Unit 18 Reading A

Biological effect

The particles or electromagnetic waves that are emitted from radioactive nuclei can have damaging effects on living cells. When they pass through living tissue they can remove electrons from atoms and molecules, leaving ionized particles. This can interfere with cell reproduction and lead to cell death, causing cancer and genetic defects. There are also constructive uses of radiation: it can be used to cure cancer and for medical diagnostic purposes.

The biological effects are directly proportional to the number of particles ionized. The number of particles ionized depends on the type of radiation and the amount of energy deposited in the living tissue. Radiation dosage is reported in terms of the amount of energy deposited in the mass of tissue that was exposed to radiation per unit mass of the tissue. The rad (*r*adiation *a*bsorbed *d*ose) is defined as

$$1rad = 10^{-2} J / kg$$

The biological effect of the same dose in rads is different for different types of radiation. A unit that takes the type of radiation into account is the roentgen equivalent man (rem). A rem is the dosage in rads multiplied by a factor that depends on the type of radiation, the relative biological effectiveness factor (RBE):

$$rem = (RBE)(rad)$$

The RBE for different kinds of radiation is given in the table below. The same dose in rem produces the same effect on tissue.

Relative Biological Effectiveness

Type and energy of radiation	RBE
X rays	1
Gamma ray	1
Beta particles of 30keV or more	1
Beta particles of less than 30keV	1.7
Neutrons, thermal to slow (<0.02MeV)	2-5
Neutrons, 1-10 MeV (fast)	10(body), 30(eyes)
Protons, 1-10 MeV	10(body), 30(eyes)
Alphas from natural radioactivity	10-20

(from Peter Paul Urone, Physics with Health Science Applications, John Wiley and Sons, NY, 1986)

Biological Hazards

The biological effects of radiation exposure are directly related to the number of rems received. The effects can be divided into two categories: immediate (within days of exposure) and long-term effects.

Immediate biological effects of ionizing radiation are observable only for moderate to large doses (see Table 18.3). Note that the effects listed are for an exposure of the entire body in a short time. If only part of the body is exposed, the effects will be less severe. If the exposure is spread out over days, weeks, months, or years, the effects are also less severe. This is because most organs in the body are able to repair some of the damage, so the doses are not completely cumulative.

The most easily produced observable effects are changes in blood count. Because radiation interferes with cell reproduction, the systems with the greatest cell division, such as bone marrow, are most sensitive to radiation. Most references say that the smallest dose that can cause blood count changes is 25 rem, but some researchers have reported changes for doses as low as 10 rem. At somewhat higher

TABLE 18.3 / IMMEDIATE EFFECTS OF RADIATION—ADULTS
Whole Body, Single Exposure

Dose (rem)	
	No observable effect
	Slight decreases in white blood cell counts
	Temporary sterility; 35 for women, 50 for men
100–200	Significant reduction in blood cell counts, brief nausea and vomiting; rarely, if ever, fatal
200–500	Nausea, vomiting, hair loss, severe blood damage, hemorrhage
450	LD50—lethal to 50% so exposed within 30 days if untreated
500–2000	Worst effects due to malfunctions of small-intestine and blood systems; survival possible if treated
>2000	Fatal within hours from collapse of central nervous system and gastrointestinal system

doses, nausea and vomiting occur because the lining of the digestive system is rapidly reproducing and is therefore more sensitive than most body systems.

Peacetime deaths from the immediate effects of radiation are rare. Death usually occurs because the immune system depends on white blood cells and is badly disrupted; the victim dies of infection or pneumonia. Treatments for very high doses of radiation include bone marrow transplants.

Fetuses and children are much more sensitive than adults. Increases in miscarriages and birth defects are noticeable in women exposed to more than 20 rem. Values of LD50, the dose that is lethal 50% of the time if untreated, vary for different types of plants and animals, the more primitive being the least susceptible. For viruses, for example, LD50 is at least 100,000 rem.

Doses of less than 10 rem will be called **low doses**, those between 10 and 100 rem **moderate doses**, and those above 100 rem **high doses**.

Long-term biological effects of ionizing radiation are well established for high doses, fairly well established for moderate doses, and poorly known for low doses. The long-term effects are the inducement of cancer and genetic defects. The risk of cancer is greater and far better known than the risk of genetic effects. Both effects are due to the interruption of normal cell reproduction.

Table 18.4 gives the risk of death from radiation-induced cancer. Organisms with rapid cell reproduction are again seen to be more susceptible. The only exception is that the risk to children for all cancers

TABLE 18.4 / RISK OF DEATH FROM RADIATION-INDUCED CANCER[a]

Age at Irradiation	Type of Cancer	Latent Period (yr)	Absolute Risk (Deaths/10^6·yr·rem)
	Leukemia	0	25
	All others	0	25
0–9 yr	Leukemia	2	2
	All others	15	1
> 10 yr	Leukemia	2	1
	All others	15	
	Breast		1.5
	Lung		1.3
	Gastrointestinal		1.0
	Bone		0.2
	Other		1.0
			5.0

[a]The actual incidence of radiation-induced cancer is greater than the risk of death given here since significant cure rates are now achieved for many types of cancer.

Source: A. Edward Profio, *Radiation Shielding and Dosimetry* (Wiley-Interscience, New York, 1979). Used with permission.

other than leukemia is 1 while the risk to adults is 5. Children are apparently able to repair more of the radiation-induced damage. The latency period for radiation-induced cancer is shortest for leukemia (blood cancer). Again, this is because of the very rapid cell division in the bone marrow. Once the latency period is over, cancer may appear anytime in the following 25–30 years.

The following example illustrates how to use Table 18.4 to calculate the risk of death from radiation-induced cancer.

Genetic defects are another long-term effect of ionizing radiation. They do not occur in humans with as high a frequency as predicted by laboratory studies with animals. It is possible that this is due to a larger incidence of miscarriages in humans exposed to radiation than in animals so exposed. The transmission of recessive genetic defects to subsequent generations is also a genuine concern. No numbers will be quoted in this text because of their large uncertainties, but it can be said with confidence that the genetic effects of radiation occur with less frequency than does radiation-induced cancer.

It is necessary to consider the relative risks of low, moderate, and high doses of radiation. The numbers in Table 18.4 are based on statistics gathered for people exposed to large doses of radiation. When they are used to estimate the risk for low doses, the **linear hypothesis** is being assumed. The **linear hypothesis** is that low doses of radiation are proportionally as dangerous as high doses. For several reasons this is an overestimation of risk for low doses. One is that the body has a known ability to repair damage. Two doses of 100 rem each separated by only a week produce significantly milder immediate effects than a single dose of 200 rem. The long-term effects of 100 rem should therefore be less than half those of 200 rem. Some researchers even con-

TABLE 18.5 / MAXIMUM PERMISSIBLE DOSES—REM/YEAR

Occupational,[a] medical diagnostics	
Whole body, adults	5.0[b]
Whole body, minors	0.5
Whole body, pregnant women	0.5
Gonads, bone marrow, lens of eye	5.0
Skin, thyroid, bone (external exposure)	30
Skin, thyroid (internal exposure)	15
Hands, forearms, ankles, feet	75
Soft tissues and most other organs	15

[a]Nonoccupational, 0.1 of occupational. From nuclear power plants, 0.001 of occupational at plant boundary.
[b]Limited to no more than 3 rem/quarter.

clude that there is a threshold below which repair is complete and that there will be no risk from an exposure less than this threshold. The subject is still controversial, and it is perhaps prudent to overestimate risk where safety is involved.

Table 18.5 gives maximum permissible doses in rems per year as set by law. Higher doses are allowed for occupational exposures and those to parts of the body where there is relatively little cell reproduction taking place. Maximum permissible doses are not set to protect the individual, because the risk to the individual from such low doses per year is negligible. The philosophy is rather to protect the public as a whole from even a small number of cancers and genetic defects nationwide. Finally, the linear hypothesis is used to set these limits, another prudent overestimation of risk.

We now turn our attention to some of the sources of ionizing radiation in our environment and methods of radiation protection.

Background Radiation

We are routinely exposed to a number of sources of radiation, referred to collectively as **background radiation**. Table 18.6 lists the yearly background doses from various sources. Only the medical and occupational exposures can be avoided. Cosmic rays from the sun and outside the solar system cause more exposure at high altitudes, where there is less atmospheric shielding, than at low altitudes. The amount of natural radioactive isotopes in the environment also varies with location. Medical exposure comes almost entirely from x rays and is a significant fraction of average annual background radiation in the United States.

The effects of background radiation are so small that no one has been able to measure them. There are places in the world, specifically parts of Brazil and India, where background radiation is far higher than in the United States. Those populations show no measurable in-

TABLE 18.6 / BACKGROUND RADIATION

Source	mrem/yr	
Natural radiation—external		
Cosmic rays,	35–70	(from sealevel to 5000 ft.)
U.S. average	44	
Radionuclides in soil, building materials,	35–70	
U.S. average	40	
Natural radiation—internal		
^{14}C	1	
^{40}K	16	
^{226}Ra	1–350	(average close to 1)
Artificial radiation—external and internal		
Medical, dental	50–100	(average 73)
Fallout (e.g., ^{90}Sr)	4	
Occupational	1	
Nuclear power, to public	0.003	
Miscellaneous	2	
Total	144–608	
Average U.S. total	182	

crease in cancer. Furthermore, workers in the nuclear weapons industry and people living at high altitudes have lower than average incidences of cancer. This does not necessarily imply that background radiation is harmless or beneficial, but rather that its effects are so small that they are masked by other effects.

Radiation Protection

Efforts are made to limit exposure to any source of radiation since all radiation causes some damage. If there is no benefit to the exposure, as in medical diagnostics, then there is no reason to sustain even slight damage. The three methods of limiting doses are to limit exposure time, use shielding, and increase distance from the source.

Time of Exposure If the source of radiation is relatively constant, the dose is directly proportional to the time of exposure. One example is the use of sensitive x ray film so that exposure times can be small.

Shielding Shielding placed between a person and a source will absorb part or all of the radiation. Heavy elements are ideal absorbers because they have many electrons and because radiation loses most of its energy by interacting with electrons in a material. Lead aprons, for example, are used to shield patients being x-rayed.

Distance If the source of radiation is nondirectional, then the radiation levels around it decrease proportional to distance squared in a vacuum. If the source is not in a vacuum, the radiation levels decrease even faster with distance because of the absorbtion of materials, including air.

Other precautions, such as using radiation monitors and personnel film badges to record radiation levels and doses, usually amount to common sense. Whenever the risk is great, the rules and procedures for working with radiation necessarily become more restrictive.

18.5 RADIATION DIAGNOSTICS AND THERAPY

Ionizing radiation is used to diagnose numerous medical conditions. The doses in rems from diagnostic procedures are usually small. Large doses of ionizing radiation are applied for therapeutic purposes, almost exclusively for the treatment of cancer. The risk of exposure versus the benefit of the medical procedure is usually carefully considered, as in any medical procedure.

Diagnostic Uses of Ionizing Radiation

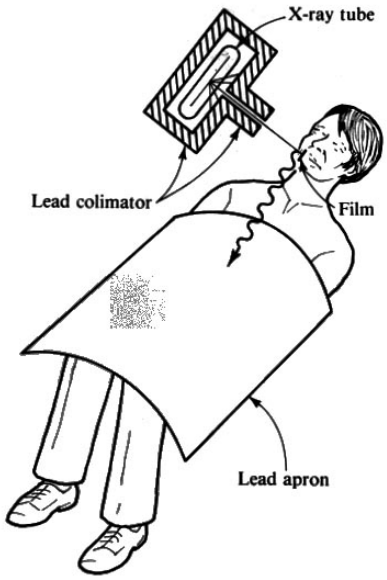
Nearly half the average background radiation in the United States comes from medical diagnostics (see Table 18.6). Most of that exposure is due to x rays.

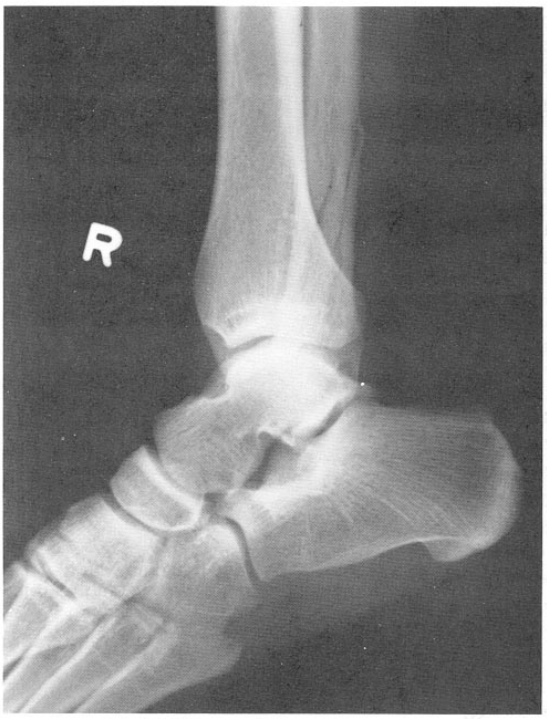
X rays were first used for medical diagnostic purposes shortly after their discovery by Roentgen in 1895. X-ray photons travel a significant distance in tissue before being absorbed. Their range depends on the density of the material encountered. The simplest medical x-ray diagnostics (called *x rays* for brevity) produce a shadow on film. The darkness of the shadow is representative of tissue density and thus can be used to detect, for example, broken bones or decay in teeth.

The typical x ray is produced as shown in Figure 18.8. Figure 18.9 shows examples of x ray photographs. Breaks in the bone in Figure 18.9(a) show clearly. In Figure 18.9(b) the patient has drunk an x-ray-absorbing contrast medium to make the upper gastrointestinal tract visible.

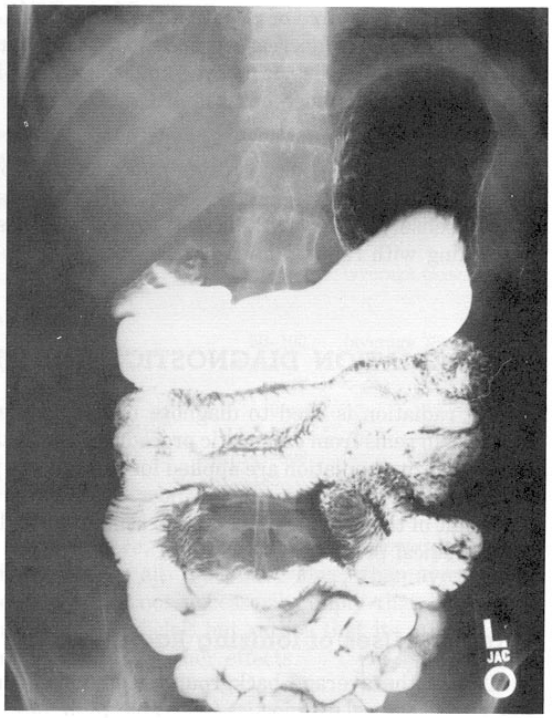
Many techniques are used to minimize radiation doses given in medical diagnostics. These include careful shielding, the use of sensitive films, and fluorescent image intensifiers. Table 18.7 lists representative doses for several x-ray diagnostic procedures. Most doses are small and their benefit clearly outweighs their risk. Indiscriminate use is still to be avoided.

Figure 18.8 X-ray machine with a colimated beam of x rays being used to photograph teeth. The lead apron shields part of the patient from scattered x rays.





(a)



(b)

Figure 18.9 **(a)** X ray showing spiral fracture of the fibula produced while shot putting. (X ray courtesy of the victim.) **(b)** X ray of the midsection of the body. Many features are recognizable, but the duodenum and small intestines are made more visible by a contrast medium containing barium. (X ray courtesy of Dr. J. Livoni, University of California, Davis Medical Center.)

Tomography and CT Scanners **Tomography** is a technique for obtaining a cross-sectional image of high quality and is most often performed using x rays and machines called computerized tomography (CT) scanners. In standard x-ray images overlapping organs shadow and block one another, but CT scanners eliminate these shadows. The scans are made by rotating the x-ray tube around the patient and using a large array of detectors, as shown in Figure 18.10(a). A computer analyzes the x rays received by each detector and constructs an image from this information, such as the one shown in Figure 18.10(b). Details as small as 1 mm are observable in CT scans. There is the added benefit that only the tissue being imaged is exposed to radiation since a very narrow beam of x rays is used. Allan MacLeod Cormack of the United States and Godfrey Hounsfield of Britain shared the 1979 Nobel Prize in medicine for developing computerized tomography.

Radiopharmaceuticals are being used increasingly in medical diagnostics. A **radiopharmaceutical** is any drug that contains a radioactive isotope. Radiopharmaceuticals can be designed to be very organ or system specific; that is, the body will concentrate them in specific

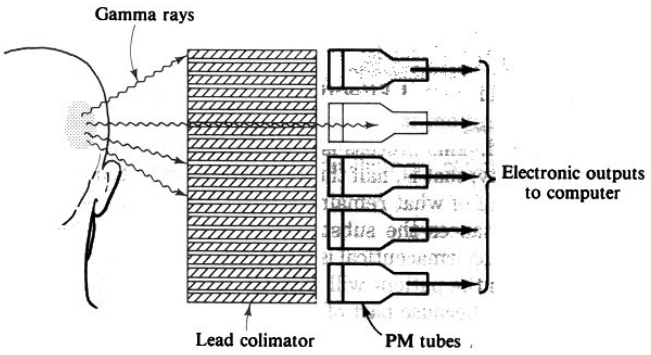
TABLE 18.7 / TYPICAL DOSES FOR X RAY DIAGNOSTIC PROCEDURES

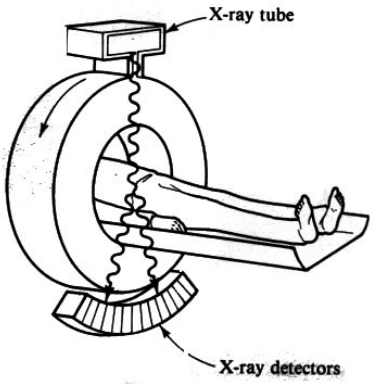
Procedure	Dose per film in rem to organ or region affected
Chest	0.07
Kidney, intravenous	0.2
Cerebral, intravenous	0.3
Skull	0.4
Dental	0.9
Spine or lower back	1–3
CT scan	1–7
Pneumoenchephalogram (brain)	9
Gastrointestinal fluoroscopic exam	
with image intensifier	1–4
without image intensifier	2.5–10

places. Diagnostic information is then obtained by measuring the nuclear radiation emitted by the selected isotope. Gamma-ray emitters are usually employed because gammas can escape the patient's body. Bone cancer, inflammation of tissues, organ function, blood supply, various tumors, and a variety of other information can be detected with radiopharmaceuticals.

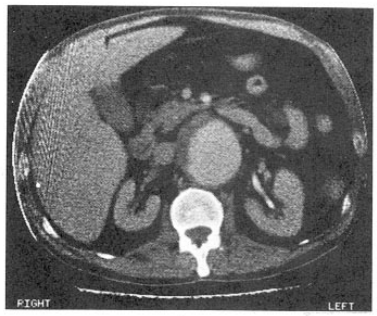
Figure 18.11 shows a detector system, called an *Anger camera*, used to measure nuclear radiation from radiopharmaceuticals. The colimator is designed to obtain position information. Detector output is sent to a computer for image construction. Figure 18.12 shows the images of two patients obtained by scanning them lengthwise with an Anger camera following injection with a drug containing ^{99m}Tc. The drug employed is concentrated in bones, indicating areas of greatest blood supply and consequently inflammation. The patient on the right has advanced bone cancer.

Table 18.8 lists some commonly used radiopharmaceuticals and their applications. The applications listed are a small fraction of those





(a)



(b)

Figure 18.10 **(a)** CT scanner taking an x-ray "slice" of a patient: The stationary array of x-ray detectors encircles the area examined so that the x-ray tube may make a 360° rotation, centered about the area of interest. The data is fed to a computer for analysis. **(b)** Cross-sectional image from a CT scanner. The liver, gallbladder, kidneys, small intestine, backbone, and spinal cord are visible. The large circle in the center is an aneurysm of the descending aorta with blood pooled around it. (CT scan courtesy of Dr. J. Livoni, University of California, Davis Medical Center.)

Figure 18.11 Anger camera used to obtain images in radiopharmaceutical diagnostics.

TABLE 18.8 / DIAGNOSTIC USES OF RADIOPHARMACEUTICALS

Procedure and Agent	Typical Activity (mCi)	Radiation Dose (rem)
Brain scan		
^{99m}Tc-pertechnetate	7.5	1.5 (colon)
^{113m}In-DTPA	7.5	4 (bladder)
Lung scan		
^{99m}Tc-MAA	2	0.7 (lung)
^{133}Xe	7.5	0.4 (lung)
Cardiovascular blood pool		
^{131}I-HSA	0.2	3 (blood)
^{99m}Tc-HSA	2	0.08 (blood)
Placental localization		
^{99m}Tc-pertechnetate	0.7	0.1 (colon)
^{113m}In-transferrin	1	0.1 (blood)
Thyroid scan		
^{131}I	0.05	75 (thyroid)
^{123}I	0.07	1.5 (thyroid)
Liver scan		
^{198}Au-colloid	0.1	5 (liver)
^{99m}Tc-sulfur colloid	2	0.6 (liver)
Bone scan		
^{85}Sr	0.1	4 (bone)
^{99m}Tc-STPP	10	0.5 (bone)
Kidney scan		
^{197}Hg-chlormerodrin	0.1	1.5 (kidney)
^{99m}Tc-iron ascorbate	1.5	0.8 (kidney)

in use, and more are being developed every year. A broad range of clever techniques is used to locate radiopharmaceuticals in specific places and to minimize the dose given in diagnostic applications. One of the most effective techniques for minimizing radiation exposures from radiopharmaceuticals is to use isotopes with short half-lives and drugs that the body excretes quickly. About 80% of all radiopharmaceutical procedures performed today employ ^{99m}Tc because of its short half-life. (The *m* in ^{99m}Tc means that the nucleus is in a metastable excited state.)

Biological Half-Life and Effective Half-Life The body removes substances by excretion, in an amount of time that depends on the chemical compound. This process is often like the decline of radiation due to nuclear decay; that is, half the substance is excreted in a certain amount of time, half of what remains in a similar amount of time, and so on. In such instances the substance is said to have a **biological half-life**. If a radiopharmaceutical is made from such a substance, then the radioactivity in the patient will decrease faster than it would from nuclear decay alone because part of the radioactivity is being excreted

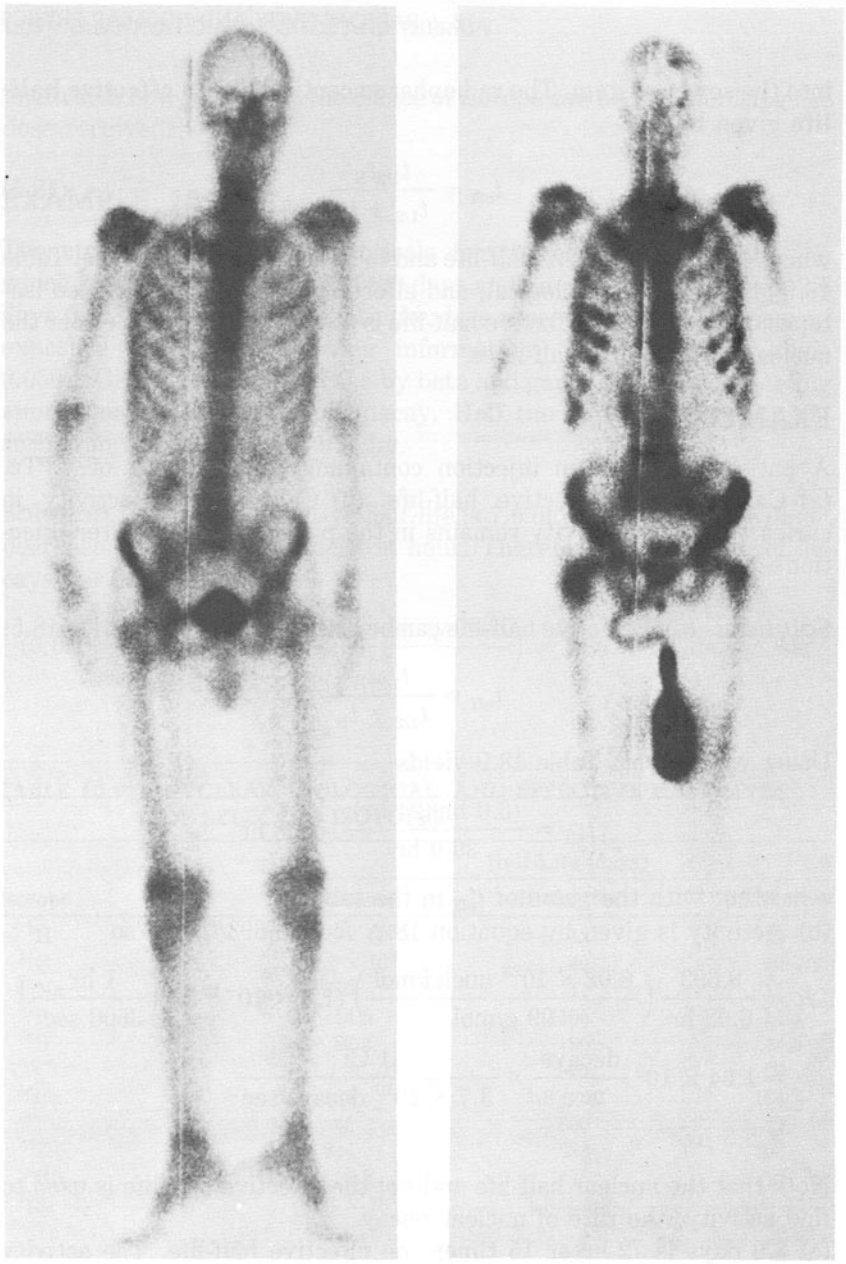


Figure 18.12 Two bone scans. The radiopharmaceutical used is concentrated in the bones and eliminated through the kidneys. The patient on the left is normal. Bone cancer is indicated in the patient on the right by the nonuniformity of exposure. (Courtesy of Dr. G. DeNardo, University of California, Davis Medical Center.)

into the sewer system. The radiopharmaceutical has an **effective half-life** given by

$$t_{\text{eff}} = \frac{t_{1/2} t_{\text{B}}}{t_{1/2} + t_{\text{B}}} \tag{18.5}$$

where t_{eff} is the effective half-life and t_{B} is the biological half-life. Table 18.9 gives nuclear, biological, and effective half-lives for selected isotopes. Note that the effective half-life is always shorter than either the nuclear or biological half-lives.

Therapeutic Uses of Ionizing Radiation

Therapeutic applications of ionizing radiation, called radiation therapy or **radiotherapy**, have existed for decades. Radiotherapy was once applied to ailments from acne to rheumatism, often with tragic consequences. It was not until the 1950s that the abuses of radiotherapy were prohibited by law. Radiotherapy is now used almost exclusively for the treatment of cancer.

Radiotherapy is appropriate for cancer treatment because cancer cells are rapidly dividing and consequently sensitive to ionizing radiation. Furthermore, there is often no effective risk-free alternative to radiation therapy. Finally, radiotherapy works; it improves survival rates for some types of cancer.

Radiotherapy is sometimes used in combination with the other two major types of cancer treatment, surgery and chemotherapy. Chemotherapy uses chemicals that, like radiation, inhibit cell division. As a result many of the side effects of chemotherapy are similar to those produced by radiation. It is usually possible to localize radiation better than chemicals, so the side effects of radiotherapy tend to be more localized than those of chemotherapy.

The central problem in radiotherapy is to concentrate radiation in abnormal tissue, giving as little dose as possible to normal tissue. The ratio of abnormal cells killed to normal cells killed is called the **therapeutic ratio**, and all radiotherapy techniques are designed to enhance this ratio. The effects of radiation on cancer cells are generally the same as those for normal cells, with two qualifications. First, rapid cell

division in cancer increases its sensitivity to radiation compared to normal tissue. Second, cancer tissue is usually oxygen poor, which decreases its sensitivity to radiation compared to normal tissue; this is known as the **oxygen effect**. Ionizing radiation produces more toxic end products when oxygen is plentiful in tissue. It is sometimes possible to oxygenate a tumor to overcome this problem, but in general larger doses of radiation must be used to compensate for the oxygen effect.

Many different forms of radiotherapy are in use. Radiation can be applied externally, as illustrated in Figure 18.13, most often using x rays or ^{60}Co gamma rays. Particle accelerators are also used to produce beams of other types of ionizing radiation, such as high-energy nitrogen nuclei, pi mesons, or neutrons. While some of these accelerator-produced beams can be more effective than x rays or gammas, they are much more expensive and much less commonly employed. Externally applied radiation is localized by focusing the beam, rotating the source, as shown in the Figure 18.13, and by shielding normal tissue.

Radiotherapy can also be administered internally with radiopharmaceuticals or implanted capsules, needles, or pellets. Internally applied radiotherapy has the advantage that radiation having a larger RBE can be used than in externally applied radiotherapy. (Large RBE implies short range, so the radiation could not penetrate from outside the body.) When capsules of radium, radioactive gold needles, or other

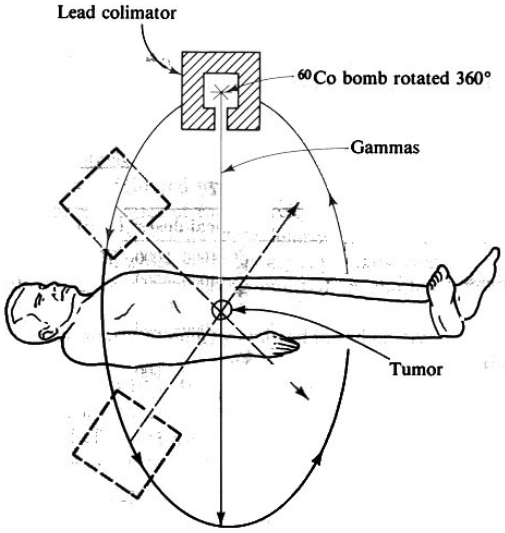


Figure 18.13 ^{60}Co treatment of malignant tumor. The dose to normal tissue is minimized by rotating the source about the patient in a circle centered on the tumor so that the common crossing point for the ^{60}Co gammas is the tumor.

radioactive isotopes are implanted in tumors, they are removed once a sufficient dose is administered.

Radiopharmaceuticals are used for cancer therapy only if they can be sufficiently localized to produce a favorable therapeutic ratio. One example is the use of radioactive iodine for thyroid cancer, but with larger doses than are used in thyroid imaging. A technique called **immunoradiotherapy**, currently being developed, attaches radioactive isotopes to antibodies produced by the patient against his cancer. The antibodies, it is hoped, will locate themselves almost exclusively in cancerous tissue.

Table 18.10 indicates typical doses given to cancerous tissue in radiotherapy. The doses are not fatal because they are localized in one part of the body and spread out over several weeks of time. The upper limit to the radiation given is always determined by the unavoidable exposure of normal tissue. Note that larger doses are given to cancers located in tissues that are relatively resistant to radiation (e.g., the adult brain, since there is no cell reproduction in it).

Radiotherapy is spread over many weeks because it is not possible to give enough radiation in a single dose to kill the cancer but spare the patient. Both the patient and the cancer recover somewhat between treatments, but cancerous tissue recovers less since the radiation is concentrated in it. Complete eradication is sometimes possible. Cures are not always achieved or even attempted. Lung cancer, for example, cannot ordinarily be cured using radiation because lung tissue and blood are too sensitive to radiation to permit doses large enough to eradicate the cancer completely. But statistics show that life is prolonged, symptoms are alieviated, and survival chances are improved by radiotherapy for many forms of cancer, including lung cancer.

The decision whether to use radiotherapy in cancer treatment and whether to use it in conjunction with surgery and chemotherapy is

TABLE 18.10 / CANCER RADIOTHERAPY

	Typical doses[a] (rem)
Lung	1000–2000
Hodgkin's disease	4000–4500
Skin	4500
Ovarian	5000–7500
Breast	5000–8000 +
Bladder	7000–7500
Head (brain)	8000 +
Neck	
Bone	
Soft tissue	
Thyroid	

[a]Usually given at 200 rem/treatment, from three to five times per week.

complex and contains an element of subjectivity. Physicians rely on an evolving body of statistical data and their own experience. Many factors must be weighed, including the possible inducement of another cancer and the chances of survival without radiotherapy.