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Inhalation von Radionukliden – physikalische und biologische Mechanismen

Werner Hofmann

Abteilung für Physik und Biophysik, Fachbereich Materialforschung und Physik, Universität Salzburg

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LUNG DOSIMETRY MODELS

Sequence of consecutive steps:

Deposition: physical and biological mechanisms
Fluid dynamics, physical deposition mechanisms, breathing parameters

Clearance: biological mechanisms
Mucociliary clearance, macrophage transport

Retention (deposition, clearance, radioactive decay): physical and biological mechanisms

Tissue dosimetry: physical and biological mechanisms
Energy deposition in cells, cellular tissue structure

Note: Deposition and clearance steps are the same for radioactive and non-radioactive particles

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LUNG DOSIMETRY MODELS

Morphometric lung model
Structure (number of generations, branching patterns), linear airway dimensions (diameters, lengths, etc.)

Respiratory physiology model
Breathing patterns related to physical activities (breathing frequency, tidal volume, breathing cycle)

Deposition model
Extrathoracic filter, physical deposition mechanisms in cylindrical airways (diffusion, impaction, sedimentation), analytical deposition equations for specified flow patterns

Clearance model
Clearance pathways and related half-times (mucociliary clearance, slow bronchial clearance fraction, transport into blood via epithelial tissue, macrophage transport)

Dosimetry model
Depth and frequency distributions of sensitive target cells in bronchial and alveolar epithelium , geometric model of alpha particle interactions with target cells

IDEAL-DOSE: Stochastic lung dosimetry model applying Monte Carlo methods

THE HUMAN RESPIRATORY TRACT

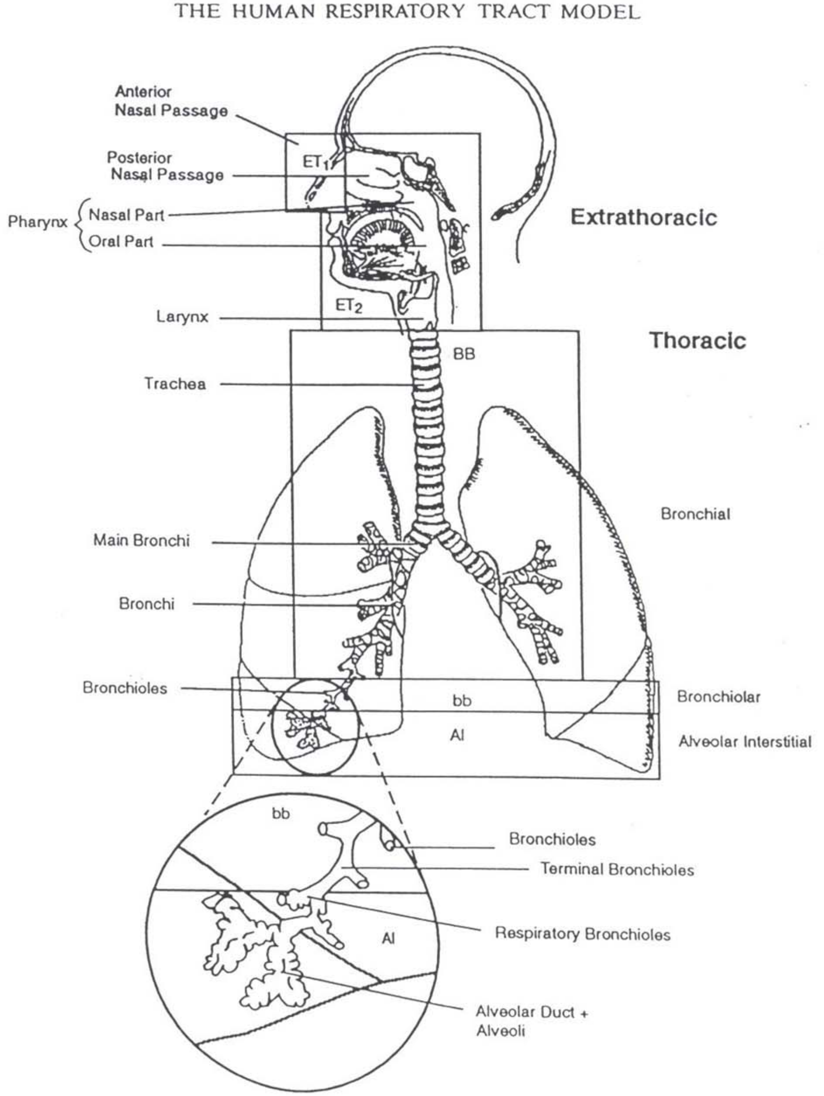
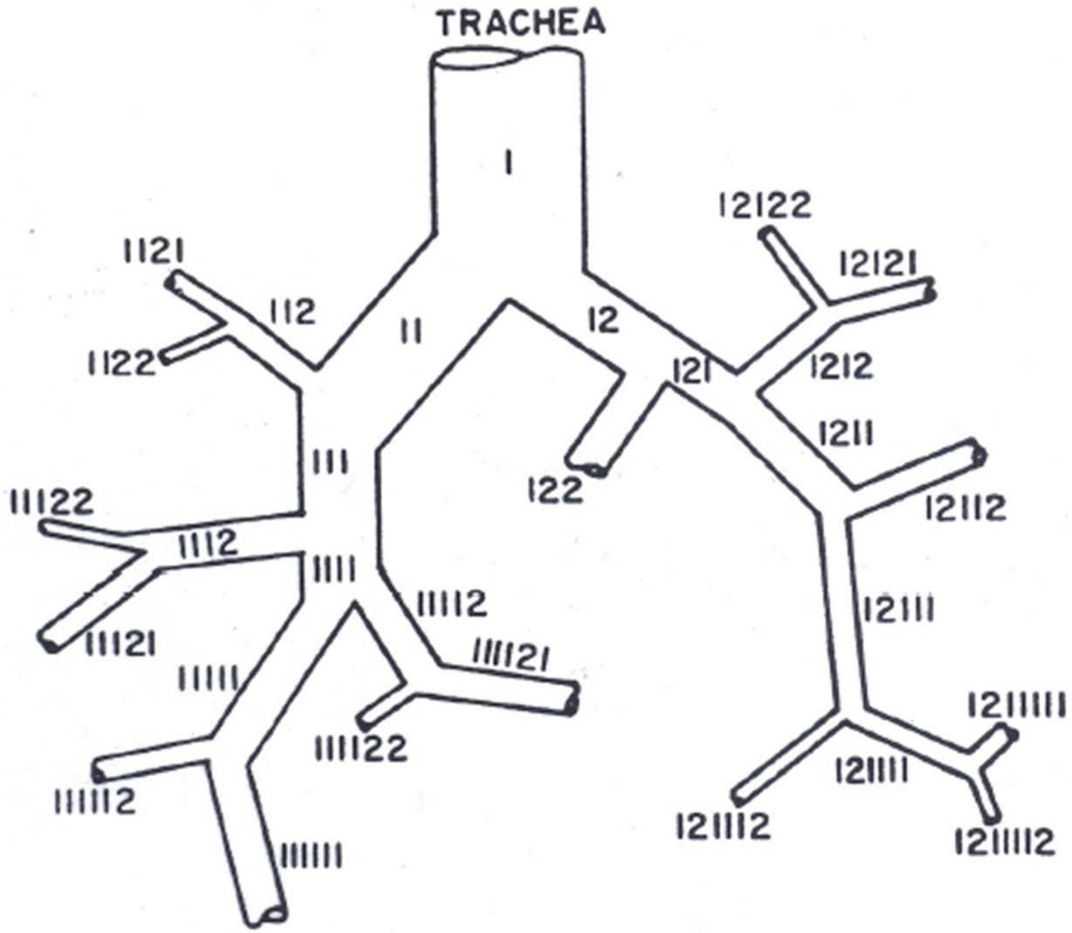


Fig. 1. Anatomical regions of respiratory tract.

AIRWAY GENERATION MODELS OF THE HUMAN LUNG

Raabe et al. (1976):
Morphometric measurements of the tracheobronchial tree (trachea to bronchial airways: 100%, bronchiolar airways to terminal bronchioles: 10-25%)



VENTILATION PARAMETERS BY AGE AND GENDER

ICRP (1994):

	Physical activity							
	Resting (sleeping)		Sitting		Light exercise		Heavy exercise	
Age \ Breathing parameters	f (min^{-1})	TV (L)	f (min^{-1})	TV (L)	f (min^{-1})	TV (L)	f (min^{-1})	TV (L)
1 y	34	0.074	36	0.102	46	0.127		
5 y	23	0.174	25	0.213	39	0.244		
Male 10 y	17	0.304	19	0.333	32	0.583		
Male 15 y	14	0.500	15	0.533	23	1.0	36	1.352
Female 15 y	14	0.417	16	0.417	24	0.903	38	1.127
Male 30 y	12	0.625	12	0.750	20	1.25	26	1.923
Female 30 y	12	0.444	14	0.464	21	0.992	33	1.364

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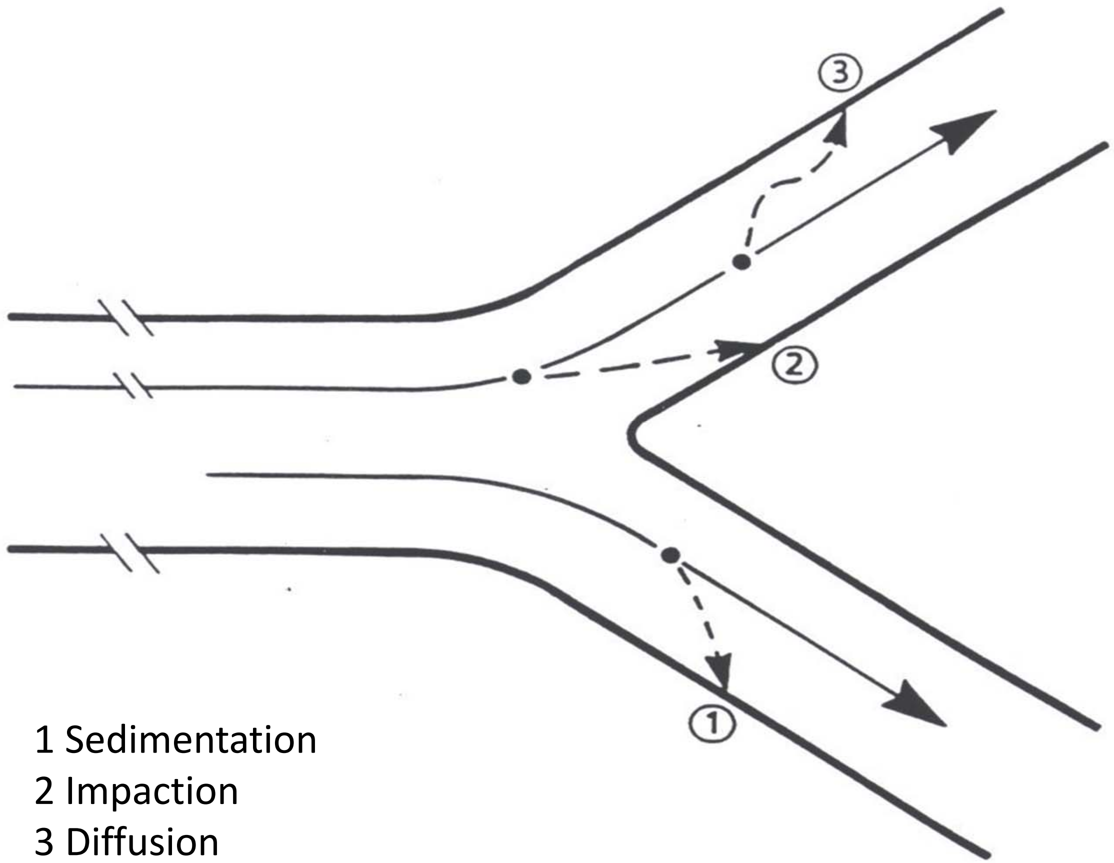
PHYSICAL DEPOSITION MECHANISMS



1 Sedimentation
2 Impaction
3 Diffusion

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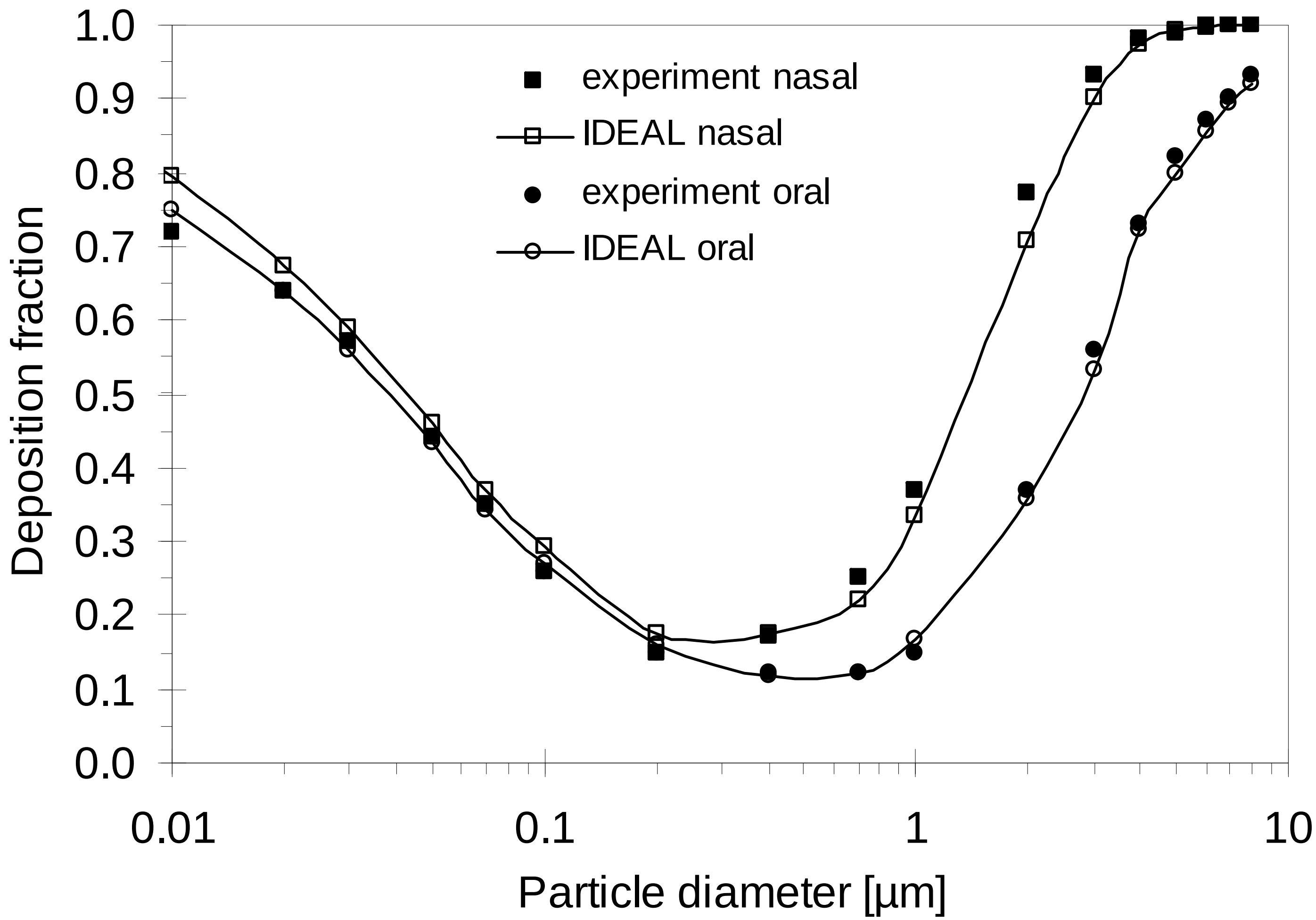
TOTAL DEPOSITION IN THE HUMAN LUNG

Heyder et al. (1986):



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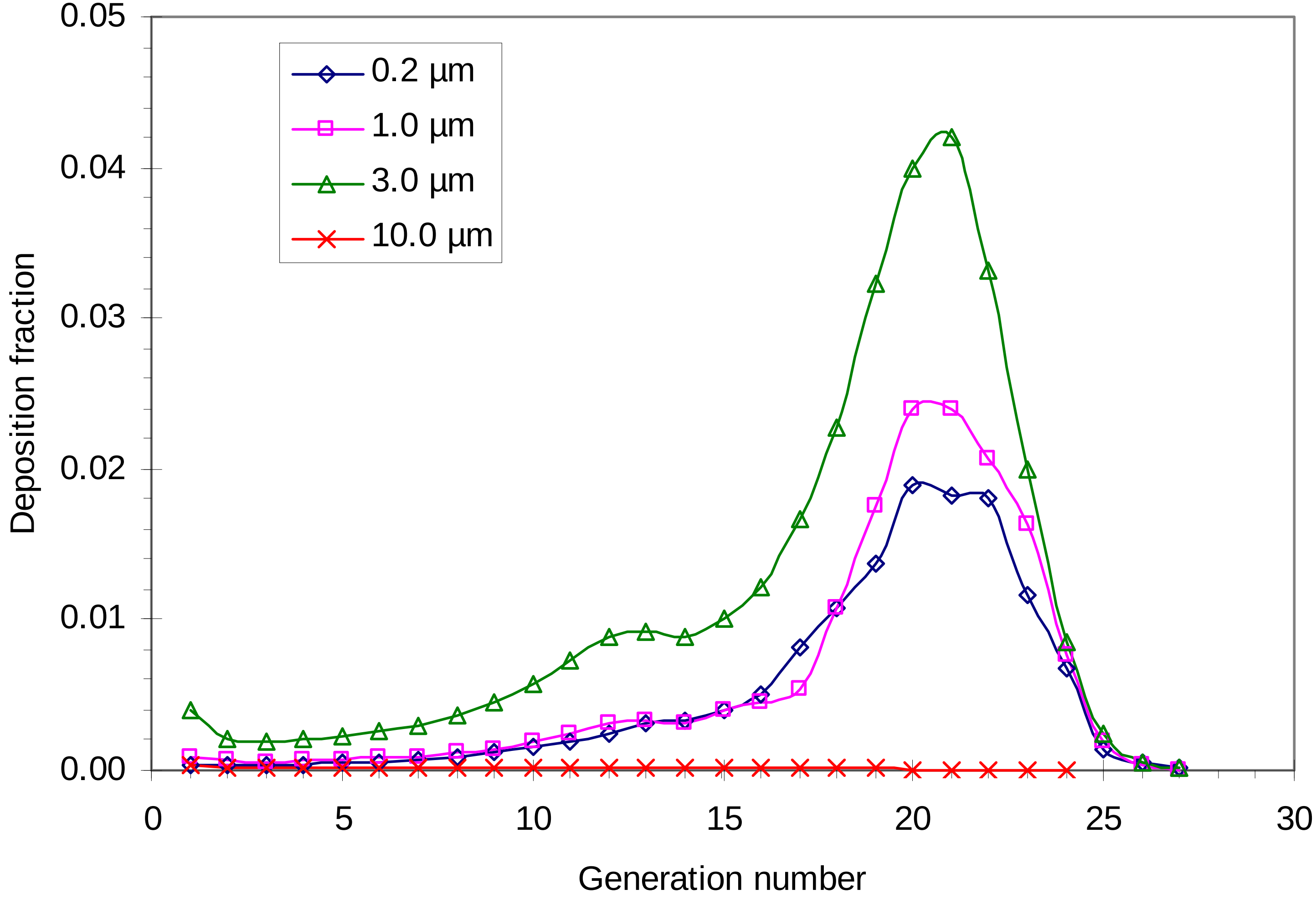
DEPOSITION IN HUMAN AIRWAY GENERATIONS



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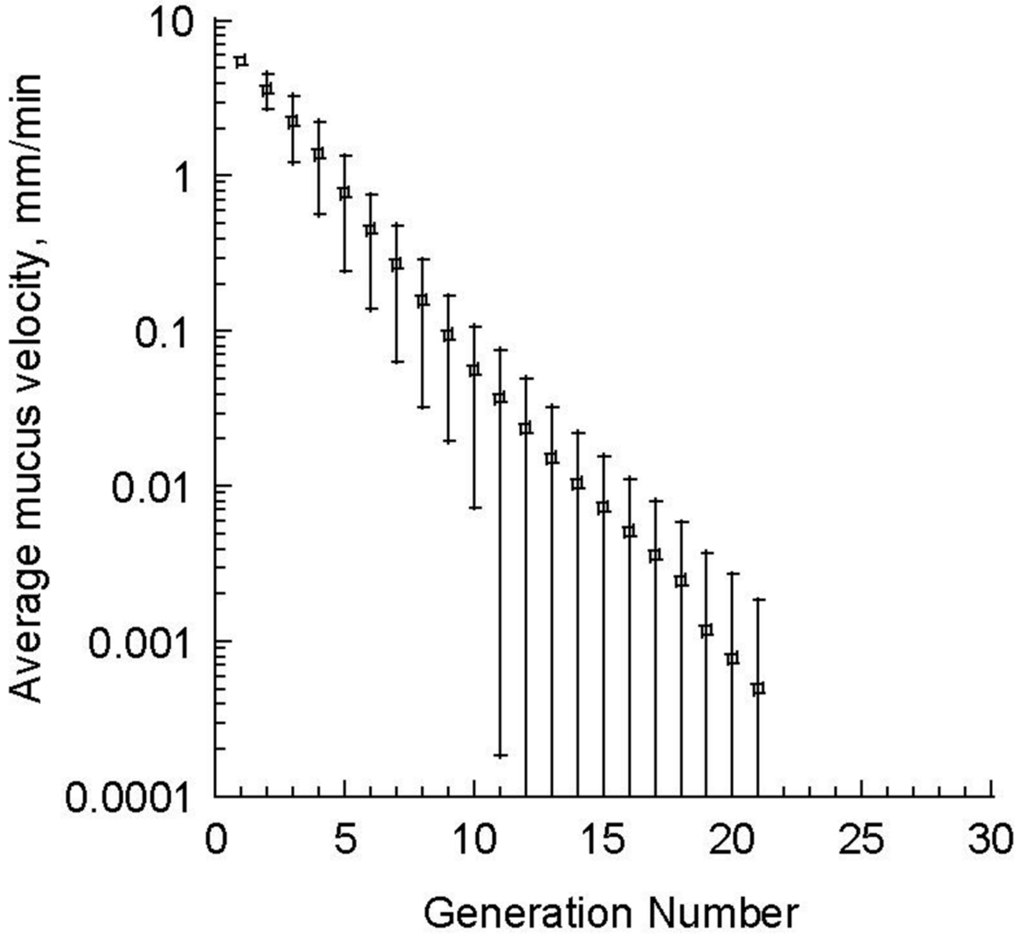
MUCOCILIARY CLEARANCE VELOCITIES IN THE BRONCHIAL REGION

Hofmann and Asgharian (2002):



GEOMETRIC ALPHA PARTICLE CELLULAR DOSIMETRY MODEL

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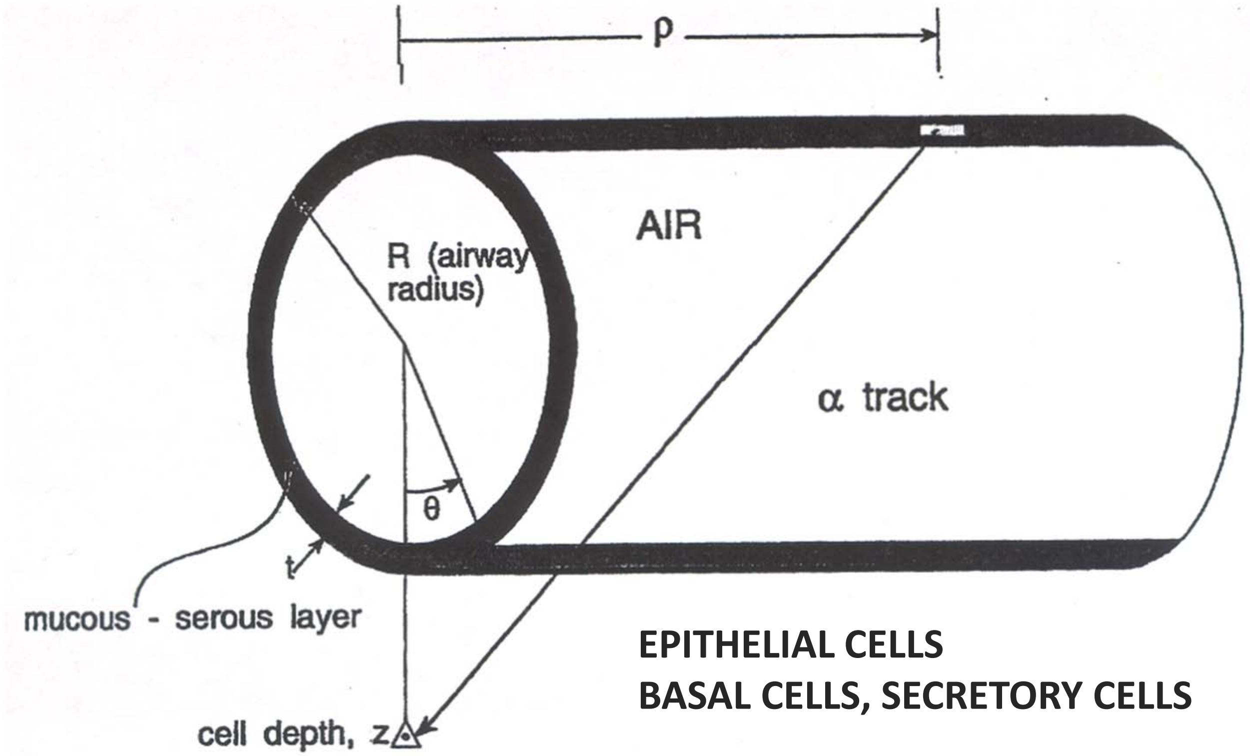
Cylindrical bronchial airway geometry



EPITHELIAL CELLS
BASAL CELLS, SECRETORY CELLS

Dose as a function of depth in bronchial epithelium is computed for uniform activities on cylindrical bronchial airway surfaces, considering both near and far wall contributions.

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INTRA- AND INTERSUBJECT VARIABILITY OF BRONCHIAL DOSES PRODUCED BY RADON PROGENY ALPHA PARTICLES

- **Breathing parameters:**
  Variations of breathing frequency, tidal volume, breathing cycle times

- **Airway morphology:**
  Size and structure of oral and nasal passages, asymmetry and variability of linear airway dimensions (diameters, lengths, branching and gravity angles) and their correlations (e.g. cross-section ratios, termination probability)

- **Mucociliary clearance:**
  Mucociliary clearance velocities, slow bronchial clearance fraction

- **Bronchial epithelium:**
  Thickness of bronchial epithelium, depths of target cells

Most important factors are:
Asymmetry and variability of the airway geometry, filtering efficiency of nasal passages, and diameter-related thickness of the bronchial epithelium

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INTRA- AND INTERSUBJECT VARIABILITY OF BRONCHIAL DOSES PRODUCED BY RADON PROGENY ALPHA PARTICLES

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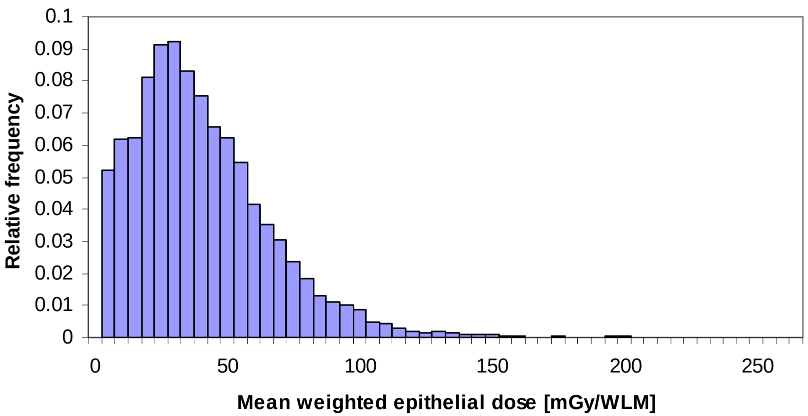
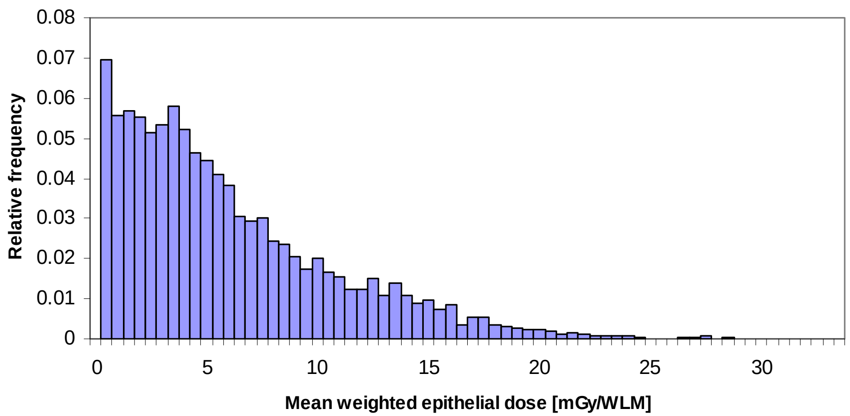
Generations 4 and 10, diameters 1 nm (unattached) and 200 nm (attached)

Generation 4

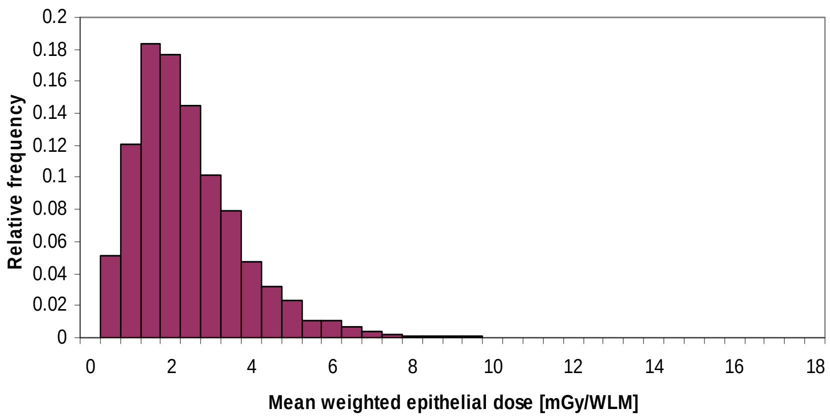
Generation 10

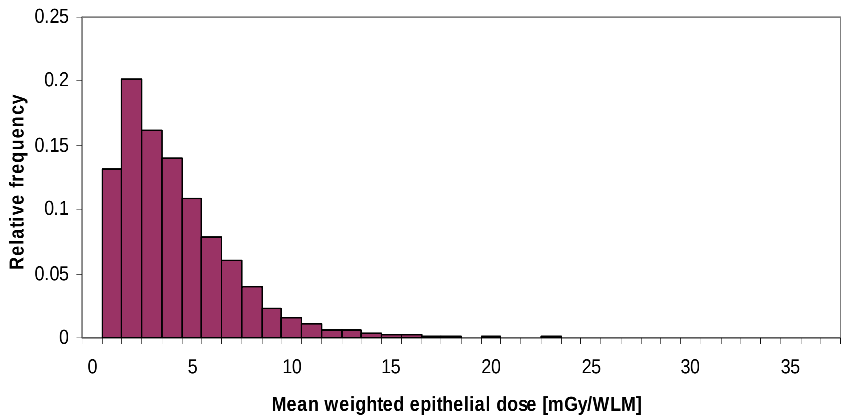
Unattached





Attached



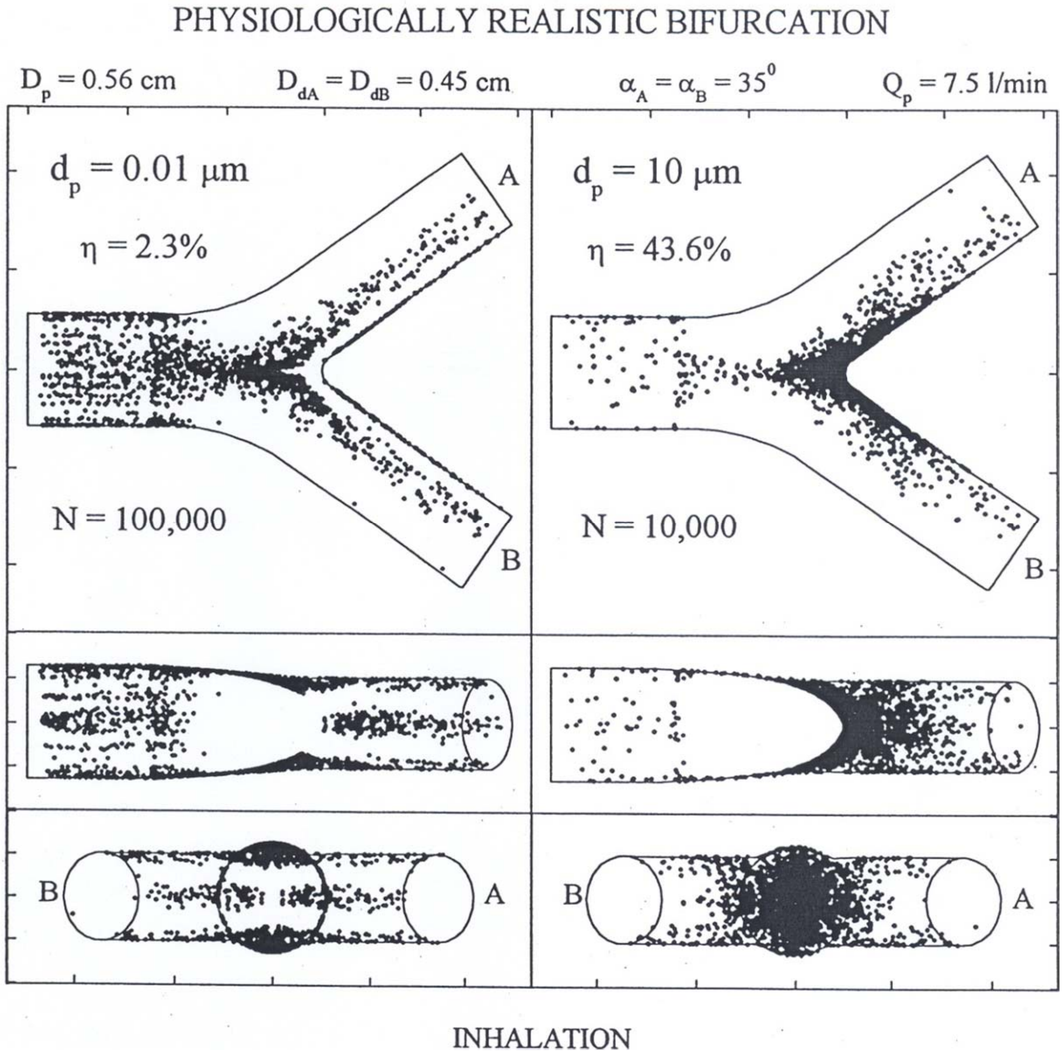


BB region: Median: 3.18 mGy/WLM
GSD: 2.28

bb region: Median: 2.25 mGy/WLM
GSD: 4.74

DEPOSITION OF INHALED PARTICLES IN A BRONCHIAL AIRWAY BIFURCATION

Balásházy et al. (1999): CFPD model

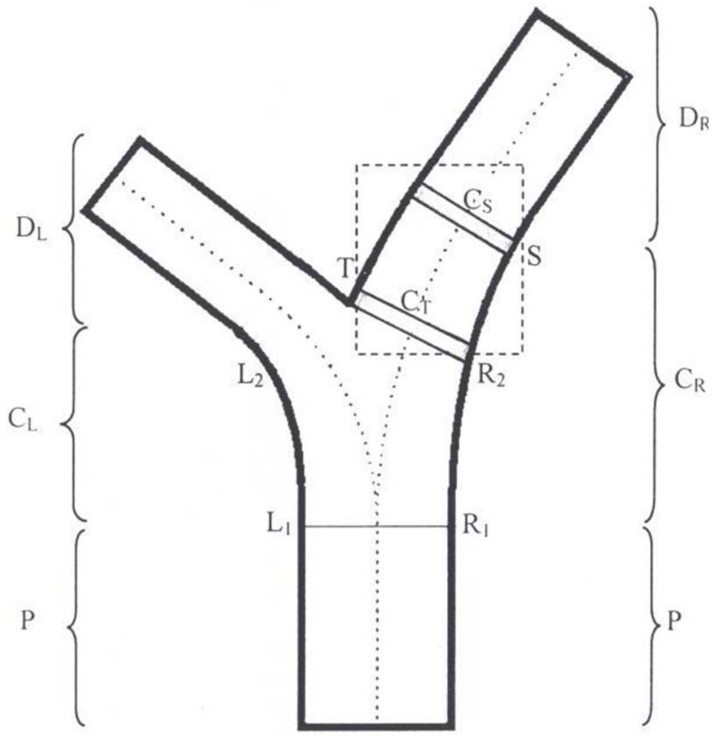


Local scale model: inhomogenous particle deposition patterns

DOSE DISTRIBUTION WITHIN BRONCHIAL AIRWAY BIFURCATIONS

Inhomogeneous activity distributions, i.e. local accumulations of activities at carinal ridges due to enhanced deposition and impaired mucociliary clearance, and non-uniform irradiation geometry lead to inhomogeneous dose distributions

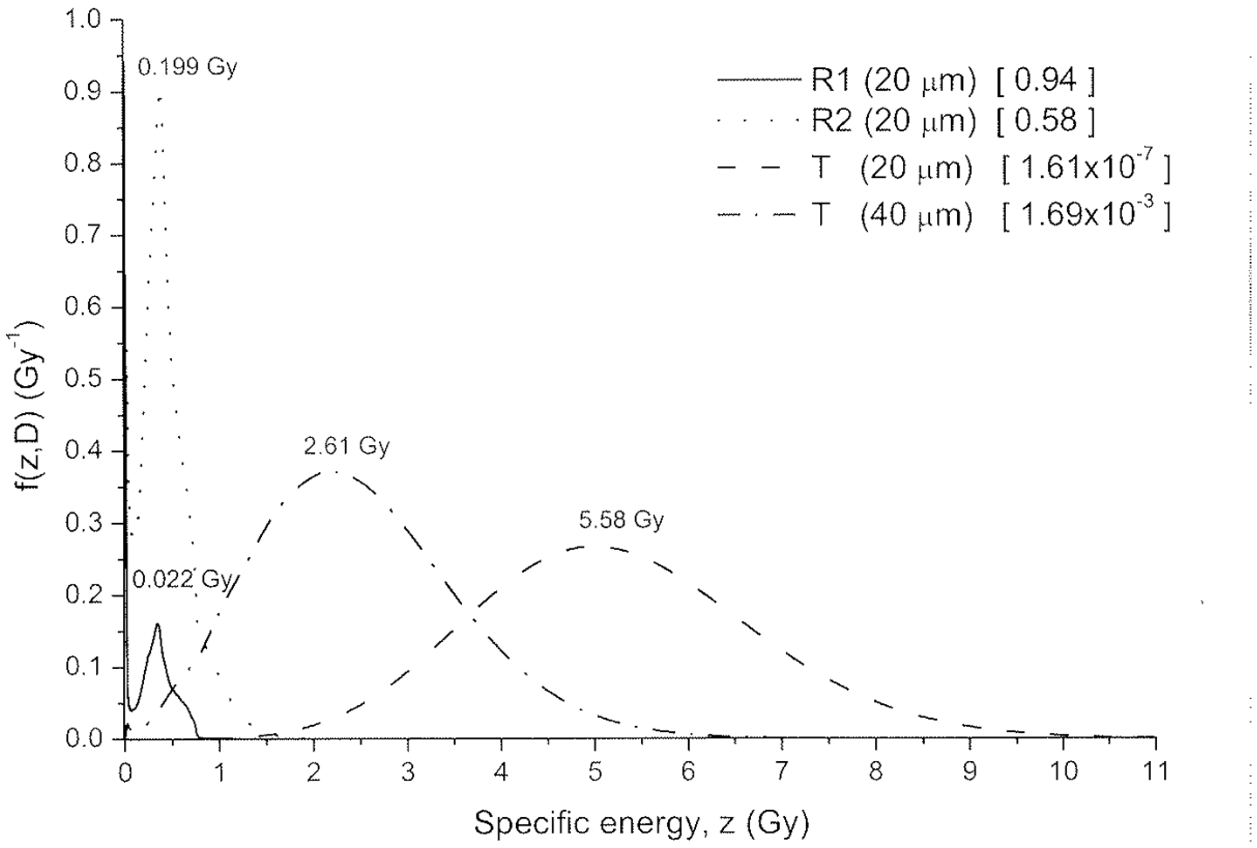
Fakir et al. (2005):



R_1: cylindrical section
R_2: transition zone
T: carinal ridge

MICRODOSIMETRIC SPECIFIC ENERGY SPECTRA AT BRONCHIAL BIFURCATIONS

Specific energy distributions (microdosimetry)
Fakir et al. (2005):



*number of zero hits

Typical result:
About 10% of the whole bifurcation surface area receives a roughly ten times higher dose than the average dose (tip of carinal ridge: factor of about 100).

INHALATION OF RADIOACTIVE GASES

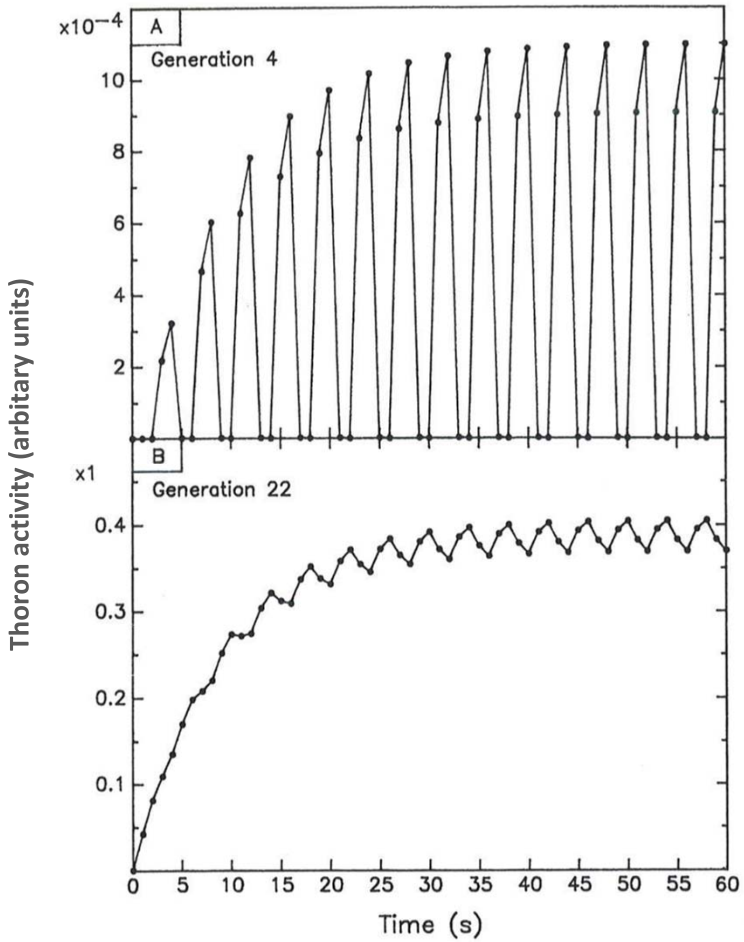
Radioactive gases, e.g. radon
Radioactive gases deposited on particle surfaces in ambient air and released from these particles during inhalation due to evaporation

- Transport of gases follows the transport of inhaled air
- Deposition on airway surfaces by diffusion either by Brownian motion or by a concentration gradient
- Uptake by the bronchial or alveolar epithelium depends on the solubility in tissue and the mass balance between air and tissue concentrations
- Gas molecules may also be released back into the air volume upon exhalation

THORON ACTIVITY CONCENTRATION IN THE EXHALED AIR

Thorotrast patients:
Thoron is produced by Thorotrast deposits in liver, spleen and bone marrow, transported to the lung by the blood, and then exhaled. The exhaled amount of thoron is a measure of the Thorotrast activity still retained in the human body.

Hofmann et al. (1990):



SUMMARY

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Inhalation of radionuclides depends on physical factors, such as deposition mechanisms and decay schemes, and on biological factors, such as airway morphometry and clearance pathways

Lung doses exhibit significant intra- as well as intersubject variations, represented by lognormal dose distributions

Deposited radionuclides exhibit significant accumulations at bronchial airway bifurcations due to enhanced deposition and reduced clearance, producing high local doses at carinal ridges

Deposition of inhaled radioactive gases, following the movement of air, is determined by the mass balance between the concentrations in air and in tissue