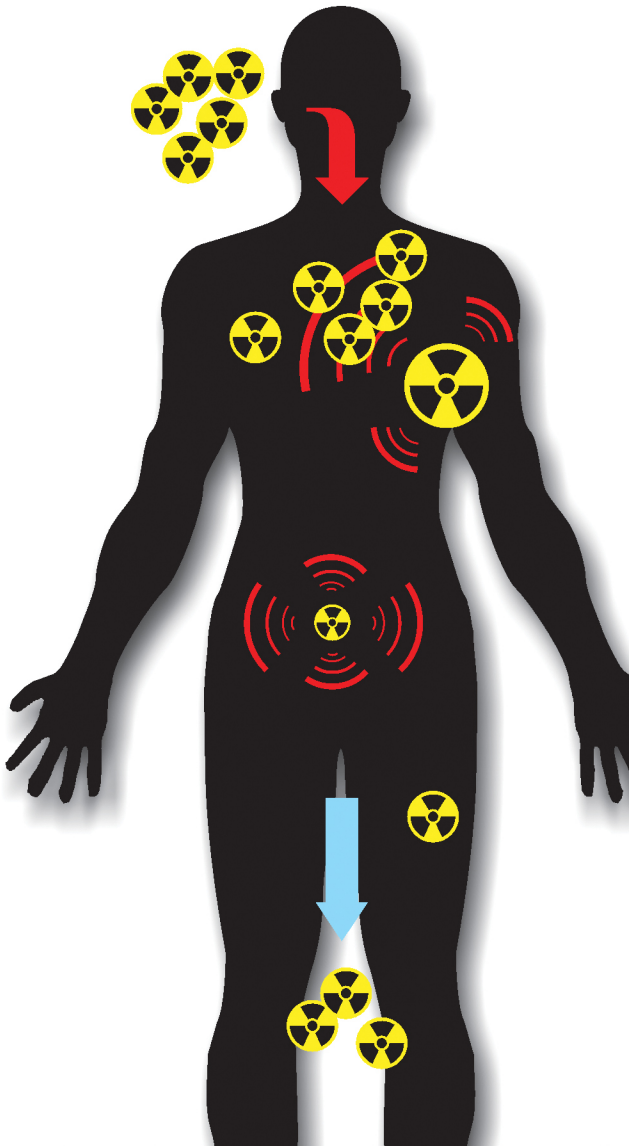
IRSN
INSTITUT
DE RADIOPROTECTION
ET DE SÛRETÉ NUCLÉAIRE

Faire avancer la sûreté nucléaire

Mémoire d'habilitation à diriger des recherches

Development and application of methods for the assessment of radiation dose from internal radioactive contamination

Éric BLANCHARDON



Collection HDR

Éditorial

L'habilitation à diriger les recherches (HDR) est un diplôme délivré par un établissement universitaire. Pour un chercheur, elle constitue la consécration d'un cycle - typiquement d'une dizaine d'année - d'activité de recherche remarquable dans son domaine et une double reconnaissance : bien sûr, celle de l'atteinte d'un haut niveau scientifique, mais surtout celle de la capacité à impulser un ensemble cohérent de travaux articulés au service d'un défi scientifique. Cette reconnaissance renforce également l'aptitude à encadrer des étudiants en formation doctorale ou postdoctorale. Elle est précieuse tant pour les chercheurs que pour l'Institut, compte tenu de sa volonté de multiplier les configurations de partenariat où la vision scientifique à moyen terme joue un rôle déterminant.

Le travail présenté dans ce dixième numéro de la collection HDR a été réalisé par Éric BLANCHARDON. Il concrétise la volonté d'une mise en lumière des travaux de recherche de l'Institut, attendue par différentes parties prenantes de la gestion des risques nucléaires et radiologiques et s'adresse plus largement à la communauté académique.

Illustration en page de couverture : overview of internal dosimetry.

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Université Paris XI
UFR Scientifique d'Orsay
Habilitation à diriger des recherches
(HDR)

Développement et application de méthodes pour l'évaluation de la dose de rayonnement résultant d'une contamination radioactive interne

Development and application of methods for the assessment of radiation dose from internal radioactive contamination

21 novembre 2012

Éric BLANCHARDON
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Contents

Glossary of abbreviations

Alpha-Risk:	European study of the risks from alpha emitters (2005-2009)
Am:	americium
AMAD:	Activity median aerodynamic diameter of particles in an aerosol
Bq:	Becquerel, unit of radioactivity (1 Bq = 1 s^{-1})
CDF:	Cumulative density function
CEA:	Commissariat à l'énergie atomique et aux énergies alternatives (French atomic energy commission)
CONRAD:	European coordinated network for radiation dosimetry (2005-2008)
DOCAL:	ICRP task group on dose calculation
DTPA:	Diethylenetriamine penta-acetic acid, chelating treatment for Pu and Am
ENVIRHOM:	IRSN study of environmental and health effects of radionuclides
EURADOS:	European network for dosimetry
F (type):	Compound rapidly absorbed from the respiratory tract
f_b:	Bound fraction of activity deposited in the respiratory tract
f_r:	Rapidly dissolved fraction of activity deposited in the respiratory tract
Gy:	Gray, unit of absorbed dose (1 Gy = 1 $J.kg^{-1}$)
HAS:	Haute autorité de santé (French authority for health)
HPA:	British Health Protection Agency
HRTM:	human respiratory tract model of the ICRP
ICRP:	International Commission on Radiological Protection
IDEAS:	European guidelines for internal dose assessment (2002-2005)
INDOS:	ICRP task group on internal dosimetry
IRSN:	Institut de radioprotection et de sûreté nucléaire (France)
ISO:	International organization for standardization
LEDI:	Laboratoire d'évaluation de la dose interne de l'IRSN (IRSN laboratory of internal dose assessment)
LEPID:	Laboratoire d'épidémiologie des rayonnements ionisants de l'IRSN (IRSN laboratory of epidemiology)
M (type):	Compound moderately absorbed from the respiratory tract
MCNPX:	Monte Carlo code for radiation transport (Los Alamos National Laboratory)
mSv:	Milli-sievert, unit of effective dose (1 mSv = 1 $mJ.kg^{-1}$)
NCRP:	United States National Council on Radiation Protection and Measurements
ORNL:	Oak Ridge National Laboratory (USA)

PDF:	Probability density function or probability distribution
Pu:	Plutonium
QA:	Quality assurance
RaFu:	Algorithm for propagation of uncertainty from possibility and probability
S (type):	Compound slowly absorbed in the respiratory tract
SAF:	Specific absorbed (in a target) fraction of energy (emitted from a source)
s_b:	Absorption rate of activity bound in the respiratory tract
SF:	Scattering factor (geometric standard deviation)
SFMT:	Société française de médecine du travail (French society of occupational medicine)
s_r:	Rapid dissolution rate
s_s:	Slow dissolution rate
ST:	Soft tissues
Sv:	Sievert, unit of effective dose (1 Sv = 1 $Gy.kg^{-1}$)
Tl:	Thallium
UNSCEAR:	United Nations Scientific Committee on the Effects of Atomic Radiation
USTUR:	United States Transuranium and Uranium Registries
WeLMoS:	Weighted likelihood Monte Carlo sampling
WLM:	Working level month, unit of radon exposure (1 WLM = 3.54 $mJ.h.m^{-3}$)

Résumé

L'exposition aux rayonnements ionisants augmente le risque de cancer en proportion de la dose reçue. Celle-ci est donc une quantité fondamentale de la radioprotection que mon travail d'expert vise à évaluer en situation de contamination radioactive interne, à partir des résultats de mesure de l'activité et par l'application de modèles biocinétiques et dosimétriques. Pourtant la variabilité observée dans les estimations dosimétriques au cours d'exercices d'intercomparaison conduit à questionner la fiabilité de ces modèles et les conditions de leur application. Une grande partie de mon travail de recherche est donc dédiée à l'évaluation de la variabilité des données de mesure et de la fiabilité des modèles biocinétiques et dosimétriques, de façon à réduire, autant que faire se peut, l'incertitude qui leur est associée. Mais aussi précis que soient les techniques et les modèles, le bon outil doit être employé dans la bonne situation pour obtenir des résultats pertinents. Afin de garantir la robustesse des méthodes, l'assurance qualité des résultats et une meilleure reproductibilité de la procédure d'évaluation de la dose interne, des guides pratiques ont été rédigés à l'intention des professionnels du domaine. Malgré l'existence de ces guides, les résultats d'un exercice récent d'intercomparaison montrent qu'il reste plusieurs façons d'aborder chaque problème, suivant les hypothèses retenues. Les erreurs de mesure, la connaissance incomplète des conditions d'exposition et des mécanismes biologiques et physiques mis en œuvre sont des sources d'incertitude qui se propagent inévitablement à la valeur de dose estimée. Nous avons donc cherché à quantifier cette incertitude, de façon à pouvoir décider si elle acceptable suivant la situation rencontrée et l'objectif recherché. Nous pensons qu'une évaluation fiable de la dose à des fins de gestion du risque est réalisable. En revanche, l'évaluation du risque pour la santé d'un individu exposé reste une question difficile, notamment parce que la plus grande partie de l'exposition aux rayonnements ionisants conduit à des doses efficaces de moins de 100 mSv, c'est-à-dire à un niveau où la relation entre dose et risque reste mal connue. La compréhension des risques à ce niveau des faibles doses est l'objet d'un important effort de recherche en épidémiologie et en radiobiologie. Nous contribuons à cette recherche par le développement de modèles dosimétriques pour apporter une évaluation aussi réaliste que possible de la dose reçue par les sujets des études épidémiologiques et des expériences animales.

Mots-clés : rayonnements ionisants, dose, contamination interne, modèle, dosimétrie, biocinétique, américium, thallium, uranium, plutonium, césium, strontium, DTPA, CIPR, incertitude

Chapitre 1
Introduction

1.1 Radiation protection

We may be exposed to ionizing radiation by external irradiation from sources outside the body or by internal contamination following intake of radionuclides. In both cases the exposure is quantified in terms of the energy deposited in biological tissues divided by the mass of the irradiated tissues. This ratio is the dose, expressed in grays (Gy).

DNA damage by radiation leads to cell killing and mutations (UNSCEAR, 2000). Above a threshold of dose, the excess of cell killing leads to deterministic effects that are the loss of function of tissues and possibly death. Mutations in key genes for cell proliferation may cause the initiation of cancer (ICRP, 1991). The epidemiological follow-up of the survivors of the Hiroshima and Nagasaki atomic bombings shows

that the risk of cancer increases broadly in proportion with the dose received (figure 1, Ozasa *et al.*, 2012). Below a hundred of mGy, the increase of the risk is not statistically significant anymore. However, for the management of risks in radiation protection, it is assumed that the relation of the risk of cancer with the dose has no threshold below which the risk would be null (ICRP, 2005).

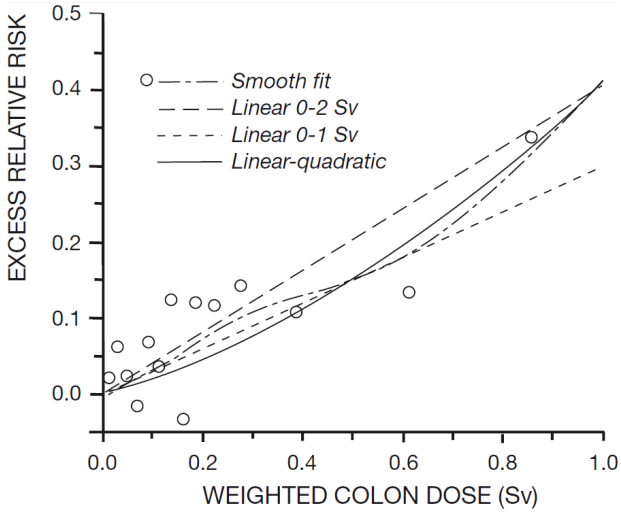


Figure 1. Dose response for solid cancer mortality based on the 2002 studies of the survivors of the atomic bombings in Japan (UNSCEAR, 2010). The trend of the data may be fitted by different models.

The dose absorbed by the radiosensitive tissues is therefore an important indication of the level of risk (ICRP, 2007a). However the same dose of different radiations has been shown to exhibit different relative biological efficiencies (RBE), in relation with the linear energy transfer and the ability to induce closely correlated damages to the DNA that are harder to repair (ICRP, 2003). For radiation protection purpose, the International Commission on Radiological Protection (ICRP, 2007) has described the effectiveness of radiations of differing qualities by means of radiation weighting factors (w_R). The absorbed dose multiplied by the appropriate radiation weighting factor is the equivalent dose (in sieverts, Sv). The relative sensitivity of the different body tissues is evidenced by the incidence of the different cancers. For radiation protection purpose, the ICRP (2007) has quantified the relative sensitivity of the different body tissues by a set of tissue weighting factors (w_T). The sum over the body of equivalent tissue doses weighted by their tissue weighting factors is the effective dose (in sieverts, Sv). Based on the epidemiological data, an effective dose of 1 Sv is broadly corresponding to an increase of 5% of the risk of lethal cancer in a reference

population. In the particular case of internal contamination, the committed effective dose is calculated as the sum of effective doses to be received over 50 years from the intake of radioactivity (box 1, [ICRP, 2007a]).

Absorbed dose D_T

$$D(r_T) = \frac{\varepsilon}{m}$$

to the region r_T of mass m due to the energy ε deposited in the region r_T

Equivalent dose H_T

$$H(r_T) = \sum_R w_R D_R(r_T)$$

to the region r_T where $D_R(r_T)$ is the dose absorbed in region r_T due to radiation of type R, and

radiation type	radiation weighting factor, w_R
photons	1
beta and muons	1
protons and charged pions	2
alpha particles, fission fragments, heavy ions	20
neutrons	between 2.5 and 20 depending on the energy

Effective dose E

$$E = \sum_T w_T \left[\frac{H(r_T)^{Male} + H(r_T)^{Female}}{2} \right]$$

is a weighted mean of equivalent doses to the tissues and organs of the reference adult male and female, with

tissue	tissue weighting factor, w_T
red bone marrow, colon, lungs, stomach, breast, remainder tissues[a]	0.12
gonads	0.08
bladder, esophagus, liver, thyroid	0.04
bone surface, brain, salivary glands, skin	0.01

[a] adrenals, extrathoracic region, gall bladder, heart, kidneys, lymphatic nodes, muscle, oral mucosa, pancreas, prostate, small intestine, spleen, thymus, uterus

Committed effective dose $E(50)$

$$E(50) = \int_{t_0}^{t_0+50} \dot{E}(t_0, t).dt$$

over 50 years after intake at time t_0

Box 1: Formulas for the main dose quantities (ICRP, 2007a).

Barring nuclear tests and major accidents such as Chernobyl and Fukushima, the general population is mainly exposed to radiation of natural origin, especially *via* the ubiquitous radioactive radon gas, and to medical irradiation for diagnosis or

treatment (figure 2, [UNSCEAR, 2008]). On the other hand, workers, notably in the nuclear industry and in medicine, may be occupationally exposed to radiation.

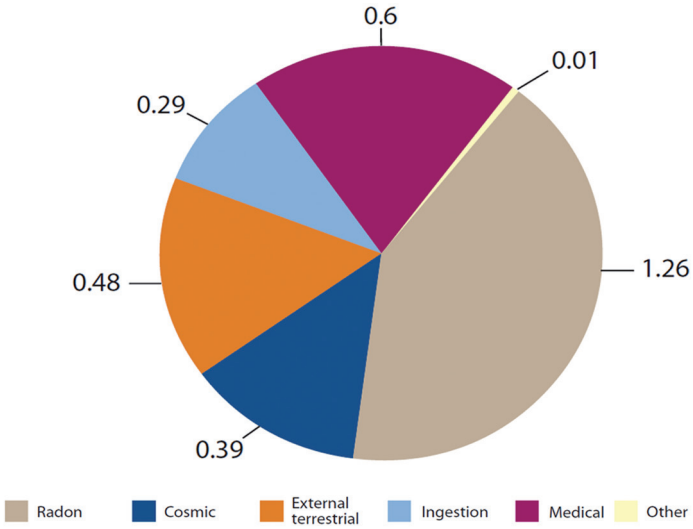


Figure 2. Estimated contributions (in milli-sieverts, mSv) to worldwide average annual exposure from different sources. "Other" includes exposure due to fallout resulting from nuclear tests, to the Chernobyl accident and to releases from nuclear power plants. All but medical and "other" is natural irradiation (UNSCEAR, 2008).

The protection of human health from exposure due to the use of ionizing radiation is the purpose of radiation protection, which is based on three principles derived from the knowledge of risk (ICRP, 2007a). Since no threshold of dose has been demonstrated below which there would be no risk, no practice involving exposure to ionizing radiation should be adopted unless it provides some benefit to the exposed individuals or population (justification). The risk of cancer increases with the dose. Therefore exposures should be maintained as low as reasonably achievable, economic and social factors being taken into account (optimization). The deterministic effects appear above a threshold. Therefore the exposure of individuals should be subject to dose limits below such thresholds (limitation). The overall system of radiation protection is developed by the ICRP as recommendations that are adapted in national regulations.

In both the retrospective assessment of risk from exposure to radiation, based on the scientific knowledge, and in the prospective management of such risk by the system of radiation protection, the (absorbed, equivalent or effective) dose appears as a central quantity to be evaluated. While a dose from external irradiation may be measured with properly calibrated dosimeters, the absorbed dose due to incorporated

radionuclides during the commitment period following the intake is not measurable at all. Instead, in internal dosimetry, the activity of the incorporated radionuclides is measured and interpreted into dose by the use of models (Blanchardon *et al.*, 2007a). My work is dedicated to the application and improvement of these models.

1.2 Internal dosimetry

Internal exposure may take place by ingestion, inhalation and percutaneous transfer of radionuclides or through contaminated wounds. Depending on its physico-chemical form, part or the totality of the intake is absorbed to blood from the site of entry. From blood it is distributed and retained in organs, depending on the metabolism of the element, and it is progressively eliminated by nuclear decay and excretion in urine and feces. Until the radionuclide is completely cleared, each contaminated region of the body becomes a source irradiating the neighboring and farther body tissues, starting with the source region itself.

The incorporated activity can be estimated prospectively from the measurement of activity in the environment or retrospectively from the individual measurement of activity in the whole body, in organs (*in vivo*) or in excreta (*in vitro*). The measurements of activity are usually arranged in routine monitoring programs where the measurements are repeated at a given frequency to spot possible intakes during the monitoring intervals or in special monitoring programs where several measurements are performed shortly after an incident (ISO, 2006).

Biokinetic models represent the time-dependant behavior of radionuclides and relate the intake to activities in the body regions and in excreta over the time following the incorporation. The integral of the activity in a region over the commitment period (50 years) is a number of nuclear transformations. Each of these nuclear transformations results in the emission of a spectrum of radiation (ICRP, 2008). Dosimetric models represent the anatomy of the body and predict the radiation-matter interactions in the transport of the radiation from the source regions to the radiosensitive target regions (ICRP, 2009). Thus, the consecutive application of biokinetic and dosimetric models enables inferring the intake from activity measurement at a given time and deducing the dose from the intake (figure 3).

The ICRP develops authoritative biokinetic and dosimetric models and apply them to publish predicted functions of activity in organs, urine and feces over time following a unit intake (ICRP, 1997), and coefficients of committed effective dose per unit intake of radionuclides (ICRP, 1995c, 1996, 2012).

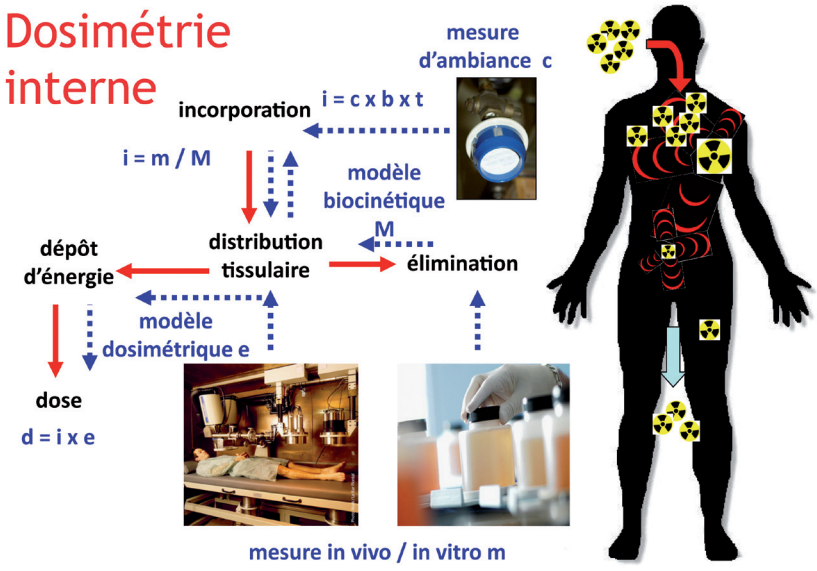


Figure 3. Overview of internal dosimetry. Black, events and quantities of interest; red, relations of cause and effect; blue, inference with models.

A significant part of my working time in the laboratory of internal dose assessment (LEDI) of the French Institute for nuclear safety and radiation protection (IRSN) is dedicated to the application of these reference models in the expertise of contamination cases, at the request of occupational health practitioners in charge of the follow-up of workers exposed to radiations in the nuclear industry, in hospitals or research laboratories, or at the order of public authorities in case of contamination of members of the public. Such expertise generally involves the collection and processing of measurement data, the clearing of the conditions of exposure to choose the appropriate biokinetic function and dose coefficient and their application to provide the committed effective doses of the exposed individuals, along with some short statement of their meaning in terms of regulation and health risk.

The validity of the models, tools and methods used is periodically evaluated in intercomparison exercises at national and international levels. Following the publication by the ICRP of a series of models and reference values for internal dosimetry, a third European intercomparison exercise was organized in 1998 (Doerfel *et al.*, 2000). The results have shown a large dispersion in the evaluation of doses from measurement data. For example, following a case of plutonium inhalation, 33 international experts evaluated committed effective doses ranging over four orders of magnitude, from nearly naught to far beyond the regulatory limits (figure 4).

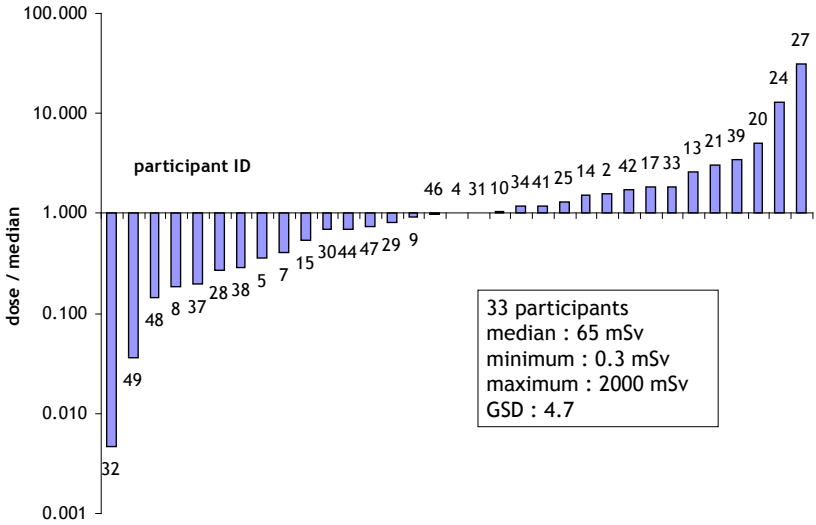


Figure 4. Third European intercomparison exercise, case 6, subject B. Results of individual participants (ID): committed effective dose normalized to the median; GSD is the geometric standard deviation (data from Doerfel et al.*, 2000).*

Beyond obvious errors in calculation and misapplication of the methods, this dispersion highlights a range of possible assumptions on the conditions of exposure, a range of choices regarding the biokinetic and dosimetric models and their numerical implementation and a range of quality in the activity measurement results. Obviously it raises questions on the scientific, technical and regulatory value of internal dosimetry. All the more because it is not an isolated result but rather symptomatic of a discipline largely considered as complex, not straightforward and sometimes unreliable. Much of my development and research activity was therefore dedicated to the quantification of the variability of measurement, to the evaluation of the reliability of biokinetic/dosimetric models and, as far as possible, to the reduction of their associated uncertainty. This activity is summarized in chapter 2.

No matter how good the techniques and models, the right tool has to employed in the right situation to obtain consistent results. In order to ensure a better reproducibility in the process of internal dose assessment, the robustness of the methods and the quality assurance of the results, an effort was made to provide guidance to professionals in the field and to harmonize the practice. This effort is summarized in chapter 3.

However, this guidance does not eliminate a range of possible assumptions, as demonstrated by the outcome of another intercomparison exercise. The errors of measurement, the incomplete knowledge of the conditions of exposure, and the underlying biological and physical processes are sources of uncertainty that inevitably propagates to the assessed dose. In chapter 4 we ask how to deal with it, whether it is acceptable, for which purpose.

We believe that a reliable dose assessment for the management of risks is achievable. However, the assessment of the actual health risk for the exposed individual remains a difficult question, not the least because most exposure to ionizing radiation results in effective doses of less than 100 mSv, in a range were the dose-risk relationship is most uncertain. The elucidation of risks in this low dose range is the subject of much research in epidemiology and radiobiology. We contribute to this research with dosimetric models to provide as good an evaluation of the dose as possible. This collaboration with epidemiologists and radiobiologists is considered in chapter 5.

To complete the information of the reader, the two last chapters include an overview of the research programs (chapter 7) and a *curriculum vitae* (chapter 8).

Chapitre 2
Reliability of models and measurement

2.1 Update of biokinetic models

Biokinetic models predict the time-dependent behavior of incorporated radionuclides: How far they are absorbed to blood, how fast they are transferred from blood to organs or to urinary and fecal excretion, how long they are retained in organs. They are built from the follow-up of incidental or volunteer intake of radionuclides, animal experiments, basic physiological data and chemical analogies. In radiation protection, they take the form of compartmental models where compartments representing an organ, a tissue, a group of tissues or a particular metabolic state of the radionuclide are related by first order transfer rates with constant coefficients. Such first order kinetics is consistent with the observed behavior of the trace levels of radionuclides. Mathematically, it translates into a system of linear first order differential equations.

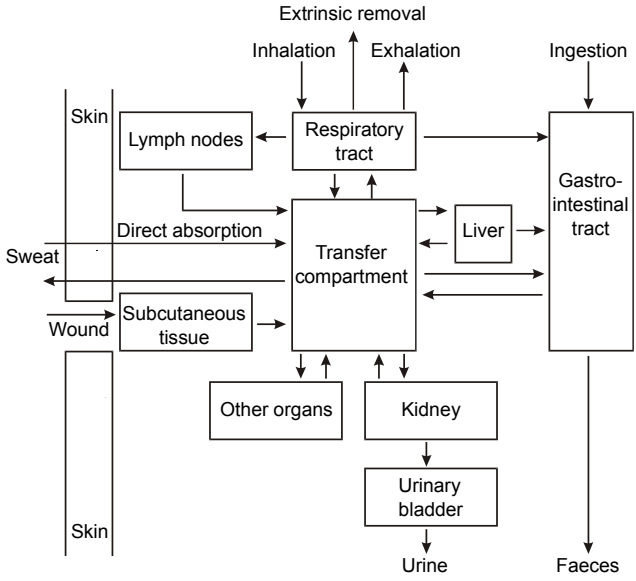


Figure 5. Summary of the main routes of intake, transfers and excretion (ICRP, 1997).

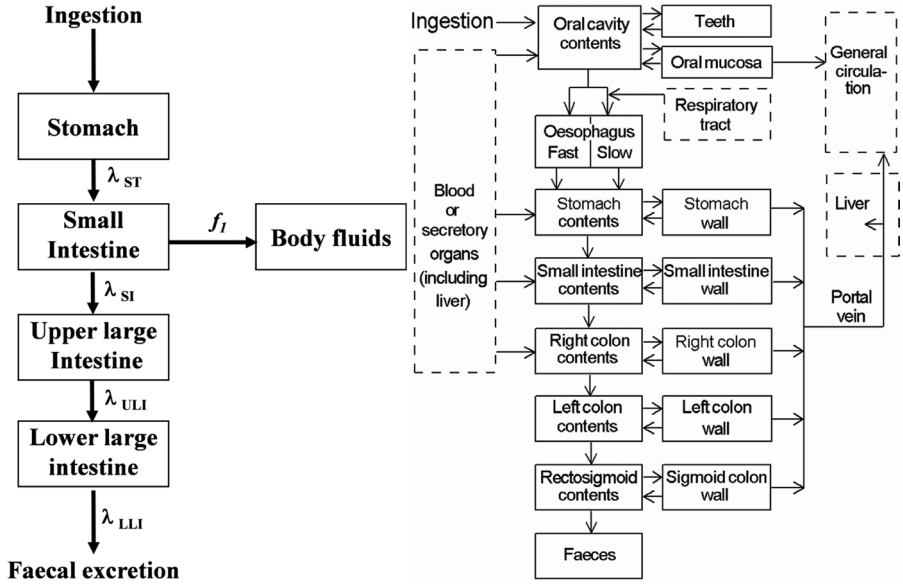


Figure 6. Structure of the gastro-intestinal tract model (left, [ICRP, 1979]) and human alimentary tract model (right, [ICRP, 2006]).

The ICRP (1979, 1989, 1993, 1994, 1995a, 1995b) has developed and published the reference biokinetic models for use in radiation protection. It distinguishes models for the main routes of intake: inhalation and ingestion, which predict the kinetics and magnitude of absorption from the site of entry to the circulation; and element-specific systemic models that describe the distribution and clearance of radionuclides in the general circulation (figure 5). These models are updated as new information on the behavior of radionuclides in the body becomes available. For instance, in 2006 a task group of the ICRP was able to update the gastro-intestinal tract model (ICRP, 1979) used for ingestion into the alimentary tract model (ICRP, 2006) based on new information on the transit times and absorption to blood (figure 6).

2.1.1 New biokinetic data for systemic models

2.1.1.1 Americium biokinetics

Following the last recommendations of ICRP (2007), its task group on internal dosimetry (INDOS) is considering the revision of all its biokinetic models (ICRP, 2012). The effort on systemic models is coordinated by Rich W. Leggett in the

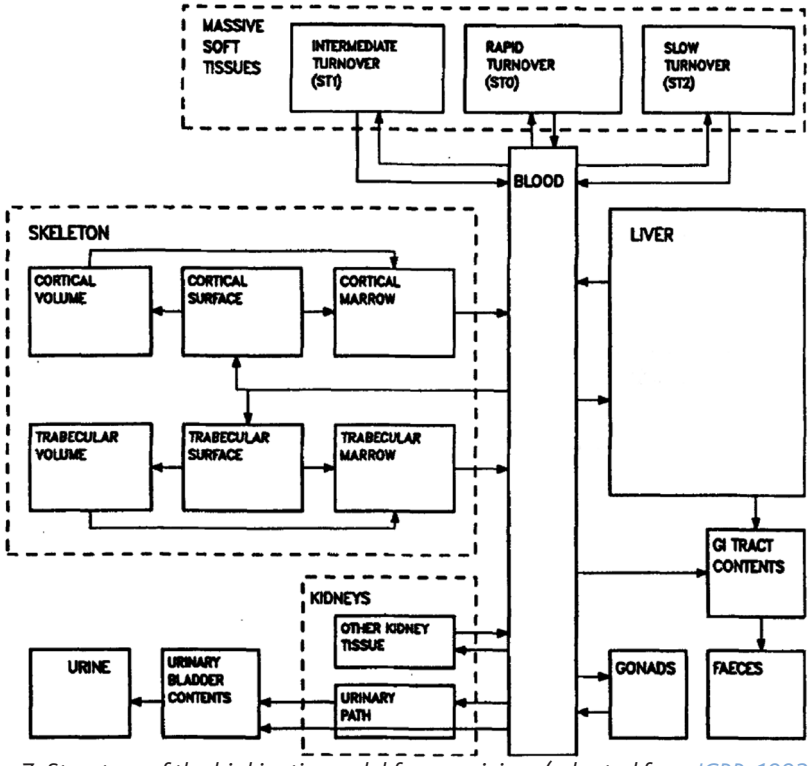


Figure 7. Structure of the biokinetic model for americium (adapted from ICRP, 1993a).

Oak Ridge National Laboratory (ORNL, USA) who recently published a series of such models (Leggett *et al.*, 2003, 2005; Leggett, 2004, 2008, 2010, 2011, 2012a, 2012b). As a slight participation to this effort, I had the chance to briefly work at ORNL (Blanchardon *et al.*, 2007b). The objective was the collection of data on americium biokinetics appeared since the publication of the current ICRP model (Leggett, 1992; ICRP, 1993a; figure 7 and table 1). The United States Transuranium and Uranium Registries (USTUR), which collect and analyze bioassay data on workers exposed to uranium, plutonium and americium, are valuable sources of information. The USTUR receive volunteer body donations which are autopsied to measure the contents of actinides in the various tissues (Filipy and Russel, 2003).

from	to	d^{-1}	from	to	d^{-1}
blood	liver	1.16e+01	soft tissues 0	blood	1.39e+00
blood	soft tissues 0	1.00e+01	soft tissues 1	blood	1.39e-02
blood	soft tissues 1	1.67e+00	soft tissues 2	blood	1.90e-05
blood	soft tissues 2	4.66e-01	cortical marrow	blood	7.60e-03
blood	cortical bone surface	3.49e+00	cortical bone surface	cortical marrow	8.21e-05
blood	trabecular bone surface	3.49e+00	cortical bone surface	cortical bone volume	4.11e-05
blood	kidneys urinary path	4.66e-01	cortical bone volume	cortical marrow	8.21e-05
blood	colon content	3.03e-01	trabecular marrow	blood	7.60e-03
blood	other kidney tissue	1.16e-01	trabecular bone surface	trabecular marrow	4.93e-04
blood	testes	8.20e-03	trabecular bone surface	trabecular bone volume	2.47e-04
blood	ovaries	2.60e-03	trabecular bone volume	trabecular marrow	4.93e-04
blood	urinary bladder content	1.63e+00	kidneys urinary path	urinary bladder content	9.90e-02
liver	blood	1.85e-03	other kidney tissue	blood	1.39e-03
liver	small intestine content	4.90e-05	testes	blood	1.90e-04
			ovaries	blood	1.90e-04

Table 1. Transfer rates for the americium model (adult, [ICRP, 1993a]).

The activity measured by USTUR in tissue samples was used to estimate the distribution of americium in the body a long time after occupational exposure. This empirical distribution was compared with the prediction of the ICRP model. On the face of it, the results seemed to show a large underestimate of the concentration of americium in the massive soft tissues (mostly fat and muscle) and to support an important revision of the model (figure 8).

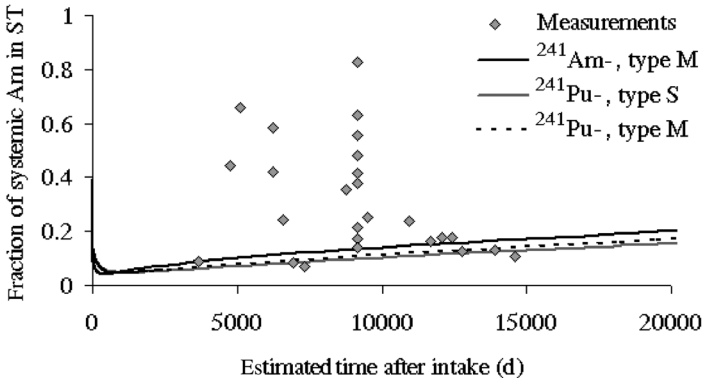


Figure 8. Comparison of the fractional retention of systemic americium (Am) in the massive soft tissues (ST) derived from the USTUR measurements with the predictions of the ICRP (1993) model after inhalation of absorption type M ^{241}Am or type M/S ^{241}Pu (Blanchardon et al., 2007b).

However the observed trend was associated with a large variability which led to question the quality of the different tissue samples measured. An empiric scale was adopted to grade the expected reliability of those samples. A cluster of highly reliable data was found to be associated with donations where the whole body could be mineralized and measured, as opposed to partial body donations where only limited samples could be measured (figure 9). Furthermore, these whole body data were consistent with the prediction of the current model. It was finally concluded that the available data did not support a significant revision of the model. Instead the inconsistent data appeared to be associated with small samples of large tissues which extrapolation to the whole body was highly uncertain.

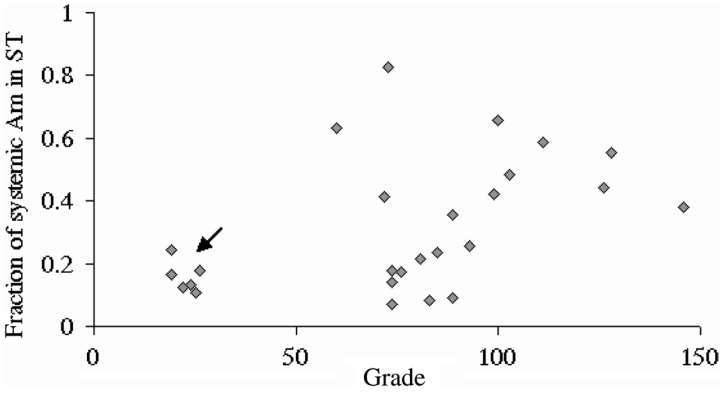


Figure 9. Fraction of the systemic Am content in the massive soft tissues (ST) derived from the USTUR measurements as a function of a grade of reliability of the corresponding autopsy case (the lesser the grade, the more reliable the data). The arrow points at a cluster of values derived from 6 particularly reliable cases (Blanchardon et al., 2007b).

This short study highlights a more general conclusion of Leggett (2001) that the reliability of biokinetic models relies directly on the quality of the measurement data they are built upon. Leggett notably distinguishes the models built on human data that are more reliable than those built on extrapolation of animal data and even more than models built through chemical analogy. Of course these data are more pertinent when they result from the direct observation of the process or quantity of interest for the model. In internal dosimetry, the observation of the late behavior of radionuclides is often limited for practical reasons and thus it is all the more valuable to document, in order to avoid the extrapolation of early kinetics to latter times. Regarding americium, beside the USTUR database, the most interesting recent information was the observation of the late urinary excretion, liver and skeleton retention (measured *in vivo*) for workers a long time after inhalation (Malátová *et al.*, 2003). Together with former data, it made clear an overestimation of the late urinary excretion by the model, which may be of importance for the dose assessment from late monitoring data (figure 10). The proper way to account for this observation in the revised americium model is under discussion in the INDOS task group.

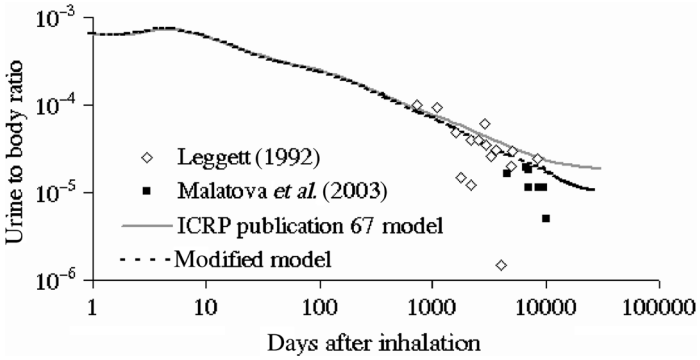


Figure 10. Fraction of systemic Am excreted per day in urine reported by Leggett (1992) and Malátová et al. (2003), compared with predictions from the ICRP (1993) model and from a tentative modified model (Blanchardon et al., 2007b).

2.1.1.2 Thallium biokinetics

In order to collect similar data for thallium (Tl), we initiated the dosimetric follow-up of an IRSN employee who underwent myocardial perfusion scintigraphy (Blanchardon *et al.*, 2005). Tl-201 is largely used in nuclear medicine for imaging of cardiac function. Its early kinetics is well known as a radiopharmaceutical and included in an ICRP (1987) model. However we had the opportunity to follow its whole body retention and urinary excretion for more than a month. The results suggested a slightly longer biological period than the one of the model (figure 11). This observation will be considered in the future revision of the biokinetic model for the element.

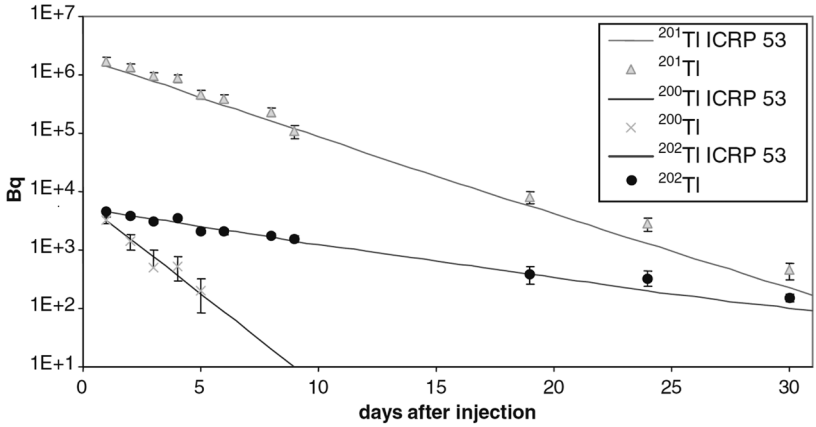


Figure 11. Urinary excretion of thallium. Daily-excreted activity of the three isotopes of thallium is represented (marks) in a semi-log graph and compared to decrease curves predicted from ICRP (1987) (Blanchardon et al., 2005).

2.1.2 Absorption kinetics in the human respiratory tract model

The inhalation of radioactive particles is the main route of occupational exposure. The assessment of doses to the lung and to other organs following inhalation is therefore an important issue of radiation protection. The human respiratory tract model (HRTM) of the ICRP (1994) is used to predict the deposition of inhaled particles in the regions of the respiratory airways, depending on their size, and the clearance of the deposited activity, by mechanical transport to the gut (mucociliary clearance) and to the regional lymph nodes, and by absorption to the blood. In its simpler form, the representation of absorption in the HRTM is a sum of two exponentials: a fraction f_r of the activity is rapidly dissolved with the fast dissolution rate s_r and the rest is dissolved at the slow dissolution rate s_s. The uptake of dissolved material to blood is supposed to be immediate (figure 12).

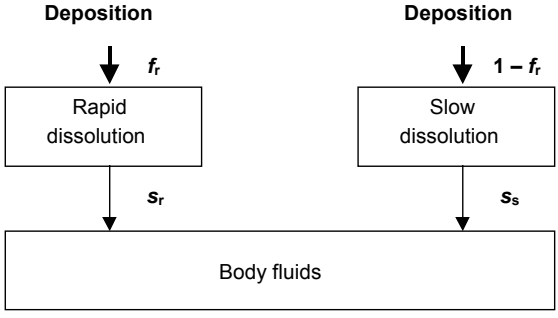


Figure 12. Compartment model representing time-dependent dissolution, followed by instantaneous uptake to body fluids (ICRP, 2002a).

The ICRP is considering three reference types of absorption for the various chemical compounds: Types F, M and S correspond respectively to fast, moderate and slow dissolution. However it was argued that those types, especially the intermediate type M, correspond to broad spectra of dissolution kinetics (ICRP, 1995b; figure 13) and include compounds of such different characteristics (*e.g.* for uranium) that they bear a large uncertainty.

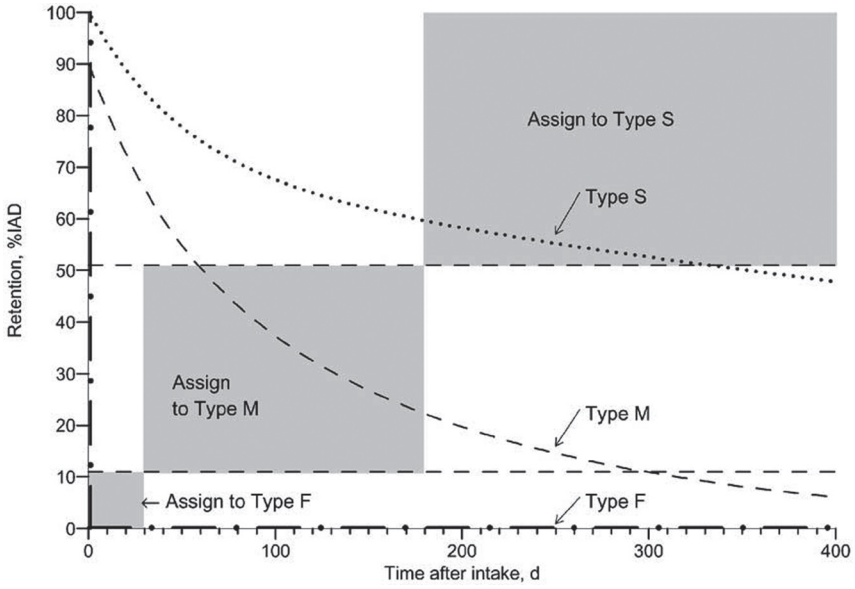


Figure 13. Retention of materials in lung as a percentage of the 'initial alveolar deposit' (IAD), following deposition in the alveolar region of the human lung. The curves show retention of hypothetical materials with absorption characteristics according to the default values for types F, M and S. The shaded areas show where observations can be used to assign materials to each type (ICRP, 2002a).

Therefore the studies related to the respiratory absorption of radionuclides are under re-analysis by the INDOS group. Our team reviewed so far the literature on the dissolution and absorption of plutonium (Davesne *et al.*, 2010a), americium and ruthenium. Experimental or empirical data were interpreted with species-specific biokinetic models to derive compound-specific values of f_r, s_r and s_s (*e.g.* figure 14).

The median of estimates for f_r and s_s from the different studies is consistent with the reference types F, M, S assigned by the ICRP to the chemical forms considered. s_r appears to be overestimated by the current default value, although few studies provide the early measurements needed to assess this parameter value. However a large variability is observed between the different compounds associated with each reference type and between the studies of each single compound. In order to improve the precision

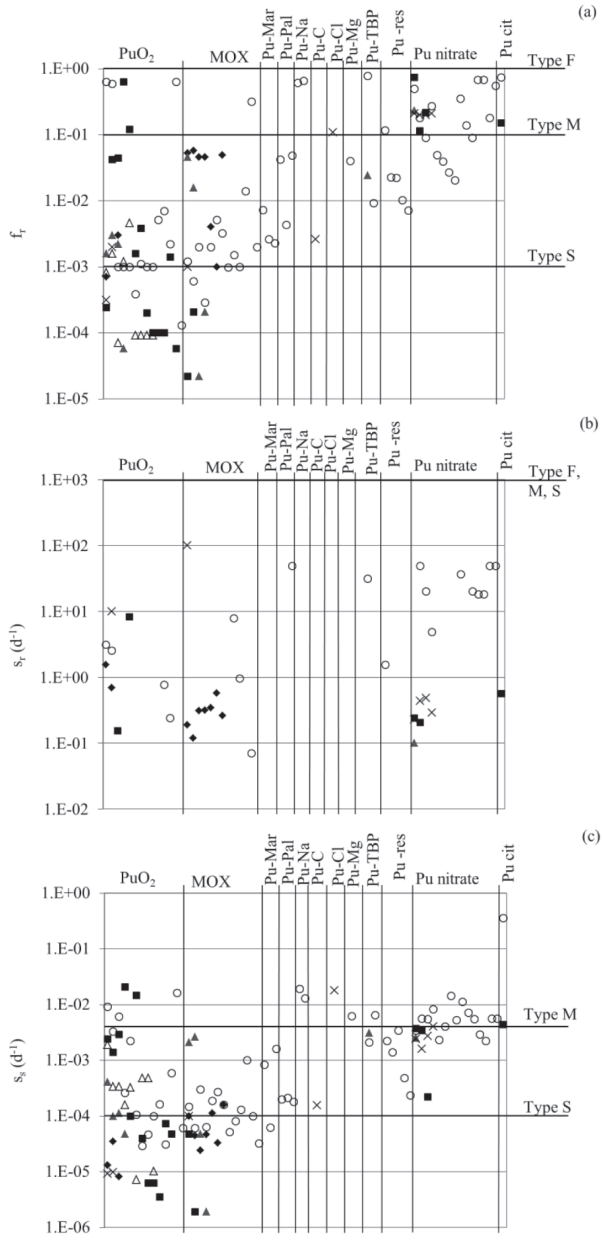


Figure 14. Rapid dissolution fraction f_r (a), fast dissolution rate s_r (b) and slow dissolution rate s_s (c) for different plutonium (Pu) compounds. Pu-Mar: soil from the Maralinga atomic weapons test range, Australia; Pu-Pal: dust from the Palomares H-bomber crash site, Spain; Pu-Na: Pu sodium alloy; Pu-C: Pu oxide graphite; Pu-Cl: Pu chloride; Pu-Mg: Pu magnesium alloy; Pu-res: residues; Pu cit: Pu citrate. In vitro (◆), dog (■), monkey (▲), mouse (△), rat (○) experiments; human contamination cases (✖) (Davesne et al., 2010a).

of the assessment of dose from inhalation, the ICRP now intends to provide specific default dissolution parameter values for each chemical compound which biokinetics is sufficiently documented (Bailey *et al.*, 2007). Our review and interpretation of data will support these values for plutonium, americium and ruthenium as well as the update of s_r values for the reference absorption types F, M and S. The sets of values estimated from the different studies also provide a mean to quantify the uncertainty on the absorption kinetics depending on the knowledge of the involved chemical compound.

One particular feature that complicates the understanding of the late kinetics is the absorption of dissolved material to blood. So far, this is assumed to be immediate. However, a provision is made in the model for a possible fraction f_b of dissolved element that could be bound to the tissues of the respiratory tract and absorbed at a rate s_b. When feasible, the ICRP now intends to provide non-zero values for these two parameters. This is well supported by experimental data for ruthenium which appears to be retained in the extrathoracic airways much longer than the mechanical clearance to the gut would suggest (Snipes, 1981). For americium (Taya *et al.*, 1994) and plutonium (James *et al.*, 2007), lighter evidence supports the choice of values and this may eventually rely on expert judgment.

2.1.3 Influence of a decorporation treatment on the biokinetic model

Blanchin and colleagues (2008) reported two occupational cases of plutonium inhalation where the reference biokinetic model appears to be inconsistent with observed individual measurements. The authors suggest than a peculiar physiological feature of the individual or a chemical property of the compound is responsible for this unusual behavior. Another reason may be the effect of a treatment with diethylenetriamine penta-acetic acid (DTPA). The observation highlights the limitation of models dedicated to the assessment of the effective dose received by a reference individual in a standard situation of exposure, for the demonstration of compliance with regulatory limits. These models of radiation protection are more interested in the radiological safety of the environment than in the individual behavior. However, in French nuclear facilities, any suspicion of contamination with plutonium is treated with an administration of DTPA (Grappin and Bérard, 2008). This chelating agent forms stable complexes with plutonium (and other metals) that are rapidly cleared in excretion, resulting in a strong increase (about 50 times) of plutonium in urines in the 24 hours after administration and in a much weaker lasting effect for up to 100 days (Ménétrier *et al.*, 2005). Despite an abundant literature, the kinetics of plutonium under DTPA treatment is not well understood, causing difficulties in dose

assessment. In common practice, data from urine measurements in the 24 h after DTPA administration are divided by 50 and those from 2 to 20 days post treatment are discarded (Piechowski *et al.*, 2003). As similar issues are encountered in other countries, I promoted the development of a model for DTPA treatment as a task (Breustedt *et al.*, 2009) in the European project "coordinated network in radiation dosimetry" (CONRAD, Lopez *et al.*, 2007) and in the European network for dosimetry (EURADOS, Lopez *et al.*, 2012). Hopefully, such model may support a more reliable dose assessment after plutonium exposure and DTPA treatment, for both regulatory and medical purposes. We chose relevant models to represent the behavior of plutonium (Leggett *et al.*, 2005) and DTPA (Stather *et al.*, 1983) that were connected by chelation with second order kinetics (figure 15).

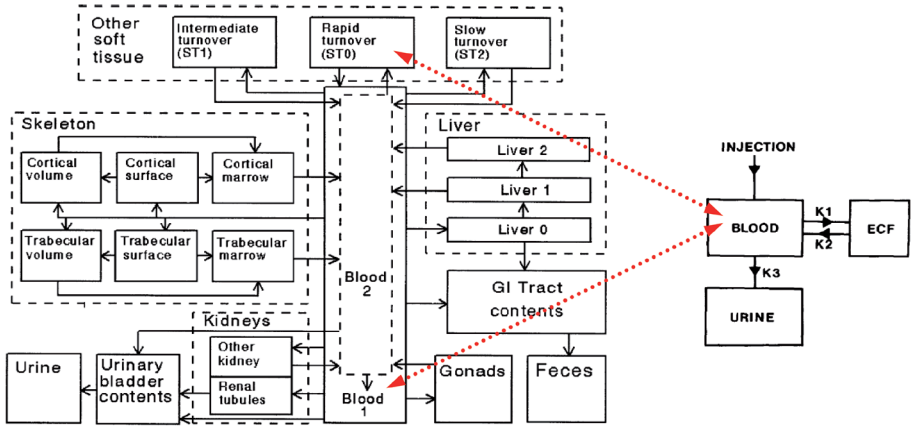


Figure 15. Structure of the biokinetic models for plutonium (left, [Leggett et al., 2005]) and DTPA (right, [Stather et al., 1983]). The chelation takes place between an atom of plutonium in 'ST0' or 'Blood 1' and a DTPA molecule in 'blood'.

The comparison of the prediction from the model with the actual follow-up of human contamination cases showed a good consistency in early kinetics but an underestimate of the latter urinary excretion (figure 16). One of the unanswered questions is the location of plutonium available for DTPA chelation: The pool of plutonium in plasma appears too small to explain a lasting effect of DTPA. Instead the few percents of DTPA distributed in the extracellulary fluids may be responsible for chelation of plutonium in such reservoir tissues as skeleton and liver to an extent that remains to be determined. Animal studies may provide the answer to this question and to others in the near future (Fritsch *et al.*, 2009; Weber *et al.*, 2012).

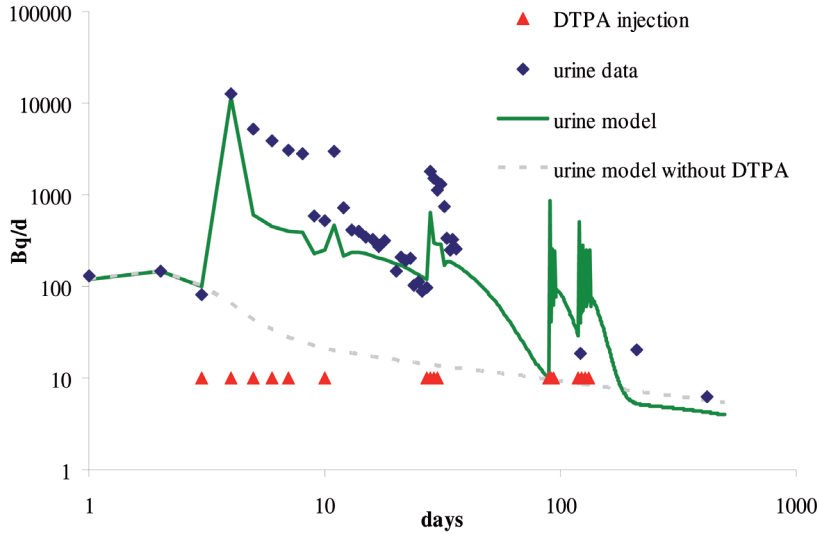


Figure 16. Interpretation of follow-up data after wound intake of plutonium (Jeanmaire et al.*, 1964) with a model for DTPA treatment. Measured and predicted values of urinary excretion.*

2.1.4 Numerical implementation of biokinetic models

Beside the major issue of reliable biokinetic data, a minor source of errors is the numerical implementation of the models. I therefore participated in a task dedicated to the quality assurance of the implementation of new biokinetic models within CONRAD and EURADOS (Nosske *et al.*, 2008). In addition to reducing to less than 1% the discrepancies in numerical results between the different organizations participating, this work allowed quantifying the consequences of possible modeling assumptions like shared *versus* independent kinetics of radionuclides within a nuclear decay chain and averaging procedures for sex-dependant models. A collaboration with the ICRP dose calculation task group (DOCAL) and the US National Council on Radiation Protection and Measurements (NCRP) allowed correcting minor inconsistencies in the alimentary tract model of the ICRP (2006) and in the wound model of the NCRP (2006) before publication.

2.2 Update of dosimetric models

Dosimetric models represent the transport of radiations recorded in nuclear databases (ICRP, 2008) from their point of emission, following the nuclear transformation of a radionuclide, to the radiosensitive regions of the body. Combined with biokinetic models they can predict the doses absorbed by the tissues and the committed

effective dose following the intake of a radionuclide. The geometry of irradiation is provided by computational anthropomorphic phantoms consistent with the volumes and densities of organs in a reference person (ICRP, 2002b). Where the precise nature and location of the cells at risk are identified (skeleton, gut, lung), specific models are available to assess doses at the cellular scale. The laws of physics are applied through Monte Carlo codes. A recent improvement was the endorsement by the ICRP of voxel phantoms (ICRP, 2009) in lieu of the former stylized phantoms where organs were represented by simple geometric shapes such as ellipsoids and cylinders (Cristy and Eckerman, 1987). The male and female voxel phantoms are based on medical images from real persons and consist in two matrices of volume elements (voxels). They provide a more precise and realistic representation of human anatomy (figure 17).

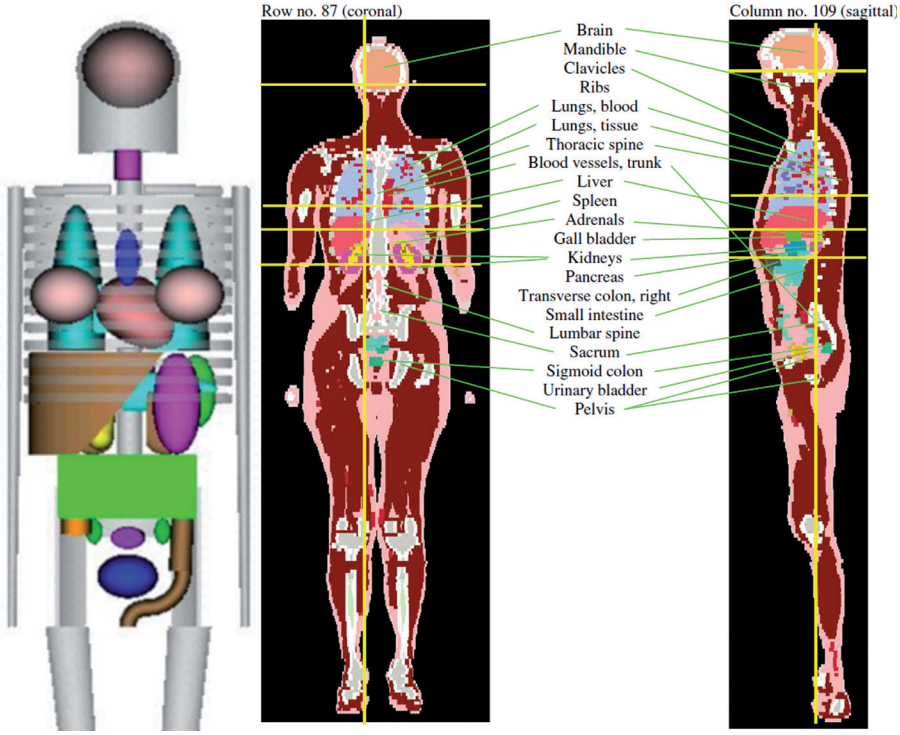


Figure 17. Left, front view of the ORNL stylized phantom (Cristy and Eckerman, 1987); right, coronar and sagittal slices of ICRP reference male computational phantom (ICRP, 2009).

The DOCAL task group took advantage of these phantoms to recalculate the specific absorbed fractions (SAF) of energy deposited in target regions following the emission of radiations in source regions. Our team participated in this work by the calculation with MCNPX (Hendricks *et al.*, 2008) of a set of photon, neutron and electron SAF for

quality assurance purpose (Gardavaud, 2009; Hadid *et al.*, 2010; figure 18). Overall, the evolution from stylized to voxel phantoms results in moderate changes in the dosimetry (Zankl *et al.*, 2012). Meanwhile an in-depth revision of the local dosimetry of the cells at risk in the alimentary tract (basal stem cells, [ICRP, 2006]) and in the skeleton (red bone marrow and endosteum) by the ICRP is under way (Pafundi *et al.*, 2010; Jokisch *et al.*, 2011).

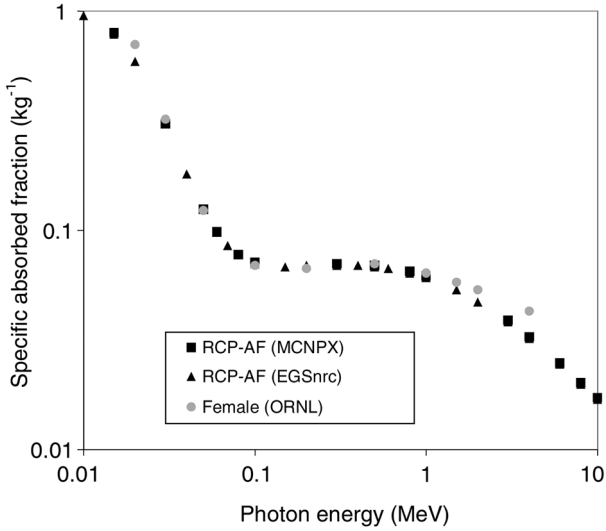


Figure 18: SAF (lungs←lungs) for the adult female reference computational phantom (voxel, RCP-AF), calculated at IRSN (MCNPX) and Helmoltz Zentrum München (EGSnrc), and for the former stylized phantom (ORNL), depending on the energy of the emitted photon (Hadid et al., 2010). The SAF is the fraction of energy emitted from the source organ that is absorbed by the target organ, divided by the mass of the target organ.

2.3 Evaluation of the uncertainty on activity measurement

The first source of uncertainty in the measurement of radioactivity is the statistic fluctuation of the quantity of interest and of the background noise. This (Gaussian) uncertainty increases as the measured activity decreases, down to the limit of detection (ISO, 2010). Increasing the counting time reduces this uncertainty. The *in vitro* measurement of urine or feces samples is also affected by the chemical yield in case of chemical separation of the radionuclide to be measured (Hurtgen and Cossonnet, 2003). When the activity is well above the limit of detection, the uncertainty is dominated by the stochastic fluctuations of excretion (figure 19). Those fluctuations are the consequence of the discontinuous and not-so-well understood mechanisms by which trace elements are cleared from the body (Usuda *et al.*, 2002). They increase dramatically when the sampling period decreases (Moss *et al.*, 1969).

I contributed to a task of the CONRAD project to quantify such fluctuations in the follow-up of contamination cases reported in the literature (Marsh *et al.*, 2007). They appear to follow log-normal distributions of geometric standard deviations (or scattering factors, SF) depending on the measured quantity, on the element and on the sampling period.

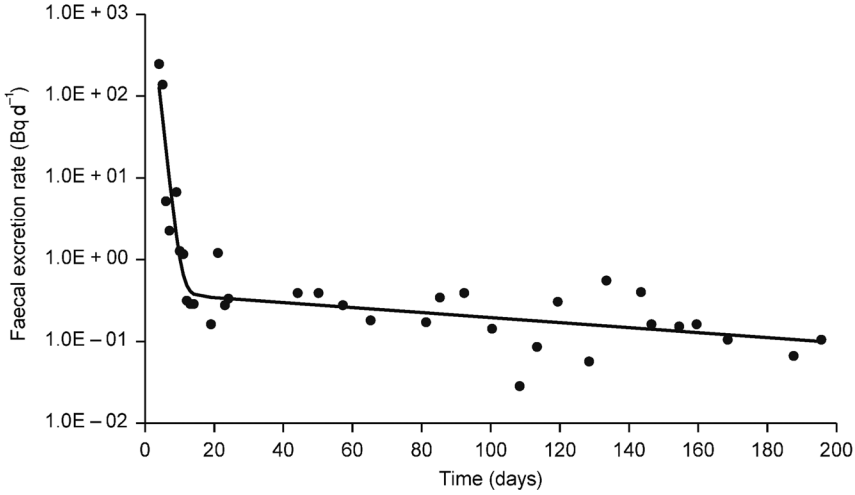


Figure 19. Stochastic fluctuations of fecal excretion around a sum of two exponential terms fitted to the data of a plutonium inhalation case (Lister, 1966). They are consistent with a lognormal distribution of geometric standard deviation (SF) = 2.2.

In addition to counting statistics, the reliability of *in vivo* measurement depends on its calibration (Toohey *et al.*, 1991). This is usually performed by the measurement of sources of known activity within physical phantoms made of tissue-equivalent material (figure 20). However these physical phantoms suffer from several limitations: their anatomical realism is not perfect; the activity is distributed in a fixed set of organs and it is homogenous inside each of these organs. Like voxel phantoms and Monte Carlo particle transport codes can be used to assess the doses absorbed by tissues, they can simulate the *in vivo* measurement of activity. A comparison between Monte Carlo simulations with voxel phantoms and measurements of a physical phantom showed only a limited influence of the shape of the phantom and of the heterogeneous distribution of activity within an organ (de Carlan *et al.*, 2007). However, the biokinetics of the radionuclide may significantly influence the result as the measurement of the organ of interest is affected by the radiations emitted from other organs.

Figure 20. In vivo measurement with 4 germanium detectors (left) and efficiency calibration using the IGOR phantom (right) at IRSN, Le Vésinet.

The PhD thesis of Stéphanie Lamart (2010), which I supervised, was therefore devoted to the integration of biokinetics in a procedure of numerical calibration of *in vivo* counting. The in house OEDIPE software (Franck *et al.*, 2003) used to process input and output data files of the MCNPX Monte Carlo code was connected to the biokinetic code ACTACAL (Eckerman *et al.*, 2001) to specify distributions of activity depending on the time since intake and on the conditions of exposure. Organ specific calibration coefficients were determined from the simulation of activity of a radionuclide in a single organ measured under a given geometry. These organ specific coefficients may be linearly combined with the distribution of activity predicted by the biokinetic model to provide a calibration coefficient dependant on the biokinetics (Lamart *et al.*, 2007). This method was applied to the measurement of americium 241 in the lungs (figure 21), liver or knee and to the measurement of cobalt 60 in the lungs or in the whole body at the *in vivo* measurement facility of AREVA La Hague reprocessing plant (Lamart *et al.*, 2009a).

The results may be used to confirm the selection of measurement geometry, to correct calibration coefficients obtained with physical phantoms and to evaluate the uncertainty due to the incomplete knowledge of conditions of exposure such as the time of intake or the absorption type of the radionuclide, or due to the uncertainty on individual parameters of the biokinetic model. In routine monitoring this uncertainty can be prospectively propagated to the dose to evaluate the suitability of the monitoring program. The developed tools were also applied to old and complex

americium 241 contamination cases (Broggio *et al.*, 2009). Several measurements in different geometries could be represented by as many linear combinations of constant organ specific calibration coefficients with the activity retained in each organ at the time of the measurement. These linear equations yielded likely values of both the biokinetic parameters and the intake, which eventually led to the organ doses.

The biokinetic and dosimetric models appear suitable for their application in radiation protection. Where they are uncertain, this uncertainty may be quantified. However guidance is needed for their proper use in order to ensure a better reproducibility in the process of internal dose assessment, the robustness of the methods and the quality assurance of the results.

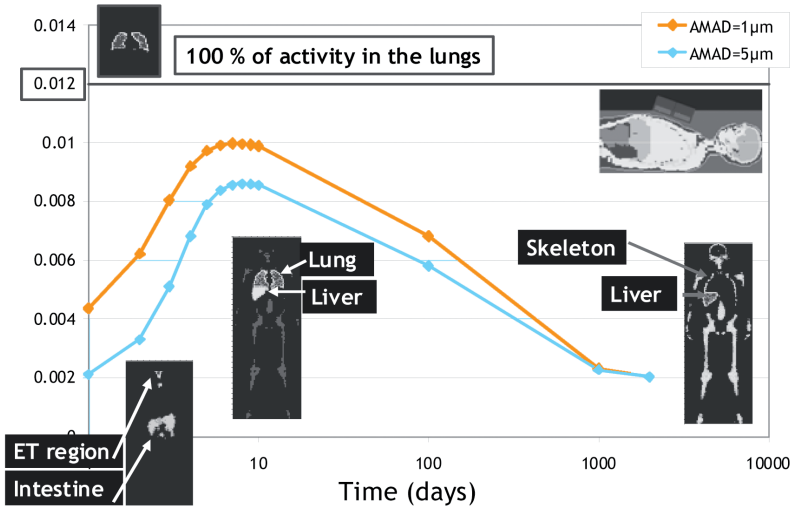


Figure 21. Efficiency calibration coefficient for lung counting of Am-241 depending on the time after inhalation of absorption type M material, comparison with the coefficient obtained with a physical phantom where all activity is in the lungs (Lamart, 2010).

Chapitre 3
Guidelines for internal dose assessment

In practice, having access to reliable models and measurement techniques is not sufficient to produce a reliable dose assessment. The right model and technique have to be applied in the right way and in the right situation. The indirect nature of the process leading from the measurement of body activity to the assessment of committed dose, the variety of available models, techniques and options regarding their parameters, as well as their relative complexity, cause internal dosimetry to be considered as a complex and difficult discipline, prone to errors and misconceptions.

3.1 Recommendations validated by the national authority for health

In France, many of the occupational health practitioners legally responsible for the dosimetric follow-up of workers exposed to ionizing radiation experience difficulties with the management of internal exposure. This was the reason for the occupational health officers of French companies managing basic nuclear facilities (AREVA, Électricité de France [EDF], the Atomic Energy Commission [CEA] and the department of radiological protection of the army [SPRA]) to build a working group of occupational health practitioners, biological pharmacists in charge of activity measurement, and experts in internal dosimetry (including me), in order to discuss these difficulties and to harmonize the practices. The French society of occupational medicine (SFMT) commissioned the group to write a guide, under the method recommended by the national authority for health (HAS, agency under supervision of the ministry of health), which could be used as a reference by professionals concerned with this risk (Blanchin *et al.*, 2012). A review of the international recommendations and standards, norms, national regulation and scientific literature, as well as the experience of professionals in the field was the basis of a series of recommendations to answer such questions as: Why assessing the dose? Who is in charge? What results should be transmitted and recorded, in which form? Which measurement technique should be applied in which situation, with which frequency? How to interpret the early indicators of exposure to evaluate its magnitude? What model and parameters to use in the dose assessment? What to do if the model does not fit the observed situation? Can we say something of the uncertainty on the dose and of the associated risk?

The recommendations on implementation, communication, traceability and records; monitoring programs; assessment of the committed effective dose; health risk and care were reviewed by a reading group of professionals. Each recommendation was graded according to the level of evidence that supports its development. Finally the guide was validated by the HAS and made freely available by the SFMT (2011) (figure 22). It aims at optimizing the protection against the risk of internal exposure and the medical follow-up of workers exposed to this risk by harmonizing the professional practice in occupational medicine, strengthening the primary prevention through an improvement of the radiological cleanliness of workplaces and improving the information of workers on the nature of the risks they are exposed to.

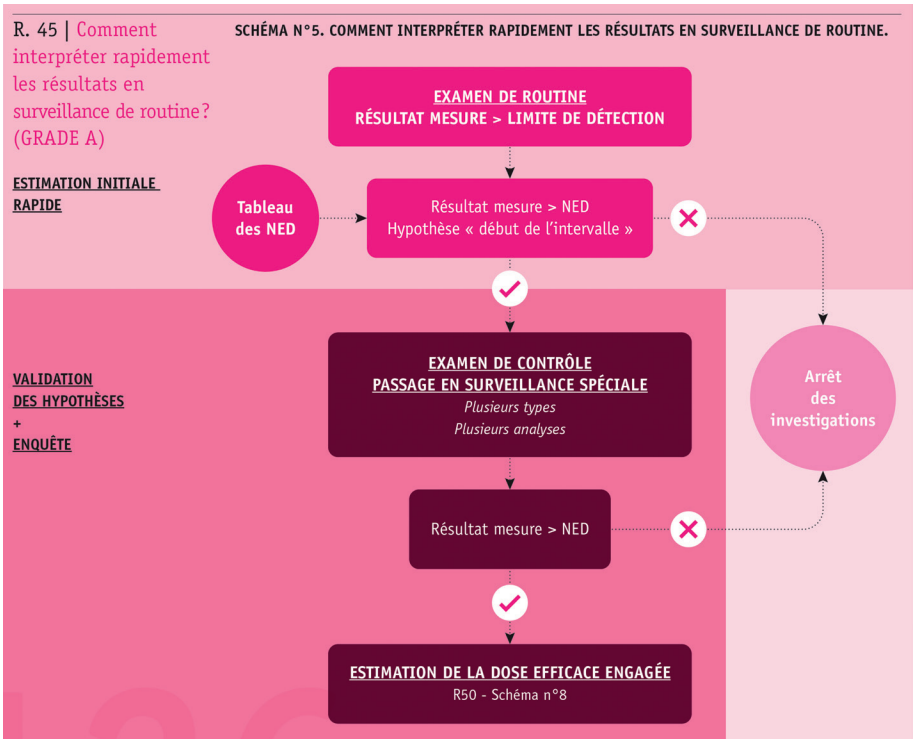


Figure 22. Diagram illustrating the rapid interpretation of routine measurement results (SFMT, 2011).

3.2 European IDEAS guidelines

At the European level, I participated in the project "General guidelines for the estimation of committed dose from incorporation monitoring data" (IDEAS) that was started as a response to the disturbing dispersion of results observed in the third European intercomparison on dose assessment (Doerfel *et al.*, 2000). It first consisted in compiling a database of contamination cases reported in the literature (Hurtgen *et al.*, 2007) and in the cross evaluation of these cases by different experts with dedicated software (Berkovski, 2000) to draw lessons on the main issues. Then guidelines were written aiming at harmonization: by following the guidelines any two assessors should obtain the same estimate of dose from a given data set; optimization: the best estimate of dose should be obtained from the available data; and proportionality: the effort applied to the evaluation should be proportionate to the dose — the lower the dose, the simpler the process should be. Unlike the guide promoted by the SFMT, the IDEAS guidelines are exclusively concerned with the assessment of committed effective dose from the results of activity measurement

and they discuss in detail the application of the models and the choice of their parameters (Doerfel *et al.*, 2006).

Three levels of task, depending on the expected dose were proposed: At level 0, the comparison of measurement results with pre-calculated values ensures that the annual committed effective dose is less than 0.1 mSv and no evaluation of dose is needed. At level 1, when the dose is typically 0.1 – 1 mSv, a simple evaluation is conducted with the reference ICRP models, their default parameter values and default assumptions regarding the conditions of exposure. At level 2, when the dose may exceed 1 mSv, several measurement results are used to fit the model to the data, in order to find optimum parameter values regarding the conditions of exposure: time of intake and physicochemical form of the radionuclide (for inhalation, the activity median aerosol diameter (AMAD) and the absorption type). At level 3, when the dose may be above 6 mSv, an advanced evaluation requires comprehensive data to adjust all the model parameters until a reasonable fit of the model to the data is obtained (figure 23). From leve 1, the value of the intake and of the other variable parameters is obtained by minimizing a chi-squared test statistic (1).

$$\chi_0^2 = \sum_{i=1}^{n} \left(\frac{\ln(M_i) - \ln[Im(t_i)]}{\ln(SF_i)} \right)^2 \qquad (1)$$

Where I is the intake, M_i is one of the n measurement results, SF_i its associated scattering factor assuming log-normal measurement uncertainty, $m(t_i)$ is the prediction of the model for the measured quantity at time t_i after the incorporation took place.

Although the IDEAS guidelines were developed in connection with the ICRP and were the basis of a draft document for public consultation (ICRP, 2007b), they were not endorsed by the Commission. They were judged to be too prescriptive for the general recommendations of the ICRP that have to be applicable in the regulation of any country and in most situations of exposure. Particularly, the individual specific adjustment of the model at the level 3 of the IDEAS guidelines is in contradiction with the definition and purpose of the effective dose. The effective dose is evaluated for a reference person, rather than a specific individual, under the exposure considered. The dose limits associated with this reference person are set well below the levels where an excess of risk is observed so that the whole population is adequately protected when the dose to the reference person fulfills the requirements of the radiation protection policy (ICRP, 2007a). Recently, much of the content of the IDEAS guidelines was integrated in an ISO (2011) norm on internal dose assessment and we are currently updating the guidelines within a task group of EURADOS (Lopez *et al.*, 2012).

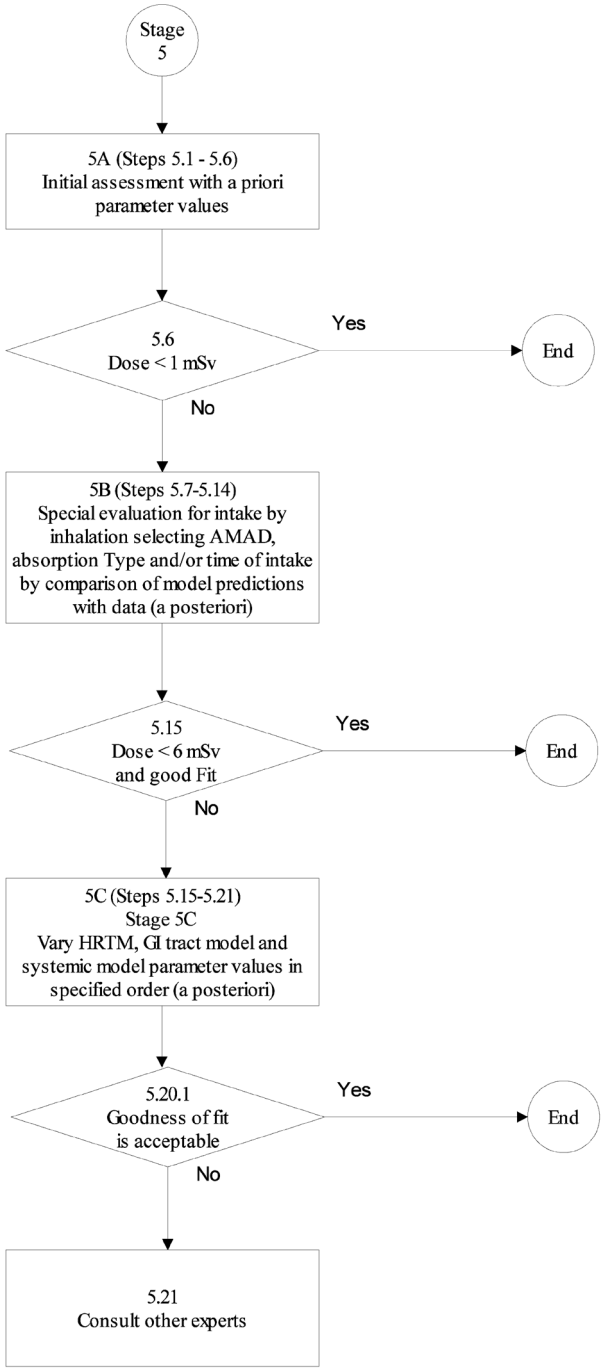


Figure 23. IDEAS stage 5-special procedure for inhalation cases above level 1-overview.

Chapitre 4
Evaluation of the uncertainty on dose assessment

The application of the IDEAS guidelines was tested in an international inter-comparison exercise of internal dose assessment organized jointly with the International Atomic Energy Agency (IAEA). The results were only partly satisfying: While the dispersion was reduced in comparison of the former European inter-comparison (Doerfel *et al.*, 2000), it stayed significant despite the application of the guidelines (Hurtgen *et al.*, 2005). Beyond errors in the process of the monitoring data and in the application of the models, this dispersion presumably hints at a remaining uncertainty due to a range of possible choices and assumptions. Furthermore while guidelines may help in harmonizing the practices, they do not cancel the uncertainty associated with both the measurement techniques and the models or the resulting uncertainty on the estimated dose.

Understanding and quantifying this uncertainty associated with the procedure of dose assessment therefore appears as an intellectual necessity and a requirement for the quality assurance of the result. In the longer term, providing the result of dose assessment as a range of possible values rather than a reference point value would appear to be more consistent with the reality. With a Russian colleague, Andrey Molokanov, we initiated a research work in this direction in the frame of collaboration between IRSN and the Moscow Federal Medical Biophysical Centre (FMBC, Russia; Molokanov *et al.*, 2004).

4.1 Position of the problem

It is useful to distinguish prospective and retrospective dose assessment (figure 24). In prospective dose assessment, a known or predicted exposure, such as the release of radioactive material from a nuclear plant, is converted into dose for the radiation protection of the exposed individual. In retrospective dose assessment, individual monitoring data are analyzed to infer the intake that took place and then to derive a value of the dose.

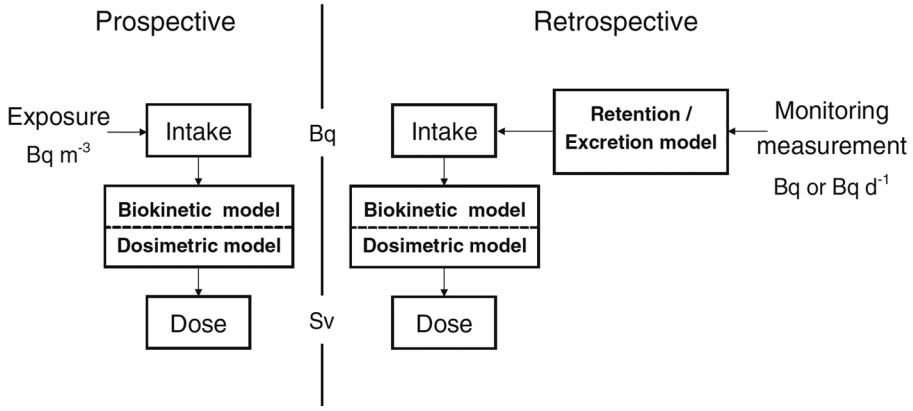


Figure 24. Types of internal dose assessment (Etherington et al., 2006).

The monitoring data are the results of the measurement of activity in the body or in excreta. They may come from routine monitoring where periodic measurements are performed to confirm the absence of contamination or to spot potential intakes that may have escaped the detection by the means of environmental or workplace monitoring (figure 25), or they may come from special monitoring when several measurements are performed after a known or suspected event to estimate the magnitude of the intake.

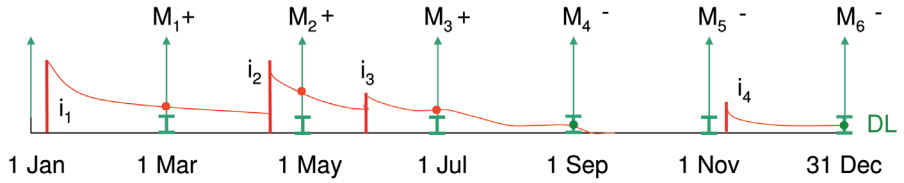


Figure 25. Illustration of routine (bimestrial) monitoring. The bars symbolize intake, the curves stand for the decreasing retention of activity. The measurement M_i (arrows) is considered positive when above the detection limit (DL). On the other hand, figures 11, 16 and 19 illustrate the outcome of special monitoring after incidents.

In prospective dose assessment, the committed effective dose is calculated as (2).

$$E = i \times e_{50}(L) \qquad (2)$$

where i is the known intake and $e_{50}(L)$ is the dose coefficient (effective dose committed over 50 years after the intake of 1 Bq) depending on the biokinetic parameters L.

In retrospective dose assessment the measured activity depends on the magnitude of intake i, the delay t between intake and measurement and the retention or excretion function m derived from the biokinetic model L for unit intake (3).

$$M = i \times m(t,L) \qquad (3)$$

The intake is thus derived from the measurement as (4).

$$i = M/m(t,L) \qquad (4)$$

If some parameters of the above equations are subject to uncertainty then the outcome of the calculations will also be uncertain.

4.2 Classical approach to the evaluation of uncertainty

We considered only inhalation intake which is the main route of internal exposure for workers. Like the IDEAS guidelines recommend three levels of task, when dealing with uncertainties we considered three stages of approximation to be applied depending on the level of exposure. At stage 1, corresponding to routine monitoring, a reference biokinetic model representing a reference person is considered; the default ICRP assumptions regarding the parameters of exposure are applied

(AMAD = 5 µm, absorption type F, M or S, intake at the middle of the monitoring interval), the measurement uncertainty is a combination of normal and lognormal dispersion. At stage 2, after an incident or when a dose limit may be exceeded, the parameters of exposure are variable (physicochemical form of the radionuclide, time pattern of intake). At stage 3, when health effects are expected and a medical follow-up or treatment is warranted, an individual specific biokinetic and dosimetric model for the exposed individual should be sought; this approximation stage 3 was only briefly discussed.

The uncertain quantities were represented by probability density functions (PDF), taking advantage of the input of chapter 2. In the situation where no clue indicated otherwise, uniform PDF were retained within the range of possible values. The uncertainty is propagated from the input to the output variables of the equations (2), (3) and (4) by Monte Carlo calculation, *i.e.* by sampling a large number of combinations of the parameters according to their PDF. The results are expressed as PDF of dose. The method was applied to evaluate the dose and its associated uncertainty for contamination cases reported in the literature (Blanchardon *et al.*, 2007c), and to study the effect of different assumptions on the time pattern of intake (Molokanov and Blanchardon, 2007a) and the stochastic variability of excretion (Molokanov and Blanchardon, 2007b).

The work was continued in the frame of an internal project that we conducted with a statistician colleague, Eric Chojnacki, from the nuclear safety division of IRSN (Molokanov *et al.*, 2008). The rational of the method was reviewed along four steps: 1) defining the physical quantity of interest and the physical process leading to measurement, 2) modeling the knowledge on the uncertainty sources, 3) choosing an inference method and target values such as mean, mode, and percentiles, 4) choosing a set of rules to aggregate the information from different sources, such as several monitoring periods or several possible biokinetic models.

In this regard the Monte Carlo calculation applied above to retrospective dosimetry where the intake appears as a random variable depending on the random measurement result (4) is in contradiction with the actual physical process where the intake is the cause and the measurement is a consequence. To correct this problem of causality, an updated method was developed where the intake is considered as a fixed but unknown quantity.

In the physical model, the activity to be measured is proportional to the intake i_0 and the measurement is subject to an uncertainty related to the bioassay sampling

and nuclear counting procedures. Probability distributions were retained to model the uncertainty sources so that we can calculate the probability distribution of the measurement M. Formally, it can be written:

$$M = i_0 \times S \qquad (5)$$

where S is a random variable of known PDF resulting from the PDFs associated to all uncertainty sources.

The value of intake i_{est} is estimated so that the observed measurement M_{obs} appears to be a chosen statistics of M: percentile, mean, etc. if the value of i_0 was i_{est}. For example, $i_{0.95}$ is the value of intake for which M_{obs} is equal to the percentile 95% of M (figure 26).

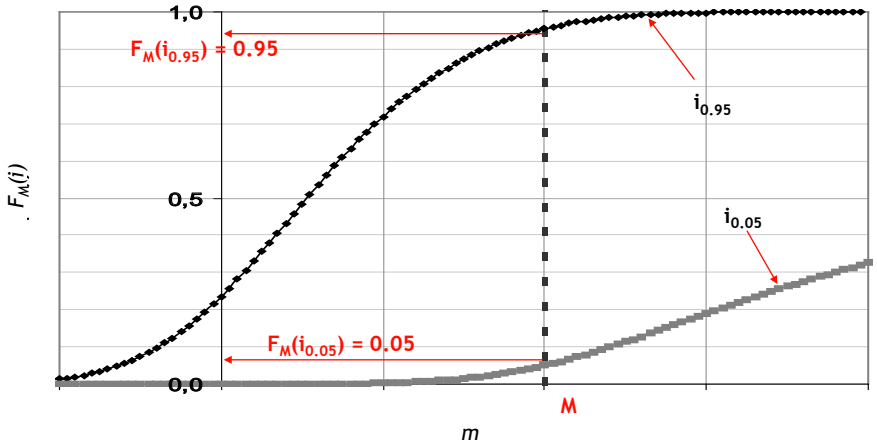


Figure 26. Determination of the 90% confidence interval of intake by a classical method (adapted from Molokanov et al.*, 2008).*

The method was applied to understand a debate on the choice of the time pattern of intake to be assumed in routine monitoring (Puncher *et al.*, 2006): The assumption of a single intake at the middle of the monitoring interval leads to the median of the distribution of intake estimates. The assumption of a constant chronic intake over the monitoring interval leads to the mean of this distribution. The present method provides any percentile of the distribution (Molokanov *et al.*, 2010). However, we were so far unable to properly apply it to multiple measurement values or to multiple intakes. To deal with such complex cases, we looked for a more flexible method in the Bayesian framework.

4.3 Bayesian approach to the evaluation of uncertainty

In the Bayesian frame, all uncertain quantities, including the intake, are modeled by random variables. The idea of the Bayesian approach is to weight each possible value of the intake by its degree of belief in the form of a PDF. Before the measurement of activity, the value of the intake is assumed to be described by the prior probability distribution $p(i)$ and the knowledge of the biokinetic model parameters by the PDF $p(L)$. The result of the measurement M gives information that is used to more precisely define the value of the intake by calculating a conditional probability of i given M. From the result of measurement, the prior probability distribution of the intake is changed to the posterior probability distribution $P(i \mid M)$ (6).

$$P(i|M) = C \,.\, \int_{-\infty}^{\infty} P(M|i,L).\, p(i).\, p(L).\, dL \qquad (6)$$

where C is a constant and $P(M \mid L,i)$ is the likelihood of observing the measurement M given L and i. In Bayesian as in frequentist statistics, uncertainty bands can be defined for a parameter to reflect the probability that it lies in the intervals.

The application of the classical and Bayesian approaches to simple cases was found to yield comparable results (Molokanov *et al.*, 2010). Within the CONRAD project, the application of the Bayesian approach at the British Health Protection Agency (HPA) and in our group resulted in a reasonable agreement (Marsh *et al.*, 2008).

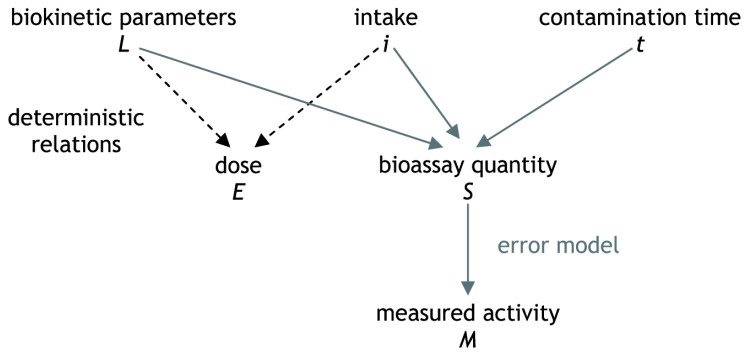
4.4 Optimization of a monitoring program

In radiation protection the models and parameter values are fixed by convention and are not subject to uncertainty (ICRP, 2007a). There is no need to evaluate the uncertainty associated with an individual dose assessment performed to demonstrate compliance with regulatory requirements. Nevertheless, the assessment of uncertainties associated with a specified monitoring procedure provides important information for the quality assurance of the monitoring program.

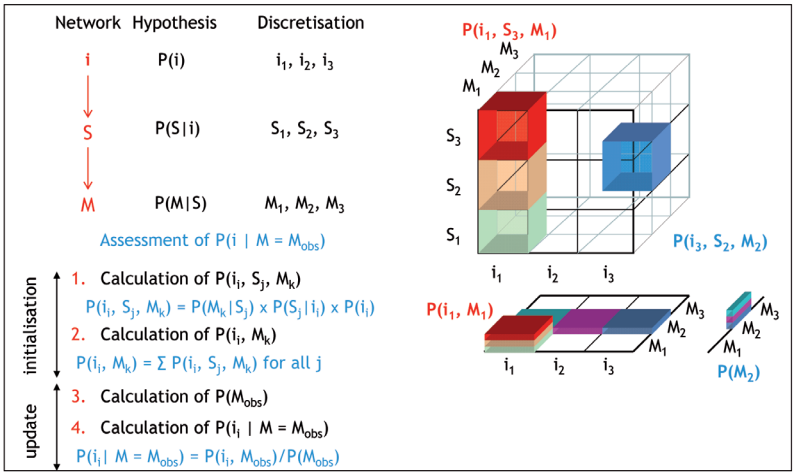
In the PhD thesis of Estelle Davesne (2010b), which I supervised, the probabilistic approach to the uncertainty was applied to determine the minimum exposure detectable by a monitoring program with sufficient (95%) confidence, as the upper bound of the confidence interval on the effective dose estimated from a negative result of measurement. This minimum detectable dose (MDD) depends on the features of the program (measurement technique and frequency) and the exposure to control (physico-chemical form of the radioactivity). It quantifies the

sensitivity of the monitoring program and it may be compared with the level of 1 mSv recommended by the ICRP (1997), the ISO (2006) and the SFMT (2011) for estimation and record of the effective dose, or with another constraint decided by the employer or the national authority.

We felt that, in the classical (frequentist) approach, the absence of assumption on the quantity of interest that is the intake may implicitly give more weight to the assumptions regarding other uncertain parameters. The Bayesian approach was preferred because all assumptions are made explicit through the prior probability distributions. It was implemented in two ways: through the Weighted Likelihood Monte Carlo Sampling (WeLMoS) method developed at HPA (Puncher and Birchall, 2008) and through a Bayesian network with the following structure:



The Bayesian network provides a clearer view of the dynamic relations between the variables at the cost of a longer calculation time or a lesser precision (box 2).



Box 2. Calculation of the posterior probability of i in a simplified Bayesian network where each of three related variables may take only three values (courtesy of E. Davesne).

It was applied to optimize the monitoring program of workers who perform the purification of plutonium in AREVA La Hague reprocessing plant (Davesne *et al.*, 2011). The potential exposure of these workers to plutonium oxide is monitored by a combination of periodic urine and fecal measurements. The optimization consisted in finding the best compromise between the cost of the measurements and the sensitivity of the program, under explicit assumptions regarding the prior probabilities of the uncertain parameters. The influence of the different parameters on the MDD was studied by varying the form of the respective prior probability distributions in view of the available information (Davesne *et al.*, 2010c). Not surprisingly the choice of the prior probability of intake has a strong influence on the MDD. Three prior distributions of the intake were considered, respectively: a uniform prior probability assuming that all intakes between 0 and 10,000 Bq have the same probability of occurrence; a decreasing exponential prior assuming that the smallest intakes are the most probable; and the alpha-prior (Miller *et al.*, 2001) consistent with the 0.001 historically observed frequency of positive measurement results in AREVA La Hague facility. The three assumptions led for the monitoring program currently in operation (fecal measurement every 6 months) to a MDD of respectively 17, 0.27 and less than 10^{-6} mSv. The uniform prior was considered as too conservative in regard of the extensive confinement of the plutonium at the workplace. The alpha prior is so informative that the other parameters have nearly no influence and it would question the need for any monitoring program at all. So, it was agreed with the medical officer of AREVA La Hague that the exponential prior was a reasonable compromise and that the resulting MDD was satisfying.

4.5 Representation of imprecise knowledge

The latter result regarding the prior probability of intake illustrates the dramatic influence of the choice of PDFs for the input variables. Probabilistic approaches, especially in the Bayesian framework, have the virtue of explicitly formulating these underlying hypotheses. The choice of prior probability distributions may be discussed in view of the scientific knowledge and hopefully agreed by all the stakeholders in the issue under consideration. However agreed, the choice of a prior probability of intake in our study looks more like a guess than the conclusion of a scientific investigation, as the limited information on the expected exposure ("it should be very low") clearly does not support assigning a degree of belief or a frequency to every single value of intake where the prior probability distributions are defined. The same could be said of other variables such as the time of intake. The three prior probabilities considered for the intake may be seen as the bounds of intervals from the most conservative viewpoint to the most optimistic one, providing a range of results consistent with the possible positions between these extreme views.

There are other ways to represent such uncertainty that results more from a lack of knowledge than from a known variability. The possibility theory (Dubois and Prade, 1988), like probability, proposes a set-function that quantifies the uncertainty of events. As for probability, the possibility π of any subset or event E of the whole set U is a real number between 0 and 1:

$$\forall E \subset U, \pi(E) \in [0,1] \text{with } \pi(\varnothing) = 0 \text{ and } \pi(U) = 1$$

But, unlike a probability, a possibility is not an additive measure:

$$\pi(A \cup B) = \max(\pi(A), \pi(B)) \qquad (7)$$

so that several subsets may be fully possible (their possibility is then 1). The imprecision associated with the possibility distribution of an uncertain variable may be evaluated as the area under its distribution. From a possibility measure, a dual measure called the necessity N of the event E can be defined by:

$$N(E) = 1 - \pi(\text{non } E) \qquad (8)$$

The possibility indicates to which extent the event E is plausible while the necessity indicates to which extent it is certain. In this way, it appears that a possibility distribution π and its dual form, the necessity distribution N, define a set of probability distributions P (9):

$$P(\pi) = \{P, \forall E, N(E) \leq P(E) \leq \pi(E)\} \qquad (9)$$

This last equation shows that a possibility distribution may be seen as an imprecise probability. In this way, a possibility distribution defines a set of PDF rather than a single one. Therefore, a possibility distribution constitutes a simple and efficient way to model a family of probability distributions.

We applied these tools to the assessment of the uncertainty in the prospective dosimetry of uranium ore dust that may be inhaled by uranium miners. Both probability and possibility distributions were used to model respectively the variability and the imprecision of the input variables, according to the available information (Davesne *et al.*, 2009). The propagation of the uncertainty was performed according to the RaFu method (Chojnacki *et al.*, 2010). In practice, this method is similar to a Monte Carlo simulation. At each iteration, N values α_i *(1* $\leq i \leq$ *N)* are sampled from a uniform distribution over [0,1]. From the K probability distributions,

parameter values corresponding to the $\alpha_{i\,(1 \le i \le K)}$ cumulative probability are sampled. From the N-K possibility distributions, the upper and lower bounds of the intervals of possibility greater than or equal to $\alpha_{i\,(K+1 \le i \le N)}$, called the α-cuts, are sampled (figure 27). Two point calculations are performed for each set of α_i, combining the sampled probabilistic parameter values with either the most pessimistic or the most optimistic (regarding the outcome) sampled possibilistic parameter values.

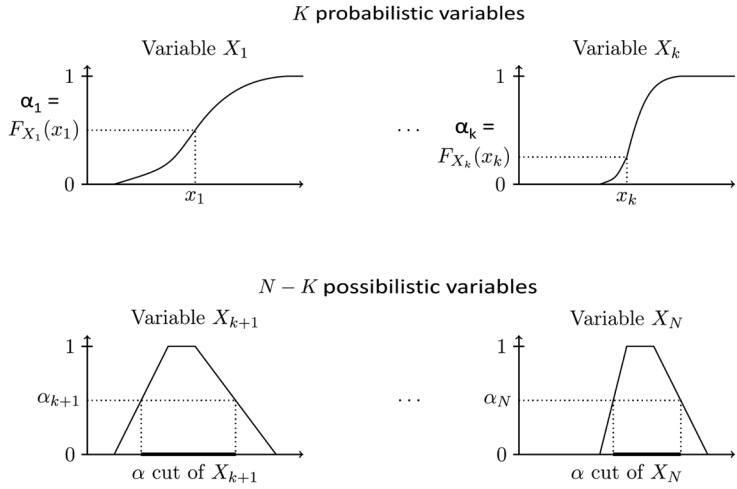


Figure 27. Sampling from possibility and probability distributions in the RaFu method (Chojnacki et al., 2010).

The outcome of the RaFu method is a set of intervals which bounds may be arranged in an upper and a lower cumulative density functions (CDF) on the quantity of interest that is the dose in our application. For simple interpretation, an uncertainty coefficient on the dose was taken as the ratio of the 95th percentile of the lower CDF to the 5th percentile of the upper CDF. This uncertainty is considered to be the combination of the imprecision represented by the distance between the same percentile of the lower and upper CDF and the variability represented by the distance between the 5th and 95th percentiles of a single CDF (figure 28).

The results were found to be more conservative, and we believe more realistic, than the outcome of a usual probabilistic approach. While we consider this first application of possibility to be satisfying for the purpose of prospective dosimetry in radiation protection, its presentation in the frame of the Alpha-Risk European project (Tirmarche *et al.*, 2010) showed that more work and discussion was needed before it could be used as an input in epidemiological studies of radiation exposure. Moreover the current method is not suitable yet for application to the inverse problem of retrospective dose calculation from monitoring data.

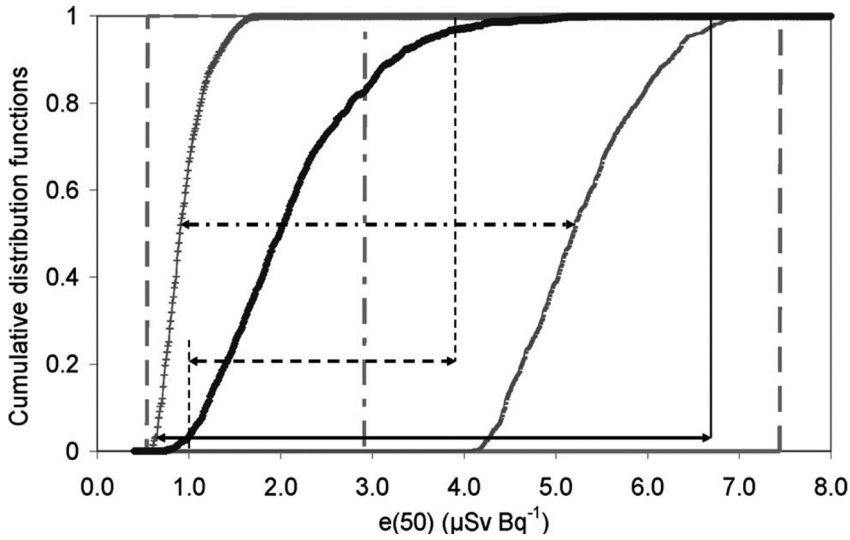


Figure 28. Example of cumulative density functions of the committed effective dose at the COMURHEX Malvesi plant for unit intake of U_3O_8 according to different representations of uncertainty: deterministic (broken grey), probabilisitc (dark gray), RaFu method (light grey). The arrows correspond to probabilistic uncertainty (broken), or uncertainty (solid) and imprecision (dotted-dashed) from the RaFu method (Davesne et al., 2009).

Chapitre 5
Study of the health effects of radionuclides

The system of radiation protection is based on knowledge of radiation health risk. It aims at restricting this risk as much as possible while retaining the benefit from the use of radiation. The exposure of individuals is quantified by the effective dose to be compared with limits, constraints and reference levels. However, the direct interest of exposed individuals is to know their own risk rather than their dose. This information is difficult to provide since most exposure is below the 100 mSv level (UNSCEAR, 2008) where the dose response curve for cancer is unclear (ICRP, 2005). The risk from the commonly heterogeneous and protracted irradiation delivered by internal emitters is especially delicate to extrapolate from the major source of information that is the follow-up of the survivors from the atomic bombings.

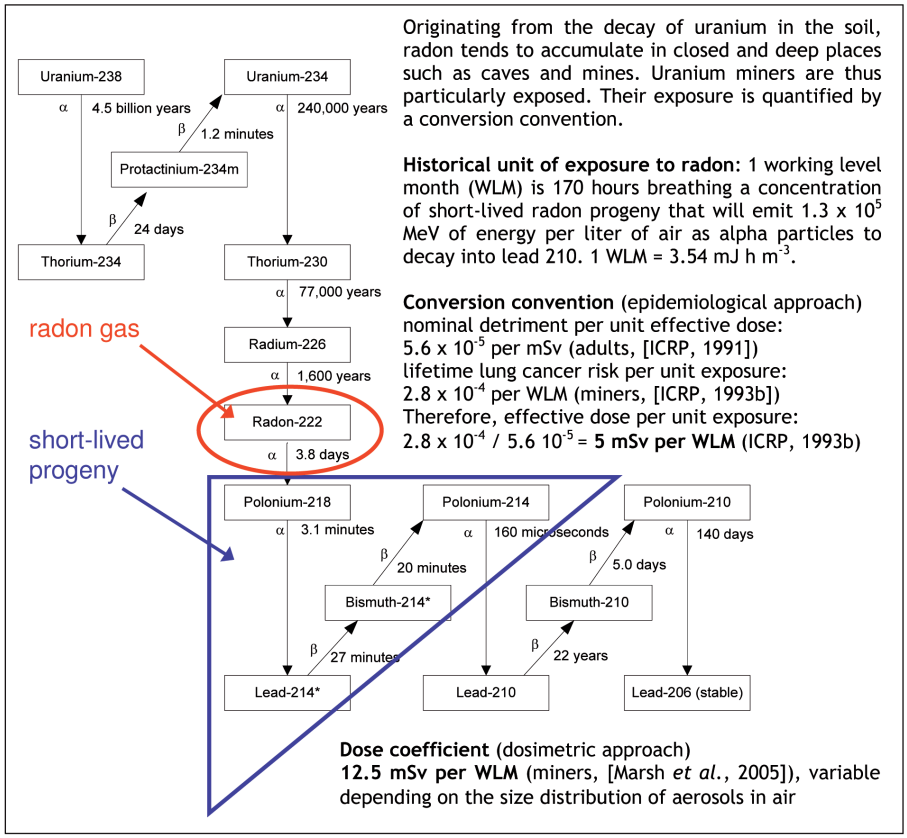
A large part of radiation research is devoted to clarify the risk of cancer and non-cancer diseases in the low dose range. IRSN is taking his share of this effort by

performing epidemiological and animal studies. I take part in the studies concerning internal exposure by providing dosimetric input.

5.1 Epidemiology of incorporated radionuclides

The epidemiology of ionizing radiation studies the incidence of diseases and the subsequent mortality in exposed populations. An excess of cancer which increases with the absorbed dose has been demonstrated notably among the survivors of the Hiroshima and Nagasaki atomic bombings, among patients treated with radiation and among nuclear workers. However the types of cancer and the excess relative risk depend on the precise nature of the exposure (as well as on the population under study). Furthermore, the size of the existing cohorts is currently not sufficient to prove a statistically significant excess of risk for a dose of less than a hundred of milligrays.

Among internal emitters, alpha emitters present a special challenge as their short range makes for a heterogeneous dose distribution and their high linear energy transfer causes heavier biological damages than photons at the same dose (ICRP, 2003). Finally the alpha-emitting actinides are also heavy metals which chemical toxicity may add up or interfere with the radiation damage. The question of the risk specifically associated with alpha emitters was therefore addressed in the European project "Quantification of cancer and non-cancer risks associated with multiple chronic radiation exposures: Epidemiological studies, organ dose calculation and risk assessment" (Alpha-Risk, [Tirmarche *et al.*, 2010]). Three work packages of this project were dedicated to the radon gas. This ubiquitous radioactive noble gas and its short-lived, alpha-emitting, progeny (box 3) are acknowledged as the prime source of exposure to ionizing radiation (figure 2) and the second cause of lung cancer ([WHO, 2009], after smoking) in the general population. Within Alpha-Risk, the risk of lung cancer was investigated in relation with domestic exposure to radon and occupational exposure of German, Czech and French uranium miners. As compared to former epidemiological studies of miners, the consideration of recent years of operation allowed for a better reconstruction of exposure and the evaluation of risk down to a relatively low level of exposure (Rage *et al*., 2012). I participated in the reconstruction of the annual individual lung dose of the miners, accounting for the respective contribution of radon gas, radon progeny, uranium ore dust and external gamma irradiation, with model parameters adapted to the working conditions depending on the location, job type and time period (Marsh *et al.*, 2012).



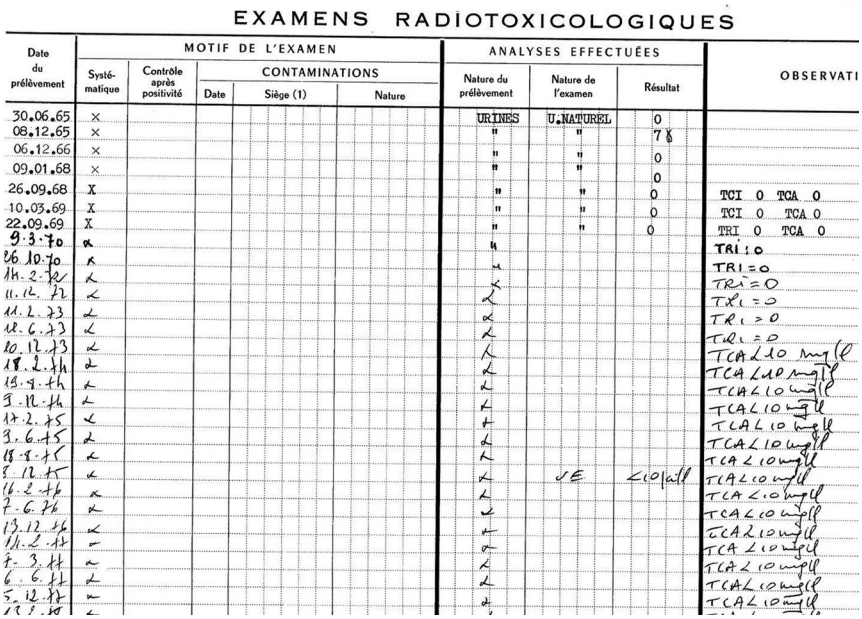
Box 3. Radon gas and its short lived progeny as part of uranium 238 decay chain. ICRP (1993b) convention for conversion of radon exposure into effective dose compared with a value of dose coefficient that was obtained by the application of the human respiratory tract model (ICRP, 1994) under specific conditions of exposure (Marsh et al., 2005).

The knowledge of lung cancer risk from radon exposure was sufficient for the ICRP to recommend managing this risk on the basis of epidemiological studies rather than dosimetric models. The effective dose per unit of radon exposure was therefore evaluated trough an "epidemiological approach" (ICRP, 1993b; box 3). In this method, the estimated health detriment associated with unit exposure to radon was divided by the detriment per unit effective dose determined by the ICRP (1991). The former is determined from miner epidemiology and the latter determined mainly from epidemiological studies of Japanese atomic bomb survivors (Marsh *et al.*, 2010). The resulting value was found to be 2 to 3 times lower than the dose coefficient that would come from the application of the human respiratory tract model ("dosimetric approach"). However the recent review of epidemiological studies of uranium miners within an ICRP task group on risk from alpha emitters (TG64) demonstrated

an updated value of detriment per unit exposure to radon that was twice higher than the former estimate (5×10^{-4} per WLM, [ICRP, 2010]). In this ICRP TG64, I participated in a review of dosimetric models that have been applied to radon. Since the finding of an increased detriment factor for radon reconciles the epidemiological and dosimetric approaches, the ICRP (2010) will now apply its dosimetric models to provide an updated dose coefficient for radon along with the revised dose coefficients for all other radionuclides (ICRP, 2012).

Two other work packages of Alpha Risk were dedicated to epidemiological studies of British, Belgian and French nuclear workers exposed to uranium and plutonium. These cohorts offer the advantages of good medical follow-up and characterization of exposure. We established dosimetric procedures for the retrospective assessment of annual individual organ absorbed doses from bioassay data (Thierry-Chef *et al.*, 2009) in a case-control study (Tirmarche *et al.*, 2010). The main issue was the documentation of work history and analytical techniques in order to understand the potential exposure in the course of time, and the bioassay data (figure 29). The low level of exposure resulted in a majority of negative bioassay results, interpreted as "less than the limit of detection", making the determination of the time-dependent limit of detection of the historical measurement techniques all the more important. We calculated the individual doses and their associated uncertainty by the Bayesian WeLMoS method developed at HPA (Puncher and Birchall, 2008). However, the number of negative bioassay data and the limited information on the chemical forms of uranium and plutonium handled at the various workplaces gave much weight to the subjectivity in the choice of prior probability distributions for intake and for lung absorption parameters. In the end the results expressed in the form of distributions of posterior probability on individual organ doses were complex to analyze for epidemiologists. This and additional practical problems explain why the assessment of the dose-risk relationship has not yet been finalized in this study.

The investigation of risk associated with plutonium exposure is continued in European (SOLO, 2009) and international projects involving notably the epidemiological study of workers at the Russian facility of Mayak. The first results show a significant increase of lung cancer risk with dose from plutonium and a weak evidence for an increased risk of liver and bone cancers (Sokolnikov *et al.*, 2008). So far, IRSN is not directly involved in those projects, but I am involved in the evaluation by ICRP TG64 of the results and of their potential impact on the radiation protection system.



EXAMENS RADIOTOXICOLOGIQUES

Date du prélèvement	MOTIF DE L'EXAMEN					ANALYSES EFFECTUÉES			OBSERVATI
	Systématique	Contrôle après positivité	CONTAMINATIONS Date	Siège (1)	Nature	Nature du prélèvement	Nature de l'examen	Résultat	
30.06.65	×					URINES	U.NATUREL	0	
08.12.65	×					"	"	7	
06.12.66	×					"	"	0	
09.01.68	×					"	"	0	
26.09.68	X					"	"	0	TCI 0 TCA 0
10.03.69	X					"	"	0	TCI 0 TCA 0
22.09.69	X					"	"	0	TRI 0 TCA 0
9.3.70	×					"			TRI : 0
26.10.70	×					"			TRI = 0
14.2.72	×					"			TRI = 0
11.12.72	×					×			TRI = 0
11.2.73	×					×			TRI = 0
12.6.73	×					×			TRI = 0
10.12.73	×					×			TRI = 0
18.2.74	×					×			TCA L 10 mg/l
19.9.74	×					×			TCA L 10 mg/l
9.12.74	×					×			TCA L 10 mg/l
17.2.75	×					×			TCA L 10 mg/l
3.6.75	×					×			TCA L 10 mg/l
18.8.75	×					×			TCA L 10 mg/l
8.12.75	×					×			TCA L 10 mg/l
16.2.76	×					×	VE	< 10 µg/l	TCA L 10 mg/l
7.6.76	×					×			TCA L 10 mg/l
13.12.76	×					×			TCA L 10 mg/l
14.2.77	×					×			TCA L 10 mg/l
7.6.77	×					×			TCA L 10 mg/l
6.12.77	×					×			TCA L 10 mg/l
5.12.78	×					×			TCA L 10 mg/l

Figure 29. Example of bioassay monitoring data for a French worker exposed to uranium (C. Challeton – de Vathaire, 2012).

The French cohort of uranium workers is currently under study by the IRSN laboratory of epidemiology (LEPID). Before we jointly start the individual dosimetry of the cohort, I supervised the master thesis of Irina Canu who characterized the exposure through the establishment and validation of a job-exposure matrix (Guseva – Canu *et al.*, 2010). As uranium may be encountered under a number of isotopic compositions (natural, depleted, enriched, reprocessed) and chemical forms covering the whole spectrum of lung absorption kinetics (from type F to type S), this matrix will allow, in particular, to document the physico-chemical forms of uranium handled by individual workers in the course of their work history.

5.2 Radiobiology of incorporated radionuclides

The limitation of epidemiology is its purely statistical approach. While it may evidence a quantitative correlation between a source of exposure and the incidence of a disease, it may demonstrate neither the cause to effect relationship nor the underlying mechanism. Moreover, the statistical elucidation of weak effects at low levels of exposure requires building very large cohorts which may prove practically difficult if not impossible. On the other hand, biological experiments conducted on laboratory animals can complement epidemiology by providing an insight into the mechanisms at work even at low level of exposure.

The effort of IRSN in radiobiology of internal emitters is conducted in the frame of the program "From environment to human" (ENVIRHOM, [Paquet, 2005]). Besides a part dedicated to the environmental effects on the vegetal and animal biotopes, ENVIRHOM studies the non-cancer effects of low level chronic ingestion of radionuclides by rats and mice, in order to predict and understand the health effects that may be experienced by populations as a consequence of enhanced natural radioactivity, releases from the nuclear industry or post-accidental situations (Chernobyl, Fukushima).

So far, the chronic ingestion of uranium at a relatively high level (40 mg of uranium per liter of drinking water) was shown to induce behavioral effects including alteration of the spatial working memory capacities, anxiety, perturbation of the sleep-wake cycle (Houpert *et al.*, 2005) and hyperactivity (Houpert *et al.*, 2007). I implemented biokinetic models for rat based on the observation of uranium retention and excretion after acute intake to investigate the specific features of uranium biokinetics under chronic ingestion (Paquet *et al.*, 2006) or inhalation (Monleau *et al.*, 2006). The accumulation of uranium in several organs was shown to be inconsistent with a direct extrapolation from the post-acute intake situation, suggesting some changes in biokinetic parameters as a response to chronic exposure (figure 30).

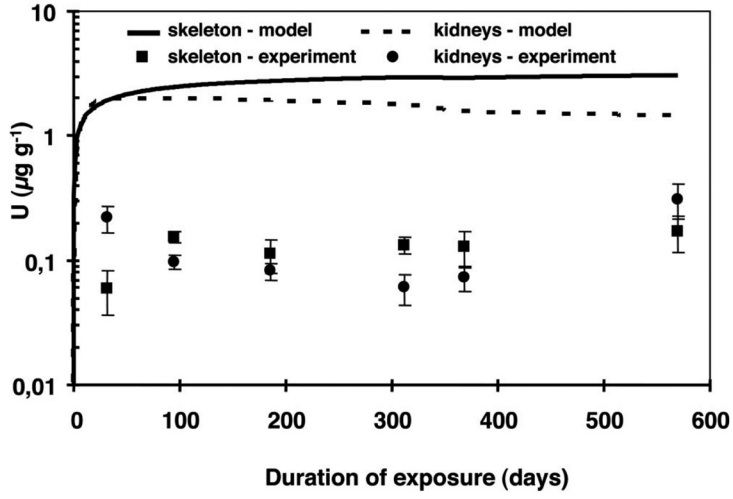


Figure 30. Discrepancy between model and observation for uranium concentration in kidney and skeleton plotted as a function of time after beginning of exposure to 1 mg uranium d^{-1}. Plotted and dashed lines represent predicted accumulation by the chronic rat model. Black squares and circles are experimental data (mean +/- SEM) (Paquet et al., 2006).

No pathology was reported following chronic ingestion of cesium 137 by rats, but several molecular effects were observed in relation with the metabolism of vitamin D (Tissandié *et al.*, 2009), steroidogenesis (Grignard *et al.*, 2008), cardiac physiology (Gueguen *et al.*, 2008) and cholesterol metabolism (Racine *et al.*, 2010). While the short range alpha particles bearing most energy emitted by uranium may be assumed, at first approximation, to be absorbed in the organ where they are emitted, the beta and gamma rays emitted by cesium 137 and its daughter barium 137m require a more sophisticated dosimetric model. Therefore, Hanane Miloudi's (2011) and Maxime Locatelli's (2012) master theses, which I supervised, were dedicated to develop such a model. Voxel phantoms were built from MRI images of the rodents studied in ENVIRHOM (figure 31). The phantoms were used to calculate specific absorbed fractions of energy (SAF) with MCNPX for the relevant organs and energies. Finally the SAF were included within rodent dose calculation software where they may be combined with experimental biokinetic data to assess organ absorbed doses. Similar work was already conducted before, notably for the dose assessment of radiopharmaceuticals in pre-clinic studies (Keenan *et al.*, 2010), but disposing of a library of voxel phantoms of the actual animals in use at IRSN (rats and mice of both sexes and three ages) should allow for an accurate dosimetry.

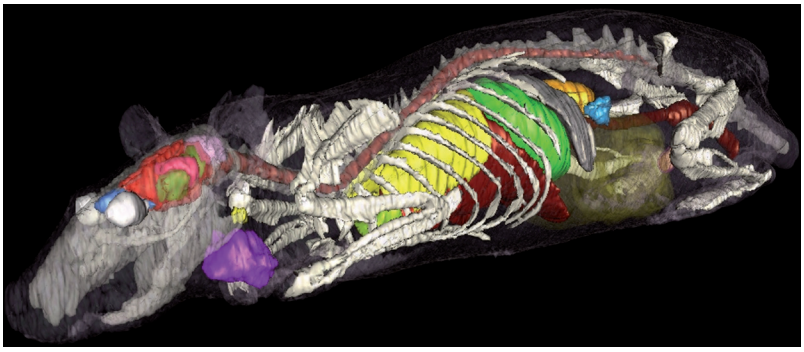


Figure 31. Voxel phantom of an old female rat (M. Locatelli, 2012).

Chapitre 6
Conclusion and perspectives

6.1 Conclusion

From the work conducted on the models for internal dosimetry and their applications, it seems that a reliable assessment of dose for regulatory purpose is achievable. Still a robust assessment of the individual risk from exposure to low doses of radiation lies as an open question and a natural topic for future research. Further work is planned in the continuation of the current activities to support radiation protection and research with updated dosimetric tools.

6.2 Perspectives in radiation protection

I plan to finish the study of the respiratory absorption of actinides and lanthanides, to review their alimentary absorption and to discuss the changes that may be required

in the systemic models for transuranium elements with the view of the update of ICRP dose coefficients for occupational intake of radionuclides and for exposure of members of the public. As the exposed members of the public may be children as well as adults, the age-specific alimentary and systemic behavior of radionuclides will be reviewed and incorporated into the biokinetic models. Accounting for exposed children will also require calculation of dosimetric SAF values with suitable children phantoms (Lee *et al.*, 2010). The round of update of ICRP reference values will finish with the revision of documents dedicated to the exposure of the embryo, fetus (ICRP, 2001) and breast-fed infant (ICRP, 2004).

I will coordinate the finalization of the model for DTPA treatment of plutonium and americium contaminations within EURADOS. We may have to distinguish two models of increasing complexity for regulatory application in radiation protection, and for medical application in the assessment of health risk and benefit. The missing key information appears to be the precise location of the one percent DTPA molecules remaining in body tissues 24 hours after the administration and of the corresponding pools of actinides accessible to chelation. The animal experiments of decorporation therapy currently conducted at the CEA Laboratory of RadioToxicology (Bruyères-le-Châtel, France) and at the Lovelace Respiratory Research Institute (Albuquerque, USA) should shed light on the issue. Ideally, experiments involving ^{14}C-DTPA would be especially valuable to clarify the distribution of DTPA molecules independently of their association with actinides.

There are more workers exposed to ionizing radiation in the medical field than in the nuclear industry (Feuardent *et al.*, 2011). The development of radiation protection in medicine is therefore a priority at the present time. While the internal exposure of workers in the nuclear industry is adequately controlled by a combination of workplace and individual monitoring, the situation of staff in nuclear medicine departments could be improved as the concern with radiation protection is relatively new. I will contribute to the development of specific guidance envisaged in an ISO norm on the "monitoring and internal dosimetry for staff exposed to medical radionuclides", which preparation is coordinated by IRSN, and in the extension of SFMT guidelines for monitoring of internal exposure from nuclear workers to nuclear medicine. However the short half-lives of radiopharmaceuticals in use (*e.g.* 110 min for fluorine 18, 6 h for technetium 99m) and the available equipment (usually nothing for the continuous assessment of exposure at the workplace but medical devices such as gamma cameras for the detection of activity in the body) raise particular issues. I therefore plan a specific study of the uncertainties in the monitoring programs of medical staff.

6.3 Perspectives in risk assessment

I aim at strengthening the collaboration with epidemiologists and biologists to support the investigation of health effects with accurate dosimetry. MELODI, the European platform under construction for low dose radiation risk research, will provide a natural framework for such exchanges (Laurier *et al*., 2012).

The dose calculation software developed in the master thesis of M. Locatelli (2012) should enable the biologist researchers of IRSN to apply dosimetric models. But owing to the few biokinetic data obtained in recent incorporation experiments, I may have to design biokinetic models to compensate for missing information. It is likely that new experiments in ENVIRHOM will involve decreasing concentrations of radionuclides in order to test whether the observed biological effects remain at the levels of exposure actually experienced by populations in contaminated areas. More interaction between biology and epidemiology is foreseen in the molecular epidemiology approach supported by MELODI to better understand the mechanisms leading to the effects evidenced by epidemiological studies (Pernot *et al.*, 2012). Meanwhile I will participate in a project initiated by the IRSN laboratory of biological dosimetry to adapt the tools (biomarkers) of biological dosimetry to the issue of internal contamination.

In collaboration with the LEPID, the lifetime annual tissue absorbed doses will have to be calculated for the thousands French uranium workers under study in the PhD thesis of Sergei Zhivin. I will supervise a master thesis to develop software for automated dose calculation. The outcome might be combined in the future with results from the Belgian and British cohorts. The epidemiological study of uranium miners will be extended by the fusion of the European and Canadian cohorts in the EUROCAN project. Since other diseases than lung cancer are to be considered, I will calculate absorbed doses to the bone marrow, kidney, brain, heart, stomach and colon, in relation with cancer and non-cancer risks. The estimated lung cancer risk from radon exposure was recently shown to increase by more than a factor of two when the uncertainties on the exposure data (WLM) are taken into account in the risk analysis for French uranium miners (Allodji *et al*., 2012). This demonstrates the need for an accurate assessment of uncertainty on doses in epidemiological studies, which I will promote as an important topic in the future of our collaboration with epidemiologists.

6.4 Required development of tools and methods

Some fundamental problems remain in our treatment of uncertainty: the representation of imprecision in probabilistic methods, the inverse problem from bioassay data to intake in the possibilist framework, the management of correlations in both approaches. I therefore plan to study the application of imprecise Bayesian (credal) networks (Cozman, 2005) in our field as they may provide a useful compromise.

Still, the bulk of work at hand is more practical: significant software development has to be performed. At present, we calculate doses, for both expert and research purposes, with software provided by other institutes: HPA's IMBA (Birchall *et al.*, 2007) and ORNL's DCAL (Eckerman *et al.*, 2001). Only the handling of voxel phantoms and the uncertainty analysis of routine monitoring programs are done with homemade codes: OEDIPE (Lamart *et al.*, 2009b) and OPSCI (Davesne *et al.*, 2010b), still connected to external ones: MCNPX and DCAL. I plan to coordinate the development of our own software for the flexibility of research and the transparency of expertise. It will be necessary to implement the biokinetic models, to combine them with values of SAF and weighting factors, to design algorithms for the assessment of organ and effective doses in situation of routine monitoring or incident and for lifetime reconstruction. The implementation of the latest models will participate in and benefit from the QA effort of ICRP DOCAL computational biokinetics subgroup and EURADOS task WG7.2 (Nosske *et al.*, 2008).

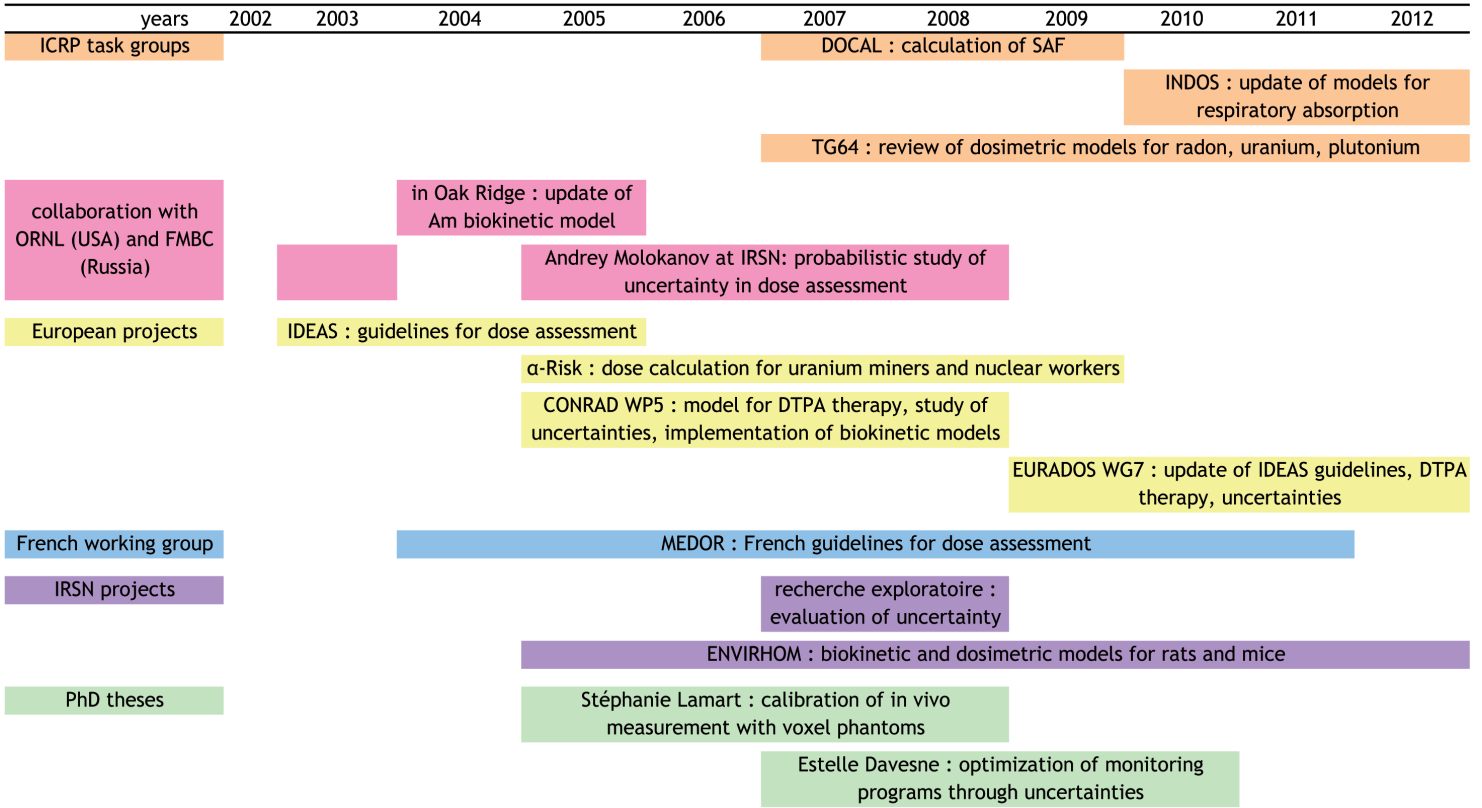
Then applications will be needed in the estimation of uncertainty on the dose assessed from multiple bioassay measurements following an incident, in the automated reconstruction of lifetime doses for uranium miners (prospective calculation from exposure to dose) and uranium workers (retrospective calculation from bioassay data to intake, then to dose), in the assessment of uncertainties in the dosimetric monitoring for staff of nuclear medicine. The assessment of the uncertainty on such dose calculation will be the subject of a PhD thesis which I will supervise.

Finally, the assessment of doses for exposed populations in the context of emergency following a major accident such as Fukushima or Chernobyl requires a specific study. Together with the development of mobile units for whole body and thyroid measurement in the field (Franck *et al.*, 2012), IRSN is building a computer database to collect *in vivo* and *in vitro* measurement results. A tool for dose calculation is also desired. In such situation, multiple individuals are exposed to several radionuclides over large areas in relatively well defined conditions. The assessment of dose is

then simple in principle. But the possibly high levels of exposure and the urgency to inform medical and political action would make the practice more complex. Before the crisis, I expect to spend a particular effort on a reliable uncertainty assessment, where imprecision should be properly represented, in order to be able to provide the relevant information when it is needed.

Chapitre 7
Overview of research projects

International and national projects are briefly indicated together with a note of the actions that I performed, contributed or supervised in their course (as 'framework: action').


years
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
ICRP task groups
DOCAL : calculation of SAF
INDOS : update of models for respiratory absorption
TG64 : review of dosimetric models for radon, uranium, plutonium
collaboration with ORNL (USA) and FMBC (Russia)
in Oak Ridge : update of Am biokinetic model
Andrey Molokanov at IRSN: probabilistic study of uncertainty in dose assessment
European projects
IDEAS : guidelines for dose assessment
α-Risk : dose calculation for uranium miners and nuclear workers
CONRAD WP5 : model for DTPA therapy, study of uncertainties, implementation of biokinetic models
EURADOS WG7 : update of IDEAS guidelines, DTPA therapy, uncertainties
French working group
MEDOR : French guidelines for dose assessment
IRSN projects
recherche exploratoire : evaluation of uncertainty
ENVIRHOM : biokinetic and dosimetric models for rats and mice
PhD theses
Stéphanie Lamart : calibration of in vivo measurement with voxel phantoms
Estelle Davesne : optimization of monitoring programs through uncertainties

Chapitre 8
About the author

8.1 Curriculum vitae

Éric Jacques Antoine BLANCHARDON
Born 05 January 1973

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92262 Fontenay-aux-Roses Cedex, France
eric.blanchardon@irsn.fr

Positions

- Researcher, IRSN/LEDI, since 2002 (expert since 2008).
- Guest scientist, dosimetry research team of the Oak Ridge National Laboratory (USA), 2004-2005.
- PhD student, CNRS Gif-sur-Yvette, 1998-2002.

Degrees

- PhD, molecular cell biology, University Paris-sud, 2002.
- Engineer, École polytechnique, 1997.

Research programs

Participation to task groups on:

- Internal dosimetry (INDOS) of the International Commission on Radiological Protection (ICRP).
- Risk from alpha emitters (TG64) of ICRP.
- Internal dosimetry (WG7) of the European network EURADOS.
- Reference dosimetric methods (MEDOR) initiated by the health practitioners of the French nuclear industry.

Participation in European contracts:

- IDEAS – "General guidelines for the assessment of internal dose from monitoring data" (2002-2005).
- α-Risk – "Quantification of cancer and non-cancer risks associated with multiple chronic radiation exposures: Epidemiological studies, organ dose calculation and risk assessment" (2005-2009).
- CONRAD - "Coordinated network for radiation dosimetry" (2005-2008).

Participation in the IRSN-AREVA collaboration program in internal dosimetry (PIC DOSINTER).

Collaborations with the Health Protection Agency (HPA, UK), Burnazyan Federal Medical Biological Centre (FMBC, Russia) and Oak Ridge National Laboratory (ORNL, USA).

Coordination of the internal IRSN research project on the "evaluation of uncertainty in the determination of doses from bioassay monitoring data of internal exposure for workers" (recherche exploratoire, 2007-2008).

Coordination of the actions "uncertainty studies on internal dose assessments" and "towards a DTPA therapy model" in EURADOS WG7.

Teaching and supervision

Teaching

- Computer science applied to biology, 64 h/year, University Paris-sud, 1998-2001.
- Radiation protection, about 20 h/year, Institut national des sciences et techniques du nucléaire, École nationale supérieure d'ingénieurs de Bourges, École des Mines de Nantes, since 2007.

Supervision PhD thesis

- Estelle DAVESNE (2007-2010), PhD thesis on the "Optimization of routine monitoring programs of internal exposure by the study of uncertainty in dose assessment" - 50% supervision – 5 publications.
- Stéphanie LAMART (2005-2008), PhD thesis on the "Study of the influence of the biokinetics of radionuclides on the *in vivo* measurement with voxel phantoms" - 25% supervision – 5 publications.

Supervision Masters

- Maxime LOCATELLI (2012), Master thesis on "Anatomical model and dose calculation software for internal contamination of rodents" - 50% supervision.
- Hanane MILOUDI (2011), Master thesis on "An anatomical model for the dosimetry of small animals" - 50% supervision – 1 publication.
- Irina CANU (2008), Master thesis on "Estimation of uranium intake by French workers in the nuclear fuel cycle: validation of a semi-quantitative approach" - 100% supervision - 1 publication.
- Estelle DAVESNE (2006), Master thesis on the "Evaluation of uncertainties in assessment of doses resulting from occupational inhalation of uranium dust" - 100% supervision.
- Lhoucin TAGHYA (2006), Master thesis on the "Development of software to assess the committed dose from an internal radioactive contamination" - 100% supervision.
- Cédric DELBOY (2004), Master thesis "Dose calculation for cells exposed to alpha ray with Monte Carlo codes" - 50% supervision.

8.2 Publications

8.2.1 Articles in international journals with review board

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Development and application of methods for the assessment of radiation dose from internal radioactive contamination

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Par Éric BLANCHARDON
Laboratoire d'évaluation de la dose interne de l'IRSN (IRSN/PSE-SANTE/SDOS/LEDI)

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