

The skeleton, an important target

Certain radioactive elements can behave in the body like calcium, and so exhibit a special affinity for bone structures.



PhotoDisc

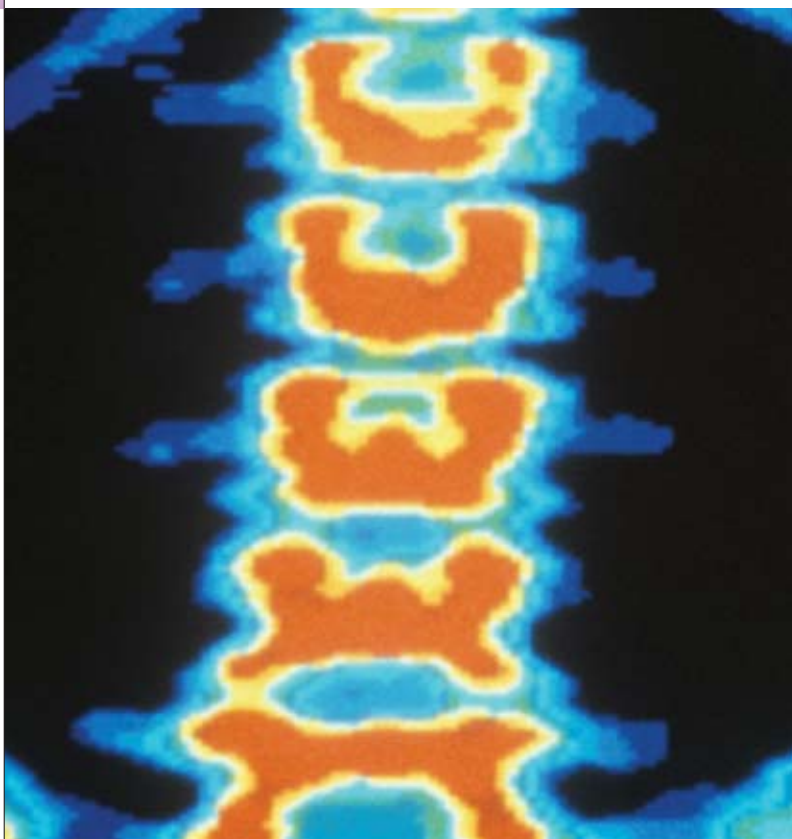
Spine. The skeleton is a preferred residence site for certain osteotropic radionuclides, which can be retained there for up to a hundred years.

Bone tissue is composed of cells (**osteoblasts**, **osteocytes**, **osteoclasts**) and a mineralised organic matrix. This mineralisation, formed essentially of hydroxyapatite crystals of calcium phosphate, gives bones their mechanical strength.

After **internal contamination** (by **inhalation**, **ingestion** or *via* wounds), certain **radioactive elements** can be retained or distributed in the body like calcium, displaying its special affinity for bone structures. Certain **alkaline earth metals** (e.g., radium and strontium), **lanthanides** or **rare earths** (e.g., cerium) and actinides (uranium or plutonium) are, for example, known **osteotropes**.

Bone deposition of radionuclides through internal contamination

For lanthanides, bone deposition occurs mainly in the well-vascularised channels of the internal bone surface (**endosteum**). Deposition is lightest on the external surface (**periosteum**). For actinides, observations in rodents show that the initial distribution in the skeleton is not uniform. As bone is naturally reshaped during life and the **radionuclides** are gradually “buried” in the bone mass, this distribution becomes more homogeneous. Plutonium is deposited preferentially



Scintigraphy of the spine. The image was obtained by rotating a gamma camera around the subject.

in the endosteum, while americium is distributed over all the surfaces. Uranium is initially deposited on the active surfaces of the bone tissue.

Considering the whole skeleton, preferential deposition of these radionuclides takes place in the vertebrae, scapular and pelvic girdles and ribs.

Radio-induced effects in the skeleton

The industrial and medical use of radioactive elements at the beginning of the twentieth century, and the ignorance of the **radiotoxicity** of the **ionising radiation** they produced, had dramatic health repercussions. Growing awareness of these adverse effects and their subsequent analysis prompted research to assess radiotoxic risk more accurately and draw up **radioprotection** standards. The case of radium can be cited as an example. Soon after its discovery it found many medical applications (e.g., radium-224 in the treatment of alkylosing spondylitis and tuberculosis) and industrial uses (e.g., radium-226 and -228, in

radium dial paint). These uses were the cause of severe complications among people exposed to the **alpha radiation** emitted by radium, with cases of bone radionecrosis⁽¹⁾ and a significant increase in the induction of bone tumours, not to mention effects on the bone marrow, which will not be dealt with here. It has been estimated that in humans there is a threshold **dose** of 0.8 **gray** (Gy) above which the **incidence** of bone tumours increases.

Experiments in rodents (single injection of lanthanides, **beta emitters**) have shown that induction of **osteosarcoma** occurs at optimal doses delivered to the skeleton of between 25 and 50 Gy. For actinides (²³⁸Pu, ²³⁹Pu, ²⁴¹Am) emitting alpha radiation, abundant American research in animals has demonstrated induction of bone tumours at skeleton doses lower than 0.5 Gy, corresponding, for example, to an initial **activity** deposited in the lungs, after inhalation, of 340 Bq.kg⁻¹.

Together, these studies show that radio-induced bone diseases are directly related to the distribution patterns of radionuclides and to how long they are retained in the skeleton. According to the retention site and the nature of the emitted radiation, the irradiation will preferentially affect the calcium bone matrix and (or) the bone cells involved in bone growth and reshaping. The average dose delivered locally in the different parts of the skeleton is the main parameter determining radio-induced biological effects such as radionecrosis and bone tumours.

Also, these studies demonstrate that the risk of development of radio-induced bone tumours is greatest in exposed young adults.

Experimental data on the distribution of **radio-elements** in the body and tumour induction after internal contamination have been obtained mainly after (intravenous or intraperitoneal) or inhalation. Importantly, after ingestion of lanthanides or actinides, the **transfer factors** (from the digestive tract to the bloodstream) are small ($2 \cdot 10^{-2}$ to $5 \cdot 10^{-4}$), lowering incorporation of the radionuclides and so lessening the associated health hazard.

> **Jean-Luc Poncy**

Life Sciences Division

CEA - DAM-Ile de France Centre

(1) **Radionecrosis** is a chronic dynamic process that corresponds to an imbalance between bone matrix and bone cells, leading to loss of substance or cell death. Bone **necrosis** can result from a complication of radiotherapy linked to failed healing.

A Natural and artificial radioactivity

Everything on the earth's surface has always been exposed to the action of **ionising radiation** from natural sources. **Natural radiation**, which accounts for 85.5% of total radioactivity (natural plus artificial), is made up of 71% **telluric radiation** and about 14.5% **cosmic radiation**. The **radionuclides** formed by the interaction of **cosmic rays** arriving from stars, and especially the Sun, with the nuclei of elements present in the atmosphere (oxygen and nitrogen) are, in decreasing order of **dose** (Box F, *From rays to dose*) received by the population, carbon-14, beryllium-7, sodium-22 and tritium (hydrogen-3). The last two are responsible for only very low doses.

Carbon-14, with a **half life** of 5,730 years, is found in the human body. Its **activity** per unit mass of carbon has varied over time: it has diminished as carbon dioxide emissions from the combustion of fossil fuels have risen, then was increased by atmospheric nuclear weapon tests.

Beryllium-7, with a half life of 53.6 days, falls onto the leaf surfaces of plants and enters the body by **ingestion** (Box B, *Human exposure routes*). About 50 Bq (becquerels) per person per year of beryllium-7 are ingested.

The main or "primordial" radionuclides are potassium-40, uranium-238 and thorium-232. Along with their radioactive decay products, these elements are present in rocks and soil and are therefore found in many building materials. Their concentrations are generally very low, but vary according to the nature of the mineral. The **gamma radiation** emitted by these radionuclides forms the **telluric radiation**, which is responsible for the **external exposure** of the body. The primordial radionuclides and many of their long-lived descendants

are also found in trace amounts in drinking water and plants: this results in an **internal exposure** by ingestion, plus an additional low exposure by **inhalation** of airborne suspended dust particles.

Potassium-40 is a **beta** and **gamma** emitter with a half life of 1.2 thousand million years, and has no radioactive descendants. This radioactive **isotope** makes up 0.0118% of all natural potassium, and enters the body by ingestion. The mass of natural potassium in the human body is independent of the quantity ingested.

Uranium-238 is an **alpha** emitter with a half life of 4.47 thousand million years. It has thirteen main alpha-, beta- and gamma-emitting radioactive descendants, including **radon-222** (3.82 days) and **uranium-234** (0.246 million years). Uranium-238 and its two descendants **thorium-234** (24.1 days) and **protactinium-234m**⁽¹⁾ (1.18 min), and **uranium-234** are essentially incorporated by ingestion and are mainly concentrated in the bones and kidneys. **Thorium-230**, derived from uranium-234, is an alpha emitter with a period of 80,000 years. It is an **osteotrope**, but enters the body mainly by the pulmonary route (inhalation). **Radium-226**, a descendant of thorium-230, is an alpha emitter with a half life of 1,600 years. It is also an osteotrope and enters the body mainly *via* food. Another osteotrope, **lead-210** (22.3 years), is incorporated by inhalation though mostly by ingestion.

Thorium-232 is an alpha emitter with a half life of 14.1 thousand million

years. It possesses ten main alpha-, beta- and gamma-emitting radioactive descendants including **radon-220** (55 s). Thorium-232 enters the body mainly by inhalation. **Radium-228**, a direct descendant of thorium-232, is a beta-emitter with a half life of 5.75 years. It enters the body mainly in food.

Radon, a gaseous radioactive descendant of uranium-238 and thorium-232, emanates from the soil and building materials, and along with its short-lived alpha-emitting descendants constitutes a source of internal exposure through inhalation. Radon is the most abundant source of natural radiation (about 40% of total radioactivity).

The human body contains nearly 4,500 Bq of potassium-40, 3,700 Bq of carbon-14 and 13 Bq of radium-226 essentially imported in food.

Natural radiation is supplemented by an **anthropic component**, resulting from the medical applications of ionising radiation and to a lesser extent from the nuclear industry. It accounts for about 14.5% of the total radioactivity worldwide, but much more in the developed countries. In the medical field (more than 1 mSv/year on average in France), irradiation by external sources predominates: radiodiagnosis (X-rays) and radiotherapy, long based on caesium-137 and cobalt-60 sources, but now more and more often using linear accelerators. Irradiation by internal routes (curietherapy with iridium-192) has more specialised indications (cervical cancer, for example). The metabolic and physico-chemical properties of some twenty radionuclides are put to use for **medical activities** and in **biological research**. The medical applications comprise radio-diagnostics (**scintigraphy** and radio-

(1) m for metastable. A nuclide is said metastable when a transition delay exists between the excited state of the atom and the stable one.

immunology), and treatment, including thyroid disorders using iodine-131, radioimmunotherapy in certain blood diseases (phosphorus-32) and the treatment of bone metastasis with strontium-89 or radiolabelled phosphonates alongside other uses of radiopharmaceuticals. Among the most widely used radionuclides are: **technetium-99m** (half life 6.02 hours) and **thallium-201** (half life 3.04 days) (scintigraphy), **iodine-131** (half life 8.04 days) (treatment of hyperthyroidism), **iodine-125** (half life 60.14 days) (radioimmunology), **cobalt-60** (half life 5.27 years) (radiotherapy), and **iridium-192** (half life 73.82 days) (curietherapy). The average contribution of radiological examinations to total radioactivity amounts to 14.2%.

The **early atmospheric nuclear weapon tests** scattered fallout over the whole of the earth's surface and caused the exposure of populations and the **contamination** of the food chain by a certain number of radionuclides, most of which, given their short radioactive half lives, have now vanished. There remain **cæsium-137** (30 years), **strontium-90** (29.12 years), some **krypton-85** (10.4 years) and **tritium** (12.35 years), and the isotopes of **plutonium** (half lives 87.7 years to 24,100 years). Currently, the doses corresponding to the fallout from these tests are essentially attributable to **fission products** (cæsium-137) and to carbon-14, rather than **activation products** and plutonium.

In the **Chernobyl accident** (Ukraine), which occurred in 1986, the total radioactivity dispersed into the atmosphere was of the order of 12 milliard milliard (10^{18}) becquerels over a period of 10 days. Three categories of radionu-

clides were disseminated. The first consisted of volatile fission products such as **iodine-131**, **iodine-133** (20.8 hours), **cæsium-134** (2.06 years), **cæsium-137**, **tellurium-132** (3.26 days). The second was composed of solid fission products and **actinides** released in much smaller amounts, in particular the strontium isotopes ^{89}Sr (half life 50.5 days) and ^{90}Sr , the ruthenium isotopes ^{103}Ru (half life 39.3 days) and ^{106}Ru (half life 368.2 days), and **plutonium-239** (24,100 years). The third category was rare gases which although they represented most of the activity released, were rapidly diluted in the atmosphere. They were mainly **xenon-133** (5.24 days) and **krypton-85**.

The contributions of the early atmospheric nuclear weapon tests and the Chernobyl accident to the total radioactivity are roughly 0.2% (0.005 mSv) and 0.07% (0.002 mSv) respectively.

The whole of the **nuclear-powered electricity production cycle** represents only about 0.007% of total radioactivity. Almost all the radionuclides remain confined inside the nuclear reactors and the **fuel cycle** plants. In a nuclear reactor, the reactions that take place inside the fuel yield **transuranics**. **Uranium-238**, which is non-**fissile**, can capture neutrons to give in particular plutonium isotopes ^{239}Pu , ^{240}Pu (half life 6,560 years) and ^{241}Pu (half life 14.4 years), and **americium-241** (432.7 years). The main fission products generated by the fission of **uranium-235** (704 million years) and **plutonium-239** are **iodine-131**, **cæsium-134**, **cæsium-137**, **strontium-90** and **selenium-79** (1.1 million years).

The main radionuclides present in releases, which are performed in a



Laurence Médard/CEA

Classical scintigraphy performed at the Frédéric-Joliot Hospital Service (SHFJ). The gamma-ray camera is used for functional imaging of an organ after administration, usually by the intravenous route, of a radioactive drug (radiopharmaceutical) to the patient. The radionuclides used are specific to the organ being studied: for example, technetium-99m for the kidneys and bones, thallium-201 for the myocardium. The injected radiopharmaceutical emits gamma photons, which are captured by two planar detectors placed at 180° or 45° according to the examination.

very strict regulatory framework are, in liquid release, **tritium**, **cobalt-58** (70.8 days), **cobalt-60**, **iodine-131**, **cæsium-134**, **cæsium-137** and **silver-110m** (249.9 days). In gaseous releases **carbon-14** is the most abundant radionuclide, emitted most often as carbon dioxide. In all the reactors in the world, the total production of radiocarbon dioxide amounts to one tenth of the annual production formed naturally by cosmic radiation.

In addition, certain radionuclides related to the nuclear industry exhibit **chemical toxicity** (Box D, **Radiological and chemical toxicity**).

B Human exposure routes

Human **exposure**, i.e., the effect on the body of a chemical, physical or radiological agent (irrespective of whether there is actual contact), can be external or internal. In the case of **ionising radiation**, exposure results in an energy input to all or part of the body. There can be direct **external irradiation** when the subject is in the path of radiation emitted by a radioactive source located outside the body. The person can be irradiated directly or after reflection off nearby surfaces.

The irradiation can be **acute** or **chronic**. The term **contamination** is used to designate the deposition of matter (here **radioactive**) on structures, surfaces, objects or, as here, a living organism. Radiological contamination, attributable to the presence of **radionuclides**, can occur by the **external** route from the

receptor medium (air, water) and vector media (soils, sediments, plant cover, materials) by contact with skin and hair (cutaneous contamination), or by the **internal** route when the radionuclides are **intaken**, by **inhalation** (gas, particles) from the atmosphere, by **ingestion**, mainly from foods and beverages (water, milk), or by penetration (injury, burns or diffusion through the skin). The term **intoxication** is used when the toxicity in question is essentially chemical.

In the case of **internal contamination**, the dose delivered to the body over time (called the **committed dose**) is calculated for 50 years in adults, and until age 70 years in children. The parameters taken into account for the calculation are: the nature and the intaken quantity of the radionuclide (RN), its

chemical form, its **effective half life**⁽¹⁾ in the body (combination of **physical** and **biological half lives**), the type of **radiation**, the mode of exposure (inhalation, ingestion, injury, transcutaneous), the distribution in the body (deposition in target organs or even distribution), the radiosensitivity of the tissues and the age of the contaminated subject.

Lastly, the **radiotoxicity** is the toxicity due to the ionising radiation emitted by the inhaled or ingested radionuclide. The misleading variable called **potential radiotoxicity** is a *radiotoxic inventory* that is difficult to evaluate and made imprecise by many uncertainties.

(1) The effective half life (T_e) is calculated from the physical half life (T_p) and the biological half life (T_b) by $1 / T_e = 1 / T_p + 1 / T_b$.

F From rays to dose

Radioactivity is a process by which certain naturally-occurring or artificial **nuclides** (in particular those created by **fission**, the splitting of a heavy nucleus into two smaller ones) undergo spontaneous **decay**, with a release of energy, generally resulting in the formation of new nuclides. Termed **radionuclides** for this reason, they are unstable owing to the number of nucleons they contain (protons and neutrons) or their energy state. This decay process is accompanied by the emission of one or more types of **radiation**, ionising or non-ionising, and (or) particles. **Ionising radiation** is electromagnetic or corpuscular radiation that has sufficient energy to ionise certain atoms of the matter in its path by stripping electrons from them. This process can be *direct* (the case with alpha particles) or *indirect* (gamma rays and neutrons).

Alpha radiation, consisting of helium-4 nuclei (two protons and two neutrons), has low penetrating power and is stopped by a sheet of paper or the outermost layers of the skin. Its path in biological tissues is no longer than a few tens of micrometres. This radiation is therefore strongly ionising, i.e., it easily strips electrons from the atoms in the matter it travels through, because the particles shed all their energy over a short distance. For this reason, the hazard due to

radionuclides that are **alpha emitters** is **internal exposure**.

Beta radiation, made up of electrons (beta minus radioactivity) or positrons (beta plus radioactivity), has moderate penetrating power. The particles emitted by **beta emitters** are stopped by a few metres of air, aluminium foil, or a few millimetres of biological tissue. They can therefore penetrate the outer layers of the skin.

Gamma radiation composed of high energy photons, which are weakly ionising but have high penetrating power (more than the **X-ray** photons used in radiodiagnosis), can travel through hundreds of meters of air. Thick shielding of concrete or lead is necessary to protect persons.

The interaction of **neutron radiation** is random, and so it is stopped only by a considerable thickness of concrete, water or paraffin wax. As it is electrically neutral, a neutron is stopped in air by the nuclei of light elements, the mass of which is close to that of the neutron.

- The quantity of energy delivered by radiation is the **dose**, which is evaluated in different ways, according to whether it takes into account the quantity of energy absorbed, its rate of delivery, or its biological effects.

- The **absorbed dose** is the quantity of energy absorbed at a point per unit mass of matter (inert or living),

according to the definition of the International Commission on Radiation Units and Measurements (**ICRU**). It is expressed in **grays** (Gy): 1 gray is equal to an absorbed energy of 1 joule per kilogramme of matter. The *organ absorbed dose* is obtained by averaging the doses absorbed at different points according to the definition of the International Commission on Radiological Protection (**ICRP**).

- The **dose rate**, dose divided by time, measures the intensity of the irradiation (energy absorbed by the matter per unit mass and per unit time). The legal unit is the gray per second (Gy/s), but the gray per minute (Gy/min) is commonly used. Also, radiation has a higher **relative biological effectiveness (RBE)** if the effects produced by the same dose are greater or when the dose necessary to produce a given effect is lower.

- The **dose equivalent** is equal to the dose absorbed in a tissue or organ multiplied by a **weighting factor**, which differs according to the nature of the radiation energy, and which ranges from 1 to 20. Alpha radiation is considered to be 20 times more harmful than gamma radiation in terms of its biological efficiency in producing random (or **stochastic**) effects. The equivalent dose is expressed in sieverts (Sv).

- The **effective dose** is a quantity introduced to try to evaluate harm

F (next)



Foulon/CEA

Technicians operating remote handling equipment on a line at the Atalante facility at CEA Marcoule. The shielding of the lines stops radiation. The operators wear personal dosimeters to monitor the efficacy of the protection.

in terms of whole-body stochastic effects. It is the sum of *equivalent doses* received by the different organs and tissues of an individual, weighted by a factor specific to each of them (weighting factors) according to its specific sensitivity. It makes it possible to sum doses from different sources, and both external and internal radiation. For internal exposure situations (*inhalation, ingestion*), the effective dose is calculated on the basis of the number of *becquerels*

incorporated of a given radionuclide (*DPUI, dose per unit intake*). It is expressed in sieverts (Sv).

- The *committed dose*, as a result of internal exposure, is the cumulated dose received in fifty years (for workers and adults) or until age 70 (for those aged below 20) after the year of *incorporation* of the radionuclide, unless it has disappeared by physical shedding or biological elimination.
- The *collective dose* is the dose received by a population, defined

as the product of the number of individuals (e.g., those working in a nuclear plant, where it is a useful parameter in the optimisation and application of the ALARA system) and the average equivalent or effective dose received by that population, or as the sum of the individual effective doses received. It is expressed in man-sieverts (man.Sv). It should be used only for groups that are relatively homogeneous as regards the nature of their exposure.

D Radiological and chemical toxicity

The chemical toxics linked to the nuclear industry include **uranium** (U), **cobalt** (Co), **boron** (B), used for its neutron-absorbing properties in the heat-exchange fluids of nuclear power plants, **beryllium** (Be), used to slow neutrons, and **cadmium** (Cd), used to capture them. Boron is essential for the growth of plants. Cadmium, like lead (Pb), produces toxic effects on the central nervous system. When the toxicity of an element can be both radiological and chemical, for example that of plutonium (Pu), uranium, neptunium, technetium or cobalt, it is necessary whenever possible to determine what toxic effects are radiological, what are chemical, and what can be either radiological or chemical (see *Limits of the comparison between radiological and chemical hazards*).

For **radioactive** elements with long physical **half lives**, the chemical toxicity is a much greater hazard than the radiological toxicity, as exemplified by rubidium (Rb) and natural uranium.

Thus the chemical toxicity of uranium, which is more important than its radiological toxicity, has led the French regulators to set the **ingested** and **inhaled** mass limits for uranium in chemical compounds at 150 mg and 2.5 mg per day respectively, regardless of the **isotopic** composition of the element.

Certain metals or **metalloids** that are non-toxic at low concentrations can become toxic at high concentrations or in their radioactive form. This is the case for cobalt, which can be **genotoxic**, selenium (Se) (naturally incorporated in **proteins** or **RNA**), technetium (Tc) and iodine (I).



Two-dimensional gel electrophoresis image analysis carried out in the course of nuclear toxicology work at CEA Marcoule Centre in the Rhone Valley.