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**Energy Deposition and Radiation Quality of
Radon and Radon Daughters**

This program was aimed at creating a quantitative physical description, at the micrometer and nanometer levels, of the physical interactions of the alpha particles from radon and its daughters with cells at risk in the bronchial epithelium. We calculated alpha-particle energy spectra incident upon the cells and also energy deposition spectra in micrometer- and nanometer-sized sites as a function of cell depth, site size, airway diameter, activities of ^{218}Po and ^{214}Po , and other parameters. These data are now being applied, using biophysical models of radiation effects, to predict cell killing, mutations, and cell transformation. The model predictions are then compared to experimental biophysical, biochemical, and biological information. These studies contribute to a detailed understanding of the mechanisms of the biological effectiveness of the radiations emitted by radon and its progeny.

Principal Investigators

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Background

The question of radon protection and health effects is a national problem of high visibility. It is important because large numbers of people are exposed to radon in their homes and the effectiveness of this radiation is not very well understood. The epidemiological data available is from uranium and other miners who work in an environment which is very different from that of the home. Therefore, such questions as the particle size of the

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aerosols involved and the size of the unattached fraction are different in these two situations.

In its study of the research needed on radon protection and health effects, the Science Panel of the Committee on Interagency Radiation Research and Policy Coordination in 1986 emphasized:

"Because of the importance of valid risk estimates in assessing health consequences resulting from indoor radon exposures, research should be accelerated in the following three areas: . . .

c. Basic research into the mechanisms of lung cancer induction by alpha radiation, development of mechanistic models of radiation-induced lung cancer, and better definition of the cells at risk in the respiratory tract and the radiation interactions with them."

The work of this project was in the area of "development of mechanistic models of radiation induced lung cancer and better definition of the cells at risk in the respiratory tract and the radiation interactions with them."

The project focussed on two aspects of the physics of energy deposition in cells: the alpha particle spectra incident upon cells (needed for input to biophysical models of cancer induction); and microdosimetric spectra and linear energy transfer (LET) spectra which give information on radiation quality.

Accomplishments

- Computer program: We adapted an analytical method previously developed for neutron radiation to write a computer program known as RADONA (for radon-analytic). This program is used to calculate alpha-particle energy spectra (scientifically known as fluence-rate spectra or slowing-down spectra). Based on these spectra, the program also calculates microdosimetric (y) spectra and LET spectra and important parameters describing these spectra. The computer program operates in three modes: MODE 1 for a thin, plane source of radon-daughter activity adjacent to the epithelium; MODE 2 for a thick source layer (the mucous-serous layer) adjacent to the epithelium; and MODE 4 for cylindrical airways of various radii, lined by the mucous-serous layer. Some calculations have been made with a different code in MODE 3, which is for a uniform distribution of radon activity throughout an organ considered homogeneous. MODE 4 has been the most utilized since it corresponds to the various generations of the bronchial airways.
- Calculational results for the "plane" or "disk source" case have been published in *Radiation Protection Dosimetry* 31, 395-8 (1990).

- **Calculational Results for Cylindrical Airways.** We have carried out many calculations, some of which were presented in at the Hanford Radon Symposium in 1990 (Caswell and Coyne, 1992). Alpha-particle spectra and microdosimetry spectra and parameters are studied as a function of cell depth, $^{218}\text{Po}/^{214}\text{Po}$ ratio, airway radius, and cell nucleus or site size. Also available from the calculation is mean dose a function of depth below the airway surface. The slowing-down spectra (MODE 4) are similar to those of MODE 2 (plane source) except that there is an additional broad peak at lower energy due to alpha particles coming through the air from serous-mucous layer on the opposite side of the airway from the cells under consideration. The y spectra are qualitatively similar to MODE 2, but the average parameters such as \bar{y}_D are slightly lower.
- **Human Lung:** Calculated the alpha particle fluence-rate spectra and LET spectra at cell nuclei for cell depths within the range of 5 μm to 60 μm , in 5 μm increments, for radon daughters, ^{218}Po and ^{214}Po , using a source layer thickness of 8 μm and airways of diameters 1.130, 0.651, 0.435, and 0.198 cm (generations 2, 4, 6, and 10 of the Yeh and Schum morphometry). These results were compared to those previously obtained for source layer thickness of 15 μm .
- **Rat Lung:** Calculated the fluence-rate spectra and LET spectra at cell nuclei for cell depths within the range of 5 μm to 15 μm , in 5 μm increments, for ^{218}Po and ^{214}Po in airways of diameters of 0.2626, 0.1636, 0.1227, 0.0778, 0.0199 cm (generations 2, 4, 6, 10, and 15). The source layer thickness used (2.6 to 1.6 μm) was dependent on the airway generation of interest.
- **Energy deposition distributions (y spectra)** were calculated for cell nuclei of 5 μm diameter for above cell depths and airway diameters for both rat and human lung models.
- **Human Lung:** Calculated the fluence-rate spectra and lineal energy for ^{214}Po and ^{218}Po in generation 4 (cell depths 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55 and 60 μm ; source thickness 8 μm for all calculations) for a target size of 1 μm and results compared with those from calculations for a target of 5 μm .
- All data have been sent to Professor Werner Hofmann of the University of Salzburg, and are being used as input to several biophysical models.
- In collaboration with Professor Hofmann and other collaborators, we have applied a microdosimetric interaction model which simulates individual interactions of alpha particles with nuclei of sensitive target cells in human bronchial airway generations 2, 4, 6, and 10. Using lineal energy spectra in a spherical nuclear target from our calculations, we obtain probabilities for cell killing, mutation and transformation by multiplying the single event chord length distribution with event specific effect probabilities per unit track length as a function of LET. These effect probabilities

are finally weighted by the depth-density distributions of basal and secretory cells. The predicted transformation probability is compared with other physical indicators of lung cancer risk, such as dose, dose equivalent, biologically weighted dose, mean lineal energy, and number of alpha particle hits.

- In collaboration with Professor Hofmann the formalism of track structure theory has been used to predict the probabilities of different cellular radiation effects in basal and secretory cells of the bronchial epithelium exposed to radon progeny alpha particles. Cellular radiosensitivity data applicable to the prediction of carcinogenic response consists of in vitro data on oncogenic transformation and survival in C3H10T1/2 cells, mutation and survival in V79 Chinese hamster cells, and chromatid aberrations and survival in CH2B₂ cells. Energy spectra of ²¹⁸Po and ²¹⁴Po alpha particles have been computed for cell nuclei located at varying depths in the bronchial epithelium of different airway generations. When track structure theory is applied, the number of observable inactivations, chromatid aberrations, transformations, and mutations can be calculated for a given alpha particle energy spectrum. The computed effect probabilities are then weighted by the depth-density distributions of basal and secretory cells. Our track structure predictions for airway generation 4 in rat and human lung models suggest that cellular radiation effects are rather uniformly distributed within the bronchial epithelium and that the lung cancer risk per unit exposure at low exposure levels is either constant or increases slightly, and then decreases at high cumulative exposure levels.

Collaborations and Outreach

Dr. J. Joseph Coyne was an active participant in the program until his retirement from NIST in 1991. He contributed particularly in questions of analysis of the physics involved in the calculation and computer programming.

Our chief outside collaborator was Professor Werner Hofmann, Institute for General Biology, Biochemistry and Biophysics, of the University of Salzburg, Austria. Dr. Hofmann is an authority on the radon problem having worked in many phases such as aerosols, deposition of activity in the lungs, and biophysical models. In addition his collaborators at Duke University (D. G. Crawford-Brown and M. G. Ménache) and at the University of Salzburg (M. Nösterer and T. Heistracher) have also participated in this research.

We have collaborated with and benefitted from discussions with Mr. Stephen Seltzer, Leader of the Radiation Interactions and Dosimetry Group, Ionizing Radiation Division at National Institute of Standards and Technology (NIST).

At the request of Dr. Pascal Pihet, Chief of the Laboratories for Study and Research in Internal Dosimetry at the Department of Human Health Protection and Dosimetry, Fontenay-aux-Roses, France, we have prepared and given him a Personal Computer version of the program for use in France. [Our standard version runs on the CRAY supercomputer at NIST].

Budget

This program was funded under two agreements:

<u>Agreement</u>	<u>Period Covered</u>	<u>Funding</u>
DE-AI05-88ER60670	4/1/88-12/30/92	\$217650
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Total		<u>\$364650</u>

The average yearly funding was about \$47,000.

Publications

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Hofmann, W., Heistracher, T., Caswell, R. S., and Karam, L. R., "Track Structure Predictions of Radon-Induced Biological Effects in Human Bronchial Epithelium," Environment International (in press).

Publications in preparation (work continuing, not supported by DOE):

Karam, L. R., Caswell, R. S., and Hofmann, W., "Radon Daughter Alpha Particle Spectra in Human and Rat Lung Models: Fluence-Rate Spectra" (about 75% complete).

Karam, L. R., Caswell, R. S., and Hofmann, W., "Radon Daughter Alpha Particle Spectra in Human and Rat Lung Models: Lineal Energy (y) and LET Spectra" (about 25% complete).