CHARACTERISATION OF LOCAL AIRWAY DEPOSITION OF THE INHALED RADIO-AEROSOLS BY COMPUTATIONAL FLUID DYNAMICS METHODS

THESIS POINTS OF THE PHD THESIS

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**Introduction and objectives**

The understanding of biological effects of low dose ionizing radiation seems to be one of the most challenging issues of current radiation protection, radiation biophysics and radiation biology. The official position on this issue is that the adverse health effects depend linearly on the radiation dose even in the low dose range. This statement is based on the so called LNT (linear-nonthreshold) dose-effect theory. However the LNT hypothesis is one of the most controversial scientific theories of the last decades.

Epidemiological studies of atomic bomb survivors and former uranium miners revealed that high radiation burdens were implicated in causal relationships with leukaemia, lung carcinomas and other health disorders. However, due to the different exposure conditions, direct extrapolation of A-bomb and miner data to low doses is not suitable. At the same time, in spite of sophisticated statistical analysis, residential radon studies yielded limited epidemiological evidence at low doses. Furthermore, due to the difficulties in measuring the true response at very low doses, experimental radiation carcinogenesis has not yet provided a plausible dose-effect relationship in the low dose range. This suggests that the understanding of mechanisms of action of radiation and the cellular changes which lead to malignancy is increasingly important in biological risk estimation. Hence, the development of biophysical mechanisms based complex risk models seems to be a promising avenue.

However, mechanistic models require exact microdosimetric quantities. Most of current lung dosimetry models are based on some
strongly simplifying assumptions, like straight cylindrical airways and uniform radon progeny deposition. In reality, the tracheobronchial tree is a system of asymmetric, sequentially bifurcating ducts and the site specificity of particle deposition has been shown both experimentally and by CFD methods. However, the systematic use of CFD techniques as a tool in microdosimetry and cancer research is still missing. Thus, the objective of my work was to elaborate a computational fluid and particle dynamics based model, capable to characterise the local burden of epithelial cells. This model was applied to exposure conditions characteristic of homes and mines.

**Methods**

Airflows and trajectories of the inhaled short – lived radon progenies have been computed by numerical methods. The model development consisted in construction and meshing of the three dimensional geometry of the upper and central airways, elaboration of methods for the characterisation of particle transport and deposition and working out of procedures for the quantification of local burdens.

I have elaborated two different methods for the generation of the three dimensional numerical surfaces of the airways, starting from their exact mathematical description. For this purpose I have applied the GAMBIT and UNIGRAPHICS commercial codes and some self-developed programs.

I have transformed the airway geometries into computational domains by the generation of velocity gradient and boundary adapted mathematical meshes.
I have implemented an Euler-Lagrange method for the modelling of two-phase (air and particles) flow. I have applied a finite volume method for the computation of airflow fields. Particle trajectories have been computed by numerical integration of the force-balance equations.

I have introduced the enhancement factors, defined as the ratio of the local to the total deposition density, for the characterisation of local particle deposition distributions.

I have used the potential alpha-energy enhancement factors, defined as a ratio of the local to the total potential alpha-energy density of the deposited radon progenies, in order to quantify the radiation burden of sensitive epithelial cells.

**Thesis points**

The main achievements of the present work can be summarised in the following thesis points:

1) I have developed a new method for the construction of morphologically realistic airway bifurcations. By this method the reconstruction of the realistic, ridge-like shape of the airway carinas has become possible.

2) I have implemented a new Brownian model for the description of the movement of inhaled nanoparticles within the airways. I have attached my program to the FLUENT commercial CFD code.

3) I have computed for the first time the airflow field and particle deposition distribution in five generation central airway geometry.


**Further publications**


7. Szőke I, Balásházy I and Farkas Á 2003 Effect of mucociliary clearance on the distribution of bronchial aerosol deposition *J. Aerosol Sci.* **34** 664-5

8. Balásházy I, Alföldy B, Osán J, Farkas Á, Szőke I and Török Sz 2003 Numerical simulation of the deposition of toxic elements originating from fossil burning in the human airway system, 12


4) I have studied the effect of breathing method, particle characteristics and lung geometry on the airway deposition by the application of laminar, turbulent steady and time dependent models.

5) I have quantified the local deposition and radiation burden in a complex airway segment by the computation of deposition enhancement factors and potential alpha-energy enhancement factors.

Conclusions

My radio-aerosol deposition modelling efforts have lead to the conclusion that the deposition efficiency of the inhaled particles is highly sensitive to the lung geometry, breathing mode and particle size.

According to my regional deposition results the unattached fraction of radon progenies deposits mainly in the upper and central airways, the probability of these nanoparticles to reach the acinar region of the lung is extremely low. At the same time the extrathoracic and bronchial deposition efficiency of the attached progenies is quite low.

Numerical investigation of the local deposition revealed that the airway deposition is inhomogeneous for any flow rate and particle size. However, progenies from the molecular fraction deposit more uniformly than the attached ones. Their degree of non-uniformity increases with the increase of the flow rate.

The radiation burden of the inhaled short-lived radon progenies is also non-uniform. The potential alpha-energy density of the most
exposed cells can be hundred and even thousand times higher than the average.

According to my simulations the local burden of the same macroscopic dose is higher for mines than for homes. This suggests that the health effects of the low-dose radiation cannot be estimated by direct extrapolation from higher doses.

Since the local radiation burden depends not only on the dose but also on many other parameters, the effect of low doses can be better described by a multidimensional surface.

This work has shown that the computational fluid and particle dynamics based models can be a powerful tool in characterising the local radiation burdens. The integration of my model with a microdosimetry model and the state vector model of radiation carcinogenesis will lead to a new, biophysical mechanisms based complex risk model.

**Publications closely related to the thesis**

1. Farkas Á, Hegedűs Cs and Pálfalvi J 2001 Realistic 3D flow calculations in the human tracheobronchial tree *J. Aerosol Sci.* **32** 803-4


10. Farkas Á, Balásházy I and Szőke I 2002 Numerical modeling of airflows and deposition patterns of radio-aerosols in central human airways *J. Aerosol Sci.* **34** 651


13. Farkas Á, Balásházy I and Szőke I 2003 Numerical modelling of local deposition patterns, activity distributions and cellular hit probabilities of inhaled radon progenies in the airways. IRPA