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Physics of diagnostic imaging for medical students

Original title:

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Comments to English edition:

This text presents the physical grounds of methods of diagnostic imaging without recourse to higher mathematics. This was not always easy; I am aware that metaphors used to bridge the formal deduction occasionally missed the parts of reality.

There are a lot of good textbooks on basic aspects of medical imaging, but the target populations are usually required to have a college background is mathematics and physics. This texts targets medical students and residents, but may be useful to other profiles, as well.

There are few details, so that student does not have to resolve important from side issues.

D.E. (January, 2013)

Chapter I
IONISING RADIATION

• Atomic nucleus

Atom is made of nucleus and electron cloud
Atom does not behave as macroscopic objects
Atomic nucleus: hidden part of atom
Isotopes: variants of the same element

• Radioactive decays

Stable nuclei have balanced numbers of protons and neutrons
Radioisotopes have unstable nuclei
Majority of radioisotopes are artificial
Unstable nucleus undergoes violent changes
Alpha decay: heavy unstable nucleus rejects helium nucleus
In beta decay some particles disappear and others are created
By gamma decay nucleus disposes excess energy
Radioactive nuclei die without getting old

• Radiation and matter

Radioactive radiation ionize matter
Particle radiation loses energy in small steps
Particle radiation ionizes most before stopping
Gamma rays loose energy once or in several steps
Gamma rays are more penetrable than particle radiation

• Dosimetry

Source and field of ionizing radiation
Two quantities describe radiation effects
The effects of radiation can be predicted or measured
Absorbed dose can be predicted by measuring exposure
Ionization is biologically harmful
We are most irradiated by natural sources

Atomic nucleus

ATOM IS MADE OF NUCLEUS AND ELECTRON CLOUD

Atomic nucleus is in center of an atom, contains almost all of its mass (99.9%), but occupies negligible fraction of its volume. In the space around nucleus is the electron cloud. Atom of an element with **atomic number** Z has Z electrons. Electron is a carrier of unit negative electric charge.

Atomic nuclei are built from **protons** and **neutrons**, or **nucleons** in common. Proton carries unit positive electric charge, while neutron is electrically neutral. Number of protons in nucleus equals the atomic number, which is also number of electrons. Therefore atom as a whole is electrically neutral. Denoting by N the number of neutrons in nucleus, total number of nuclei is $Z+N$. This is the **mass number,** A. Therefore:

$$A=Z+N$$

Coulomb force is attractive between protons and electrons, keeping the later confined to space around nucleus. Nucleons are kept together by attractive **nuclear (strong) force**, overcoming Coulomb repulsion between protons. On small intranuclear distances the nuclear force is by far stronger than electric (Coulomb) force, but, as the distance increases, it quickly vanishes to zero.

ATOM DOES NOT BEHAVE AS MACROSCOPIC OBJECTS

The events in atom, and especially in its nucleus, can be related to events in our macroscopic world only rarely and approximately. It is naive to consider the atom as a solar system, with nucleus as the Sun and planets as electrons, where the attractive electric force stands for gravitation. The satisfactory description of an atom provides **quantum mechanics**, not classical physics. Quantum physics describes atom as bound microsystem: the electrons are confined to space around nucleus, having however discrete energies, which cannot be infinitely close. By absorption of exact energy quanta the electrons can jump to higher energy states, and the same energies are released when they return to lower energy states. The similar holds for nucleons, but their energy stairs are much higher, due to much stronger forces acting between them.

ATOMIC NUCLEUS: HIDDEN PART OF ATOM

When two atoms come close their electron clouds only partially overlap, each cloud blocking the space around its nucleus. When two or more atoms join into molecule, their outer electrons make up the common electron cloud. Relatively intensive exchanges in energy and other electron characteristic that occur in these reactions do not affect the atomic nuclei, due to their isolation and very high energy differences between possible energy states. Thus, nucleus is an isolated part of

atom; it interacts with electron clouds and take part in electron rearrangements (chemical reactions), but does not change itself.

This is valid for great majority of atomic nuclei that make up our surrounding. Our interest, however, are exceptions from this rule, which will be discussed in the remaining sections of this chapter.

ISOTOPES: VARIANTS OF THE SAME ELEMENT

Generally, an atom of the chemical element having symbol X is denoted as X-*A*, and its nucleus as ${}_{z}^{A}\mathrm{X}$. Atoms having the same proton/electron number Z, but different neutron number *N* are **isotopes** of the same chemical element. Isotopes of the given element do not differ chemically, sharing the same arrangement of electron clouds, unaffected by electrically neutral neutrons. The isotopes of an element also share many other (than chemical) characteristics, like rigidness, viscosity, color. However, isotopes of an element differ in nuclear (and thus atomic) masses; therefore their macroscopic densities vary. In nature the majority of elements are present as mixtures of isotopes, with one of them prevailing.

Example 1. *There are three oxygen isotopes, each having* Z=*8, while neutron numbers are* N=*8,* N=*9 and* N=*10. Their mass numbers are* A=*16,* A=*17 i* A=*18, which is denoted by: O-16, O-17 i O-18. In nature 99.758% is O-16 isotope, 0.03 % O-17 isotope, and the rest of 0.204% O-18 isotope.*

Aside from density and details of nuclei (that capture interest of nuclear physicists), isotopes of an element can sometimes differ in one extreme characteristic. The nuclei of some isotopes of an element are stable, while other isotopes have nuclei that change their structure, resulting in enormous bursts of energy. The unstable isotopes of an element are called **radioisotopes**.

Example 2. *There are three hydrogen isotopes: hydrogen-1 (H-1), deuterium (H-2) and tritium (H-3). The nuclei of deuterium and tritium comprise a proton and one or two neutrons, respectively. In natural hydrogen there is 99.985% hydrogen-1 and only 0.01 % deuterium. Tritium is artificially produced in scientific laboratories and extremely rarely in natural nuclear processes induced by cosmic rays. However, tritium is unstable and disappears.*

Isotope means "on the same spot". When a single element is referred (the place in periodic system defined), the term isotope (X-A) is thus adequate. When isotopes of different elements are referred, more adequate term is **nuclide**, or **radionuclide**, if unstable.

Radioactive decays

STABLE NUCLEI HAVE BALANCED NUMBERS OF PROTONS AND NEUTRONS

Nuclear force dominates over repulsive Coulomb force only on short distances between neighboring protons. However, more separated protons interact only by electrical repulsive force. Neutrons play role in overcoming this repulsion since they attract the neighboring nuclei (protons and neutrons, irrespectively), but do not have repulsive component, like protons. In order that a nucleus is stable the number of neutrons should exceed the number of protons, especially in case of heavier elements (FIGURE 1.1).

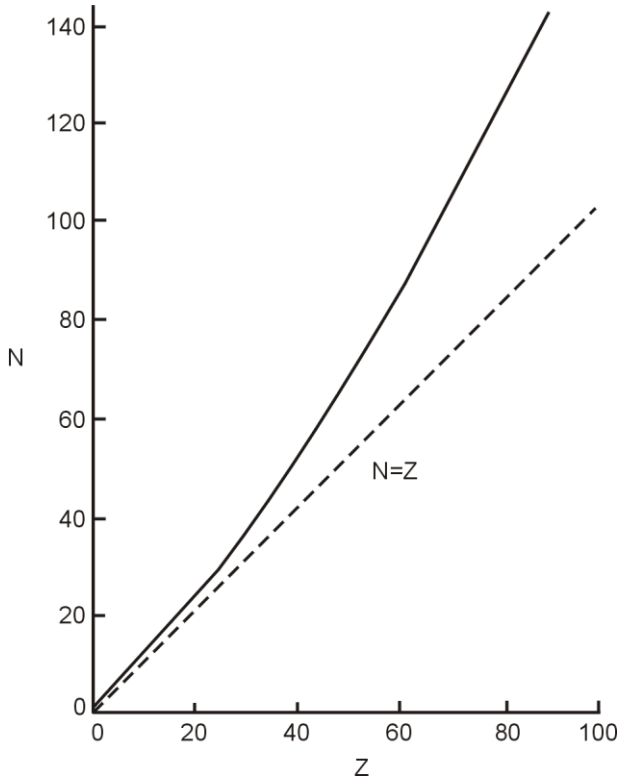


FIGURE 1.1 Association between number of neutrons N and number of protons Z in nuclei of various nuclides. Stable nuclei are in close vicinity to full line, called the stability line. At the beginning, the stability line is closed to line N=Z, i.e. in light stable nuclei the number of protons and neutrons is roughly equal. As Z increases, for stable nuclei, N/Z ratio approaches 1.5.

RADIOISOTOPES HAVE UNSTABLE NUCLEI

When Earth was created various elements emerged, each having various isotopes. Some isotopes of an element had unfavorable *N/Z* ratio and disappeared quickly, other, less stable, can be found even today. These are **natural radioisotopes**. The isotopes that were created with favorable *N/Z* ratio make the vast majority of matter. Most elements have several stable isotopes. Also, most elements do not have natural radioisotopes.

MAJORITY OF RADIOISOTOPES ARE ARTIFICIAL

Natural radioisotopes are rare and, for medical use, have unfavorable characteristics (slow, chain decay). For medical and other uses most commonly one uses **artificial radioisotopes**, obtained in nuclear reactors and particle accelerators. We can now make radioisotopes of all elements; over 1000 radionuclides have been synthesized as yet. Heavier elements have more radioisotopes; for example iodine has 15 radioisotopes and hydrogen only one (tritium).

UNSTABLE NUCLEUS UNDERGOES VIOLENT CHANGES

Unstable nucleus spontaneously tends to achieve the stable state, in a single step, or in several steps. The spontaneous change of a nucleus, without external influence, is called **radioactive decay**, while particles and photons thus created is **radioactive radiation**. The basic characteristic of radioactive radiation is enormous energy of created particles and photons. This energy (E) results from a loss in mass (m) of unstable nuclei upon transformation, according to famous Einstein equation $E=mc^2$, where c is the speed of light; 300 000 km/s. In consequence, a single particle of a radioactive radiation has sufficient energy to change structure of 10 000 molecules of a body, and, also, can be detected by our macroscopic electronic devices.

→ *Often in medicine we use radioactive sources with very low intensity of radiation (unable to raise a temperature of 1 dl of water for 1 °C in 1 hour).This means that we are dealing with very small number of particles (or photons) that are emitted by unstable nuclei in unit time. However, the energy of a single particle is enormous, so that the penetrating power and biological effects by far exceed the effects of non-radioactive radiation (e.g. visible light) or mechanical waves of the same intensity.*

ALPHA DECAY: HEAVY UNSTABLE NUCLEUS REJECTS HELIUM NUCLEUS

Some heavy unstable nuclei transform to a stable state by emitting high-energy projectile, which is helium nucleus, composed of two protons and two neutrons. This spontaneous process is **alpha-decay**, and the ejected helium nucleus is **alpha-particle (α-particle)** or **alpha-radiation**. In this process the initial nucleus (parent nucleus) transforms to another nucleus (daughter nucleus), which has 2 protons and two neutrons less.

The example is alpha decay of radium-226 nucleus into nucleus of radon-222, which is symbolically presented:

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

Kinetic energy of this alpha particle is about 4.8 MeV, an enormous energy in micro-world.

Alpha-emitters (radioisotopes which stabilize by alpha decay) are rarely used in medicine, mainly in oncology, as implants which destroy the neighboring tumor tissue (brachy-therapy). They have no place in medical diagnostics.

IN BETA DECAY SOME PARTICLES DISAPPEAR AND OTHERS ARE CREATED

Negative beta particle (β^-) is a very fast electron emitted by nucleus that underwent **beta-minus decay**. Beta particle should be distinguished from orbital electron. Radioisotopes having excess of neutrons usually stabilize in this way; one neutron from the nucleus transforms to proton, which stays in the nucleus, and an electron, which is ejected from the nucleus. The nucleus also emits **antineutrino** (ν^-), which accounts for the part of energy released. Antineutrino (as its antiparticle neutrino) has no mass and no charge, and thus no effect on a matter.

Upon beta-minus decay the nucleus retains its mass number, but its atomic number increases for one, i.e. it becomes the nucleus of another element. In this way the nucleus of phosphorus-32 transforms to sulphor-32 nucleus:

$$^{32}_{16}\mathrm{P} \rightarrow ^{32}_{17}\mathrm{S} + \beta^- + \nu^-$$

Artificial beta-minus emitters (radioisotopes which stabilize by beta-minus decay) are produced in nuclear reactors by exposing the stable isotopes to flux of slow neutrons. Beta-minus emitters are the commonest radioisotopes in medical applications. They are used in brachy-therapy, and phosphorus-32, which in blood binds to erythrocytes, in therapy of polycytemia rubra vera. More commonly beta-minus emitters are used as radioindicators in in-vitro measurements (hydrogen-3, carbon-14) and as secondary sources of gamma rays in imaging diagnostics (see next section).

Positive beta-particle (β^+) is a very fast **positron**, particle which has the same mass as electron and carries the charge of the same magnitude, but opposite sign. It is emitted by a nucleus having excess of protons (lack of neutrons). So, in the process of stabilization, one proton transforms to neutron and stays in the nucleus, while positron and neutrino are ejected from the nucleus. After **beta-plus**, the daughter nucleus has the same mass number as the parent nucleus, while her atomic number decreases for one. Beta-plus decay is always accompanied by **annihilation radiation**. The created positron decelerates in traversing matter. When it almost stops and comes in the vicinity of electron (his antiparticle), after short mingling (‘death dance’), they both disappear. The energy equivalent of their masses emerges in form of two gamma rays, each having 511 keV of energy, leaving in opposite direction. This is used in creating the image of distribution of beta-plus nuclides in body (2. chapter).

The energy of β^- particle varies from zero (all energy of decay taken by antineutrino) to total energy of decay (all energy taken by β^- particle). On average the energy of β^- particle equals 1/3 of total energy of decay. The same is valid for beta-plus decay (FIGURE 1.2).

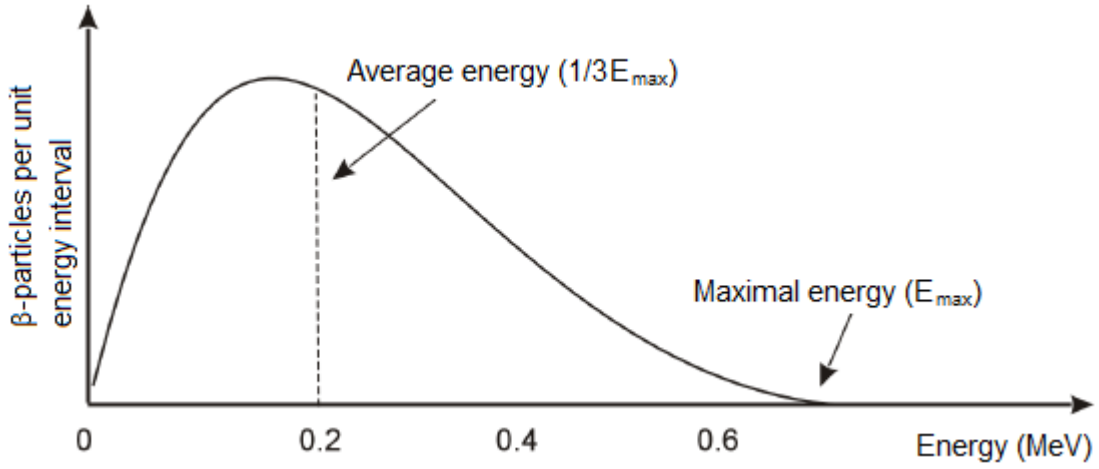


FIGURE 1.2 Beta-plus energy spectrum of Cu-64.

Beta-plus decay is also called **positron decay**, and radionuclides prone to this type of stabilization are **positron emitters**. There are no natural positron emitters. They are produced by exposing stable isotopes to flux of fast particles (mostly protons) in particle accelerators. In order to incorporate in nucleus foreign proton has to have sufficient energy to overcome repulsion of protons in the nucleus, until it is in the range of attractive nuclear forces. That's why it is easier to produce light positron emitters, which have only few protons. Thus, available for medical use are positron radioisotopes of oxygen (O-14), carbon (C-11), nitrogen (N-13), etc. The positron emitters are used as radiotracers in exploiting the metabolism of these elements (2. chapter). Positron emitters decay rapidly since the excess of protons is relatively large (unfavorable *N/Z* ratio).

Instead of beta-plus decay, unstable isotope having excess of protons can transform by **electron capture (EC)**. Example is nucleus of iodine-125; by 'eating' its own orbital electron one proton transforms to neutron, as in beta-plus decay, producing the nucleus of tellurium-125.

*Beta decays show that elementary particles can transform one into another. The transformation of nucleons (proton into neutron and vice versa) in beta-decay is caused by **weak force** (weaker than electric force, and by far than strong, nuclear force).Weak force acts between particles called **leptons** (electron, neutrino and their antiparticles are leptons). The transformation of nucleons, mediated by weak force, is always accompanied by ejection of two leptons, which are particle-antiparticle pair.*

BY GAMMA DECAY NUCLEUS DISPOSES EXCESS ENERGY

Stable nuclei are in their ground state, which, unlike orbital electrons, is unaffected by atom structural changes due to interactions with neighboring atoms. Stable nuclei can climb (or descent) over their energy stairway only in extreme, laboratory conditions.

Huge energies, comparable to height of nucleus energy stairs, are released during radioactive decays. After alpha or beta decay the daughter nucleus is often not in its state of lowest energy (ground state), but in one of possible states of higher energy. This, however, lasts very shortly; the nucleus fast descents to the ground state, releasing the energy surplus in the form of a photon, which is called **gamma photon** or **gamma ray.** Such photon has energy up to million times greater than light photon. The process is called **gamma decay.** Strictly speaking this is ill-coined phrase since in gamma decay the atomic number does not change.

→ *Thus, in gamma decay, unlike in beta and alpha decays, no new element is created*

The excited nucleus can jump to the bottom of its stairways in one or several steps. Thus gamma decay may result in one or several gamma rays of varying energies.

Sometimes, instead of gamma decay, the nucleus uses other way to dispose the excess energy. Take, for example, the nucleus of tellerium-125, created by electron capture of iodine-125. The daughter nucleus has 35 keV energy surplus, which can be given off by emission of gamma ray of energy $E_\gamma = 35$ keV. More often the nucleus hands over this energy to its K electron, which then leaves the atom. Subsequently, the electrons from higher energy orbitals fill the empty state of lower energy. The emitted photons, which take off the energy differences, are called **characteristic X radiation** and this type of decay **internal conversion** or **isomeric transition**. Gamma decay and internal conversion are often concurrent processes.

Electromagnetic force, which causes gamma decay, is stronger than the weak force. This implies that gamma decay is almost instantaneous, while beta decay is much slower. Exceptionally, relatively slow gamma decay occurs. This happens when, following beta decay, the daughter nucleus is in **metastable state.** This is the state of increased energy, but transitions to lower states are hardly possible, so that nucleus remains in elevated energy state for a relatively long time.

In radionuclide imaging diagnostics only gamma rays are useful; the beta radiation is absorbed in tissues, causing unwanted radiation burden. Metastable emitters are most useful for radionuclide diagnostics for two reasons:

1. If isolated from parent radio emitter (commonly beta emitter), one gets pure gamma emitters, without unwanted particle radiation.
2. Relative slow decay enables use, without necessity to always have in close vicinity the parent radio emitter.

RADIOACTIVE NUCLEI DIE WITHOUT GETTING OLD

Unstable nuclei transform suddenly, without gradually changing their structure. They are not like living beings which gradually get older, having the life-span

around the average expectations. In contrast, the radioactive decay can be compared to a game of roulette or tossing the dire, where some outcomes are fatal, the other not. The older nucleus that survived many dire tossing is not structurally different than the newly born nucleus, which has not been in the game yet. In fact there are no old and new nuclei (‘a dire has no memory’).

→ *Unstable nucleus has a certain probability of decay in unit time, irrespectively on past, i.e. this probability is constant in time.*

This probability is characteristic to each radionuclide and is called the **decay constant (λ)**, with measuring unit 1/second.

Let as start with 1 million nuclei of some radionuclide at a given time. Comparing their destiny with outcome of tossing a coin, assume that ‘head’ implies life and ‘tail’ means death. After first tossing there would be about 500000 survivors since both probabilities are equal to 0.5. After subsequent tossings there would be first about 250000 parent nuclei, then 125000, etc. In other words, after some time, (given by frequency of ‘tossing a coin’, which increases with radionuclide instability), there will be ½ of the parent nuclei, then, after the same time intervals, ½ (1/2) = ¼, 1/8, 1/16, etc. This specific time is the greater the smaller the decay constant, and is called the **half-life ($T_{1/2}$)**.

In case of Tc-99m the half-life is 6 hours (FIGURE 1.3).

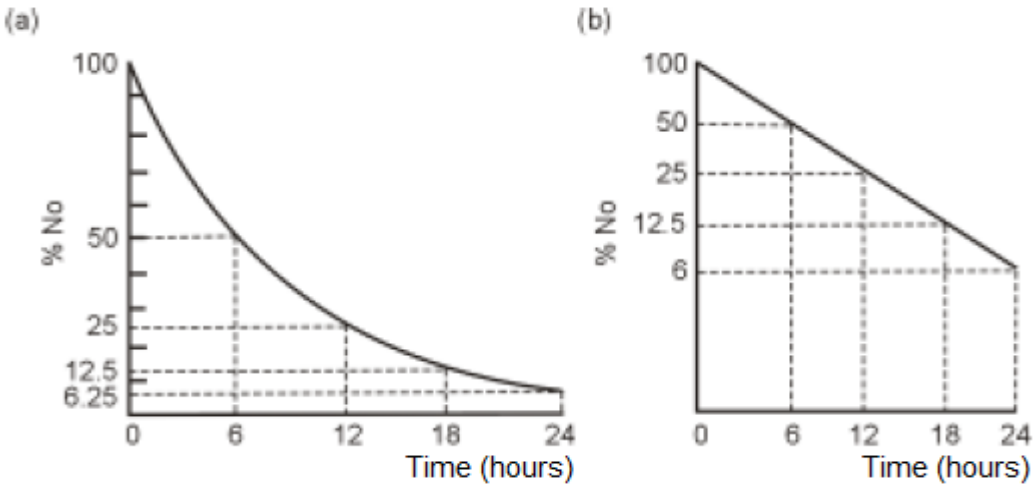


FIGURE 1.3 The initial number No of radionuclide Tc-99m in time, presented in linear (a) and logarithmic scale (b).

Radionuclides which decay slowly (have small λ and great $T_{1/2}$) can be found in nature, while radionuclides with more unstable nuclei are only produced artificially (TABLE 1.1).

TABLE 1.1 Half-lifes ($T_{1/2}$) of some radionuclides

Radioisotope	Element	$T_{1/2}$
Natural		
U-238	Uranium	4.5 billion years
Ra-226	Radium	1600 years
K-40	Potassium	1.3 billion years
C-14	Carbon	5760 years
H-3	Hydrogen	12 years
Artificial		
Cs-137	Cesium	33 years
I-131	Iodine	8 days
I-125	Iodine	60 days
Co-60	Cobalt	5.3 years
P-32	Phosphor	14.3 days
Na-24	Sodium	15 hours
Tc-99m	Technetium	6 hours

(1.2)

Observe what is happening with our 100000 nuclei in the very short time, when the change in their number can be neglected. Assume that the decay constant is 0.1% in a second, i.e. λ=0.001/s. The statistically expected number of transformations in one second will be 0.001x1000000 = 1000. In reality this number may be, for instance 940 or 1080, and very rarely exactly 1000.

→ *Radioactive decay is a random event, described by statistical laws, and one can never predict the exact outcome.*

Generally, if in a time *t* there are *N(t)* nuclei of a radionuclide with decay constant λ, the expected number of transformations in 1 second equals the product of a probability of a transformation of a single nuclei (λ) and the number of nuclei present *N(t)*. The number of transformations of nuclei of a radionuclide in unit time ($-\Delta N(t)/\Delta t$) is called **radioactivity**, or, short, **activity**- *A(t)*. Thus:

$$A(t) = -\Delta N(t)/\Delta t$$

$$\Delta N(t)/\Delta t = -\lambda N(t)$$

The minus sign accounts for a decrease of *N* in time. The solution of the above differential equation shows that *N* decreases mono-exponentially in time:

$$N(t) = N_0 e^{-\lambda}$$

where N_0 is the number of nuclei in time t=0. The above equation gives the association between decay constant and half-life:

$$\lambda = ln(2)/T_{1/2}$$

It also follow that radionuclide activity follows the same law:

$$A(t) = A_0 e^{-\lambda t}$$

In SI system the unit for radioactivity is Becquerel (Bq). One Becquerel is one transformation in one second. The old unit is Curie. One Curie equals $3.7 \cdot 10^{10}$ Bq.

The table below summarizes the main features of alpha, beta and gamma decays. 'Pure' alpha, beta or gamma emitters are rare. The combined decays alpha/gamma and beta/gamma are commonest.

TABLE 1.2 Main characteristics of different modes of radioactive decay

Decay	Parent nucleus	Daughter nucleus	Radiation
alpha	Z/N	Z-2 / N-2	He-4 nucleus
beta-minus	Z/N	Z+1 / N-1	electron
beta-plus	Z/N	Z-1 / N+1	positron
gamma	Z/N	Z/N	gamma photon

Sometimes the daughter nuclei, granddaughter and even grand-granddaughter are unstable. These are chain radioactive decays (TABLE 1.3).

TABLE 1.3 Gradual transformation of U-238 in stable Pb-206.

Element	Isotope	Half-life	Radiation
Uranium	U-238	4.55×10^9 years	α
Thorium	Th-234	24.1 days	β,γ
Protactinium	Pa-234	1.14 minutes	β,γ
Uranium	U-234	2.69×10^5 years	α
Thorium	Th-230	8.22×10^4 years	α,γ
Radium	Ra-226	1600 years	α,γ
Radon	Rn-222	3.8 days	α
Polonium	Po-218	3.05 minutes	α
Lead	Pb-214	26.8 minutes	β,γ
Bismuth	Bi-214	19.7 minutes	α,β,γ
Polonium	Po-214	1.5×10^{-4} seconds	α
Lead	Pb-210	22.2 years	β,γ
Bismuth	Bi-210	4.97 days	β
Polonium	Po-210	139 days	α,γ
Lead	Pb-206	Stable	-

There can also be the **branching**, when some radionuclide can undergo more than one type of decay, as for example K-40 (FIGURE 1.4).

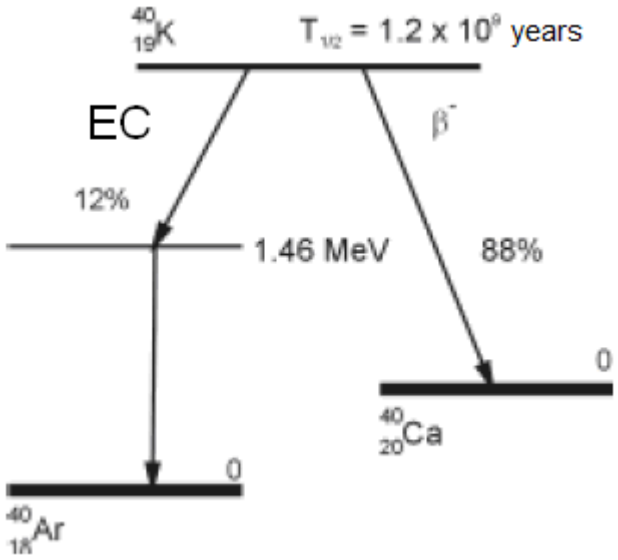


FIGURE 1.4 Potassium-40 decays very slowly, in two ways: in each 100 transformations, there are on average 88 β-minus decays, the rest is electron capture, followed by gamma emission.

Radiation and matter

RADIOACTIVE RADIATION IONIZE MATTER

In traversing matter, infrared radiation and visible light give off energy to facilitate molecular rotations and vibrations, which is seen as an increase in temperature of a medium. Other than thermal interaction, visible light and especially ultraviolet light, can release weekly bound valence electrons of a medium. In contrast to these radiations and mechanical waves, gamma radiation, and especially particle radiation (alpha and beta particles) have sufficient energy to eject even tightly bound electrons from inner orbitals of atoms of a medium. Moreover a single gamma photon or fast charged particle can **ionize** several thousand of atoms of a matter.

→ Ionization is the main effect of radioactive radiation in traversing matter; therefore radioactive radiation is also called **ionizing radiation**.

PARTICLE RADIATION LOSES ENERGY IN SMALL STEPS

Alpha and beta particles lose energy mostly in interacting with orbital electrons of a medium. Small portions of their tremendous energy are gradually spent on excitation (rising to higher energy levels) and ionization of thousands of electrons, mostly in outer orbitals. Alpha particle has large mass and, therefore, travels in straight line, with little staggering (FIGURE 1.5). In this way, the total trace of an alpha particle in a medium, its **range**, equals its **penetration depth**. The range of alpha particles of the same energy is approximately equal (FIGURE 1.6A). The range of alpha particle increased with its energy, but does not exceed several cm in air in majority of cases. This does not contradict the large energy of alpha particles since they spend their energy extremely densely, so that it is given off on a small distance. In this way the **specific ionization** of alpha particles, which is the number of ion pairs released on unit distance traversed, is very great.

→ *Alpha particles are stopped by the outer layer of human skin, so that they cannot reach internal organs. However, alpha particles are very dangerous when taken by ingestion or breathing, since they are absorbed in a small volume of tissue, completely destroying it. As a joke, one can say that alpha emitters are not dangerous as external source of radiation, but eating them is not recommendable.*

Beta particle has about 7000 times less mass than alpha particle; which is the same mass as orbital electrons. Therefore it straggles when going through matter, exhibiting tortuous trace (FIGURE 1.5). Beta particles of the same energy may not have the same range, and especially their depth of penetration differ. However, due to lower specific ionization, maximal penetration depth of beta particles in a medium is many times greater than in case of alpha particles of the same energy (FIGURES 1.6 A i B).

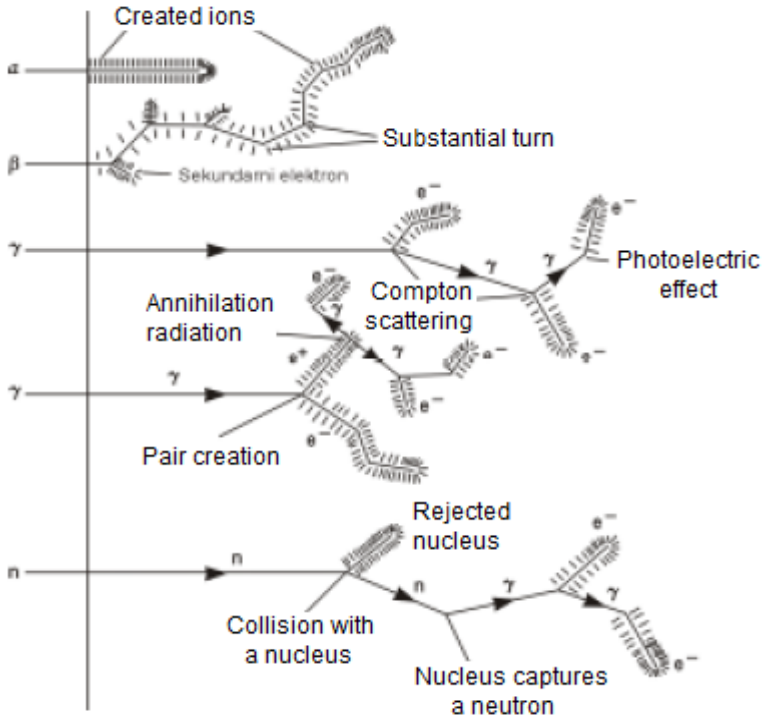


FIGURE 1.5 Schema of traces of ionizing radiation.

Aside from interacting with orbital electrons, the fast, light charged particles (beta particles or electrons accelerated in strong electric field) loose a part of their energy in interacting with nuclei of atoms of a medium. By this, the electrons decelerate, and the energy lost reapers as high-energy electromagnetic radiation called **X rays** or **Roentgen rays**. X photons differ from gamma photons in the way they are created, but both are high-energy, electromagnetic (non-particle) ionizing radiation. The energies of X photons used in diagnostic radiology are lower than majority of gamma radiations, while in radiotherapy one uses X photons having energy over 1 MeV. If one does not know the origin of high energy photon, there is no way to tell whether it is X or gamma photon; as far as interaction with matter is consider, these radiations are indistinguishable.

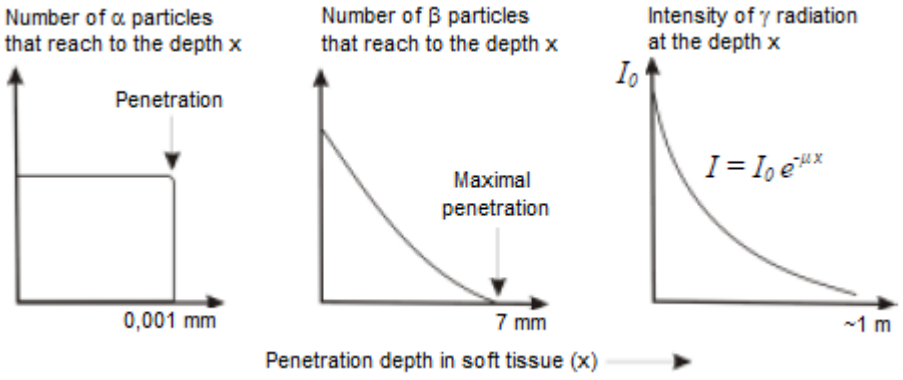


FIGURE 1.6 Penetration of ionizing radiation of 1MeV energy in soft tissue.

PARTICLE RADIATION IONIZES MOST BEFORE STOPPING

Compared to beta particle, alpha particle have greater specific ionization, because, due to larger mass, it moves slower, having more time to interact intensively with orbital electron it passes by. In the same way the slow stone does more damage to a glass than the fast bullet, that only makes a tiny hole. The same arguments explain why the specific ionization of alpha and beta particles increase as they decelerate and lose energy, being maximal at the end of journey (FIGURE 1.5).

GAMMA RAYS LOOSE ENERGY ONCE OR IN SEVERAL STEPS

In contrast to particle radiation, gamma photon traverses matter unchanged, without any interaction, until it reacts violently, delivering all or significant part of energy to the surrounding. In the same way as in radioactive decay one cannot tell when a certain nucleus transforms, one cannot tell which atom is to interact with gamma photon and how much energy will be transferred. There are, however, statistical probabilities of such events, which depend both on 'projectile' (energy of gamma ray Eγ) and 'target' characteristics (density and atomic numbers of elements of a medium). There are three ways of interaction of gamma (or X) photon and matter (FIGURE 1.7):

1. In **photoelectric effect** gamma (or X) disappears, delivering **all** its energy to tightly bound orbital electron, which gets high kinetic energy, leaves the atom and performs subsequent ionizations (similarly to beta particle, as described above). Photoelectric effect (photo-effect) is more probable for inner electrons in strong electric field of nucleus, than in weakly bound outer electrons. The probability of photo effect increases with cube of atomic number, so that heavy elements with high *Z* absorb electromagnetic radiation by this effect very efficiently. Of course, it is necessary that gamma ray energy E_γ at least equals the electron energy of binding. Since the binding energy of K electron (electron in first shell of atomic electron cloud) in iodine atom is 33 keV, and in lead atom 88 keV, the photons having energy in the range 33 to 88 keV can ionize K electrons of iodine, but not lead. Photo-effect is most probable when E_γ slightly exceeds the electron binding energy. As photon energy increases the probability of photo-effect decreases (FIGURE 1.8).
2. High energy photon can also interact with weakly bound (or free) electron in the way that resembles collision of billiard balls. In this collision electron receives a **part** of photon energy E_γ and, as in photo-effect, leaves the atom as a high energy projectile. The rest of E_γ is taken away in form of **lower** energy photon, going in **other** direction than the original photon (FIGURE 1.**7**). In the process, called **Compton scattering (or Compton effect)**, small changes in energy and direction of photon are more probable than large changes. As in case of collision of balls of equal masses, the Compton effect is most probable when E_γ equals the energy equivalent or electron mass, which is 511 keV (FIGURE 1.8). Since almost free electrons are involved, the atomic nuclei has no effect, so that Compton scattering does not depend on type of 'target' (atomic numbers of medium elements), but only on density of a free electrons.

The later is approximately proportional to medium density. Therefore, given $E_{\gamma,}$ the probability of Compton effect depends only on medium density.

3. There is still another way the very high energy photons interact with matter. When such photon happens to be in strong electric field, near the heavy nucleus, sometimes it will disappear; on account of creating the electron/positron pair (FIGURE 1.7). The energy equivalent of masses of electron and positron being 1.02 MeV (2 x 511 keV), E_{γ} has to be at least that much or greater (when the rest converts to kinetic energy of newly created particles). Since positron is an antiparticle, this process, called **pair creation**, is always accompanied by annihilation radiation as in the case of beta-plus decay. Pair creation is of concern only for photons having very large energies (only some gamma rays and X photons used in radiotherapy), in the medium containing elements with high atomic numbers.

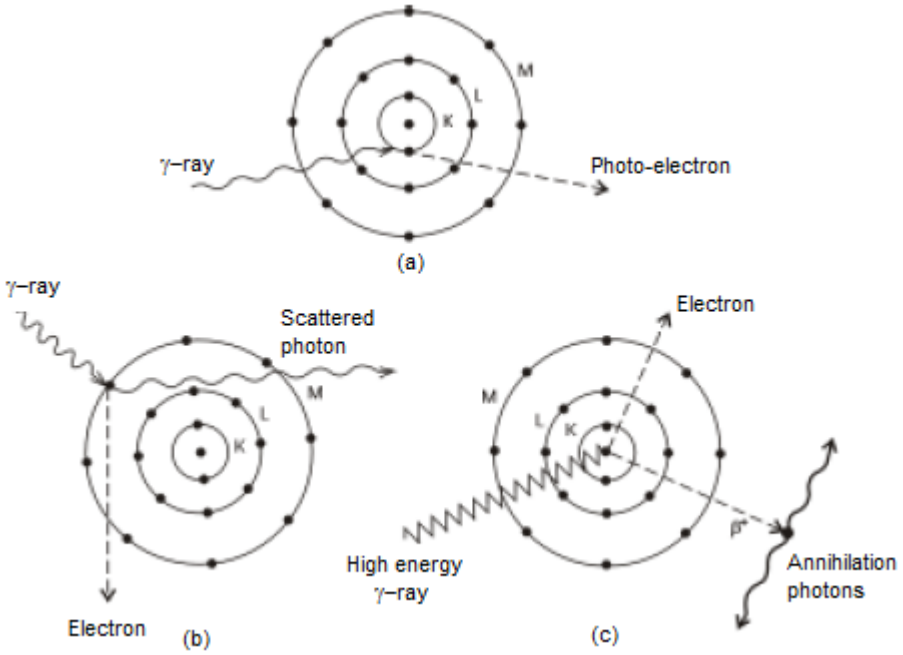


FIGURE 1.7 Gamma photon loses energy in three ways: (a) in photoelectric effect all energy is delivered to electron, (b) in Compton scattering a part of energy is delivered to electron, while weakened photon continues the journey in other direction, and (c) in pair creation gamma ray is converted to electron/positron pair. After short journey, annihilation of positron results in two gamma rays of 511 keV, leaving the battlefield in opposite directions.

Irrespectively on type of interaction a single gamma (or X) photon ionizes only one atom, whereas thousands of other ionizations are due to fast charged particles ejected from the atom following the initial ionization, and the couple of then may be due to photons created by Compton scattering.

→ *Particle radiation ionize matter directly, gamma photons indirectly. .*

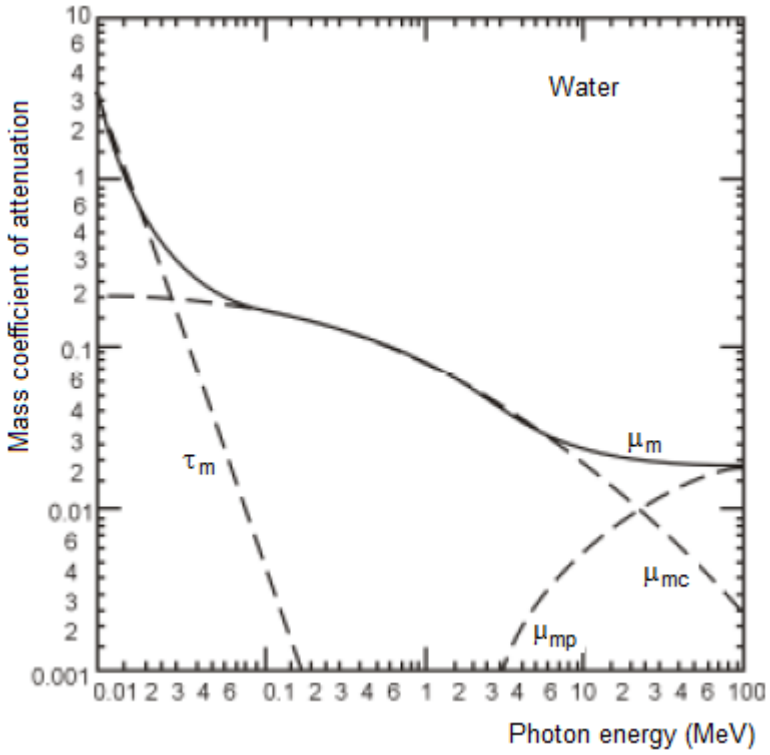


FIGURE 1.8 Mass coefficient of attenuation (μm) as function of photon energy, presented as sum of three components: mass coefficients of attenuation for photoelectric effect (τm), Compton scattering (μmc) and pair creation (μmp).

GAMMA RAYS ARE MORE PENETRABLE THAN PARTICLE RADIATION

In contrast to fast charged particles, which lose energy continuously, gamma (or X) photons don't have the defined range. The transport of high-energy photons resembles the transformation of unstable nucleus: photon that traversed some path in matter has the same energy and thus the same probabilities of interaction as it had on the beginning, in the same way as an unstable nucleus does not change before it transforms to a more stable formation. Thus, in the same way as the number of radioactive nuclei decays in time exponentially (equation 1.2), the initial

intensity (power per unit surface of a beam) of radiation of photon energy E_γ, I_0, decreases upon traversing the thickness d of an absorber according to relation

$$I = I_0 e^{-\mu d} \quad (1.4)$$

where μ is the sum of probabilities of all effects capable of elimination of photon from its direction of propagation (photoelectric effect, Compton effect and pair creation), per unit distance travelled. This quantity is **linear coefficient of attenuation** and depends on energy of gamma ray and on medium:

$$\mu = \mu(E_\gamma, \text{medium})$$

Linear coefficient of attenuation is large in materials of high density and high atomic number, which are thus good absorbers of electromagnetic radiation.

From equation (1.4) it follows that the depth of an absorber which halves the initial radiation intensity- **half-value thickness ($d_{1/2}$)** relates to linear coefficient of attenuation through:

$$d_{1/2} = ln2/\mu$$

Instead of linear coefficient of attenuation, μ, one also uses so called **mass coefficient of attenuation $\mu_\rho = \mu/\rho$.** In this way, by screening the effect of density, one emphasizes the importance of type of absorber. So, μ_ρ for water is the same for liquid water, ice or water vapor. The equation (1.4) can also be expressed as:

$$I = I_0 e^{-\mu_\rho (\rho \cdot d)}$$

where the product of absorber depth and density is called **area density** (dimension is mass/area). In FIGURE 8 we see that the total probability of interaction of gamma photon decreases with increase in photon energy, so that:

→ *The greater energy of gamma photons the deeper they penetrate in matter.*

Generally, gamma and X radiations are more penetrable than particle radiation, and complete protection behind the shield is hard to achieve. This penetrability is useful in radiological diagnostics and therapy and in radionuclide imaging.

Two reasons hinder direct applicability of equation 1.4:

1. Some of the photons diverted from beam by Compton scattering experience further multiple scatterings which redirect those photons back to the beam. These events can be neglected only in conditions of narrow beam. In wide beam geometries, radiation intensity can exceed several times the value predicted by equation 1.4

2. When the beam contains photons of several energies (more than one type of gamma decay or X ray beam, which is always polychromatic), equation 1.4 stands for each E_γ, separately.

Dosimetry

SOURCE AND FIELD OF IONIZING RADIATION

The source of ionizing radiation can be the assembly of unstable nuclei, *X* ray cathode or some other artificial device. In the former case, the essential source characteristics are:

1. geometry (point source, or source spread in space);
2. decay mode, defining energies of particles and photons and decay constant λ;
3. number of unstable nuclei in some time N_0.

Knowing N_0 and λ one can, by using equations 1.1 i 1.3, calculate the initial source activity $A_0 = \lambda N_0$, as well as the subsequent changes: $A(t) = A_0 e^{-\lambda t}$. From source activity, types and energies of radiation, one can calculate the radiation power of the source, *P*. Finally, the radiation power and source geometry determine the **radiation intensity**, *I* (power per unit surface area) at some point in space exposed to radiation; i.e. in the **radiation field**.

Consider the simple case of a *point source* in vacuum, so that there is no interaction of radiation with matter before it reaches the point of interest. In that case, the intensity of radiation decreases with distance *R* from the source only due to spatial spreading of ionizing particles spherically symmetric in all directions from the source. This intensity decay should be distinguished from decrease in intensity due to interaction with absorber.

Since the surface area of a sphere containing our point of interest is $4\Pi R^2$, it follows that **intensity of radiation decreases with square of distance from the source***:*

$$I = P/4\Pi R^2$$

Since radiation power is proportional to source activity, it follows:

$$I \sim A/4\Pi R^2$$

Thus, if one finds himself in the radiation field, the effects (to be discussed later) will be proportional to *activity of the source* and *time of exposure*, and inversely proportional to *square distance* from the source. Since one cannot change the source activity, two basic principles of **radiation protection** are:

1. **short time**
2. **large distance,**

where distancing from the source is more effective measure, due to quadratic dependence.

TWO QUANTITIES DESCRIBE RADIATION EFFECTS

The radiation effects depend on:

(i) intensity of radiation at the point of interest, and

(ii) interaction probabilities of radiation with matter

These effects are quantified by:

1. **Absorbed dose**, which is the energy the radiation deposited to unit absorber mass. The unit is **Grey (Gy)**. One Grey is 1 Joule/kilogram (J/kg).

2. **Exposure,** which is the total number of all ions (positive and negative) which *X* or gamma radiation released in unit mass of air. The unit is **Coulomb/kilogram (C/kg)**.

TABLE 1.4 Typical radiation doses

Source	Absorbed dose (mGy)
Natural sources of radioactivity	1-5 yearly
Single X-ray of thorax	
best	0.1
average	2
fluoroscopic examination	100
Local radiotherapy dose	30 000-70 000

Absorbed dose and exposure indicate cumulative effects of ionizing radiation on the unit mass of the exposed medium during non-specified time spent in the radiation field. Dividing these quantities with time, one gets the time independent quantities; these are **absorbed dose rate**, measured in Gy/s, and **exposure rate**, measured in C/(kg·s).

TABLE 1.5. The new and old radiation units

Quantity	New units	Old units	Conversion
Activity	Bq	Curie (Ci)	1 Bq ≈ 2.7×10^{-11} Ci
Exposure	C kg^{-1}	Röntgen	1 C kg^{-1} ≈ 3876 R
Absorbed dose	Gy	rad	1 Gy = 100 rad
Equivalent dose	Sv	rem	1 Sv = 100 rem

THE EFFECTS OF RADIATION CAN BE PREDICTED OR MEASURED

In case of point source of gamma radiation in vacuum, the exposure rate is constant on the surface of the sphere with radius *R*, and is proportional to source activity:

$$\text{rate of exposed dose} = \Gamma \cdot A/R^2$$

where the proportionality constant Γ (gamma constant) depends on gamma rays energy E_γ (since all process of interaction of radiation with matter depend on energy of photons). The gamma constant describes the different effects of sources of gamma radiation of the **same** activity. Although the probability of interaction decreases as gamma photon energy increases (FIGURE 1.8), the higher the energy of gamma ray, the more ions are released, and the summary effect is that, in general, radionuclides emitting higher energy gamma rays have also larger gamma constants E_γ (TABLE 1.6). Besides, due to larger penetrability of high energy gamma and *X* ray photons, their effects protrude deeper in the body, i.e. are not confined to skin and superficial tissues, as in case of lower energy radiation.

TABLE 1.6. Radiation parameters of common radionuclides

	Eγ (keV)	**Γ(Cm^2/kg Bq s)x10^{14}**	**μ (cm^{-1}) –in lead**
Tc-99m	140	0.14	23
Hg-203	279	0.23	2.3
I-131	360	0.43	2.3
Au-198	412	0.45	2.3
F-18	512	1.11	0.76
Cs-137	667	0.60	1.20
Co-60	1250	0.52	0.58

ABSORBED DOSE CAN BE PREDICTED BY MEASURING EXPOSURE

In case of live tissue the absorbed dose indicates the damage that radiation produced. On the other hand, the exposure can be measured relatively easy. Luckily, these quantities are related, so that it is possible to predict the absorbed dose due to electromagnetic ionizing radiation from the corresponding exposure.

To make it plausible, observe that that the average energy needed to create a pair of ions in air (to release one electron from atom) is 34 eV (34 x 1.6 x 10^{-19} J). Since 1 C/kg = $(1/1.6)\cdot 10^{19}$ electron charges per kg, it follows:

absorbed dose (Gy) = 34 x exposure (C/kg), in air

Generally, for any absorber, it holds:

absorbed dose (Gy) = f · exposure (C/kg)

where factor *f* depends on type of absorber, and, for low photon energy (less than 100 keV), in media with relatively heavy elements (e.g. bones), also on photon

energy (FIGURE 1.9). For photon energies above 100 keV, the association between absorbed and exposure is practically the same for air, soft tissues and bones (try to explain why, considering that: 1. above 100 keV the dominant process of interaction is Compton scattering and 2. the absorbed dose relates to unit mass of an absorber).

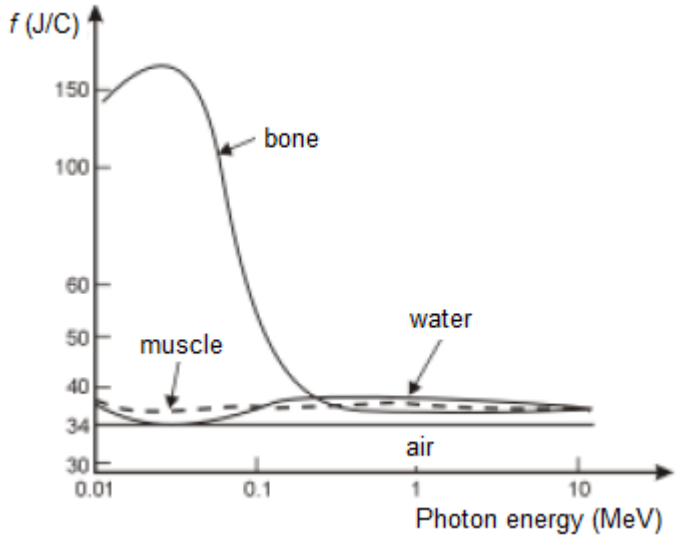


FIGURE 1.9 The ratio (f) between absorbed and exposed dose depends on photon energy differently for different tissues.

Observe that the above applies only for X and gamma radiation, since exposure is not defined for particle radiation. The reason behind is that particle radiation, except ionizing air molecules, deliver energy on exciting molecules and raising their kinetic energy (heating matter). Further complication is that the probability of these processes change as particle decelerates. Similar occurs in case of low energy wave radiation in heavy materials, which explains the dependence of *f* factor on photon energy in bones (FIGURE 1.9).

Often one does not know the characteristics of the radiation source. In that case one can only rely on measuring the radiation effects. Measurements of the rate of exposed dose are done by **ionization chambers**. Commonly, it is the chamber with air on atmospheric pressure containing positive and negative electrodes. When radiation enters the chamber and ionizes air, the relieved positive and negative ions are collected on cathode and anode, respectively. This creates the current in an external circuit, which can be measured (FIGURE 1.10).

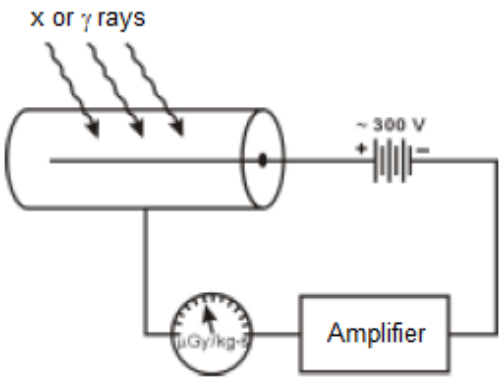


FIGURE 1.10 Transportable ionization chamber (Cutie Pie) consists of chamber with gas, high voltage source and device that measures the current produced.

In ionization chambers the potential of electrodes is that great to collect only the ions released by primary ionization; i.e. the electric field is insufficient to accelerate ions enough to produce secondary ionizations. Ionization chambers use for precise measurements of ionization field, which is especially important in radiotherapy planning.

On the contrary, in **Geiger-Müller (GM) counters** the voltage is greater, so that the primary ions, rushing towards the respective electrodes, create the avalanche of secondary ions. In consequence, GM counters do not measure the exposure rate, but only the ionization rate. However, their unique advantage lies in internal signal amplification, allowing for detection of relatively low energy radiation (insufficient to produce detectable primary ionization current). In practice GM counters are used for surveillance and radiation detection, in applications not requiring great precision.

IONIZATION IS BIOLOGICALLY HARMFUL

Ionizing radiations can cause serious damage to body cells, depending on:

(i) part of body exposed (cells that divide intensively are most sensitive)

(ii) absorbed dose

(iii) type of ionizing radiation

(iv) absorbed dose rate (longer time enables recuperation)

The examples of radiation effects are: skin burns, nausea, hair loss, sterility, cataract, bone marrow damage, changes in genes and induction of carcinoma. Excessive doses may cause death in a couple of days.

Radiation harms cells by ionizing biologically important molecules like DNA, which is the **direct effect,** or by chemically altering intracellular water, which is **indirect effect.** Interaction of radiation and water may produce **free radicals** H and OH. They are electrically neutral, but have uncoupled electrons and are thus very reactive. Their binding produces hydrogen peroxide (H_2O_2), a potent oxidant which harms DNA, enzymes and other vital molecules. The indirect effects of

radiation are much more common that the direct ones, since water is much more abundant than DNA (around 10^7 times).

The effects of radiation can be **hereditary** or **somatic.** Hereditary effects are caused by damage inflicted upon reproductive cells, which are transmitted to offspring. Somatic effects inflict only person exposed.

Biological effects of radiation are also classified as **stochastic** (randomly occurring) and **non-stochastic** (regularly occurring). Stochastic effects are due to cell mutation. They have no threshold, i.e. can occur even after very low absorbed dose. However, the probability of occurrence increases with absorbed dose. On the other hand, it such an effect occurs, its seriousness does not depend on the absorbed dose (all-or-none effect). All hereditary effects are stochastic, as well as some somatic (carcinoma induction).

Non-stochastic effects are caused by cell death or permanent damage, disabling cell proliferation. Thus they can occur only after some threshold of absorbed dose, and their seriousness increases with absorbed dose. Evidently, all non-stochastic effects are somatic; the examples include: erythema, cataract, leukopenia, glomerulonephritis, and sterility.

Doses received in medical imaging which use ionizing radiation do not exceed the great majority of thresholds of non-stochastic effects. Therefore the diagnostic use of *X* rays and radionuclides is primarily associated with stochastic radiation risks.

Biological damage inflicted by ionizing radiation does not depend only on absorbed dose; the type of radiation matters also. Namely, large number of ionizations within a single cell, or single macromolecule, is more harmful than the same number of ionizations (and thus absorbed energy) distributed over more cells (molecules). Neutrons and alpha particles ionize very densely, producing more commonly multiple, irreparable damages, than gamma or beta radiation. To account for this, one defines the **equivalent dose**:

$$\text{Equivalent dose} = Q \cdot \text{Absorbed dose}$$

where Q is **quality factor**. In case of alpha particles Q is 20, for neutrons range 5 to 20 applies (depending on energy), while beta particles and gamma photons have Q=1. The unit of equivalent dose is **Sievert (Sv)**. The old unit is **rem** (1 rem=0.01 Sv).

Besides, the sensitivity to radiation (radiosensitivity) depends on type of tissue (rate of proliferation is essential!). So, we also introduce the quantity called **effective equivalent dose.** To each part of a body one assigns the specific weight factor, which accounts for differential radiosensitivity. The effective equivalent dose equals the product of the weight factor and equivalent dose in the part of body considered. The unity is Sievert.

WE ARE MOST IRRADIATED BY NATURAL SOURCES

We are all constantly in the low-intensity field of ionizing radiation, so called **background radiation.** Background radiation primarily is primarily caused by natural radioactivity sources. The most important natural source is an alpha emitter-radon, a link in radioactive decay chain of U-228 (TABLE 1.3). This is a gas, emerging from uranium-containing rocks (most rocks contain traces of uranium, especially the granite ones), and especially from uranium mines. Thus, exposure to radon strongly depends on geographical location and time of a day (maximum is in the morning, when air is steady). It was also observed that radon accumulates more in some buildings. On average 1 m^3 of air contains about 10^6 radon atoms. Other sources of background radiation are cosmic rays (gamma rays of enormous energy) and natural radionuclides in soil, construction materials and food.

Production of artificial radionuclides accounts for minority of background radiation. The examples are: escape of radionuclides in nuclear accidents, radioactive waste material, and marketing of general-use products containing radionuclides (smoke detectors, illuminating watch-heads, etc.

Some of us are exposed to additional radiation due to radiological examinations or professional exposure. The average absorbed dose due to diagnostic use of electromagnetic radiation (mainly *X* rays) accounts for over 95% of absorbed dose from artificial sources. Radiotherapeutic doses are not considered here.

The details presented in TABLE 1.7 are only average values. Some persons are much more exposed; depending on place they live, their profession, need for medical diagnostics, etc.

Table 1.7 Average effective equivalent dose of Great Britain inhabitants (1991).

Source	Dose/μSv	Percent	Notion
Natural sources			
Radon	1300	50.1	
Gamma rays from soil and construction materials	350	13.5	
Natural radionuclides in food	300	11.6	
Cosmic radiation	260	10.0	airplane crews can get 10 times more
Artificial sources			
Medical use	370	14.3	excluding radiotherapy
Professional exposure	7	0.27	
Radioactive falls	5	0.19	declining from 1962, except for Chernobyl accident in 1986
Leakage of radionuclides	0.4	0.02	
Common market devices	0.4	0.02	smoke detectors, illuminating watch-heads, etc.

Self assessment

Out of five statements, only one is correct.

1.1 *Majority of stable, heavy nuclei*:

a) have equal numbers of protons (Z) and neutrons (N)
b) have $N<Z$
c) have $N>Z$
d) inclines to alpha decay
e) are artificial

1.2 *Annihilation radiation occurs in*:

a) beta-minus decay
b) alpha decay
c) gamma decay
d) beta-plus decay and in pair-creation
e) only in beta-plus decay

1.3 *Continuous energy spectrum is present*:

a) in alpha and beta decay
b) only in alpha decay
c) only in beta decay
d) in alpha and gamma decay
e) only in gamma decay

1.4. *The wooden plate put in front of the collimated source of ionizing radiation halves its intensity. If two such plates attenuate the beam to zero intensity, one can undoubtedly conclude:*

a) source does not emit gamma rays
b) source emits only gamma rays
c) source emits only alpha rays
d) source does not emit beta particles
e) source emits only beta particles and gamma rays

1.5 *Somatic effects of ionizing radiation*:

a) do not refer to exposure of gonads
b) do not have threshold
c) cannot be stochastic
d) comprise all non-stochastic effects
e) cannot be due to irradiation of gonads

Chapter II

PHYSICS OF NUCLEAR MEDICINE

- What is nuclear medicine?

  Radioisotopes are used in diagnostics and in therapy
  Diagnostic activities don't have physiologic effects
  Tc-99m: the most used radioisotope in nuclear medicine
  Scintigram is an image of organ function

- Measurements of radioactivity

  Registration of gamma radiation requires massive detector
  Gamma rays are detected by conversion to visible light
  Scintillation counters can measure the gamma ray energy
  Sodium iodide crystal: the commonest gamma ray detector
  RIA: way to measure extremely low concentrations
  Volumes of body fluids can be measured by dilution of radiotracer
  Collimator selects radiation from parts of body
  Radiohistogram je graf funkcije organa

- Imaging of radioactivity distribution

  Scintigram can be created by successive scanning
  Gamma camera creates live scinitigrams
  Scintigram is also a table of numbers
  Functionality and quantitative aspect: distinctive scintigram features
  Two factors of scintigram (dis)advantages
  Hot lesions are better seen than cold lesions
  Radiotracer kinetics: an insight into functional parameters
  Effective half-life: determinant of absorbed dose of introduced radionuclide

- Imaging of body slices

  SPECT: single-photon emission computed tomography
  Imaging from many angles enables slice isolation
  Singling out slices increases contrasts
  Tomograms have inferior resolution than planar images
  PET: positron emission tomography
  No collimator required- recording of a projection is almost instantaneous
  Positron emitters give insight into metabolic processes

What is nuclear medicine

RADIOISOTOPES ARE USED IN DIAGNOSTICS AND THERAPY

Nuclear medicine comprises a set of diagnostic and therapeutic procedures that use radioisotopes. Diagnostic methods include laboratory, in-vitro procedures and in-vivo imaging of distribution of radioisotopes within a body. In-vivo diagnostics utilize gamma emitters since, once introduced in the body, gamma rays can penetrate the body tissues and be detected outside. For therapeutic purposes beta emitters are more suitable since they have short range and produce high therapeutic absorbed doses only locally, without damming the neighboring tissue.

DIAGNOSTIC ACTIVITIES DON'T HAVE PHYSIOLOGIC EFFECTS

Our primary interest is radioisotope diagnostics. In diagnostic procedures very small activities of radionuclides are used (around 1 GBq), having masses below 1 μg. Such small amounts do not produce physiologic effects, but the accompanying radiation suffices for diagnostic information.

Tc-99m: THE MOST USED RADIOISOTOPE IN MEDICINE

Artificial beta emitters are produced in nuclear reactors or particle accelerators. They are also secondary beta emitters, while the pure gamma emitters are obtained by isolating the meta-stable (relatively long living) offspring of a beta emitter. In radionuclide imaging diagnostics the most commonly used radioisotope is technetium-99m (Tc-99m), having half-life of 6 hours. Index *m* denotes the meta-stable isotope of technetium-99, with surplus of energy. Tc-99m is a beta-minus offspring of molyibdenum-99 (an isotope produced by reactions in nuclear reactor). By gamma decay Tc-99m becomes Tc-99 (which is not strictly stable, but decays so slowly that its radiation can be neglected). At most occasions the emitted gamma ray has energy of 140 keV. The advantages of Tc-99m include:

1. it is a pure gamma emitter, without unwanted beta radiation,

2. the photon energy is sufficient to penetrate the body, but not too large for detection and protection,

3. the half life is long enough to complete the investigation, but not too long to produce excessive radiation dose,

4. it has chemical affinity towards many molecules,

5. it is relatively cheap.

The half life of Mo-99 is 2.5 days. This enables the average nuclear medicine institution to satisfy its weekly needs for Tc-99m by purchasing about 3 GBq Mo-99. The product is called (molybdenum)-technetium generator. It has massive lead protection with Mo-99 inside in the form of ammonium molybdenate, adsorbed on

aluminum column. When one needs Tc-99m (accumulated by decay of Mo-99), the solution of sodium chloride is allowed to perfuse the column, where chloride ions are exchanged for pertechnetate ions. Technetium, in the form of pertechenetate ($Tc\text{-}99mO_4^-$) is sucked in the evacuated bottle and afterwards distributed in daily and individual activities (FIGURE 2.1).

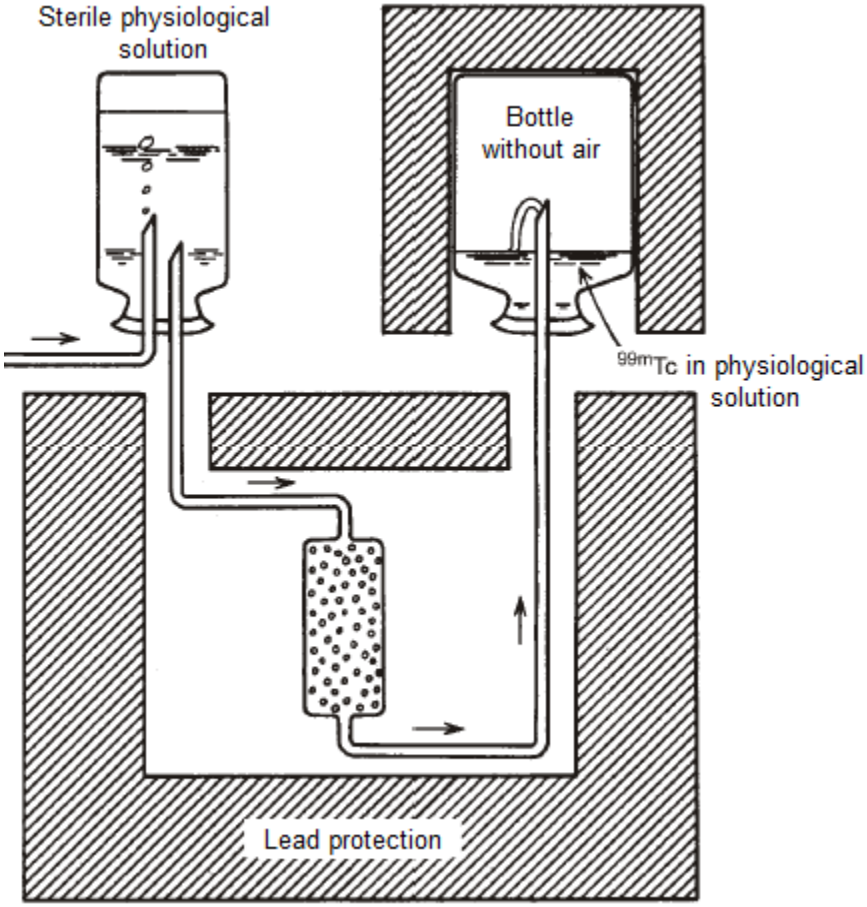


FIGURE 2.1 Schema of technetium generator

SCINTIGRAM IS AN IMAGE OF ORGAN FUNCTION

In contrast to morphological image, created by X rays, that originate from the source outside and traverse the body, nuclear medicine image (scintigram) displays the physiologic function and is created by gamma rays originating from the body.

Accumulation of radionuclide in body depends exclusively on chemical and physical characteristics of a molecule that contain radioactive atom. For example radioactive isotopes of iodine (I-131, I-123, I-125, etc.) accumulate in thyroid which makes no distinction between any of them and stable iodine (I-127).

In this case the anion of radioactive iodine is both radioindicator- radioisotope that emits gamma rays, providing for detection, and tracer- the chemical entity with specific affinity for a tissue of interest.

However, when investigating the renal plasma flow, one uses I-131 incorporated in ortho-iodine-hypurric acid, in place of stable iodine. Now I-131 is radioindicator, and the whole complex ortho-iodine-131-hypurric acid is radiotracer, which behaves analog to para-iodine-hypurric acid, the well known marker of renal plasma flow. In most cases the radioactive atom is added to a stable tracer, which insignificantly changes its characteristics. The nuclear medicine institution purchases radioindicator (or its generator), which can be attached to a variety of tracers, that are purchased separately.

Thus, in most cases:

RADIOTRACER = RADIOINDICATOR + TRACER

where characteristics of a tracer determine localization and radioindicator enables registration in space and time.

Nuclear medicine diagnostic potentials base on variety of tracers; the new tracers are constantly synthesized in radiopharmaceutical companies and scientific institutions. Since the diagnostic quantities of tracers are physiologically negligible, there are no problems with adverse reactions, like in drugs.

One has to consider only the absorbed radiation doses. However, in nuclear medicine diagnostics one uses relatively small activities of short-lived radioisotopes. In consequence, like in radiologic diagnostics, the absorbed doses only pose the risk of stochastic effects of ionizing radiation. These risks must be acceptable when compared with benefits of diagnostic procedure.

Measurements of radioactivity

REGISTRATION OF GAMMA RADIATION REQUIRES MASSIVE DETECTOR

Nuclear medicine radioactivity measurements have two purposes: 1. determination of radionuclide concentration (indirectly: hormones or other attached substances) in tissue sample, and 2. registration of distribution of radionuclide in the body. In both cases, due to large energy of gamma rays, one needs a massive detector.

The x ray may leave a point trace on a film, while efficient registration of gamma ray requires several centimeters of a heavy absorber. This is one of the reasons why resolution of details on nuclear medicine images is relatively poor.

→ *Necessity of massive detector restricts the potentials of nuclear medicine imaging diagnostics.*

GAMMA RAYS ARE DETECTED BY CONVERSION TO VISIBLE LIGHT

When some materials absorb ionizing radiation, a part of absorbed energy excites the atoms of a material in higher energy states, from which they return by emitting visible light. The effect is called luminescence, the bursts of emitted light scintillations, and such materials scintillators (or phosphors). The image acquired by using scintillation detector is called scintigram. Intensity and duration of a single scintillation are too small for routine detection. Therefore one uses photomultiplicator tubes. Scintillator and photomultiplicator tube make up the scintillation counter (FIGURE 2.2).

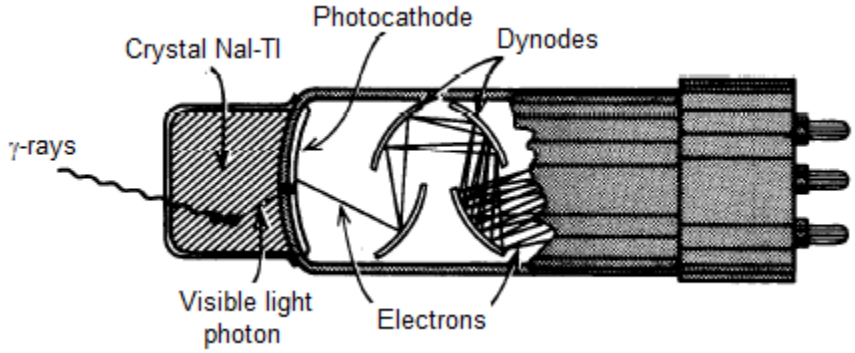


FIGURE 2.2 Absorption of gamma ray in a scintillator creates visible photons, which traverse the material without significant absorption. Thus, a larger part of this light reaches the back of a scintillator, with photocathode attached. Light photons release photo-electrons from photocathode surface. This primary

signal is intensively amplified (10^5 do 10^8 times) by accelerating the electrons on assembly of dynodes on successively greater potentials; each time one primary electron ejects about 10 secondary electrons.

SCINTILLATION COUNTERS CAN MEASURE THE GAMMA RAY ENERGY

The larger the gamma ray energy the larger energy of light photons created in a scintillator, which is then amplified by a constant factor. Thus, the energy pulse coming from the scintillation counter is proportional to the absorbed energy of gamma ray. This enables:

1. use of scintillation counters as detectors, and

2. possibility to select only those absorption events that create a pulse of predefined height, which is the spectral analysis.

In the later case one needs the electronic device known as pulse height discriminator. Its function is to select the pulses with height (voltage) within the window defined by lower and upper threshold. In this way one can separate out a single isotope from a mixture or register only certain processes of gamma ray absorption.

The photon absorbed by photo effect leaves larger energy than photon after Compton scattering. Multiple Compton scatterings leave smeared, ill defined track in the absorber. By omitting these events (taking into account only photo-effects) significantly improves scintigram resolution.

SODIUM IODIDE CHRYSTAL: THE COMMONEST GAMMA RAY DETECTOR

The most convenient scintillator is the crystal of sodium iodide, activated by around 5% of thallium iodide (NaI-Tl). Addition of thallium enables scintillations at room temperature. The advantages of NaI-Tl crystal are:

1. high sensitivity of detection of gamma radiation, due to high density and high iodine atomic number,

2. relatively high conversion rate of gamma radiation to visible light (around 10%) and

3. short time of a scintillation enables high count rates (above 10^4 in second), without ‘dead time’ of a counter.

The gamma rays can also be detected by other counters, as much as NaI-Tl crystal can measure other types of ionizing radiation.

When NaI-Tl crystal is used in in-vitro diagnostics, it has the shape of a well counter. The sample is put in the center of a crystal, which surrounds it almost in total, while massive lead protection shields from background radiation (FIGURE 2.3). This maximizes the measurement sensitivity.

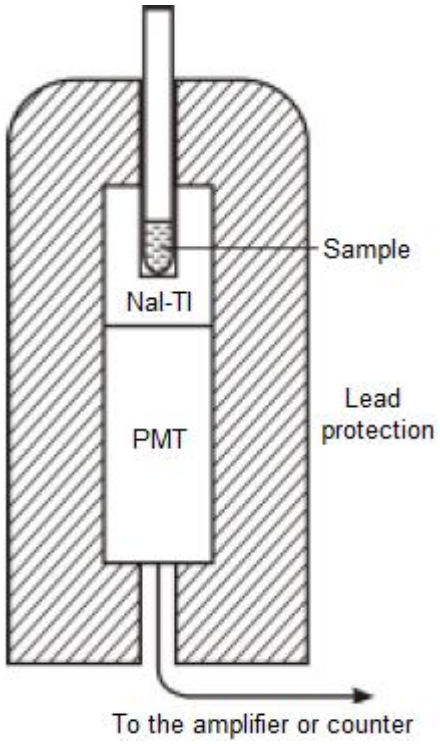


FIGURE 2.3 Well counter comprise the hollow NaI-Tl crystal, photomultiplier tube (FMC) with electronics and massive lead shield which absorbs the surrounding background radiation.

RIA: WAY TO MEASURE EXTREMELY LOW CONCENTRATION

The most important nuclear medicine in-vitro test is radioimmunoassay (RIA). RIA can measure very low concentrations of hormones, drugs and other substances, which cannot be detected by standard laboratory diagnostics. The method relies on marking the substance (or its antibody) by radioindicator. The investigated stable substance is mixed with its complement, labeled with known activity of radionuclide. After reaching the steady state, the unbound complement is removed. The greater the concentration of a substance investigated the greater concentration of antigen-antibody complex, assessed by counting radiation. High sensitivity of RIA relies on two factors:

1. high sensitivity of registration of gamma radiation (recall it is possible to detect a single gamma ray), and

2. high specificity of antigen-antibody reaction.

VOLUMES OF BODY FLUIDS CAN BE MEASURED BY DILUTION OF RADIOTRACER

The volumes of body fluids can be assessed by dilution of intravascularly injected radioindicator. For example, the examinee is injected with 9 MBq Tc-99m, bound to human serum albumin, intravenously in 1 ml of saline. After a couple of minutes the radioindicator distributes evenly in plasma volume. The sample of blood is then

taken, 1 ml separated and its activity counted. If the result is, for example, 3 kBq, this implies that 1 ml of injected volume has diluted in 3000 times larger pool (9 MBq:3 kBq=3000), i.e. the plasma volume of our examinee is 3 liters. Similarly, using radioindicator that binds for erythrocytes (Cr-51), one can assess the total erythrocyte volume. In the same way, if the distribution volume of an indicator is the total body water (tritium), one can assess this physiologic parameter.

The use of radioindicators in these measurements has the advantage of a high sensitivity. Thus one can use minute amounts of tracers, without possibility of allergic or other adverse reactions.

COLLIMATOR SELECTS RADIATION FROM PARTS OF BODY

In nuclear medicine in-vivo diagnostics one records the radiation from certain body parts- regions of interest. The radionuclide is commonly dispersed in space (for example in blood and kidneys), but we want to record the radiation of only a single organ or its part (for example- kidneys). For that purpose one uses the open collimator of gamma rays. It is a massive part of lead which absorbs all gamma photons outside its field of view, defined by its hole (FIGURE 2.4).

RADIOHISTOGRAM IS A GRAPH OF ORAGAN FUNCTION

Attaching the pen recorder on the output of collimated scintillation counter, one can record the time changes in radioactivity within the body part in the collimator's field of view, which is the radiohistogram (FIGURE 2.4). We use radioindicators which transport reflects the organ function.

→ *Radiohistogram displays the time course of radioindicator in an organ (or its part), which points to its function.*

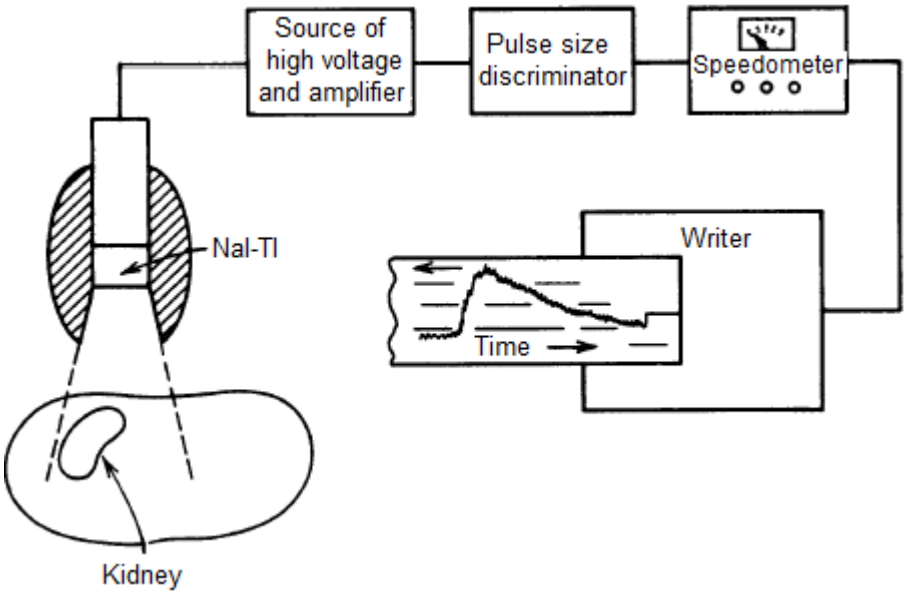


FIGURE 2.4 The principal parts of a device that record kidney radiohistogram-renogram. Usually two such devices record simultaneously each kidney.

Imaging of radioactivity distribution

SCINTIGRAM CAN BE CREATED BY SUCCESSIVE SCANNING

More demanding application is to image the distribution of radiotracer in a body. If this is thyroid scintigram, one should allow only radiation from small part of a thyroid to reach the scintillation crystal at a time. However, the excited nuclei emit radiation from all parts of a thyroid simultaneously. To deal with it one uses focusing collimator, a device that absorbs all radiation outside the small volume of its focus (FIGURE 2.5). The image is created as the collimator slowly sweeps over the region of an organ, successively scanning its parts. Simultaneously a light source, mechanically coupled to the collimator, exposes the film. The light intensity is proportional to count rate of a scintillation counter attached to collimator. Such device is called scanner.

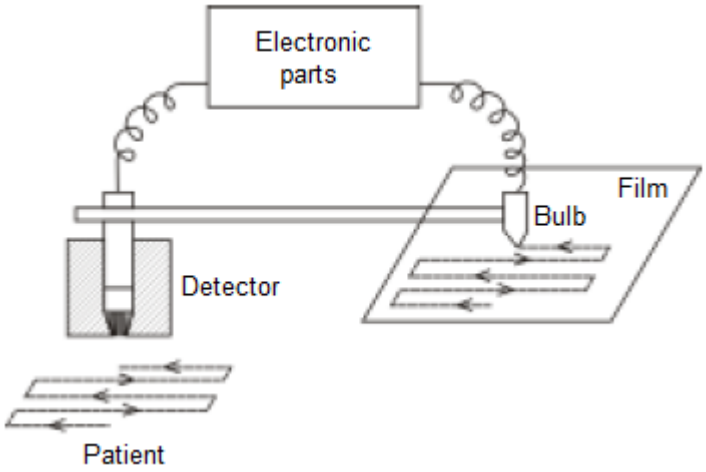


FIGURE 2.5 Principal scheme of a scanner.

Scintigram obtained by scanner is a two-dimensional image of radiotracer organ distribution in a layer defined by the depth of its focus. Focusing collimator significantly decreases the sensitivity of radiation detection (compared to open collimator) and such imaging has relatively poor resolution, since the focus of a device is not a point, but the finite volume. Successive scanning imaging is slow, and only static images can be produced. For those reasons scanner is currently out of use.

GAMMA CAMERA CREATES LIVE SCINTIGRAMS

The gamma camera is a revolutionary invention in nuclear medicine imaging. It has a large about 4 cm wide NaI-Tl crystal with parallel holes collimator in front (at most occasions). This collimator is a several centimeters thick lead cylinder plate with thousands of narrow parallel channels (holes several millimeters wide),

running at right angle to the cylinder bases. This ensures that radiation absorbed by the spot in a crystal originates only from the area under this particular spot. One should further reveal the spot of a crystal that absorbed the photon at a time. To accomplish this there are many photomultiplier tubes (up to 75) on the back of crystal (about 1 cm thick). Each scintillation sheds light on several photocathodes, the more the closer photocathode to absorption spot is. Based on differential outputs of the tubes, the position of a spot is determined by an algorithm, executed by a computer (FIGURE 2.6).

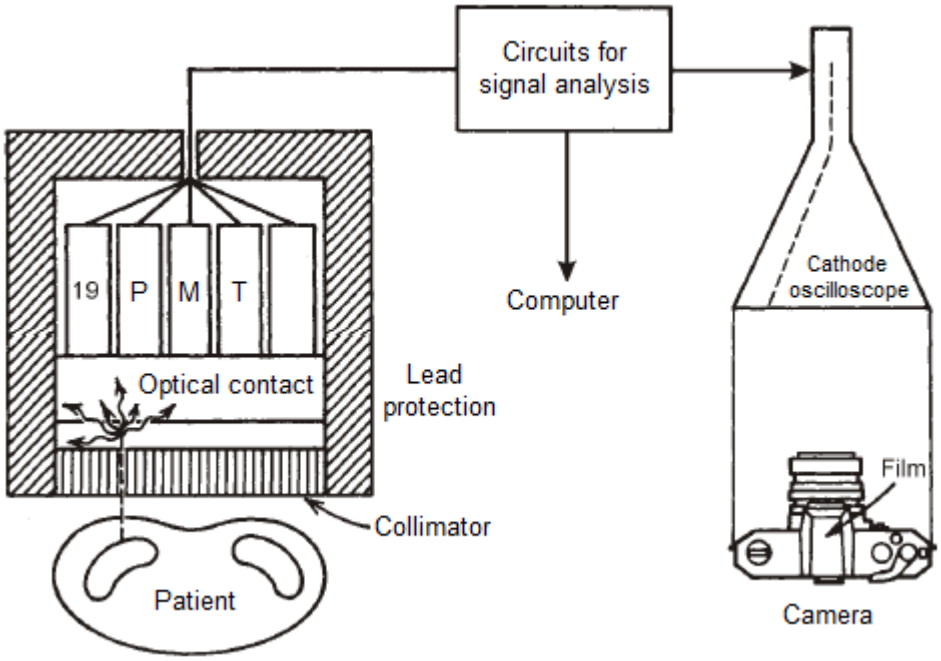


FIGURE 2.6 Components of gamma camera. Detector and photomultiplier tubes (FMC) are protected by lead shield. Scintillation in a crystal causes largest signal in the nearest FMC. Dedicated circuits determine (x, y) position of a scintillation, which is both stored in computer memory (digital image) and used to illuminate the corresponding spot of the analog camera film.

In contrast to successive scanning of a scanner, gamma camera is at all times sensitive to the whole area beneath the crystal. This enables making images in a short time, enough to monitor fast changes, i.e. to make movies of indicator kinetics.

To make an image of a small organ (notably a thyroid) one uses the special, pinhole collimator, which creates an enlarged, inverse image on a face of a crystal, like the dark camera (FIGURE 2.7).

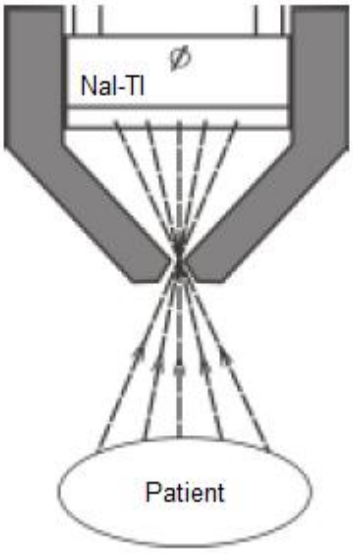


FIGURE 2.7 The original gamma camera had a pinhole collimator, which is still used to image small organs or organ parts.

SCINTIGRAM IS ALSO A TABLE OF NUMBERS

The gamma camera image can be displayed in two ways:

1. analog image, obtained by transferring the position of a scintillation on the cathode oscilloscope screen, which then illuminates the photographic film, and

2. digital image, obtained by storing the position of a scintillation in a cell of matrix (typically 64x6); each cell contains the numbers of events in a given time.

The advantage of digital image lies in its quantitative aspects, amenable to subsequent numerical, in addition to visual analysis. These analyses result in diagnostics and quantification of various morphological and physiologic parameters, like: volume of heart cavities, presence and magnitude of various abnormalities (intracardiac shunts, valvular insufficiencies, vesico-ureteral refluxes), magnitude of renal blood flow and filtration fraction, etc.

The nuclear medicine specialist devotes only a faction of her (his) time to visual analysis of scintigrams, usually the quantitative analyses on a computer take the majority of her (his) attention.

FUNCTIONALITY AND QUANTITATIVE ASPECT: DISTINCTIVE SCINTIGRAM FEATURES

In conclusion, although gamma camera scintigrams do not have resolution comparable to other imaging modalities (ultrasound, radiologic diagnostics, magnetic resonance imaging) the unique scintigram advantages are:

- functionality (radiotracer accumulation depends on function), and

- quantitative aspect (image is a table of numbers).

TWO FACTORS OF SCINTIGRAM (DIS)ADVANTAGES

All in all, there are two grounds of nuclear medicine imaging:

1. large energy of a gamma ray, and

2. distribution of gamma ray sources in a body.

These facts determine both the comparative advantages and disadvantages of radioisotope imaging. The unique advantage of large energy of gamma rays is an extreme sensitivity of registration; however, the price paid is a need for massive detector, which worsens image resolution. The distribution of gamma emitters in a body is the primary information of a scintigram, providing insight into body functions. The price paid is a need for collimation, which deteriorates image resolution, even to a grater extent than large detector volume

Not only that collimation severely limits the resolution of a scintigram; it also drastically decreases the sensitivity of registration- the radiation absorbed by collimator is several thousand times larger than radiation let through collimator channels. However, in spite of these losses, the extreme sensitivity of registration of a single gamma ray suffices that small quantities of radiotracer, unable to affect body functions, provide diagnostic images in a fraction of a second.

HOT LESIONS ARE BETTER SEEN THAN COLD LESIONS

Lesion is a pathologically altered accumulation of radiotracer, mostly in part of an organ. Abnormal increase in accumulation is hot lesion, abnormal decrease- cold lesion. Thus, lesions are displayed with abnormal contrast to surrounding tissue, where by contrast one means the difference in accumulation of radiotracer. In case of cold lesion, the maximal abnormal contrast occurs when some tissue did not accumulate radiotracer at all; the contrast is then given by (normal) accumulation of radiotracer in the surrounding tissue. The contrast of hot lesions can be much greater. In an extreme example, the hyperfunctional nodule in a thyroid can take up all radioactive iodine, so that the surrounding tissue is not seen at all. This explains why cold lesions are harder to detect, especially if a lesion is small. Due to relatively poor resolution of a scintigram, the small cold lesions can be covered by the activity of the surrounding tissue.

The detectablitiy of a lesion primarily depends on its contrast, which can be greater in hot than in cold lesions. Secondly, the lesion detectability increases with lesion size, and, in case of cold lesions, the image resolution is also important. Digital image can be manipulated on a computer to enhance the visual contrast. Also, scintigrams are tables of numbers, and lesion detection can be automated on a computer by dedicated algorithms. This may be more objective and bypass some limitations of visual analysis, but also introduce artifacts. Some physicians are skeptic about information which cannot be seen by bare eyes.

RADIOTRACER KINETICS: AN INSIGHT INTO FUNCTONAL PARAMETERS

The amount of radiotracer able to traverse the kidneys changes depending on the way of absorption (filtration, tubular secretion or both), the eventual tubular reabsorption, dynamics of tubular transport, openness of the channeling system, in short- on renal function. Similar is valid for dynamics of radiotracer passage through central circulation (blood vessels of heart and lung), as well as for other organs which function influence upon radiotracer kinetics.

There are three phases of radiotracer kinetics: 1. transport to the organ; 2. localization in the organ and 3. elimination from an organ or body.

After an intravenous application the radiotracer is convectively carried by blood with varying degree of diffusion to extravascular space. So called intravascular (blood) indicator remain confined to blood vessels, with negligible escape during the time of examination. Since the blood carries it, kinetics of intravascular indicator reflects hemodynamic parameters. On gamma camera scintigrams one can identify the areas of lung and heart cavities. Radiohistograms of those areas are input data, used by dedicated algorithms (often based on complex models and numerical analyses), to assess various hemodynamic parameters, like cardiac blood flow (cardiac output), volume of blood in lungs, ejection fraction of the left ventricle (fraction of blood in a ventricle ejected in a single contraction), presence and degree of malfunction of heart valves, presence and degree of left-to-right shunt (blood flow through abnormal opening in the heart septum), parameters of left ventricular diastolic (filling) function (FIGURE 2.8).

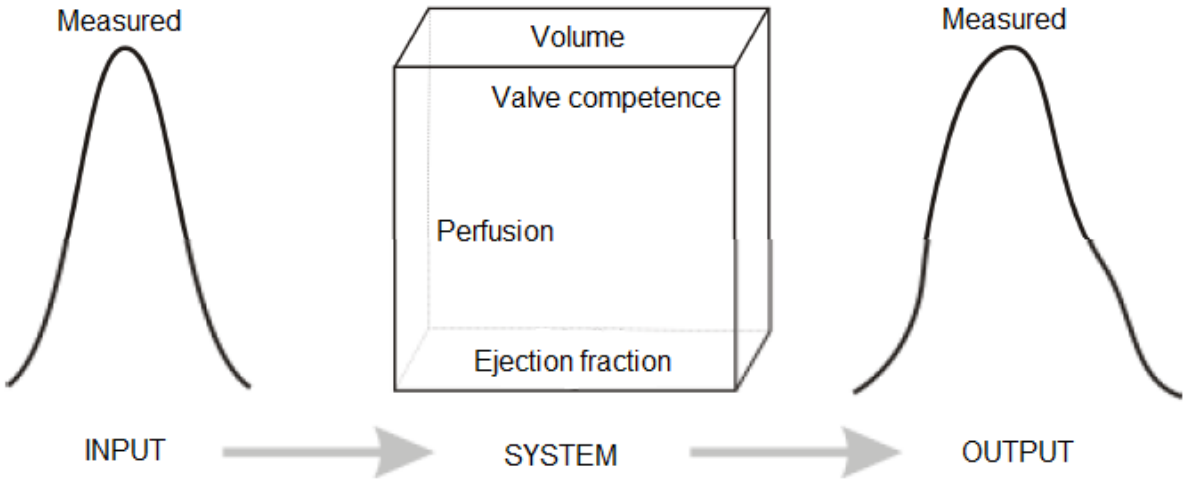


FIGURE 2.8. System modifies input according to its characteristics. By measuring input and output one can indirectly assess the system characteristics.

In other cases one uses radiotracers which leave the blood to accumulate specifically (preferentially) in certain organs. Typical mechanisms of radiotracer accumulation are presented in TABLE 2.1.

TABLE 2.1 Examples of radiotracer localization

Mechanism	Organ	Radiotracer
active transport	thyroid	J-131
active transport	kidney	ortho-I-131-hypurric acid
active transport	myocardium	Tl-201
capillary blockade	lungs	Tc-99m-macroaggregate
filtration	kidney	Tc-99m-diethilene-triamine-pentaacetic acid
dilution	blood	Tc-99m-human serum albumin
phagocytosis	liver	Tc-99m-sumphor colloid
sequestration	spleen	Tc-99m-sumphor colloid

At most cases the radiotracers are eliminated by kidneys or (and) liver, whether unchanged or not, depending on the metabolism of a tracer.

EFFECTIVE HALF-LIFE: DETERMINANT OF ABSORBED DOSE DUE TO INTRODUCED RADIONUCLIDE

In most cases the rate of tracer elimination is proportional to its concentration. The same law is followed by most drugs and other exogenous substances introduced instantly (as a bolus) into circulation. It follows that the amount of a tracer declines exponentially, with rate called constant of biological elimination (λ_B). In this point, there is a complete analogy with the law of radioactive decline (equations 1.1 and 1.2). Accordingly one defines the biological half-life $(T_{1/2})_B$:

$$(T_{1/2})_B = ln(2)/\lambda_B$$

If a tracer is radioactive, the activity of radioindicator in a body declines even faster, with rate equal to sum of constant of biological elimination and constant of radioactive decay, λ. This sum is the constant of effective elimination (λ_{EF}):

$$\lambda_{EF} = \lambda_B + \lambda$$

Accordingly (recall equation 1.2.), the initial activity of radioindicator in a body (A_0) declines in time:

$$A(t) = A_0 \, exp(-\lambda_{EF} \, t)$$

where the symbol *exp* stands for *e* raised to the expression in the bracket.

One also uses the inverse quantity, the effective half-life $(T_{1/2})_{EF}$:

$$(T_{1/2})_{EF} = ln(2)/\lambda_{EF}$$

Taking into account that the (physical) half-life of radioindicator, $T_{1/2}$ is an inverse of the decay constant,λ the two above equations give:

$$(T_{1/2})_{EF} = T_{1/2}\,(T_{1/2})_B \,/(\, T_{1/2} + (T_{1/2})_B)$$

It follows that the effective half-life of radiotracer is always less than both the half-life of a tracer and the physical half-life of radioindicator:

$$T_{1/2} > (T_{1/2})_{EF} < (T_{1/2})_B$$

EXERCISE 1. Calculate the effective half-life of I-131 anion in a body, taking into account that the biological half-life of iodine anion is 15 days, while I-131 decays with half-life of 8 days. Try to explain the relatively long biological half-life of iodine anion, in spite of the fact that kidneys eliminate this compound by glomerular filtration, without subsequent reabsorption (recall the physiologic function of iodine).

Disappearance from body of a radiotracer which decays very slowly is only by biological elimination. Similarly, the radiotracer which incorporates in a body compartment (e.g. radioactive strontium in bones) diminishes in activity exclusively by radioactive decay.

EXERCISE 2. Show that from the above equations follows: if the physical half-time greatly exceeds the biological half-life, the effective half-life practically equals the biological half-life and vice versa. Calculate the effective half-life of orto-iodine-131-hyppuric acid, if one half of a complex is excreted in urine in 1 hour.

Clearly, upon radioactive decay, the radioindicator does not disappear from body, only the daughter nucleus replaces the parent nucleus. If a daughter is not radioactive, from the absorbed dose point of view, one may consider that physical decay means elimination from body. In that case the absorbed dose due to introduction of radionuclide in body is proportional to effective half-life of the radiotracer complex (radionuclide + tracer). Aside from effective half-life, the absorbed dose is proportional to activity of radionuclide and depends on type of decay and radiation energies.

In assessing the radiation dose due to introduction of a radionuclide in a body (for diagnostic or therapeutic purposes, or due to contamination), one should primarily consider the effective half-life of a radioactive compound. This is because in practice this parameter varies widely (from couple of seconds to thousands of years), while other factors (activity, type of decay) vary less.

In diagnostics, the activities of radionuclides must suffice for obtaining good quality images. However, only complexes with short effective half-life are used. In consequence, the absorbed radiation doses are acceptable (have favorable price/ gain ratio), resulting in only stochastic risks of ionizing radiation (TABLE 2.2).

Table 2.2 Absorbed doses in common nuclear medicine procedures

Procedure	Radiotracer	Activity	Dose in critical organ (Gy)[a]	Dose in gonads (mGy)
Brain scintigraphy	^{99m}Tc pertechnetate	500 MBq (~ 15 mCi)	Intestines, 0.02	4
Liver scintigraphy	^{99m}Tc sulphor colloid	150 MBq (~ 4 mCi)	Liver, 0.02	0.85
Lung scintigraphy	^{99m}Tc macroaggregate	100 MBq (~ 3 mCi)	Lungs, 0.009	0.3
Bone scintigraphy	^{99m}Tc pyrophosphate	500 MBq (~ 15 mCi)	Bladder, 0.06	4
Renography	^{131}I hyppuric acid	8 M Bq (~ 200 μCi)	Bladder, 0.02	0.2
Thyroid function	^{131}I sodium iodide	300 kBq (~ 8 μCi)	Thyroid, 0.08	0.6
Thyroid scintigraphy	^{99m}Tc pertechnetate	150 MBq (~ 4 mCi)	Intestines, 0.01	0.8

[a] critical organ has the largest absorbed dose

Imaging of body slices

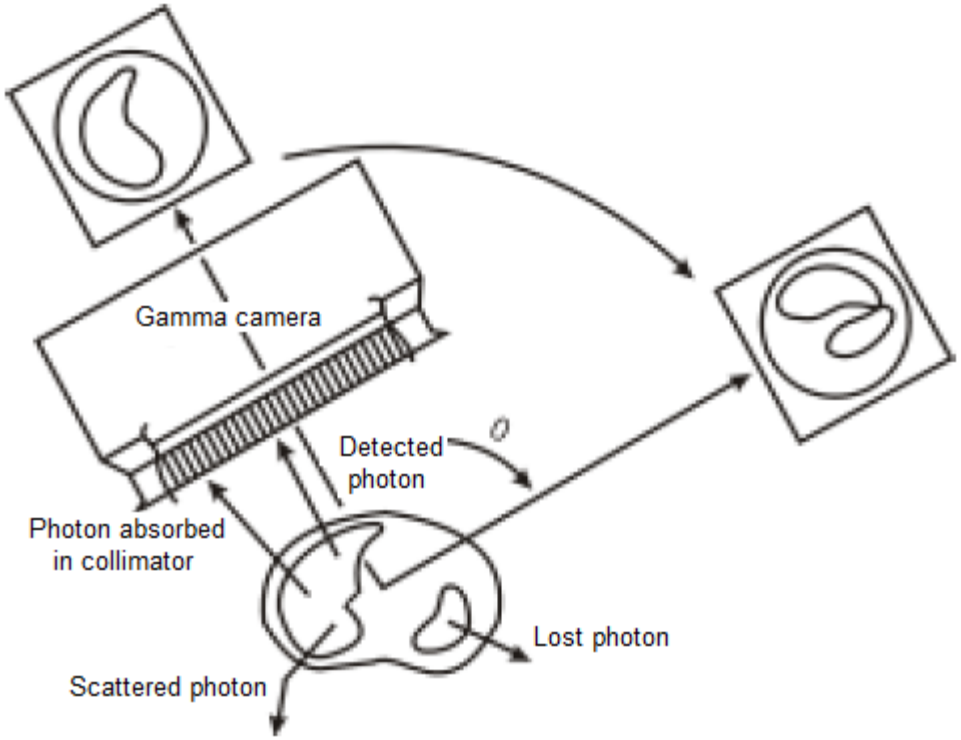
SPECT: SINGLE-PHOTON EMISSION COMPUTED TOMOGRAPHY

Recall that scintigrams are planar projections of a three dimensional distribution of radiotracer in body. The activities above and beyond superimpose with activity of a tracer in the region of interest. Those activities are biological noise that obstruct lesion detectability and increase errors in numerical analysis of tracer kinetics.

The method of imaging tiny slices of body- tomography overcomes this problem. The tomogram is an image of a body slice. One of two such nuclear medicine procedures is single-photon emission computed tomography (SPECT). The attribute ‘single-photon’ distinguishes the method from positron tomography, which we shall address later. The attribute ‘emission’ emphasizes that the source of radiation is within body, in contrast to radiological transmission tomography, with radiation source outside the body.

IMAGING FROM MANY ANGLES ENABLES SLICE ISOLATION

In SPECT one uses gamma camera, like in ordinary planar scintigraphy. However, the camera is not stationary, but rotates around body. Thus obtained scintigrams are not final images, but inputs to a computer, which reconstructs images of body slices. Ordinarily the slices are cross sections in a plane perpendicular to long axis of a body, around which the camera rotates (FIGURE 2.9).



FUGURE 2.9 SPECT imaging. Computer uses the set of planar scintigrams, registrated during rotation of the gamma camera head around patient to reconstruct the images of body slices.

A single projection scintigram is a set of parallel strips, the activity profiles, (FIGURE 2.10). Each profile displays the depth-averaged radiotacer concentration along the line perpendicular to the strips. We are, however, interested in depth distribution of activity in a strip, not only the summary, average value. By singling out a certain depth of a stripe would give us the image of a cross-sectional slice, i.e. the third dimension of radiotracer distribution. This is possible using the profiles from many angles, obtained during detector rotation around the long axis of a patient (FIGURE 2.10).

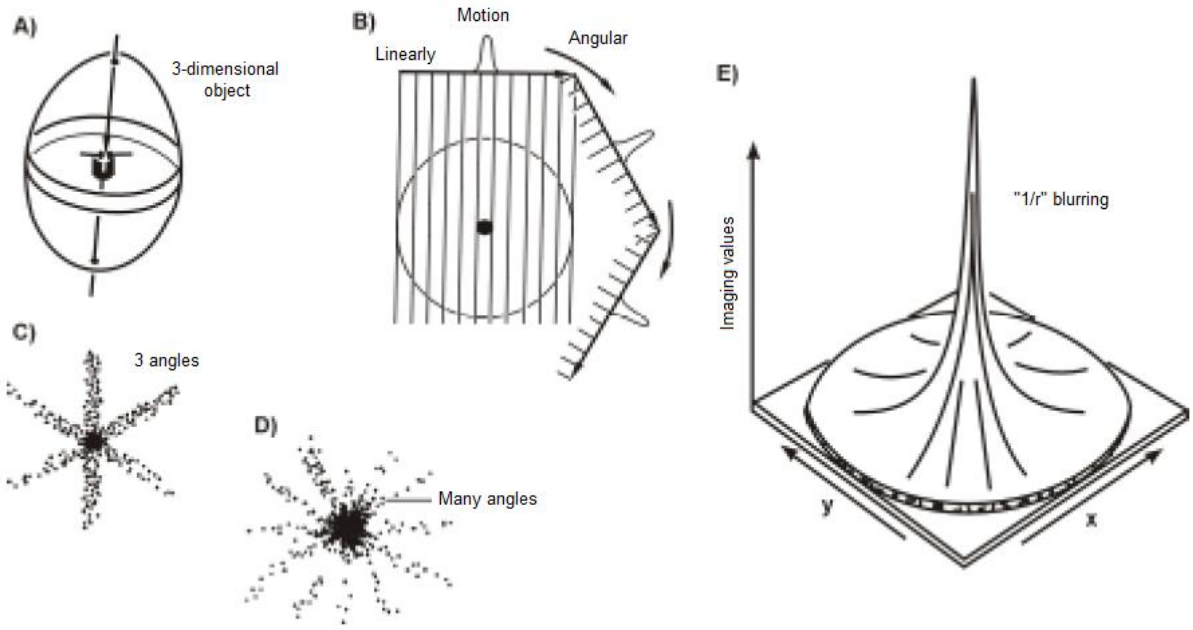


FIGURE 2.10 Principles of back-projection reconstruction algorithm. The unknown object (A) for simplicity is only one point source of radioactivity. The activity profiles are taken from several angles around object (B). By back projection, to each point of a profile one assigns the proportional activity density, constantly along the body depth bellow. These uniform activity distributions are then superimposed, and the approximation improves with number of projections (C and D). However, even in case of infinite number of projections (angles), the residual blurring remains, which looks like 1/r function, r being the distance between source and detector. The cause is the final resolution of imaging device, so that profile strips cannot be infinitely thin, but have certain width. In consequence the image of a point is not a point, but smeared divergently from the center.

SINGLING OUT SLICES INCREASES CONTRASTS

A lesion deep into the body is hard to detect on planar scintigram, even it has accumulated much more or much less radiotracer than the surrounding tissue. This is due to biological noise, which increases with volume of a tissue above and under lesion. Singling out a slice at the depth of a lesion increases the apparent contrast of a lesion, which facilitates its detectability (FIGURE 2.11).

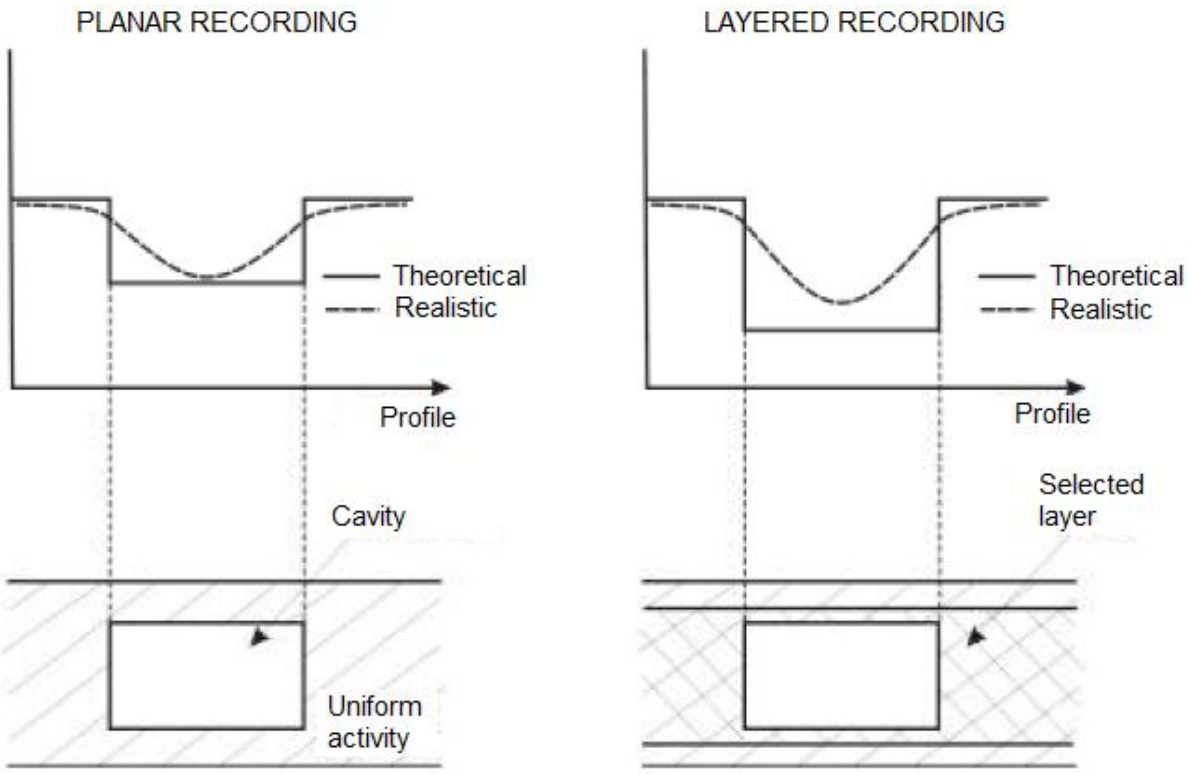


FIGURE 2.11 The effect of singling out a slice on lesion contrast.

TOMOGRAMS HAVE INFERIOR RESOLUTION THAN PLANAR IMAGES

Scintigram resolution (the ability to separate close objects) depends on how smeared is the image of a point source. In ideal conditions tomogram resolution is hardly better than 1 cm, primarily due to collimation, massive detector and errors in electronic localization of scintillation. Tomogram is a result of a mathematical analysis of hundreds scintigrams. The reconstruction algorithm cannot be perfect due to problems arising from attenuation of gamma rays in a body. In addition the input data are only the limited set of statistically limited scintigrams. Because of all these factors the tomogram resolution is inferior to resolution of planar scintigrams, from which it is built of.

Beside this limitation, the lesion detectability is improved, due to prevailing effect of contrast enhancement

In addition to planar resolution, in tomography there is an axial resolution- the ability to resolve details on axis cutting the tomogram at right angle. The later depends on thickness of the slices. It is therefore independent on determinants of planar resolution and can be set at the desired value. However, the price paid for an excellent axial resolution is an increase in acquisition time, needed to reconstruct

large number of tiny slices (recalling the statistical nature of radioactive decay, try to answer why!).

Clearly, imaging from many angles takes considerable time, so that this method provides only static images of radiotracer distribution.

PET: POSITRON EMISSION TOMOGRAPHY

In addition to SPECT there is another tomographic method which uses radionuclides. The method uses positron emitters and is called **positron emission tomography (PET).** Recall that positron decay results in a piece of antimatter-positron, which shortly traverses matter until colliding with electron. In these encounter both particles disappear, while their energy equivalent appears in form of two gamma rays, each having the energy of 511 keV. A decisive fact for PET is that those two gamma rays leave the creation spot in different directions along the same line (recall the law of conservation of momentum (FIGURE 2.12).

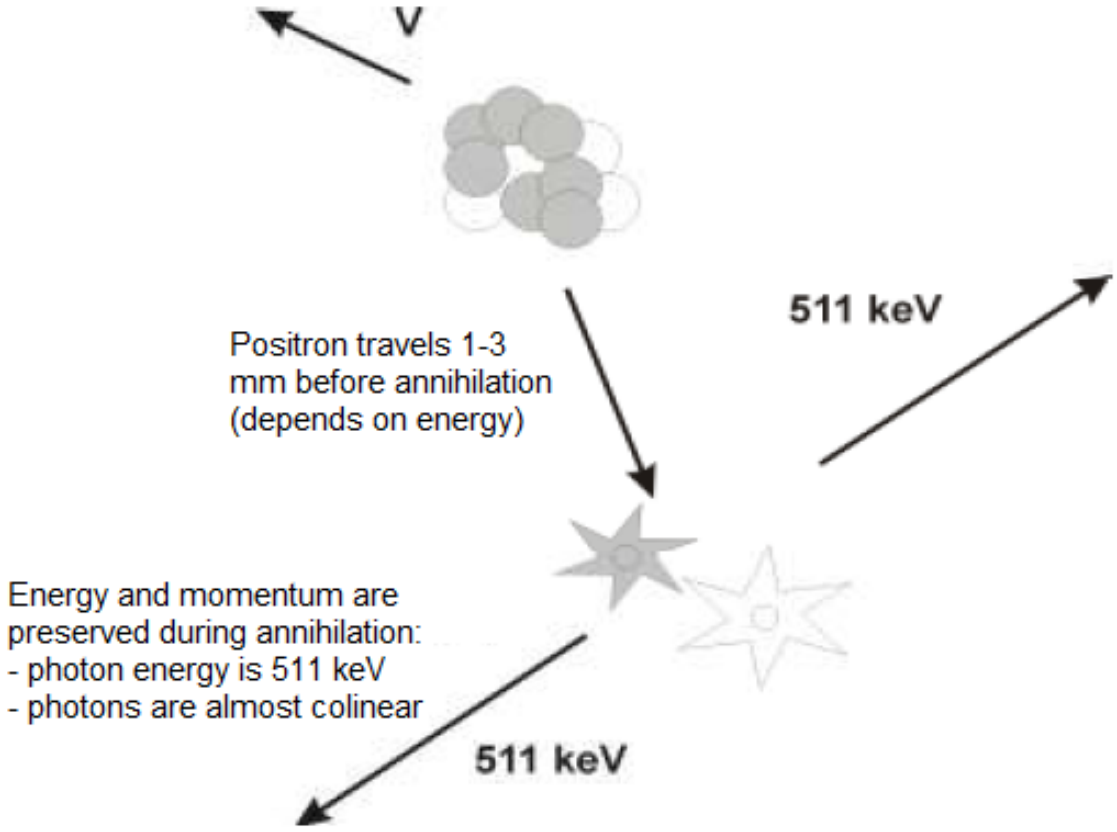


FIGURE 2.12 Events after positron decay.

NO COLLIMATOR REQUIRED- RECORDING OF A PROJECTION IS ALMOST INSTANTANEOUS

The system of small detectors, positioned circularly around the body part investigated, detects the diametrically opposite gamma rays, created by electron-positron collision. The pair of detectors that simultaneously detected a gamma ray defines the line crossing the position of annihilation. Positron source emits radiation in all directions; its position is identified as the section of lines identified by simultaneous detection of detector pairs (FIGURE 2.13).

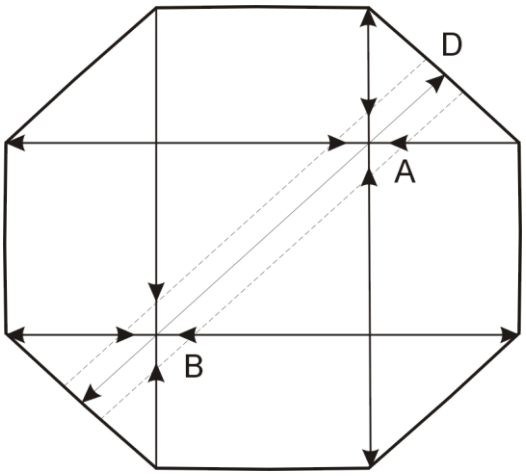


FIGURE 2.13 The position of positron sources (A,B) are on the sections of straight lines of the detector pairs which registered annihilation photons.

Thus, PET reconstruction algorithm resembles the SPECT back-projection algorithm. The crucial difference is that PET does not require collimation of gamma rays. Almost simultaneous arrival of annihilation photons on opposite detectors (the difference is within several nanoseconds) makes it possible to accept only those, coincident events and discard the gamma ray detections that miss the coincident pair. Thus, based on the principle of **coincident detection** the imaging device electronically removes the photons coming from different positron sources, which should otherwise be eliminated physically, by collimation (FIGURE 2.14).

The absence of collimation results in striking advantages of PET when compared to other scintigraphic imaging methods:

1. significantly better resolution (comparable to ultrasound), and

2. drastical gain in sensitivity of radiation detection.

A gain in sensitivity allows for stationary PET detectors, which results in much faster reconstruction of slices than in SPECT, opening the possibility for dynamic tomographic imaging.

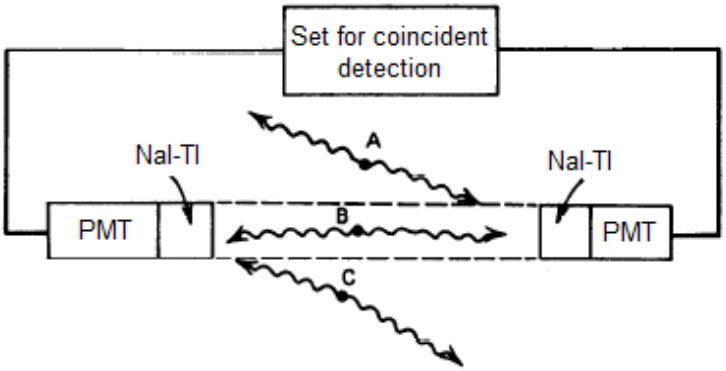


FIGURE 2.14 PET camera utilizes coincident arrival of two annihilation photons on the pair of opposite detectors. In most cases only photons originating from the dotted lines produce coincident pulse in two photomultiplier tubes (FMC). Positrons outside the sensitive volume are usually detected by only one of the detectors. If, by accident, the events in positions A and C are simultaneous, they also produce coincident detection. Those events are rare and cause localization errors.

POSITRON EMITTERS GIVE INSIGHT INTO METABOLIC PROCESSES

Recall that positron emitters are light elements, present in almost each biologically important molecule. Having relatively large excess of protons, they decay fast (TABLE 2.3). These are key features for their diagnostic use.

TABLE 2.3 Common PET radionuclides

Radionuclide	Half-life (min)	Tracer	Use
Carbon-11	20.5	Nitric acid	Clinical research
Nitrogen-13	10	Cardiology	Cardiology
Oxygen-15	2.1	H_2O, CO, CO_2	Clinical research
Fluorine-18	110	FDG and F-dopamine	Oncology, cardiology, neurology
Rubidium-82	1.3	Potassium analogs	Cardiology

Carbon-11, nitrogen-13 and oxygen-15 are radionuclides of elements which are present in virtually all organic molecules, providing opportunity for many applications. Unfortunately, due to fast decay, these radionuclides can only be used in vicinity of cyclotrons. Rubidium- 82 is also short-lived, but can be obtained from a generator.

Some atoms can also be substituted for analogs. The example is fluorine, as hydrogen analog. F-18 is available as the positron emitter, which can be incorporated in radiotracer F-18-fluorine-deoxy-glucose (F-18-FDG). This is by far the commonest PET radiotracer. The applications are practically unlimited since every cell uses glucose as fuel in aerobic metabolism.

Self assessment

Out of five statements, only one is correct

2.1 *The characteristic of radionuclide 99m-Tc IS NOT*:

a) it is ‘“pure” gamma emitter
b) it can be bound to many compounds
c) it is relatively cheap
d) its half-life is 6 hours
e) energy of its gamma photon is 360 keV

2.2 *Radionuclide is both radioindicator and radiotracer in example*:

a) thyroid scintigraphy with J-131
b) renography with ortho-iodine-131-hippuric acid
c) renal scintigraphy with Tc-99m-diethylene-triamine-pentaacetic acid
d) lung scintigraphy with Tc-99m-macroaggregate
e) liver scintigraphy with Tc-99m-sulphor colloid

2.3. *The advantage of radionuclide indicators in measurement of volume of body liquids is*:

a) possibility to collimate gamma rays
b) use of massive detector
c) high specificity of antigen-antibody reaction
d) high sensitivity of registration of gamma radiation
e) stochastic nature of radioactive decay

2.4 Scintigrams have poor resolution because:

a) necessity of collimation and use of massive detector
b) necessity of collimation of gamma rays and fast radioactive decay
c) necessity of massive detector and fast radioactive decay
d) low contrast lesions and collimation of gamma rays
e) low contrast lesions and use of massive detectors

2.5 The advantages of positron tomography over other scintgraphies are:

a) better resolution and easier availability of positron emitters
b) due to imaging without collimation
c) due to large energy of annihilation photons
d) better sensitivity of registrations and easier availability of positron emitters
e) better resolution and possibility of tomography

Chapter III

PHYSICS OF MR IMAGING

- **Magnetic properties of atomic nuclei**
  - Some nuclei are tiny magnets
  - Nuclei in external magnetic field
  - Resonance induction
  - Relaxation times
- **MR imaging**
  - What MR image is and how it is created
  - Diagnostic parameters of MR image

Magnetic characteristics of atomic nuclei

SOME NUCLEI ARE TINY MAGNETS

Let us recall that electric charges, except producing static electric field, can produce magnetic field, as well. The magnetic field is created by a moving charge. That field is proportional to the product of the particle's charge and angular momentum, shortly- **magnetic momentum.** We distinguish the **orbital momentum** of a nucleon, produced by its movement as a whole, and the self angular momentum or **spin**, which can imagined as due to spinning of a nucleon around its own axis. Although the effective charge of neutron is zero, this particle has a complex structure and non-zero angular momentum, including spin. In atomic nucleus, two protons, as well as two neutrons make couples with equal and opposite angular momentums that cancel out. That is why the nuclei with even numbers of protons and neutrons do not have magnetic characteristics. About 2/3 of atomic nuclei have odd number of either protons or neutrons and behave as tiny magnets. The nucleus of interest in medical diagnostics is hydrogen nucleus-proton. The reason is its prevailing abundance in body.

Magnetic resonance (MR) is the phenomena based on magnetic characteristics of atomic nucleus. The abbreviation for the related diagnostic imaging is **MRI (magnetic resonance imaging)**. The term NMR (nuclear magnetic resonance) was abandoned for commercial reasons, since it could misleadingly suggest the presence of ionizing radiation.

NUCLEI IN EXTERNAL MAGNETIC FIELD

Although the individual nuclei are tinny magnets, the macroscopic sample of such nuclei may not produce the gross magnetic field. The reason is that random thermal movement orients the individual magnets randomly in space and individual magnetic momentums cancel out (here we do not consider the possible magnetic effects due to atomic electrons).

The exception occurs when the macroscopic sample is put in the external, permanent magnetic field. As two macroscopic magnets interact aligning their axes, the nuclei 'feel' the external field, orienting in its direction or opposite, i.e. in parallel or antiparallel orientation. However, the alignment is never perfect; in fact the individual magnets exhibit precession around the axis of external magnetic field (FIGURE 3.1).

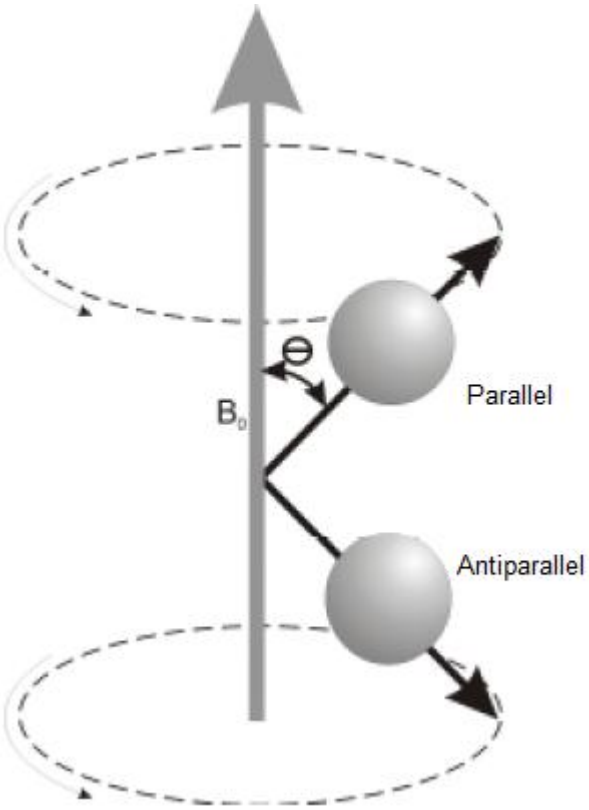


FIGURE 3.1 Possible orientations of nuclear magnetic momentums in external magnetic field B_0.

In steady state there is a tiny surplus of nuclei in parallel orientation, since this is a state of lower energy. In consequence, the external magnetic field magnetizes the sample, producing a non-zero total (net or macroscopic) magnetic momentum facing in its direction (FIGURE 3.2).

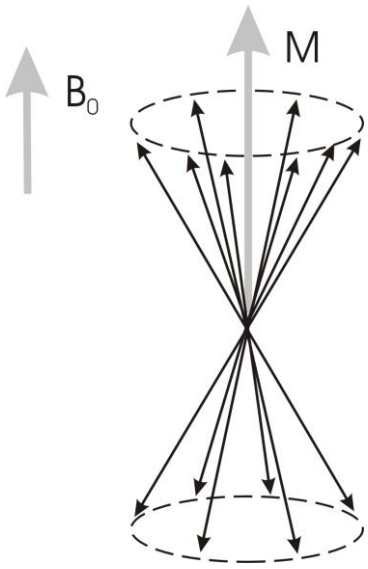


FIGURE 3.2. The addition of individual vectors of magnetic momentums results in macroscopic magnetization M, in the direction of external magnetic field B_o. This happens because the components of individual magnetic moments in transversal plane rotate in randomly different phases

and thus cancel out. On the contrary, the components in direction of B_o do not cancel out because of surplus of nuclei in parallel orientation.

MR signal is due to unequal occupation of energy levels of nuclei, which increases with strength of external magnetic field. That is why in MRI one uses very strong static magnets. However, even in case of magnets producing the magnetic field of 2T, only 16 hydrogen nuclei out of million is the surplus of lower energy (parallel orientation). Therefore:

→ *MR signal is inherently weak, requiring repetition and shielding from noise.*

The difference in energy of nuclei between parallel and antiparallel orientation also increases with strength of an external field. For hydrogen, in magnetic fields commonly used in practice, this energy lies in the range of radiofrequency photons. This is crucial, since our body is transparent for those photons. Recall that our body is only partially transparent to very energetic X and gamma rays, the lower the energy the less penetrable are photons; light and infrared photons cannot go through. However, the reverse occurs for very low energy radiofrequency photons, they simply lack energy required for transition of body molecules to higher states. In MRI, the radiofrequency photons both induce the signal and are the signal itself.

RESONANCE INDUCTION

Next, a small, oscillating electromagnetic field is applied, with magnetic component at right angle to the external magnetic field, rotating with the frequency of precession of individual nuclei. This has two consequences: (i) the nuclei in lower energy state take up the energy of radiofrequency photons to jump to higher energy state and (ii) the individual nuclei are forced to rotate in phase with radiofrequency field. This generates the rotating, transversal component of macroscopic magnetization. This phenomenon, along with fading out of longitudinal component of macroscopic magnetization (parallel with external magnetic field) may be viewed as spiraling- simultaneous nutation of macroscopic magnetization away from *z*-axis to *x-y* plane and precessing of this vector around *z*-axis (FIGURE 3.3).

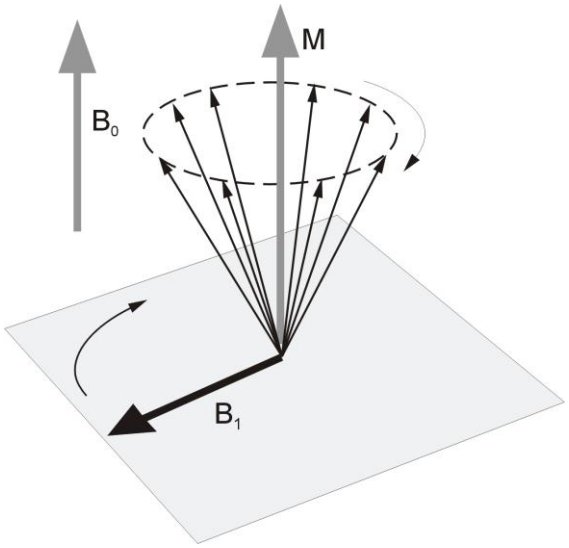


FIGURE 3.3 Transversal magnetization occurs due to individual magnets rotating in synchrony (in phase) with external radiofrequency field B_1.

We say that radiofrequency field induces **resonance** of individual magnetic moments of nuclei, creating the oscillating macroscopic magnetization in transversal plane (perpendicular to longitudinal, z-axis of external magnetic field). This is exactly what makes the MR signal; according to the **Faraday's law**, the oscillations of macroscopic magnetization induce the voltage in a receiver coil, positioned in *x-y* plane (FIGURE 3.4).

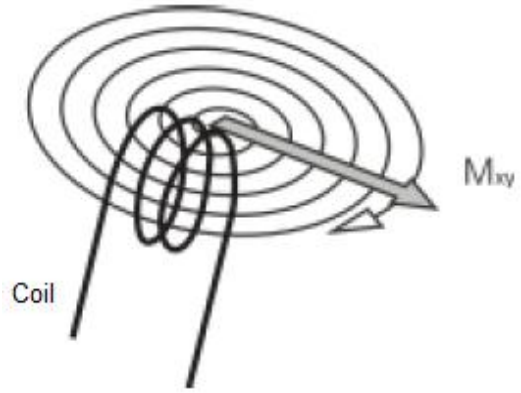


FIGURE 3.4 After applying the radiofrequency pulse the transversal magnetization M*xy* rotates around the direction of steady magnetic field, which, according to Faraday's law, induces electromotor force in a coil in transversal plane.

RELAXATION TIMES

The stronger radiofrequency field and the longer it lasts the more tilt of macroscopic magnetization it produces. The radiofrequency pulse which tilts the macroscopic magnetization to transversal plane, where it rotates synchronously with the field, is **Π/2 pulse**. By then the longitudinal magnetization has vanished

since the nuclei energy levels are equally populated. **Π pulse** corresponds to 180 degrees tilt, reflecting the inverse occupancy of energy levels. After radiofrequency field is turned off the excited nuclei begin to release the surplus energy, returning to a steady state of lower energy. The signals emitted during this period comprise the MR image.

Two partially independent parameters characterize the recovery of assembly of excited nuclei into original state:

T_1 is the time required to restore 63% of longitudinal macroscopic magnetization after Π/2 pulse; this is **spin-lattice relaxation time**;

T_2 is the time required for the transversal magnetization to decay to 37% of its initial value, following Π/2 pulse; this is **spin-spin relaxation time**.

Unlike one would expect, the return of the vector of macroscopic magnetization from transversal plane to longitudinal axis cannot be pictured as the vector of constant magnitude that spirals back from *x-y* plane to *z* axis; i.e. we cannot unroll back the movie of its flipping from z axis to x-y plane. That would wrongly imply that the times T_1 and T_2 are equal. On the contrary, the times T_1 and T_2 are only weakly related. For instance, after complete restoration of longitudinal magnetization (requiring several T_1 times) the relaxation is completed and there can be no residual transversal magnetization. This means that always:

$$T_2<T_1$$

However, it is possible that transversal component quickly vanishes, after which the longitudinal magnetization slowly recovers (elongates) on *z* axis.

These facts are related to mechanisms by which the excited nuclei return to lower energy state.

• Time T_1 relates to the rate of transitions of nuclei from higher to lower energy state. This builds up the longitudinal component of macroscopic magnetization. The energy quanta released equal the energy of radiofrequency photon. These processes may be spontaneous, but the presence of local electromagnetic fields in radiofrequency spectrum significantly accelerates them. For a given nucleus this requires vicinity of the molecules with dipole momentum that rotate in radiofrequency spectrum. For excited protons in pure water T_1 is relatively long, around 3 s, because unbound water molecule rotates too fast. In biological tissue T_1 covers the wide range, from 2 s to several ms. Short T_1 is due to protons in water bound to proteins, or protons in large molecules (lipids), which relax faster, because macromolecules rotate much slower than water, in radiofrequency spectrum.

• Time T_2 relates to loss of resonance and thus the loss of transversal magnetization. This occurs due to slight energy transitions between neighboring nuclei, inducing slightly different rates of rotation and loss of resonance (phase coherence). These processes are not related to gross relaxation of excited nuclei, where much larger energy quanta are released. Therefore, short T_2 does not imply short T_1. In contrast to time T_1, which relates to interaction of nucleus with water

molecule as a whole, the loss of resonance occurs in interaction of two neighboring nuclei (therefore the names for times T_1 and T_2).

In water T_1 and T_2 are approximately equal (around 3 seconds). T_1 shortens with mobility of relaxation centers, since it is advantageous that a nucleus has an access to as many neighboring molecules as possible. This is why in solids T_1 is relatively large. In contrast, the loss of resonance is the faster the more fixed neighboring nuclei are; the fields of many neighboring nuclei cancel out. That is why in solids T_2 is very short. Thus, it generally holds:

$$T_1(\text{solid}) > T_1(\text{liquid}) \approx T_2(\text{liquid}) >> T_2(\text{solid})$$

MR imaging

WHAT MR IMAGE IS AND HOW IT IS CREATED

The coil that creates the oscillating radiofrequency field (excitation) is usually also the detector of signals that follow that excitation. The MR signal is the electromotor force generated on the coil ends due to changes in transversal component of macroscopic magnetization. The signal strength increases with number of nuclei resonating in phase. In case of hydrogen nuclei in a biological sample the signal is strong in areas rich in water.

→ *Thus, MR image is primarily body water map.*

The density of water in body is the source of primary contrast in MRI. This primary contrast can be greatly enhanced by selecting the imaging method which accentuates the spatial differences in relaxation times T_1 and (or) T_2. Let us recall that MR signal is inherently weak, requiring 'sticking' of several thousand of consecutive images one on top of other. Every particular image results from one excitation/relaxation cycle. However, in order to amplify the primary contrast, the pause between two consecutive excitations is intentionally too short for overall recovery of a sample. In this way the fast relaxing nuclei (protons in bound water) dominate in signal over slower relaxing nuclei (protons in free water).

→ *The fast rate of repetition of certain combinations of radiofrequency pulses selectively attenuates the areas with long times T_1 and (or) T_2.*

The coil simultaneously receives signals from different body parts. To create an image it is necessary to resolve signals coming from different spatial locations. The *z* coordinate is unveiled by selective excitation of transversal sample slices- slice by slice.

Thus, MR image is obtained slice by slice, which, in conjunction with repetition of many cycles of excitation/relaxation, causes relatively long imaging time.

The position in *x-y* plane is determined by superimposing the linear gradients to permanent external magnetic field in both dimensions (B_x and B_y). In this way one assigns specific, slightly different external magnetic field (and thus slightly different resonance frequency) to each single position in *x-y* plane. Slightly different permanent magnetic field implies also slightly different frequencies of excitation and relaxation signals. Finally, out of mixture of received signals, one needs to separate out the intensities of different frequencies, i.e. the signal strength corresponding to the particular position in the body (this makes an image). Computer performs those complex mathematical analyses.

DIAGNOSTIC PARAMETERS OF MR IMAGE

The primary *contrast* of MR image is the density of hydrogen nuclei (protons in other nuclei do not contribute to signal). Since body is abundant in water molecules, each having two hydrogen nuclei, the density of proton nuclei approximately equals the density of water.

The primary contrast in MRI would not suffice that this expensive diagnostics competes with CT and ultrasound. Fortunately, tissues having the same amount of water can be displayed with contrast if they differ in relaxation times T_1 and (or) T_2. In this way some malignant tumors display thinner than the surrounding soft tissue because they contain less fast relaxing, bound water.

Due to extremely short T_2, no MR signal emerges from the bones (recall that MR signal reflects the changes in magnetic flux in transversal plane, which is almost immediately lost in bones). That does not mean that bones are not seen in MRI, on the contrary, there is an extreme contrast between bones and soft tissue.

The hydrogen atom is present in other molecules that provide additional contrast. For instance the white matter in brain contains more cholesterol than gray matter, providing stronger MR signal, due to shorter relaxation time of protons in cholesterol compared to protons in water.

Resolution of MR image primarily depends on:

1. homogeneity (space uniformity) of static magnetic field B and

2. magnitude of space gradients B_x and B_y.

Theoretically, the more homogeneous the static magnetic field and the greater its space gradients the better image resolution is. In practice, in imaging of living body, it is also important that the static magnetic field is as large as possible. Strong magnetic field produces strong MR signals, requiring less repetitions and shorter acquisition time. This decreases blurring and image artifacts due to movement of a patient and periodic movements of organs like heart and lungs. Also, the stronger the signal the lesser are effects of electromagnetic noise of a surrounding.

However, the price of a device exponentially grows with strength of a static magnet. In practice we encounter the devices with static magnets that produce magnetic field up to 2 T strong. The uniformity requirement means that this field does not differ in space occupied by a part of a body investigated (better than $1{:}10^{-6}$).

Occasionally, the supraconductive magnets are used. They have coils made of niobium-titanium, a material that, when cooled below temperature of liquid helium, conducts electrical current without resistance. These magnets do not require electrical energy, but must be cooled with liquid helium, which is expensive. The other possibility is use of common electromagnets (coils made of copper or aluminum). Their initial price is lower, but the maintenance is even more expensive, since such magnets require about 40 kW of electric energy.

Self assessment

Out of five statements, only one is correct

3.1 *All nuclei with magnetic characteristics have:*

a) equal numbers of protons (Z) and neutrons (N)
b) N>Z
c) N<Z
d) odd N or Z
e) odd N and Z

3.2 The magnetic resonance signal is weak (A) because

The occupancies of nuclei energy states differ very little (B)

a) A and B correct and associated
b) A and B correct but unassociated
c) A correct, B incorrect
d) A incorrect, B correct
e) A and B incorrect

3.3 *Primary contrast of MR image is amplified by:*

a) use of contrast media
b) increase in strength of static magnetic field
c) increase in strength of radiofrequency field
d) rapid repetition of excitation/relaxation cycles
e) prolonging imaging time

3.4 *Relaxation times T_1 and T_2 of a tissue sample:*

a) do not depend on temperature
b) depend on tissue density
c) depend on abundance of water in tissue
d) depend on abundance of bound water in total water
e) do not differ in bone tissue

3.5 *Localization of MR signal is possible due to:*

a) homogeneity of static magnetic field
b) signal collimation
c) space gradients of static magnetic field
d) inhomogeneity of water distribution in tissue
e) space gradients of radiofrequency field

Chapter 4

PHYSICS OF DIAGNOSTIC RADIOLOGY

What are X-rays?

X-rays are produced by breaking the electrons
Diagnostic X-rays have smaller energies than γ-rays
Roentgen's tube emits photons of various energies
Source of X-rays is described by the quality and beam intensity
Interaction of X-rays with matter
Beam filtration decreases irradiation of a patient

Characteristics of radiograph

Differences in attenuation of X-rays are visible on radiograph
Tube voltage determines the image contrasts
Tube current determines the speed of the image formation
Time of exposition is adjusted to the imaging media
Roentgen's films contain fluorescent enhancers
The size of the beam changes by collimation
The size of the source determines image resolution
Scattered radiation is removed by lead grids

Radiographic methods

The most common in practice are planar radiographs
Contrast agents are injected in bloodstream and body cavities
Fluoroscopy: obtaining of radiograph *in-vivo*
Slice imaging increases contrasts
Each new generation of CT devices is becoming faster and faster

What are X-rays?

X-RAYS ARE PRODUCED BY BREAKING THE ELECTRONS

X-rays were discussed in Chapter 1. It is a high-frequency (energy) electromagnetic radiation, above ultraviolet part of the spectrum. They behave as particles (packets of energy) when they interact with matter. As opposed to smaller frequency light, they cannot be focused. The same is valid for γ-rays; the difference is only in the way of formation. While excited atomic nuclei emit γ-rays, x-rays are produced by breaking the electrons in the medium with high atomic number (heavy metal). The most commonly, X-rays are produced in synthetic sources, the devices made by man (FIGURE 4.1).

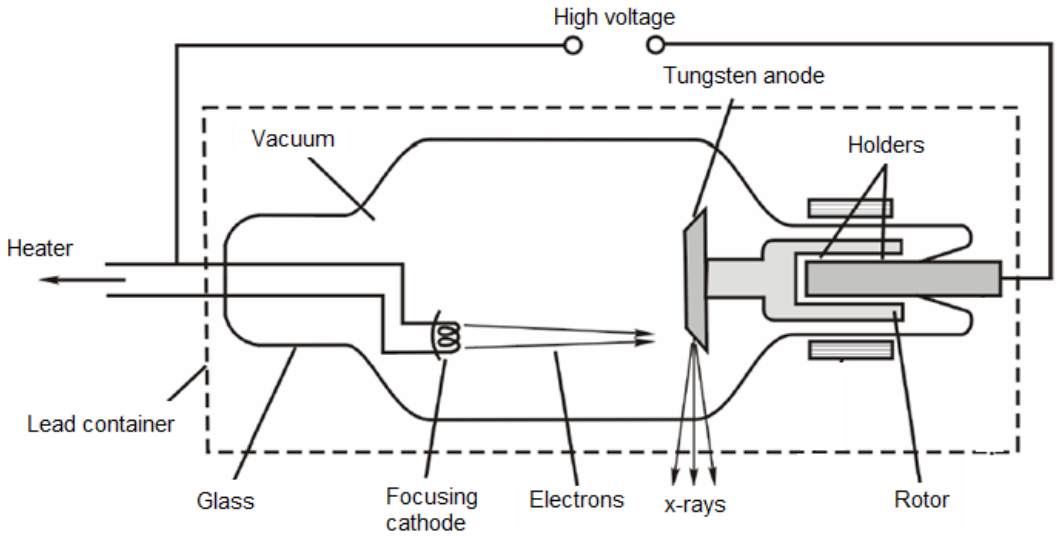


FIGURE 4.1. Device for X-ray production consists of evacuated glass tube that contains two electrodes: negative (cathode) and positive (anode). There is a high voltage difference between them (order of magnitude 10^4 V). Separate heater worms up the cathode and, as a consequence, electrons are released and accelerated towards the anode. These electrons have high kinetic energy. They stop abruptly at the moment of hitting the anode and only small part of their kinetic energy (usually less than 1%) is released in the form of electromagnetic radiation. That is Roentgen's or X radiation. Bigger part of the electron's energy warms up the anode. The anode has relatively small surface (in order to create approximately point source of radiation) and therefore it is necessary to prevent melting of the anode. This can be achieved using the rotating anode. The anode is disc usually made of tungsten that rotates fast around molybdenum arbor. At any time only smaller part of the disc surface is exposed to electron beam. At the same time the rest of the anode is cooling down (more by thermal radiation than conduction).

DIAGNOSTIC X-RAYS HAVE SMALLER ENERGIES THAN γ-RAYS

Gamma rays are relatively weakly absorbed in tissue because they have high energy. In imaging diagnostics their absorption in the body is simply neglected. As opposed to that, images recorded using X-rays (radiographs) are based on absorption of radiation inside of the body. As a consequence, photons with lower energy than the majority of the gamma rays are used.

ROENTGEN'S TUBE EMITS PHOTONS OF VARIOUS ENERGIES

Phenomena when charge breaks and loss of energy releases in the form of photon is called **breaking radiation** (*'bremmstrahlung'*). Photon energy depends on how rapidly the charge breaks. Therefore energies range from zero (big wavelengths) to value equal to initial kinetic energy of the electron. Latter case corresponds to complete arrestment of the electron. Upon arrival at the anode all electrons have the same kinetic energy, which is equal to the product of electron charge and tube voltage eU. This means that the energies emitted by X-tube range from zero to maximum (specified by tube voltage). The frequency of various energies in that range represents spectrum of X-rays. Its shape depends on the material that anode is made from and consists of two parts which differ in origin (Figure 4.2):

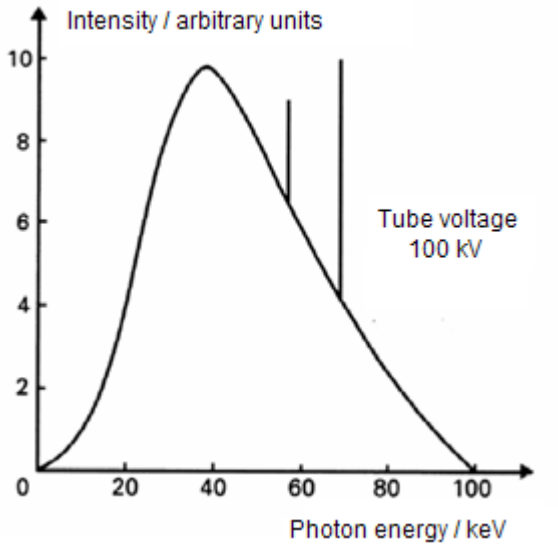


FIGURE 4.2. Spectrum of tungsten X radiation as a function of photon energy

- Continuous spectrum is generated by described breaking radiation. Graphically it is a modal, continuous line, tilted to the right (the most common energy is ~40% of the maximal energy).
- Line spectrum is generated as a result of emission of several discrete energies, visible as thin lines sticking above the continuous part of the spectrum. It is produced by fast electrons that ionize atoms of the anode, having enough energy to eject well-bounded inner electrons (from K and L shells). After that, electrons from the higher energy shells descend to the empty spots of the lower energy shells. The energy difference is released in the form of photon with, for anode, characteristic energy. Therefore, the position of these lines depends only on the material that the anode is made of.

SOURCE OF X-RAYS IS DESCRIBED BY THE QUALITY AND BEAM INTENSITY

X-ray beam quality describes its penetration. It is determined by the shape of its spectrum. If high energy rays predominate in the spectrum, the beam is penetrative, so called **hard X-rays**. In contrast, **soft X-rays** have low energy and they penetrate weekly. Increase in beam quality means a shift of its spectrum to the right (towards higher energies).

Intensity of the X-ray beam represents sum of intensities of all parts of the spectrum (energy intervals), what corresponds to the area under the spectral curve.

- If tube voltage increases, starting energy that electrons have when they hit the anode also increases. As a consequence:

1. more energy is available for x-rays production, therefore the radiation intensity increases
2. posible losses of electron energy are bigger, what increases *quality* of radiation.

It can be concluded if tube voltage increases, spectrum of radiation will be increased and shifted towards right (FIGURE 4.3A)

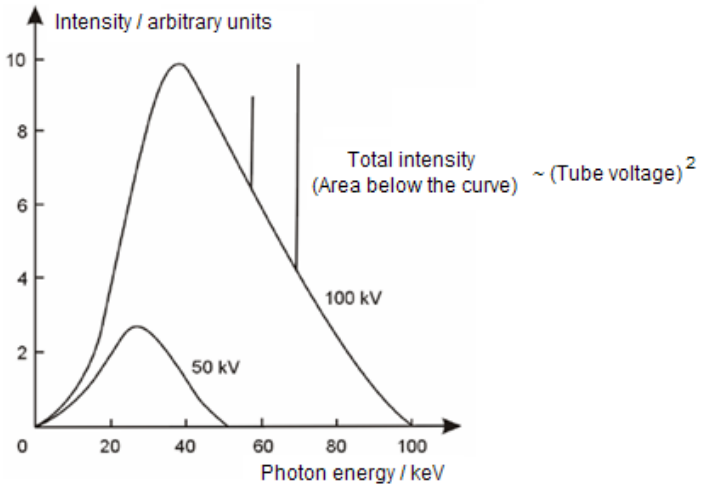


FIGURE 4.3A. Effect of tube voltage on spectrum of X-radiation

- If the heating current increases, number of electrons released from cathode pet time unit also increase. This increases only radiation intensity, spectrum of radiation increases without any shifting (FIGURE 4.3B).

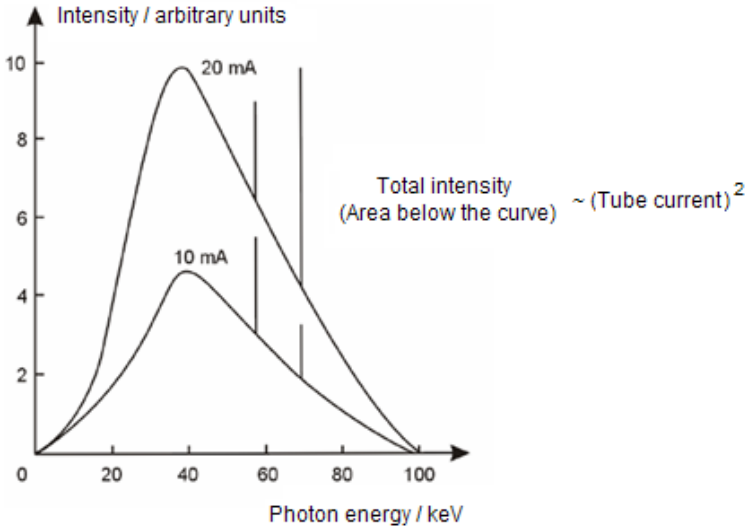


FIGURE 4.3B. Effect of tube current on spectrum of X-radiation

INTERACTION OF X-RAYS WITH MATTER

The intensity of an X-ray beam, which in vacuum spreads from point source as a spherical wavefronts, depends on the inverse square of distance from the source because the surface of the sphere, where X-ray beam spreads around, increases (Chapter 1).

In the case of parallel X-ray beam (the source is located far away or the beam is collimated) its intensity will fall only because of interaction with matter in which X-ray beam spreads around. Mechanisms of interactions are the same as for γ-rays: photoelectric effect, Compton scatter and pair production, for energies bigger than 1.022 MeV (TABLE 4.1). Besides, there is a possibility of simple scatter for smaller energies in which X-ray changes direction without any loss of energy.

TABLE 4.1. Probability of interaction between X photon (with energy *E*) and matter (atomic number *Z*).

Mechanism	**Dependence on E**	**Dependence on Z**	**Comment**
Simple scatter	Falls with E	Rises with Z	Important only for E<20keV
Photoelectric effect	Falls fast with E ($\sim 1/E^3$)	Rises very fast with Z ($\sim Z^3$)	Dominant process in diagnostic devices
Compton scatter	Falls very gradually with E	Independent	Dominant process in therapeutic devices
Pair production	Rises with E	Rises with Z	Important above 5MeV, happens above 1.02MeV

If sum of probabilities of that processes per distance unit in some medium (for X-rays of only one energy) is labeled with μ (the total linear attenuation coefficient), the incident beam intensity I_0 falls with the thickness d of the medium according to the equation:

$$I=I_0 e^{-\mu d}$$

Reminder: mass attenuation coefficient ($\mu_\rho=\mu/\rho$) is also in use.

In reality, X-rays are heterogeneous, thus for the whole beam upper equation is not valid (it is valid only for each energy separately). The half value thickness, $\boldsymbol{d_{1/2}}$, is defined as the thickness of the material which reduces the incident intensity to half of its original value.

The attenuation coefficients are smaller for high energy photons, it is more difficult to attenuate high energy X-rays. Therefore, when energetically heterogeneous X-ray beam passes through matter it becomes harder and its half value thickness is not constant anymore. It increases up to value determined by maximal photon energy.

In radionuclide imaging diagnostic we were interested in interaction between γ-rays and radiation detectors, while its transition through body did not contain diagnostic information. Contrary, in diagnostic radiology, image content is determined by interaction between radiation and body.

The most common voltage in diagnostic X-tubes is ~30kV, so the highest photon energy is 30keV. Photoelectric effect is dominant way of attenuation in tissues for those energies. Because of the fact that the probability of photoelectric effect rises very fast with Z ($\sim Z^3$), bones ($Z \approx 14$) absorb radiation more intensively than soft tissue ($Z \approx 7$). Bigger bones density (1.5 to 2 times) contributes to that phenomenon additionally. Therefore, there will be a big contrast on radiograph between bones and soft tissue.

The majority of devices for radiotherapy produce high energy X-rays, from 0.5 to 5 MeV (except when used for skin tumor irradiations).Compton scatter is dominant process at that energies. Because of the fact that Compton scatter is independent on atomic number, preferred bone irradiation is not too expressed (the most commonly, that is not a goal).

BEAM FILTRATION DECREASES IRRADIATION OF A PATIENT

In radiologic diagnostics are useful photons of energies that partly pass through body and partly absorb in it (depend on thickness and kinds of tissues on its way). Low energy photons are not useful because tissue absorb them completely, it does not matter which direction they pass. Therefore the primary X-ray beam is directed through thin layer of absorber first (process called **filtration**).

Passing through absorber the beam becomes harder, lower energies are less present in its spectrum (FIGURE 4.4). Materials with high atomic number are used and, as a consequence, photoelectric effect becomes dominant way of attenuation. In this process low energy photons are absorbed. Contrary, in Compton scatter they are being replaced with photons that have smaller energy and changed direction.

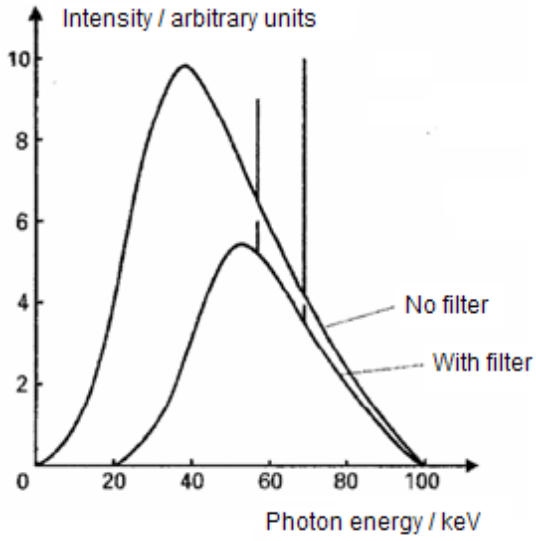


FIGURE 4.4. X-ray beam spectrum, after filtration, has smaller intensity and smaller frequency of low energies

Few millimeters thick aluminum filters (Z=13) are used in diagnostic devices. In therapeutic devices, filters are made of heavier metals (copper, lead or gold).

Characteristics of radiograph

DIFFERENCES IN ATTENUATION OF X-RAYS ARE VISIBLE ON RADIOGRAPH

Divergent X-ray beam is emitted from almost point source and enters the body. Image forms on the medium located behind the body (FIGURE 4.5). Each X-ray has different direction. Therefore, when they pass through body without interaction they illuminate roentgen film at different positions. Certain part of the film will become blacker if more X-rays illuminate it. This will be fulfilled if:

1. the body in the direction of illumination is thin
2. the matter on the way of illumination is less dense and consisted of lighter atoms.

Radiograph can be described as a plane display of divergent X-ray beam attenuation in the body. Two presented dimensions are almost vertical on the majority of X-rays in the beam. Third dimension represents the body thickness in the direction of the beam center and it is not displayed.

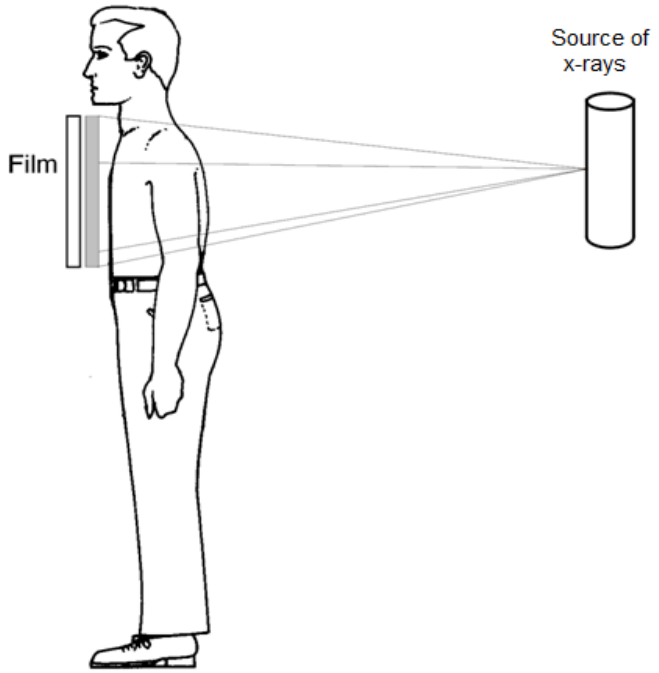


FIGURE 4.5. Schematic display of radiograph creation

In this imaging diagnostic method the source of radiation is point (unlike in scintigraphy method that displays the distribution of radioactivity) and it does not have to be collimated. Additionally, X-rays have lower energies than the majority of γ-rays and therefore they can be detected at relatively thin media. These are crucial advantages regarding image resolution.

TUBE VOLTAGE DETERMINES THE IMAGE CONTRASTS

Radiograph is determined by two different factors:

1. dimension and a kind of tissue projected on the film

2. quality of X-ray beam

Both factors determine imaging contrasts, while only the later can be influenced (by changing tube voltage)

In principle, changing of tube voltage causes changes in relative frequency of photoelectric effect and Compton scatter in the patient body. Lower tube voltages are used if we want to present bone structures better (FIGURE 4.6A). Contrasts inside of soft tissues can be increased by increasing of tube voltage (FIGURE 4.6B).

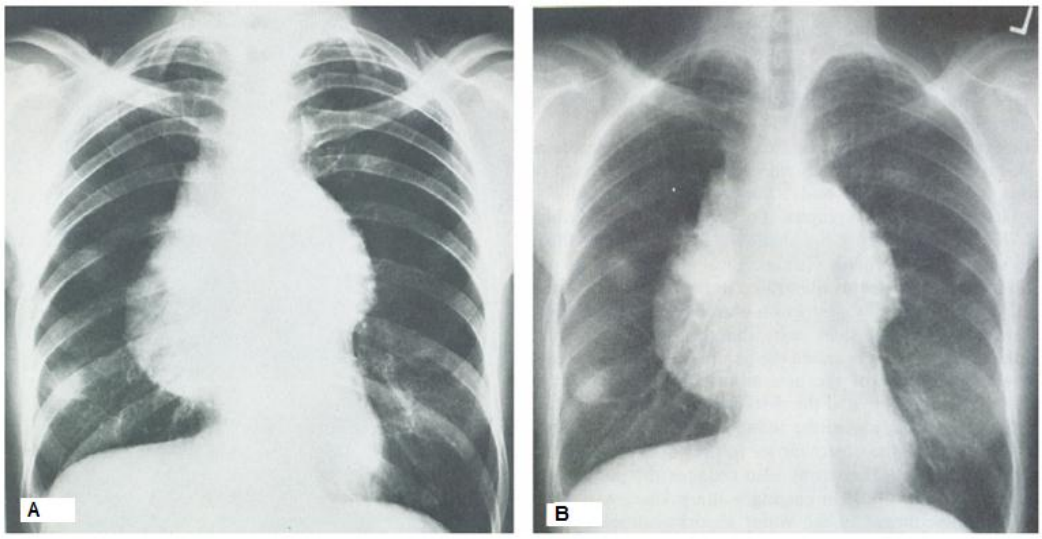


FIGURE 4.6. Two radiographs of the chest recorded for the same patient. Figure A is recorded using tube voltage 80kV. Ribs are shown with high contrast. Figure B is recorded using tube voltage 350kV. Ribs are visible with smaller contrast, while soft tissues are visible much better.

TUBE CURRENT DETERMINES THE SPEED OF THE IMAGE FORMATION

Increasing of cathode heating current does not change radiation quality but it increases number of emitted photons pet time unit. As a consequence, the speed of film or some other detecting device (fluorescent monitor) illumination increases. In order to decrease influence of a patient motion and unavoidable periodical moves of inner organs on the image quality it is necessary to record image in the shortest possible time.

TIME OF EXPOSITION IS ADJUSTED TO THE IMAGING MEDIA

Too small film exposition means insufficient radiation intensity or too short recording time, and vice versa. Radiation intensity increasing (by increasing of cathode heating current) is limited by anode overheating. Thus, for specified tube voltage (determined based on the type of check up) and specified cathode heating current (determined by mechanical properties of anode), optimal film exposition is achieved by adjusting a time of exposition. The size of the patient is a factor that should be considered too. An absorption and beam scattering increase when X-ray beam passes through bigger person. The beam divergence is bigger as well.

ROENTGEN'S FILMS CONTAIN FLUORESCENT ENHANCERS

Unlike γ-rays, X-rays can be detected on a film. Simple photographic film is not used than special film. Roentgen's film is a photographic film positioned between fluorescent layers (usually zinc sulfate crystal). Usually, X-rays interact with fluorescent layers, than they emit visible light that makes film blacker (FIGURE 4.7).

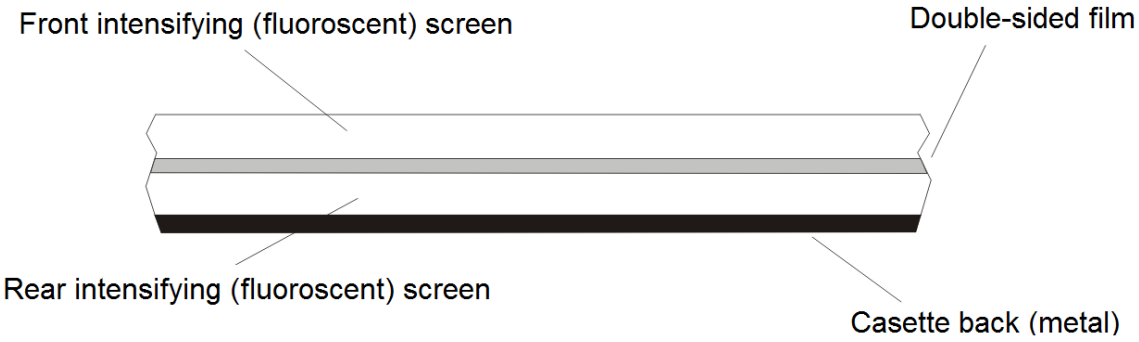


FIGURE 4.7. Cross-section of Roentgen film.

Fluorescent layers amplify the speed of film illumination rapidly. But one fluorescent point source will illuminate limited film area; at higher distances it will be bigger (depends on the thickness of fluorescent layer). Such image scatterings, from primary (fluorescent layer) to secondary media (film) mean small loss in image resolution.

THE SIZE OF THE BEAM CHANGES BY COLLIMATION

The shape and size of X-ray beam at the exit from tube is adjustable by massive absorber, which allows radiation to pass only through changeable hole located in the middle (diaphragm). In that way certain part of the body can be chosen for recording and the system can be adjusted to the patient size. The device contains a bulb and mirror that creates the same shape beam like X-ray beam. In that way the area exposed to X-rays becomes visible (FIGURE 4.8).

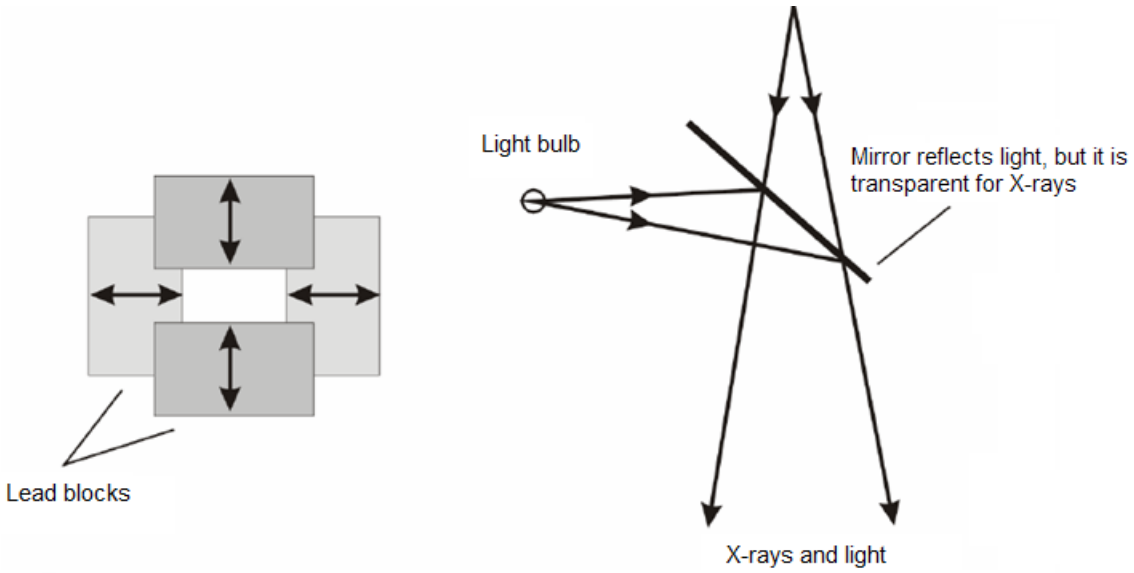


FIGURE 4.8. Collimator of Roentgen's film: (A) changeable diaphragm system, (B) optical control

THE SIZE OF THE SOURCE DETERMINES IMAGE RESOLUTION

In order to form sharp image (object shadow) it is necessary to have point source because X-rays cannot be focused. In reality source is not a point than small square

surface called focal spot. Therefore, radiograph is not perfectly sharp image, it has finite resolution (FIGURE 4.9A).

Anode has to have sufficient surface in order to prevent melting caused by heating. If the cathode tilts towards the beam vertical the dimension of the focal spot can be decreased. That is the way how effective size of the focal spot becomes smaller than its actual size (FIGURE 4.9B).

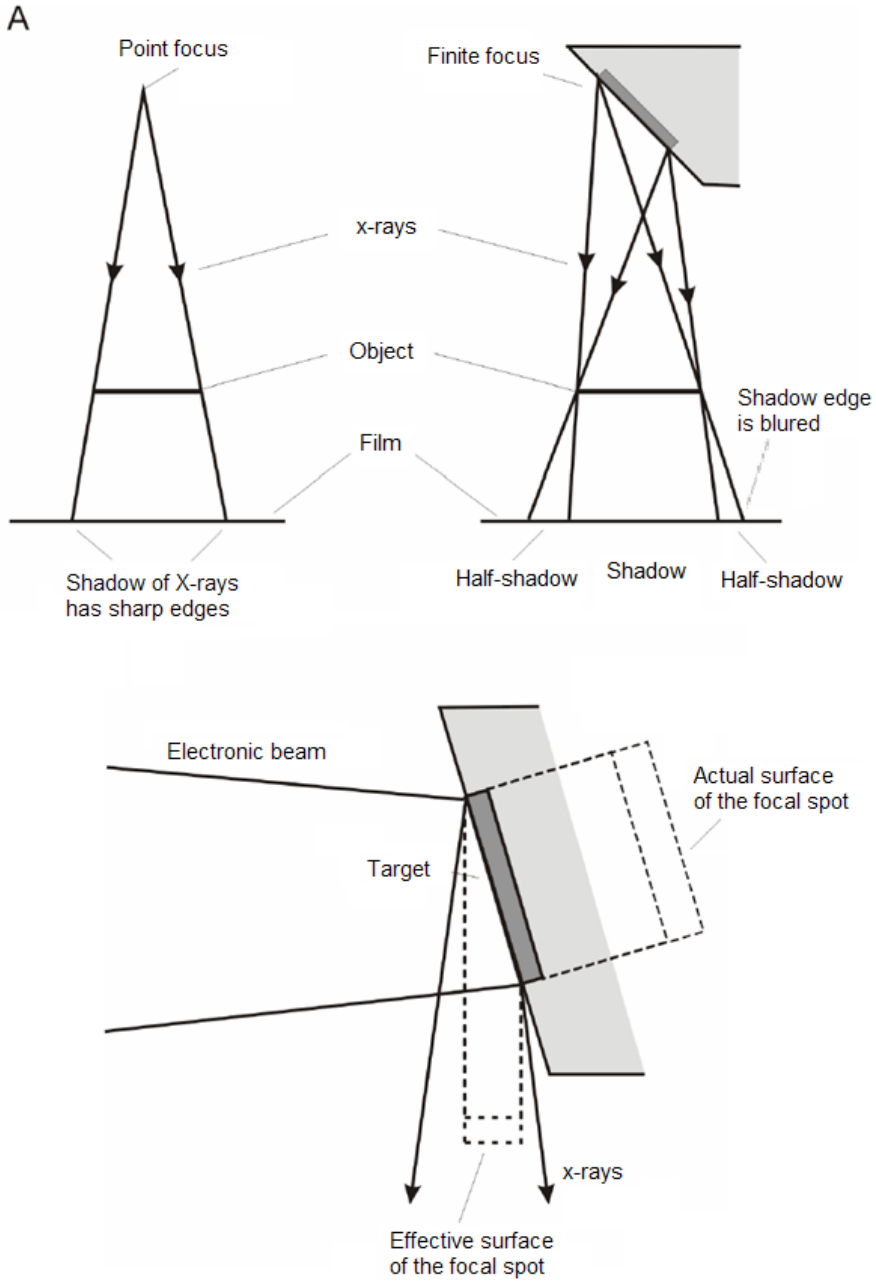


FIGURE 4.9. Factors that influence sharpness of the radiograph (half-shadow)

Decreasing the effective size of focal spot makes radiograph sharper but, as a consequence, number of photons used for image formation gradually decrease (space angle under which the object "see" the anode becomes smaller). Thus, as a final result the radiation intensity declines. It becomes necessary to increase an exposition time (loss of dynamic information).

The best possible resolution is required in clinical practice if we record relatively static structures. In the case of dynamic structures it is necessary to find optimum between opposite requirements for sharpness and dynamic information (between a space and time resolution).

Finite size of radiation source causes formation of half-shadow on radiograph. It is obvious, from FIGURE 4.9, that half-shadow dimension has properties:

1. rises depend on effective size of the focal spot
2. rises when the distance between object and film rises
3. falls when the distance between source and film rises

Increasing the distance between the source and patient (as well as the distance between the source and film) improves the resolution of radiograph. But the radiation intensity falls depend on the distance from the source. So, for that way of image improvement the same limitations like for decreasing the size of effective focal spot surface are valid (anode overheating, loss of dynamic information caused by longer exposition).

Distance between the object and film is determines by anatomic relations and relative position of the film and body. Therefore, it is significant if we record some organ from front towards back (anterior-posterior) or vice versa. Structures located closer to film will be shown clearer than these located at bigger distances, but magnification will be smaller.

SCATTERED RADIATION IS REMOVED BY LEAD GRIDS

Both, photoelectric effect and Compton scatter in the patient body influence contrast of radiograph. Photoelectric effect is preferred interaction regarding image resolution. In that process photon is completely absorbed (disappears), while Compton's scattered photon can exit the body and illuminate film at the "wrong" position. Such events decrease sharpness and imaging contrasts. It can be prevented by using specific **lead grids** (FIGURE 4.10).

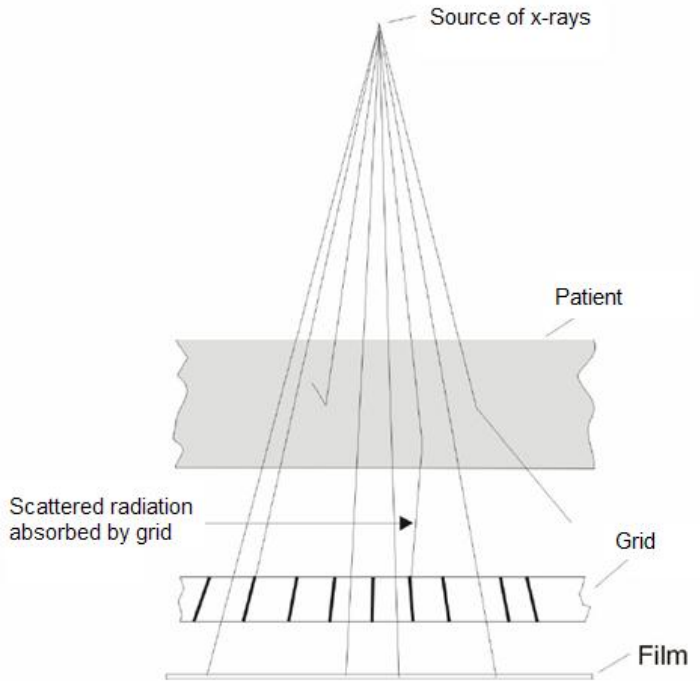


FIGURE 4.10. Lead grid cross-section used to remove scattered X radiation. Lead strips are positioned with bigger dimension (5 mm) in the direction of X-rays, inside of the material in which X-rays pass through. In the direction of the surface they are only 0.05 mm wide and positioned ~ 0.5 mm apart. In that way the majority of primary (unscattered) photons will pass, while the grid absorbs scattered radiation. Influence of half-shadow (created by grid) is eliminated by shifting of the grid during recording.

Radiographic methods

THE MOST COMMON IN PRACTICE ARE PLANAR RADIOGRAPHS

Planar radiography is the most common method of radiographic imaging diagnostics. It represents two-dimensional display of X-rays attenuation in the part of the body where the beam passed through. Its advantages are: simplicity, speed, low price and relatively low dose of, by patient, absorbed radiation.

Sometimes, information that we get using planar radiography is not sufficient. Disadvantages of this method are:

1. it is static
2. it is difficult to make a difference between tissues with different thickness (dimension that is not presented)

Therefore, developed are methods that improve imaging contrasts and can monitor movements.

CONTRAST AGENTS ARE INJECTED IN BLOODSTREAM AND BODY CAVITIES

Drastic increasing of radiographic imaging contrasts is achieved by synthetic contrast agents' application in the bloodstream and body cavities. Usually, agents with high atomic numbers (iodide and barium) are used. These agents completely absorb radiation and create sharp shadow compare to surrounding tissue. Another possibility is replacing liquids from the space with air. That also increases visibility of monitored part, but in an opposite way, using increased film expositions. Methods achieve incomparably detail displays of anatomic structures.

Disadvantages of using contrast agents are:

1. possibility of allergic and other unwanted reactions
2. invasiveness, in the case of artery or body spaces punction.

FLUOROSCOPY: OBTAINING OF RADIOGRAPH *IN-VIVO*

In order to display time changes (dynamics), it is necessary to exchange film by medium where images are not recorded permanently. It is possible using fluorescent screens. "Alive" Rontgen's image is created in this way. Chest movement during breading, heart work, flow of contrast carried by blood and other physiological functions can be monitored.

Unfortunately, radiation intensities that create immediately visible image are very often unacceptably big. Therefore, the lightening of primary image amplifies ~1000 times using **image amplifiers** (FIGURE 4.11).

Method is called fluoroscopy and provides unique diagnostic information. Compared with film recordings, disadvantages are:

1. much bigger absorbed doses
2. worse resolution.

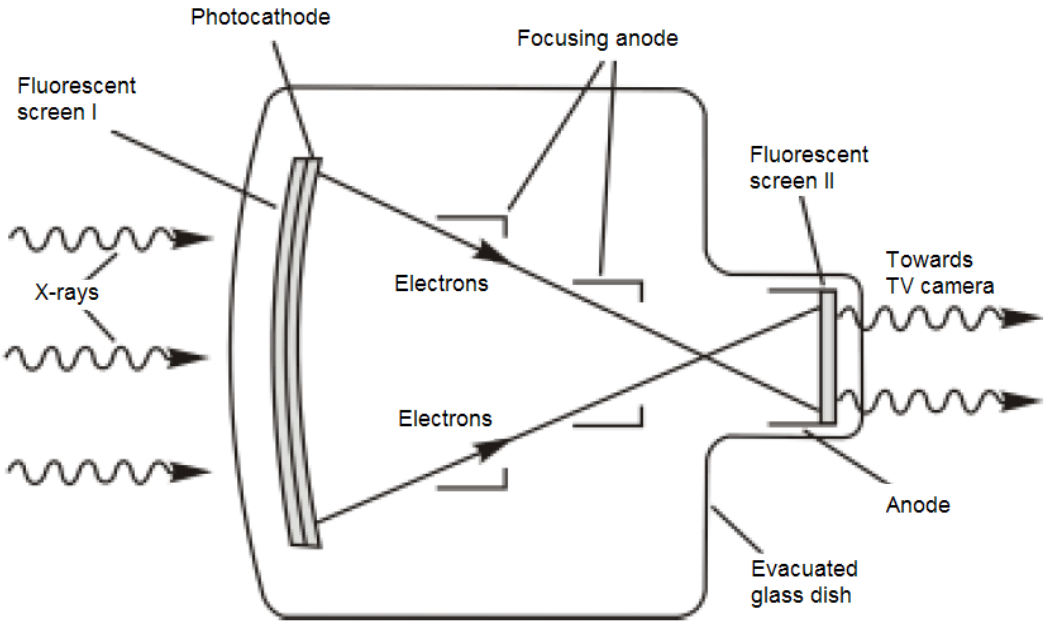


FIGURE 4.11. Part of X rays energy absorbed by fluorescent screen is released by emission of visible light photons (Chapter 1.). Light photons release electrons in sticked photocathode. That electrons speed up than and focus on the row of anodes adjusted at successively higher potentials. One electron kicks out few secondary electrons at each anode. Finally, multiply amplified electron beam falls at the second fluorescent screen. Created secondary image is additionally recorded by camera or video recorder.

SLICE IMAGINGS INCREASE CONTRASTS

Radiographs are three-dimensional structures projected in the plane of film (or fluorescent monitor). This is similar like scintigrams that represent plane display of three-dimensional distribution of radioindicators. Different thicknesses of neighboring tissues make difficult to differ them. Separating the slice of interest eliminates this problem, because all details have the same thickness.

There are two methods of radiologic diagnostics: **classic tomography** and **computerized tomography (CT).** In the first one tomogram is obtained directly, in the way that film and radiation source move during recording (FIGURE 4.12).

Contrary, CT is reconstruction method; image of the body cross-section is obtained by computer.

Entering data are X-rays' attenuations that pass through body under different angles, in the plane of chosen cross-section. The way of obtaining this data is to compare radiation intensities that leave the body (measured by scintillation detectors) with starting (unattenuated) intensity (FIGURE 4.13).

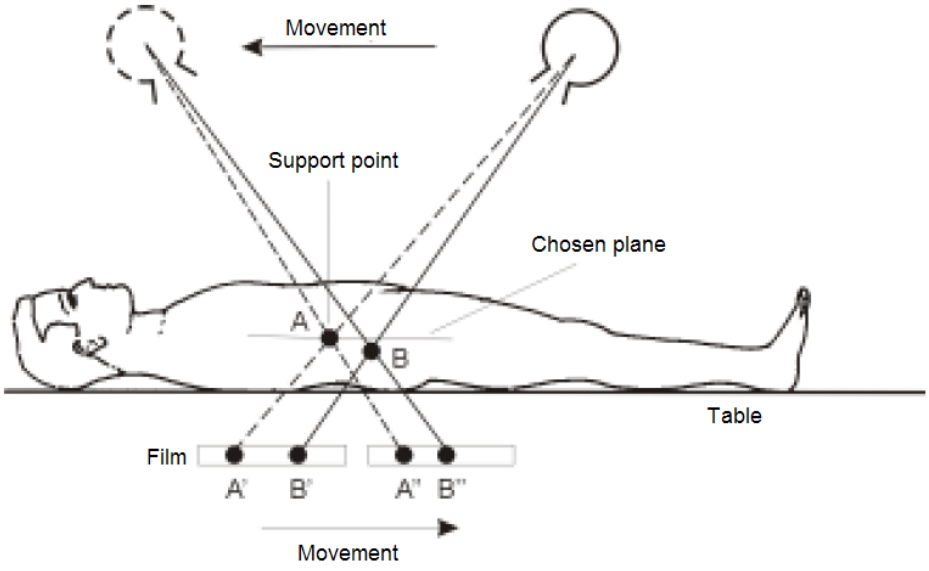


FIGURE 4.12. Device for linear tomography. Roentgens' tube and film are mechanically connected in a way that they move parallel and have support in the plane of chosen slice. In that way the object images are in the chosen plane (i.e. A), always at the same place on film (A'), while the object images are blurred outside of that plane (i.e. B), because they are created at the different places on the film (B' and B'').

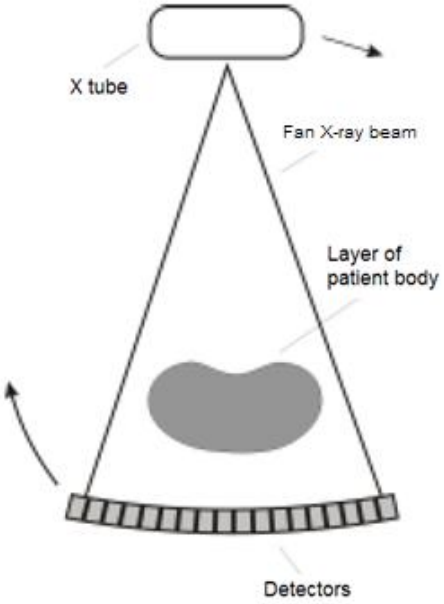


FIGURE 4.13. Third generation of CT devices. The source emits X-ray beam that passes through investigated body cross-section. Their intensity is measured by few thousands of small detectors, which create circular section. The source and detector move around chosen slice during recording. After that patient moves along axis of a device, and recording of the next parallel slice starts. The data are sent to computer that reconstructs the image.

There are a few reconstruction algorithms. One of them is similar to method of SPECT data backward projecting (Chapter 2). The difference is in output data; instead of radioindicator density, coefficients of linear attenuation (μ) in chosen body slice are used. In computer memory CT tomogram is matrix of numbers. Coefficients of attenuation are shown as relative numbers, called **CT numbers**:

$$\text{CT number} = 1000 \times (\mu_{tissue} - \mu_{water})/\mu_{water}$$

Usual range of CT numbers is from -500 (air) to 500 (compact bone). Soft tissues CT number is around zero (FIGURE 4.14). CT number is also called **radiological density**. Even though it has no dimension, sometimes radiological density is expressed in Hounsfield's units (HU) as an honor to investigator that developed the first commercial CT device in 1972.

CT tomography provided drastic improvements compared to planar radiography. Planar radiographs can sharply differentiate soft tissues compared to bones, while details of soft tissues (like blood vessels) can be differentiated only when contrast agents are used. Tissues that only slightly (less than 1%) differ in linear coefficient of attenuation of X-rays can be differentiated at CT tomograms because thin body slice (few millimeters thick) is separated. Imperfections of reconstruction process degrade image resolution just like in other tomography methods. Therefore the resolution of CT tomogram is ~1mm, while it is little bit smaller (better) for planar radiograms. This small loss in resolution is less significant than drastic improvement of imaging contrasts.

Besides, CT tomogram is primarily qualitative image that can be mathematically analyzed. That contributes to visual estimation of image on the video screen.

EACH NEW GENERATION OF CT DEVICES IS BECOMING FASTER AND FASTER

In the first CT device the source of X-rays was collimated, creating practically only one ray (pencil beam). One slice recording lasted three minutes, while the whole check up lasted much longer (usually, the area of interest covers ~10 slices, each of them 2-3 mm thick). Clinical application of this method was limited to the head (it was possible to fix it mechanically) because patient movement can significantly degrade a CT image quality. The chest and abdomen images were significantly blurred because of respiratory moves of the inner organs.

The second and following generations use fan collimated source of rays (*fan beam*). In devices of third and fourth generation the beam is wide; it covers the whole cross-section of the body (FIGURE 4.14). The time of one slice recording is shortened to 4-5 seconds; that is comparable to the time that source requires for

completing one rotation around the patient. This allows application of this method to the chest and abdomen (patient is supposed to keep breath during recording).

After one slice is recorded patient moves parallel to the detector axis and the second slice recording can start. Improvement in image quality is provided in device variant of fourth generation, called **spiral CT**. In that case patient movement parallel to the detector axis is not intermittent than permanent. The source of the rays moves spirally around a patient. The device was named after that.

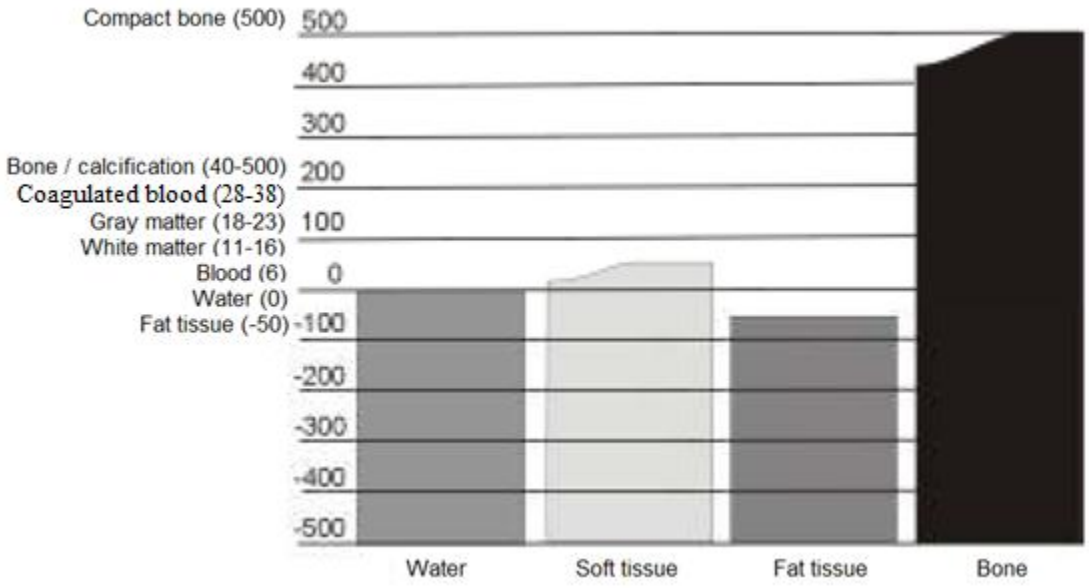


FIGURE 4.14. Typical radiological densities of the head tissues.

Tomograms can be recorded quite fast using CT devices of third and fourth generation, with possibility to control respiration movements. These are still cell recordings; unavoidable and fast moves of heart and pulsating blood vessels still blur the image.

Big step forward is provided by fifth generation of CT devices. In this case there is no moving of mechanical parts. Electronic beam moves fast by round target using electronic collimation. The time of slice recording is shortened to ~10 milliseconds. Besides, using bigger number of targets it became possible to record more slices simultaneously (*multi-slice CT*). This provides dynamic CT recordings, and images of heart and organs well supplied by blood (like liver) are much clearer.

Self assessment

Out of five statements, only one is correct.

4.1. *After hitting the anode of Roentgen tube, kinetic energy of electron:*

a) mainly transfers to heat
b) mainly transfers to X-ray energy
c) completely transfers to X-ray energy
d) partly transfers to kinetic energy of anode rotation
e) exponentially falls to zero

4.2. *Positions of characteristic lines of X radiation spectrum depend on:*

a) tube voltage
b) intensity of X radiation
c) cathode heating current
d) speed of anode rotation
e) material that anode is made of

4.3. *Rise of X radiation beam quality:*

a) means rise of photoelectric effect frequency in exposed material
b) as a consequence has increased anode heating
c) is achieved by increased cathode heating
d) it can be achieved by X-ray beam filtration
e) is achieved by tube voltage decrease

4.4. *If we want to see clearer the ribs on the planar radiograph of the chest:*

a) we will increase the time of exposition
b) we will use the special film
c) we will increase the cathode heating current
d) we will increase tube voltage
e) we will decrease tube voltage

4.5. *Planar radiograph resolution depends on everything EXCEPT on:*

a) effective size of focal spot
b) distance object-film
c) distance focus-film
d) tube voltage
e) target orientation

4.6. *Transmission computerized tomography (CT) is an advancement compared to planar methods regarding:*

a) increased image resolution
b) decreased radiation dose of a patient
c) allows registration of dynamic processes
d) decrease the image blur caused by body movements (organs)
e) detection of soft tissue lesions

Chapter 5

PHYSICS OF ULTRASOUND DIAGNOSTICS

- Formation, propagation and detection of ultrasound

  Ultrasound is used because of negligible diffraction
  Piezoelectric crystal creates and detects ultrasound
  Reflections occur at the boundaries of different materials
  Loss of sound energy depends on the material and sound frequency

- Displays of ultrasonic echoes

  The A-scan measure a depths of reflective boundaries
  The B-scan is alive image of the body cross-section
  The M-scan is graphical record of the motion velocities
  Motion velocities are measured by Doppler effect too

- Parameters of echogram

  Tissues with different density and elastic properties are shown with contrast
  Two parameters of ultrasound image resolution
  Ultrasound image artifacts

Formation, propagation and detection of ultrasound

ULTRASOUND IS USED BECAUSE OF NEGLIGIBLE DIFFRACTION

Ultrasound is sound wave of frequencies above those which the human ear can hear (above 20 kHz). Frequencies used in imaging diagnostics are in the range from 1 to 20 MHz. Physical properties ultrasound do not differ from sound waves of other frequencies. It is used in diagnostics because of relatively small diffraction.

Essentially, the ultrasound source sends short pulses of high frequencies in the body. Time that passes until the reflected pulse returns to the source represents the information about position of various structures in the direction of the pulse propagation. Therefore it is important that the pulse spreads straight, without turning. However, sound waves turn beyond the edges of cavities (diffraction). The effect is more pronounced if the wavelength is greater. Ultrasound wavelengths in soft tissue are usually smaller than 1mm, and the turning of an ultrasound pulse from the standpoint of imaging diagnostic is negligible.

PIEZOELECTRIC CRYSTAL CREATES AND DETECTS ULTRASOUND

Piezoelectric crystals (quartz or synthetic ceramic - lead zirconate titanate) change the size in an electric field. Also, if the external force deforms the crystal, they generate an electric field. These phenomena are a consequence of the separation of centers of positive and negative charges in the crystal lattice (FIGURE 5.1).

If the external electric field is alternating, the crystal will vibrate with field's frequency. If the frequency is large enough, the vibrations will be a source of ultrasound. Contrary, if the ultrasound wave excites crystal to vibrate, an alternating electric field of the same frequency will be generated. This means that the piezoelectric crystal can be used as a source and detector of ultrasound, i.e. as a **piezoelectric (electro-mechanical) transducer**.

These phenomena will be most pronounced if the crystal vibration frequency is equal to its **own frequency**, when the crystal **resonates**. The crystal resonates when one half of the wavelength is equal to its thickness. Thus, the own frequency of crystal is larger when the crystal is thinner. When we talk that certain transducer has certain frequency (e.g. 2 or 5 MHz) we think about its own frequency, although he can emit (and more importantly detect) ultrasound waves of slightly smaller or larger frequencies than its own.

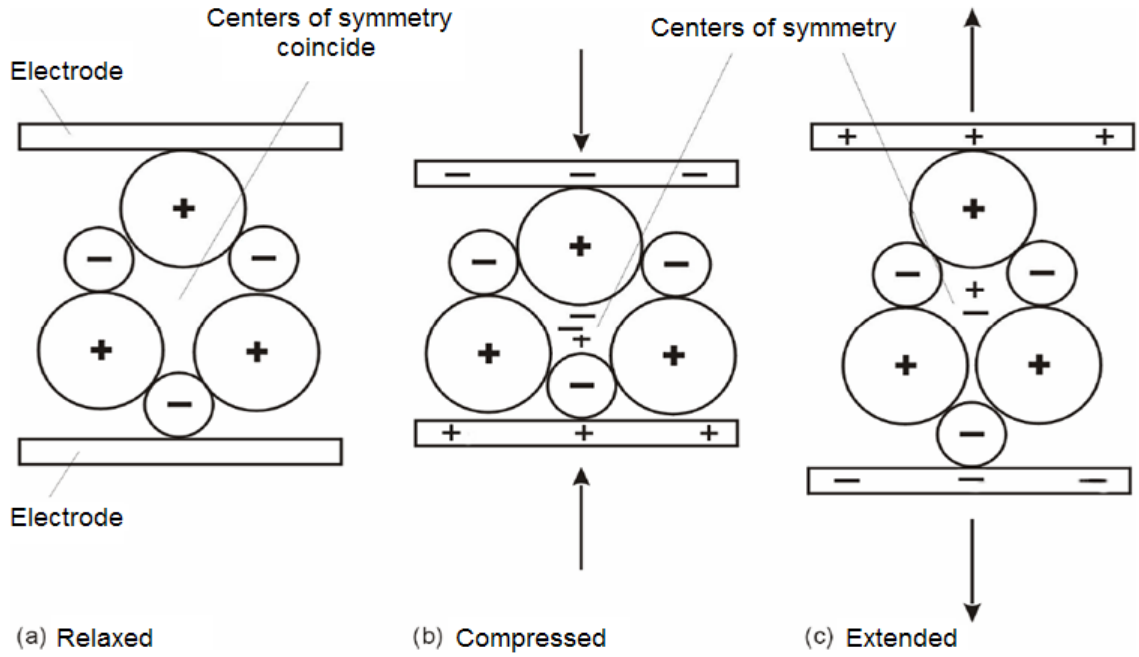


FIGURE 5.1. In the relaxed state the centers of symmetry of positive and negative charges in the crystal lattice fall into the same point, and on the surfaces of the crystal has no effective charge (a). If, however, the crystal deforms (b and c), the opposite free charges appear on the surfaces, which creates a potential difference between them (**piezoelectric effect**). Also, if the crystal surfaces are connected to different potentials, the centers of symmetry of the charges shift, which deforms the crystal (**the inverse piezoelectric effect**).

The ultrasound transducer is composed of thin crystals (a few tenths of a millimeter), on which opposite surfaces are placed film spreads of silver electrodes (Figure 5.2). The electrode in contact with the patient is grounded (connected to a grounded metal container), while the second electrode is connected to the source of voltage by coaxial cable (when the transducer is a source), or with amplifier and cathode oscilloscope (when the transducer is a detector).

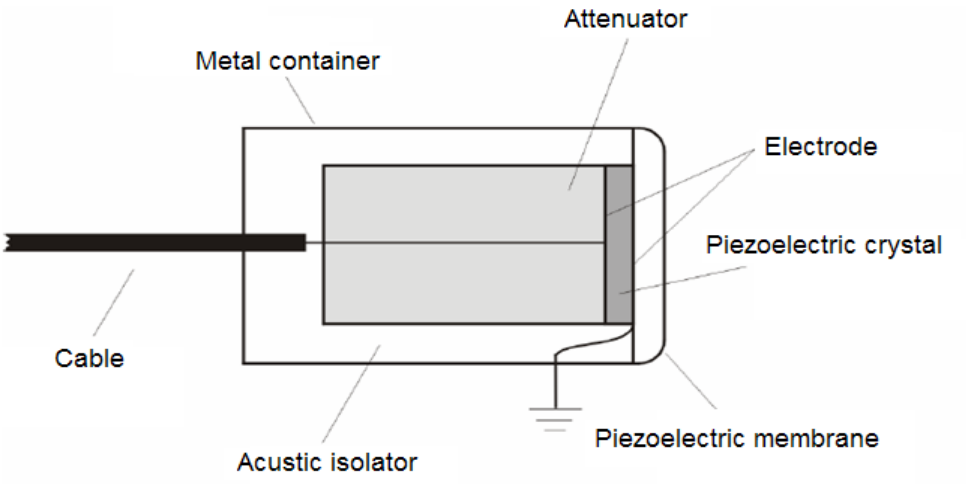


FIGURE 5.2. Scheme of piezoelectric transducer. The thickness of the crystal is equal to a half of the resonant wavelength.

In order to differentiate incoming echoes as good as possible at the time scale, very short pulses must be used (lasting for 1μs or less). This requires that, after excitation, the vibration of crystal attenuate quickly. Therefore, behind the back of the transducer is massive attenuating material (araldite or other epoxy resin), additionally wrapped with acoustic insulator (cork with rubber).

It is easier to attenuate the high frequencies than lower. This fact, together with smaller diffraction, is in the background of the fact that the ultrasound transducers of high own frequencies provide better resolution than low frequency transducers. The use of high frequencies is limited by their strong absorption in the tissue. About all we will read more below.

REFLECTIONS OCCUR AT THE BOUNDARIES OF DIFFERENT MATERIALS

The product of density (ρ) and velocity of sound in the medium (v) is called **the acoustic impedance (*Z*)**. So:

$$Z = \rho v$$

When the sound, spreading through the medium of the acoustic impedance Z_1, encounters the medium of acoustic impedance Z_2, part of the vibration energy is transmitted to the second medium, while the rest is reflected. Reflected intensity (Ir), the part of the incident intensity (Ii), is greater when the difference between the acoustic impedances is greater. In the case of vertical intrusion:

$$\text{Reflection coefficient } (\alpha) = Ir/Ii = ((Z_1\text{-}Z_2)/(Z_1 + Z_2))^2$$

It should be noticed:

- If $Z_2 = Z_1$ there is no reflection and
- If Z_1 and Z_2 are differ drastically, almost all the incident energy is reflected.

TABLE 5.1 shows the acoustic parameters of various tissues.

TABLE 5.1. Sound in biological materials

Medium	**Density (ρ) kgm^{-3}**	**Velocity (v) ms^{-1}**	**Acoustic impedance (Z=ρv) kgm^{-2}s^{-1}**
Air	1.3	330	429
Water	1000	1430	1.43×10^6
Blood	1060	1570	1.59×10^6
Brain	1025	1540	1.58×10^6
Fat tissue	952	1450	1.38×10^6
Muscle	1075	1590	1.70×10^6
Bone (variable)	1400	4000	1.60×10^6
	1908	4080	1.78×10^6

Based on it we can conclude:

- On the border of the soft tissues, e.g. muscle/fat tissue only 1% of sound energy reflects. It is however sufficient for detection, while the rest penetrates deeper and can give further echoes (images).
- Stronger reflections appear on the border of the soft tissue/bone. Too little of the incident wave penetrates deep enough, and only a few different surfaces can be detected. Consequently, the ultrasound examination of the brain is easier in newborn children, who do not have fully developed bone structure of the skull, than in adults.
- Almost complete reflection of sound occurs at the border air/soft (or other) tissue (99.9% in the case of soft tissue). This requires the use of special gels, which eliminates the air in the space between the transducers and the skin, from which they do not differ in acoustic impedance. Therefore it is also impossible examine the lungs by ultrasound.

In the case of intrusion at an angle on the border, reflected and transmitted waves have different directions compared to the incident wave. If the border is smooth (flat areas are bigger than its wavelength), the incident and reflected directions make equal angles with normal to the border, while the direction of the transmitted wave deflect towards the normal in medium where the velocity of propagation is

smaller (Snell's law). Also, in relation to the vertical intrusion, the reflection coefficient is reduced, and increases the proportion of transmitted intensity.

LOSS OF SOUND ENERGY DEPENDS ON THE MATERIAL AND SOUND FREQUENCY

The intensity of plane, sound wave, I_0, of certain frequency decreases with distance x which the wave passes through medium according to the equation:

$$I=I_0\, e^{-\mu x}$$

Causes of the attenuation are: absorption of sound energy (its conversion into heat because of friction), and the wave turning because of diffraction and scattering (small particles absorb part of the sound energy, which is reemitted in all directions). Attenuation coefficient μ depends on the wave frequency and the medium (TABLE 5.2).

TABLE 5.2. Sound attenuation coefficients (μ) for different tissues

Tissue	**Frequency (MHz)**	**μ (cm^{-1})**	**Half-attenuation thickness: ln2/μ (cm)**
Muscle	1	0.26	2.7
Fat tissue	0.8	0.1	6.9
Brain	1	0.22	3.2
Bone	0.6	0.8	0.95
	0.8	1.8	0.34
	1.2	3.4	0.21
	1.6	6.4	0.11
	1.8	8.4	0.08
	2.25	10.6	0.06
	3.5	15.6	0.045
Water	1	5×10^{-4}	1.4×10^{3}

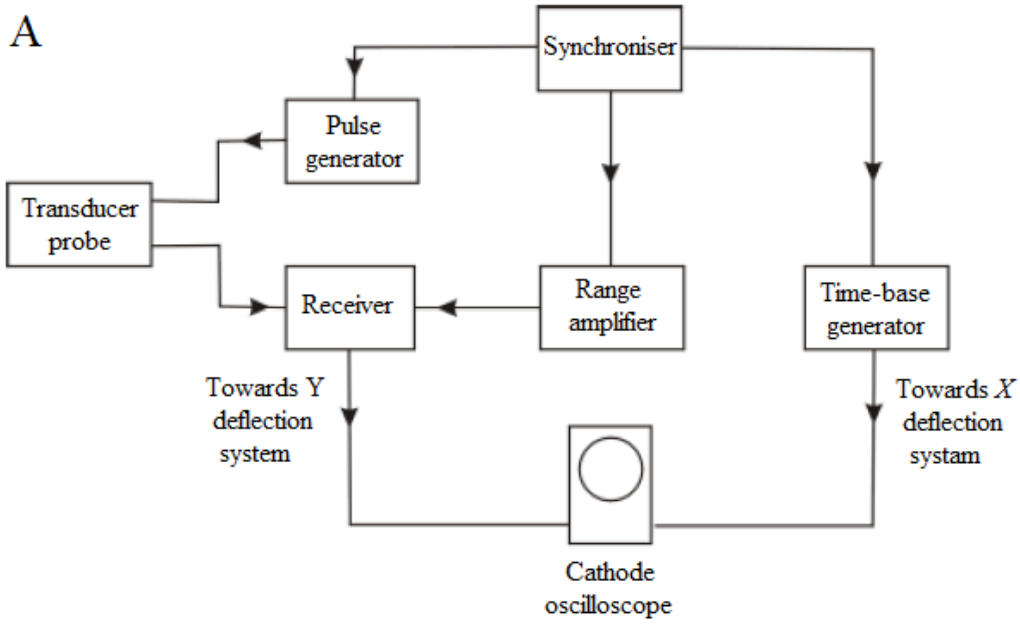
→ The higher frequencies are absorbed stronger (converted to heat) than the lower, which limits the diagnostic use of ultrasound high frequencies to superficial organs.

It should be noted that the attenuation of sound in bones is significantly greater than the attenuation in soft tissues, primarily due to bigger bone density. Also important fact is that the sound in the water attenuates much less than in the soft tissues, even though the difference in density is negligible (the difference is in the presence of macromolecules). Therefore, acoustic communications is possible in the water.

Displays of ultrasonic echoes

THE A-SCAN MEASURE A DEPTHS OF REFLECTIVE BOUNDARIES

The A-scan (A-scope or A-mode) is the easiest way to display the ultrasound echoes. Although this approach provides only one-dimensional information, the same principle is used in recording of ultrasound images in two dimensions. The method is based on measuring the time during which the ultrasound pulse travels till the specific medium border, and returns back the same way (FIGURE 5.3).



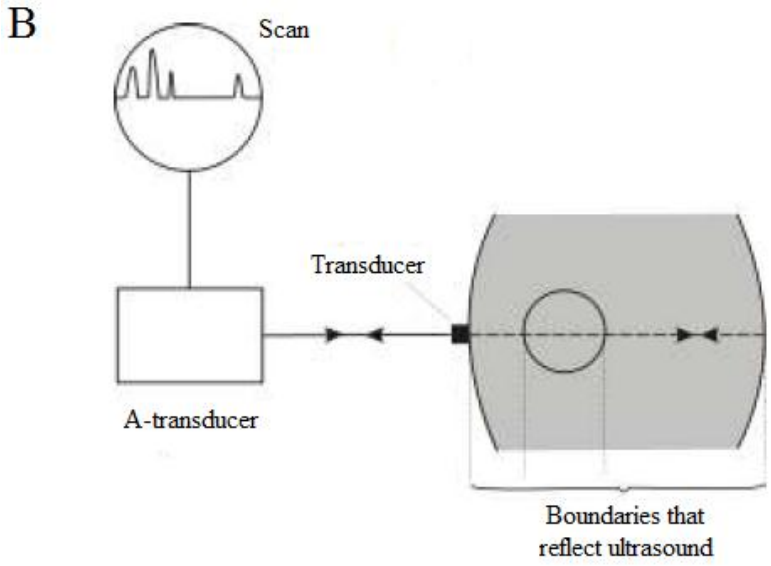


FIGURE 5.3. Electrical **pulse generator** excites the transducer to the emission of short (about 1 μs) ultrasound pulse. Excitation comes from the synchronizer, which simultaneously activates the time-base generator and range amplifier (swept-gain amplifier). Time-base generator provides voltage which causes a constant horizontal shift of the bright spot on the screen of cathode oscilloscope. After the pulse enters the body, a series of reflected pulses with smaller intensities returns to the transducer, which then works as a detector. Each reflected pulse generates a small voltage between the opposing surfaces of the transducer. These voltages are transmitted to the **receiver**, where they amplify first. This function performs the range amplifier. Echoes from the deeper parts of the body suffer greater attenuation than echoes from the surface. Based on time information, obtained from the synchronizer, the range amplifier amplifies the deeper echoes more than the surface echoes (A). Corrected voltages are then transmitted to the system for the vertical deflection of the cathode oscilloscope, where they appear as a series of pulses on the screen (B). If we divide the time between two echoes by two and multiply by the velocity of sound in soft tissue (approximately 1500 m s) we obtain the distance between the reflective surfaces. In this way the cathode ray oscilloscope can be calibrated in a way that the distances between the pulses correspond to actual distances.

In order to get a realistic picture in time, the transducer works as a emitter at even time intervals, several thousand times per minute. This frequency is called the **frequency of pulse repetition**. It is large enough for a good time resolution of moving structures, and small enough that all the echoes that originate from one pulse come back into the transducer before emitting the next one. In a typical example of repetition frequency of 1 kHz and pulses lasting 1 μs, the transducer only 0.1% of the time (1 ms within one second) works as an emitter, while the remaining time is available for detection.

Given that, after correction because of attenuation, the size of the voltage pulse is proportional to the reflection coefficient, A-scan indicates the type of reflective surfaces.

A-scan is used in obstetrics, cardiology, ophthalmology and neurology, and as an aid in complex representations. A-scan is just one-dimensional information about the reflections along the axis of the transducer. Because of a variety of leaning reflections (which do not return to the transducer), the obtained image is highly dependent on the orientation of the transducer toward the tested structures. Therefore its application is limited to:

-structures that are easily identifiable, such as: echoes on opposite sides of the skull (measuring of the biparietal diameter of the fetus), echoes of the central brain (detection of its displacement due to tumor mass, hematoma or abscess), echoes of various ocular tissues (separation of the retina and sclera echoes indicates the retinal ablation), as well as
-structure whose periodic motion assists in the orientation of the transducer (heart valves).

THE B-SCAN IS ALIVE IMAGE OF THE BODY CROSS-SECTION

B-scan (B-scope or B-mode) is the extrapolation of the A-scan in two dimensions. This gives images of the body cross-section.

The device electronics can serve only one transducer at one time. Therefore, the transducers turned on and off one by one, in a way that a whole sequence of transducers activates about 25 times per second. In that way sufficient time resolution is achieved. (Serial activation of transducers in the sequence is not only a necessity, but also has the following advantage: leaning reflections echoes can activate "false" transducers, because they are not in function at that time.)

Image quality is limited by:

- The finite size of the transducer, so that in the lateral direction we cannot distinguish objects smaller than the size of the transducer (a few millimeters).

Perpendicular intrusions to the surface are relatively rare, and only such echoes are detected, while others disappear. Two cases can be distinguished. (1) The smooth rounded surfaces (e.g., diaphragm) should be monitored from multiple angles, which is achieved by continuously rotating the axis of the probe. (2) Irregular surfaces, consisting of differently oriented parts, smaller than the wavelength of sound (e.g. parenchyma Jere), always reflect sound in different directions. The part that is returned in the same direction (detected part) does not depend on the intrusion angle, so the probe does not have to be rotated.

B-scan is the most common method of ultrasound diagnostics. It is used routinely to monitor the pregnancy and to detect cysts, tumors and other abnormalities in almost all organs. It is also used as a guide in percutaneous surgery techniques and biopsies.

Since the partial reflection of sound at the borders of the different structures is the basic image information, ultrasound imaging diagnostics is shortly called **echography**, and the images itself **echograms**. It should be noted that echography

is the only imaging method in which the body section images are obtained directly, without the mathematical reconstruction. In addition, these sections are obtained in real time, which is extremely difficult to achieve with other topographies.

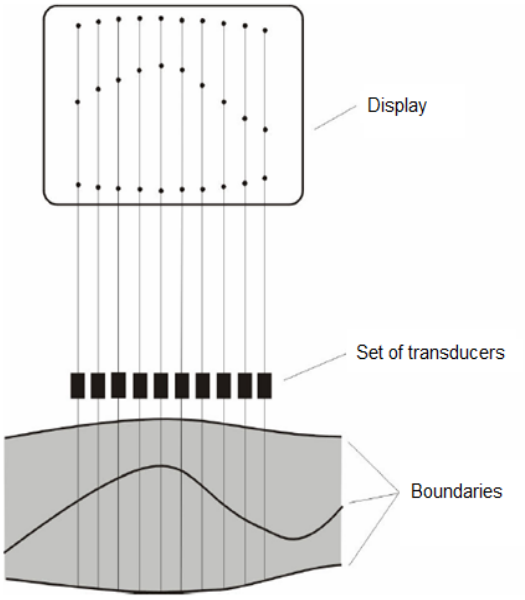


FIGURE 5.4. The most commonly used is so-called **Linear Array Scanner**. In order to obtain the second dimension, instead of one, we use a series of around hundred small transducers arranged side by side. Each of them emits and receives the echoes of structures that are located in front of him, which is presented by bright spots on the screen of cathode oscilloscope. The brightness of the point is determined by the echo intensity. Position is determined by the position of the transducer which detects echo (x coordinate) and time between emission and echo, as in A-scan (y coordinate). Other parts of the device are the same as in FIGURE 5.3.

M-SCAN IS GRAPHICAL RECORD OF THE MOTION VELOCITIES

Although A and B scans are alive images in real measurement, ultrasound motion velocities are measured by special techniques. In the case of cardiac structures is used so called M-scan (M-scope or M-mode).

It is the A-scan with a different graphic solution, which directly shows the velocity. Reflections along the axis of the transducer are measured here too, but the echoes are displayed as bright spots in a plane whose x-axis is time a y-axis is depth of echo. In this way the motion velocity appear as slopes of the image linear structures (FIGURE 5.5).

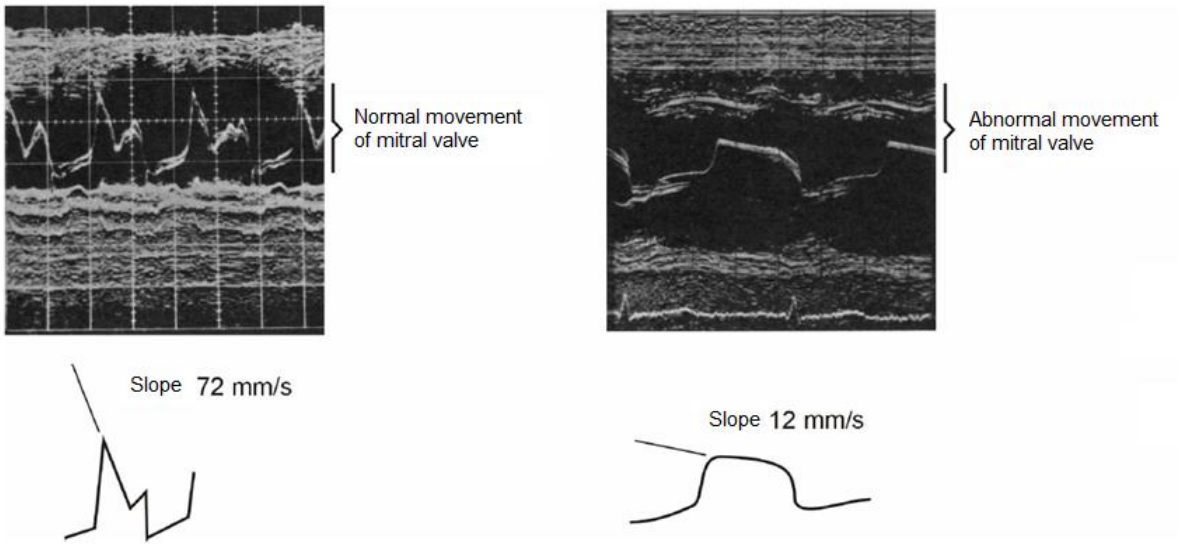


FIGURE 5.5. M-scan of mitral valve motion. Valve closing velocity is shown by slope, whose scheme is separately presented under each image. In the first case (A) normal function is presented, when the closing velocity is around 72 mm/s. The second image (B) refers to severe mitral stenosis that causes very slow valve closure. Otherwise, the sign of mitral stenosis are considered to be the closing velocity less than 35 mm/s.

MOTION VELOCITIES ARE MEASURED BY DOPPLER EFFECT TOO

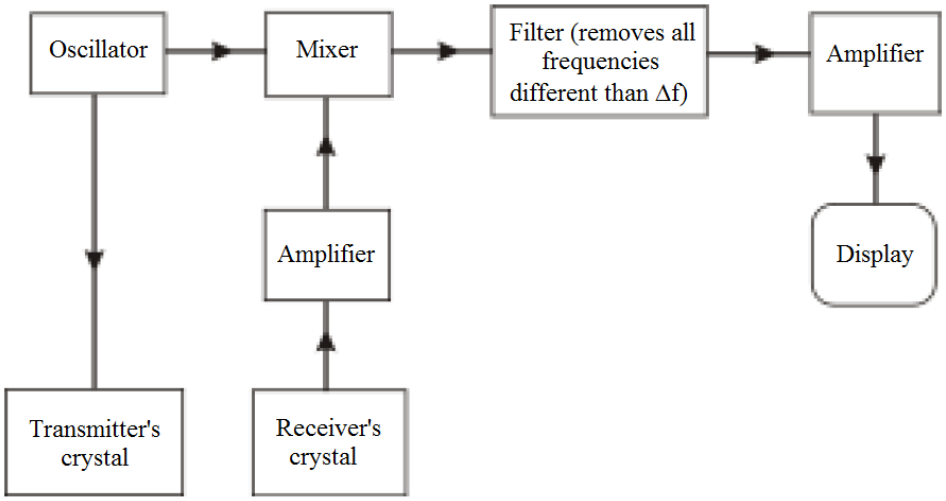
When sound wave of frequency f reflects from object that moves with velocity v (which is much smaller than the velocity of sound propagation in the medium c), its frequency changes for:

$$\Delta f = 2fv/c$$

This is a case of the Doppler effect, and the relation is valid for the case when the source is moving directly towards the receiver (which is stationary in the medium of wave propagation). The change is positive if the subject moves toward the receiver (observer) and negative if it moves from the receiver.

This phenomenon is used in ultrasound measurements of blood velocity and movement of organs in the fetus. The most commonly used are continuous ultrasound waves rather than pulses. Therefore the ultrasound emitter and detector are separate parts of the device. Emitted and reflected waves mix electronically, creating so-called **beats**. The frequency of beats is equal Δf. It is measured electronically, recalculated to velocity v, which is displayed on the screen (FIGURE 5.6). Also the beats themselves can be heard over headphones or

speakers (fetal heart produces frequency range that reminds of horse gallop and experienced ear can recognize many abnormalities).



FGURE 5.6. The components of an ultrasound device used to measure velocities by Doppler method.

In practice, it is often impossible to direct transducer in the direction of motion of the object of interest, especially in the case of measuring blood flow velocity. If the direction of motion of the object makes an angle θ to the observer (FIGURE 5.7), only the component of velocity toward the observer, $v\cos\theta$, causes a change in frequency, and the next equation is valid:

$$\Delta f = 2fv\cos\theta/c$$

It should be noted that in the measurements of blood flow the waves reflect of erythrocytes, which have a maximum velocity in the center of the blood vessels, while the velocities towards the periphery decrease to zero. Therefore, the measurement result should be averaged across the whole vessel cross-section. In the case of pulsating arteries it is should be averaged by time too.

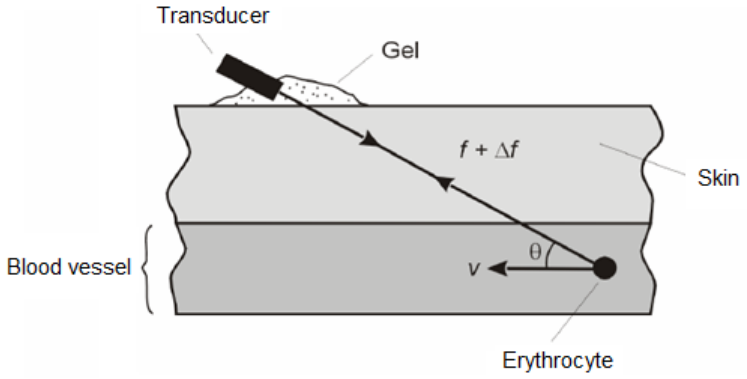


FIGURE 5.7. Blood flow measurement by Doppler method

Parameters of echogram

TISSUES WITH DIFFERENT DENSITY AND ELASTIC PROPERTIES ARE

SHOWN WITH CONTRAST

Echogram is an image of echoes that occur at the borders of media with different acoustic impedance, i.e. products of medium density and velocity of motion of the sound in that medium. Sound velocity in the fluid increases with medium density and the elastic forces that connect the medium particles. The dependence of the acoustic impedance on strength of intermolecular forces is comparative advantage of ultrasound diagnostics. In the background is the fact that some types of soft tissue we differentiate better by ultrasound than by radiological method (where the contrast is provided only with differences in density).

Tissues with ultrasound acoustic impedances equal in space (e.g. cysts filled with fluid) are recognized as dark structures, with no echo. We call them **anechogenic**. Parenchyma tissues give a characteristic echoes (because they consist of different structures). If different structures that build tissue are uniformly distributed in the volume of tissue, the echoes are displayed also uniformly, i.e. **isoechogenic** (e.g., thyroid). Some organs (such as breast) are composed of many different tissues and are displayed **heteroehogenic**. Presence of pathologically altered tissues inside of the healthy tissue is visible as areas of increased echoes, i.e., **hyperechogenic lesion**, or as areas of reduced echoes, ie, **hypoechogenic lesions**. It is easier to observe lesions in the organs with isoechogenic display are, than in heteroechogenic structures.

TWO PARAMETERS OF ULTRASOUND IMAGE RESOLUTION

Axial resolution is the resolution of details in the direction of the transducer axis. It is determined by the duration of the ultrasound pulse. Namely, ideally the pulses should be instant, so that the distance between them can be small enough, and that they do not overlap. In reality, each pulse lasts for some time and the next pulse can be detected only after the expiration of that time. It follows that the two objects cannot be distinguished if they are located closer than the distance which the wave passes during the duration of one pulse (FIGURE 5.8). For pulses of 1 μs, this distance in the soft tissue is 1.5 mm (1μs x 1500 m/s).

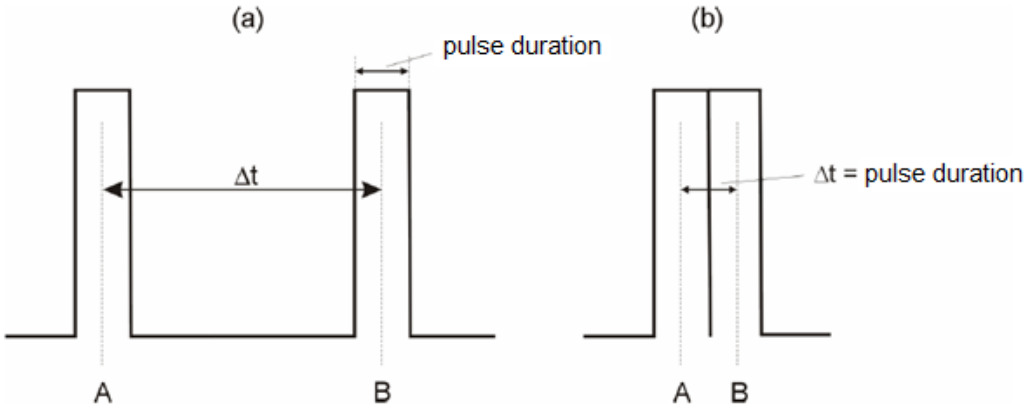


FIGURE 5.8. Distances between points A and B are equal to the sound velocity multiplied with the time interval between successive reflections, i.e., with the distance of corresponding pulses amplitudes Δ*t* (a). This principle cannot be applied if the pulses overlap. Borderline case, which displays resolution of the system, is the pulses touching. This corresponds to the case when the distance between objects is equal as much as the wave passes during the duration of the pulse (b).

The duration of the pulse is determined by the rate of the attenuation of piezoelectric crystal's vibrations. Bigger frequencies can be attenuated faster. In current practice, one ultrasound pulse must last at least three periods of crystal's vibrations (or contain at least 3 wavelengths). It means:

→ *Axial resolution of echogram increases with the frequency of piezoelectric transducer.*

Unfortunately, with increase in the ultrasound frequency its attenuation also increases, so in practice, the most commonly, we use the frequencies that can still provide required penetration. Thus, while frequencies 10-20 MHz are used in ophthalmology, for most of other organs probe frequencies of 5 MHz or less are used.

Generally, because of diffraction, it is not possible to echographicaly distinguish two object located closer than the sound wavelength. Since the ultrasound pulses consist of several wavelengths, the resolution limitation due to their finite duration is bigger than the diffraction limitation. In other words, the ultrasound diagnostics the phenomenon of diffraction can be neglected.

Lateral resolution is the resolution of details in the direction perpendicular to the transducer axis. It is determined by the width of the ultrasound beam. Namely, we talk about the ultrasound beam instead of ray, because the source is not the point, but the transducer with finite dimensions. Width of the transducer is the order of magnitude of several millimeters. Beam width is equal to the transducer width in the area directly behind the transducer; the beam then (after the sudden convergence) begins to diverge and quickly becomes larger than the transducer (FIGURE 5.9). The divergence is smaller in the case of higher frequencies. Therefore, high frequency, except improving the axial resolution, reduced depth

deterioration of lateral resolution.
So:

→ *Lateral resolution is worse than axial, it is determined by the size of the transducer and gets worse with depth, the faster if the transducer frequency is lower.*

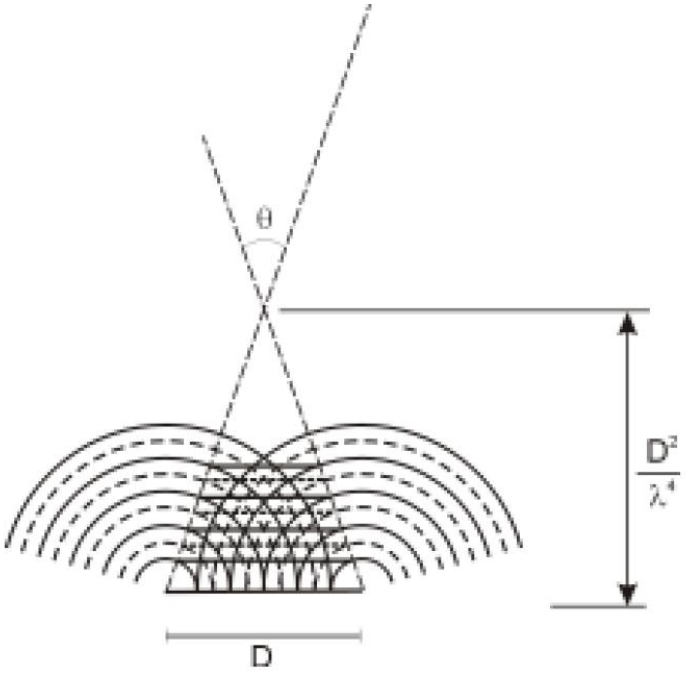


FIGURE 5.9. Each part of the crystal surface is a source of hemispherical waves. These elementary waves superimpose, first creating the convergent field of alternating maximal and minimal intensities (Fresnel zone), then field diverges (Fraunhofer zone), faster if the crystal expands and if the frequency is lower (i.e. wavelength, λ, is bigger).

ULTRASOUND IMAGE ARTIFACTS

Few phenomena generate false information (artifacts) on echogram. These phenomena may complicate interpretation of ultrasound images, if we do not know the causes and characteristic imaging patterns. In contrast, an experienced specialist can use such phenomena in making diagnosis more reliable.

Acoustic shadow occurs behind the structures that strongly reflect the sound, and part that enters them is absorb more than by the soft tissues (calcifications, air bubbles). Therefore, the area under them is not displayed (FIGURE 5.10). In a such posterior shadows the false echoes, so-called **reverberancies (re-reflections),** are sometimes shown. Namely, after almost complete reflection, the pulse, only slightly weakened, returns back to the transducer, partly reflects, again returns to

the reflector and repeats a whole process a few times in a row. Each new detected echo appears (wrongly) as a reflection on, each time more distal, equidistant boundaries (FIGURE 5.11).

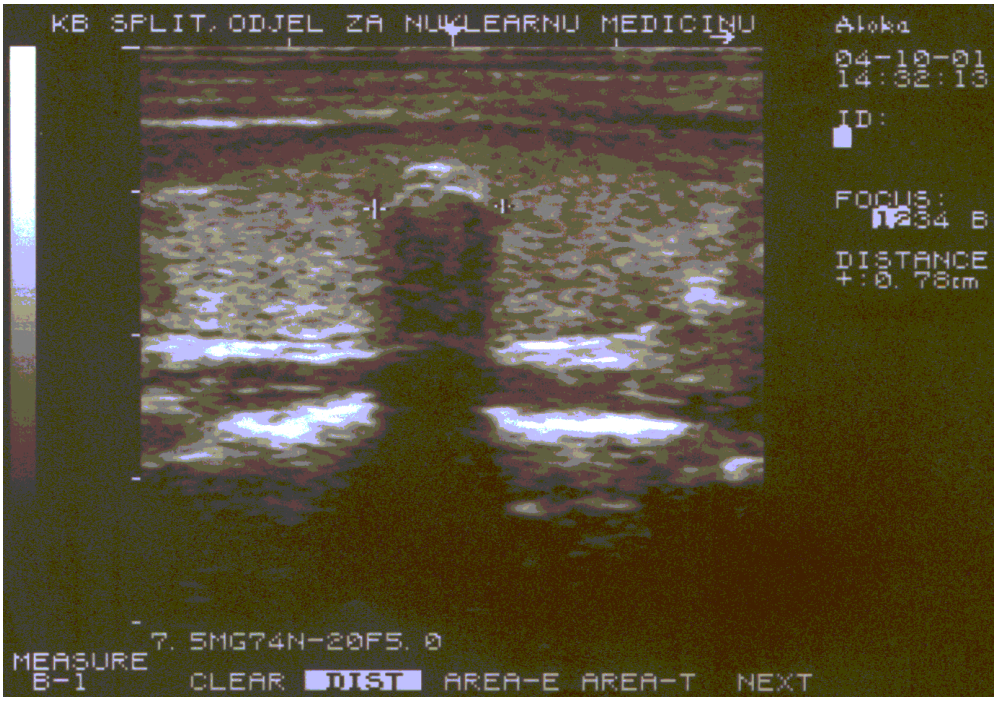


FIGURE 5.10. Calcification in thyroid tissue creates acoustic shadow (courtesy of Dr. D. Radović).

Another source of artifacts is tilted intrusion of the wave on a smooth surface (e.g. on the side of the cystic formation). In this case, the intensity of the reflected wave is small, because of the predominant transmission. Transmitted wave can have such a huge intensity that it prevents all distal reflections in the area of its shadow, determined by the angle of refraction (FIGURE 5.12 A). Term is called **edge shadowing**.

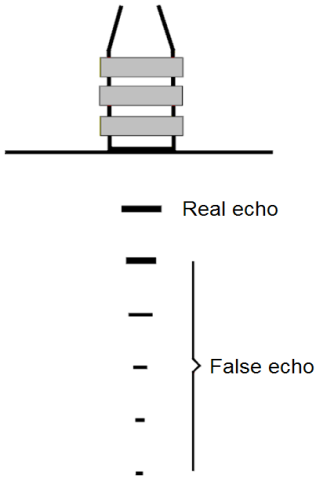


FIGURE 5.11. Scheme of ultrasound artifact formation - reverberancie.

The third phenomenon occurs only in formations filled with fluid. It is called **through transmission sign**. It appears as an area of stronger echoes behind such formation. In fact this is not a stronger echo, but the consequence of the fact that sound attenuates much less in liquids than in the soft tissues (TABLE 5.2.). As a consequence the ultrasound beam that exits behind the back side of the fluid-filled cysts is stronger than the one that passes through the cyst (FIGURE 5.12 B).

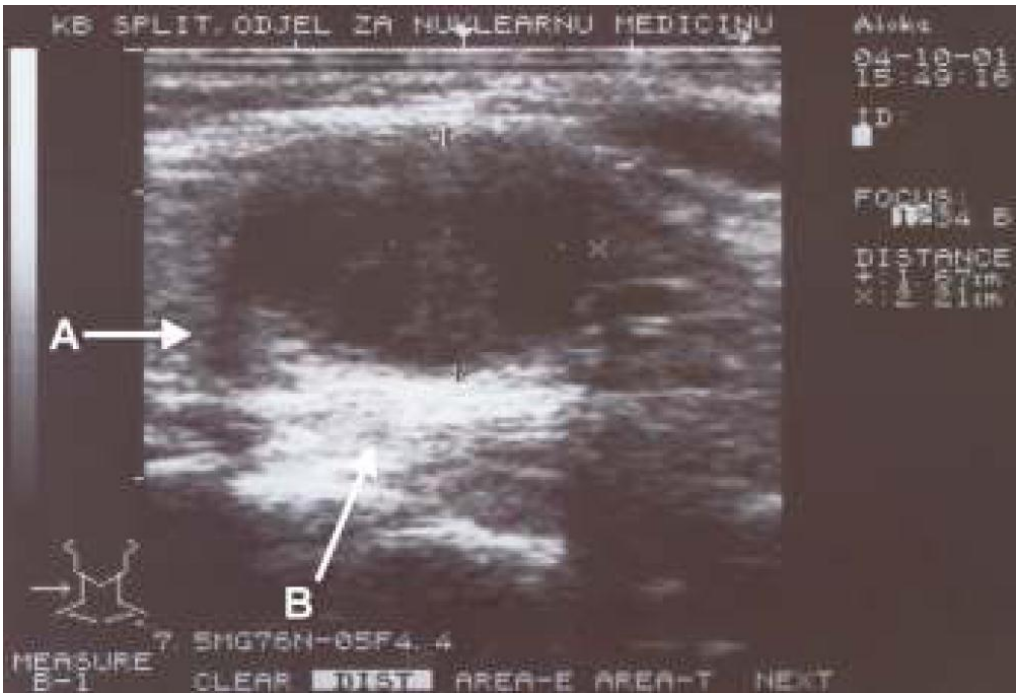


FIGURE 5.12. Echogram of cystic formations in the thyroid tissue next artifacts can be seen: edge shadowing(A) and increasing the back echoes (B) (courtesy of Dr. D. Radović).

We mentioned that the fluid-filled formations appear as dark formations, with no echoes. In most other tissues reflections do occur. There are however some solid tissues (e.g., lymphoma), which are homogeneous sound wise, practically with no echo (anechogenic). However, the absorption of sound in them is equal as in other soft tissues, so and increasing the back echoes do not appear. This is an important example of how image artifacts can be helpful in the interpretation of echogram.

Self assessment

Out of five statements, only one is correct.

5.1. *Phenomenon that in echography prevents the use of frequencies in audible range is:*

f) reflection
g) diffraction
h) refraction
i) interference
j) dispersion

5.2. *Medium that is placed between the ultrasound transducers and the skin:*

f) provides reflection of ultrasound wave on the skin
g) has the same density as skin
h) has the some elasticity as skin
i) has the same absorption coefficient as skin
j) ensures that the ultrasonic beam enters the body

5.3. *In order to improve the axial resolution of echogram we use:*

f) big frequency of pulse repetition
g) small frequency of pulse repetition
h) long ultrasound pulses
i) short ultrasound pulses
j) probes with a lots of small transducers

5.4. *Increasing the back echoes is echographic artifact that occurs behind the bone formations or gas bubbles (A) because: The sound in these tissues is less absorbed than in the soft tissue (B)*

f) A and B correct and connected
g) A and B correct and not connected
h) A correct, B incorrect
i) A incorrect, B correct
j) A and B incorrect

5.5. *Improving the dynamics (time resolution) in echogram is achieved:*

f) increasing the pulse repetition frequency
g) using the transducer with larger characteristic frequencies
h) using Doppler effect
i) using shorter ultrasound pulses
j) using the probe with a lots of small transducers

Chapter VI

COMPARISON OF METHODS OF DIAGNOSTIC IMAGING

- Image parameters

  Diagnostic imaging is art in part
  Images develop on film or computer memory
  Image is mosaic of contrasts
  Contrast quantification- a gain in objectivity
  Resolution is separability of close details

- What and why an image displays

  Image shows anatomy or function
  Fast generating images provide insight in dynamics
  High contrast lesions are best detectable

- Relative roles of imaging methods

  Diagnostic potentials of methods
  Accessibility and non-invasiveness

Image parameters

DIAGNOSTIC IMAGING IS ART IN PART

Diagnostic imaging shares features of both science and art. Both human activities transmit to brain an abstract correlate of outside (so called 'reality'), which elucidate mental activities. The difference is that art predominantly affects emotions, and diagnostic imaging intellect. The sharp discrimination exists only when, instead of man, automatic computer algorithms are used as part of a process. In all other instances we should be aware that both limitations of the method and limitations of an observer stand between reality and diagnostic conclusion (FIGURE 6.1).

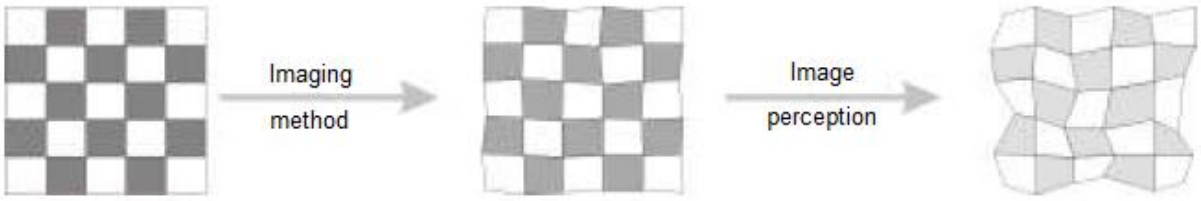


FIGURE 6.1 Imaging method assigns the primary image to an object, which we subsequently perceive by eye-brain system with limitations and in subjective manner.

IMAGES DEVELOP ON FILM OR COMPUTER MEMORY

Digital image is comprised from discrete elements, which are areas of finite size. The contents of these discrete elements are saved in digital matrix of computer memory. An image on a continuous medium (like photographic film) is an **analog image**.

We distinguish 1. intrinsically digital images (tomograms obtained by scintigraphy, CT or MR devices), 2. planar scintigrams, which can be both realized as digital and analog images, 3. display of ultrasound echoes, which are analog, but can be digitalized in real time (rare in practice) and 4. intrinsically analog images, like planar radiograms. Information contained in matrix element of digital image is the number. This number relates to a precisely defined body position and, depending on a method may be: instant radiotracer concentration, radiologic density, acoustic impedance or relaxation pondered water density.

IMAGE IS MOSAIC OF CONTRASTS

Image is a part of a plane, mostly rectangle or circle, composed of details. The details differ in intensity or spectrum of reflected light (analog images; displayed in grey or color scale), or in number attached to each matrix element (digital images).

Image **contrast** is the intensity of distinction of image details.

Different diagnostic methods produce different images of an object; thus achieving different contrasts. Diagnostic potentials of a method primarily depend on spectrum of image contrasts. The applications and comparative advantages of an imaging method are determined by ability of a method to display certain features with certain degree of contrast.

CONSTRAST QUANTIFICATION- A GAIN IN OBJECTIVITY

Image contrasts are perceived by our vision system in a complicated, partly known way. Anyhow, there are several limitations:

1. The range of imaging contrasts is reduced and distorted (non-linearity).

2. The same image is seen differently by different observers (subjectivity).

3. Analog images are secondary information. The primary contrast (e.g. the difference in tracer concentration between hyperfunctional thyroid nodule and surrounding thyroid tissue) is displayed as the difference in intensity of grey, which aside from primary contrast, depends on time of exposure and film characteristics.

The important advantage of digital images is that they contain quantitative (objective) information. Digital image can be visually displayed in several ways, changing the size, field of view, visual contrasts, etc. Aside from visual insight, the observer can analyze the quantitative contents, alone or with an aid of a computer. For example, in this way one can more reliably diagnose the tumor lesion by observing that its radiologic density is exactly 22% less than the surrounding tissue. Contrast quantification is especially useful when the same person is evaluated several times (intra-observer variability), or when one wishes to decrease the variations in findings of different observers (inter-observer variability).

RESOLUTION IS SEPARABILITY OF CLOSE DETAILS

The smallest detail of digital image is a tiny square (less than a millimeter in one dimension), an element of a digital matrix. Potentially, the photographic film can display even finer details, but the resolution of diagnostic imaging methods is too poor (at best slightly under 1 mm) to make it an advantage over digital image (if matrix fineness matches the resolution of imaging device).

Theoretically, image perception could be limited by resolution of human sight (determined by size of retinal light receptors and light diffraction on pupil aperture). In ideal conditions (sufficient light intensity and strong contrasts) a person with good vision can distinguish two objects, separated 0.025 mm, on 25 cm distance from eye. This resolution is by far superior to resolution of diagnostic images, posing no additional limitations (contrary to contrast perception).

Analogously to light diffraction on a pupil, causing smeared retinal image of a point source (light and dark rings of radially decaying intensity), each imaging method has a finite **resolution**. Descriptively, resolution of a method is its ability to separate out close details.

There are two ways to quantify it:

1. The least separation of two objects (commonly two straight lines) presented separately, if having large contrast toward the background.

2. Space dispersal of a point source, defined as **half-width at full-maximum (FWHM)**, of a curve displaying the radial decay in image intensity from center towards periphery (FIGURE 6.2).

Unfortunately, those two definitions do not produce the same estimates, and the difference depends on a method. Numerical data in this text imply the later definition.

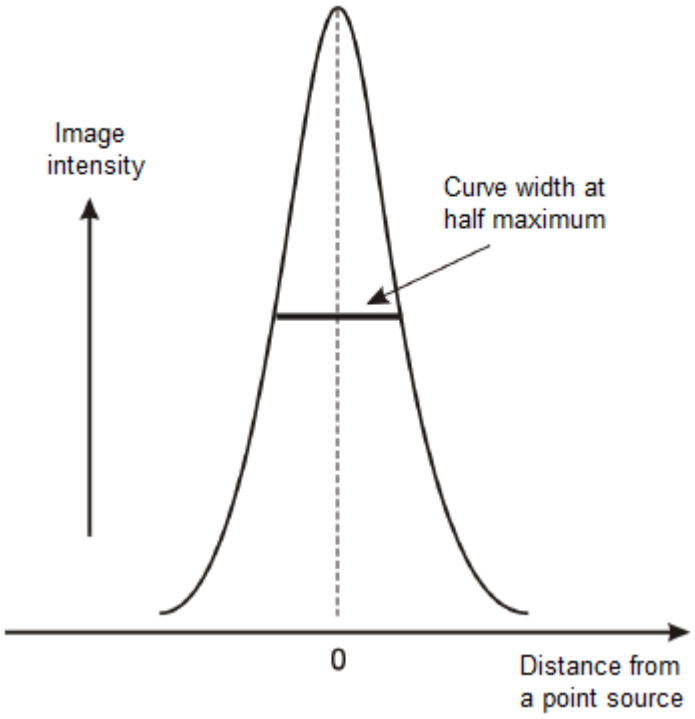


Figure 6.2 With definition of space resolution

Resolution of a method cannot be easily assessed on a routine image, due to limited contrasts. Thus, unclear separation between structures can be due to both, poor resolution or small contrast.

What and why an image displays

IMAGE SHOWS ANATOMY OR FUNCTION

Diagnostic imaging methods differ in characteristics that determine the intensity of image detail. In scintigraphy this is the radiotracer concentration, in radiogram the tissue density and atomic numbers of elements (the relative weights depending on 'hardness' of X rays), in echogram tissue density and elasticity and in MR imaging water density and relaxation surrounding of proton.

Some of the above features define primarily anatomy, other function. Radionuclide scintigrams are typical functional images, while planar radiograms, CT and B scans provide anatomical relations. MR tomograms define morphology, but have significant functional dependence

FAST GENERATING IMAGES PROVIDE INSIGHT IN DYNAMICS

The above division is no longer valid if anatomical methods can generate images sufficiently fast to show changes in time, which can be functional information (for example B scan of cardiac structures and fluoroscopy). Some anatomical methods provide functional information by application of contrast medium (on contrast CT scan one can assess blood flow).

HIGH CONTRAST LESIONS ARE BEST DETECTABLE

Lesion is functionally or (and) morphologically altered tissue. In diagnostic imaging lesion is an object displayed on image more intensively (hot scintigraphic lesion, hyperechogenic structure, radiologically denser region) or less intensively (cold scintigraphic lesion, hypoechogenic structure, radiologically thinner region) than normally expected. Lesion detection and classification is most common goal of diagnostic imaging. It is therefore necessary to summarize the factors affecting lesion detection.

Contrasts on an image are due to functional and morphological variations in normal and pathological conditions. Those variations are given and cannot be influenced upon; exceptionally, one can amplify them pharmacologically or by physical exercise.

Generally, the factors affecting lesion detection, which *cannot* be influenced upon, are:

- degree of functional derangement
- lesion size
- lesion position

However, we can choose the method which displays the physiological contrasts with largest image contrasts. By choosing the method one chooses the image resolution. Thus, factors of lesion detection that can be influenced upon are:

- image contrast (given by interplay of physiologic contrast and choice of method)
- image resolution (given only by choice of method).

In most cases image contrast influences most on lesion detection. One will regularly detect high-contrast lesion even if it is smaller than image resolution. Certainly, in that case, one cannot see the details or estimate lesion size, since image is smeared (FIGURE 6.3). High-contrast lesions are regularly displayed more intensively than surrounding tissue. Contrast of a lesion displayed less intensively than surrounding is limited by surrounding intensity. However, even such contrasts can be high (e.g. scintigram of non-functional cyst in thyroid tissue). On the other hand, low contrast lesions are hard to detect or classify (e.g. malignant vs. non-malignant lesion), even if large in size.

In case of small, low-contrast lesion image resolution is decisive. Then, poor resolution is an obstacle since smeared images of neighboring structures 'fill-in' the area of lesion (noise exceeds signal). Final resolution does not matter much in high-contrast lesions, since image contamination from neighboring structures is usually small (signal exceeds noise). Irrespectively on lesion detection, poor resolution of a method obstructs detection of morphological details and assessment of size of a structure.

One should also observe that:

1. in planar methods and in echograms, image resolution worsens with lesion distance from active body surface;
2. image contrast sometimes depend on choice of imaging time (radiotracer has a dynamics, radiographic contrast is rapidly washed-out by blood, etc.), body posture and other factors;
3. primary contrast of digital image can be manipulated on a computer; such *a posteriori* image modifications can aid our vision in detecting lesion, but also introduce false information (artifacts).

Relative roles of imaging methods

DIAGNOSTIC POTENTIALS OF METHODS

The methods which primarily reflect function are used as early diagnostics in circumstances when functional changes precede morphological changes. For example, the bone scintigraphy reflects osteoblastic activity, and this method uses as early diagnostics of changes that induce (hot lesions, in cases of fractures) or suppress (cold lesions, in case of loss of bone mass of various etiologies) bone remodeling. FIGURE 6.3 is an example of traumatic bone fracture, clearly visible on chest scintigram, and unobservable on chest radiogram. Radionuclide methods are also used to quantify function, like the magnitude of intracardial shunt, vesico-ureteral reflux, renal filtration, etc. On the other hand, the morphological methods have advantage of finer resolution, enabling much more precise definition of morphological relations.

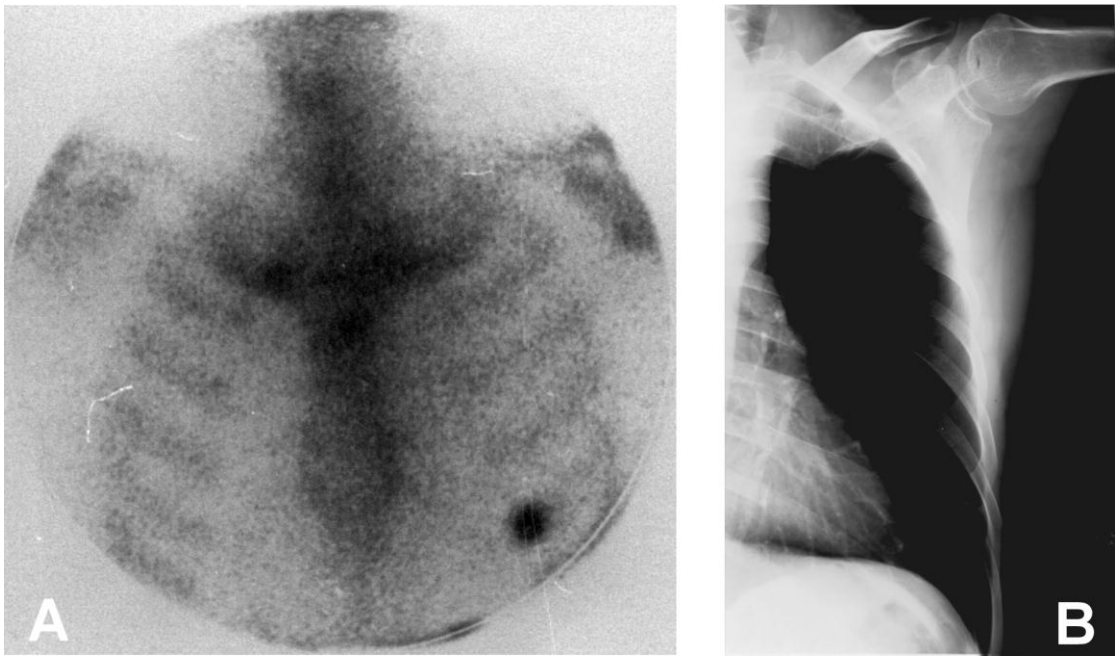


FIGURE 6.3 Traumatic rib fracture is clearly seen on the scintigram (A), as an area of intensive accumulation of radiotracer. Fracture is without dislocation, i.e. without morphological changes, hindering its presentation on chest X ray radiogram (B), despite evident superior resolution of image (courtesy of dr. V. Marković).

Total reflection of ultrasound prohibits display of structures behind air bubbles (lungs). These waves cannot also reach brain, due to excessive reflection at soft

tissue-bone interface and intense attenuation of the remainder in bone tissue. However, differences in structure of soft tissues are regularly presented with more intensive contrast with ultrasound than X-ray. The explanation is that ultrasound contrast depends not only on differences in density, but also elastic properties of tissues. On the other hand, radiologic methods are more objective and have wider application, due to superior resolution, more often detect small lesions, and achieve large contrast between bone and soft tissue. MR images have slightly inferior resolution compared to CT tomograms, but are able to distinguish soft tissues which only slightly differ in density (TABLE 6.1).

TABLE 6.1 Comparison of methods of diagnostic imaging

	Scintigram	**Echogram**	**Radiogram**	**CT tomogram**	**MR tomogram**
	≈ 1cm	2-5 mm	≈ 1 mm	≥ 1 mm	≥ 2 mm
RESOLUTION	Limited by necessity of collimation and massive detector, deteriorates in SPECT	Limited by absorption of high frequencies (axial) and size of transducer (lateral)	Determined by size/mechanical characteristics of anode (focus)	Technologically dependent, possible improvements	Determined by quality and strength of permanent magnet
CONTRASTS	Theoretically unlimited, given by tissue function, amplified by tomography	Determined by differences in tissue density and elastic properties	Determined by differences in tissue density and atomic numbers	Like in radiogram, but amplified by slice selection	Determined by differences in water density and proton relaxation surrounding
SPECIAL VIRTUES	Quantitative aspect, insight in dynamics	Non-invasiveness, insight in dynamics	Simplicity	Insight in morphologic details	Insight in morphologic details

Aside from radionuclide, radiological, ultrasound and MR diagnostics, there are other methods of diagnostic imaging. The examples are:

1. **termography**, imaging temperatures of various body parts;
2. **applied potential tomography (APT)**, imaging of tissue electrical resistance;
3. **diphanography**, imaging of light absorption in visible and infrared spectrum.

These methods are rare in clinical practice and are currently under investigation.

ACCESSIBILITY AND NON-INVASIVENESS

In clinical practice we don't always use the method with best diagnostic potential. The reasons against may be non-accessibility, high cost, discomfort or the associated health risks.

Ultrasound diagnostics is an example of accessible, low cost and fast diagnostics, without proven health risks. It is therefore widespread, especially as the first method in diagnostic algorithm.

The use of ionizing radiation in diagnostics bears the risk of very serious adverse effects, which, however, are very rare. Some radiologic methods are also invasive, including arterial punctures and catheterization. However, such procedures often save life, so that the expected benefit by far surpasses the associated discomforts and risks.

MR diagnostics costs most, due to both cost of a device and its maintenance, as well as relatively long time required for imaging and data analysis. This is the reason why the method is used less often than really needed. The frequency of use depends on the community standard of health care. There are no proven health risks.

Self assessment

Out of five statements, only one is correct

6.1 *The order of methods of diagnostic imaging regarding image resolution is:*

a) planar radiography, CT, echography, MRI, scintigraphy
b) CT, planar radiography, MRI, echography, scintigraphy
c) MRI, CT, planar radiography, echography, scintigraphy
d) CT, planar radiography, MRI, echography, scintigraphy
e) planar radiography, CT, MRI, echography, scintigraphy

6.2 *The order of methods of diagnostic imaging regarding distinction of soft tissue types is:*

a) echography, MRI, planar radiography
b) MRI, planar radiography, echography
c) planar radiography, MRI, echography
d) MRI, echography, planar radiography
e) echography, planar radiography, MRI

6.3 *Diagnostic image resolution:*

a) depends on image contrasts
b) matters in case of small, high-contrast lesions
c) is principal factor in lesion detection
d) depends on lesion size
e) is not important for detection of large or high-contrast lesions

6.4 *Image contrast of a lesion:*

a) depends on lesion size
b) does not depend on imaging method
c) is primary factor in lesion detection
d) does not depend on physiologic contrast
e) depends on image resolution