Radiation Protection Dosimetry (2014), Vol. 158, No. 2, pp. 135–147 doi:10.1093/rpd/nct218
Advance Access publication 19 September 2013

A REVISED MODEL FOR THE DEPOSITION AND CLEARANCE OF INHALED PARTICLES IN HUMAN EXTRA-THORACIC AIRWAYS

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Received February 1 2013, revised August 15 2013, accepted August 17 2013

The International Commission on Radiological Protection (ICRP) Task Group that developed the Human Respiratory Tract Model for Radiological Protection (HRTM) identified a lack of published information on aspects of the clearance of inhaled particles deposited in the human nasal passage. Using the results of a recent human volunteer study on the clearance of inhaled particles from the nose, a revised model of clearance from the extra-thoracic (ET) airways has been developed that addresses important issues for which simplifying assumptions had to be made in the ICRP Publication 66 HRTM ET model. This ET clearance model has been adopted by ICRP for inclusion in the revised HRTM. The derivation of the model and parameter values from the experimental data are explained.

INTRODUCTION

The International Commission on Radiological Protection (ICRP) Committee 2 Task Group that developed the Human Respiratory Tract Model (HRTM) found in its review of published data that there was a lack of information on the clearance of inhaled particles that deposit in the human nasal passage (ICRP Publication 66, Paragraph E83[(1)]). Two studies did provide limited data on nasal clearance in the first 10 h after intake[(2, 3)] with some data available from studies on clearance by nose blowing[(4)], but no information was available on nasal clearance at times >10 h.

The Task Group acknowledged this lack of information and the use of simplifying assumptions in the HRTM when modelling deposition and clearance within the extra-thoracic (ET) airways (Figure 1a). The ET airways are modelled in the HRTM as two regions: ET_1, the skin-lined anterior nasal passage and ET_2, the epithelium-lined posterior ET airways, as the tissues in these two parts of the ET airways have very different clearance patterns and perceived radio-sensitivities.

Information available on clearance from ET_1 and its implementation in the HRTM was summarised as follows in paragraph 242[(1)]:

> Studies of mucus flow patterns, and of the retention of radiolabelled particles inhaled by humans, suggest that most of the material deposited in the anterior nasal passages (compartment ET_1) is removed by extrinsic means (nose-blowing, wiping etc.) and that the retention time is of the order of 1 day (Section E.4.1). It is also likely, however, that some of the material deposited in ET_1 is transported to the posterior nasal passages (which are included in ET_2) by mucus flow and sniffing. To take account of this, while avoiding the additional complexity of a pathway from ET_1 to ET_2, the deposition fraction of ET_2 is rounded upward and that for ET_1 is correspondingly rounded downward. Thus it is assumed that the activity deposited in the nasal part of ET is equally divided between ET_1 and the nasal part of ET_2 (Section D.7.1), although for typical occupational exposures to aerosols with AMADs of a few micrometers or more, it would be expected that deposition in ET_1 would be somewhat greater than that in the nasal part of ET_2[(1)].

As explained in paragraph D78 of ref. (1) there was, at that time, insufficient experimental data to determine the partitioning between ET_1 and ET_2.

Deposition in the HRTM is modelled as a set of filters in series, the filters corresponding to the regions of the respiratory tract (RT) that the aerosol passes through as it is inhaled and then exhaled. Following the first filter, which models the inhalability of the aerosol, the first and last filters in the sequence represent the ET airways (ET_1 and ET_{2n} for nasal inhalation and ET_{2m} for oral inhalation). Total deposition in a specific region of the RT is given by the sum of deposition in the inhalation and the exhalation

[†]The Health Protection Agency became part of Public Health England on 1 April 2013.

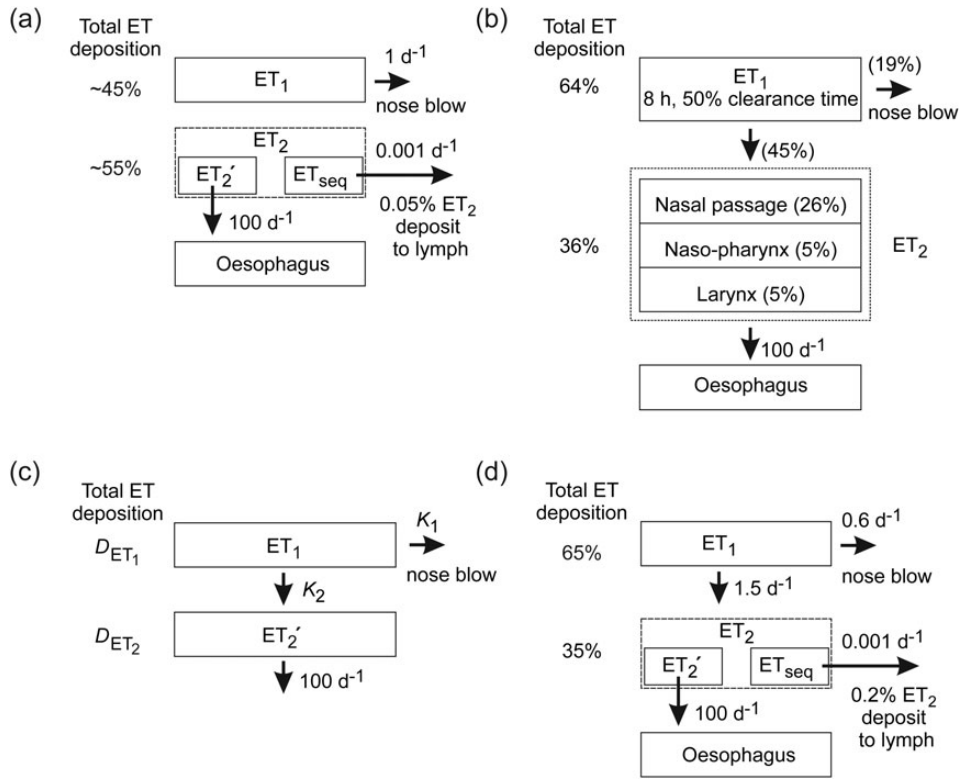

Figure 1. (**a**) ICRP Publication 66 HRTM model of ET clearance[1], (**b**) schematic summary of experimental results of nasal clearance study, (**c**) simple model of biokinetic behaviour of inhaled aerosol in the ET region used to determine clearance rates K_1 and K_2 for fixed deposition fractions D_{ET_1} and D_{ET_2} and (**d**) complete revised ET clearance model.

filters. The deposition efficiencies are determined using a semi-empirical approach that depends on particle size, air flow rate and airway dimensions. As the most appropriate interpretation of the available information, constraints were made so that for both very small and very large particles there is equal deposition in ET_1 and ET_2. This gave an approximate partitioning of 50:50 between ET_1 and ET_2 for all aerosol sizes and air flows. While the model constrains the ratio to exactly 50:50 at the model's maximum and minimum particle sizes, the ratio does vary to a small degree over the intervening particle size range and with breathing rates. This variation is an artefact of the model, caused by the requirements of modelling deposition on both inhalation and exhalation for both thermodynamic and aerodynamic processes and ensuring that the modelled deposition in all regions of the RT is in agreement with the experimental data then available. As ET_1 and ET_2 are the first, second, last and penultimate compartments in the RT deposition model (Tables 12 and 13 in ref. (1)) it was not possible to make the sum of deposition on inhalation and exhalation for these two compartments exactly match for all particle sizes without compromising deposition calculated for other, more radiosensitive, regions of the RT.

In the original (Publication 66) HRTM, all particles deposited in ET_1 are cleared to the environment with a clearance rate 1 d^{-1} with no absorption to blood. Of the particles deposited in ET_2, 99.95 % are cleared by transport to the gastro-intestinal tract (GI tract) at a rate of 100 d^{-1}. Particles deposited and then cleared in this way are represented by compartment ET_2' in Figure 1a. The remaining 0.05 % of particles deposited in ET_2 are sequestered into the airway's epithelium and eventually cleared to the lymphatic system at a rate of 0.001 d^{-1} (ET_{seq} in Figure 1a). For both fractions, absorption to blood competes with particle transport and is modelled using the same model and parameter values as that used for particles deposited elsewhere in the RT. No route for clearance from ET_1 to ET_2, and hence to the GI tract or blood, is present in this model.

This paper supports a revision of the transport model for the ET airways for particles inhaled through

the nose. The ET_2 sequestered fraction is also reassessed, taking into account the revision of the ET model and data presented in ICRP Publication 66[1]. The revised model does not affect the modelling of the deposition or clearance of particles inhaled through the mouth that deposit in ET_2, nor the biokinetic modelling of absorption to blood of particles in ET_2.

The revised model is derived from the results of a human volunteer study of nasal clearance of inhaled particles that was conducted to address the need for information identified by the Task Group[5, 6]. The revised ET model was submitted to the ICRP's Internal Dosimetry Task Group, who accepted it and incorporated it into the revised HRTM which was submitted to the ICRP Main Commission in October 2011 as part of the draft ICRP Publication 'Occupational Intakes of Radionuclides: Part 1'[7].

EXPERIMENTAL VOLUNTEER STUDY OF INHALED PARTICLE CLEARANCE FROM THE HUMAN NASAL PASSAGE

The volunteer study of inhaled particle clearance from the human nose and its results are comprehensively described in refs (5) and (6) and so only a summary is given here. To investigate the variation of nasal clearance with aerosol size and the subjects' work rate, a series of experiments were performed in which healthy volunteers inhaled insoluble monodisperse ^{111}In-labelled polystyrene particles ranging in size from 1.5- to 6-μm aerodynamic diameter (d_{ae}) through the nose while either sitting at rest or performing light exercise [Table B.14 in ref. (1)]. All nine subjects inhaled 3-μm aerodynamic diameter particles while sitting at rest to enable inter-subject variation to be assessed, while sub-groups of three or four inhaled 1.5- or 6-μm particles at rest, and 3- or 6-μm particles while performing light exercise. These particle sizes and exercise rates were selected as being typical of occupational exposure. The particles' retention in the ET airways and their clearance by nose blowing were followed for at least 2 d, until ET retention was <5 % of the initial ET deposit (IETD). In the first hour after intake a series of 1- and 5-min measurements was made to measure the fraction and clearance rate of particles deposited on the ciliated nasal epithelium and cleared to the GI tract by mucociliary action. Subjects blew their noses at will through the course of the experiment using standardised tissues, which were bagged and their time of collection recorded. Sample activities were measured by gamma-ray spectrometry. Activities in the subjects' lungs and GI tract (in the stomach and beyond) were also measured throughout the experiment. Information on intra-subject variation was gained from subjects participating in both a pilot experiment, using ^{99m}Tc labelled particles, and a main experiment for the same particle size and breathing rate.

To compare the results of the individual inhalation experiments, all retention and clearance data from each experiment were corrected for radioactive decay since the time of intake and normalised by expressing all data as fractions of the IETD[5, 6]. Measurement and calibration uncertainties were propagated through all such calculations and other sources of uncertainty were taken into account. Ref. (6) provides a compilation of the experimental data, sources of uncertainties, their magnitudes and treatment. Intake activities and count times were selected to ensure adequate measurement precision[5].

No overall trends were found between nasal clearance and particle size, exercise rate or any other parameter related to deposition[5]. Regression analysis was also used to detect any trends between nasal clearance and the subjects' age, weight, height and body mass index. A linear fit to the two sets of data being compared was used, rather than a more complex relationship, because of the limited number of pairs of data available. The P test was used to identify correlations, using the criterion that a statistically significant relationship between the two parameters was indicated if P was ≤ 0.05. No statistically significant relationships were found. However, it should be noted that the volunteers were a small group of nine white Europeans, only one of whom was female. Such trends may exist but be masked by inter-subject variation. The fraction cleared by nose blowing was correlated with the frequency of voluntary nose blowing and was therefore considered to be a characteristic of an individual. Significant inter- and intra-subject variation in the clearance rates and fractions was observed. Therefore, it was considered appropriate to typify the nasal clearance by considering the average behaviour observed for the whole study for all particle sizes and inhalation conditions. A generic model of ET clearance was derived from the results of the study using parameters derived as directly as possible from the experimental data to prevent it being influenced by modelling artefacts.

Four modes of clearance for particles deposited in the ET airways were identified:

- The ET retention fraction cleared by nose blowing.
- A fraction presumed to deposit in the extreme posterior of the ET airways, e.g. the pharynx, that is promptly swallowed and present in the stomach within a few minutes of inhalation.
- A fraction deposited on the ciliated epithelium of the posterior nasal passage and cleared by mucociliary action to the GI tract with a clearance half-time of tens of minutes.
- A fraction deposited in the anterior of the nasal passages, cleared by mucociliary action to the GI tract with a clearance half-time of hours.

These fractions are the same as or closely related to the following four clearance fractions directly measured by the study.

Fraction of IETD cleared by nose blowing

Total clearance by nose blowing was determined by summing the decay-corrected activities of all the nose blows produced. The total fractions cleared by nose blowing were highly variable, ranging from 0.5 to 49 % IETD, although the results for each subject tended to be similar. On average, 19 % IETD was cleared by nose blowing with a geometric mean 50 % clearance time of 8.2 h (Table 1).

All but one of the nose blow samples collected in the study were produced more than an hour after intake. Measurements showed that particles retained in the ET airways at times >1 h after intake are predominantly in the anterior of the nose[5], confirming the findings of the earlier nasal inhalation clearance studies[2, 3]. Therefore, particles cleared by nose blowing are considered to be from the fraction deposited in the ET_1 compartment of the HRTM.

The fraction cleared from the ET airways to the stomach by the time of the first measurement

The first measurements of aerosol retention in the subject's ET airways, lungs and stomach were made as soon as possible after inhalation, typically ~5 min later. The activity present in the stomach at that time varied from 0.5 to 57 % IETD, with an average value of 15 % IETD (Table 1). This activity is taken to be predominantly from particles deposited in the ET airways rather than in the lung as both the study's measurements of lung retention and the modelling of particle deposition and clearance from the lung using the HRTM[1] indicate that there will be negligible particle clearance from the lung to the GI tract in this period after intake[5].

This fraction is considered to be predominantly constituted of particles deposited in and around the pharynx and promptly swallowed. A secondary component may be from particles deposited on the nose's ciliated epithelium and cleared by mucociliary action. ET mucociliary clearance is estimated to contribute one-third (e.g. 5 % IETD) of average clearance to the stomach in this time interval (see below). However, both of these contributions to this clearance fraction deposit in the ET airways in areas designated as within ET_2 in the HRTM.

Clearance from the ET airways to the GI tract between the first measurement and approximately an hour after intake

Clearance in this time interval, between the first measurements made in the aerosol administration laboratory and the first using the Centre for Radiation

Table 1. Summary of clearance fractions determined for particles retained in the ET airways and their half-times[5].

ET retention clearance fractions	Fraction of IETD		50 % clearance time	
	Arithmetic mean	Standard deviation	Geometric mean (h)	Geometric standard deviation
Total IETD	1	N/A	2.5	3.2
Extraneous clearance				
Nose blow fraction	0.19	±0.15	8.2	3.0
Clearance from ET airways to GI tract				
Fraction swallowed promptly[a]	0.15	±0.13		
Total ET to GI tract mucociliary fraction	0.66	±0.22	4.1	2.9
ET to GI tract rapid mucociliary fraction[b]	0.21	±0.15		
ET to GI tract slow mucociliary fraction[c]	0.45	±0.20	8.9	2.0
HRTM compartment fractions				
ET_1 (nose blow plus slow mucociliary fractions)	0.64	±0.13	8.2	1.9
ET_2, (swallowed plus rapid mucociliary fractions)	0.36	±0.13	0.24	2.4

[a]The fraction of IETD that clears to the stomach by the time of the first *in vivo* measurement, typical <5 min after intake. Therefore, it is not possible to assign a 50 % clearance time to this fraction.
[b]The fraction of IETD that clears from ET to the GI tract between the time of the first *in vivo* measurement, <5 min after intake, and the first LBIDA measurement, made ~1 h after intake. A 50 % clearance time is not given for this fraction as it is likely to be influenced by the timing of those measurements and hence be an artefact of the experimental design.
[c]The fraction of IETD that clears from ET to GI tract after the first LBIDA measurement, that is at times >1 h.

Chemical and Environmental Hazards' (CRCE) highly sensitive low background *in vivo* measurement detector array (LBIDA), is expected to be dominated by mucociliary clearance of particles deposited on the ciliated epithelium of the nasal passage. The ET retention fractions cleared in this time interval ranged from 0 to 50 %, with an average value of 21 %.

A 50 % clearance time is not given for this fraction as it may be an artefact of the experimental design. However, the previous nasal inhalation clearance studies[2, 3] detected a clearance fraction with a half-time of a few tens of minutes in approximately half of their experiments. The fitted clearance half-times are consistent with the measured ET to GI tract clearance half-times of 10–30 min obtained by studies where particles were directly deposited onto the ciliated epithelium[1]. The results of those studies were consulted when setting the ET_2' to the GI tract clearance rate in the original HRTM at 100 d^{-1}. As the findings of this study are consistent with that data, the assignment of this clearance fraction to the ET_2 compartment in the HRTM and its clearance rate are unchanged in the revised model (see Figure 1a and d and Table 2).

A small fraction of the clearance seen in this time interval may result from the slow mucociliary clearance mechanism responsible for ET clearance to the GI tract seen at times >1 h.

Clearance from ET airways to the GI tract at times >1 h

The ET retention fraction cleared to the GI tract at times >1 h ranged from 15 to 85 % IETD, with an average value of 45 % IETD and a geometric mean 50 % clearance time of 8.9 h.

As discussed above, particles retained in the ET airways at times longer than an hour after intake are known to be predominantly in the anterior of the nose. The anatomy of the anterior nasal passage is complex, evolving from the skin-lined nasal vestibule into the well-ciliated epithelium of the posterior nasal passage. The location of the retained particles and the measured clearance of this clearance fraction suggest that the particles experience slow, probably intermittent, mucociliary clearance until, on reaching the posterior nasal passage, they are cleared to the GI tract in minutes. The similar values for the 50 % clearance times for this slow mucociliary clearance fraction and the fraction cleared by nose blowing suggest that the particles contributing to these two clearance fractions experience a common environment. Therefore, this clearance fraction is taken to be of particles deposited in ET_1.

The study results therefore indicate that of the four modes of clearance from the ET airways, two, nose blow and slow mucociliary clearance, are associated with particles deposited in the anterior nasal passage, the ET_1 compartment in the HRTM; and two, rapid mucociliary clearance and the promptly swallowed fraction, are associated with particles deposited in the posterior of the ET airways, the ET_2 compartment of the HRTM.

Therefore, the following information from the inhalation study (Figure 1b) was used in constructing the revised model of particle deposition and clearance within the ET airways:

- On average, ET_1 deposition is 64 % of IETD, of which 19 % IETD is cleared by nose blowing and 45 % IETD is cleared by slow mucociliary action to ET_2. Both modes of clearance have 50 % clearance times of ~8 h.
- The remaining 36 % IETD deposits in ET_2, ~10 % IETD in the naso-pharynx and larynx,

Table 2. Comparison of original HRTM ET model and revised ET model parameter values.

Regions and compartments[a]	Deposition, % total ET deposition		% Distribution between compartments		Clearance route	Clearance rates (d^{-1})	
	HRTM ET[b]	Revised ET	HRTM ET	Revised ET		HRTM ET	Revised ET
ET_1	46	65	100	100			
					To environment	1	0.6
					To ET_2	N/A[c]	1.5
ET_2	54	35					
ET_2'			99.95	99.8	To GI tract[d]	100	100
ET_{seq}			0.05	0.2	To LN_{ET}	0.001	0.001

[a]LN_{ET}, the ET lymphatic tissue region, is not included as particles neither deposit nor clear from it. Note that for reasons that are outside the scope of this paper, in the ICRP Publication 'Occupational Intakes of Radionuclides Part 1'[7], the ET and thoracic lymphatic tissues will not be included in the revised HRTM, but included in the lymphatic nodes remainder tissue.
[b]Values for 5-μm AMAD aerosol; see Figure 2 for variation with the particle size.
[c]N/A : not applicable.
[d]GI tract : gastro-intestinal tract.

which is promptly swallowed, with 26 % IETD depositing on the ciliated epithelium of which ~one-fifth (~5 % IETD) clears to the stomach within ~5 min. However, as the subdivision of the fraction deposited in ET_2 does not affect dosimetry modelling in the HRTM it is not considered further in this paper. Both particles deposited in ET_2 and those transferred to it from ET_1 are assumed to be cleared to the GI tract at a rate of 100 d^{-1}.

DERIVING A REVISED MODEL FROM THE EXPERIMENTAL DATA

The results of the experimental study indicate a need to adjust both the HRTM deposition and clearance models of the ET airways. Over the range of particle sizes and intake conditions used in the nasal clearance study, relative deposition in ET_1 and ET_2 calculated using the ICRP Publication 66 HRTM are 44 and 56 %, respectively (see Table 3). The relative deposition fractions observed in the study were 64 % in ET_1 and 36 % in ET_2.

The ET_1 and ET_2 compartments are the second and third filters and the last two filters in the HRTM deposition model. Because the filters are in series, altering their deposition efficiencies would affect deposition in all subsequent regions of the RT, requiring a complete recalculation of the deposition model over the ranges of all aerosol and intake parameters: a major undertaking in itself. Therefore, initial attempts were made to retain the ET_1:ET_2 relative deposition fractions given by the deposition model, and compensate for this by assigning appropriate rate constants so that the combination of the depositions and rates would be consistent with the observed experimental data.

Separate attempts were made to develop such a model at CRCE and at Nagoya University, both based on the simple biokinetic model shown in Figure 1c, and both using ET deposition fractions of $D_{ET_1} = 45$ % for ET_1 and $D_{ET_2} = 55$ % for ET_2, but placing different emphases on specific derived clearance fractions and 50 % clearance times.

Several attempts were made to derive values for the rate constants, K_1 and K_2, which when used with the fixed deposition values of 45 % in ET_1 and 55 % in ET_2 would yield good agreement with the experimental data. This was partially successful as to some extent the values of K_1 and K_2 can be changed to compensate for the incorrect deposition values, but the optimised values depend on which quantity they are optimised to, i.e. either to dose or to predict bioassay data (e.g. faecal excretion), but they cannot be optimised to both. In view of this, it was decided to change the deposition model so that the results of both bioassay and dosimetric assessments would give results consistent with the experimental data.

Modification of the original ICRP HRTM deposition model

As described above, the ICRP HRTM deposition model for nose breathing consists of a series of filters each with its own deposition efficiency that depends on both the aerodynamic and thermodynamic properties of the aerosol. The equations governing these deposition efficiencies were fitted to experimental data of total deposition in each region. At the time, the best interpretation of the available experimental data was equal deposition in ET_1 and ET_2 (see the section Introduction).

In the original HRTM deposition model the equations are constrained in the limit for both very small sizes (dominated by thermodynamic processes) and very large sizes (dominated by aerodynamic processes) to give 50:50 deposition in ET_1 and ET_2. However, as stated above, at intermediate particle sizes the need for the deposition fractions for all RT regions calculated using the model to be in reasonable agreement with the

Table 3. Relative deposition fractions in ET_1 and ET_2 calculated using the original HRTM for the aerosol sizes used in the volunteer experiments, and ICRP default breathing parameters for 'rest' and 'light exercise'[5].

Aerodynamic diameter[a]	No. of experiments	Exercise rate[b]	ET_1 deposition, % total ET deposition	ET_2 deposition, % total ET deposition
1.50	3	Rest	45.64	54.36
2.93	12	Rest	42.41	57.59
3.19	3	Light exercise	43.22	56.78
5.80	3	Rest	45.02	54.98
6.16	4	Light exercise	47.39	52.61
Weighted average			44.00	56.00

[a]Measured aerodynamic diameter of inhaled particles. Geometric standard deviation (σ_g) = 1.2, density = 1.05 g cm^{-3} (polystyrene), shape factor = 1.
[b]As defined in ICRP Publication 66, Table B.14[1].

available experimental data causes the ratio of the calculated ET_1 and ET_2 deposition fractions to vary from this ideal. For aerosols that are most frequently of interest for radiological protection the ratio of the calculated ET_1:ET_2 deposits is actually closer to 45:55. Figure 2 shows relative deposition fractions for ET_1 and ET_2 as a function of diameter for a monodisperse unit density aerosol calculated using the original HRTM deposition model for a nose breather. To circumvent the need for a complete recalculation of the deposition model a simple, alternative, pragmatic approach is used here.

The ICRP default assumption for workers performing light work, a combination of the sitting and light exercise work rates, is 100 % nose breathing:

- Use the original HRTM deposition model to calculate total deposition in ET arising from inhalation through the nose i.e. $Dep(ET) = Dep(ET_1) + Dep(ET_2)$
- Set $Dep'(ET_1) = 0.65 \times Dep(ET)$
- Set $Dep'(ET_2) = 0.35 \times Dep(ET)$

where $Dep(ET)$, $Dep(ET_1)$ and $Dep(ET_2)$ are the deposition fractions for ET, ET_1 and ET_2, respectively, calculated by the original HRTM deposition model and $Dep'(ET_1)$ and $Dep'(ET_2)$ are the revised deposition fractions, and 0.65 and 0.35 are rounded values of the measured relative deposition fractions for ET_1 and ET_2.

However, for workers performing heavy work the ICRP default is a combination of light and heavy exercise, with oro-nasal breathing (50 % nasal inhalation, 50 % mouth inhalation) occurring during heavy exercise. In these circumstances, or others when oral-augmented breathing is the appropriate assumption, the above reapportionment between ET_1 and ET_2 for deposition from air inhaled through the nose is performed and the total ET_2 deposition determined by summing the reapportioned fraction from nasal inhalation with that deposited from breath inhaled through the mouth.

$$\text{Set } Dep'(ET_2) = Dep_{mouth}(ET_2) + Dep'_{nose}(ET_2)$$

where $Dep'_{nose}(ET_2)$ is the reapportioned ET_2 deposition fraction from inhalation through the nose and $Dep_{mouth}(ET_2)$ is the ET_2 deposition fraction due to inhalation through the mouth. Note that that this procedure does not change total deposition in ET.

In this way the revised model keeps total ET deposition to that determined by the original HRTM deposition model but re-assigns the ET deposition from nasal inhalation between ET_1 and ET_2 in a ratio of 65:35. Since the HRTM deposition fractions in the ET regions were determined from experimental data based on total deposition in ET, the new methodology for calculating ET deposition remains consistent with that data[1]. Also, since the proposed modification only affects deposition in ET_1 and ET_2, there would be no change in the BB, bb and AI regional depositions.

Figures 3 and 4 show the ET_1 and ET_2 deposition fractions as a function of aerosol size for the default ICRP occupational aerosol parameters for a 100 % nose breather and, for direct comparison, a mouth-augmented breather both performing light work [see

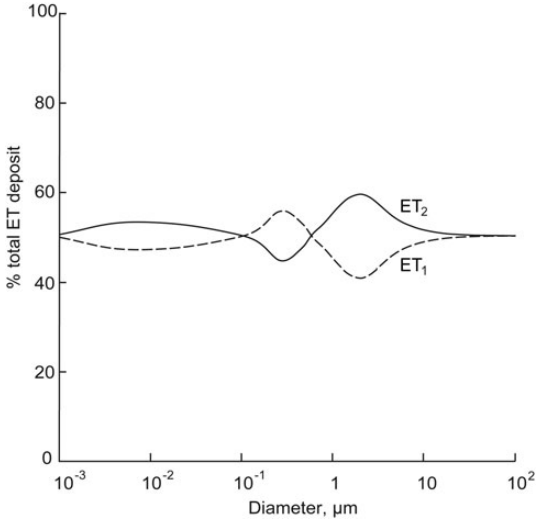

Figure 2. Relative ET_1 (dashed) and ET_2 (solid) deposition calculated using the ICRP Publication 66 deposition model (monodisperse unit density aerosol, shape factor = 1).

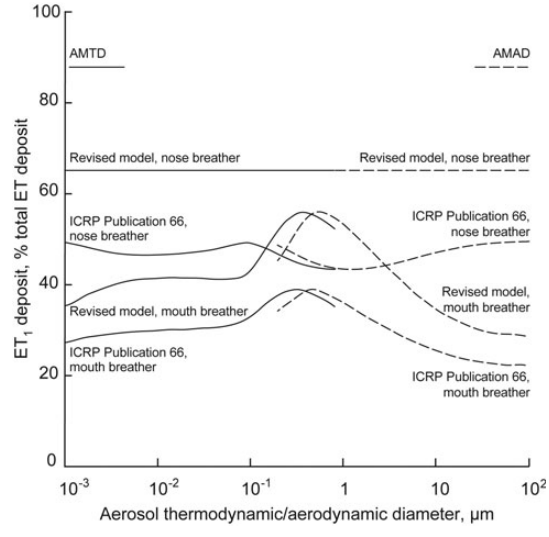

Figure 3. Comparison of calculated ET_1 deposition as a fraction of total ET deposition for the original HRTM ET model and the revised ET model.

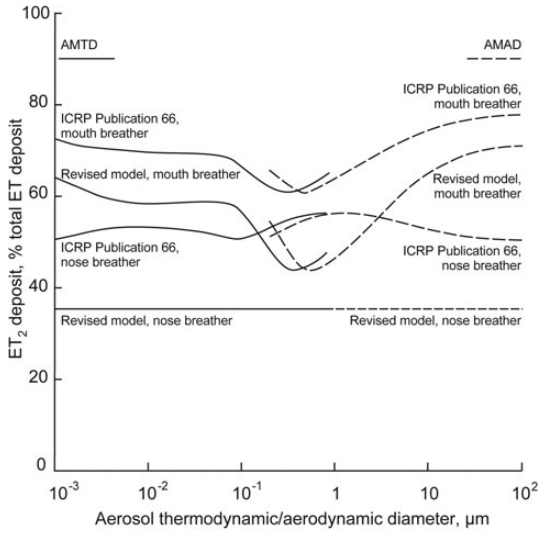

Figure 4. Comparison of calculated ET_2 deposition as a fraction of total ET deposition for the original HRTM ET model and the revised ET model.

Table 11 in ref. (1)] calculated using the ICRP Publication 66 HRTM and revised ET models using the software package IMBA[8].

The revised clearance model for ET_1 was obtained using the model shown in Figure 1c with the values of D_{ET_1} and D_{ET_2} fixed at 65 and 35 % of total ET deposition, respectively. The clearance rates to the environment (nose blow) and to ET_2' (mucociliary clearance) are derived from the experimental results given in Table 1. The clearance half-times for both modes of clearance from ET_1 are of the order of 8 h, which corresponds to a clearance rate (λ_{ET1}) for ET_1 of 2.0794 d^{-1}. Retention in ET_1 at a time t after intake (time $t = 0$) can be expressed as:

$$N_t = N_0 \times e_1^{-\lambda ET} t = N_0 \times e^{-\lambda NBt} \times e^{-\lambda MCt} = N_0 \times e^{-(\lambda NB + \lambda MC)t}$$

where N_0 is the initial deposit, N_t the fraction retained in ET_1 at time t, λ_{NB} is the clearance rate to the environment and λ_{MC} is the clearance rate by mucociliary clearance to ET_2'. As the clearance rate from ET_1 is 2.0794 d^{-1}

$$\lambda_{NB} + \lambda_{MC} = 2.0794\ d^{-1}$$

The relative values of the clearance rates for two modes reflect the fractions of the total ET deposit cleared by them, 19 % to the environment and 45 % to ET_2', so that:

$$\frac{\lambda_{NB}}{\lambda_{NB} + \lambda_{MC}} = \frac{19}{19 + 45} \quad \text{and} \quad \frac{\lambda_{MC}}{\lambda_{NB} + \lambda_{MC}} = \frac{45}{19 + 45}$$

and

$$\lambda_{NB} = 0.617 \quad \text{and} \quad \lambda_{MC} = 1.462$$

Rounding these values for use in the revised ET model gives the rate constants:

$$K_1 = 0.6\ d^{-1} \quad \text{and} \quad K_2 = 1.5\ d^{-1}$$

The value of K_2 is given to two significant figures because, as its value is close to the clearance rate unit of d^{-1}, rounding its value to 2 or 1 d^{-1} would significantly affect both the clearance half-time for ET_1 and the relative fractions cleared by the two modes.

The complete revised ET model, including the ET_2 sequestered fraction, is shown in Figure 1d and its parameter values are compared with those of the original HRTM ET model in Table 2. Note that all clearance from ET_1 to ET_2 is to the ET_2' compartment and hence to the GI tract with a half-time of 100 d^{-1}. Figure 5a and b compare ET retention for the different clearance fractions for the original HRTM ET model and the revised ET model for idealised insoluble particles. Figure 6 shows for nasal deposition the cumulative fractions cleared to the environment, the GI tract and to lymph nodes for the original HRTM and the revised ET clearance models.

It should be noted that the revised ET model is consistent with comments made in the text of ICRP Publication 66 that deposition in ET_1 is likely to be higher than ET_2 (see the section Introduction).

Revision of the modelling of the ET sequestered fraction

For insoluble forms of some radionuclides (e.g. plutonium isotopes), the main contribution to the dose to the ET region comes from the small fraction (F_{seq} = 0.05 %) that is considered to be sequestered (retained for a long time). This is because the alpha particles have barely enough energy to penetrate the mucus layer, but sequestered activity, which is assumed to be uniformly distributed throughout the epithelium, is, on average, closer to the radiosensitive cells. There is no sequestered activity in ET_1 and so the total amount of a radionuclide sequestered in ET is obtained by multiplying deposition in ET_2 by F_{seq}. Data from ICRP Publication 66 on the value of the sequestered fraction came from animal experiments where the total fraction of total ET activity retained was measured[9, 10].

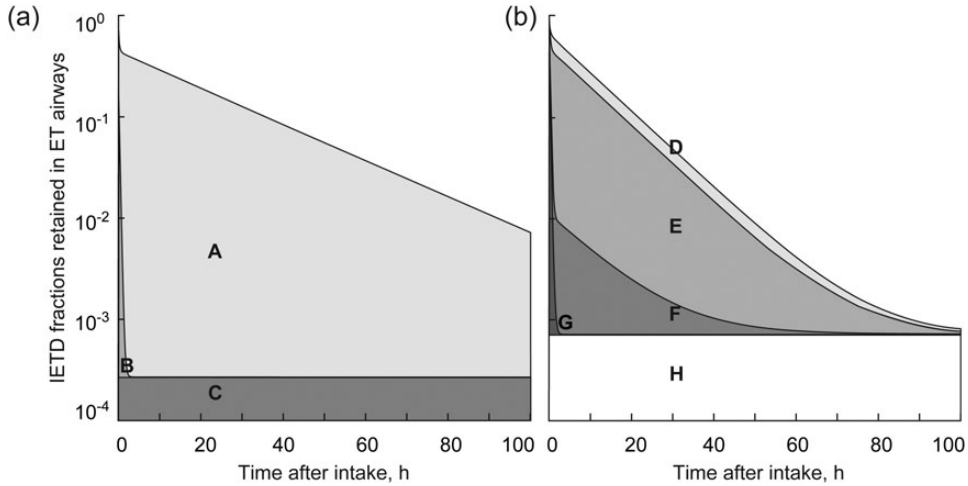

Figure 5. Retention in the ET airways in the first 100 h after intake: (**a**) original HRTM ET model; (**b**) revised ET model. Keys: A—ET_1 retention: fraction that will be cleared by nose blowing, B—ET_2 retention: fraction that will be cleared to GI tract, C—ET_2 retention: sequestered fraction retained in nasal tissue. D—ET_1 retention: fraction that will be cleared by nose blowing, E—ET_1 retention: fraction that will be cleared to ET_2, F—ET_2 fraction: ET_1 deposit clearing through ET_2 to GI tract, G—ET_2 retention: ET_2 deposit that will be cleared to GI tract, H—ET_2 retention: sequestered fraction retained in nasal tissue.

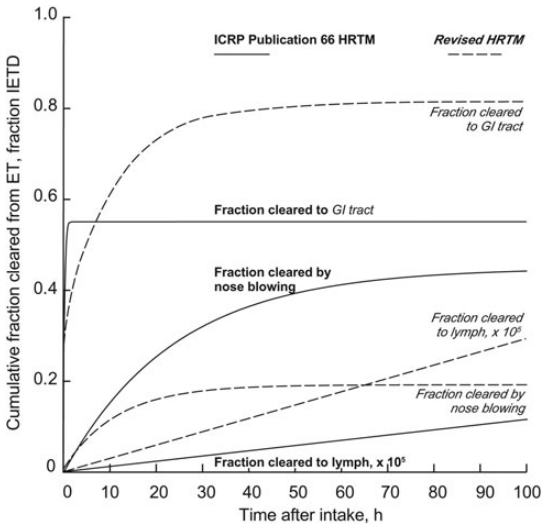

Figure 6. Cumulative clearance to the environment, the GI tract and lymph nodes compared for the original HRTM ET model and the revised ET model.

Clearly, if the same fraction of ET deposit is required to be retained in ET as is currently assumed, then F_{seq} must change because it applies to the ET_2 deposit only, and this has changed from 55 to 35 % of total ET deposition. In ICRP Publication 66, Table E.6 gives the sequestered fraction of total ET deposit for different animals[1, 9, 10]. The median value is 0.058 %. To arrive at this fraction for deposition in ET_2, F_{seq} must be set such that $0.35\ F_{seq} = 0.058$ %. This gives a value of 0.17 % for F_{seq} which, in view of the large variation observed, is rounded here to 0.2 %.

A review of other aspects of the HRTM was conducted at the same time as the review of ET clearance[7]. It concluded that the F_{seq} values for the sequestered fractions of the material deposited in the bronchial (BB) and bronchiolar (bb) regions should be lower than the value of 0.7 % set in ICRP Publication 66, and recommended that the value of 0.2 % chosen for the ET region be applied. It also recommended that the clearance rates for the BB and bb sequestered fractions should be changed from 0.01 to 0.001 d^{-1}, the clearance rate set for the ET_{seq} fraction[1]. Hence, the revised HRTM has adopted ET_2, BB and bb F_{seq} values of 0.2 % of the material deposited in those regions, with all three sequestered fractions having a clearance rate to lymph nodes of 0.001 d^{-1}[7].

Hereafter, the effective dose will simply be referred to as 'dose' unless otherwise stated.

In order to compare the effects on effective and equivalent dose per unit intake of using the revised F_{seq} value of 0.2 % ET_2 deposition, rather than the original value of 0.05 %, doses from inhalation of 1 Bq ^{239}Pu (5-μm activity median aerodynamic diameter (AMAD), absorption Type M) were calculated using the original HRTM ET model, and using the revised ET model (Table 4). (Dose per unit measurement for a 24-h faecal sample collected 4 d after intake is also given for the purposes of the discussion of the implications for dose assessment of the revised ET model in

Table 4. Doses per unit intake and per unit bioassay measurement for three radionuclides illustrating the effect of the revised ET model.

Inhalation of a ^{239}Pu 5-μm AMAD aerosol, absorption Type M, $f_1 = 0.0005$, radioactive half-life = 24 100 y, alpha emitter

ET model and value of ET_{seq} used[a]	Equivalent dose to each region per unit intake (Sv Bq^{-1})[a]				Effective dose per unit bioassay measurement[a]	Effective dose[a] (Sv Bq^{-1})
	ET_1	ET_2	LN_{ET}	ET	Sv Bq^{-1} Day 4 24-h faecal sample[b]	
ICRP 66 HRTM ET, $F_{seq} = 0.05\,\%$[c]	3.2×10^{-6}	1.5×10^{-5}	2.3×10^{-6}	1.5×10^{-5}	9.7×10^{-4}	3.2×10^{-5}
Revised ET, $F_{seq} = 0.05\,\%$[d]	3.0×10^{-6}	1.1×10^{-5}	2.4×10^{-6}	1.1×10^{-5}	5.6×10^{-4}	3.7×10^{-5}
Revised ET, $F_{seq} = 0.2\,\%$[e]	3.0×10^{-6}	3.6×10^{-5}	3.5×10^{-6}	3.6×10^{-5}	5.7×10^{-4}	3.8×10^{-5}

Inhalation of a ^{137}Cs 5-μm AMAD aerosol, absorption Type F, $f_1 = 1$[f], radioactive half-life = 30.05 y, beta/gamma emitter

ET model and value of ET_{seq} used[a]	Equivalent dose to each region per unit intake (Sv Bq^{-1})[a]				Effective dose per unit bioassay measurement[a]	Effective dose[a] (Sv Bq^{-1})
	ET_1	ET_2	LN_{ET}	ET	Sv Bq^{-1} whole-body Day 10[g]	
ICRP 66 HRTM ET, $F_{seq} = 0.05\,\%$[c]	1.9×10^{-6}	1.1×10^{-8}	1.1×10^{-8}	1.3×10^{-8}	1.4×10^{-8}	6.6×10^{-9}
Revised ET, $F_{seq} = 0.05\,\%$[d]	1.3×10^{-6}	1.2×10^{-8}	1.2×10^{-8}	1.4×10^{-8}	1.6×10^{-8}	9.3×10^{-9}
Revised ET, $F_{seq} = 0.2\,\%$[e]	1.3×10^{-6}	1.2×10^{-8}	1.2×10^{-8}	1.4×10^{-8}	1.6×10^{-8}	9.3×10^{-9}

Inhalation of an ^{132}I 5-μm AMAD aerosol, absorption Type F, $f_1 = 1$[f] radioactive half-life = 2.3 h, beta/gamma emitter

ET model and value of ET_{seq} used[a]	Equivalent Dose to each Region per unit intake (Sv Bq^{-1})[a]				Effective dose per unit bioassay measurement[a]	Effective dose[a] (Sv Bq^{-1})
	ET_1	ET_2	LN_{ET}	ET	Sv Bq^{-1} Thyroid 24 h after intake[h]	
ICRP 66 HRTM ET, $F_{seq} = 0.05\,\%$[c]	2.3×10^{-7}	2.6×10^{-9}	2.2×10^{-9}	2.8×10^{-9}	1.7×10^{-6}	1.6×10^{-10}
Revised ET, $F_{seq} = 0.05\,\%$[d]	2.9×10^{-7}	3.0×10^{-9}	2.7×10^{-9}	3.3×10^{-9}	1.3×10^{-6}	1.5×10^{-10}
Revised ET, $F_{seq} = 0.2\,\%$[e]	2.9×10^{-7}	3.0×10^{-9}	2.7×10^{-9}	3.3×10^{-9}	1.3×10^{-6}	1.5×10^{-10}

[a]All dose calculations were performed using ICRP Publication 60 dosimetry with the minor modification that the remainder tissue weighting factor of 5 % was split and set to 1 % for ET and 4 % for all other remainder tissues (see text). Lung doses were calculated using the ICRP Publication 66 HRTM with standard parameters.
[b]Typical special monitoring plutonium bioassay measurement: 24-h faecal sample collected 4 d after the intake.
[c]Doses calculated using the ICRP Publication 66 HRTM ET model with the ET_2 sequestered fraction, ET Fs_{eq}, set at the ICRP Publication 66 default value of 0.05 % of ET_2 deposition.
[d]Doses calculated using the revised ET model with ET $F_{seq} = 0.05\,\%$ (see text).
[e]Doses calculated using the revised ET model with ET $F_{seq} = 0.2\,\%$ (see text).
[f]In compliance with the guidance given in ICRP Publication 67 for materials for which $F_1 = 1$ is recommended, calculations were performed using $F_1 = 0.99$.
[g]Typical special monitoring caesium bioassay measurement: whole-body measurement made 10 d after intake.
[h]Typical bioassay measurement for a short-lived iodine radionuclide: Thyroid measurement made 24 h after intake.

the following section.) Effective and equivalent doses were calculated using ICRP Publication 60[11, 12] dosimetry using the ICRP Publication 66 HRTM[1], the ICRP Publication 30 gastro-intestinal tract model[13] and the ICRP Publication 67 systemic model for plutonium[14]. For the purposes of this comparison the remainder tissue weighting factor of 5 % was set at the fixed fractions of 1 % for ET and 4 % for all the other remainder tissues. This was done to prevent the activation of the ICRP Publication 60 rule for splitting the

remainder tissue weighting factor if the equivalent dose to one of its constituent tissues exceeds that to any of the 12 organs with specified weighting factors[11, 12]. The value of 1 % was chosen as a rounded value for 0.92 %, 1/13th of 12 %, which is the sum of the tissue weighting factors for the 13 remainder tissues specified for each sex in ICRP Publication 103[7, 15].

Table 4 shows that for ^{239}Pu:

- Leaving F_{seq} at 0.05 % would artificially reduce the equivalent dose to ET_2 by a third.
- Using $F_{seq} = 0.2$ % leads to a doubling of the equivalent doses to ET_2 and ET, but the dose per unit intake and dose per unit faecal excretion are not significantly different from the values predicted using the revised ET model with $F_{seq} = 0.05$ %.

In summary, the value of the ET_2 sequestered fraction, F_{seq}, has been set at 0.2 % in the revised ET model, as this represents the best estimate based on current scientific knowledge. The clearance rate for the sequestered fraction remains at 0.001 d^{-1} (Figure 1d).

THE REVISED ET MODEL AND ITS IMPLICATIONS FOR DOSE ASSESSMENT

The most significant change introduced by the revised ET model is the introduction of the clearance route from ET_1 to ET_2. By enabling material retained in the anterior of the nose at times greater than an hour to clear through the nasal passage to the GI tract, the revised model enables both deposition within ET and excretion by nose blowing, urine and faeces to be modelled more realistically.

The effect of the revised ET model on assessed doses and intakes will differ with the radionuclide inhaled and its chemical form. A full investigation of this topic, including an uncertainty analysis of the model parameters, is beyond the scope of this paper. For some radionuclides (see below) the adoption of the revised ET model will significantly affect assessed doses and intakes. For many radionuclides, differences are expected to be small and with respect to the modelling of retention and bioassay data, not statistically significant. However, the impact of the revised model on operational practice may be greater than one would expect, because for regulatory purposes, such as recording occupational exposures, ICRP provides single best estimates of dose coefficients. A relatively small change in a dose coefficient (~10 %) may cause a change in a reference level such as an investigation level and therefore impact on operational procedures.

Table 4 illustrates how the revised ET model affects different categories of radionuclides. In Table 4 an intake of Type M ^{239}Pu is used to illustrate the revised ET model's effect on dose coefficients and doses assessed from bioassay measurements for a long-lived moderately soluble alpha emitter with a small gastro-intestinal uptake factor ($f_1 = 0.005$). Table 4 uses the examples of ^{137}Cs and ^{132}I to illustrate the impact of the revised ET model for a long-lived soluble beta/gamma emitter and a short-lived soluble beta/gamma emitter, respectively. The effective and equivalent doses for ^{137}Cs and ^{132}I were calculated using the same method as that used for the ^{239}Pu doses (see above) using the systemic models for the radionuclides referenced in ICRP Publication 67[14].

Table 4 shows that for radionuclides with half-lives significantly >8 h (the effective clearance half-time of ET_1) the principal effect of the revision of the ET model is to increase the fraction of material deposited in the nose that is potentially available for either absorption to blood or clearance to the GI tract, from 55 to 81 %. This 50 % increase in material passing through ET_2 and the gastro-intestinal tract results in higher equivalent doses per unit intake for ET_2, and ET, as well as for the GI tract and systemic organs, resulting in the higher effective and equivalent doses per unit intake shown in Table 4. Equivalent doses to ET_1 are slightly reduced because the higher ET_1 deposition fraction is more than offset by the faster clearance rate of the revised model (see Figure 1a and d, and Table 2). Note that as the tissue weighting apportionment factor for ET_1 is 0.001[1, 7], changes in the equivalent dose to ET_1 tend not to influence the equivalent dose to ET significantly.

As discussed above, Table 4 shows that for Type M ^{239}Pu the use of the revised model increases the equivalent dose to ET_2 arising from the increased sequestered fraction by ~240 %. As the sequestered fraction is the major contributor to equivalent dose to ET_2 for a long-lived alpha emitter such as ^{239}Pu, this also causes a similar increase to the ET equivalent dose. However, it should be noted that for Type M ^{239}Pu the 16 % increase in dose per unit intake is caused by increased systemic uptake by the liver, bone surface and other organs, not the increased ET_2 sequestered fraction. For most radionuclides the increase in the sequestered fraction is not significant, as shown in Table 4 for ^{137}Cs and ^{132}I, as the ET_2 equivalent dose is dominated by the equivalent dose to ET_2'.

Any change in doses per unit intake will cause doses assessed from air sampling data to change proportionately when assessed using the revised ET model. However, changes in clearance to the GI tract and systemic uptake from both ET and the GI tract will have a more complex impact on intakes and doses assessed from bioassay measurements. For instance, the faecal excretion of Type M ^{239}Pu in the week after intake is a factor of 2 higher when assessed using the revised ET model. This causes the dose per unit measurement assessed from faecal sample bioassay using the revised ET model to be ~40 % lower than that assessed using the original HRTM ET model. Similarly for long-lived radionuclides, and most notably for soluble materials, intakes assessed from whole-body measurements and urinary

excretion data will also be lower when assessed using the revised ET model. As shown in Table 4 increased systemic uptake per unit intake causes the dose per unit intake of ^{137}Cs assessed with the revised ET model to be 41 % higher than for the original HRTM ET model. This is off-set by the higher activity present in the body when measured 10 d after intake, causing the dose per unit measurement assessed from whole-body activity measurement to be only 12 % higher. This cancelling effect is likely to cause most doses assessed from bioassay measurements to change by only a few tens of per cent from their values assessed using the original HRTM ET model.

Table 4 illustrates how adopting the revised ET model will affect doses for short-lived radionuclides with a high gastro-intestinal uptake factor. The half-life of ^{132}I is 2.3 h, short compared with the ET_1 clearance half-time of both the original HRTM ET model and the revised ET model. For the revised model this limits the fraction of ET_1 deposition that clears to ET_2 which, combined with the smaller deposition fraction in ET_2, decreases the fraction of intake available for systemic uptake from ET_2 and the GI tract, and consequently decreases the dose per unit intake by 7 %, and the dose per unit measurement for thyroid measurements by ~24 %. However, the equivalent doses to ET_1, ET_2 and ET are each increased with the revised ET model. This is due to the higher ET_1 deposition fraction, which increases the irradiation of ET_1 and of it neighbouring tissues, ET_2 and LN_{ET}, by penetrating radiations (i.e. X- and gamma radiation). Therefore, the revised ET model will tend to reduce both dose per unit intake and dose per unit bioassay measurement for radionuclides with half-lives <8 h but for X- or gamma emitters, can increase the equivalent dose to ET.

The effect of the revised ET model on radon dosimetry has some similarities to that for ^{132}I as the dose from inhaled radon decay products is dominated by that from its short-lived progeny, especially ^{218}Po and ^{214}Po. However, as ^{218}Po and ^{214}Po decay by non-penetrating alpha emissions, the increased ET_1 deposition does not irradiate the other ET regions and so does not increase the equivalent doses to ET_2 and LN_{ET}. The changes that the use of the revised ET model will cause to ET equivalent dose and effective dose per unit exposure to radon progeny have been calculated for a typical exposure in the home[16]. The equivalent dose to ET is ~10 % lower when calculated using the revised ET model. The effective dose from the inhalation of radon and its progeny is dominated by the dose to the central airways of the lung (BB and bb regions in the HRTM[1]) and so dose per unit exposure for radon inhalation is only decreased by ~1 %.

CONCLUSION

Compared with the original HRTM ET model, the revised ET model enables more realistic modelling of material transfer from the anterior nasal passage to the gastro-intestinal tract, as well as clearance by nose blowing and similar mechanisms. Hence, the use of the revised model should improve the assessment of intake and dose for inhaled radionuclides.

The revised model increases the fraction of material deposited in the nose that is potentially available for absorption to blood or clearance to the GI tract. This may potentially affect intakes and doses assessed from excretion bioassay samples, and the calculated values for systemic absorption and inhalation dose coefficients. For example, for radionuclides with half-lives significantly >8 h, intakes assessed from bioassay data will tend to be lower than those assessed using the ICRP Publication 66 HRTM ET model. On the other hand, doses per unit intake will tend to increase for these radionuclides. Therefore, in most cases, it is expected that the net impact of adopting the revised ET model is that the committed effective doses assessed from bioassay will change by a few tens of per cent at most from values assessed using the ICRP Publication 66 HRTM ET model. Doses assessed from air sampling data will change only in proportion to the change in dose coefficient and therefore may be subject to larger changes. However, there could be exceptions to these general trends.

As the revision of the ET model is taking place at the same time as the revision of other aspects of the HRTM, a comprehensive review of the impact of revising the ET model has not been conducted. In addition to the revision of the HRTM, and of RT and GI tract absorption parameter values for many elements, revisions are being made to the systemic biokinetic models for the same elements[7]. Dose coefficients that will be published in forthcoming parts of ref. (7) will be the first to have been calculated using the ICRP Publication 100 Human Alimentary Tract Model (HATM)[17], the ICRP Adult Reference Computational Phantoms[18] and revised nuclear decay data for dosimetric calculations[19]. The effect of the revised ET model on doses and bioassay assessments should be assessed in conjunction with the other revisions to the HRTM and other models so that the full impact of the updating of ICRP internal dosimetry methodology on radiation protection practice can be determined.

ETHICS STATEMENT

All the volunteer studies referred to in this report were conducted at the Centre for Radiation, Chemical and Environmental Hazards (CRCE), in accordance with the ethical approval gained from the Central Oxford Research Ethics Committee (references: C95.289—Study of the deposition and clearance of inhaled particles in the nasal passage and C00.038—Study of the deposition and clearance of inhaled particles in the nasal passage: Part 2). All administrations of radionuclides to the volunteer subjects were made in accordance with the Administration of Radioactive Substances

Advisory Committee (ARSAC) certification of the studies (certificate numbers: RPC 530-1114 (9080) issued 14 December 1995, extended 24 November 1997 and RPC 530-2417 (13 912)).

ACKNOWLEDGEMENTS

The views expressed in this publication are those of the authors and not necessarily those of the NHS, the National Institute for Health Research, or the Department of Health. The authors wish to thank Dr James Marsh (CRCE) for dosimetric calculations made using the revised ET model for intakes of radon and its progeny in a domestic environment.

FUNDING

The volunteer studies discussed in this paper were supported by part funding from the European Commission (contract no. F14P CT950026 'Inhalation of Radionuclides') and British Nuclear Fuels plc (agreement number BW4/15822). The ET clearance modelling work was supported through the Joint Coordinating Committee on Radiation Effects Research (JCCRER) supported by the governments of the Russian Federation and the United States of America and managed by the U.S. Department of Energy (cooperative agreement DEFC0397 AF21354). The compilation of this publication was supported by funding from the National Institute for Health Research (NIHR project 102082, 'Inhalation Studies').

REFERENCES

1. International Commission on Radiological Protection. *Human respiratory tract model for radiological protection*. ICRP Publication 66. Ann. ICRP. Pergamon Press. **24**(1–3) (1994).
2. Fry, F. A. and Black, A. *Regional deposition and clearance of particles in the human nose*. J. Aerosol Sci. **4**, 113–124 (1973).
3. Lippmann, M. *Deposition and clearance of inhaled particles in the human nose*. Ann. Otol. Rhinol. Laryn. **79**, 519–528 (1970).
4. Hounam, R. F., Black, A. and Morgan, A. *Removal of particles deposited in human nasal passages by nose blowing*. Health Phys. **44**, 418–422 (1983).
5. Smith, J. R. H., Bailey, M. R., Etherington, G., Shutt, A. L. and Youngman, M. J. *An experimental study of clearance of inhaled particles from the human nose*. Exp. Lung Res. **37**(2), 109–129 (2011).
6. Smith, J. R. H. and Shutt, A. L. *Human biokinetics of nasal clearance by particle transport: a compilation of experimental data*. HPA CRCE Science and technology report, HPA-CRCE-031, Centre for Radiation, Chemical and Environmental Hazards. Health Protection Agency (2012). http://www.hpa.org.uk/Publications/Radiation/CRCEScientificAndTechnicalReportSeries/HPACRCE031/ (accessed 11 September 2013).
7. International Commission on Radiological Protection. *Occupational intakes of radionuclides*. Part 1, Ann. ICRP, Accepted for publication.
8. Birchall, A., Puncher, M., Marsh, J. W., Davis, K., Bailey, M. R., Jarvis, N. S., Peach, A. D., Dorrian, M-D. and James, A. C. *IMBA Professional Plus: a flexible approach to internal dosimetry*. Radiat. Prot. Dosim. **125**(1–4) 194–197 (2007).
9. Snipes, M. B., Boecker, B. B. and McClellan, R. O. *Retention of monodisperse or polydisperse aluminosilicate particles inhaled by dogs, rats and mice*. Toxicol. Appl. Pharmocol. **69**, 345–362 (1983).
10. Snipes, M. B., Olson, T. R. and Yeh, H. C. *Deposition and retention patterns for 3-, 9- and 15-μm latex microspheres inhaled by rats and guinea pigs*. Exp. Lung Res. **14**, 37–50 (1988).
11. International Commission on Radiological Protection. *1990 Recommendations of the International Commission on Radiological Protection*. ICRP Publication 60. Ann. ICRP. Pergamon Press. **21**(1–3) (1991).
12. International Commission on Radiological Protection. *Dose coefficients for intakes of radionuclides by workers*. ICRP Publication 68. Ann. ICRP. Pergamon Press. **24**(4) (1994).
13. International Commission on Radiological Protection. *Limits for intakes of radionuclides by workers*. ICRP Publication 30. Part 1. Ann. ICRP. Pergamon Press. **2**(3–4) (1979).
14. International Commission on Radiological Protection. *Age-dependent doses to members of the public from intakes of radionuclides: Part 2: Ingestion dose coefficients*. ICRP Publication 67. Ann. ICRP. Pergamon Press. **23**(3–4) (1993).
15. International Commission on Radiological Protection. *The 2007 recommendations of the International Commission on Radiological Protection*. ICRP Publication 103. Ann. ICRP. Elsevier. **37**(2–4) (2009).
16. Marsh, J. W. and Bailey, M. R. *A review of lung-to-blood absorption rates for radon progeny*. Radiat. Prot. Dosim. **157**(4), 499–514 (2013).
17. International Commission on Radiological Protection. *Human alimentary tract model for radiological protection*. ICRP Publication 100. Ann. ICRP. Elsevier. **36**(1/2) (2006).
18. International Commission on Radiological Protection. *Adult reference computational phantoms*. ICRP Publication 110. Ann. ICRP. Elsevier. **39**(2) (2009).
19. International Commission on Radiological Protection. *Nuclear decay data for dosimetric calculations*. ICRP Publication 107. Ann. ICRP. Elsevier. **38**(3) (2008).