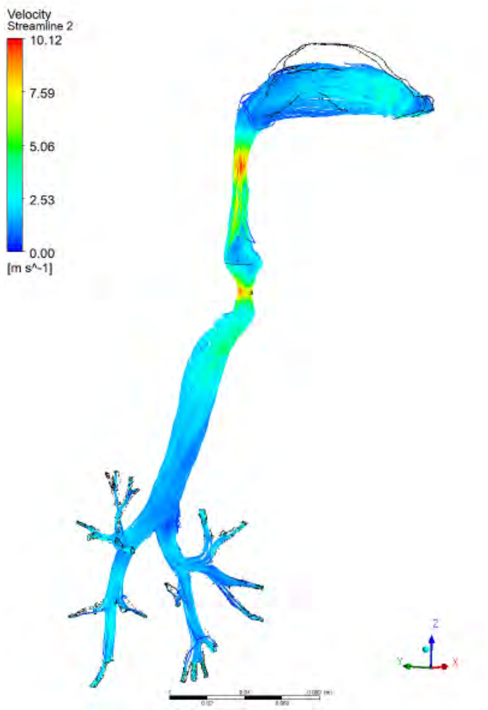

Figure 8. The air velocity lines and field
in the airways in the middle of inhalation

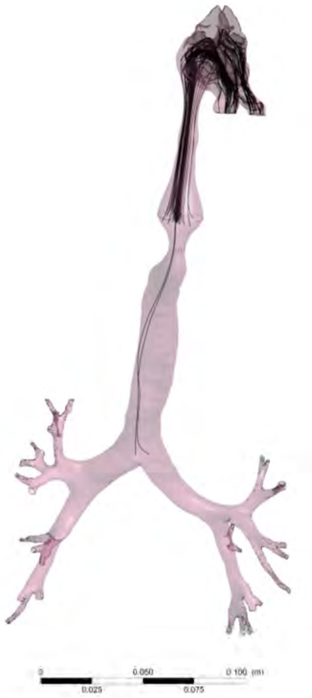

Figure 9. The motion paths of solid particles
sized 10 µm in the airways

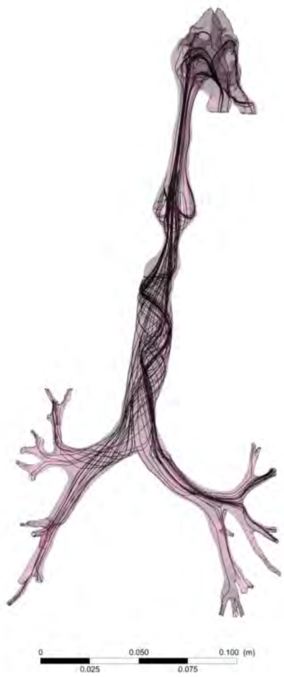

Figure 10. The motion paths of solid particles
sized 2.5 µm in the airways

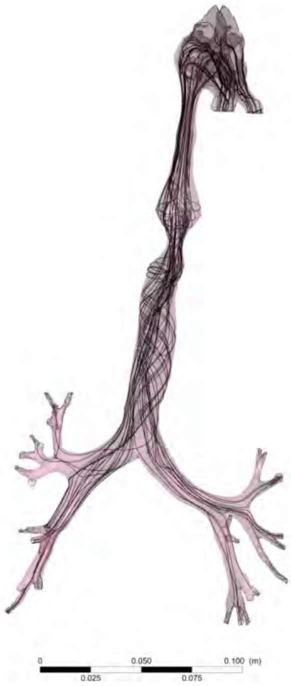

Figure 11. The motion paths of solid particles
sized 1 µm in the airways

apparent in the right lung and predominantly localized in the middle and lower lobes[7] [32], which is in line with our findings obtained by numeric modeling.

Within this research, we performed numeric modeling of a dusty air flow in the airway section from the nasal cavity to the 5th generation of bronchi (using a finite element mesh made of 582 thousand elements). As a result, we established that 95.12 % of particles sized 10 μm, 65.55 % of particles sized 2.5 μm, and 61.43 % of particles sized 1 μm were deposited in this section under calm respiration. Thirty four point forty five percent of particles sized 2.5 μm and 38.57 % of particles sized 1 μm were able to reach the lower airways and lungs and be deposited in them. These calculations are consistent with a field experiment accomplished by experts from the Federal Scientific Center for Medical and Preventive Health Risk Management Technologies with its aim to investigate regularities of distribution of airborne dust particles in the human airways [33].

Fine fractions move along with an airflow and penetrate to the maximum depth of the respiratory system; accordingly, an area with their greatest deposition can be found in lung alveoli. Particles contact the walls and thus are able to be deposited, accumulate over time and cause development and / or exacerbation of pathologies.

It is advisable to identify sites in the human lungs where the highest health risks occur relying on changes in air masses during the respiratory cycle. The bigger a mass of an air mixture enters a section in the lung tissue during respiration, the higher likelihood exists for particles to be deposited in this section. Figure 12 provides the ratio between the air mass in the human lungs at the moment of their greatest expansion and their initial state.

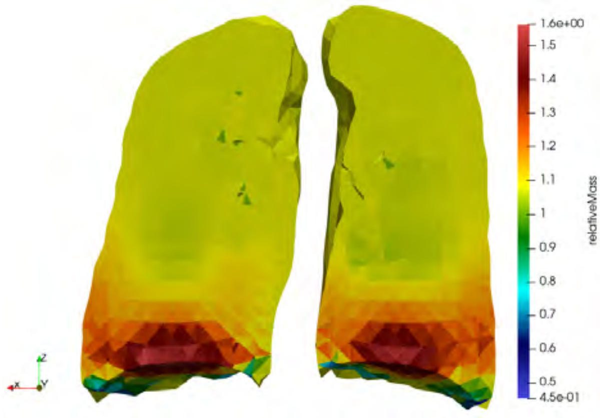

Figure 12. The ratio between the air mass in the human lungs at the moment of their greatest expansion and their initial state

The greatest changes in the air mass occur in the lower lobes of the lungs; differences reach 1.6 times against their initial state. The results are quite similar for the right and left lung. Still, we should bear in mind that the use of the submodel describing an air mixture flow in the airways established that more particles were able to penetrate the right lung than the left one. Accordingly, we can expect more negative outcomes in the right lung. These findings are also in line with the established medical fact that pathological changes in the lungs at the initial stages of silicosis first occur in the lower lobes (as a rule, these changes are symmetrical but sometimes more apparent in the right lung)[8] [32].

Particulate matter contacts the airway walls and thereby causes negative outcomes in the respiratory system (both upper and large

[7] Kostyuk I.F., Kapustnik V.A., Brykallin V.P., Kalmykov A.A. Professional'nye bolezni [Occupational diseases]: manual. Kharkov, Kharkov State Medical University Publ., 2007, 155 p. (in Russian); Artemova L.V., Baskova N.V., Burmistrova T.B., Buryakina E.A., Bukhtiyarov I.V., Bushmanov A.Yu., Vasilieva O.S., Vlasov V.G. [et al.]. Federal clinical recommendations on diagnosis, treatment and prevention of pneumoconiosis. In: N.F. Izmerov ed. Moscow, 2014, 46 p. (in Russian).

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lower airways and smaller ones as well as lung alveoli). Negative outcomes may vary depending on a component structure and size of particles, duration of exposure, and individual peculiarities of a given body. A comprehensive review by L.M. Fathudinova and others [34] analyzes and summarizes findings reported in Russian and foreign research works over 1990–2021 that focus on effects of fine-dispersed particles as ambient air pollutants on population health. The review provides an extensive list of negative responses, both in the respiratory organs and other organs and systems in the human body (the circulatory system included), as well as potential pathological pathways. 'Potential pathological pathways of exposure to particular matter include oxidative stress, inflammations, disrupted autonomic regulation and heart rate, particles penetrating through the alveolar-capillary barrier into the vessels together with damage to endothelium and blood clot formation, and genotoxicity' [34, p. 862]. The authors also note that pathways and effects of chronic long-term exposure to dust particles have still not been investigated completely. Identifying sites with high risks of negative outcomes relying on numeric modeling of respiration provides a solid basis for predicting risks of negative health outcomes.

Conclusion. This study presents a mathematical model that describes an air mixture flow in the human airways and lungs. The mathematical model is described by using continuum mechanics relationships. Personalized three-dimensional geometry of the human airways and lungs is based on CT-scans. Spatial distribution of air-dust flows in various sections of the respiratory system was investigated relying on numeric modeling (using engineering software and a self-developed software package); in addition to that, areas where dust particles would be deposited were established. These areas are sites with elevated risks of negative health outcomes in the respiratory organs. The presented model of the respiratory system is the basis for further modeling of effects produced in the human body by airborne health risk factors as well as for modeling of respiration in case a disease is already present in the body.

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Competing interests. The authors declare no competing interests.

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