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ALPHA PARTICLE MICRODOSIMETRY IN THE LUNG

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Alpha particle microdosimetry in the lung

Alpha particle microdosimetry in the lung comprises problems of

internal dosimetry, such as the spatial and temporal distribution of alpha-emitting radionuclides, and

cellular microdosimetry, such as the distribution of energy deposition at the cellular level characterized by hit probabilities and specific energy distributions

Radon progeny microdosimetry in the human lung

Short-lived radon progeny:

^{222}Rn decays into ^{218}Po, ^{214}Pb, ^{214}Bi/^{214}Po

Alpha emitters:

^{218}Po: E = 6.0 MeV, R(tissue) = 47 µm

^{214}Po: E = 7.69 MeV, R(tissue) = 72 µm

Exposure parameters:

Radon progeny concentrations in the inhaled air

Fractions and size distributions of attached and unattached radon progeny

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Inhalation of short-lived radon progeny

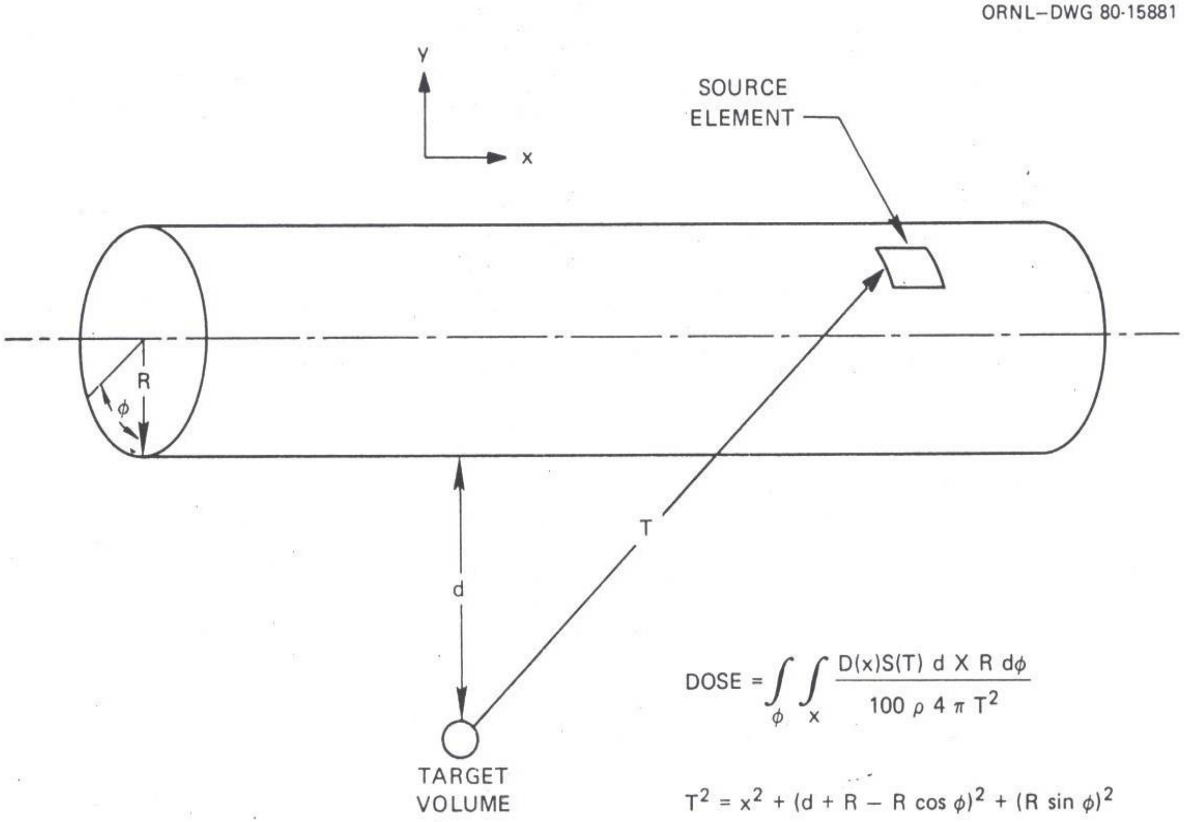
From inhalation to equilibrium surface activities on bronchial airway surfaces

- Deposition on bronchial airway surfaces
- Mucociliary clearance from deposition sites
- Radioactive decays between daughter nuclides

Source term for irradiation of bronchial target cells:
Equilibrium bronchial surface activities of alpha-emitting ^{218}Po and ^{214}Po nuclides

Irradiation of target cells in bronchial epithelium

From bronchial surface activities to cellular doses



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Internal microdosimetry for inhaled radon progeny

Internal microdosimetry encompasses problems of internal dosimetry and microdosimetry

- Variability of radon progeny surface activities
- Microdistribution of radon progeny on bronchial airway surfaces
- Spatial correlation between microdistribution and bronchial target cell distribution
- Variability of energy deposition in cell nuclei

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Variability of radon progeny surface activities on bronchial airway surfaces

Sources of variability:

Inter- and intrasubject variations

Deposition: Size and structure of nasal and oral passages
Lung volume
Asymmetry and variability of bronchial airway dimensions
Breathing parameters

Clearance: Mucociliary clearance velocities

Monte Carlo deposition, clearance and dosimetry code IDEAL-DOSE

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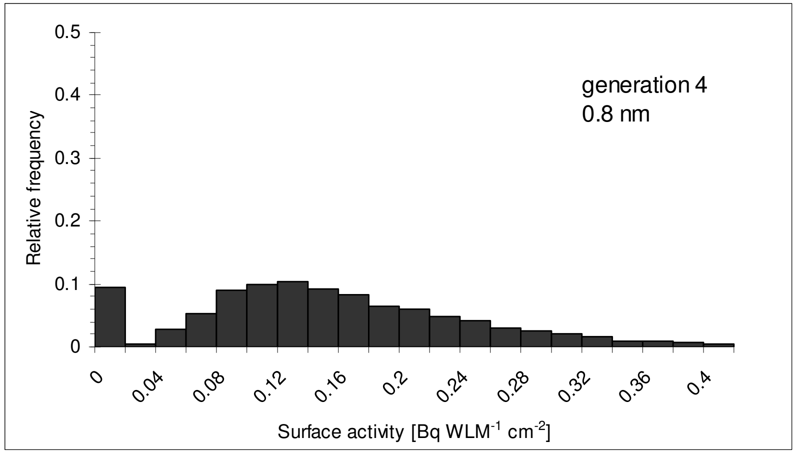
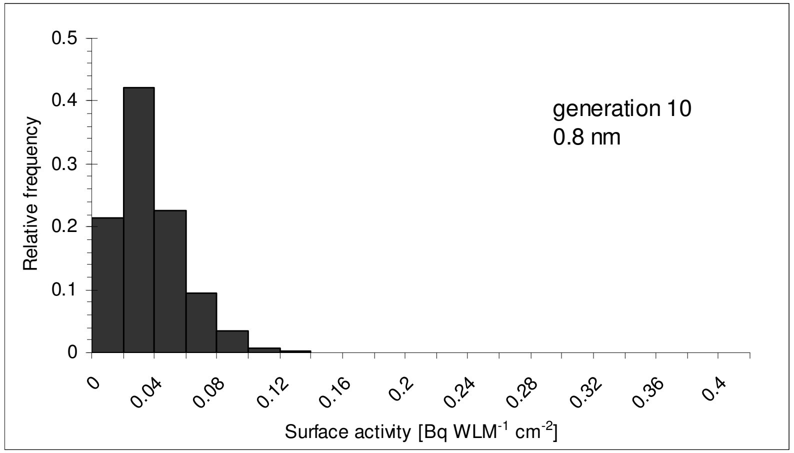
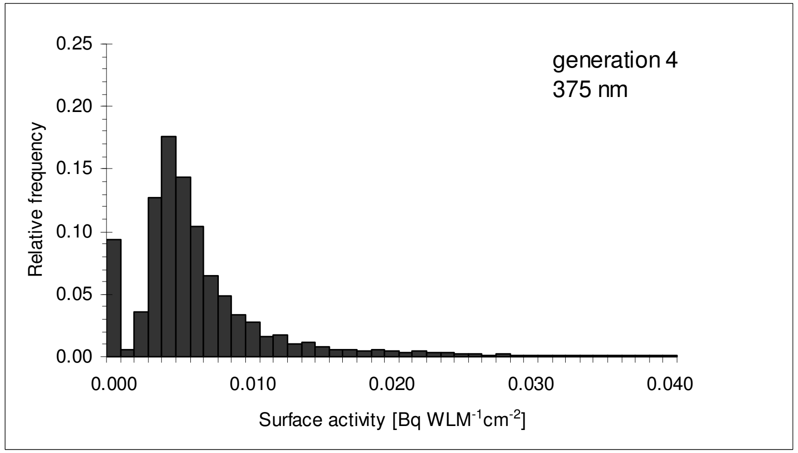
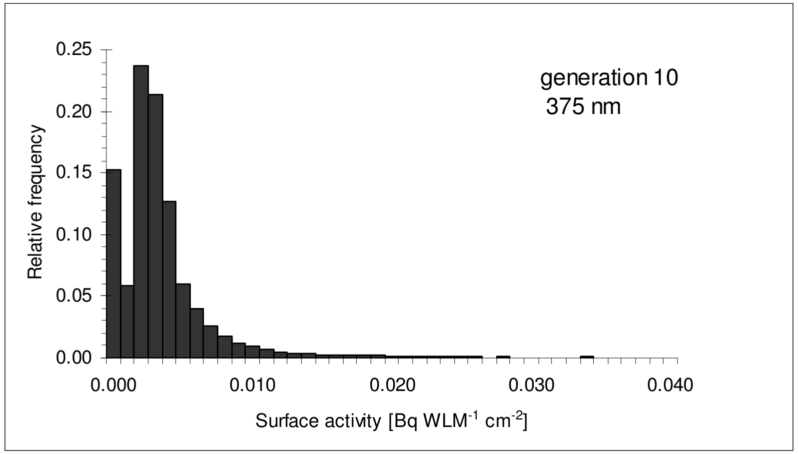
Variability of radon progeny surface activities on bronchial airway surfaces

^{218}Po surface activities



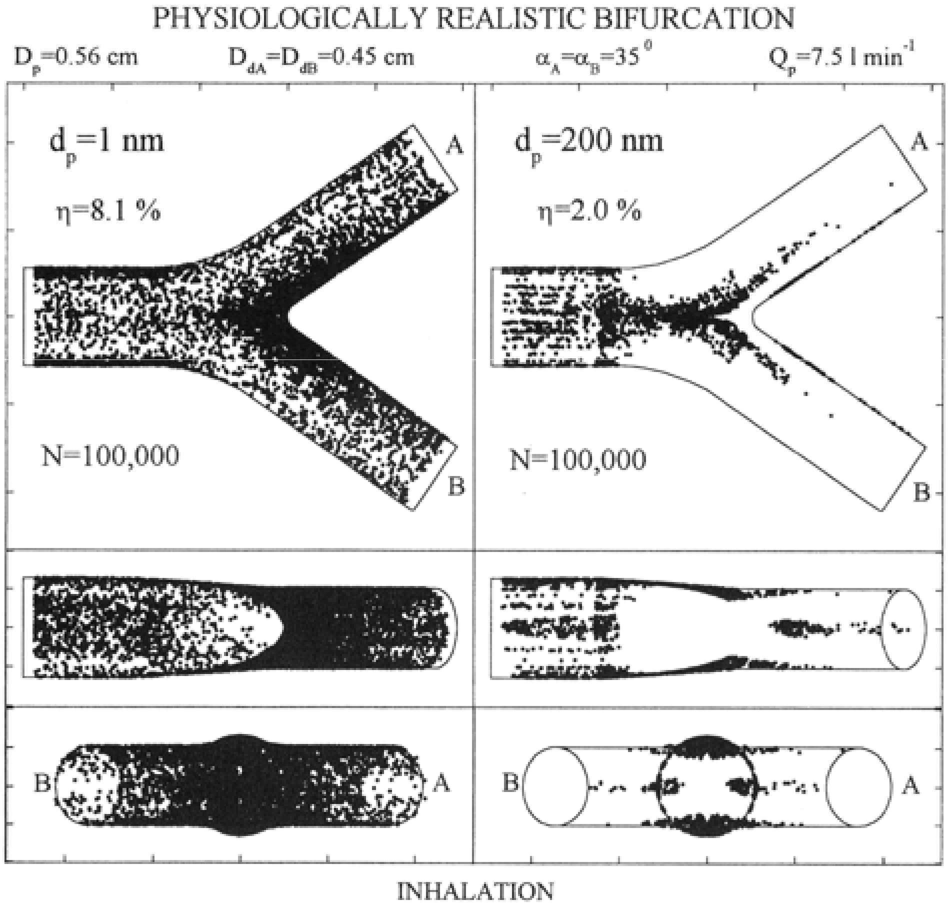






Microdistribution of radon progeny in airway bifurcations

Balásházy and Hofmann (2000)



Spatial deposition patterns of unattached and attached radon progeny in human bronchial airway bifurcations

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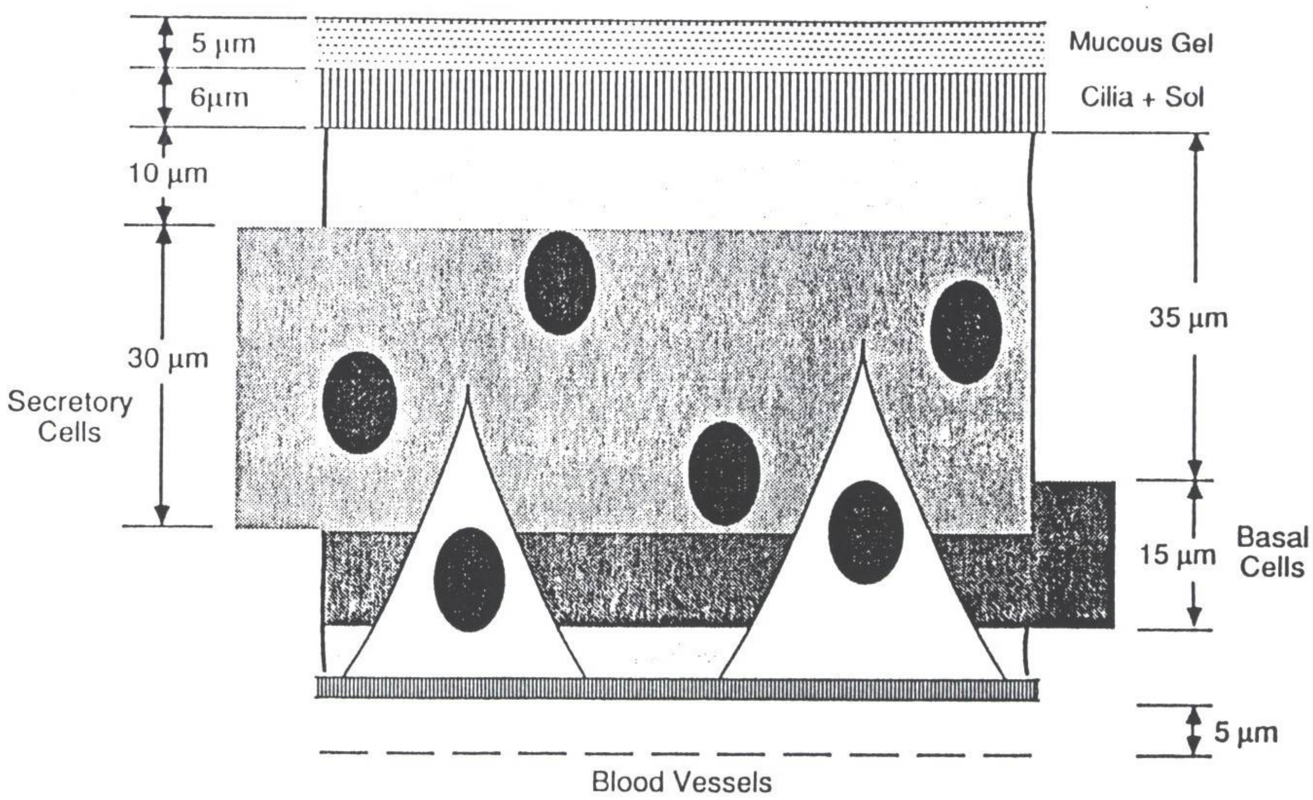
Spatial correlation between surface activities and target cells

Non-uniform target cell distribution across the bronchial epithelium

Volumetric densities (generation 2): 6% basal cells, 1.2% secretory cells



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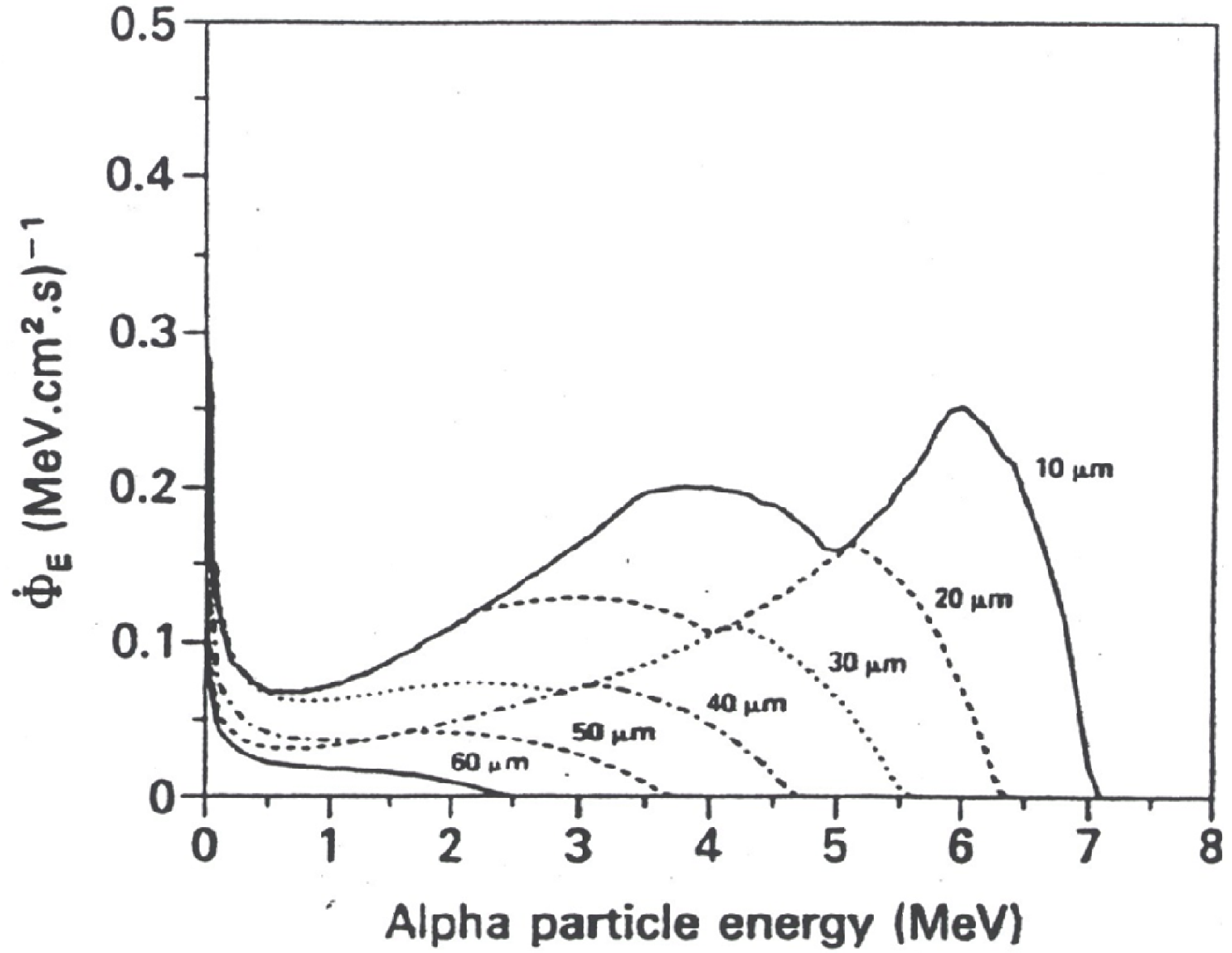
Variability of energy deposition in cell nuclei

- Probability of hitting the target due to the limited range of alpha particles (single and multiple hits)
- Alpha particle intersection of target cells: Random track lengths in a spherical nucleus (crossers, stoppers)
- Random energy deposition along traversal as a result of the spatial correlation between emission site and target site (Bragg curve)

Monte Carlo code MICROS: calculation of microdosimetric spectra in bronchial airways and airway bifurcations

Alpha particle energy spectra for different target cell depths



Alpha particle fluence rate spectra for ^{218}Po and ^{214}Po in generation 2.

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LET spectra for different depths (^{214}Po)

Hofmann et al. (2000)

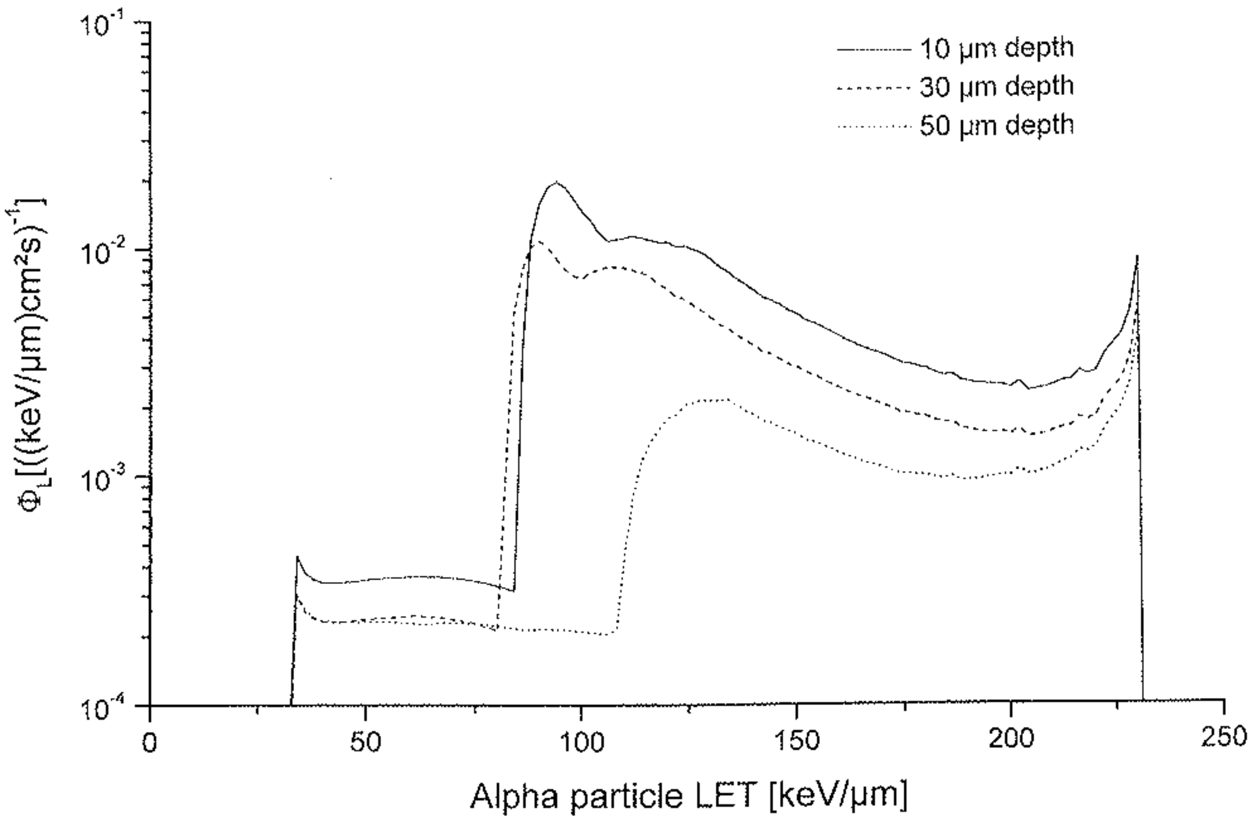

Fig. 2. LET spectra for ^{214}Po alpha particles at various depths (10, 30, and 50 μm) in airway generation 4 of the human lung for a source density of 1 Bq cm^{-2}, illustrating the dependence of the shape of the LET spectra on depth in bronchial epithelium.

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Comparison of ^{214}Po and ^{218}Po LET spectra

Hofmann et al. (2000)

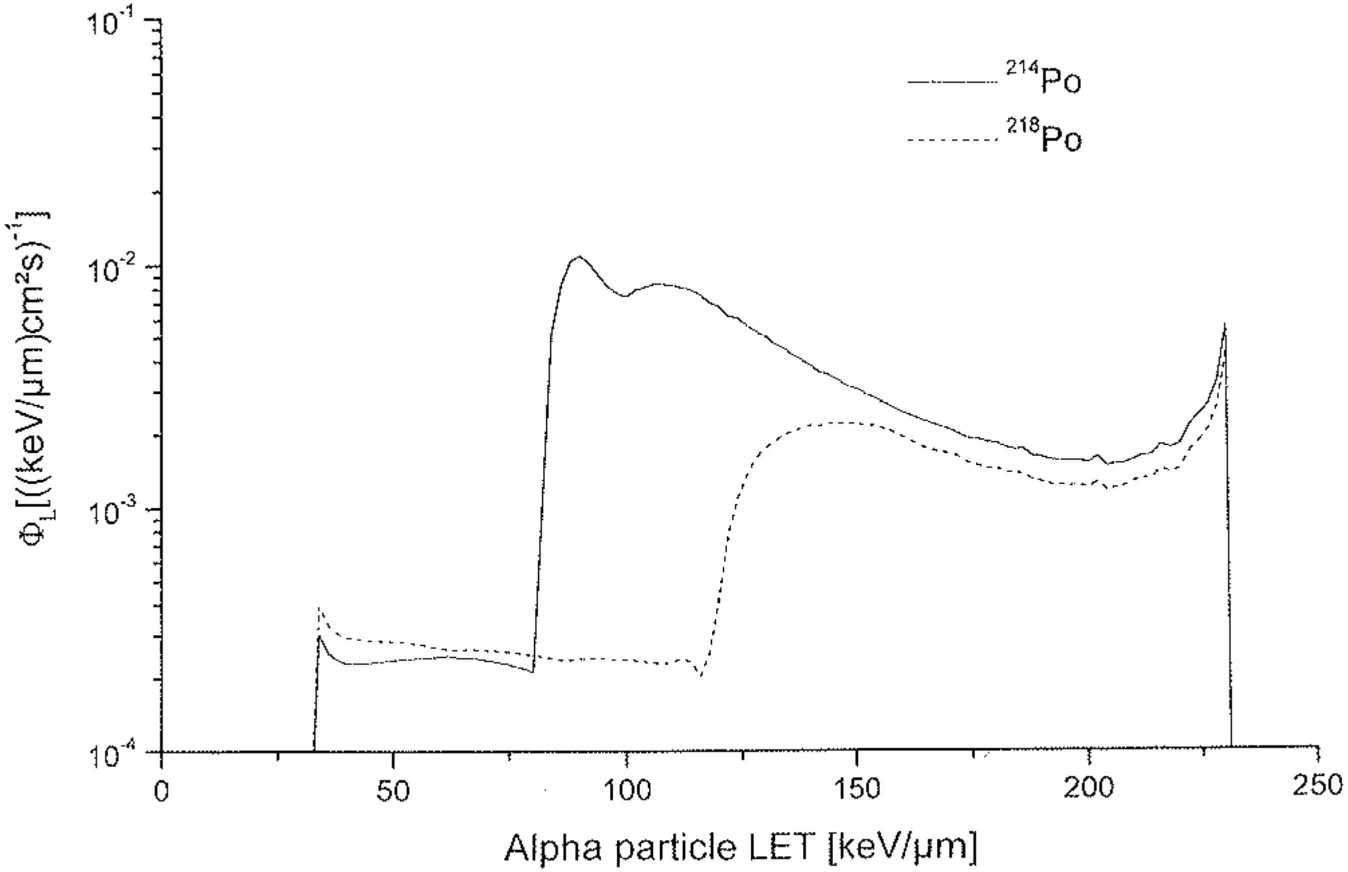

Fig. 1. LET spectra for ^{218}Po and ^{214}Po alpha particles in human airway generation 4 at a depth of 30 µm for a source density of 1 Bq cm^{-2}, illustrating the effect of initial alpha particle energy on the resulting LET spectrum.

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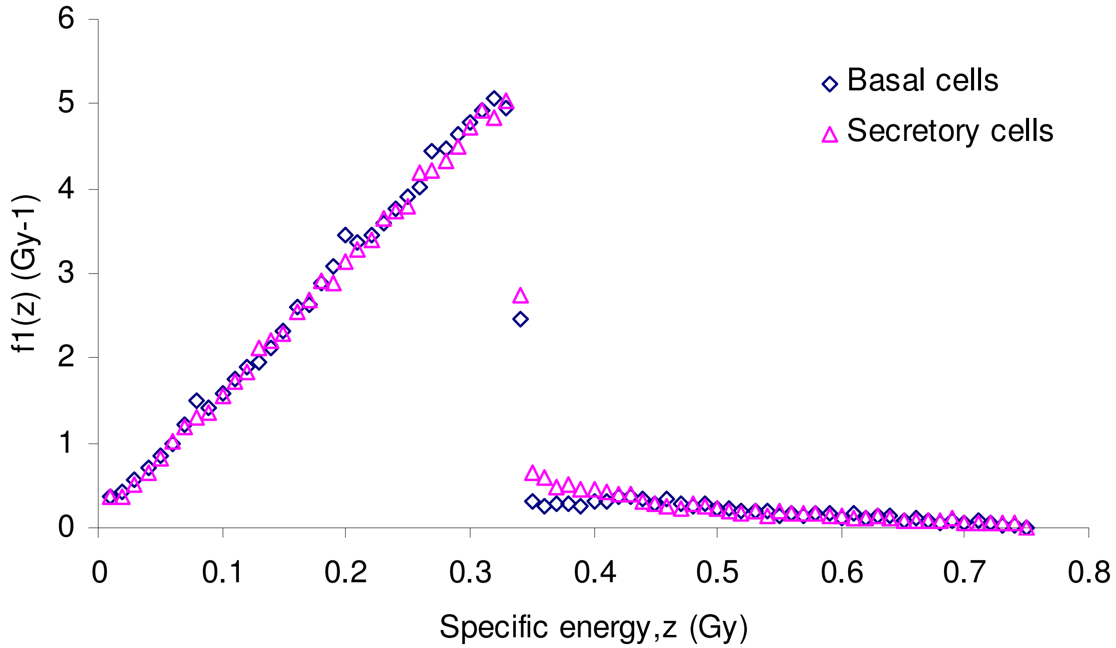
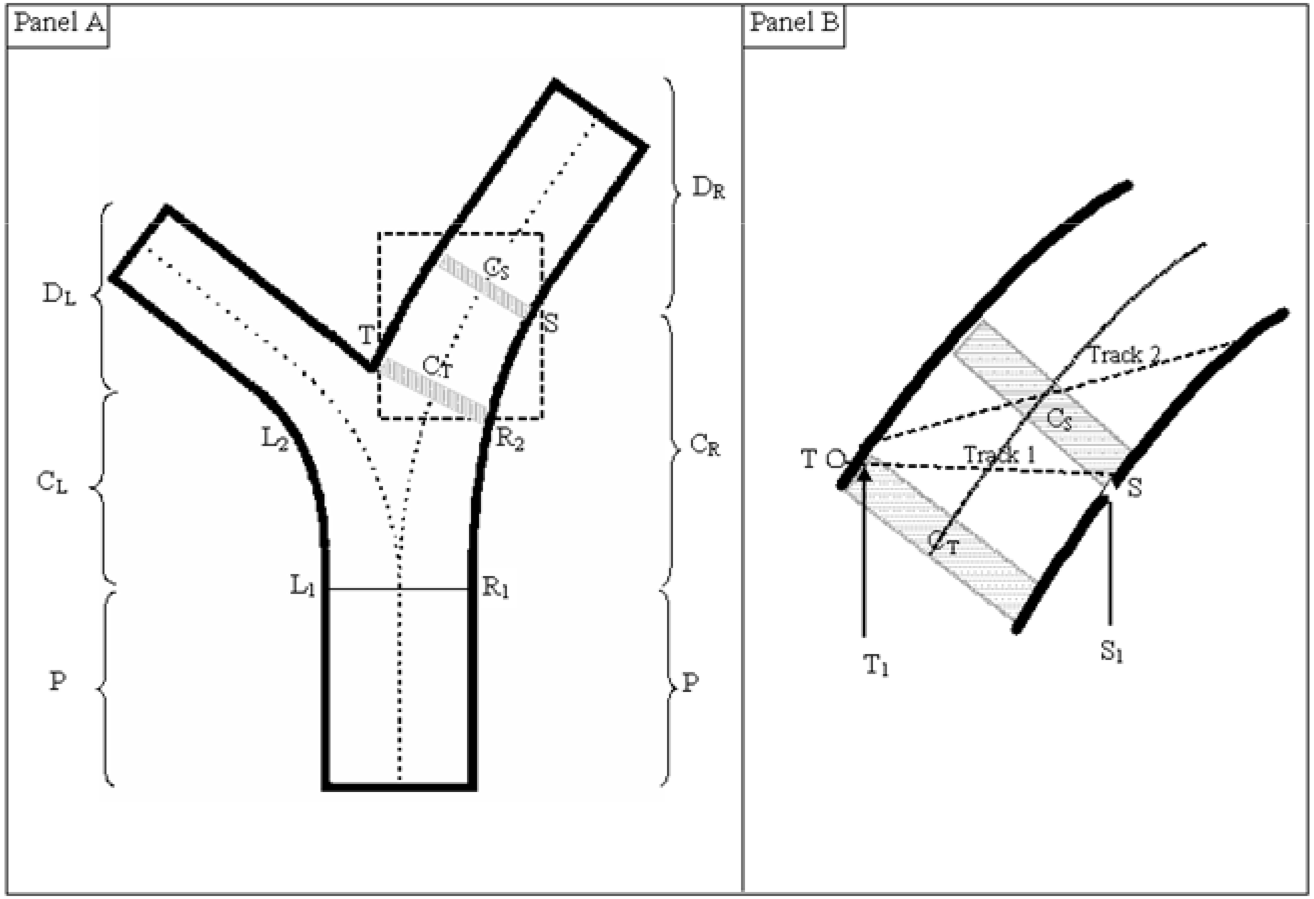
Specific energy distribution for single hits



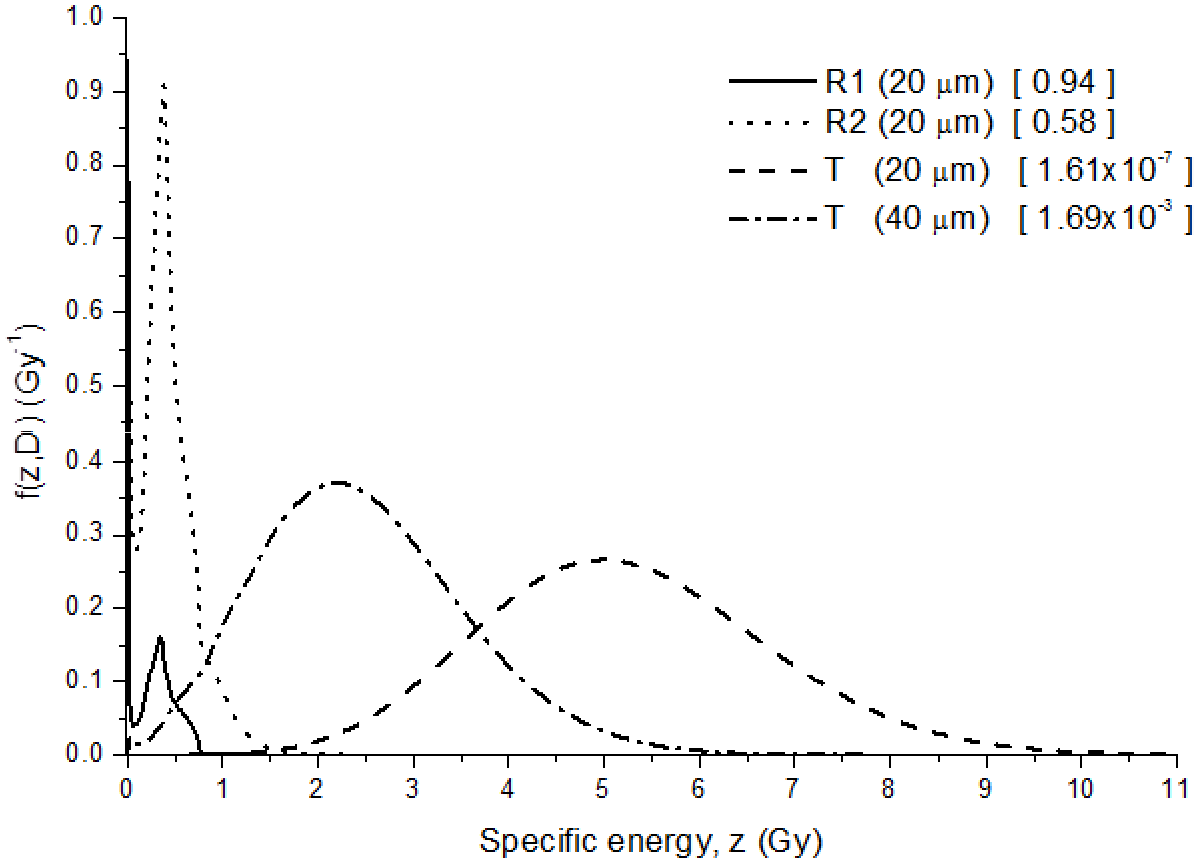
Single-event distributions (normalized) in both basal and secretory cells of a bronchial airway in human airway generation 4, calculated by Monte Carlo methods.

Spatial correlation between non-uniform activity microdistribution and target cell distribution

Correlation due to limited range of alpha particles



Dose dependent specific energy spectra for 20 WLM



Residential radon exposures (20 WLM). **Non-uniform** surface activity distribution.

In parenthesis are the probabilities of zero events, indicating the fraction of cells not hit at all.

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Acute vs. chronic exposure to radon progeny

Leenhouts and Chadwick (1994)

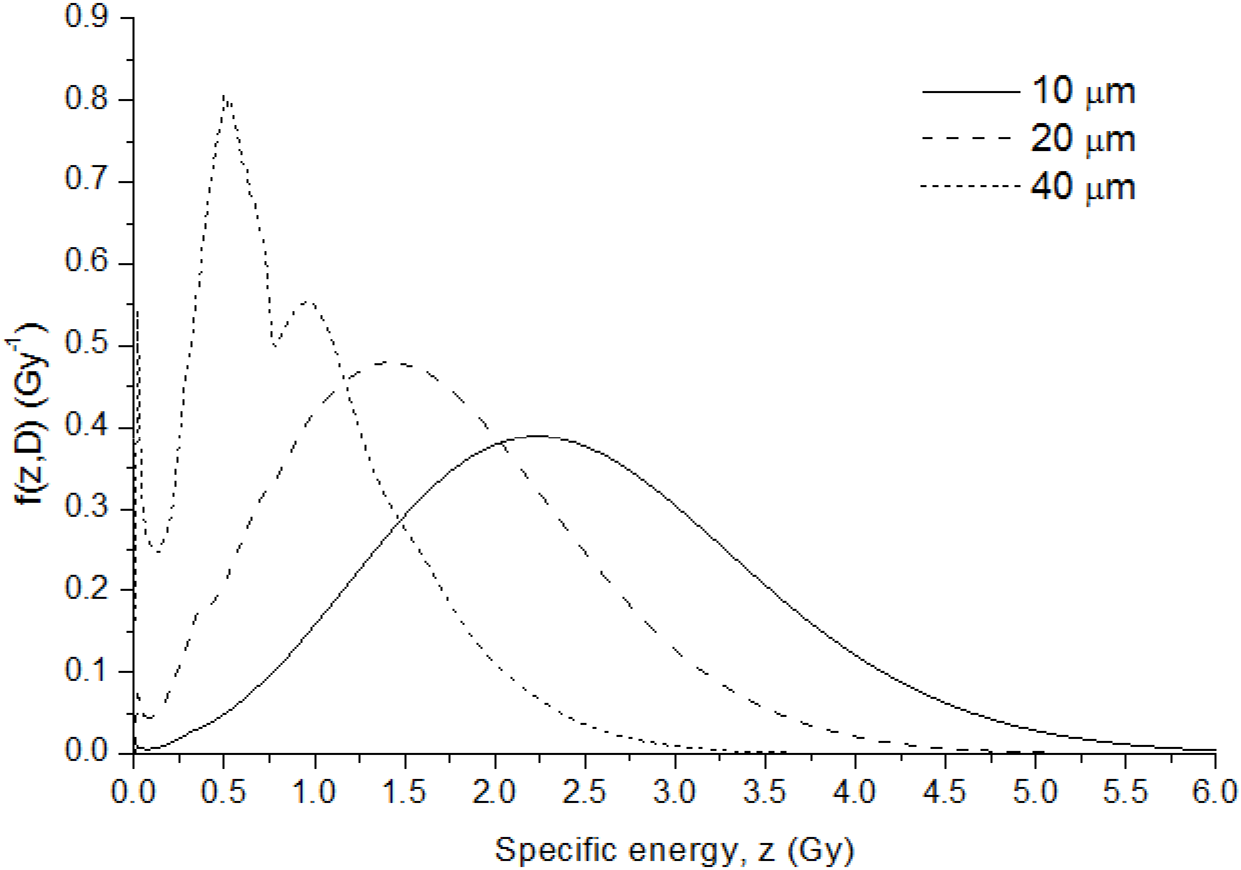
Acute radiation exposure:

The relevant dosimetric quantity to determine cellular radiation effects is the **total dose**.

Chronic or protracted exposure:

The crucial radiation quantity for cellular effects is the **dose rate**, i.e. the dose per cell cycle (typical cell turnover time in the lung: 30 days)

Dose dependent specific energy spectra for uranium miners (30 day exposure)



uranium miners: Colorado (578.6 WLM)

Non-uniform surface activity distribution

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How to relate microdosimetry to cellular radiobiological effects?

Cellular radiation effects relevant for carcinogenesis:

Oncogenic transformations, cell killing

Effect-specific track length model

Microdosimetric parameters: track length (T), LET (L)

Probability per unit track length as a function of LET

$$P_{\mathrm{TS}}(L,T)=\left[\sum_{i=0}^{m-1}\frac{(P_{\mathrm{D}}(L)\times T)^i}{i!}\cdot\exp(-P_{\mathrm{D}}(L)\times T)\right]\times\left[1-\sum_{i=0}^{n-1}\frac{(P_{\mathrm{T}}(L)\times T)^i}{i!}\cdot\exp(-P_{\mathrm{T}}(L)\times T)\right]$$

Integration over all track lengths T_j

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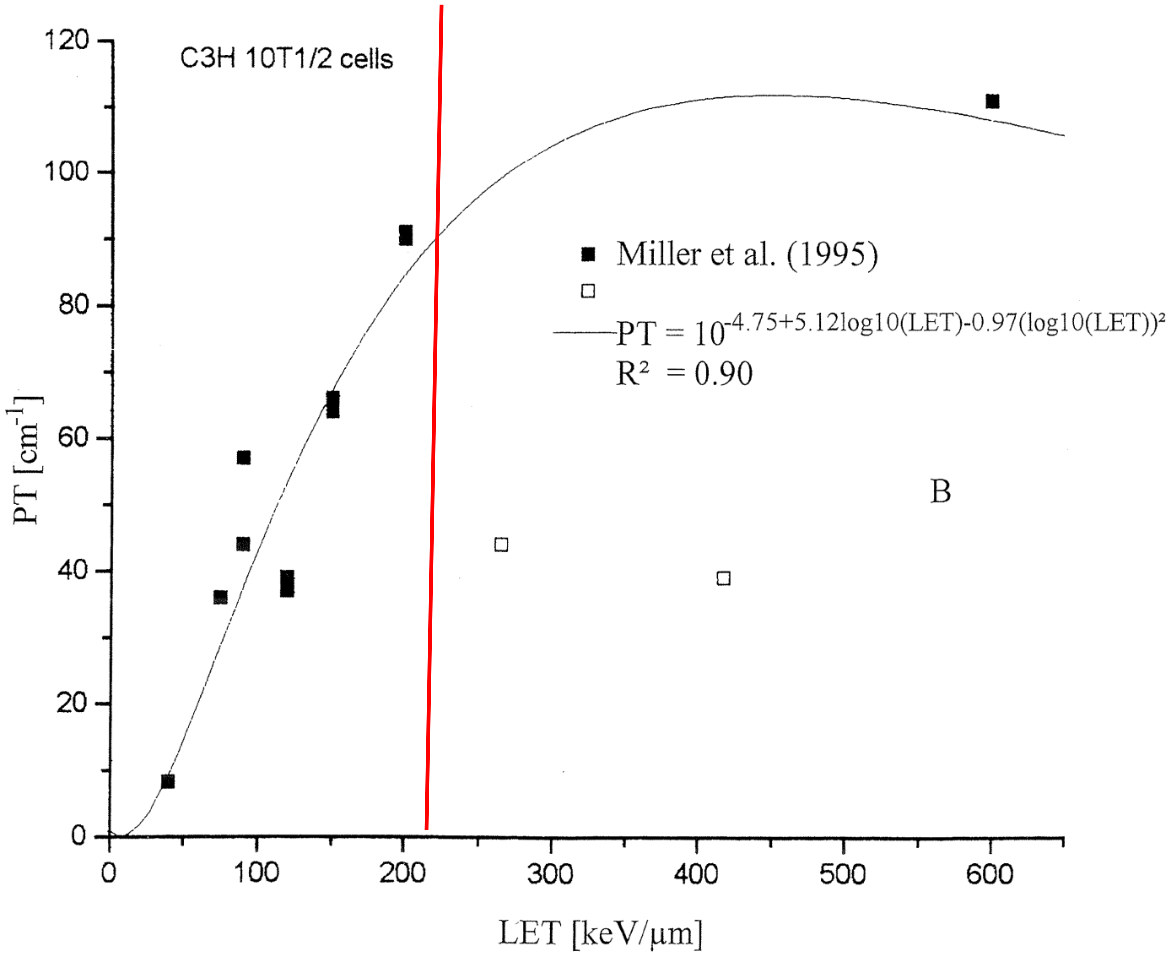
Probability per unit track length for transformation as a function of LET



Transformation frequency distributions

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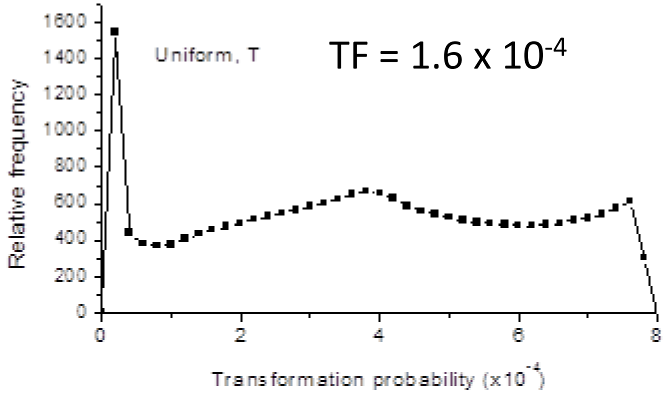
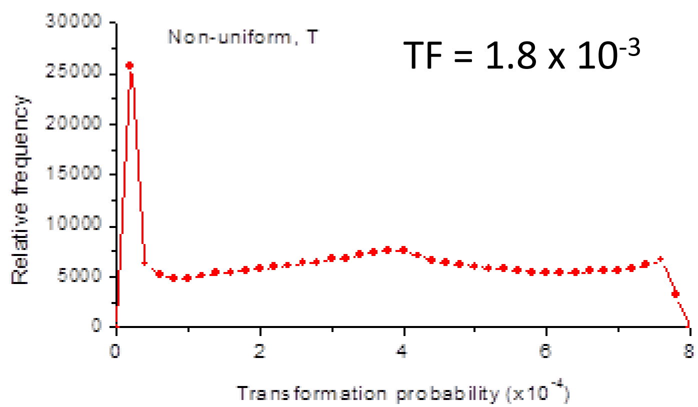
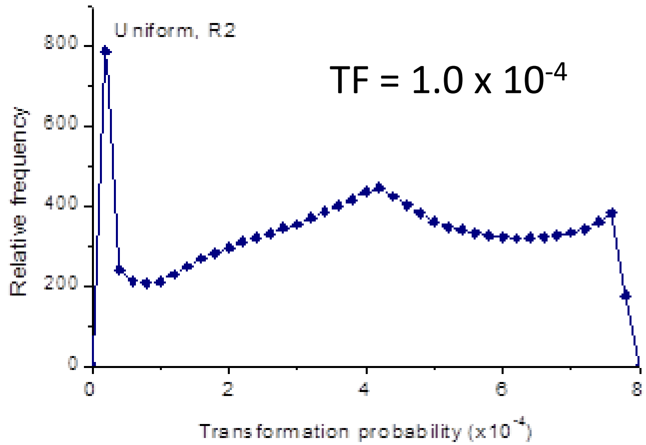
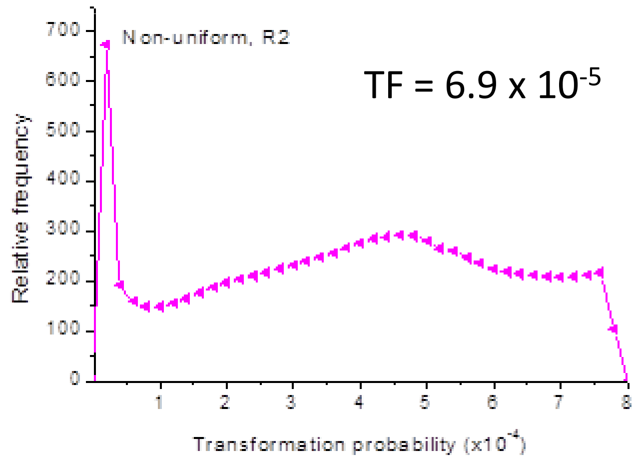






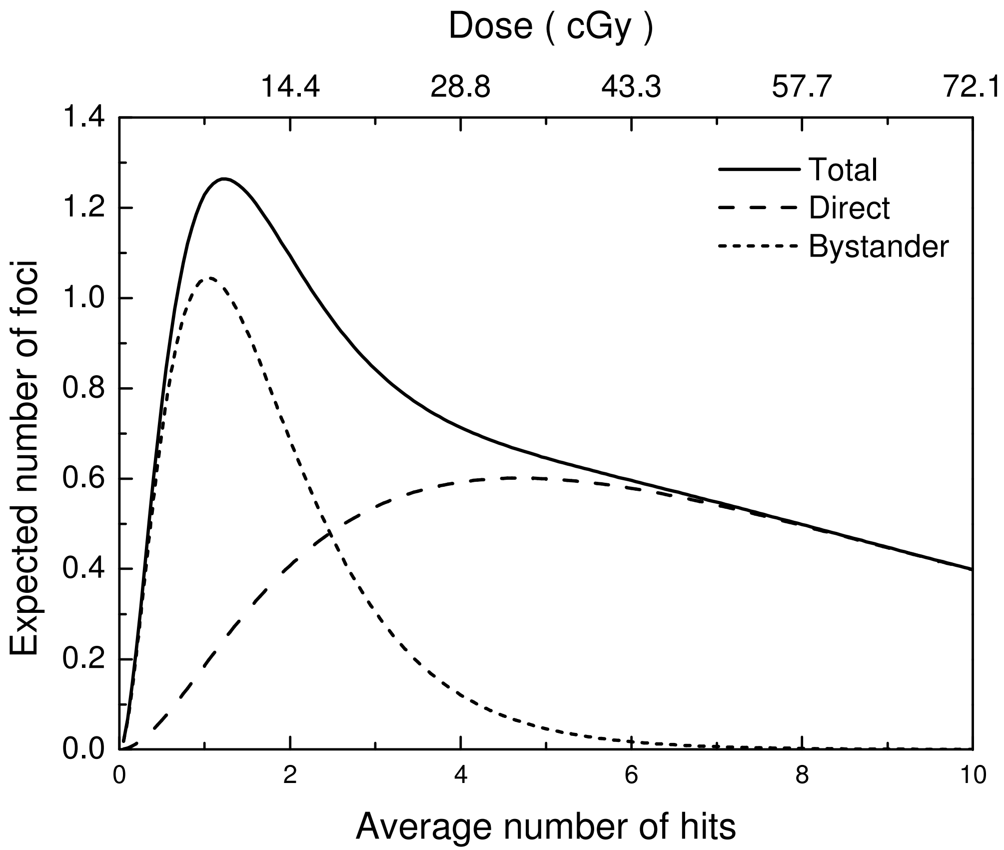


Target cell nuclei at 20 µm depth

Cumulative exposure: 578.6 WLM

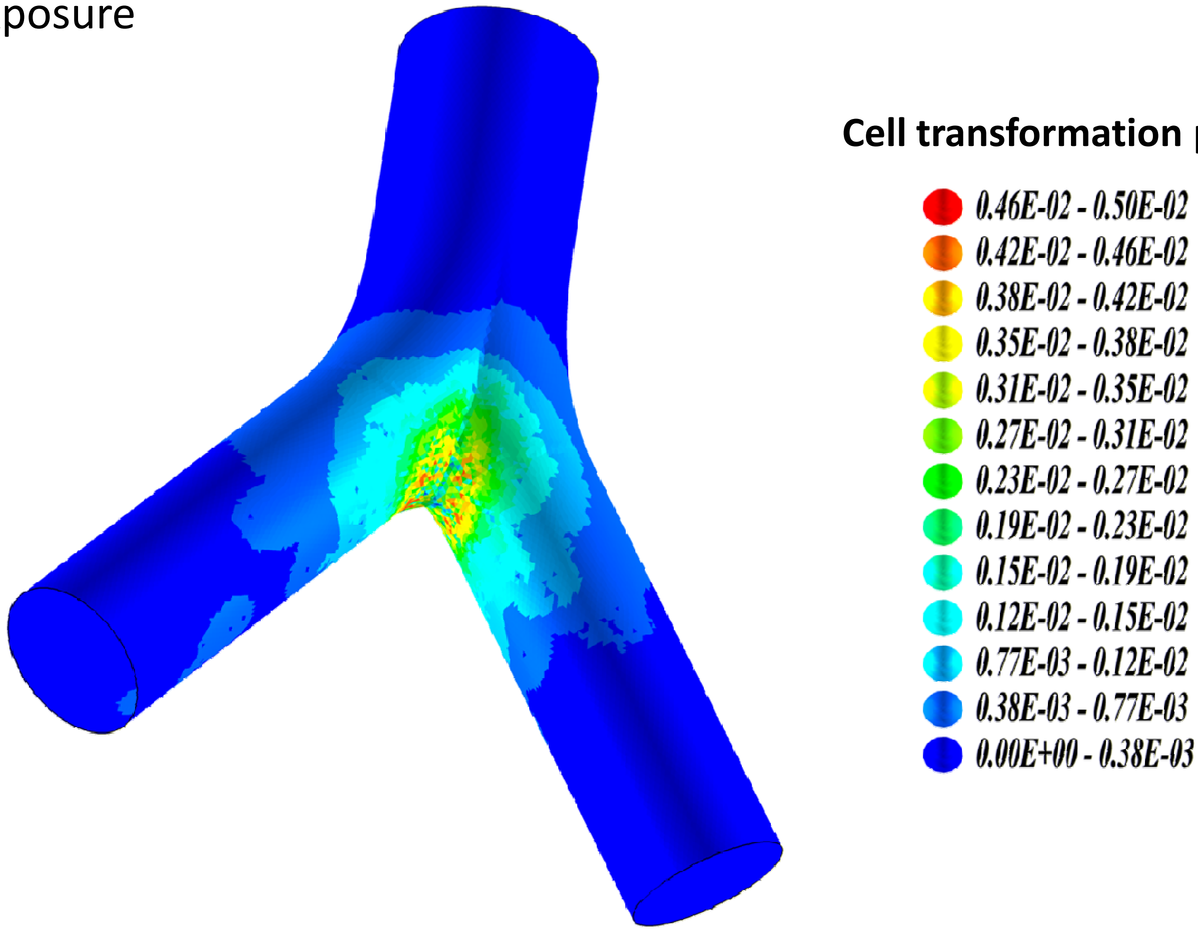
Transformation: Direct vs. bystander mechanisms

Fakir et al. (2007)
Microdosimetric bystander model for transformation frequencies induced by alpha particles
Ratio of total (direct + indirect) / direct as a function of the average number of hits



Distribution of cell transformations in a bronchial airway bifurcation

Balásházy et al. (2012)
Low exposure



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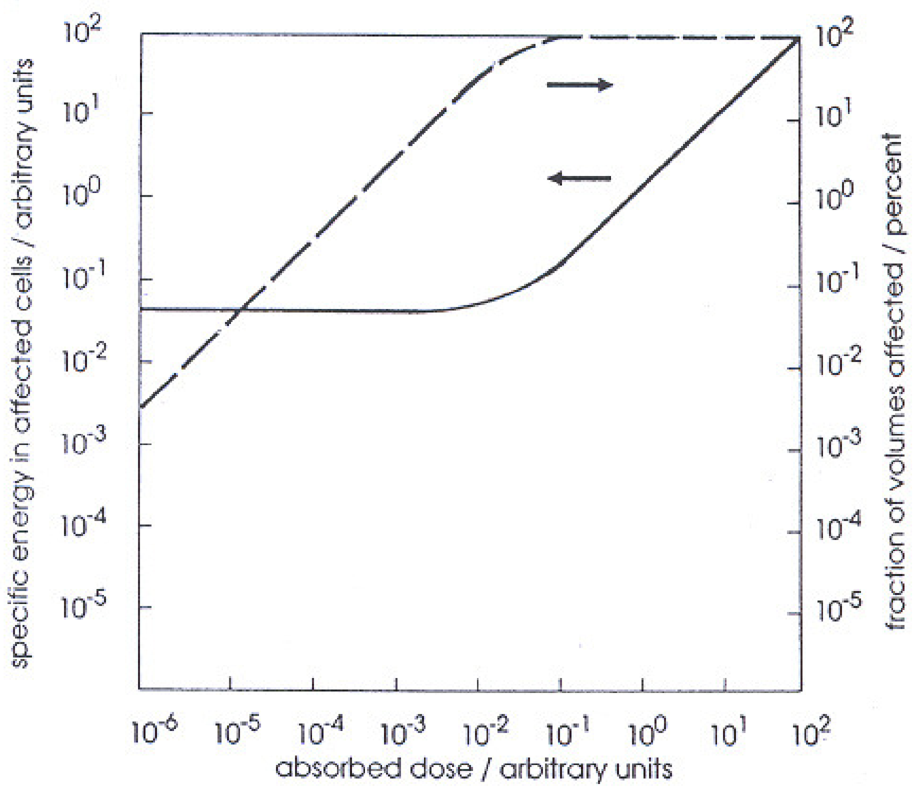
Low dose effect of alpha particles

Number of cellular hits and average specific energy of low doses of alpha particles



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Application of internal microdosimetry to cancer risk estimation at low doses

Alpha particles:

Only few cells are hit, but these cells experience high energy deposition events

Gamma rays:

Practically all cells are hit, and these cells experience relatively small energy deposition events

Low doses and dose rates of alpha particles typical of radon exposures in homes are characterized by a small number of cells affected over an extended period of time

Relevant microdosimetric parameters for radon progeny in the lung:

- **Number of cell nuclei hit by alpha particles**
- **Specific energy distributions due to single and multiple alpha particle traversals**

Acknowledgements

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