GENERAL REMARKS

1. Internal irradiation

1.1 *General aspects*

Radiation sources can be either external to the body, such as medical X-rays, or internal. The latter can result from the ingestion, inhalation, dermal absorption or injection of radionuclides. The effects of radiation are directly related to the dose that an organ receives, and any difference between the effects of external and internal sources is in large part related to the distribution of dose within and among body organs. Volume 75 of the *Monographs* (IARC, 2000) addressed the carcinogenic potential of external X-rays, γ-rays and neutrons in exposed populations; at least for X-rays and γ-rays, the effects are reasonably well known, and the carcinogenic risks have been quantified. Internal sources of radiation are more difficult to evaluate because of problems in determining the distribution of doses in tissues and organs. The dose received from external sources depends on the parts of the body that were irradiated, whereas the distribution of dose from internal sources can be affected by biological processes and metabolism. For example, radioactive iodine concentrates in the thyroid gland, and no other organs receive doses of any comparable magnitude.

Table 1 lists epidemiological studies of populations exposed to external and internal sources of radiation. The external sources include direct exposure to ionizing radiation from the atomic bombs exploded over Hiroshima and Nagasaki, radiotherapy for malignant and benign conditions, medical diagnostic procedures such as repeated chest X-ray fluoroscopies, occupational exposure such as received by radiologists and external exposure related to reactor accidents, such as that of Chernobyl clean-up workers. The distinction between external and internal sources is not complete in all cases. Brachytherapy, for example, involves the insertion of encapsulated radioactive materials such as radium within body cavities and thus could be considered an 'internal' source, but for the purposes of this monograph it is considered to be external and is not covered. Nuclear industry workers could inhale or ingest small amounts of radionuclides during their occupational exposure in addition to receiving external γ-rays.

Internal sources of radiation include radioactive fall-out from nuclear weapons tests or the Chernobyl accident, radiotherapy for malignant conditions such as ^{131}I to

Table 1. Sources of external and internal exposure to radiation, with examples of exposed populations

Type of exposure	Source	Examples of populations exposed
External	Atomic bombs	Japanese bomb survivors Marshall Islanders
	Radiotherapy for neoplastic disease	Patients with: Cervical cancer Childhood cancer Retinoblastoma Breast cancer Endometrial cancer Hodgkin disease Bone-marrow transplants
	Radiotherapy for benign conditions	Patients with: Ankylosing spondylitis Benign gynaecological disorders Peptic ulcer Breast disease Tinea capitis Thymus enlargement Tonsil enlargement Haemangioma
	Diagnostic procedures	Pregnant women (X-rays) Patients with: Tuberculosis (fluoroscopic X-rays) Scoliosis (X-rays)
	Occupation	Radiologists, technologists, nuclear workers
	Reactor accident	Workers in the Chernobyl nuclear power plant, clean-up workers and neighbouring populations
Internal	Atomic bombs	Marshall Islanders
	Radiotherapy	Patients with: Bone disease (^{224}Ra) Hyperthyroidism (^{131}I) Polycythaemia vera (^{32}P)
	Diagnostic procedures	Patients undergoing: Angiography (Thorotrast; ^{232}Th) Thyroid uptake and scans (^{131}I)
	Occupation	Radium-dial painters (^{226}Ra and ^{228}Ra) Underground miners (radon and progeny) Plutonium workers

Table 1 (contd)

Type of exposure	Source	Examples of populations exposed
Internal (contd)	Reactor accident	Workers in the Chernobyl nuclear power plant, clean-up workers and neighbouring populations
	Environmental contamination	Inhabitants of the Techa River area
	Radon	House dwellers
	Monoazite sands	Inhabitants of India and Brazil

From UNSCEAR (1994); Boice *et al*. (1996); IARC (2000); UNSCEAR (2000)

treat thyroid cancer, radiotherapy for non-neoplastic conditions such as ^{224}Ra to treat bone tuberculosis and ankylosing spondylitis, diagnostic radiographic procedures such as cerebral angiography with Thorotrast (^{232}Th), occupational exposure such as that to plutonium of workers at the Mayak military plant in the Russian Federation, and environmental contamination such as that of the Techa River, also in the Russian Federation.

Ionizing radiation interacts randomly with atoms in cells and can alter molecular structure, the most important alteration being damage to DNA that is either unrepaired or is accurately or inaccurately repaired. These alterations can be amplified by biological processes to result in observable effects. The biological effects, however, depend not only on the total absorbed dose but also on the local density of ionization. Linear energy transfer (LET), defined in section 3.2, is a measure of the energy loss per unit distance travelled and depends on the velocity, charge, energy and mass of a charged particle or other secondary charged particles (electrons) from neutrons, or of secondary X-rays or γ-rays. High-LET radiations such as α-particles (helium nuclei) release energy in short tracks (< 100 μm) of dense ionizations. They are not penetrating and can be stopped in the outer layers of skin. Low-LET radiations such as β-particles (electrons), X-rays or γ-rays, are more sparsely ionizing, on average, although there is some clustering of low-energy secondary electrons. The depth of penetration of β-particles can vary from a few micrometres up to several millimetres, depending on their energy. X-rays and γ-rays are generally much more penetrating and are attenuated exponentially, as they occasionally interact to produce secondary electrons as they pass through tissue.

In experimental studies, the induction of many cancers by low-LET radiation appears to follow a sigmoidal relationship with dose, risk per unit dose being somewhat lower at low doses and high doses owing to repair and cell killing, respectively. The induction of cancer by exposure to high-LET radiation (particularly neutrons) often appears to follow a more linear dose–response relationship. Protraction and

fractionation of doses tend to decrease the risk for cancer after exposure to low-LET radiation but not high-LET radiation, possibly because of a reduction in the competing effect of cell killing (UNSCEAR, 1993).

The relative biological effectiveness (RBE) of radiation characterizes its ability to have a specific level of effect (e.g. frequency of chromosomal aberration, cell death or neoplastic transformation) when compared with a standard, usually X-rays or γ-rays. A RBE of 20 for α-particles at an absorbed dose of 0.1 Gy, for example, would imply that the level of biological effect from 0.1 Gy of α-particles is the same as that from 2 Gy of γ-rays. For the purposes of radiation protection, the International Commission on Radiological Protection (ICRP) has defined the equivalent dose and effective dose, both expressed in units of sievert (Sv), which include specified radiation and tissue weighting factors. The radiation weighting factor for α-particles is specified as 20 and that for β-particles, γ-rays and X-rays as 1 (ICRP, 1991; IARC, 2000).

Another difference between external and internal sources of radiation is the duration of exposure: an internal source might stay in the body for a long time and irradiate tissues. Once the external exposure is over, however, there is no longer delivery of ionizing radiation within body cells. Internal sources can remain in the body for many years. For example, ingested ^{226}Ra is incorporated into bone and for all practical purposes affects tissues in the body continually. Some radionuclides, such as ^{99m}Tc, have shorter half-lives, so that the radiation dose is delivered within a period of hours after exposure.

The difficulties in determining or quantifying the effects of internal sources also include the problem of non-uniform distribution of dose in organs and tissues. For example, the risk for thyroid cancers in humans due to incorporated ^{131}I would result from absorption of β-particle energy not in the colloid of the thyroid but rather in the radiation-sensitive follicular cells, which are at risk for cancer development.

1.2 *Nomenclature*

(*a*) *Radiation dose*

The *absorbed dose* is defined as the radiation energy absorbed per unit mass of an organ or tissue and is expressed in grays (Gy); 1 Gy is equal to 1 J/kg.

The *equivalent dose* (H) takes account of different types of radiation and differences in ionization densities: to calculate the equivalent dose, the average absorbed dose in an organ or tissue is multiplied by a radiation weighting factor w_R. The radiation weighting factors currently recommended by ICRP (1991) are listed in Table 2. The equivalent dose is expressed in sieverts (Sv); 1 Sv is equal to 1 J/kg.

The *effective dose* (E) takes into account variations in equivalent dose among radiosensitive organs and tissues and is calculated by multiplying the equivalent dose by a tissue-weighting factor w_T. The effective dose gives a measure of the impact of radiation irrespective of how the dose was received. This approach allows effective doses from internal and external sources to be aggregated and correlates well with the

Table 2. Radiation weighting factors

Type and energy range	Radiation weighting factor
Photons, all energies	1
Electrons and muons[a], all energies[b]	1
Neutrons, energy:	
< 10 keV	5
10–100 keV	10
> 0.1–2 MeV	20
> 2–20 MeV	10
> 20 MeV	5
Protons, other than recoil protons, energy > 2 MeV	5
α-Particles, fission fragments, heavy nuclei	20

From ICRP (1991); all values relate to the radiation incident on the body or, for internal sources, emitted from the source.

[a] One of the elementary particles, a member of a category of light-weight particles called leptons which also include electrons and neutrinos

[b] Excluding Auger electrons (280–2100 eV) emitted from nuclei bound to DNA, which are ejected after excitation by an incident electron beam

total of the stochastic effects. The tissue weighting factors currently recommended by ICRP (1991) are listed in Table 3. The effective dose is expressed in sieverts (Sv).

The *committed effective dose* is defined as the time integral of the effective dose rate over a period of 50 years for an adult and from the time of intake to age 70 years for children.

The *total effective dose*, $E(t)$, during any time, t, from external and internal sources of radiation is given by:

$$E(t) = H_p(d) + \sum_j e_{j,inh}(50) \times I_{j,inh} + \sum_j e_{j,ing}(50) \times I_{j,ing}$$

where $H_p(d)$ is the personal dose equivalent from external radiation during time t at a depth d in the body, normally 10 mm for penetrating radiation; $e_{j,inh}(50)$ and $e_{j,ing}(50)$ are the committed effective doses per unit activity intake by inhalation and ingestion, respectively, from radionuclide j, integrated over 50 years; and $I_{j,inh}$ and $I_{j,ing}$ are the intake of radionuclide j by inhalation and ingestion, respectively, during time t (UNSCEAR, 2000).

(*b*) *Radiation dose and exposure to radon and its decay products: working-level month*

Potential α energy is used as a quantity to describe the amount of short-lived decay products of ^{220}Rn (also known as thoron) and ^{222}Rn (known as radon) in air and the ensuing exposure by inhalation. It is defined as the total α energy (in J) emitted during the decay of ^{220}Rn or ^{222}Rn to ^{208}Pb or ^{210}Pb, respectively. The total α energy

Table 3. Tissue weighting factors

Tissue or organ	Tissue weighting factor
Gonads	0.20
Bone marrow (active)	0.12
Colon	0.12
Lung	0.12
Stomach	0.12
Bladder	0.05
Breast	0.05
Liver	0.05
Oesophagus	0.05
Thyroid	0.05
Skin	0.01
Bone surface	0.01
Remainder[a]	0.05

From ICRP (1991). The values were derived on the basis of data for a reference population of equal numbers of males and females and a wide range of ages. In the definition of effective dose, these factors apply to workers, to the whole population and to males and females.

[a] For the purposes of calculation, the 'remainder' is composed of the following additional tissues and organs: adrenal glands, brain, upper large intestine, small intestine, kidney, muscle, pancreas, spleen, thymus and uterus. The list includes organs that are likely to be irradiated selectively and some organs which are known to be susceptible to cancer induction. If other tissues and organs are subsequently identified as being at significant risk for induced cancer, they will either be given a specific weighting factor or included in the 'remainder'. In the exceptional case in which one of the 'remainder' tissues or organs receives an equivalent dose in excess of the highest dose received by any of the 12 organs for which a weighting factor is specified, a weighting factor of 0.025 should be applied to that tissue or organ and a weighting factor of 0.025 to the average dose for the rest of the 'remainder', as defined above.

concentration of any mixture of short-lived ^{220}Rn or ^{222}Rn decay products is the sum of the potential α energy of these atoms per unit volume of air (expressed in J/m^3). The potential α energy concentration has also been expressed in terms of working level (WL). One WL is defined as a concentration of potential α energy of 1.30×10^8 MeV/m^3. The exposure to ^{220}Rn or ^{222}Rn and their decay products is the time integral of the potential α energy concentration in air, expressed in J h/m^3 or in working-level months (WLM). Because the WLM was initially defined to specify occupational exposure, one month corresponds to 170 h. In SI units, the historical unit WLM can be written as 3.54×10^{-3} J h/m^3. In terms of effective dose, 1 WLM is usually taken to correspond to 5 mSv for workers (ICRP, 1993).

(*c*) *Dose and dose limits of radiation from internalized radionuclides*

When radionuclides have entered the body, cells and tissues will continue to be exposed to the emitted radiation until the radionuclide has been completely excreted or has fully decayed. Dose limits for occupational exposure are generally derived from the dose of the radionuclide integrated over 50 years after the intake. The committed effective dose for occupational exposure, E(50), is defined as the sum of the products of the committed organ or equivalent doses and the appropriate organ or tissue weighting factors, where '50' indicates the integration time in years after intake. In calculating the E(50), the dose coefficient, i.e. the committed effective dose per unit intake, expressed in Sv/Bq, is frequently used.

The recommended upper limit for annual intake of radionuclides is based on a committed annual effective dose of 20 mSv (ICRP, 1991). The annual limit on intake in becquerels can be calculated by dividing this value (0.02 Sv) by the dose coefficient. For inhalation and ingestion, the dose coefficients for occupational exposure to radionuclides are given by ICRP (1994).

1.3 *Routes of internal exposure to ionizing radiation*

The human body is, and always has been, exposed to background radiation. This irradiation may arise from outside the body, for example from cosmic rays from outer space and γ-rays from the decay of the natural radionuclides of the uranium and thorium series that are present in rocks and other components of the earth's crust. In addition, some individuals or groups may receive whole- or partial-body external radiation from occupational exposure, medical procedures such as X-ray examinations, radiation therapy or accidents in nuclear facilities resulting in the release into the environment of radionuclides that emit γ-rays (IARC, 2000). All human beings are also irradiated by the radiation emitted within organs and tissues by the decay of natural and anthropogenic radionuclides that have entered the body by inhalation or by ingestion of food and drinking-water. This irradiation arises naturally from the decay of the radioactive isotope of the essential element potassium, ^{40}K, and from uranium and thorium and their radioactive decay products, especially radon (IARC, 1988; UNSCEAR, 1988, 1993). In addition, there are contributions from fall-out from atmospheric nuclear weapons testing, from accidents at nuclear facilities or from nuclear medicine, i.e. diagnostic or therapeutic medical procedures with radionuclides.

Overviews of the exposures resulting from sources of radiation and the resulting health effects have been published by the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR, 1982, 1988, 1993, 1994, 2000). Recommendations on appropriate radiological protection standards are made by the ICRP (ICRP, 1991).

The passage of ionizing radiation through the human or animal body results in the deposition of energy within the irradiated tissue volume. The amount of radiation energy deposited will depend on the length of time over which the individual is

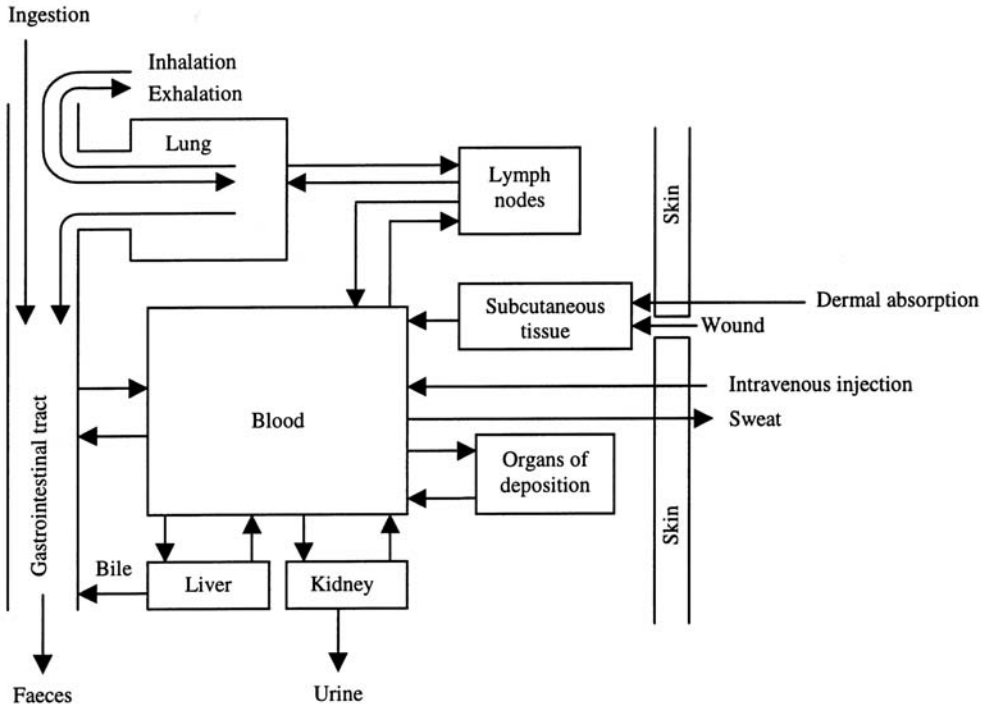
irradiated, the strength of the source and the physical nature of the radiation, e.g. X- or γ-rays, cosmic rays, α-, β- or other particles (see section 2). The immediate result of the energy deposition is the production of ion pairs and, subsequently, free radicals and other highly reactive species, predominantly through the breakdown of water molecules, which comprise about 65–70% of most tissues, but also directly in DNA and other molecules. These highly reactive species can damage sensitive biological macromolecules such as DNA, RNA and proteins. The damage to DNA may be severe enough to produce cell death or may result in various degrees of non-lethal damage. Non-lethal damage is particularly important since it may result in heritable changes in gene expression that, after one or more cell divisions, may manifest themselves as cancers or serious genetic disorders. In broad terms, cell death and other effects result largely from unrepairable DNA damage or DNA damage that is inadequately repaired.

α-Radiation is not normally regarded as an external radiation hazard (except perhaps to skin) because it is poorly penetrating, but once α-particle-emitting radionuclides are in the body they can become a health hazard. However, X- and γ- radiations and neutrons can generally penetrate sensitive organs of the body. As the higher-energy β-radiation can penetrate to about 10 mm into tissue, it can pose both an external hazard and an internal hazard when emissions occur within the body. Unlike exposure to internal radiation, that to external radiation can usually be controlled by reducing the duration of exposure, increasing the distance from the radiation source and/or using shielding. Radioactive materials may pose an insignificant external hazard, but once they come into contact with or penetrate the body they increase the risk.

The biological effects of deposited radionuclides within the body depend on the amount of radionuclide deposited, the type of radiation emitted, the physical half-life of the isotope, the organs and tissues in which the radionuclide is retained and the duration of retention. Once inside the body, the exposure rate of the radionuclide is maximized, and it will continue to irradiate the body until either the radioactivity has decayed (physical half-lives may vary from fractions of a second to millions of years) or until the substance has been excreted from the body. The rate of excretion, expressed as retention half-time in the body, may vary from a few days to tens of years, depending primarily on the physical and chemical characteristics and chemical form of the radionuclide. The chemical properties of the radionuclide (or the compound in which it may be incorporated) determine its behaviour within the body, including absorption, elimination route, elimination rate and also transfer to and retention at deposition sites and subsequent redistribution. Furthermore, the health effects of some elements with low specific activity may also be related to their chemical properties (e.g. heavy metals) rather than their radiation.

Four main routes result in internal exposure to radionuclides (Figure 1): inhalation, ingestion, dermal absorption and direct injection (or through a wound).

Figure 1. Absorption, distribution and elimination of radionuclides in the body



Modified from ICRP (1968)

(*a*) *Inhalation*

Radioactive gases, vapours or particulate materials enter the body when inhaled. The respiratory tract has a total surface area of about 75 m^2, beginning with the nasal and other air passages of 10–20 mm in diameter and ending in a large number of extremely fine tubes and ducts closed by tiny air pockets which are a fraction of a millimetre across. The vital capacity of the adult lung is about 4 L, and about 23 m^3 of air are inhaled per day (ICRP, 1975). The epithelial layer of the larger bronchi is about 40 μm thick, becoming thinner as the bronchi diminish in size. In the terminal bronchioles, the single-cell layer of the epithelium is only a few micrometres thick.

Gases can pass freely into the lungs and are rapidly absorbed into the bloodstream through the thin alveolar membranes and the highly vascularized alveoli. Generally, the uptake is governed by the dissolution rate, partition coefficient, solubility and residence time of the gas in the respiratory tract.

Liquid or solid radioactive compounds inhaled in the form of aerosols have a number of possible fates, depending on their physicochemical properties. The extent to which particulate matter is deposited is a function of particle size and shape, the density of the aerosol, the lung structure and respiratory characteristics. Only a

fraction of the inhaled material is deposited in the respiratory tree, and the remainder is exhaled. The size of inhaled particles is likely to cover a wide range. Particles are deposited in the respiratory tract by one of three mechanisms: diffusion, impaction and sedimentation, and the efficiency of these processes varies greatly with particle size. Large particles and ultra-fine particles are deposited in the nasal passages by impaction and diffusion and intermediate-sized particles in the bronchial tree by impaction and in the alveoli by sedimentation. Ultra-fine particles are also deposited in the alveoli by diffusion. Deposited material in the upper respiratory passages may be expelled into the gastrointestinal tract by ciliary action. Phagocytes in the air sacs and on the alveolar walls can remove particulate matter by either migrating up to where they can be removed by ciliary action or by entering the lymphatic system through the alveolar epithelium. Depending principally on the chemical nature and reactions of the radioactive compound, soluble radionuclides may be completely and rapidly absorbed. Otherwise, they are partially eliminated and partially absorbed and may persist in the lungs for many months or years. Models are used to estimate the deposition and retention of airborne contaminants in the respiratory tract (see section 4.1.23(*a*) of the monograph; ICRP, 1994; National Council on Radiation Protection and Measurements, 1997).

Gases that are inhaled include radon (Burkart, 1991) and tritium (^{3}H) (Hill & Johnson, 1993). Studies of volunteers who inhaled ^{3}H showed that only about 0.1% of that inhaled was dissolved in the body fluids and tissues (Hill & Johnson, 1993).

An example of an inhaled material with long pulmonary retention is the highly insoluble actinide oxide, $^{239}PuO_2$; studies in dogs indicate an exponential clearance of 98% of the inhaled material, with a half-time of approximately three years (ICRP, 1986). In contrast, after inhalation of the more soluble compound $^{239}Pu(NO_3)_4$, about 40% of the initial lung burden was lost within three months and about 80% within one year (Dagle *et al*., 1983).

It has been suggested that inhalation of a few highly radioactive particles (hot particles) might lead to highly non-uniform pulmonary irradiation and to a higher risk for tumours than that resulting from inhalation of the same amount of radioactivity at a lower specific activity (Dean & Langham, 1969). Anderson *et al*. (1979) reported a study in which Syrian hamsters received different numbers of radioactive microspheres by intratracheal instillation to induce localized or diffuse irradiation of the lungs. When only 1 or 5% of the lung was irradiated by α-particles, no tumours were observed in 85 animals; however, when the fraction of the lung irradiated was increased to 28%, the tumour incidence rose to 19 tumours in 160 animals. This suggests that intense irradiation of a small area of the lung with a hot particle does not increase the risk for tumour induction.

Table 4 summarizes the known or predicted absorption pattern after inhalation of 20 elements. The data indicate that, depending on the chemical form of the inhaled radioactive material, irradiation of the lung may be essentially complete within a few days or may continue for several years.

Table 4. Absorption of elements in the human lung after inhalation

Z[a]	Element	Chemical form	Absorption to blood[b]
1	Hydrogen	Gas, water, other compounds	Fast
6	Carbon	Dioxide, monoxide, methane, other compounds	Fast
15	Phosphorus	Most compounds except poorly soluble phosphates	Medium
16	Sulfur	SO_2, COS, H_2S, CS_2	Fast
31	Gallium	Most soluble compounds	Medium
38	Strontium	Most soluble compounds	Fast
43	Technetium	Pertechnetate	Fast
53	Iodine	Iodide, iodate	Fast
55	Caesium	Most soluble compounds	Fast
75	Rhenium	Perrhenate	Fast
83	Bismuth	Most compounds	Medium
84	Polonium	Most compounds	Medium
85	Astatine	Most compounds	Medium
86	Radon	Gas	Fast; small proportion[c]
88	Radium	Most compounds	Medium
90	Thorium	Soluble compounds Oxides	Medium Slow
92	Uranium	UF_6, UF_4, $UO_2(NO_3)_2$	Medium
93	Neptunium	Most compounds	Medium
94	Plutonium	Soluble compounds Oxides	Medium Slow
95	Americium	Most compounds	Medium
96	Curium	Most compounds	Medium

[a] Atomic number

[b] Defined by default categories in the ICRP model and expressed as approximate half-times for one or two components of clearance. The rates correspond to: fast, 10 min (100%); medium, 10 min (10%), 140 days (90%); slow, 10 min (0.1%), 7000 days (99.9%). Specific data on absorption are used when available for a particular chemical form of a radionuclide.

[c] Only a small proportion of radon is rapidly absorbed; the remainder is exhaled.

(*b*) *Ingestion*

Radionuclides may be ingested in food and drink, and are absorbed principally from the small intestine, facilitated by its immense surface area of about 200 m^2 (ICRP, 1975) provided by the epithelial villi. If the material is not absorbable, most traverses the gastrointestinal tract and is excreted in the faeces. For absorbable materials, a significant fraction is absorbed into the blood and lymphatic system. The actual degree of absorption may depend on the metabolism and nutrition of the individual as well as the chemical compound in which the radionuclide is ingested.

Harrison (1995) reviewed the anatomical, physiological and radiobiological aspects of radionuclide ingestion. Ingestion is an important route of entry into the human body since, in addition to those radionuclides present in drinking-water and the diet, a fraction of any inhaled material is swallowed. Some radionuclides such as ^{3}H, ^{40}K, ^{131}I and ^{137}Cs are almost completely absorbed from the human gastrointestinal tract into the systemic circulation, but the absorption of others is incomplete, from about 30% of ^{90}Sr to < 0.05% of highly insoluble oxides like $^{239}PuO_2$ (< 0.001%). The degree to which any given radionuclide compound is actually absorbed cannot be predicted precisely because absorption is influenced by both the chemical form of the ingested radionuclide and the chemical environment in the absorptive regions of the upper small intestine; the latter varies depending on the presence or absence of food residues and other complexing ligands.

(*c*) *Injection and entry through wounds or intact skin*

The direct entry of a radioactive nuclide into the body as a result of intravenous injection is normally a deliberate act, undertaken mainly for medical purposes. In such situations, the chemical form of the radionuclide will have been selected to achieve a desired pattern of deposition in the organs and tissues through normal or pathological biochemical processes. A radionuclide may, however, be injected accidentally into the body through a puncture wound. Under these circumstances, its fate will be determined by its physicochemical properties. In some instances, the injected material may pass relatively quickly from the entry site into the blood; but in others, the material reacts with tissue components to form a poorly soluble deposit, from which absorption into the blood may occur over a period that ranges from hours to many months. In other cases, insoluble material may remain *in situ* or become located in regional lymph nodes.

Generally, intact skin provides an effective barrier against the entry of radioactive materials into the body. An exception of practical importance is the absorption of $^{3}H_2O$ as a liquid or a vapour. Since the surface area of the skin is about 1.7 m^2 (ICRP, 1975), the extent of transport may be sufficient to pose a radiological hazard even if the rate of transport is low. Transport typically occurs by diffusion through and between epidermal cells. Similarly, many ^{3}H- and ^{14}C-labelled compounds may be absorbed through the skin, especially if it has been shaved.

Contamination of the intact skin by α- and β-particle- or very weakly γ-ray-emitting radionuclides that are not absorbed into the systemic circulation may be a special case. Irradiation of the body tissues is confined to a few micrometres below the skin surface, because of the poor penetrating power of these types of radiation, or even to the most superficial layers of the skin itself. Highly radioactive 'hot particles' that may arise during reactor operations or as a result of nuclear accidents may be fragments of fuel or highly radioactive metallic particles and produce energetic particles. If such particles remain on the skin for even a short time, they can cause intense irradiation of a small volume of tissue, resulting in the death of cells in interphase in various layers of the skin. The depth of the skin at which cells are killed depends on the energy of the emitted α- or β-particles and the total radiation dose. The damage may be severe enough to cause open ulcerative lesions and/or scabs within 1–3 weeks of irradiation. These changes occur faster than those normally associated with radiation-induced moist desquamation (Hopewell *et al.*, 1993).

1.4 *Transport and deposition*

The subsequent behaviour of radionuclides in the body depends on the element concerned and the chemical form of the exposure, which determine the solubility of the radionuclide and the extent to which it is dissolved and absorbed into blood. On reaching the blood, the distribution, redistribution and retention in body tissues depend on the chemical nature of the element. Radionuclides may be distributed throughout the body, be deposited selectively in a particular tissue or be deposited in significant quantities in a number of tissues.

Insoluble materials may move intact from wounds or the lungs through the lymphatic system. Movement along lymphatic vessels can lead to accumulation of radionuclides in regional lymph nodes and then to their discharge into the circulatory system. Particles may reach the bloodstream, from which they are removed rapidly by phagocytic cells of the reticuloendothelial system in the liver, spleen and bone marrow.

1.5 *Elimination*

Radionuclides may be eliminated from the body principally by exhalation and excretion in urine, faeces, sweat, saliva and potentially in milk. Exhalation is a major pathway for the undeposited fraction of inhaled aerosols, $^{3}H_2O$ vapour and gases such as those containing ^{14}C and ^{220}Rn and ^{222}Rn produced in the radioactive decay of internally deposited thorium and radium. In the course of urinary excretion, certain radionuclides deliver a dose to the kidney and bladder. Radionuclides in the faeces result either from ingested radionuclides that have not been absorbed during gastrointestinal transit or from radionuclides absorbed and subsequently excreted back into the gastrointestinal tract — most often via biliary excretion.

1.6 *Doses from internal irradiation*

The absorbed doses in various organs and tissues calculated for reference infants, children and adults for unit intakes of radionuclides are given in recent ICRP publications (ICRP, 1989, 1993, 1994, 1995a,b, 1996). Calculated coefficients are also provided for workers (ICRP, 1995c) and for patients given radiolabelled pharmaceuticals (ICRP, 1988, 1998). The ICRP database is available on CD-ROM (ICRP, 1999). The ICRP evaluations are based on reviews of the biokinetics of radionuclides in humans and animals. Internal doses are determined from measurements of nuclides in exhaled air, tissues, excreta or the whole body.

2. Modes of decay of radionuclides

Each atom has a small, very dense nucleus with a radius of about 10^{-6} nm, composed of positively charged protons and neutral neutrons, collectively known as nucleons. The nucleus is surrounded by electrons, equal in number to protons, making the atom electrically neutral and occupying a space with a radius of about 0.1 nm.

The atoms of different elements differ in the constitution of their nuclei and the number and arrangement of their electrons. Each atom of a particular chemical element has the same number of protons, which is defined as the atomic number (Z). Any nuclide is uniquely defined by the number of protons (Z) and the number of neutrons (N) in the nucleus. The atomic mass number ($A = Z + N$) gives the total number of nucleons. The nuclide is specified as ${}^{A}_{X}X$, where X represents the letter symbol for the particular chemical element (e.g. ${}^{12}_{6}\mathrm{C}$ for stable carbon-12). Table 5 shows the main characteristics of electrons and nucleons.

Most elements consist of a mixture of several atomic species with the same extranuclear structure but different nuclear masses, i.e. mass number A, owing to different numbers of neutrons. Atoms composed of nuclei with the same number of protons (Z) but different number of neutrons (N) are called isotopes. They have a different mass number (A) but are the same chemical element and generally have identical chemical properties. More than one isotope of an element may be found naturally within the environment; for example, the natural abundance of uranium is 99.27% ^{238}U, 0.72% ^{235}U and 0.01% ^{234}U, and that of potassium is 93.26% ^{39}K, 6.73% ^{41}K and 0.01% ^{40}K. Atoms composed of nuclei with the same total number of nucleons (A) but

Table 5. Main characteristics of electrons and nucleons

Name	Symbol	Charge	Mass (kg)	Relative mass
Electron	e	–1	9.109×10^{-31}	1
Proton	p	+1	1.6726×10^{-27}	1836
Neutron	n	0	1.6749×10^{-27}	1839

different numbers of protons (Z) are called isobars. They are different chemical elements. Isotopes and isobars may be stable or unstable and undergo change in their nuclear structure, and sometimes atomic structure, spontaneously, with the emission of energetic particles and/or photons. This process is called radioactive decay. Any nuclear species that is capable of undergoing spontaneous radioactive decay is called a radionuclide.

The atom consists of a positively charged nucleus surrounded by sufficient electrons in closed shells to make the atom electrically neutral. These electron shells are identified by sequential letters of the alphabet, the innermost shell being identified as the K shell. Each electron in the shell or sub-shell structure has a uniquely defined energy state determined by quantum numbers. The maximum number of electrons that can exist in a shell is $2n^2$, where n is the principal quantum number ($n = 1$ for the K shell, which is closest to the nucleus), as a result of the Pauli exclusion principle which states that no two electrons can have the same set of quantum numbers and exist in the same energy state. The atom is in the ground state, or most stable configuration, when all the electrons are in the lowest possible energy state. The binding energy of an electron in a specific shell of an atom is defined as the energy that must be given to the electron to remove it completely from the atom and make it a free electron.

Mass, m, is a form of energy, E, and they are related by the equation, $E = mc^2$, where c is the velocity of light in vacuum. Therefore, the atomic mass unit (u) which is defined as 1/12 the mass of the ^{12}C atom can also be defined in terms of energy:

$1\ u = 1.66054 \times 10^{-27}$ kg = 931.5 MeV (where 1 eV = 1.6022×10^{-19} J).

The energy that holds the nucleus together (i.e. the nuclear binding energy) is produced when a small proportion of the mass of each nucleon is given up. The binding energy of the nucleus can therefore be determined by calculating the difference between the total mass of the individual nucleons and the mass of the composite nucleus.

Six emissions can result from radioactive decay, as presented in Table 6.

The α-particle consists of two neutrons and two protons and therefore has a charge of +2. It is the nucleus of the helium atom, ^4_2He. The β^--particle is a negatively charged

Table 6. Modes of emission in relation to electrical charge and mass

Particle	Symbol	Charge	Mass (kg)
α	α	+2	6.645×10^{-27}
Electron (β^-)	e^- (β^-)	–1	9.109×10^{-31}
Positron (β^+)	e^+ (β^+)	+1	9.109×10^{-31}
Neutrino	ν	0	~ 0
Antineutrino	$\bar{\nu}$	0	~ 0
Electromagnetic radiation (photon)	γ or X	0	0

electron and the β^+-particle or positron (the antiparticle of the electron) is a positively charged electron. The neutrino and its antiparticle, the antineutrino, are particles with essentially no 'rest' mass and no charge. γ- and X-rays are high-frequency electromagnetic radiation that travel at the speed of light. These photons are essentially identical except for their origins: γ-rays result from de-excitation of the nucleus, while characteristic X-rays result from de-excitation of an atom (electronic shells). The term X-ray also refers to *bremsstrahlung*, which is the electromagnetic radiation produced by deceleration of charged particles (typically electrons) as they pass through matter.

A radioactive atom may decay by one of several processes: by emission of α-particles; by emission of β-particles, including β^- (electron) and β^+ (positron) emission; isomeric transitions such as γ emission (excited state and metastable state) with internal conversion being a competing process; and spontaneous fission (not considered in this monograph).

2.1 *Decay by emission of α-particles*

α-Particles are emitted mainly from heavy nuclei. In such disintegrations, a helium nucleus, consisting of two protons and two neutrons, is ejected. Thus, the decay product (*D*) has an atomic number that is two less, and a mass number four less than that of the parent (*P*), as characterized by the following equation:

$$ {}^{A}_{Z}P \rightarrow {}^{A-4}_{Z-2}D + {}^{4}_{2}\alpha, $$

e.g. $ {}^{226}_{88}\mathrm{Ra} \rightarrow {}^{222}_{86}\mathrm{Rn} + \alpha. $

The energy, *Q*, released as a result of the decay, arises from the net loss in mass:

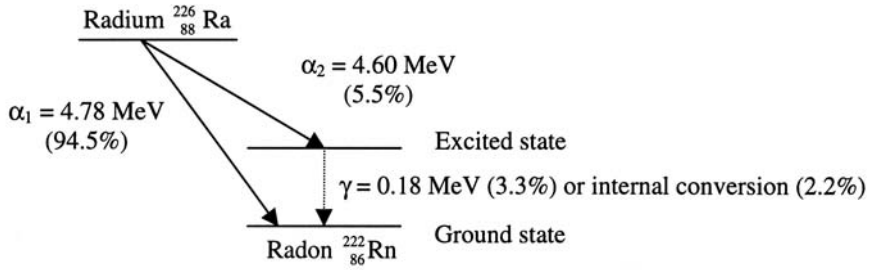
$$ Q = m_P - m_D - m_\alpha. $$

This energy is shared between the α-particle and the recoil nucleus. The α-particles emitted from a given type of decay are monoenergetic and carry most of the energy because their mass is smaller than that of the residual nucleus. Some α-particle emitters decay not only directly to the ground state but also to various excited states of the progeny nuclei, with different probabilities. If the parent decays to the excited state of the progeny, then a monoenergetic α-particle will be emitted with an energy less than *Q*. The nucleons in the excited progeny then reconfigure to the most stable configuration, the ground state, and release the additional energy by emitting one or more photons (γ-rays). Part of the energy of the excited state can also set electrons in motion by internal conversion in the K, L and M shells (discussed in section 2.2).

For instance, in 94.5% of its disintegrations, natural radium ($ {}^{226}_{88}\mathrm{Ra} $) decays directly to the ground state of its decay product, radon ($ {}^{222}_{86}\mathrm{Rn} $), by emitting a monoenergetic α-particle with an energy equal to *Q* of 4.78 MeV (Figure 2). In the remaining 5.5% of the disintegrations, radium decays to an excited state of radon, emitting a lower-energy α-particle of 4.60 MeV; the additional energy is released either by the emission

of a photon (γ-ray) of 0.18 MeV (3.3%) or an internal conversion electron (2.2%), as the nucleus moves to the ground state.

Figure 2. An example of α-particle decay is the decay of $^{226}_{88}$Ra to $^{222}_{86}$Rn



2.2 *Decay by emission of β-particles*

(*a*) *β⁻-Particles (electrons)*

A nuclide undergoing β-particle decay emits a negatively charged electron (known as a β-particle, β^-) from the nucleus, resulting in a decay product with an atomic number that is one higher than that of the parent but with the same atomic mass number. This is illustrated by the following equation:

$$^{A}_{Z}P \rightarrow {}^{A}_{Z+1}D + \beta^- + \bar{\nu}\,.$$

e.g. $^{131}_{53}\mathrm{I} \rightarrow {}^{131}_{54}\mathrm{Xe} + \beta^- + \bar{\nu}\,.$

This process results from the transformation of a neutron (n) into a proton (p) in the nucleus with the emission of an electron (β^-) and an antineutrino ($\bar{\nu}$), following the equation:

$$^{1}_{0}n \rightarrow {}^{1}_{1}p + \beta^- + \bar{\nu}\,.$$

The difference in energy between the initial atom and the final atom is Q, which is shared between the electron and antineutrino. The electron can be emitted with a range of energies from 0 to $E_{max} = Q$ because this is a three-body decay. Of interest is the mean energy, $\bar{E}$, deposited in tissue from a β-particle emitter. The ratio $\bar{E}/E_{max}$ is different for each β-particle-emitting radionuclide but is usually about 1/3.

Some β-particle emitters decay not only to the ground state but also to various excited states of the progeny nuclei, with different probabilities. If the parent decays to the excited state of the progeny, then β-particles will be emitted with a correspondingly reduced range of energies. The nucleons in the excited progeny decay subsequently to the ground state with the emission of one or more photons (γ-rays) or by ejecting atomic electrons by internal conversion.

(*b*) *β^+-Particles (positrons)*

A nuclide undergoing positron decay emits a positively charged electron, called a positron, from the nucleus, resulting in a decay product with an atomic number that is one less than that of the parent but with the same atomic mass number. This is illustrated by the following nuclear equation:

$${}^{A}_{Z}P \rightarrow {}^{A}_{Z-1}D + \beta^+ + \nu,$$

e.g. ${}^{15}_{8}\mathrm{O} \rightarrow {}^{15}_{7}\mathrm{N} + \beta^+ + \nu.$

This process results from the transformation of a proton (*p*) into a neutron (*n*) in the nucleus with the emission of a positron (β^+)and a neutrino (ν), following the equation:

$${}^{1}_{1}p \rightarrow {}^{1}_{0}n + \beta^+ + \nu.$$

The difference in energy between the initial atom and the final atom is *Q*, which is shared between the positron and neutrino. Since the combined mass of the neutron and positron is greater than that of the proton, this process is possible within the nucleus only if the nuclear masses of the parent and progeny differ (because of different binding energies) by two times the energy equivalent to the rest mass of the electron (2×0.511 MeV).

The positron can be emitted with a range of energies, from 0 to *Q*, because this is a three-body decay. The total kinetic energy shared between the positron and the neutrino (i.e. the maximum energy given to the positron) is the difference between the atomic masses of the parent and progeny nuclei reduced by 1.022 MeV.

The positron, after losing its kinetic energy, is subsequently annihilated by interaction with a negatively charged electron, which results in the conversion of the masses of the two particles into energy (1.022 MeV). Since this process usually occurs when the particles are at rest, the annihilation process produces two photons, equivalent to γ-rays, each with an energy of 0.511 MeV, travelling in opposite directions from the annihilation site.

(*c*) *Electron capture*

Electron capture decay is characterized by the absorption of an atomic inner-shell electron by the parent nucleus. This is illustrated by the following equation:

$${}^{A}_{Z}P + e^- \rightarrow {}^{A}_{Z-1}D + \nu\,,$$

e.g. ${}^{125}_{53}\mathrm{I} + \mathrm{e}^- \rightarrow {}^{125}_{52}\mathrm{Te} + \nu\,.$

The captured electron combines with a proton to form a neutron, and the excess energy is carried off by the emission of a neutrino, following the equation:

$${}^{1}_{1}p + e^- \rightarrow {}^{1}_{0}n + \nu.$$

This results in a decay product that has the same atomic mass number and an atomic number that is one less than that of the parent.

In electron capture most of the available energy is radiated from the system as neutrinos. After electron capture the nucleus may still be in an excited state, and the excess energy is subsequently emitted as γ-rays or an electron by internal conversion.

The captured electron is typically from the K shell, although capture from the L and M shells can also occur. This leaves the atom in an unstable state because of the vacancy created in the inner shell of the atom. This hole can be filled in many ways, outer-shell electrons dropping down to fill the inner-shell vacancies, resulting in the emission of X-ray or Auger electrons characteristic of the decay product (Figure 3; discussed in section 2.4). The energy of the characteristic X-rays emitted is determined by the difference between the corresponding atomic energy levels involved.

2.3 *Isomeric decay processes*

The nucleus is often left in an excited state after α- and β-particle emission. The excess energy is subsequently emitted as γ-rays or an electron by internal conversion. The nucleus before and after an isomeric decay is identical, apart from the energy state.

(*a*) *Production of γ-rays*

Usually the nucleus de-excites into a more stable configuration by γ-ray emission, the atomic number and atomic mass number remaining unchanged. This process may occur in one step with the emission of a single γ-ray or via one or more intermediate excited states resulting in the emission of two or more γ-rays. Typically more than one de-excitation pathway exists with various competing probabilities.

The life-times of nuclear excited states vary, but 0.1 ns can be regarded as typical for these nuclear electromagnetic decays. In some cases, the excited state may be almost stable, and the nucleus may remain in this state for seconds, minutes or even days. Nuclei in this state appear experimentally to act like separate isotopes and are called isomers. The transition to the ground state is called isomeric transition, and the excited state is referred to as a metastable state. An example of an isobaric transition to form a metastable state is the decay of $^{99}_{42}$Mo to $^{99m}_{43}$Tc. The isomeric transition then occurs as $^{99m}_{43}$Tc decays to $^{99}_{43}$Tc with a 6-h half-life.

(*b*) *Internal conversion*

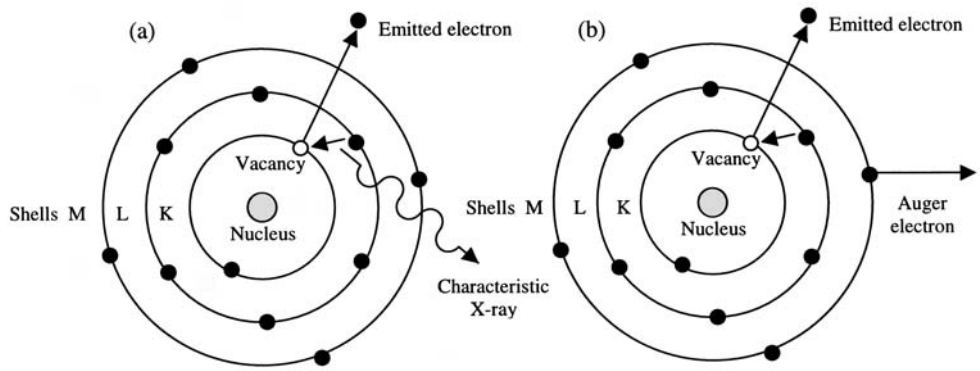
As an alternative to the emission of a γ-ray (energy, γ_1), an excited nucleus may lose its excess energy by internal conversion. In this process, the energy released in the transition of an excited nuclear state to a lower state is transferred to an inner-shell electron (typically K or L shell). This results in ejection of the electron from the atom with energy $E = \gamma_1 - E_B$, where E_B is the binding energy of the electron to its atom. As is the case with electron capture, the atom is left in an unstable state after this process because of the vacancy created in an inner shell of the atom.

Internal conversion competes with γ-ray emission, resulting in a decrease in measured γ-ray intensity. The ratio of the total number of electrons emitted to the total number of γ-rays emitted is called the internal conversion coefficient, which increases as Z^3 and decreases with γ_l. Therefore, γ-ray decay predominates in light nuclei, and internal conversion is prevalent for heavy nuclei especially in the decay of low-lying excited states.

2.4 *Auger electrons and characteristic X-rays*

If the energy transferred to an electron exceeds the binding energy, the electron is ejected from the atom with a kinetic energy equal to the difference between the absorbed energy and the binding energy. The ionization of the atom results in an ion pair (the electron and the positively charged ion). Electrons can be removed from the K, L or M shell by electron capture, internal conversion or by passage of ionizing radiation resulting in an electron hole. The atom is left in an unstable state. The energy released by this transition may be radiated in the form of characteristic X-rays of an energy equal to the difference in the binding energies of the two shells involved in the transition, or alternatively by the ejection of monoenergetic Auger electrons, with an energy equal to that of the characteristic X-ray minus the binding energy of the emitted electron. This process continues until the vacancy moves to the outermost shell and is subsequently filled by a free electron. These processes are illustrated in Figure 3.

Figure 3. Competing processes of (a) characteristic X-ray emission and (b) Auger electron production, after removal of an inner-shell electron



The relative probability of the emission of characteristic radiation to emission of an Auger electron is called the fluorescent yield. The fluorescent yield increases with increasing atomic number, *Z*.

The decay of Auger electron-emitting radionuclides is initiated when electron capture or internal conversion creates a vacancy in an inner atomic shell. The filling of this vacancy produces a cascade of inner-shell electron transitions with the emission

of numerous Auger electrons from the single atom. This can result in a high density of ionizing particles close to the point of decay and also leave the residual atom in a highly positively charged state by loss of electrons.

3. Exposure to internal sources of radiation

3.1 *Radionuclides considered in this monograph*

As described in section 2, the decay of a radioactive atom may occur through one of several processes which give rise to the emission of four major types of radiation: α, electron (β^-), positron (β^+) and γ-radiation (in this discussion we ignore neutrino and antineutrino radiation). Many types of radioactive decay produce more than one type of radiation: decay of a radionuclide to an excited state of its decay product can result in subsequent stabilization of the progeny nucleus and atom by emission of γ-radiation (or conversion electrons) and X-rays, respectively. One example is the β-particle decay of $^{131}_{53}$I to an excited state of $^{131}_{54}$Xe, which is stabilized by the release of a substantial amount of γ-radiation (see Figure 4; discussed in detail below). In other cases, the primary decay of a radionuclide may lead directly to the ground state of its progeny nuclide. The progeny nuclide may also be radioactive and subject to further decay. An example is the α-particle decay of radium (^{226}Ra) directly to radon (^{222}Rn), which subsequently enters an extensive series of disintegrations that terminates with the stable isotope ^{206}Pb. The biological effects observed after internal deposition of these types of radionuclides must be considered to result from the sum of the interactions with cells and tissues of the various types of radiation emitted during each step of the decay chain. For this reason, a previous IARC working group that evaluated the radioactive gas radon, classified 'radon and its decay products' as *carcinogenic to humans (Group 1)* (IARC, 1988).

Evaluation of the human cancer hazard of these radionuclides would not be adequate if it were based on a simple distinction between α- and β-particle-emitting radionuclides. Secondary emissions (e.g. γ- and X-rays) produced by the excited atom after release of an α- or β-particle may contribute considerably to the radiation dose, as may the characteristic X-rays produced after electron capture decay (see section 2.2). It should be noted that both X- and γ-radiation have been classified as human carcinogens (Group 1; IARC, 2000). With most internally deposited radionuclides that emit α-radiation, the dose of α-particles in the organs where the radionuclide accumulates is substantially greater than that from the accompanying β-particle and γ-ray emissions.

(*a*) *Categorization of radionuclides*

The radionuclides considered in this monograph are listed in Tables 7 and 8 in order of increasing atomic mass number. Table 7 shows the decay mode of the radionuclide, the energy of the emitted radiation, its half-life, its decay product (stable/unstable), the presence of other types of emitted radiation and — when relevant — the

Table 7. Radionuclides mentioned in this monograph that undergo decay by emission of α- and/or β-particles

Radio-nuclide	Decay	Energy[a] (keV)	Half-life	Decay product[b]		Emitter type[c]	Other emissions[d]	Δ/ΣΔ (%)[e]	Truncation[f]	Cate-gory[g]
^{3}H	β^-	18.6	12.33 y	^{3}He	(stable)	Pure β	None	β, 100	–	A-1
^{14}C	β^-	156.5	5730 y	^{14}N	(stable)	Pure β	None	β, 100	–	A-1
^{32}P	β^-	1710.7	14.26 d	^{32}S	(stable)	Pure β	None	β, 100	–	A-1
^{33}P	β^-	248.5	25.34 d	^{33}S	(stable)	Pure β	None	β, 100	–	A-1
^{35}S	β	167.1	87.32 d	^{35}Cl	(stable)	Pure β	None	β, 100	–	A-1
^{45}Ca	β^-	256.8	162.6 d	^{45}Sc	(stable)	Pure β	None	β, 100	–	A-1
^{89}Sr	β^-	1495.1	50.53 d	^{89}Y	(stable)	Pure β	γ-Rays (0.01%)	β, 100	–	A-1
^{90}Sr	β^-	546.0	28.79 y	^{90}Y	(unstable)	Pure β	None[h]	β, 100	Full chain	A-2
^{90}Y	β^-	2280.1	64.0 h	^{90}Zr	(stable)	Pure β	γ-Rays (0.01%)[h]	β, 100	–	A-1
^{91}Y	β^-	1544.8	58.5 d	^{91}Zr	(stable)	Pure β	γ-Rays (0.3%)	β, 100	–	A-1
^{106}Ru	β^-	39.4	373.59 d	^{106}Rh	(unstable)	Mixed β	γ-Rays	β, 88; γ, 12	Full chain	B-2
^{106}Rh	β^-	3541	29.8 s	^{106}Pd	(stable)	Mixed β	γ-Rays	β, 87; γ, 13	–	B-1
^{131}I	β^-	970.8	8.02 d	^{131}Xe	(stable)	Mixed β	γ-Rays	β, 34; γ, 66	–	B-1
^{137}Cs	β^-	1175.6	30.07 y	^{137}Ba	(stable)	Mixed β	γ-Rays	β, 31; γ, 69	–	B-1
^{140}Ba	β^-	1050	12.75 d	^{140}La	(unstable)	Mixed β	γ-Rays	β, 25; γ, 75	Full chain	B-2
^{141}Ce	β^-	580.7	32.50 d	^{141}Pr	(stable)	Mixed β	γ-Rays	β, 69; γ, 31	–	B-1
^{144}Ce	β^-	318.7	284.89 d	^{144}Pr	(unstable)	Mixed β	γ-Rays	β, 96; γ, 4	Full chain	B-2
^{147}Pm	β^-	224.1	2.623 y	^{147}Sm	('stable')	Pure β	γ-Rays (0.01%)	β, 100	^{147}Sm (10^{11} y)	A-1
^{188}Re	β^-	2120.4	17.00 h	^{188}Os	(stable)	Mixed β	γ-Rays	β, 93; γ, 7	–	B-1
^{210}Pb[i]	β^-	63.5	22.3 y	^{210}Bi	(unstable)	Mixed β	γ-Rays	α, 92; β, 8	Full chain	B-2
^{210}Bi[j]	β^-	1162	5.01 d	^{210}Po	(unstable)	Pure β	None	α, 93;β, 7	Full chain	A-2
^{210}Po	α	5407.5	138.38 d	^{206}Pb	(stable)	Pure α	γ-Rays (0.001%)	α, 100	–	A-1
^{212}Bi[k]	β^-	2254.0	60.55 m	^{212}Po	(unstable)	Mixed α/β^-	γ-Rays	α, 79; β, 7; γ, 14	Full chain	B-2
	α	6207.1		^{208}Tl	(unstable)		γ-Rays			
^{220}Rn	α	6404.7	55.6 s	^{216}Po	(unstable)	Mixed α	β/γ -Rays	α, 89; β, 4; γ, 7	Full chain	B-2
^{222}Rn	α	5590.3	3.82 d	^{218}Po	(unstable)	Mixed α	β/γ -Rays	α, 88; β, 4; γ, 8	^{210}Pb (22.3 y)	B-2

Table 7 (contd)

Radio-nuclide	Decay	Energy[a] (keV)	Half-life	Decay product[b]		Emitter type[c]	Other emissions[d]	Δ/ΣΔ (%)[e]	Truncation[f]	Cate-gory[g]
^{224}Ra	α	5788.9	3.66 d	^{220}Rn	(unstable)	Mixed α	β/γ-Rays	α, 92; β, 3; γ, 5	Full chain	B-2
^{226}Ra	α	4870.6	1600 y	^{222}Rn	(unstable)	Mixed α	β/γ-Rays	α, 90; β, 3; γ, 7	^{210}Pb (22.3 y)	B-2
^{228}Ra	β^-	45.9	5.75 y	^{228}Ac	(unstable)	Mixed β[l]	γ-Rays	β, 34; γ, 66	^{228}Th (1.91 y)	B2
						Mixed α[l]	β/γ-Rays	α, 89; β, 4; γ, 7	Full chain	
^{227}Th	α	6146.4	18.72 d	^{223}Ra	(unstable)	Mixed α	β/γ-Rays	α, 96; β, 3; γ, 1	Full chain	B2
^{228}Th	α	5520.1	1.91 y	^{224}Ra	(unstable)	Mixed α	β/γ-Rays	α, 93; β, 3; γ, 4	Full chain	B2
^{230}Th	α	4770.0	7.54×10^4 y	^{226}Ra	(‘stable’)	Pure α	None	α, 100	^{226}Ra (1600 y)	A1
^{232}Th	α	4082.8	1.41×10^{10} y	^{228}Ra	(unstable)	Mixed α[m]	β/γ-Rays	α, 90; β, 4; γ, 6	Full chain	B2
						Pure α[m]	None	α, 100	^{228}Ra (5.75 y)	
^{233}U	α	4908.6	1.58×10^5 y	^{229}Th	(‘stable’)	Pure α	None	α, 100	^{229}Th (7.3×10^3 y)	A1
^{234}U	α	4858.5	2.44×10^5 y	^{230}Th	(‘stable’)	Pure α	None	α, 100	^{230}Th (7.7×10^4 y)	A1
^{235}U	α	4678.7	7.04×10^8 y	^{231}Th	(unstable)	Mixed α	β/γ-Rays	α, 92; β, 4; γ, 4	^{231}Pa (3.3×10^4 y)	B2
^{238}U	α	4270.0	4.47×10^9 y	^{234}Th	(unstable)	Mixed α	β/γ-Rays	α, 82; β, 17; γ, 1	^{234}U (2.4×10^5 y)	B2
^{238}Pu	α	5593.2	87.7 y	^{234}U	(‘stable’)	Pure α	None	α, 100	^{234}U (2.4×10^5 y)	A1
^{239}Pu	α	5244.5	24110 y	^{235}U	(‘stable’)	Pure α	None	α, 100	^{235}U (7×10^8 y)	A1
^{240}Pu	α	5255.8	6537 y	^{236}U	(‘stable’)	Pure α	None	α, 100	^{236}U (2.34×10^7 y)	A1
^{237}Np	α	4959.1	2.14×10^6 y	^{233}Pa	(unstable)	Mixed α	γ-Rays	α, 90; β, 5; γ, 5	^{233}U (1.6×10^5 y)	B2
^{239}Np	β^-	721.8	2.36 d	^{239}Pu	(‘stable’)	Mixed β	γ-Rays	β, 60; γ, 40	^{239}Pu (2.4×10^4 y)	B1
^{241}Am	α	5637.8	432.2 y	^{237}Np	(‘stable’)	Mixed α	γ-Rays	α, 98; β, 1; γ, 1	^{237}Np (2.1×10^6 y)	B1
^{242}Cm	α	6215.6	162.8 d	^{238}Pu	(‘stable’)	Pure α	None	α, 100	^{238}Pu (88 y)	A1
^{243}Cm[n]	α	6168.8	29.1 y	^{239}Pu	(‘stable’)	Mixed α	β/γ-Rays	α, 96; β, 2; γ, 2	^{239}Pu (2.4×10^4 y)	B1
	EC/β^+	8.9		^{243}Am	(‘stable’)				^{243}Am (7370 y)	
^{244}Cm	α	5901.6	18.1 y	^{240}Pu	(‘stable’)	Pure α	None	α, 100	^{240}Pu (6537 y)	A1
^{249}Cf	α	6295.0	351 y	^{245}Cm	(‘stable’)	Mixed α	β/γ-Rays	α, 94; β, 1; γ, 5	^{245}Cm (8.5×10^3 y)	B1

Table 7 (contd)

Radio-nuclide	Decay	Energy[a] (keV)	Half-life	Decay product[b]	Emitter type[c]	Other emissions[d]	$\Delta/\Sigma\Delta$ (%)[e]	Truncation[f]	Cate-gory[g]
^{252}Cf[o]	α	6216.9	2.65 y	^{248}Cm (‘stable’)	Mixed α	β/γ -Rays	α, 65; β, 1; γ, 34	^{248}Cm (3.4×10^5 y)	B1
	SF					Fission neutrons			

d, days; m, months; y, years

[a] Difference (in keV) between the energies of the decaying radionuclide and its first decay product. For β^- decay, the maximum energy value is given (E_{max}); it should be noted that the average energy (E_{ave}) of β-radiation is often 30–40% of the E_{max} (^{3}H, 5.7 keV; ^{35}S , 48.6 keV).

[b] Decay products of the first decay step are listed. Stable: the decay product is non-radioactive; unstable: the decay product is radioactive; ‘stable’: the decay product is radioactive, but it has a long half-life, which justifies truncation of the decay chain at this point for calculation of energy contributions (see footnote e).

[c] α- and β-Particle-emitting radionuclides producing ≤ 1% energy contribution from ‘other emissions’ are considered pure emitters.

[d] ‘Other emissions’ refer to the first decay step only.

[e] Values were calculated from the nuclear data tables of Martin and Blichert-Toft (1970) or were provided by the National Radiological Protection Board; the data from these two sources show good agreement; the energy components of the conversion and Auger electrons have been included with β-particles, those of X-rays with γ-rays; for nuclides with unstable decay products, energy contributions were calculated for the entire decay chain or up to a long-lived decay product (see footnote b).

[f] Point in the decay chain beyond which the energy contributions are ignored; the radioactive half-life of the corresponding radionuclide is indicated.

[g] A-1/A-2: pure emitters with stable/unstable decay products, respectively (first decay step only); B-1/B-2: mixed emitters with stable/unstable decay products, respectively (first decay step only)

[h] The two-step disintegration $^{90}Sr \rightarrow {}^{90}Y \rightarrow {}^{90}Zr$ can be considered pure β^- decay.

[i] In short-term experiments, ^{210}Pb acts as a nearly pure β-particle emitter (β, 99%; γ, 1%); over the full decay chain, α-radiation from ^{210}Po predominates.

[j] In short-term experiments, ^{210}Bi acts as a pure β-particle emitter (β, 100%); over the full decay chain, α-radiation from ^{210}Po predominates.

[k] This radionuclide disintegrates by α-particle (36%) and β^- decay (64%); the energy contributions are calculated for the combined decay pathways.

[l] The radionuclide ^{228}Ra may be considered a mixed β-particle emitter in two-year carcinogenicity bioassays with rodents (with truncation of the decay chain at ^{228}Th; half-life, 1.91 years), whereas the effects of α-radiation predominate in long-term human exposure.

[m] The radionuclide ^{232}Th may be considered a pure α-particle emitter in two-year carcinogenicity bioassays with rodents.

[n] This radionuclide disintegrates by α-particle decay (99.7%) and electron capture (EC) + β^+ decay (0.3%); the energy contributions are calculated for the combined decay pathways.

[o] This radionuclide disintegrates by α-particle decay (97%) and spontaneous fission (SF; 3%); the dose from the fission neutrons is not included in the calculation of energy contributions.

Table 8. Radionuclides mentioned in this monograph that undergo electron capture (EC) and internal conversion (IC) decay

Radio-nuclide	Decay	Energy[a] (keV)	Half-life	Decay product[b]		Emitter type	Other emissions[c]	$\Delta/\Sigma\Delta$ (%)[d]	Truncation[e]	Category[f]
^{40}K[g]	β^-	1311.1	1.277×10^9 y	^{40}Ca	(stable)	Mixed β	γ-Rays	β, 76; γ, 24	–	B1
	EC	1504.9		^{40}Ar	(stable)					
^{55}Fe	EC	231.4	2.73 y	^{55}Mn	(stable)	Mixed Ae^-	X-Rays	Ae^-, 73; X, 27	–	B1
^{67}Ga	EC	1000.5	3.26 d	^{67}Zn	(stable)	Mixed Ae^-	γ-Rays	Ae^-, 21; γ, 79	–	B1
^{111}In	EC	865.5	2.80 d	^{111}Cd	(stable)	Mixed Ae^-	γ-Rays	Ae^-, 8; γ, 92	–	B1
^{125}I	EC	185.8	59.40 d	^{125}Te	(stable)	Mixed Ae^-	γ-Rays	Ae^-, 32; γ, 68	–	B1
^{211}At[h]	α	5982.4	7.214 h	^{207}Bi	(unstable)	Mixed α	γ-Rays	α, 94; γ, 6	Full chain	B2
	EC	786.1		^{211}Po	(unstable)					
^{99m}Tc	IC	142.7	6.01 h	^{99}Tc	('stable')	Mixed γ	ce^-	ce^-, 11; γ, 89	^{99}Tc (2.1×10^5 y)	B1

Abbreviations: d, days; y, years; Ae^-, Auger electrons; ce^-, conversion electrons

[a] Difference (in keV) between the energies of the decaying radionuclide and its first decay product

[b] Decay products of the first decay step are listed. Stable: the decay product is non-radioactive; unstable: the decay product is radioactive; 'stable': the decay product is radioactive, but it has a long half-life, which justifies truncation of the decay chain at this point for calculation of energy contributions (see footnote d).

[c] 'Other emissions' refer to the first decay step only.

[d] Values were calculated from the nuclear data tables of Martin and Blichert-Toft (1970) or were provided by the National Radiological Protection Board; the data from these two sources show good agreement; the energy components of the conversion and Auger electrons have been included with β-particles, those of X-rays with γ-rays; for nuclides with unstable decay products, energy contributions were calculated for the entire decay chain or up to a long-lived decay product (see footnote b).

[e] Point in the decay chain beyond which the energy contributions are ignored; the radioactive half-life of the corresponding radionuclide is indicated.

[f] B-1/B-2: mixed emitters with stable/unstable decay products, respectively (first decay step only)

[g] This radionuclide disintegrates by β^- (89%) and electron capture (EC) decay (11%); the energy contributions are calculated for the combined decay pathways.

[h] This radionuclide disintegrates by α-particle (42%) and electron capture (EC) decay (58%); the energy contributions are calculated for the combined decay pathways.

relative energy contribution of this 'contaminating' radiation, expressed as a percentage of the equilibrium rate constant (see below).

To distinguish radioactive decay processes of different complexity, radionuclides can be categorized into groups according to the 'purity' of the emitted radiation and the stability of their decay products, as follows:

Category A. 'Pure' emitters: decay occurs through emission of solely α- or β-particles.

This category includes those radionuclides that emit almost exclusively α- or β-particles (Tables 7 and 8). These radionuclides may also produce γ- and X-ray emissions, but their contribution to the dose is ≤ 1% (see below). Although some α-particle emitters have a low probability of spontaneous fission, this decay process and the irradiation of tissues by fission fragments is not reviewed in this monograph. Furthermore, although all β^-- and β^+-particle emissions are accompanied by the emission of a neutrino or antineutrino, these particles do not cause biological damage and have been ignored.

Category B. 'Mixed' emitters: α- or β-particle decay also involves emission of γ-radiation and/or X-radiation.

For each of the categories A and B, subcategories exist:

Subcategory 1. Nuclides with stable progeny, i.e. with a stable isotope as the decay product.

Subcategory 2. Nuclides with decay products that are also radioactive.

Data on radioisotopes of category A-1, i.e. pure α- or β-particle-emitting radionuclides with stable decay products, would theoretically provide the most straightforward basis for evaluating the carcinogenic hazard of α- or β-radiation *per se* from internally deposited sources. For a number of pure β-particle emitters (e.g. ^{3}H, ^{32}P) with stable progeny (^{3}He, ^{32}S, respectively), relevant data are available on which to evaluate the carcinogenic hazard of internal exposure. For most of the α-particle-emitting radionuclides — even for those of group A-1 — the situation is somewhat different, owing to secondary radiation (γ- and/or X-radiation) from the excited nucleus and atom (see above). Pure α-particle emitters in the strict sense are, therefore, rare. The effects of α-particle emitters should not be evaluated without considering the amount and possible impact of these 'contaminating' radiations. Radionuclides in categories A-2 and B-2 often result in a more complex situation because of the additional effects of the emissions in the decay chain after the primary decay. The decay sequence of a radionuclide in category A-2 may be considered only in rare instances to represent a pure emission (e.g. the two-step β-particle decay of ^{90}Sr via ^{90}Y to ^{90}Zr; see Table 7).

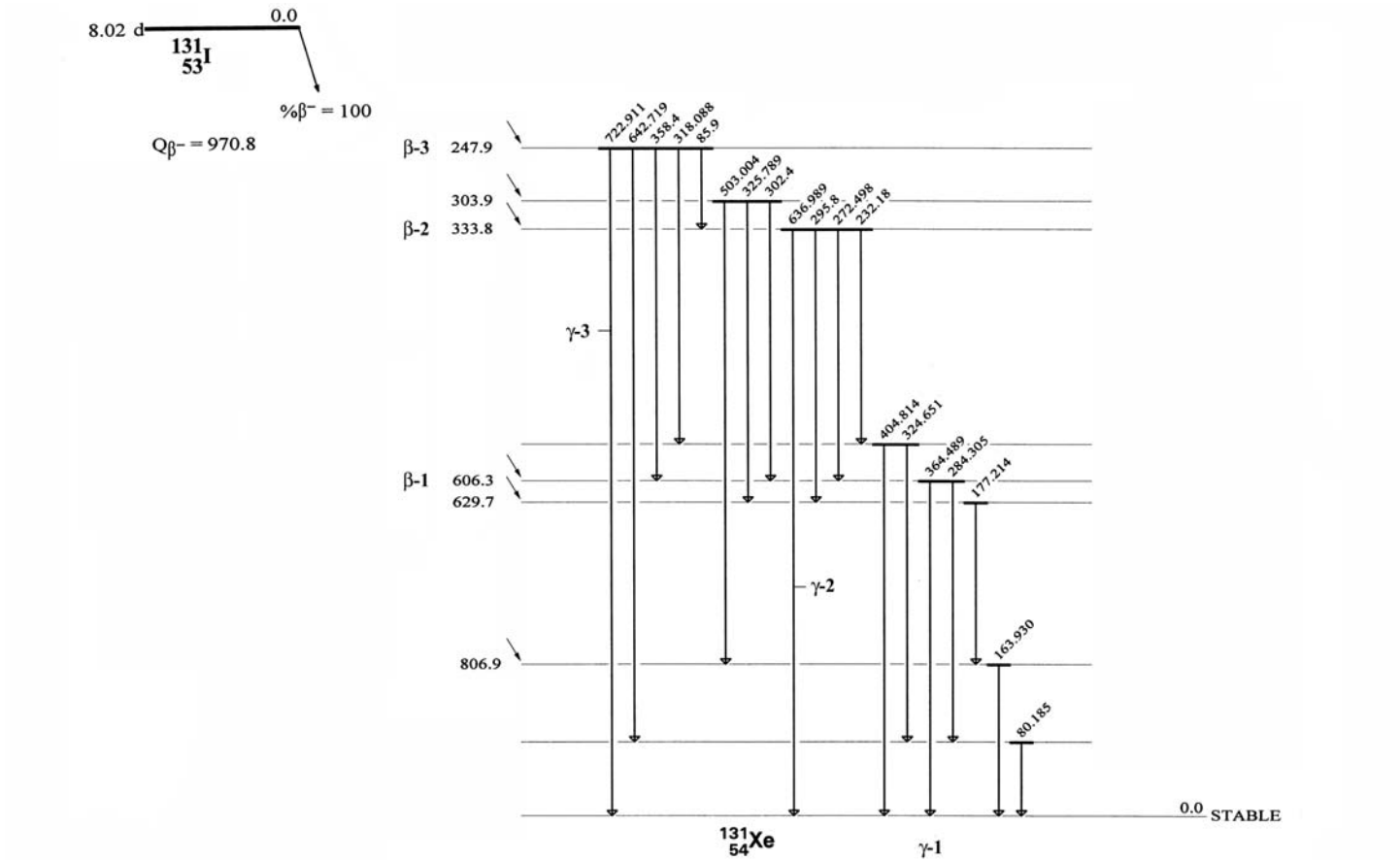
(*b*) *Types of radiation produced during decay of 'mixed' emitters*

The relative contributions of the various emissions produced during the radioactive decay of 'mixed' emitters is often considered at the state of 'ideal equilibrium', i.e. at the stage of the decay at which the activity of the decaying radionuclide is equal to the activity of the decay product. For example, the β-particle decay of ^{131}I gives rise to an excited state of the xenon isotope ^{131m}Xe, which is stabilized by emission of (mainly) γ-radiation, producing the stable nuclide ^{131}Xe (Figure 4). Assuming that the ^{131}I is initially pure, it can be calculated that the state of ideal energy equilibrium is reached after 14.1 days. The β-particle decay of ^{131}I occurs along three major emissions (β-1, β-2 and β-3), and, subsequently, the intermediate product ^{131m}Xe releases its energy by emission of a series of three major γ-rays (γ-1, γ-2 and γ-3). The relative contributions of the β- and γ-radiation emissions during the decay of ^{131}I can be assessed by calculating for each emission the energy emitted per disintegration (Δ, defined for an infinite medium), and then the relative energy contribution over all emissions ($\Delta/\Sigma\Delta$%). The calculated values for all emissions with intensity > 0.01% can be found in the nuclear data tables of Martin and Blichert-Toft (1970). Table 9 shows the results for the three major β- and γ-radiation emissions from ^{131}I mentioned above. During the decay of the 'mixed' β-particle emitter ^{131}I, the energy contribution from γ-radiation is approximately twice that from β-radiation. The relative contribution of energy imparted to the surrounding medium (or the absorbed dose) by γ-rays will, however, be much lower in finite volumes because of the escaping fraction of this penetrating radiation. Therefore, the values of $\Delta/\Sigma\Delta$ for the α- and β-particle emissions, which have low penetration, represent lower limits to the relative contribution to dose of these emissions in cells and tissues.

3.2 *Physical aspects of exposure: Linear energy transfer*

Interactions of ionizing radiations in mammalian cells induce a large number of different types of molecular damage, which subsequently lead to a diversity of cellular responses, including cell killing, chromosomal aberrations, mutations and carcinogenesis. Most effects of direct relevance to humans are due to damage to individual cells, much of which is caused by alterations to macromolecules such as DNA. The effects that radiation has on the medium through which it passes and therefore its efficiency in producing biological effects are related not only to the amount of energy transferred per unit mass, i.e. the absorbed dose, but also to the microdistribution of energy, determined by the type of radiation. For different types of ionizing radiations, the numbers of moving charged particles (per unit dose) and the structures of their radiation tracks are different at all tissue, cellular and subcellular levels. Ionizing radiation deposits energy in the form of molecular ionizations and excitations from interaction of the individual moving particles with the medium. The highly structured spatial pattern of interactions from a particle and its secondary particles is termed the *radiation track* of the particle. Energy depositions within the

Figure 4. Decay of ^{131}I, showing the major β-particle and γ-ray emissions



Total energy difference between ^{131}I and ^{131}Xe is ~ 970 keV. The majority of the β-particles (~ 90%, β-1) have a maximum energy (E_{max}) of ~ 606 keV; the remaining 364 keV are contributed by γ-ray emission (γ-1). About 7% of the β-particles (β-2) have an E_{max} of ~ 334 keV, which is complemented by 636 keV of γ-ray emission (γ-2), while about 2% of the β-particles (β-3) have an E_{max} of ~ 248 keV, leaving 722 keV for γ-ray emission (γ-3). In each case, the γ-ray emission may in fact be a combination of various lower-energy γ-ray decays, as indicated. The remaining β-particle emissions (with maximum energies of ~ 807, 630 and 304 keV) together constitute about 1% of all β (see also Table 9).

Table 9. Energy contributions of the major β^- and γ-radiation emissions during radioactive decay of ^{131}I

^{131}I decay[a]	Energy (keV)[b]	Intensity (%)	Δ (kg.Gy/Bq.s)[c]	$\Delta/\Sigma\Delta$ (%)[d]
β-1	606.3 (192.2)	90.2 of all β	2.77×10^{-14}	32.2
β-2	333.9 (96.8)	7.0 of all β	0.11×10^{-14}	1.35
β-3	247.9 (69.5)	1.9 of all β	0.02×10^{-14}	0.2
γ-1	364.5	82.4 of all γ	4.81×10^{-14}	55.9
γ-2	636.9	6.9 of all γ	0.71×10^{-14}	8.2
γ-3	722.9	1.6 of all γ	0.19×10^{-14}	2.2

From Martin & Blichert-Toft (1970)

[a] Of the β^- and γ-radiation emissions, only the three major ones are listed (see Figure 4).

[b] For the β-particle emissions, the maximum energy is given; the value in parentheses is the average energy.

[c] Δ, energy emitted per disintegration for an infinite and homogeneous medium in which a source is homogeneously dispersed

[d] Relative contribution of this emission, expressed as percentage of all emissions

track occur as isolated ionizations and also as clusters of ionizations. This interaction is qualitatively different from the reactions of most other mutagens or carcinogens with a medium. At the cellular level, there is considerable non-uniformity at natural background doses, and at the DNA level there is massive non-uniformity at all doses. Measurements in randomly selected microscopic volumes yield energy concentrations or concentrations of subsequent radiation products that deviate considerably from their average values. These variations depend in intricate ways on the size of the reference volume, the magnitude of the dose and the type of ionizing radiation (ICRU, 1983; Kellerer, 1985; Goodhead, 1987, 1992).

The quality of radiation is commonly described in terms of LET, which is a measure of the average energy deposited per unit path length along the tracks of charged particles of given type and energy. Sparsely ionizing radiation, such as electrons, X-rays and γ-rays, produces on average only a few interactions per micrometre of track and is referred to as 'low-LET', whereas charged particles such as slow α-particles, which produce dense ionizations along their tracks, are generally referred to as 'high-LET' radiation.

Ionizing radiations produce tracks of ionizations and excitations which vary greatly with the stochastic nature of each atomic interaction. The stochastic aspects can be simulated down to atomic levels (sub-nanometre) by theoretical track structure codes, which provide most of the submicroscopic descriptions currently available (Paretzke *et al*., 1995; Nikjoo *et al*., 1998). Stochastic properties can also be measured experimentally by a variety of techniques, but mostly only over dimensions greater than about 0.3 μm (ICRU, 1983).

Over the dimensions of a mammalian cell and its internal structures, the tracks of ionizing radiations are the primary determinants of the nature and consequence of the damage. Radiolysis of water molecules, which constitute much of the cell contents, leads to the production of reactive free radicals (e.g. •OH), which diffuse on average only a few nanometres because of the high reactivity of the cellular environment (Roots & Okada, 1975). Therefore, the pattern of their points of reaction largely preserves the spatial structure of the track. For most biological end-points, DNA is believed to be the critical target. Damage to DNA can result either from direct interaction of the radiation with the DNA or from reactions with nearby radicals (•OH in particular) or from combinations of these two. Ionizing radiations can produce many different possible clusters of ionizations within a track and therefore of spatially adjacent damage within a macromolecule. Analyses of track structures caused by different types of radiations show that clustered DNA damage more complex than a single double-strand break can occur at biologically relevant frequencies with all types of ionizing radiations (Goodhead, 1987; Brenner & Ward, 1992; Goodhead, 1994). Such clustered damage in DNA is produced mainly within a single track, with a probability that increases with increasing ionization density. Damage from a single track can also be seen over larger dimensions in a cell, including within the chromatin structure, among chromosomes and among adjacent cells if the particle range is sufficient.

At the level of DNA and its structure, most of the information comes from theoretical simulations (Pomplun *et al*., 1996; Nikjoo *et al*., 1997), which led to quantitative estimates of the spectra of DNA damage, including single-strand breaks, simple double-strand breaks and complex double-strand breaks (simple double-strand breaks with additional damage within a few base-pairs). Calculations and experimental measurements showed that the total yield of double-strand breaks per unit absorbed dose is fairly independent of LET for a variety of common radiations; however, the complexity of double-strand breaks and their association with additional damage along the track is greater with higher LET radiations. In general, a substantial proportion of the double-strand breaks produced by ionizing radiations are more complex. It has been estimated that with low-LET radiations such as γ-rays and X-rays, about a quarter of all double-strand breaks have at least one additional break within a few base-pairs. α-Particle radiation induces a higher proportion of complex double-strand breaks, estimated as > 70% for 2-MeV α-particles, and much greater complexity (Goodhead & Nikjoo, 1997). The degree of complexity of the damage induced by all ionizing radiations is even greater if base damage is taken into account.

For a given absorbed dose, the total number of ionizations per unit mass is approximately independent of the type of ionizing radiation, i.e. the average energy per ionization is approximately constant. Nevertheless, the spatial distribution of the ionizations (i.e. radiation track) affects the spectrum of microscopic damage within the cell, as described above; in addition, the average ionization density or LET determines the fluence of particles per unit dose. The consequence for low-level radiation is that individual cells may receive no track at all or only single tracks well isolated in time

and space. For example, for a typical uniform, environmental γ-ray dose of 1 mGy/year (equivalent-dose rate, 1 mSv/year), each cell nucleus in a tissue will experience on average approximately one electron track per year. For 1 mGy of α-radiation (equivalent dose, 20 mSv), such as from radon, only about 0.3% of the nuclei in the irradiated tissue is struck by a track; the remaining 99.7% is totally unirradiated. The energy deposited in such individual single-track events does not depend on dose, and, therefore, the effect on individual cells does not change with tissue dose. At these low doses, only the proportion of cells that is subject to a track will vary linearly with the tissue dose.

Tracks not only directly affect cell nuclei, but there is now evidence that cellular effects, including mutations and chromosomal aberrations, can result from radiation tracks through the cell cytoplasm (Wu *et al*., 1999), and some responses can be induced even in nearby cells — an effect commonly referred to as the 'bystander effect' (Little, 2000).

Nevertheless, for uniform low-level exposures, individual radiation tracks usually remain quite isolated in time and space, unless very long-range and/or long-lived biological processes are involved. Exceptions may be seen after exposure of particular tissues to highly localized low-LET energy, for which the average whole-body effective dose is described as low level but the numbers of tracks in the target cells may be quite substantial.

The dose of all radionuclides to individual target cells within the body depends on the biodistribution of radionuclides. Even for high-energy penetrating radiations such as γ-rays, the dose to distant organs is reduced by geometric factors. For charged particle emissions, the location is even more critical, depending on the range of particles. The ranges can extend to several millimetres for high-energy β-particle emitters such as ^{32}P but are mostly < 0.1 mm for α-particle emitters. In the case of Auger decay, most Auger electrons are confined to single cells or subcellular compartments, and the biological effects vary greatly depending on whether the Auger emitter is attached to DNA, free in the nucleus or in the cytoplasm. Large differences in energy deposition, even at the organ and tissue levels, can occur with different radionuclides or radiolabelled compounds because of heterogeneous distribution of radionuclides, the stochastic nature of the radionuclide decay processes and the emission of short-range radiation (i.e. α-particles, low-energy β-particles, Auger electrons and low-energy X-rays). Detailed knowledge of the cellular and subcellular localization in the relevant tissue of the particular radionuclide and any associated molecule may be relevant before a full assessment can be made of the implications of the internal emitter.

Additional mechanisms of DNA damage may result from the presence of the nuclide within the cell. These include molecular effects after transmutation of a radionuclide to a different progeny nuclide, recoil of the progeny nucleus and charge accumulation on the progeny atom after an Auger cascade. If the decaying atom is appropriately positioned, the recoil nucleus may have considerable energy and can

cause considerable cellular damage. The effects of the recoil nucleus are not considered in this monograph.

(*a*) *γ-Rays*

γ-Rays typically travel long distances (many centimetres) from the emitting radionuclide before interacting in the tissue to eject low-LET electrons with ranges of micrometres to millimetres. The LET of electrons from ^{60}Co γ-rays averaged over their track is about 0.2 keV/μm. Typically high-energy electrons, such as those set in motion by interactions of X-rays and γ-rays, produce a spectrum of low-energy secondary electrons as they slow down and their LET increases, with an increase in scatter. A major part of the energy of high-energy electrons is deposited as sparse ionizations and excitations well isolated from others, but about 30% or more is deposited as more concentrated clusters of ionizations from secondary low-energy electrons, with energies ranging from about 100 eV to 5 keV (Nikjoo & Goodhead, 1991) and approximate values of LET ranging from 30 to 4 keV/μm, respectively (based on mass stopping powers).

(*b*) *α-Particles*

All natural α-particle emitters produce high-LET particles with a range in tissues of approximately 35–90 μm. The low-energy α-particle emitter ^{226}Ra produces α-particles of 4.8 MeV which have an initial LET of about 100 keV/μm. The high-energy emitter, ^{214}Po, produces α-particles of 7.7 MeV, which have a LET of about 70 keV/μm at the point of emission, rising to a maximum of about 200 keV/μm at the Bragg peak (about 0.6 MeV) and then decreasing for the remaining very short track. Due to the high ionization density of the α-particle tracks, they can cause gross and, presumably, unrepairable local damage at the DNA level and associated structures, over and above that achievable by low-LET radiations.

(*c*) *β-Particles*

β-Particles (electrons or positrons) have short to moderate ranges. For example, low-energy electrons from ^{3}H have a maximal range of about 7 μm, while higher-energy electrons from ^{40}K have a maximal range of about 6 mm. Low-energy electrons from β-particle decay have a higher LET. For example, 1-keV electrons have an average LET of about 13 keV/μm, and the effective ionization density is further enhanced by the high scatter and tortuous path of the electron. If β-particle emitters are incorporated into DNA, there is the additional possibility of biological effects due to transmutations of the nuclides themselves.

(*d*) *Auger electrons*

Depending on the radionuclide, Auger emitters emit multiple electrons with a typical range of energies from a few electron volts up to a few tens of kiloelectron

volts. The majority of Auger electrons are of low energy and are often emitted in large numbers after the decay of a single radionuclide (Humm *et al*., 1994). For example, ^{125}I decays first via electron capture to a metastable state of tellurium (^{125m}Te), which usually (93% of the transitions) undergoes electron capture. The number of electrons emitted in a single decay of ^{125}I may vary from 1 to about 50, many with energies < 1 keV and ranges of < 50 nm (Charlton *et al*., 1978; Charlton & Booz, 1981; Pomplun *et al*., 1996). Therefore, the ionization density is greatly enhanced very locally (within a few nanometres) around the point of decay, because of the proximity of many electrons. For this reason, Auger emitters are sometimes regarded as having the properties of high-LET radiation. Four general situations can be considered, depending on the location of the Auger-emitting radionuclides:

- Excluded from the target cell, the Auger electrons should have little mutagenic potential.
- Randomly distributed, the effect of the Auger electrons should be generally similar to that of β-particles.
- Selectively concentrated within cell nuclei, they should lead to a substantial enhancement of the effect.
- Incorporated into the DNA, Auger electrons from a single decay are capable of delivering a very localized dose which is larger than that delivered by a traversing α-particle. Therefore, the damage produced to DNA can be similar to that produced by high-LET radiation but without the substantial associated damage to other parts of the genome and adjacent cells.

3.3 *Biological aspects of exposure*

(*a*) *Non-uniform distribution of radionuclides in organs and tissues*

The third component of background exposure to ionizing radiation after cosmic rays and terrestrial γ-rays is that from the inhalation and ingestion of long-lived natural radionuclides. In terms of dose, the primordial radionuclides are ^{40}K (half-life, 1.3×10^9 years), ^{232}Th (1.4×10^{10} years) and ^{238}U (4.5×10^{10} years), with ^{87}Rb (4.7×10^{10} years) and ^{235}U (7.0×10^8 years) being of secondary importance (IARC, 2000).

Apart from specific exposures to ^{40}K, the concentrations of this radionuclide in soft tissues do not depend on those in food, water or air and are relatively constant, because the concentration of potassium is under homeostatic control in the body. The body content of potassium is about 0.2%, and the isotope abundance of ^{40}K is about 0.012%. The internal radiation is delivered mainly as β-particles and amounts to an annual effective dose equivalent of 165 μSv for adults and 185 μSv for children (UNSCEAR, 1993).

The internal doses from the radionuclides ^{232}Th, ^{238}U and their decay products reflect their intake from diet and air. Age-weighted annual intakes have been calculated by UNSCEAR (1993). The total annual effective doses associated with the

intake of long-lived radionuclides in the uranium and thorium series are 52 μSv by ingestion and 10 μSv by inhalation. Approximately 65% of this dose is from ^{210}Pb and is delivered mainly as β-particles (UNSCEAR, 1993; IARC, 2000).

It should be noted that radon is the most significant source of human exposure to radiation from natural sources. The average annual effective dose resulting from inhalation of radon and its short-lived decay products is estimated to be 1200 μSv (UNSCEAR, 1993).

Depending on the radionuclide, its radiation characteristics and the chemical form in which it enters the body, the subsequent radiation energy deposited may range from short, more or less uniform irradiation of all tissues to a highly heterogeneous distribution of dose. For example, $^{3}H_2O$ irradiates all the tissues of the body more or less uniformly, but, because the radionuclide is eliminated from the body with a biological half-time of about 10 days, the vast majority of the radiation dose is delivered within a period of ~ 15 days; the situation with ^{137}Cs is similar (see section 4.1), except that the radiation dose is delivered over a period of up to about one year. In such circumstances, the pattern of radiation effects may be very similar to that observed after a similar dose of external irradiation. When ^{137}Cs was injected into beagles, the pattern of late effects was similar to that observed after an equal dose of external γ-irradiation (Nikula *et al*., 1994).

In contrast, for bone-seeking radionuclides such as ^{239}Pu or ^{226}Ra, the combination of the long physical half-life of the radionuclide and its tenacious retention in the human skeleton means that this tissue will be irradiated for the remainder of the subject's life, and the major late effect of radiation is the induction of bone tumours. Similarly, the deposition of ^{232}Th (from the X-ray contrast medium Thorotrast) in the liver may lead to liver tumours, and the accumulation of ^{131}I in the thyroid may lead to malignancies in that gland. The biodistribution of radionuclides in human adults is shown in Table 10.

If the amount of the radionuclide that enters the body is sufficiently large, the resulting irradiation may lead to the appearance of acute effects. For example, damage to the intestinal mucosa has been observed in animals given large oral doses of insoluble radionuclides (Harrison, 1995). Varying degrees of bone-marrow depression were observed in some individuals exposed to ^{137}Cs internally and externally in an accident in Goiânia, Brazil (IAEA, 1988), and a variety of haematological deterministic effects have been reported in dogs exposed to bone-seeking radionuclides (Dougherty *et al*., 1962). Unplanned human intakes of radionuclides large enough to cause acute effects should be rare, however, and the major concern lies in the smaller intake of radionuclides which may result in the induction of neoplasia.

An important finding is that the carcinogenicity of the α-particle-emitting actinide radionuclides often differs quite markedly from that of ^{226}Ra. Lloyd *et al*. (1994) calculated the relative risks for induction of skeletal tumours in humans (Table 11). It can be seen that the bone surface-seekers ^{224}Ra, ^{228}Th, ^{239}Pu and ^{241}Am are five or more times more effective in inducing bone tumours than the bone volume-seeker ^{226}Ra, and the toxicity is attributed to decay of a greater fraction of these radionuclides

Table 10. Biodistribution of elements in human adults

Element	Principal deposition sites (% entering blood)	Retention half-time
Hydrogen	^3H_2O; similar concentration in all tissues	~ 10 days
Carbon	Similar concentrations in all tissues; dependent on type of compound	Up to 40 days
Phosphorus	Skeleton (30%)	> 20 years
Sulfur	Similar concentrations in all tissues; dependent on type of compound	Weeks to years
Gallium	Skeleton (30%), liver (~ 10%)	1–50 days
Strontium	Skeleton (25%)	≥ 20 years
Technetium	Pertechnetate; thyroid (4%), stomach (10%), liver (3%)	Thyroid, 12 h; other tissues, 2–22 days
Iodine	Thyroid (30%; range, 5–55%)	80 days
Caesium	Similar concentrations in all tissues	50–200 days
Plutonium	Liver (30%), skeleton (30%)	~ 20 years, > 20 years
Astatine	Stomach (14%), liver (5%), kidneys (3%), thyroid (2%)	Up to 2 days
Radon	Similar concentrations in all tissues except fatty tissues, where it is higher	
Radium	Skeleton (25%)	≥ 20 years
Thorium	Skeleton (~ 50%)	≥ 20 years
Uranium	Skeleton (~ 10%)	≥ 20 years
Neptunium	Liver (10%), skeleton (45–50%)	2–3 years, > 20 years
Polonium	Liver (~ 30%), kidney (10%), red bone marrow (10%)	~ 50 days
Americium	Liver (50%), skeleton (30%)	2–3 years, > 20 years
Curium	Liver (50%), skeleton (30%)	2–3 years, > 20 years

Based on data reviewed by ICRP (1979, 1980, 1981, 1989, 1993, 1995a,b)

close to bone surfaces. Decay close to bone surfaces is considered to be more effective in producing bone tumours because the cells of these tumours are in the soft tissues within bone spaces. The dosimetry is complicated considerably, however, by the growth processes within bone which result in redistribution of surface-deposited radionuclides. Accordingly, the dosimetry of bone-seeking radionuclides in general has been the topic of considerable research (Polig, 1978; Spiers *et al.*, 1978, 1981; Thorne, 1985; Spiers, 1988; Priest, 1990; Priest & Tasker, 1990; Austin *et al.*, 1999).

Table 11. Estimated risk coefficients for the induction of bone tumours by ^{226}Ra and other bone-seeking radionuclides, based on the human risk coefficient for ^{226}Ra and the relative toxicity of the other nuclides in beagle dogs

Radionuclide	Risk (%/Gy average skeletal dose) ± standard deviation
^{90}Sr	
High dose	0.17 ± 0.09
Low dose	0.009 ± 0.005
Very low dose	0.002 ± 0.002
^{224}Ra	
Single exposure	0.43 ± 0.14
Chronic exposure	2.74 ± 0.86
^{226}Ra	0.171
^{228}Ra	0.34 ± 0.09
^{228}Th	1.45 ± 0.40
^{239}Pu	
Monomeric	2.74 ± 0.86
Polymeric	5.50 ± 2.00
^{241}Am	1.00 ± 0.13

From Lloyd *et al*. (1994)

(*b*) *Non-uniform deposition of radionuclides at the cellular and subcellular level*

Non-uniform deposition at the cellular or subcellular level must also be taken into consideration. Inhaled, insoluble radioactive particles may be taken up by phagocytosis into macrophages, in the airway wall or in the alveoli of the lungs. If the particle contains an α- or soft β-particle-emitting radionuclide, high local doses may be given to the lung tissue immediately surrounding the macrophage. Dean and Langham (1969) pointed out that the local dose to the surrounding cells from a single particle of 0.2-μm diameter containing 590 Bq of ^{239}Pu engulfed in a fixed macrophage could be more than five orders of magnitude greater than the dose to the lung calculated on the assumption that the radiation is uniformly distributed throughout the lung tissue (1.4×10^4 Gy compared with 32 mGy).

Radioactive atoms of radionuclides of the actinide and lanthanide series and other easily hydrolysable metallic radionuclides (e.g. ^{67}Ga) may tend to aggregate and concentrate within lysosomes (Taylor, 1972; Berry *et al*., 1983; Tsan & Scheffel, 1986; Galle *et al*., 1992; Duffield *et al*., 1994). This creates a non-uniform distribution of the radioactivity at the intracellular level, which could in principle lead to more intense radiation-induced changes in the immediate vicinity of the decaying atom.

Other investigations have shown that, at least in liver cells, the intracellular distribution of plutonium and neptunium may also be mass dependent. Comparative studies of the intracellular distribution of ^{238}Pu and ^{239}Pu in rat hepatocytes *in vitro* indicated that ^{239}Pu tended to localize in the cell nuclei, whereas the higher-specific activity nuclide ^{238}Pu localized predominantly in the lysosomes (Schuler & Taylor, 1987). A mass-dependent difference in intracellular localization has been observed for neptunium. In rats 24 h after intravenous injection of 1.2 mg/kg bw ^{237}Np or 17 pg/kg bw ^{239}Np, the association of ^{237}Np with the liver cell nuclei was double that found with ^{239}Np (Paquet *et al*., 1996). Although these studies clearly indicated mass differences in the intracellular localization of neptunium and plutonium, the practical radiotoxicological significance of these observations remains to be assessed. Nevertheless, any possible nuclear association of radionuclides may have radiotoxicological importance, especially as the nuclides emit Auger electrons (e.g. ^{67}Ga and ^{125}I). The radiobiological effects of the various ^{125}I-labelled DNA precursors have been described (Hofer, 1998). The nuclear association of the Auger-emitting radiopharmaceutical ^{67}Ga citrate has been shown to be very low, probably less than several percent of the total cellular radioactivity being deposited in the cell nucleus.

Certain ^{3}H- and ^{14}C-labelled compounds, such as [^{3}H]- or [^{14}C]thymidine, may be incorporated preferentially into the DNA of dividing cells. In the case of ^{3}H, this may result in doses to the cell nucleus as much as 50 times those resulting from uniform distribution of ^{3}H throughout the cell. However, the average energy of the ^{14}C β-particle is about nine times larger than that of ^{3}H; thus, tissues are irradiated more uniformly from ^{14}C than they are from ^{3}H incorporated into DNA. It has been shown that the absorbed dose in a ^{14}C-labelled cell nucleus does not differ significantly from the mean dose from uniformly distributed ^{14}C compounds. The β-particle dose is not the only consideration, however, and transmutation effects could be important if ^{14}C is placed in molecular positions where such effects may arise, although there is little probability of incorporation of ^{14}C into such positions from most ^{14}C-labelled compounds (ICRP, 1981).

(*c*) *Factors that may modify radionuclide metabolism and toxicity*

A number of factors may modify radiotoxicity by altering the biokinetics of the radionuclide or influencing the tissue response. For example, pregnancy reduces the retention of ^{137}Cs (Thornberg & Mattsson, 2000), and sex influences its retention (Melo *et al*., 1997). The behaviour of a radionuclide after inhalation may be affected by allergies and diseases such as chronic bronchitis and emphysema. These conditions may affect the pattern of particle deposition and retention within the lung and may even influence the absorption of radionuclides from the lung. Smoking, which may cause chronic obstructive lung disease, can also alter the clearance of radionuclides and increase the risk for lung cancer (ICRP, 1994). Similarly, acute or chronic renal disease may decrease the natural rate of elimination of radionuclides from the body, thus increasing the radiation dose to organs and tissues.

Ever since the recognition that radionuclides deposited in the human body could induce cancer and related diseases, there has been wide interest in methods to accelerate their elimination from the body. This can be achieved either by preventing or decreasing their uptake into the systemic circulation from the site of entry and/or by enhancing their natural rate of excretion; the latter approach is often called decorporation therapy. The assumption made is that such treatment reduces the risks for radiation-induced late effects (Taylor *et al*., 2000).

The management of radionuclide contamination has been reviewed, including discussion of such questions as the radiation doses at which treatment is appropriate and the indications and contraindications for treatment (Volf, 1978; Bhattacharrya *et al*., 1992; Hengé-Napoli *et al*., 2000). The medical aspects of decorporation treatment of workers and the general public have also been reviewed (Wood *et al*., 2000). Possible treatment includes lung washing (lavage) (Nolibé *et al*., 1975) and decorporation therapy with chelating agents such as salts of diethylenetriaminepentaacetic acid (Breitenstein & Palmer, 1989).

3.4 *Target tissues*

(*a*) *Liver*

In the period 1930–55, a large number of patients were injected intravenously with a colloidal suspension of thorium dioxide (Thorotrast) to allow visualization of the vascular system. Because of its colloidal characteristics, most Thorotrast is deposited within the reticuloendothelial system, principally in the liver, spleen, bone marrow and lymph nodes, for life. Approximately 60% of injected Thorotrast remains in the liver, where it induces deterministic effects (fibrosis, cirrhosis and peliosis) and causes cancer after a latency of more than 10 years (Ishikawa *et al.*, 1989; Andersson *et al.*, 1994; van Kaick *et al.*, 1995; Mori *et al.*, 1995). The relative risk of these patients for dying from liver cancer has been found to be 129 in Germany and 36 in Japan. In comparison with the general population, the risk for liver cancer was 121 in Denmark and 71 in Portugal (see section 2 of the monograph) (van Kaick *et al.*, 1999; Andersson, 1997; Mori *et al.*, 1999a,b; Martling *et al.*, 1999; dos Santos Silva *et al.*, 1999).

In the Danish study, three types of liver cancer were observed: hepatocellular carcinoma, cholangiocarcinoma and angiosarcoma, about two-thirds being carcinomas and one-third angiosarcomas. A specific feature of Thorotrast-induced liver cancers is the high proportion of cholangiocarcinomas and angiosarcomas (Andersson *et al.*, 1994).

(*b*) *Lung*

Radioactive gases and particles may enter the body by inhalation. The main exposure of concern for public health is inhalation of the short-lived decay products (^{218}Po and ^{214}Po) of the noble gas ^{222}Rn. A number of studies, including a joint analysis of 11 cohorts of underground miners, revealed carcinogenic effects of radon and its decay products (IARC, 1988; Lubin *et al*., 1994a). A combined analysis of the studies

of miners showed that the excess relative risk for lung cancer was linearly related to cumulative exposure to radon progeny, estimated as WLM. The overall estimate of excess relative risk per WLM was 0.49% (Lubin *et al.*, 1994). Whether residential exposure to radon is also carcinogenic is more controversial and is discussed in the monograph.

The commonest primary lung tumours in the male population of the USA are squamous-cell carcinoma (35%), small-cell carcinoma (17%), adenocarcinoma (25%) and large-cell carcinoma (9%) (Percy & Sobin, 1983). The distribution of the histological types of the lung cancers observed in the case–control studies of residential exposure to radon presented in section 2 of the monograph reflects these proportions. In uranium miners (especially in the 1950s), small-cell carcinomas represented the majority of cases until the late 1970s (Saccomanno *et al.*, 1996; Wiethege *et al.*, 1999).

(*c*) *Bone*

Exposure to external radiation or to bone-seeking radionuclides may result in damage to the skeletal system including growth disturbances, degenerative and reparative processes in the osseous tissue and the formation of bone tumours. An extensive review of the literature on the pathological effects of irradiation on the skeleton was published (Vaughan, 1973). The first cases of malignant bone tumours occurring after therapeutic X-irradiation were reported by Beck (1922), and detailed reports of post-irradiation neoplasia in bone after therapeutic external irradiation have been published (Unni, 1996). Bone sarcomas subsequent to internal radiation from ^{226}Ra and ^{228}Ra were first reported in radium-dial workers by Martland and Humphries (1929). About 64 cases of malignant bone tumours were observed in about 2600 patients (Rowland, 1994; Fry, 1998). A detailed study of the histopathology of ^{226}Ra- and ^{228}Ra-induced bone sarcomas in humans has been published (Schlenker *et al.*, 1989). Induction of bone sarcomas was also observed in patients with tuberculosis or ankylosing spondylitis treated with the short-lived α-particle-emitting ^{224}Ra. In a cohort of 899 patients (455 with tuberculosis, including 214 under the age of 21 years) treated with high doses of ^{224}Ra (mean bone surface dose, about 30 Gy), 56 malignant bone tumours occurred, with less than one expected (Nekolla *et al.*, 2000). In 1577 patients exposed to ^{224}Ra as therapy for ankylosing spondylitis (mean bone surface dose, about 5 Gy), four bone tumours were found, with 1.3 cases expected from statistics for the general population (Wick *et al*., 1999).

A revision of the histology of bone tumours in patients treated with ^{224}Ra revealed a high proportion of bone sarcomas of the fibrous connective tissue type. A comparison with bone sarcomas arising after incorporation of ^{226}Ra, ^{228}Ra and external irradiation and with tumours arising at sites of pre-existing bone lesions (Paget disease) showed the same spectrum of tumours. These results suggest that the cells at risk are not fully committed to bone formation (probably multipotent mesenchymal precursors) and that a close histogenetic relationship may exist between disorders of

the microenvironment caused by deterministic radiation damage (osteodysplasia) and the induction of these fibrous connective tissue-type bone sarcomas (Gössner, 1999).

(*d*) *Thyroid gland*

The only radionuclides that are actively absorbed in the thyroid gland are the radioiodines. The healthy thyroid gland absorbs 20–30% of ingested ^{131}I, but a patient with hyperthyroidism could absorb as much as 60%, and almost none might be absorbed after administration of stable iodine. ^{131}I is essentially a β-particle emitter, contributing 85% of the absorbed tissue dose, while the contribution of γ-radiation is 15%. This fact is used in medical practice, where radioiodines have been administered for the last 50 years in the treatment of hyperthyroidism and thyroid cancer. Radioiodine not only locally irradiates the thyroid gland but also becomes associated with thyroid hormones, thus influencing other organs of the body.

Thyroid cancers can be differentiated (papillary, follicular and medullary) or undifferentiated (anaplastic carcinoma). The thyroid cancer known to be caused by ionizing radiation is papillary carcinoma, as shown among the atomic bomb survivors (Wood *et al.*, 1969) and recently in the Chernobyl area. In a study of 577 Ukrainian patients less than 19 years of age in whom thyroid cancer was diagnosed, 290 cases were evaluated histopathologically and > 90% were found to be papillary carcinomas (Tronko *et al.*, 1999). Similar frequencies were seen in a study in the USA of 4296 patients previously irradiated for benign disorders: thyroid cancers were found in 41 children (mean age at diagnosis, 16 years), of which 95% were papillary carcinomas (Visvanathan *et al.*, 1994). Thyroid nodules have also been related to exposure to radioiodine (Hall *et al.*, 1996).

(*e*) *Haematopoietic tissues*

Various types of leukaemia, with the exception of chronic lymphocytic leukaemia and adult T-cell leukaemia, are known to be caused by external irradiation, as shown among the atomic bomb survivors (Preston *et al.*, 1994).

The studies of patients treated with Thorotrast showed that 10–25% of the injected dose is deposited in the bone marrow; the effects are deterministic (aplastic anaemia) and carcinogenic (myelodysplastic syndrome and leukaemia). In a combined analysis of patients in Germany and Denmark, the following subtypes of leukaemia were seen: acute myeloid leukaemia (52%), myelodysplastic syndrome (39%), chronic myeloid leukaemia (7%) and acute lymphoblastic leukaemia (2%). The corresponding figures for the atomic bomb survivors are 39%, 8%, 20% and 33%, respectively. A much higher frequency of myelodysplastic syndrome and a lower frequency of acute and chronic leukaemia were found among the Thorotrast-treated patients than among the atomic bomb survivors (Visfeldt & Andersson, 1995).

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