

**Topic:** *“Biological bases of radiation therapy. Classification and planning of radiation therapy.*

**Purpose of the lesson :** To have an idea about radioactivity and radioactive emissions, their properties. The structure of the atom. The biological effect of ionizing radiation and the basics of radiation therapy.

**Specific objectives of the lesson:**

***Know:***

1. The structure of the atom.
2. What is radioactivity, its qualitative and quantitative characteristics.
3. The biological effect of ionizing radiation and the basics of radiation therapy.
4. Dependence of biological action on physical factors (dose , power, irradiation time and irradiated surface area).
5. Classification of methods of radiation therapy.

***Be able to:***

1. Determine: the activity of a radioactive substance, the choice of irradiation mode.
2. Determine indications and contraindications for radiotherapy.
3. Determine the method of radiation therapy

***The base for conducting and material support of the lesson:***

1. Study room.
2. Cabinet of gamma therapy of the department of radiation therapy of the ROD.
3. Test cards.
4. Study tables.
5. Video films, multimedia presentations.
6. Case histories, radiographs of patients served by the gamma room.

**Literature.**

1. Kishkovsky A.N., Dudarev A.L. "Radiation therapy of non-tumor diseases". M, 1977.
2. Zetgenidze G.A. "Clinical radiology". M.1985
3. Lindenbraten L.D., Korolyuk I.P., "Medical radiology and radiology", M. "Medicine", 2000
- 4.G.E. Trufanov "Radiation diagnostics and radiation therapy", St. Petersburg, 2005.
5. "Radial diagnostics ". A textbook for universities. Under the editorship of Prof. Trufanov G.E. M, 2007

**Information block:**

## PHOTON AND CORPUSCULAR RADIATION

**electromagnetic radiation.** Radiation therapy uses x-ray radiation from x-ray machines, gamma -radiation of radionuclides and bremsstrahlung (X-ray) radiation of high energies.

**X-ray radiation** - photon radiation, consisting of bremsstrahlung and (or) characteristic radiation.

**Bremsstrahlung** is a short-wavelength electromagnetic radiation that occurs when the speed (braking) of charged particles changes when they interact with atoms of a braking substance (anode). The wavelengths of bremsstrahlung X-ray radiation do not depend on the atomic number of the retardant substance, but are determined only by the energy of the accelerated electrons. The bremsstrahlung spectrum is continuous, with a maximum photon energy equal to the kinetic energy of decelerating particles.

**Characteristic radiation** arises when the energy state of atoms changes. When an electron is knocked out of the inner shell of an atom by an electron or a photon, the atom goes into an excited state, and the vacated place is occupied by an electron from the outer shell. In this case, the atom returns to its normal state and emits a quantum of characteristic X-ray radiation with an energy equal to the energy difference at the corresponding levels. Characteristic radiation has a linear spectrum with wavelengths determined for a given substance, which, like the intensity of the lines of the characteristic X-ray spectrum, are determined by the atomic number of the element  $Z$  and the electronic structure of the atom.

The intensity of bremsstrahlung is inversely proportional to the square of the charged particle mass and directly proportional to the square of the atomic number of the substance in whose field the charged particles decelerate. Therefore, to increase the yield of photons, relatively light charged particles are used - electrons and substances with a large atomic number (molybdenum, tungsten, platinum).

*The source of X-ray radiation for the purposes of radiation therapy is the X-ray tube of X-ray therapy devices, which, depending on the level of generated energy, are divided into close-focus and remote ones. X-ray radiation of close-focus X-ray therapy devices is generated at an anode voltage of less than 100 kV, remote - up to 250 kV.*

**High-energy bremsstrahlung**, like bremsstrahlung x-rays, is short-wavelength electromagnetic radiation that occurs when the velocity (deceleration) of charged particles changes when interacting with target atoms. This type of radiation differs from high-energy X-rays. High-energy bremsstrahlung sources are linear electron accelerators - LUE with bremsstrahlung energy from 6 to 20 MeV, as well as cyclic accelerators - betatrons. To obtain high-energy bremsstrahlung, deceleration of sharply accelerated electrons in vacuum systems of accelerators is used.

## Linear electron accelerator



**Gamma radiation** is short-wavelength electromagnetic radiation emitted by excited atomic nuclei during radioactive transformations or nuclear reactions, as well as during the annihilation of a particle and an antiparticle (for example, an electron and a positron).

Sources of gamma radiation are radionuclides. Each radionuclide emits  $\gamma$ -quanta of its specific energy. Radionuclides are produced at accelerators and in nuclear reactors.

The activity of a radionuclide source is understood as the number of decays of atoms per unit time. Measurements are made in Becquerels (Bq). 1 Bq is the activity of the source, in which 1 decay occurs per second. The non-systemic unit of activity is the Curie (Ci). 1 Ci  $\approx$   $3.7 \times 10^{10}$  Bq.

Sources of  $\gamma$ -radiation for remote and intracavitary radiation therapy are  $^{60}\text{Co}$  and  $^{137}\text{Cs}$ . The most widely used preparations are  $^{60}\text{Co}$  with an average photon energy of 1.25 MeV (1.17 and 1.33 MeV).

For intracavitary radiation therapy,  $^{60}\text{Co}$ ,  $^{137}\text{Cs}$ ,  $^{192}\text{Ir}$  are used.

**Corpuscular radiation** - streams of charged particles: electrons, protons, heavy ions (for example, carbon nuclei) with energies of several hundred MeV, as well as neutral particles - neutrons. Particle beam irradiation is now called hadron therapy. Hadrons (from the Greek word *hadros* - "heavy") include nucleons, their protons and neutrons, as well as  $n$ -mesons, etc. The sources of particles are accelerators and nuclear reactors.

**The high-energy electron beam** is generated by the same electron accelerators as in the production of bremsstrahlung. Electron beams with energy from 6 to 20 MeV are used. High-energy electrons have a high penetrating power. The mean free path of such electrons in the tissues of the human body can reach 10-20 cm. The electron beam, being absorbed in the tissues, creates a dose field at which the ionization maximum is formed near the surface of the body. Beyond the ionization maximum, the dose falls off quite rapidly. On modern linear accelerators, it is possible to regulate the energy of the electron beam, and, accordingly, create the required dose at the required depth.

**A neutron is a** particle that has no charge. The processes of interaction of neutrons (neutral particles) with matter depend on the energy of neutrons and the atomic composition of matter. The main effect of thermal (slow) neutrons with an energy of 0.025 eV on biological tissue occurs under the action of protons formed in the reaction (n, p) and losing all their energy at the birthplace. Most of the energy of slow neutrons is spent on the excitation and splitting of tissue molecules. Almost all the energy of fast neutrons with energies from 200 keV to 20 MeV is lost in the tissue

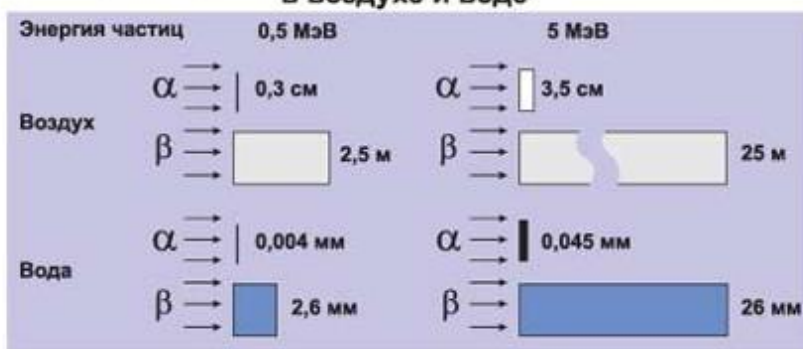
during elastic interaction. Further release of energy occurs as a result of ionization of the medium by recoil protons. The high linear energy density of neutrons prevents the repair of irradiated tumor cells.

**A proton is a** positively charged particle. The method of irradiation at the "Bragg peak" is used, when the maximum energy of charged particles is released at the end of the run and is localized in a limited volume of the irradiated tumor. As a result, a large dose gradient is formed on the surface of the body and in the depth of the irradiated object, after which a sharp attenuation of the energy occurs. By changing the beam energy, it is possible to change the place of its complete stop in the tumor with great accuracy. Proton beams with an energy of 70-200 MeV and the technique of multifield irradiation from different directions are used, in which the integral dose is distributed over a large area of superficial tissues. During irradiation at the synchrocyclotron at PNPI (Petersburg Institute of Nuclear Physics), a fixed energy of the extracted proton beam is used - 1000 MeV and the continuous irradiation technique is used. Protons of such high energy easily pass through the irradiated object, producing uniform ionization along their path. In this case, a small scattering of protons in the substance occurs, therefore, a narrow proton beam with sharp boundaries formed at the entrance remains practically the same narrow in the irradiation zone inside the object. As a result of the application of continuous irradiation in combination with the rotational irradiation technique, a very high dose ratio in the irradiation zone to the dose on the surface of the object is provided - about 200:1

**n-mesons** are spinless elementary particles with a mass, the value of which occupies an intermediate place between the masses of an electron and a proton. **n** mesons with energies of 25-100 MeV pass all the way into the tissue with practically no nuclear interactions, and at the end of the path they are captured by the nuclei of the tissue's atoms. The act of absorbing the  **$\pi$ -meson is accompanied by the escape of neutrons, protons, os-particles, Li, Be ions, etc.** from the destroyed nucleus. The high cost of the technological support of the process has so far prevented the active introduction of hadron therapy into clinical practice.

**alpha radiation** - corpuscular radiation, consisting of  $^4\text{He}$  nuclei (two protons and two neutrons), emitted during radioactive decay of nuclei or during nuclear reactions, transformations. alpha particles are emitted during the radioactive decay of elements heavier than lead or formed in nuclear reactions. Alpha particles have a high ionizing ability and low penetrating power, they carry two positive charges.

Длина пробега альфа-частиц и бета-частиц в воздухе и воде



The radionuclide  $^{225}\text{Ac}$  with a half-life of 10.0 days in combination with monoclonal antibodies is used for radioimmunotherapy of tumors. In the future, the use of the  $^{149}\text{Th}$  radionuclide with a half-life of 4.1 hours for these purposes will be used.

**B - radiation** - corpuscular radiation with a continuous energy spectrum, consisting of negatively or positively charged electrons or positrons ( $\text{B}^-$  or  $\text{B}^+$  particles) and arising from the radioactive B - decay of nuclei or unstable particles. B -emitters are used in the treatment of malignant tumors, the localization of which allows direct contact with these drugs.

Sources of B radiation are  $^{106}\text{Ru}$ , B ~-emitter with an energy of 39.4 keV and a half-life of 375.59 days,  $^{106}\text{Rh}$ , B - an emitter with an energy of 3540.0 keV and a half-life of 29.8 s. Both B -emitters  $^{106}\text{Ru} + ^{106}\text{Rh}$  are included in the sets of ophthalmic applicators.

B ~-emitter  $^{32}\text{R}$  with an energy of 1.71 MeV and a half-life of 14.2 days is used in skin applicators for the treatment of superficial diseases. The  $^{89}\text{Sr}$  radionuclide is a practically pure B -

emitter with a half-life of 50.6 days and an average  $\beta$ -particle energy of 1.46 MeV. A solution of  $^{89}\text{Sr}$ -chloride is used for the palliative treatment of bone metastases.

$^{153}\text{Sm}$  with  $\beta$ -radiation energies of 203.229 and 268 keV and with  $\gamma$ -radiation energies of 69.7 and 103 keV, a half-life of 46.2 h is part of the domestic drug samarium-oxabiphor, designed to affect bone metastases, as well as used in patients with severe pain in the joints with rheumatism.

$^{90}\text{Y}$ , with a half-life of 64.2 hours and a maximum energy of 2.27 MeV, is used for a variety of therapeutic purposes, including labeled antibody radioimmunotherapy, treatment of liver tumors, and rheumatoid arthritis.

The radionuclide  $^{59}\text{Fe}$  as part of a tableted radiopharmaceutical is used in the Russian Scientific Center for Roentgen Radiology (Moscow) for the treatment of patients with breast cancer. The principle of action of the drug, according to the authors, is the distribution of iron by blood flow, selective accumulation in tumor tissue cells and exposure to  $\beta$ -radiation.  $^{67}\text{Cu}$  with a half-life of 2.6 days is combined with monoclonal antibodies for radioimmune therapy of tumors.

$^{186}\text{Re}$  as part of the drug (rhenium sulfide) with a half-life of 3.8 days is used to treat joint diseases, and balloon catheters with sodium perrhenate solution are used for endovascular brachytherapy. It is believed that there is a prospect for the use of  $\text{P}^+$ -emitter  $^{48}\text{V}$  with a half-life of 16.9 days for intracoronary brachytherapy using an arterial stent made of an alloy of titanium and nickel.

$^{131}\text{I}$  is used in the form of solutions for the treatment of diseases of the thyroid gland.  $^{131}\text{I}$  decays with the emission of a complex spectrum of  $\beta$ - and  $\gamma$ -radiation. Has a half-life of 8.06 days.

## CLINICAL DOSIMETRY

**Clinical dosimetry** is a section of ionizing radiation dosimetry, which is an integral part of radiation therapy. The main task of clinical dosimetry is to select and substantiate irradiation means that provide the optimal spatial and temporal distribution of the absorbed radiation energy in the body of the irradiated patient and a quantitative description of this distribution.

Clinical dosimetry uses computational and experimental techniques. Calculation methods are based on already known physical laws of interaction of various types of radiation with matter. With the help of experimental methods, treatment situations are modeled with measurements in tissue-equivalent phantoms.

The tasks of clinical dosimetry are:

- measurement of radiation characteristics of therapeutic radiation beams;
- measurement of radiation fields and absorbed doses in phantoms;
- direct measurements of radiation fields and absorbed doses on patients;

measurement of radiation fields of scattered radiation in canyons with therapeutic installations (for the purpose of radiation safety of patients and personnel);

carrying out absolute calibration of detectors for clinical dosimetry;

conducting experimental studies of new therapeutic methods of irradiation.

The basic concepts and quantities of clinical dosimetry are absorbed dose, dose field, dosimetric phantom, target.

**Dose of ionizing radiation:** 1) a measure of the radiation received by the irradiated object, the absorbed dose of ionizing radiation;

2) quantitative characteristics of the radiation field - exposure dose and kerma.

**The absorbed dose** is the main dosimetric value, which is equal to the ratio of the average energy transferred by ionizing radiation to a substance in an elementary volume, to the mass of the substance in this volume:

$$D = E / m,$$

where  $D$  is the absorbed dose,

$E$  is the average radiation energy,

$m$  is the mass of the substance per unit volume.

As a unit of absorbed radiation dose in SI, Gray (Gy) is adopted in honor of the English scientist

Gray ( L. N. Gray ), known for his work in the field of radiation dosimetry. 1 Gy is equal to the absorbed dose of ionizing radiation, at which 1 krthe energy of ionizing radiation equal to 1 J is transferred to a substance of mass b. In practice, an off-system unit of absorbed dose, rad ( radiation absorbed dose ). **1 rad =  $10^{-2}$  J/kg = 100 erg/g =  $10^{-2}$  Gy or 1 Gy = 100 rad.**

The absorbed dose depends on the type, intensity of radiation, its energy and quality composition, exposure time, and also on the composition of the substance. The dose of ionizing radiation is the greater, the longer the radiation time. The dose increment per unit time is called **the dose rate**, which characterizes the rate of accumulation of the dose of ionizing radiation. It is allowed to use various special units (for example, Gy/h, Gy/min, Gy/s, etc.).

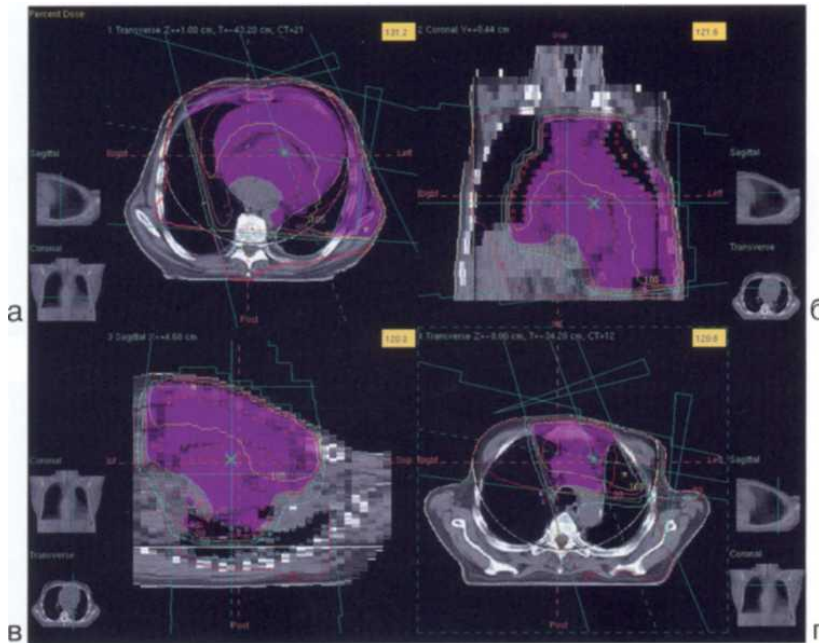
The dose of photon radiation (X-ray and gamma radiation) depends on the atomic number of the elements that make up the substance. Under the same irradiation conditions in heavy substances, it is, as a rule, higher than in the lungs. For example, in the same X-ray field, the absorbed dose in bones is greater than in soft tissues.

In the field of neutron radiation, the main factor determining the formation of the absorbed dose is the nuclear composition of the substance, and not the atomic number of the elements that make up the biological tissue. For soft tissues, the absorbed dose of neutron radiation is largely determined by the interaction of neutrons with nuclei of carbon, hydrogen, oxygen, and nitrogen. The absorbed dose in a biological substance depends on the energy of the neutrons, since neutrons of different energies selectively interact with the nuclei of the substance. In this case, charged particles,  $\gamma$  - radiation , and also radioactive nuclei can be formed, which themselves become sources of ionizing radiation.

*Different types of ionizing radiation at the same absorbed dose have a different biological effect on the tissues of a living organism, which is determined by their relative biological effectiveness - RBE*

**The dose field** is the spatial distribution of the absorbed dose (or its power) in the irradiated part of the patient's body, tissue -equivalent medium or dosimetric phantom that models the patient's body according to the physical effects of the interaction of radiation with matter, the shape and size of organs and tissues and their anatomical relationships. Information about the dose field is presented in the form of curves connecting points of identical values (absolute or relative) of the absorbed dose. Such curves are called **isodoses**, and their families are called isodose maps. For a conventional unit (or 100%), you can take the absorbed dose at any point in the dose field, in particular, the maximum absorbed dose, which should correspond to the target to be irradiated (that is, the area covering the clinically detected tumor and the expected area of its spread)

*Central lung cancer. Conformal irradiation from two parallel fields with wedge-shaped filters. Dose distribution: cross-sectional diagrams at different levels. a) diagram of the frontal section; b) sagittal section diagram*



The physical characteristic of the irradiation field is characterized by various parameters. The number of particles that have penetrated the vereda is called **fluence**. The sum of all penetrating particles and particles scattered in a given medium is the **flux** of ionizing particles, and the ratio of the flux to the area is **the flux density**. Radiation **intensity**, or energy flux density, is understood as the ratio of energy flux to the area of an object. The radiation intensity depends on the particle flux density. In addition to **linear energy transfer (LET)**, which characterizes the average energy loss of particles (photons), the linear **ionization density (LID)**, the number of pairs of ions per unit path length (track) of a particle or photon, is determined.

Physical quantity	Unit, its name, designation		Ratio between units
	(Russian)	(International system)	
Nuclide activity in the radioactive source	Becquerel (Bq, Bq)	Curie (Ci, Ki)	$1 \text{ Bq} \approx 2.7 \times 10^{-10} \text{ Ci}$ $1 \text{ Ci} \approx 3.7 \times 10^{10} \text{ Bq}$
Exposure dose	Coulomb per kg (C/kg, C/kg)	Roentgen (R, R)	$1 \text{ C/kg} = 3876 \text{ R}$ $1 \text{ R} \approx 2.58 \times 10^{-4} \text{ C/kg}$
Equivalent dose	Ampere per kg (A/kg, A/kg)	Roentgen per second (R/s, R/s)	$1 \text{ A/kg} = 3876 \text{ R/s}$ $1 \text{ R/s} \approx 2.58 \times 10^{-4} \text{ A/kg}$
Absorbed dose	Gray (Gy, Gr)	Rad, Gray	$1 \text{ Gy} = 100 \text{ rad}$ $1 \text{ rad} \approx 0.01 \text{ Gy}$

Power absorbed dose	ray per second (Gy/s, Gy/s)	per second (rad/s, rad/s)	0.01 Gy/s	1 Gy/s = 100 rad/s 1 rad/s = 0.01 Gy/s
Integral radiation dose	oule (J, J)	gram (rad • g, rad ■ g)	= 10 <sup>-5</sup> J	1 J = 10 <sup>5</sup> rad • g 1 radg = 10 <sup>-5</sup> J
Equivalent radiation dose	event (Sv, Sv)	(rem)	Sv	one Sv = 100 rem 1 rem = 0.01 Sv
Dose equivalent rate	event per second (Sv/s, Sv/s)	per second (rem/s)	0.01 Sv/s	1 Sv/s = 100 rem/s 1 rem/s = 0.01 Sv/s

Formation of the dose field depends on the type and source of radiation. When forming the dose field with photon radiation, it is taken into account that the intensity of the photon radiation of a point source falls in the medium in inverse proportion to the square of the distance to the source. In dosimetric planning, the concept of average ionization energy is used, which includes the energy of direct ionization and the excitation energy of atoms, leading to secondary radiation, which also causes ionization. For photon radiation, the average ionization energy is equal to the average energy of ion formation of electrons released by photons.

The dose distribution of the  $\gamma$ -ray beam is uneven. The 100% isodose section has a relatively small width, and then the relative dose value falls along the curve quite steeply. The size of the irradiation field is determined by the width of 50% of the dose. When the bremsstrahlung dose field is formed, there is a steep drop in the dose at the field boundary, which is determined by the small size of the focal spot. This leads to the fact that the width of 100% isodose is close to the width of 50% isodose, which determines the dosimetric value of the size of the irradiation field. Thus, in the formation of the dose distribution during irradiation with a bremsstrahlung beam, there are advantages over a  $\gamma$ -ray beam, since the doses of irradiation of healthy organs and tissues near the pathological focus are reduced.

### Depth of 100%, 80% and 50% isodoses at the most commonly used radiation energies

type and energy of radiation	Depth of location of percentage depth doses (cm)		
	one hundred%	80%	fifty%
X-ray radiation 230 kV ( 2 mCi)	0	3.0	6.8



U -Emission <sup>60</sup> Co 1.25 MeV	0.5	4.7	11.6
Photons 6 MB	1.2	6.8	15.6
Photons 10 MB	2.0	7.8	19.0
Electrons 6 MeV	1.2	1.4	1.8
Electrons 10 MeV	2.0	2.8	3.6

**dosimetric devices.** Dosimetric instruments can be used to measure doses of a single type of radiation or mixed radiation. Radiometers measure the activity or concentration of radioactive substances.

According to the method of operation, dosimetric devices are distinguished as stationary, portable (can be carried only in the off state) and wearable. A dosimetric device for measuring the radiation dose received by each person in the radiation zone is called an individual dosimeter.

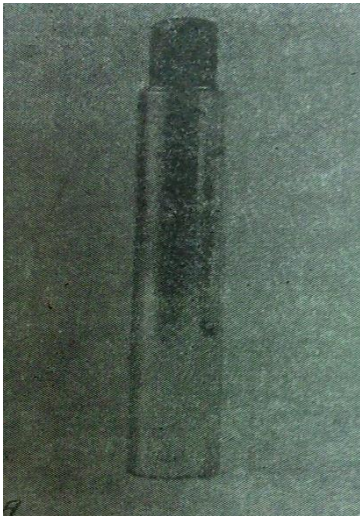
Depending on the type of detector, there are ionization dosimeters, scintillation, luminescent, semiconductor, photodosimeters , etc.

## Dosimeters



**An ionization chamber** is a device for the study and registration of nuclear particles and radiation. Its action is based on the ability of fast charged particles to cause gas ionization. The ionization chamber is an air or gas electric capacitor, to the electrodes of which a potential difference is applied. When ionizing particles enter the space between the

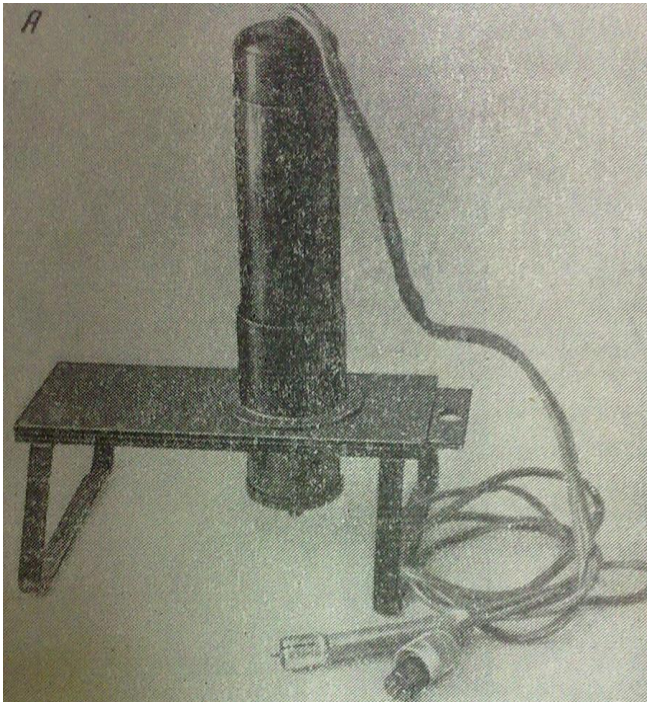
electrodes, electrons and gas ions are formed there, which, moving in an electric field, are collected on the electrodes and recorded by the recording equipment.



***External view of the ionization chamber with a stand***

*In scintillation dosimetric devices, light flashes that occur in the scintillator under the action of radiation are converted by a photomultiplier into electrical signals, which are then recorded by the measuring device. Scintillation dosimeters are most often used in radiation protection dosimetry.*

**Luminescent dosimetric devices use** the fact that phosphors are capable of accumulating absorbed radiation energy and then releasing it by luminescence under the action of additional excitation, which is carried out either by heating the phosphor or by irradiating it.



**Semiconductor** (crystalline) dosimeters change conductivity depending on the dose rate. Widely used along with ionization dosimeters.

### **Biological action of ionizing radiation .**

The biological effect of ionizing radiation is a complex phenomenon characterized by a variety of interrelated and interdependent reactions that occur in an irradiated organism. Its external manifestation, and in particular the damaging effect of ionizing radiation, is only the final link in the chain of reactions developing in the irradiated organism. The biological effect of ionizing radiation in strength and nature significantly exceeds the biological effects of other types of radiation.

The indisputable merit of the Russian school of radiobiology is the formulation and deep study of the problem of the participation of the nervous system in radiation damage to the body.

Some time after the discovery of X-rays, I.R. Tarkhanov was the first to set up a series of experiments on animals, which made it possible to study motor reflexes to chemical stimuli after irradiation of the animal with X-rays.

Tarkhanov emphasized that on the basis of his work, one should conclude that chemical rays can not only be photographed and diagnosed (as was known until now), but also influence the course of vital functions, moderating their main regulator, i.e. centers of the cerebrospinal axis.

Goldberg in 1904 with his research he also emphasized that animals exposed to radium die from "damage" to the nervous tissue.

London is a prominent Soviet pathophysiological, biochemist and radiobiologist. Studying the biological effect of radiation on the body, he revealed a number of patterns that were of decisive importance for the development of radiobiology. He was the first to establish that radium radiation in certain doses can kill animals. London was the first researcher who showed that under the influence of radium rays, the earliest and most pronounced changes occur in the hematopoietic, genital and lymphatic organs.

Already some time after the discovery of X-rays, radiation damage to the skin was discovered. Already in 1897, at the International Medical Congress, a classification was proposed and the pathology and clinic of radiation damage to the skin were described. Insufficient information about the dosage of radiation, the lack of accurate equipment for determining the dose led to the fact that radiologists and radiologists who worked in those years were systematically exposed to large radiation and in a short time received certain skin lesions. A number of specialists who worked with sources of penetrating radiation had to stop working in this area, and some of them later died from occupational skin cancer. Among these specialists were scientists Rosenblat, Isachenko, Goldberg, who irradiated his own skin to study morphological changes. This scientist erected an obelisk in Berlin.

Turning to the question of the mechanism of the biological action of radiation, one should, first of all, answer the question: is there direct ionization and excitation of high-molecular polymers that form the basis of living matter (proteins, enzymes, nucleoproteins, glucoproteins, lipoproteins), or these processes first occur in water, in which the indicated substances are dissolved and suspended, and the products of water decomposition already act on them. In the first case, one speaks of the direct action of radiation, in the second, of the indirect action of rays through the products of water radiolysis.

Even with a small number of irradiated cells, a direct action can have very important biological consequences if it concerns molecules such as enzymes or intracellular structures such as genes or chromosomes.

The probability of hitting a molecule is proportional to its volume. The larger the molecules, the more data for their absorption of energy. So nucleic acid molecules, whose role is the main one in the life of cells, are very large molecules.

The earliest hypothesis of radiobiology was the theory of hits and sensitive volumes, or the so-called target theory. According to this theory, inside each cell there is a sensitive volume (target), which is many times smaller than the volume of the cell, and the protoplasm of the cell is not sensitive to radiation. Only those ionizing particles that enter this sensitive volume have a damaging effect. Different cell sensitivity was associated with different target volumes. The authors of the target theory tried to connect this assumption with the morphological structures that actually exist in cells. The main sensitive elements of the cell are the nucleus, the nucleolus of the chromosome, genes, as well as biochemical substances that are part of enzymes, nucleoproteins, lipoproteins.

The significance of this theory is recognized by many authors at the present time. Although a number of facts were accumulated that contradicted the theory. However, if earlier radiobiology mainly adhered to the theory of sensitive volumes, then at present a large part of the biological effect is attributed to the indirect action of radiation associated with physical or chemical phenomena that occur during the passage of an ionizing particle.

It is known that all body tissues that are in a state of active life contain water, which is the medium for living organisms. It makes up 70-80% of their weight. For young or embryonic tissues, this ratio reaches 90-95%. Since Curie (1901) it has been known that radiation can decompose water, and relatively recent studies have shown that the substances released during this can be very active.

The initial process is the ionization of water, requiring only 13 electron volts. And so two free radicals H and OH are formed, which have great activity. In the presence of dissolved oxygen in water, the hydrogen radical, reacting with it, forms a new unstable  $\text{HO}_2$  radical, the formation of such a strong oxidizing agent as  $\text{H}_2\text{O}_2$  is possible. Free radicals interact not only with each other, but also come into contact with biologically important substances of the cell, and primarily with SH sulfhydryl groups, which are part of most enzymes. The binding of sulfhydryl groups, alteration, inactivation of enzymes and other important systems is accompanied by a violation of metabolic and biochemical processes.

Of particular importance under these conditions is the disorder of tissue respiration, the ability to synthesize certain types of protein, and the violation as a result of this reduplication of complex macromolecules. As a result of violation of the reduplication of protein molecules, mutations occur, i.e. cells with genetically modified properties appear. In the development of the biological effect, a special role is played by the nervous, endocrine, humoral systems, in which the ionization of atoms and molecules and the primary radiation-chemical processes also occur. In this regard, the neuroendocrine regulation of the physiological processes of various organs and systems of the body is immediately disrupted.



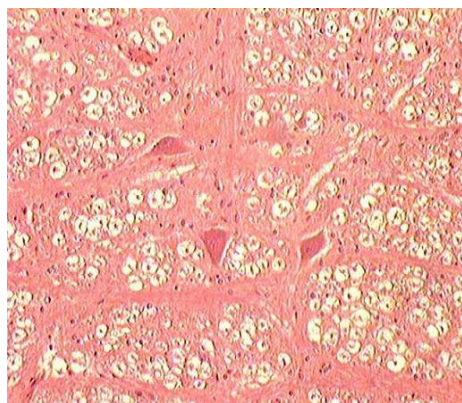
Thus, the biological effect of ionizing radiation is a complex process that takes place in living organisms. The primary ionization of atoms and molecules is a trigger, which is necessarily followed by secondary changes that develop in the form of a chain reaction according to biological laws. Secondary processes, representing in their essence damage to the body as a whole, are the main ones in the clinical picture of the biological effect of radiation.

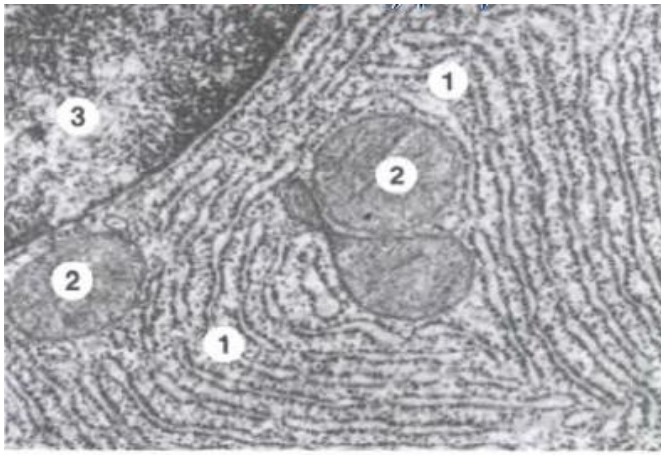
Structural changes are manifested by cell vacuolization, pycnosis and disintegration of nuclei, as well as gross damage to cell organelles, ending in their death. At the same time, there are processes of restoration of dead elements, autosensitization, and compensation of impaired functions.

### Cell vacuolization

Inhibition and suppression of cell function:

- restriction of their mobility
- ability to grow and reproduce
- change in the permeability of cell membranes
- restructuring and disorganization of metabolism in the nucleus and protoplasm.





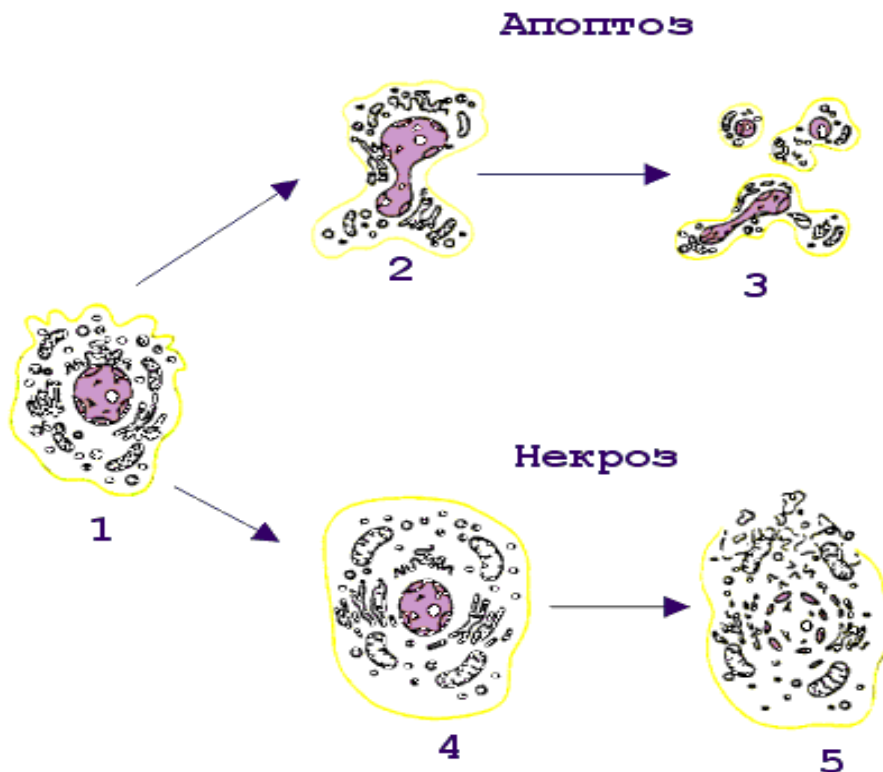
1 — гранулярная ЭПС: содержит мембраносвязанные рибосомы (на которых идет синтез экспортных и мембранных белков).

2 — митохондрии;

3 — ядро клетки.

Cells are damaged:

- chromosomes of the nucleus, nucleoli of microsomes, lysosomes, mitochondria, cytoplasm.
- appearance of mutations in cell populations
- the appearance of unusual forms of daughter cells
- gross morphological changes
- swelling of the cell, the formation of vacuoles in it, pycnosis of the nucleus, its decay.



Thus, biological action is a complex process, where regressive phenomena are combined with restorative and compensatory processes. This serves as the basis for the use of ionizing radiation for therapeutic purposes in some cases to suppress pathological growth and destruction of tumor tissue, in others - for a reactive increase in the recovery, regenerative abilities of individual tissues and organs.

It should be noted that the severity of radiation reactions depends on the type of radiation and the content of oxygen in the tissues. If light quanta of X-rays or gamma rays easily slip between the atoms of a substance, only occasionally touching their electron shells, then heavy alpha particles, like powerful “tanks”, crush all obstacles encountered in their path, break electron shells and quickly waste their energy.

On the way to 1 micron, alpha particles form 5000 pairs of ions, electrons of  $\beta$  - particles, depending on speed and energy, from 5 to 20 pairs, and Ro and  $\gamma$ -quanta from 0.5 to 2 pairs. Consequently, per unit path, alpha particles have an effect 1000 times greater than  $\gamma$ -quanta and hundreds of times more intense than  $\beta$ -particles.

To assess the destructive effect of different types of radiation, not only the specific ionization density, but also the depth of penetration of the rays into the body is of great importance. According to this sign of radiation, the rays are arranged in the reverse order. Gamma radiation passes through, and alpha radiation is absorbed by the surface layer of the skin. Therefore, if we compare these radiations in terms of their danger to the health and life of a healthy organism, it is clear that gamma and Ro rays represent the greatest danger.

It has been established that the content of oxygen in the tissues at the time of irradiation has a certain significance for the severity of the biological effect. Namely, the absence or reduction of partial pressure in tissues reduces the effectiveness of X-ray and gamma radiation. This phenomenon is known in radiobiology as the oxygen effect.

Biological action also has other features that play a positive role when used for medicinal purposes. The first of them is the subjective imperceptibility of the impact, which determines the painlessness of diagnostic and therapeutic procedures. At the same time, this feature requires great care of the personnel so as not to be imperceptibly exposed to harmful radiation.

The second feature is the dependence of the degree of tissue damage on the magnitude of the absorbed dose. This dependence can be well traced on the reactions of the skin to irradiation.

## **Radiation reaction of the skin.**



The third feature of the biological effect of radiation is the presence of a latent period. Although changes in tissues occur immediately after irradiation, they manifest themselves clinically after a certain time. The duration of the latent period is inversely proportional to the absorbed dose.

Another feature of biological action deserves attention: it lies in the fact that different cell organelles, different cells and tissues, and even different organisms have different sensitivities. As a result, to obtain the same effect in different tissues, a different dose is needed.

Radiosensitivity is understood as the body's ability to respond to the effects of ionizing radiation with various functional, destructive or degenerative disorders.

In radiobiology, species radiosensitivity is distinguished. Thus, the lethal dose for a dog is 600 rad, rats - 800 rad, mice - 550 rad, rabbit - 1250 rad.

There is intraspecific or individual sensitivity. Thus, some dogs survive at a total exposure of 600 rads, while others die at 275 rads.

Different cells of the body also have different radiosensitivity. In some organs, no destructive changes are detected, in others, profound morphological and genetic effects are observed. Long-term experimental and clinical studies have made it possible to draw up a schematic classification of the radiosensitivity of healthy cells and tissues in descending order based on the gross morphological manifestations of radiation injuries.

At the dawn of the study of the mechanism of biological action, a law was formulated, which is now a guideline in assessing the radiosensitivity of tissues.

This position, then called the law of Bergonier and Tribondeaux, states that tissue sensitivity is directly proportional to mitotic activity and inversely proportional to tissue differentiation. (Radiosensitivity scale).

This rule is confirmed by the high sensitivity of the lymphatic tissue, spleen, etc. However, in practice there are many contradictions and exceptions to this rule. Based on this rule, the spleen and ovaries are very sensitive to radiation. Previously, it was believed that the radiation effect is an excellent tool for painless sterilization. However, later it turned out that germ cells are affected sublethally. A dose of 250 r makes a person sterile, but after a year, infertility stops, the



cells that have become carriers of the mutation are involved in fertilization and, therefore, can cause irreparable harm to the offspring.

The issue of radiosensitivity of pathological tissues is solved in two ways....

Based on the rule of Bergonier and Tribondo, one can also explain the radiosensitivity of pathological tissues.

As a result, to obtain any specific effect for different cells, a different dose of radiation is required. This property is called relative or differentiated radiosensitivity.

There are also real and conditional radiosensitivity. The actual radiosensitivity is constant for a given cell type. Conditional radiosensitivity depends on the functional state of the cell, changes in the environment and other factors.

existing difference in sensitivity between healthy and pathological tissue is called the radiotherapy interval.

### **Cancericidal doses.**

In the light of the foregoing, the ability of ionizing radiation to have a biological effect, expressed in the suppression of the function of growth and reproduction, as well as in deep damage and death of elements of tissues and organs, is the basis for their therapeutic use, i.e. radiation therapy of malignant neoplasms. From the point of view of radiobiology, the treatment must meet two conditions: to sterilize the cancerous tissue and not cause severe damage in the surrounding healthy tissues that could threaten the patient's life.

In addition, the main principles of radiation therapy include:

1) the timeliness of the use of radiation therapy in the possibly early stages of the disease,

2) choice of the most rational technique,

3) delivering the required dose to the tumor,

4) simultaneous radiation exposure to the primary tumor and regional pathways of metastasis,

5) the complexity of the treatment of the patient, i.e. along with radiation therapy, the use of funds aimed at improving the general and local reactivity of the body.

Consider some of the factors that affect the effectiveness of radiation therapy. The sensitivity of the tumor depends on the histo - structure, the degree of differentiation of cellular elements, on the ratio of stroma and parenchyma. Stroma-rich tumors are highly resistant. This is due to poor oxygen supply. Small tumors with a well-developed blood supply are more radiosensitive. Large tumors are known to be less sensitive, except in their peripheral regions. Radiosensitivity is greatly influenced by previous irradiation at a dose that did not cause the death of tumor cells. As a result of such treatment, the tumor acquires resistance to the subsequent application of radiant energy. This once again proves that the first course of radiation therapy should be complete.

The success of radiation therapy of malignant neoplasms largely depends on the applied irradiation technique, which is determined by the depth of occurrence, the size of the tumor, the involvement of regional nodes in the process, as well as the dose. The choice of the optimal dose determines the degree of the body's response to radiation.

The biological effect is determined not only by the quality of the radiation, the magnitude of the single and total absorbed dose, but also by its distribution over time. This takes into account the length and fragmentation of irradiation. The length is understood as the time during which the dose of radiation is supplied without interruption.

The therapeutic effect increases significantly with increasing exposure time and dose fractionation. That is, the total dose is divided into separate fractions - portions and the tumor is irradiated many times, each time with one dose fraction. In the same way, an increase in the radiotherapy interval is achieved, i.e. differences in radiosensitivity of healthy altered tissue areas.



Another way to increase the radiotherapy interval is to protract the dose. In this case, each exposure is lengthened by reducing the dose rate. The beneficial effect of protraction and fractionation is due to the fact that healthy tissues surrounding the tumor recover faster after each irradiation than cancer cells. Taking into account the position and size of the tumor, the dimensions and direction of the radiation beam are chosen in such a way that the radiation energy is absorbed within the tumor and, to a minimum extent, in the surrounding tissues.

In each individual case, for each patient undergoing radiation treatment, a radiation therapy plan is drawn up. When drawing up a radiation therapy plan, both physical and biological and, above all, the main information complexes are taken into account: a complete diagnosis, data on the radiotherapy interval and a picture of the distribution of absorbed radiation energy in an object under different irradiation conditions.

In order to fulfill the main tasks of radiation therapy, it is necessary to choose such physical and technical conditions of irradiation so that the maximum absorption of the intended

amount of energy in the irradiated object occurs, sparing healthy tissues as much as possible. And for this, it is necessary to accurately determine the location, size and shape of the tumor in the position in which the patient will be irradiated. The localization of tumors of the internal organs is determined by X-ray and radiometric studies and cross sections of the body are built at the level of the middle of the tumor. (Topometric maps). Templates of isodose curves are then superimposed on the cross section and thus the depth absorbed dose is calculated. The most optimal irradiation conditions are selected.

We have considered the general, basic principles of radiation therapy, which should be taken into account in each particular case of radiation treatment.

Consider the classification of radiation therapy.

Depending on the goals and objectives, the following types of radiation therapy are distinguished:

1. Radical: the goal is to create in the focus the dose necessary for destruction.
2. Preoperative: the goal is to suppress the ability to grow and metastasize.
3. Postoperative: the goal is to suppress the ability to grow and metastasize.
4. Preventive - aimed at preventing possible metastasis in the existing primary focus.
5. Palliative - alleviating the suffering of the patient, painkiller.

Depending on the nature of the radiation used for therapy, 5 types are also distinguished:

1. X-ray therapy;
2.  $\beta$  -therapy;
3. gamma therapy ;
4. radiotherapy with high energy bremsstrahlung;
5. radiation therapy with high energy electrons.

Depending on the relationship between the radiation source and the irradiated object, the methods of radiation therapy are divided into:

1. remote outdoor,
2. intracavitary,
3. interstitial,
4. contact,
5. internal.

Test questions.

1. What is meant by the biological action of penetrating radiation?
2. What is the primary mechanism of the biological action of penetrating radiation?
3. What is the essence of biochemical and pathomorphological processes occurring under the influence of penetrating radiation.
4. Radiosensitivity of tissues, biological patterns of radiosensitivity.
5. The effect of ionizing radiation on the tumor.
6. The main tasks of radiation therapy.
7. Choice of optimal irradiation conditions.
8. The concept of the optimal dose.
9. The value of fractional irradiation.
10. Radiosensitivity management.
11. Preparation of patients for radiation therapy.
12. The concept of absorbed dose. Units. Exposure dose rate. Units.

Test tasks:

**1. Discovered natural radioactivity**

- A . Curie M.
- B . Rego K.
- B . Curie P.
- G. Becquerel A.

**2. What is measured with radiometers?**

- A . Activity of radioactive substances
- B . Dose of penetrating radiation
- B. The degree of penetrating power of radiation**
- G . The energy of emitted particles and quanta

**3. What are isotopes?**

- A. Varieties of the same element with different atomic weights
- B . Varieties of chemical elements with different numbers of protons
- B . Varieties of chemical elements with different numbers of electrons
- G . Elements with different numbers of electronic levels
- D . Elements with different serial number

**4. How can the rate of radioactive decay be changed?**

- A . By heating
- B . By cooling at ultra-low temperatures
- B . Through chemical exposure
- G. By increasing the pressure
- D. Cannot be changed

**5. What are the components of the natural radiation fund?**

- A. Emissions from industrial enterprises
- B. Radiation from nuclear power plants
- B . Radiation from x-ray rooms
- D. Radiation from naturally distributed radioactive substances and cosmic radiation
- D . Radiation from living organisms

**6. Unit of absorbed dose**

- A. Gray
- B. Sievert
- W. Roentgen
- G Curie

**7. What will happen to the atom of matter during alpha decay?**

- A. will shift in the periodic table two cells to the right
- B. atomic weight will not change
- The shift in the periodic table two cells to the left
- G. will release two electrons

**8. The radiopharmaceutical must meet the following requirements:**

- BUT . be harmless
- B. is quickly excreted from the body
- B . have affinity for the organ under study
- D. half-life must be short
- D is correct

**9. What physical changes occur in the atoms of tissue cells and body fluids under the influence of penetrating radiation?**

- A. Ionization and excitation of atoms.
- B. Increase in the number of electronic layers.
- B. Transformation of a nuclear proton into a neutron.

**10. Ionizing radiation includes:**

- A. quantum (photon) and corpuscular
- B. light (visible part of the spectrum).
- V. ultraviolet.
- G. laser
- D. infrared.

**Answers :**

- 1. G**
- 2. BUT**
- 3. BUT**
- 4. D**
- 5. G**
- 6. BUT**
- 7. IN**
- 8. D**
- 9. BUT**
- 10. BUT**