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Modelling Intersubject Variability of Bronchial Doses for Inhaled Radon Progeny

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Stochastic lung dosimetry model

Intersubject variability of bronchial doses is defined in this study as the effect of morphological and physiological parameter variations among a group of subjects on bronchial doses for defined exposure conditions, where each subject is characterized by a dose distribution (**intrasubject variability**).

Intersubject variability:

Breathing parameters for defined physical activities

Physical activity patterns

Size and structure of nasal and oral passages

Size of the lung (FRC)

Mucociliary clearance rates for the whole bronchial tree

Inter- and intrasubject variability:

Lung structure: Asymmetry and variability of linear airway dimensions in bronchial and alveolar airways

Parameters related to stochastic airway geometry:

Mucociliary clearance velocities and transit times in bronchial airway generations (diameter, length)

Depth of target cells (diameter)

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Extrathoracic deposition

Nose and mouth act as filters preventing inhaled particles from entering the lungs via the trachea. Only deposition upon inspiration is relevant for lung dosimetry.

Semi-empirical equations expressed as functions of flow rate, diffusion coefficient, Stokes number or impaction parameter, derived from:

(i) in-vivo experiments with volunteers, or

(ii) in-vitro experiments with oral and nasal casts

Nasal deposition:
Cheng et al. (1996, 2003):
Diffusion regime: Diffusion coefficient D and flow rate Q
Impaction regime: Aerodynamic diameter d_{ae} and flow rate Q

Sources of intersubject variability:
Diffusion regime: shape factor of the nasal turbinate region S_f
Impaction regime: minimum nasal cross-sectional area A_{min}

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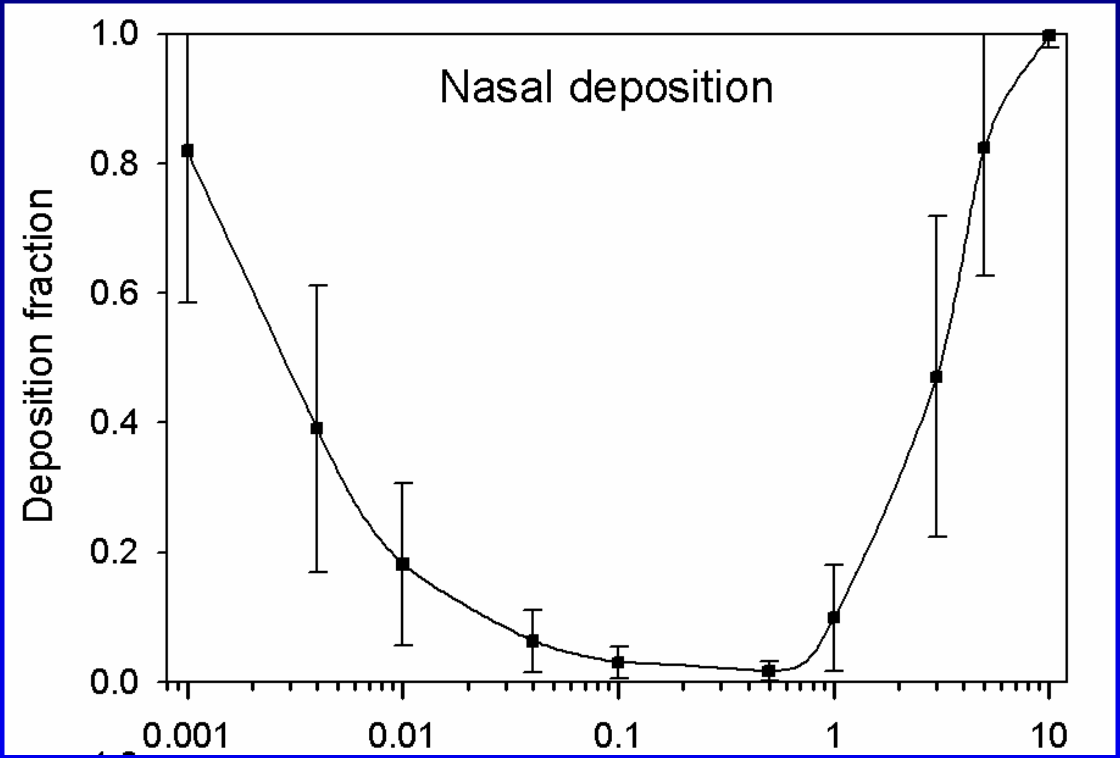
Effect of intersubject variability on nasal deposition upon inspiration



Unattached fraction: 0.8 nm (D = 8.48 x 10^{-2} cm^2 s^{-1})

Attached fraction: 375 nm (250 nm x 1.5) (D = 9.37 x 10^{-7} cm^3 s^{-1})

Sitting breathing conditions (adult male): V_T = 750 ml, f = 12 min^{-1} (Q = 300 cm^3 s^{-1})

Intersubject variability: ± 2 SD

Sources of intersubject variability of breathing

Random variations of breathing conditions for a defined physical activity:

Tidal volume
Breathing frequency
Ratio of nose/mouth breathing
Breathing cycle (inspiration, expiration and breath-hold times)
Flow rate (constant vs. variable)

Random variations of physical activity patterns:

Typical activity patterns (fractions of specific physical activities during a work day or during a full 24-hour day)

Effect of breathing variability on:

Deposition fractions in a single breath (all factors)
Amount of inhaled activity per unit time (only tidal volume and breathing frequency)

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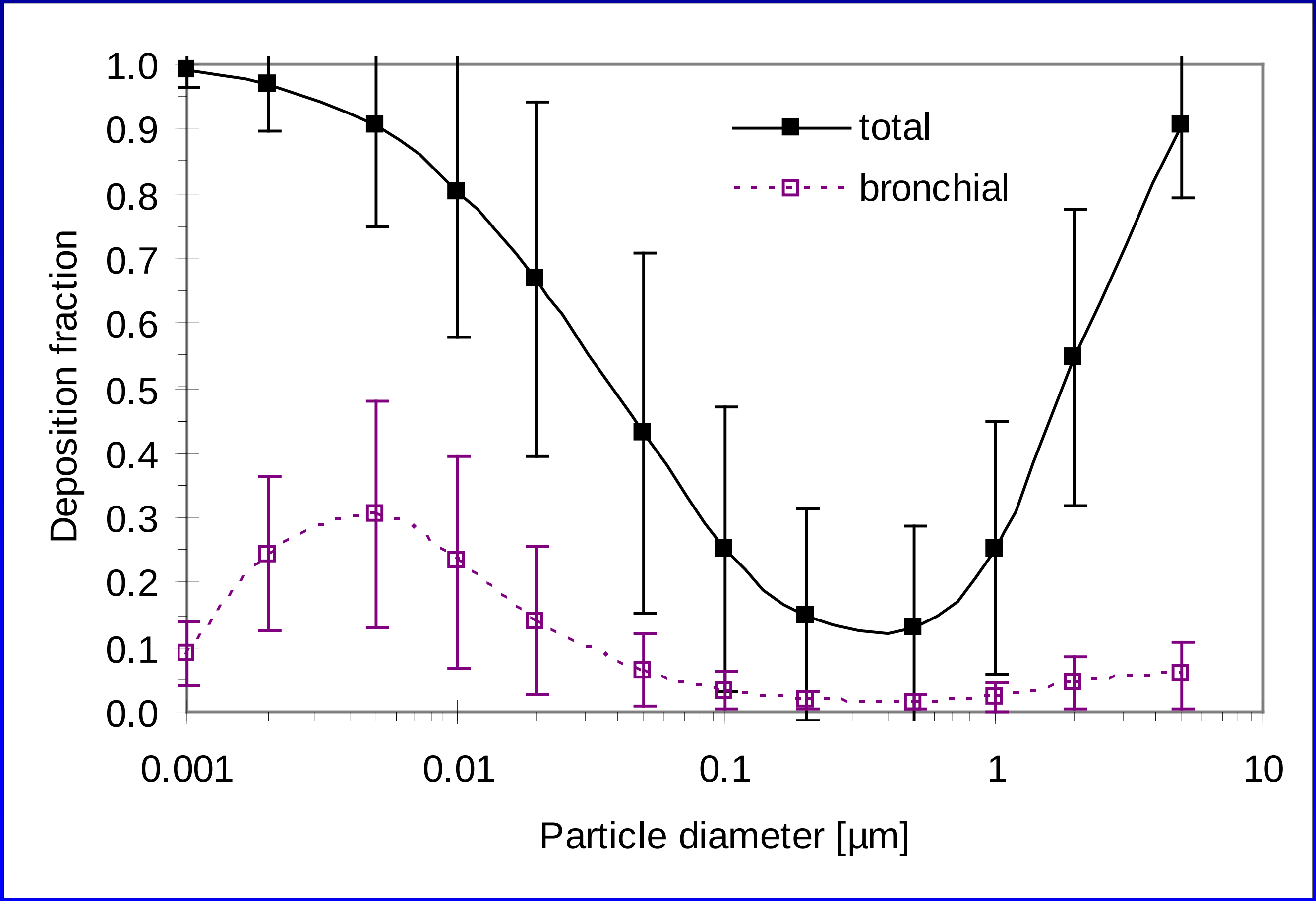
Effect of intersubject variability of breathing parameters on particle deposition

Sitting breathing conditions (adult male): V_T = 400 - 1500 ml, f = 12 - 20 min^{-1} (Coates, 1979)

Total and bronchial deposition



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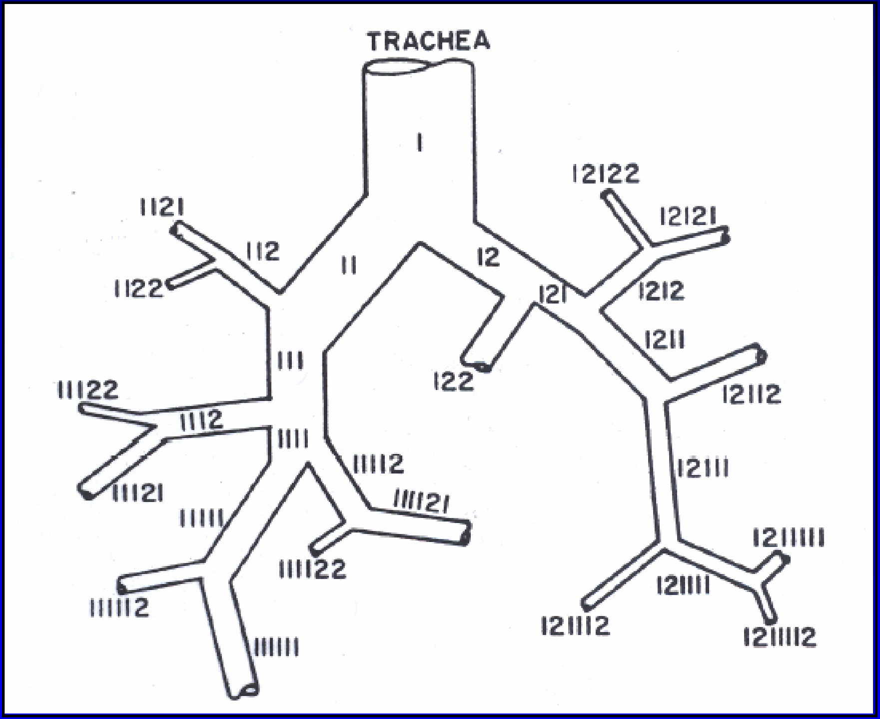
Sources of intra- and intersubject variability of lung morphology



Volumetric variability:
Functional residual capacity (FRC)

Structural variability:
Asymmetry and variability of linear airway dimensions (e.g. diameters, lengths) and their correlations (e.g. cross-section ratios) in bronchial and alveolar airways

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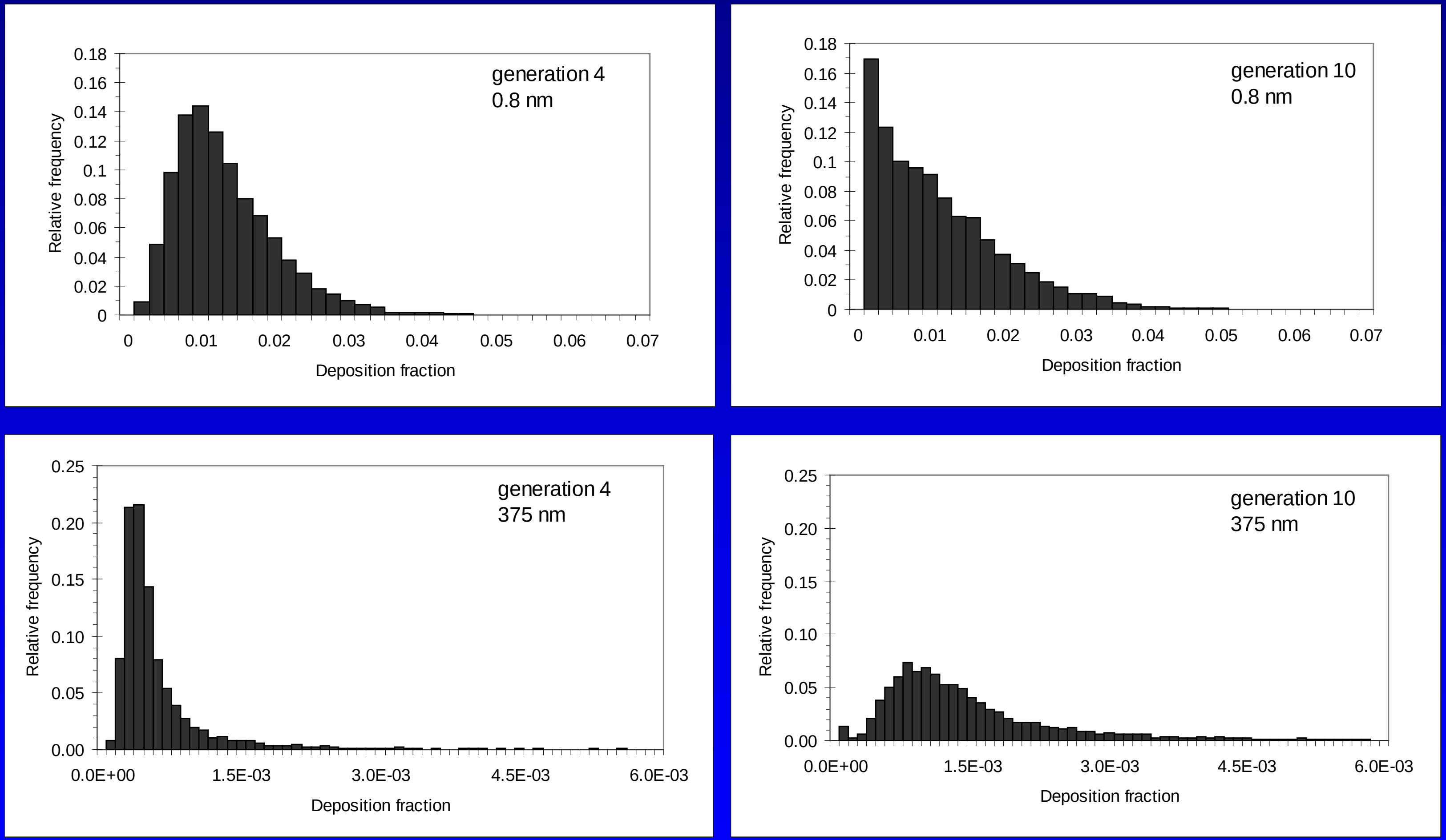
Effect of morphological variability on particle deposition

Breathing parameters: V_T = 1250 ml , f = 20 min^{-1} (light exercise)



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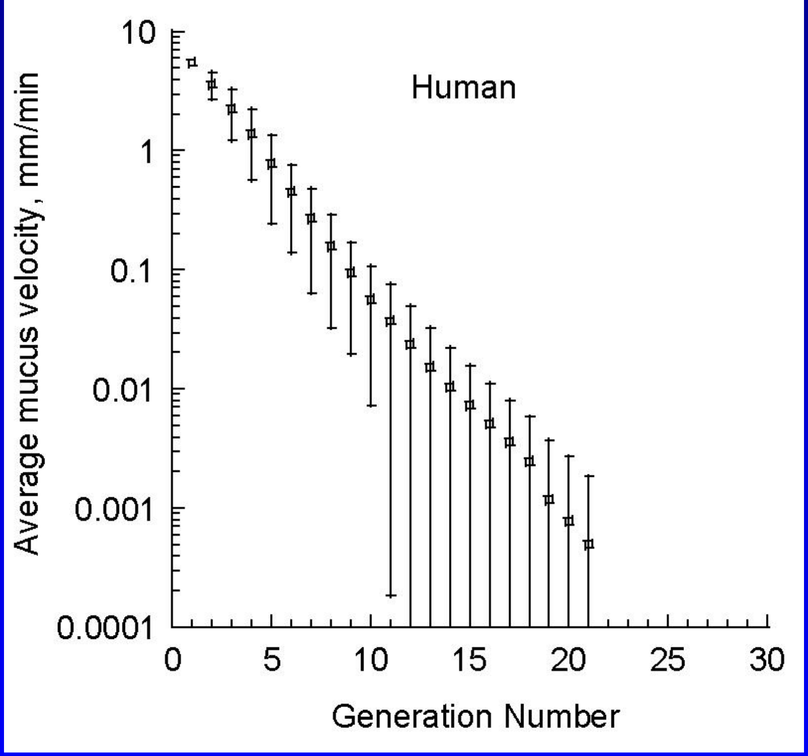
Sources of intra- and intersubject variability of mucociliary clearance

Intrasubject variability:

Mucus velocity and mucus transit time in a given aiway are related to the diameter and length of that airway (variability of airway diameters and lengths)



Intersubject variability:

Yeates et al. (1975, 1982):

Tracheal mucus velocity: Median = 4.2 mm min^{-1} (normalized to 5.5 mm min^{-1}), GSD = 1.8

Mucus velocities are rescaled in relation to the randomly selected tracheal mucus velocity

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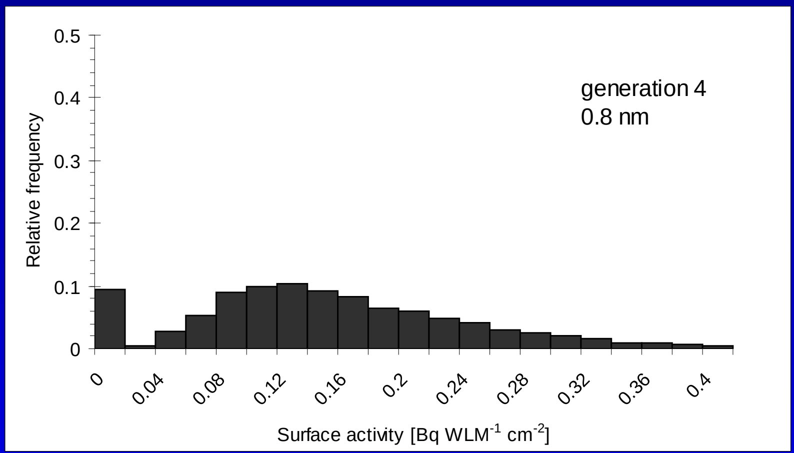
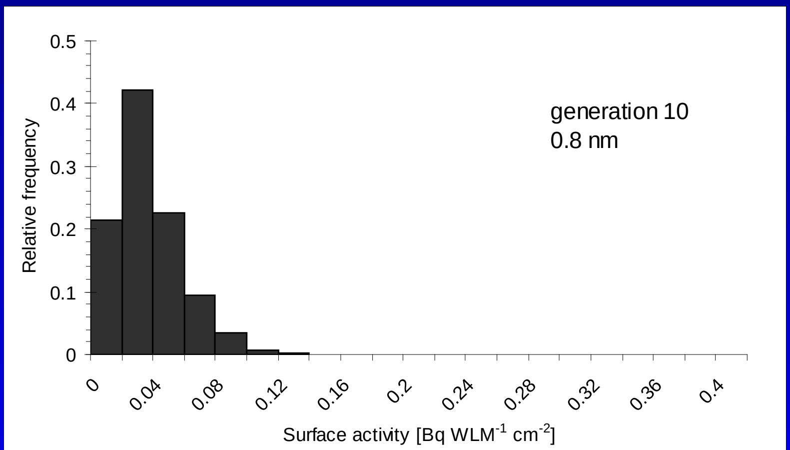
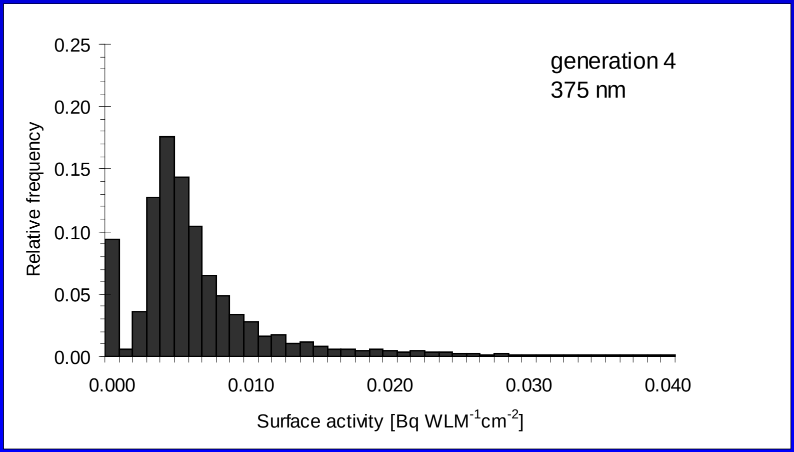
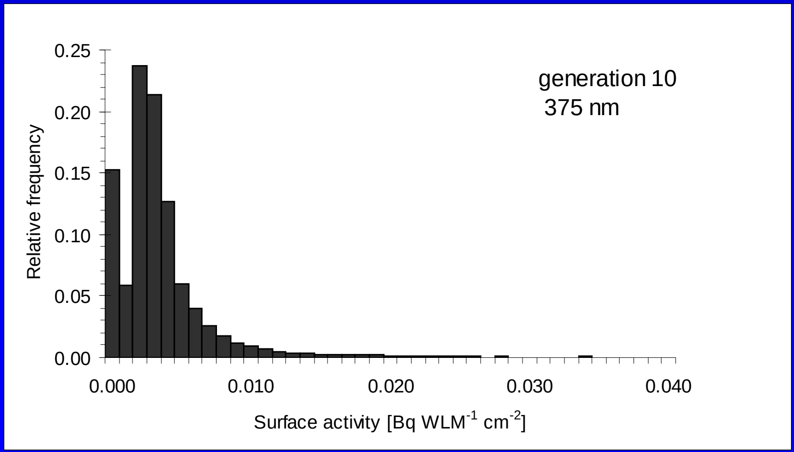
Steady-state surface actvities on bronchial airway surfaces

Deposition, clearance and radioactive decay → source strength for dose calculations
Breathing conditions (light exercise)
Surface activity of ^{218}Po in bronchial airways









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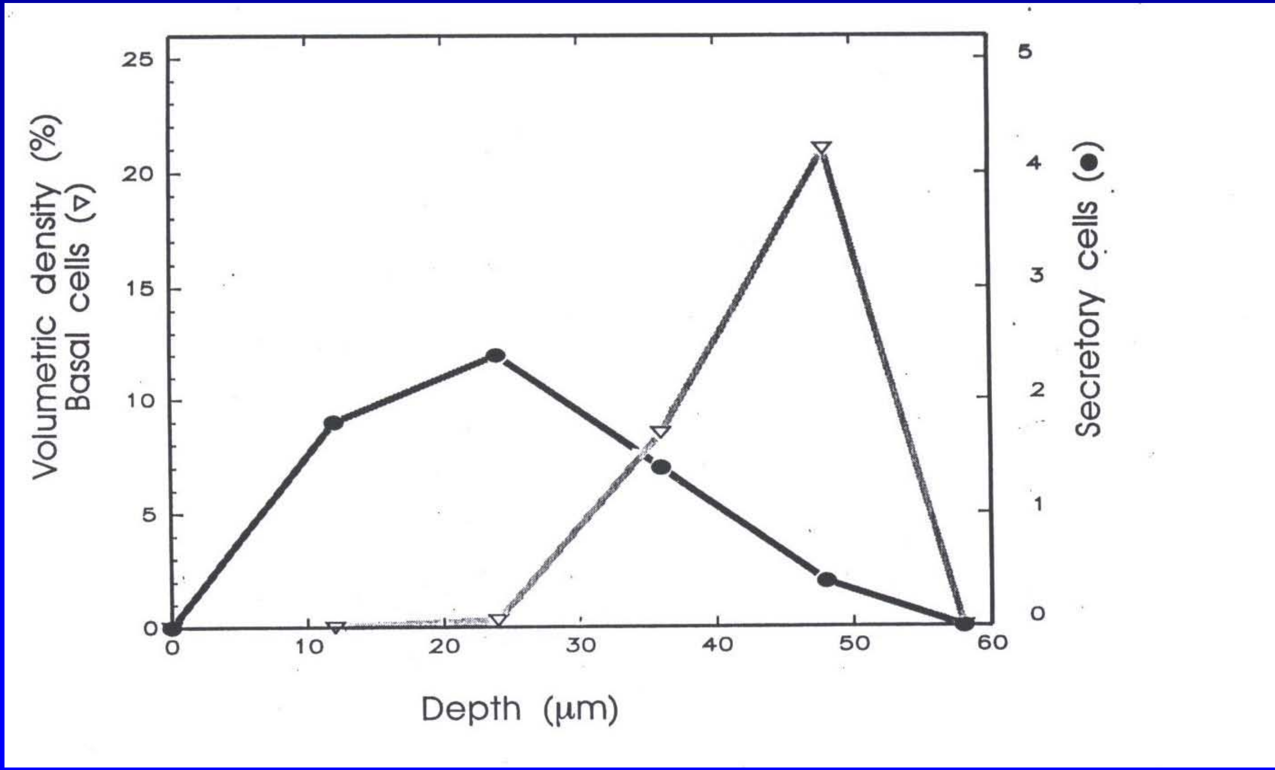
Sources of intra- and intersubject variability of target cell parameters

Thickness of bronchial epithelium:
Correlation with the corresponding airway diameter through a polynomial function
Depths of basal and sceretory cells in bronchial epithelium:
Depth distributions and relative frequencies of basal and secretory cells

Mercer et al. (1991):



Large bronchi

(generation 2)

ICRP (1994):
Basal and secretory cells are uniformly distributed across defined depth ranges in bronchial (BB) and bronchiolar (bb) regions

Uranium miner exposure conditions

Winkler-Heil et al. 2007:

Breathing parameters:

Reference worker (ICRP 1994), defined as an adult, nasal breathing male, with 31.25% sitting and 68.75% light exercise, which yields an average breathing rate of 1.2 $m^3\ h^{-1}$.

Aerosol parameters:

Unattached mode:

AMTD = 0.8 nm, GSD = 1.3, unit density, HGF = 1

Attached mode:

AMTD = 250 nm, GSD = 2.2, unit density, HGF = 1.5

Nuclide parameters:

F = 1 is assumed for simplicity (dose per WLM is relatively insensitive to F).
Exposure of 1 WLM with the short-lived radon progeny in equilibrium yields an exposure of 6.369×10^5 h Bq m^{-3} for ^{218}Po, ^{214}Pb and $^{214}Bi/^{214}Po$.

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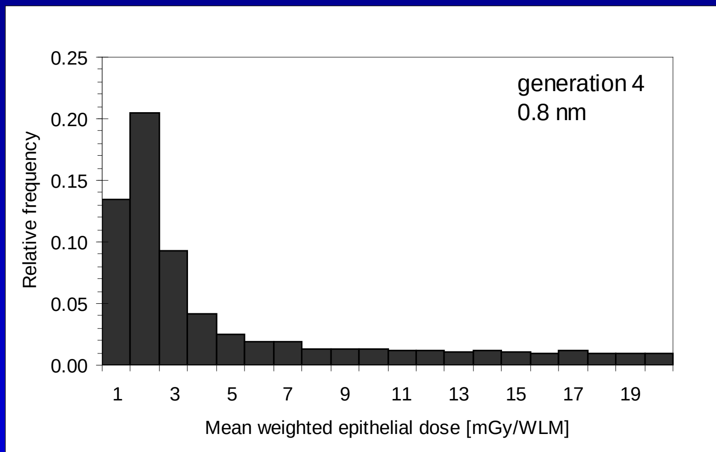
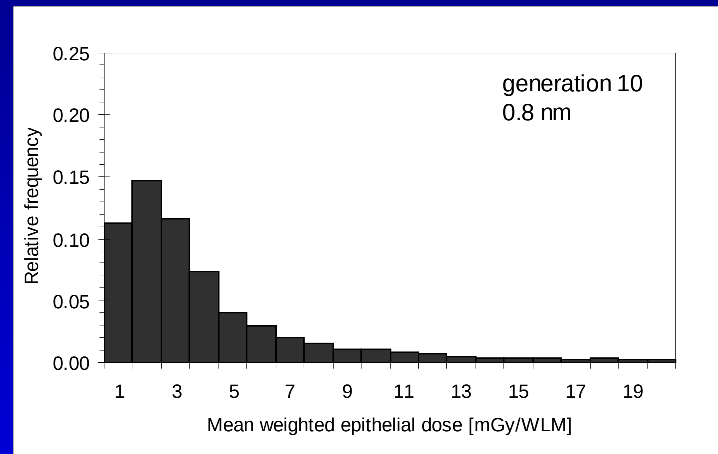
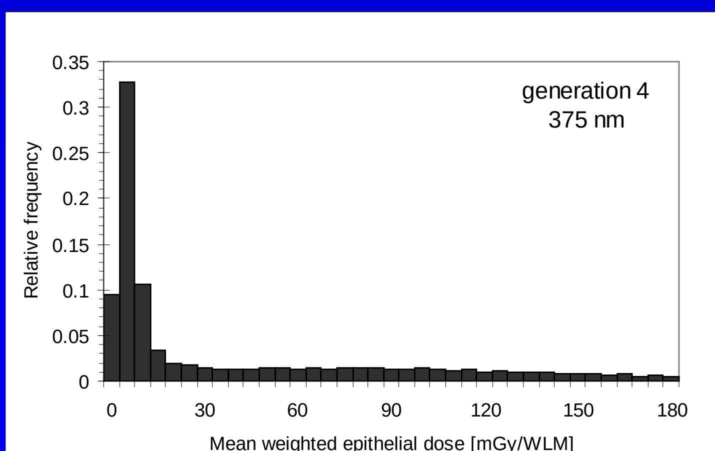
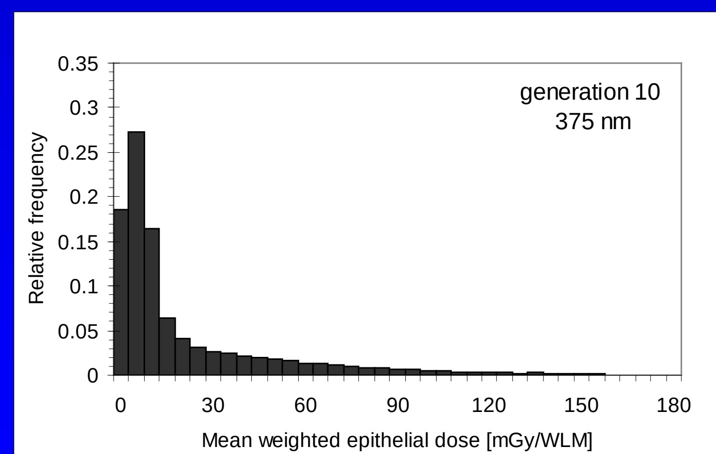
Intra-and intersubject variability of bronchial doses

Mean weighted epithelial dose, produced by ^{218}Po and ^{214}Po for uranium miner conditions









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Intra- and intersubject variability of bronchial doses

Mean weighted epithelial dose for uranium miner conditions

Generation no.	Median	GSD
1	2.41	1.97
2	4.46	2.12
3	4.44	2.15
4	3.60	2.20
5	3.16	2.19
6	2.86	2.27
7	2.69	2.34
8	2.46	2.48
9	2.57	2.78
10	3.42	3.11
11	3.61	3.59
12	3.32	4.38
13	2.73	5.09
14	2.01	6.57
15	1.65	6.85
16	1.51	6.55
17	1.67	4.87
18	1.69	3.95
19	1.64	3.47
20	1.55	3.66

BB region

Median: 3.18 mGy/WLM

GSD: 2.28

bb region

Median: 2.25 mGy/WLM

GSD: 4.74

Conclusions (I)

Intersubject variability of bronchial doses is defined in this study as the effect of morphological and physiological parameter variations among a group of subjects on bronchial doses for defined exposure conditions, where each subject is characterized by a dose distribution (intrasubject variability).

The primary sources of intersubject variability are the asymmetry and variability of airway dimensions, the filtering efficiency of the nasal passages and the depths of the bronchial epithelium, while fluctuations of the respiratory parameters and mucociliary clearance velocities seem to partly compensate each other.

Bronchial dose distributions can be approximated by lognormal distributions, characterized by median and geometric standard deviation (GSD).

Conclusions (II)

Geometric standard deviations of weighted bronchial doses range from 1.97 in the trachae to 6.85 in peripheral bronchiolar airways for defined uranium miner exposure conditions. GSDs for the BB and bb regions are 2.28 and 4.74, respectively.

Geometric standard deviations in airway generations 1 – 11, where all airways are bronchial airways, range from 1.97 to 3.59. In airway generations 11 to 20, the fraction of bronchial airways decreases from 100% in generation 11 to zero in generation 20, while the remaining airways are already alveolated. Hence the higher GSDs in peripheral bronchiolar airways are caused primarily differences of the paths of inhaled particles.

The observation that a fraction of cells in each airway generation may receive doses which are roughly an order of magnitude higher than the related median doses may have important implications for radiation protection and lung cancer risk assessment.

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for
your attention !