

# МОЛЕКУЛЯРНАЯ И КЛЕТочНАЯ РАДИОБИОЛОГИЯ

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## RADIATION BIOLOGY. MOLECULAR AND CELLULAR ASPECTS

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по специальностям «Медико-биологическое дело»,  
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Материал учебного пособия содержит систематизированные научные знания по молекулярным и клеточным аспектам воздействия ионизирующего излучения на биологические системы. Рассмотрены вопросы взаимодействия ионизирующего излучения с веществом. Освещены вопросы теоретических основ в развитии радиобиологического ответа организма. Особое внимание уделено проблемам выживаемости клеток при облучении и формам клеточной гибели. Большой раздел посвящен немишенным эффектам действия ионизирующего излучения в современной интерпретации. Подробно описаны механизмы радиационно-индуцированного канцерогенеза.

Адресовано студентам, магистрантам, аспирантам и преподавателям биологических, биомедицинских и экологических специальностей учреждений высшего образования, а также научным работникам и практикам, работающим в области молекулярной и клеточной радиобиологии, радиационной медицины, радиационной генетики, патологической физиологии.

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# INTRODUCTION

The material presented for publication contains for the first time systematized modern scientific knowledge on molecular and cellular aspects of the impact of ionizing radiation on biological systems and includes the following sections: “Physical and chemical mechanisms of interaction of ionizing radiation with matter”, “Fundamental radiobiological theories”, “Damage and repair of DNA”, “Radiation-induced effects of the cell cycle”, “Types of cell death and survival mechanisms”, “Cell survival curves”, “Radiobiology of normal tissue damage”, “Non-target effects”, “Radiation-induced cell cycle effects”, “Radiation carcinogenesis”.

In comparison with previously published textbooks, the manuscript deeply considers the issues of interaction of ionizing radiation with the matter, and also provides a detailed analysis of the issues of theoretical foundations in the development of radiobiological response of the organism.

A distinctive feature of the presented material is that special attention is paid to the problems of cell survival under ionizing radiation and forms of cell death.

For the first time the section devoted to non-missile effects of ionizing radiation is presented in modern interpretation and the mechanisms of radiation-induced carcinogenesis are described in detail.

It is intended for students and teachers of ecological, biological, biomedical specialties of higher educational institutions.

The textbook can be used in teaching such special courses and subjects as “Radiation Medicine”, “Radiation Genetics”, “Radiation Biochemistry”, “Pathological Physiology”, “Life Safety”.

# LIST OF ABBREVIATIONS

AIDS – acquired immune deficiency syndrome  
ATP – adenosine triphosphoric acid  
ChNPP – Chernobyl Nuclear Power Plant  
ICRP – International Commission on Radiological Protection  
ICRU – International Commission on Radiation Units  
IL – interleukin  
IR – ionizing radiation  
LD – lethal dose  
LET – linear energy transfer  
LID – linear ionization density  
MC – mitotic cycle  
NPP – nuclear power plant  
PRT – primary radiotoxins  
RBE – relative biological effectiveness  
ROS – reactive oxygen species  
TNF – tumor necrosis factor  
UNSCEAR – United Nations Scientific Committee on the Effects of Atomic Radiation

# PART 1

## PHYSICS AND CHEMISTRY OF RADIATION INTERACTION WITH THE MATTER

### 1.1. General characteristics of the mechanisms of interaction of ionizing radiation with the matter

The processes occurring when ionizing radiation (IR) goes through the matter have practical significance both for Nuclear Physics and the areas of science and technology associated with it. Without good knowledge of these process, it is impossible to comprehend nuclear particle detection methods or, for example, calculate the thickness of biological radiation shielding from nuclear radiation for a particle accelerator or a nuclear power facility.

The greatest practical interest is the energy range of  $1 \cdot 10^{-3} \dots 10$  MeV. The energies of particles passing through the matter in this entire area can be called high, meaning that they are greatly compared to the average ionization potential in the matter. The pattern of the passage of high energy particles through matter is extremely complex. The particles interact with electrons located on different shells, are scattered by the Coulomb fields of the nuclei, and causing various nuclear reactions at sufficiently high energies. In addition, at sufficiently high particle energies, various secondary effects inevitably arise. For example, a beam of high-energy electrons generates a powerful stream of secondary  $\gamma$ -quanta in the matter, which must be considered when calculating a radiation protection. However, this does not mean that the processes of passing through the matter are completely incalculable. A number of the most important quantities characterizing these processes can be calculated fairly accurately or at least estimated. The following reasons contribute to it:

- First, with the passage of charged particles and  $\gamma$ -quanta through the matter, well-studied electromagnetic interactions play a major role. The role of nuclear interactions in most cases is not significant because of the short-range nuclear forces and because the electrons in the substance are much larger than the nuclei.
- The second simplification arises due to the fact that the energy of passing particles significantly exceeds the binding energy of electrons in an atom and these electrons can be considered free.

According to the mechanism of the ionization of the matter, IR can be divided into two groups:

- direct ionizing radiation;
- indirect ionizing radiation.

Thus, direct ionizing radiation can be divided into:

- heavy charged particles with a mass greater or equal to the proton mass ( $p$ ,  $d$ ,  $\alpha$ , fragments of nuclear fission, and etc.);
- light charged particles with electrons and positrons with a mass less than 200 electron masses ( $e^-$ ,  $e^+$ ,  $\mu^+$ ).

Indirect ionizing radiation include:

- $\gamma$ -quanta;
- X-rays;
- neutrons.

## 1.2. The interaction of electromagnetic ionizing radiation with the matter

### 1.2.1. Nuclear interactions of $\gamma$ -quanta

The methods of nuclear interaction of  $\gamma$ -quanta are rarely used (the use of radioactive isotopes as indicators).

**Nuclear reactions.**  $\gamma$ -quanta of very high energy (above 6 MeV) can interact with the nucleus causing excitation of nucleons. This can lead to the ejection of a particle, usually a neutron and to the transformation of an atom into another nuclide (reaction  $\gamma$ , n).

**Nuclear resonance scattering.** In some situations, the  $\gamma$ -quantum can be absorbed by the nucleus without subsequent particle emission. The core remains in this excited state for a short but immeasurable period of time. Subsequent emission of the  $\gamma$ -quantum restores the stability of the nucleus. An atom that has been exposed to the  $\gamma$ -quantum remains the same without any transformations.

**Bragg scattering (diffraction).**  $\gamma$ -quanta of low energy can be scattered by the crystal matrix without an energy loss. X-ray diffraction can be effectively used to study the molecular structure; however, this phenomenon is of no importance for the method of the labeled atoms.

### 1.2.2. Photoelectric effect

*Photoelectric effect* means that the energy of the incident quantum is completely absorbed by the substance; as a result, free electrons appear that have a certain kinetic energy, the value of which is equal to the energy of

the radiation quantum minus the work of releasing of the given electron from the atom. A free electron, associating with one of the neutral atoms, generates a negative ion.

The probability of the photoelectric effect depends on the energy of the incident quantum and the atomic number of the absorbing medium. The photo effect is characteristic just of long-wave X-ray radiation. Its probability depends on the atomic number and is proportional to  $Z^3$  (Fig. 1).

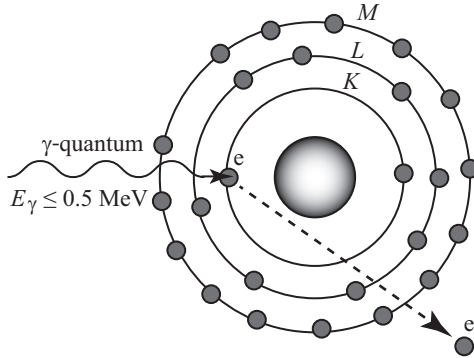


Fig. 1. Photoelectric effect

With the increase of the radiation energy, the probability of the photoelectric effect decreases; for radiation with the energy that is much higher than the intra-atomic binding energies ( $> 1 \text{ MeV}$ ), its contribution to the interaction can be neglected. The main role belongs to another way of energy exchange – *Compton effect*.

### 1.2.3. Compton effect

In the Compton effect, elastic scattering of the incident photons of radiation occurs on free (or weakly bound) electrons; only part of the photon energy is transferred to them. The rest of the energy is carried away by new photons resulting from this interaction (Fig. 2). Then, the secondary photon can again undergo the Compton effect, etc.

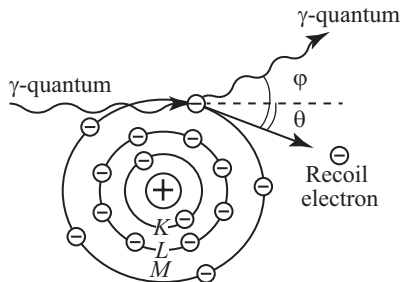


Fig. 2. Compton effect

Thus, the Compton recoil electrons, despite the fact that their occurrence is due to the monoenergetic beam of incident  $\gamma$ -quanta, have an extended energy spectrum. When such electrons interact with an absorbing matter; naturally, considerable ionization occurs. Moreover, the scattered  $\gamma$ -quantum of lesser energy can undergo some several collisions of the same nature before it loses all its energy when interacting with the matter.

The incident photon knocks out the orbital electron of the atom of the irradiated matter. Part of the photon energy is transmitted in the form of kinetic energy to the electron. The resulting secondary photon has less energy and another direction.

The average energy of recoil electrons increases with increasing energy of the incident radiation. The proportion of energy absorbed by Compton electrons in the total amount of absorbed energy increases with increasing hardness of radiation. If the source of short-wave radiation, which is dominated by the Compton effect, is calibrated using a standard ionization chamber, then the results of these measurements can be used to obtain data on energy absorption by various materials. Under the action of soft X-rays, when the photoelectric effect prevails, this cannot be done without appropriate corrections (it is not simple to introduce them), since serious errors in estimating the absorbed radiation doses can occur.

In water and biological tissues, the absorption of radiation with a photon energy of more than 300 keV mainly occurs due to the Compton effect.

As a result of several successive Compton interactions, the quantum energy decreases so much that it can already be completely absorbed as a result of the photoelectric effect. If the energy of an incident quantum exceeds 1.022 MeV, a third type of interaction becomes possible, i.e., the effect of the pair formation.

#### 1.2.4. Formation of electron-positron pairs

This type of interaction of radiation with the matter is characterized by the possibility of converting a high-energy  $\gamma$ -quantum ( $> 1$  MeV is equivalent to the rest mass of one electron and one positron) into a *pair of charged particles* — *an electron and positron*, which are ejected from the place of their occurrence with different energy. This process is caused by the interaction of the  $\gamma$ -quantum with some atomic nucleus; *an electron-positron pair* is formed in its field. The likelihood of such a process is proportional to  $Z^2$ ; therefore, for heavy elements it is more than for the light ones. The resulting electron and positron, arising from this, spend their energy



mainly on ionization. After stopping, the positron annihilates, throwing two  $\gamma$ -quanta with the energy of 0.51 MeV in opposite directions (Fig. 3).

Consequently, depending on the energy of the incident electromagnetic radiation, one or another type of its interaction with the matter prevails (Fig. 4). In most cases, when biological objects are irradiated, the energy of the used electromagnetic radiation is in the range of 0.2–2 MeV; therefore, the Compton effect is most likely to occur.

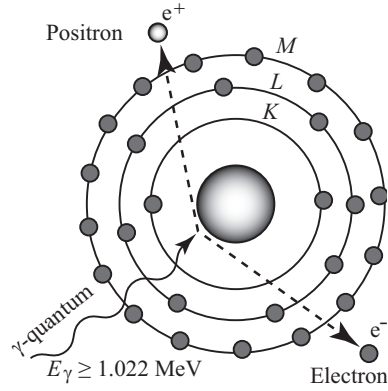


Fig. 3. Formation of electron-positron pairs

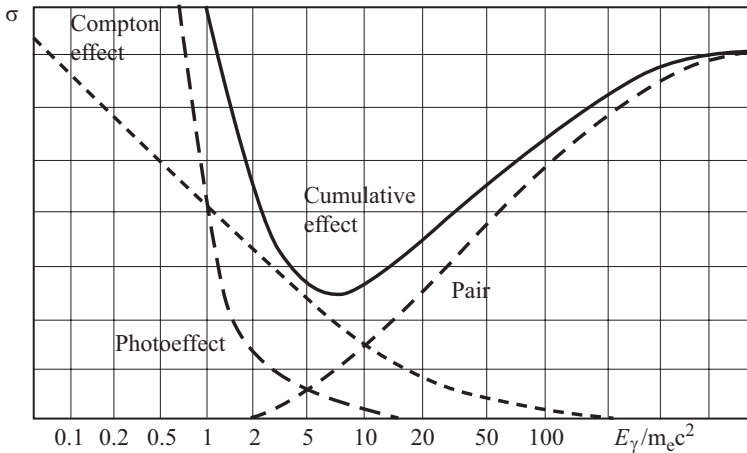


Fig. 4. The relative role of the three types of interaction of  $\gamma$ -radiation with the matter

With increasing the energy of  $\gamma$ -quanta, the formation of pairs plays an highly important role in the mechanism of absorption of  $\gamma$ -radiation. It is especially large in absorbers with a high atomic number. The photoelectric effect and the Compton effect play a smaller role with the energy increase; starting from 3 MeV, the effect of the formation of pairs makes compensation for the decrease of the absorption.

### 1.2.5. Patterns of absorption of $\gamma$ -radiation

*Linear absorption coefficient* ( $\mu_L$ ). Absorption of  $\gamma$ -radiation occurs exponentially (the thicker the absorber, the greater the absorption is), so this type of radiation does not have a strictly defined range. It is usually calculated per centimeter (1 / cm). The linear absorption coefficient depends on the energy of  $\gamma$ -quanta and the material of the absorber (Table 1).

Table 1. Linear absorption coefficients in some absorbers

The energy of incident beam, MeV	Linear absorption coefficient, $\text{cm}^{-1}$			
	H <sub>2</sub> O	aluminium	iron	lead
1.0	0.071	0.168	0.44	0.79
1.5	0.057	0.136	0.40	0.590
2.0	0.050	0.117	0.33	0.504

*Mass absorption coefficient* ( $\mu_M$ ). This value is equal to the linear absorption coefficient divided by the density of the absorber. The advantage of this value is that it doesn't depend on the nature of the absorber. Mass absorption coefficients ( $\text{cm}^2/\text{g}$  or  $\text{cm}^2/\text{mg}$ ) are approximately equal in the media considered earlier.

Sometimes the following is used

- atomic absorption coefficient ( $\mu_a$ ), which takes into account the actual number of atoms in the absorbing material to be equal to the fraction of energy absorbed per absorber atom;
- electronic absorption coefficient ( $\mu_e$ ), which is the fraction of radiation absorbed by the electron absorber. It is applied for  $\gamma$ -quanta of low energy, which interact mainly with orbital electrons.

*The thickness of the semi-absorption layer* is the value that is defined as the thickness of the layer of the material of the absorber, which halves the intensity of the incident radiation. It is used in calculating the protection required to reduce the intensity of the  $\gamma$ -radiation to the required levels.

## 1.3. The interaction of corpuscular ionizing radiation with the matter

### 1.3.1. The types of interaction of $\alpha$ -particles with the matter

The mechanism of energy transfer in the object from all charged particles is the same. When passing through the matter, a charged particle loses

its energy, causing ionization and excitation of atoms until the total energy supply decreases so much that the particle loses its ionizing ability. Depending on the charge, during the particle transit in the matter, it is attracted or repelled from positively charged nuclei, experiencing an electrostatic interaction. The larger the mass of a particle, the less it deviates from the original direction. Therefore, the trajectory of protons and heavier nuclear particles is almost rectilinear, and the trajectory of electrons is strongly broken due to scattering on orbital electrons and atomic nuclei.

The interaction of charged particles with a substance, elastic and inelastic interactions are defined.

In case of *elastic interaction*, the total kinetic energy of the particles before the interaction is equal to the total kinetic energy after their interaction. The consequence of this interaction is the change in the direction of the movement of the particles.

*Inelastic interaction* is a process in which a part of the kinetic energy of particles is spent on ionization and excitation of atoms, excitation of nuclei, nuclear fission or bremsstrahlung. In this case, the total kinetic energy of the particles before the interaction will be equal to the total kinetic energy of the particles after the interaction plus the energy spent on ionization and excitation of the atoms, excitation and fission of nuclei or bremsstrahlung.

Both types of interaction are characteristic of  $\alpha$ -particles: inelastic interaction of  $\alpha$ -particles with orbital electrons (the result is ionization and atomic excitation); elastic scattering of  $\alpha$ -particles on atomic nuclei. The strong electrostatic field surrounding the  $\alpha$ -particle has a significant effect on the orbital electrons of atoms lying near the path of the particle. In many cases, electrons located in external orbits can be completely detached from the atom. In other cases, electrons from internal orbits can move to orbits farther from nuclei. In this interaction with the orbital electrons, the kinetic energy of the  $\alpha$ -particle is scattered.

*Excitation* is an interaction when orbital electrons receive energy from an  $\alpha$ -particle passing through, but don't leave their atoms. Then, the electrons are again transferred to their orbits and emit the excess energy in the form of photons of visible or close to the region – scintillation. The amount of energy transferred in this process is usually small.

*Ionization* is the disruption of an orbital electron by an  $\alpha$ -particle from an atom with which it interacts, the loss of a negatively charged electron leaves the atom in the form of a positively charged ion. Making a pair of ions with an electron and a positive atom is called an ionization process.

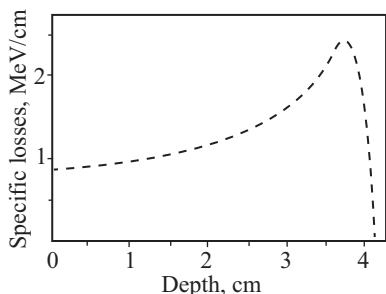


Fig. 5. The curve of distribution of the energy of  $\alpha$ -radiation in the air, cm

The formation of each pair of ions requires an average cost of about 34 eV of the kinetic energy of an  $\alpha$ -particle: an  $\alpha$ -particle with an energy of 6.8 MeV forms until its energy is completely consumed, about  $2 \cdot 10^5$  ion pairs. Therefore, ionization is the most important process of energy transfer of an  $\alpha$ -particle to the matter interacting with it. The tracks of the  $\alpha$ -particles are almost straight.

**Specific ionization** is the number of ion pairs formed per unit path (cm) in an  $\alpha$ -particle track (or other ionizing particle) in the air at normal pressure, that is, *the intensity of ionization*. Fig. 5 shows the curve of the change in the specific energy loss of the  $\alpha$ -particle along its path in the air. It is called *the Bragg curve*.

The specific ionization of the  $\alpha$ -particle beam sharply increases at the end of their path. This happens as a result of many collisions, the  $\alpha$ -particles lose most of their kinetic energy, and their speed decreases. Due to the reduced speed, they remain longer near the molecules along their path; thus, the probability of  $\alpha$ -particles interacting with these molecules significantly increases. The specific ionization reaches a maximum and then drops off sharply. At this point, the  $\alpha$ -particles, which have lost their kinetic energy, capture two electrons and become neutral atoms of helium-4. Since the energy of the  $\alpha$ -radiation emitted by a given radioactive source is discrete,  $\alpha$ -particles fly a strictly defined distance in the air (Table 2). The run of the  $\alpha$ -particles in medium other than gas will be significantly less due to the higher density of liquids and solids. In practice, they are very small and are expressed in micrometers ( $\mu\text{m}$ ).

Table 2. Linear paths of  $\alpha$ -particles with the energy of 7 MeV in some absorbers,  $\mu\text{m}$

Air	Water (tissue)	Aluminum	Mica	Copper	Lead
57,000	74	34	29	14	2

Since the measures of these ranges are very small, the term *equivalent thickness* is used; the thickness (in cm) of the absorber (which is equivalent

to 1 cm of the air by absorption of  $\alpha$ -radiation) multiplied by the matter density (in  $\text{g}/\text{cm}^3$  or if multiplied by 1,000, in  $\text{mg}/\text{cm}^2$ ). Equivalent thickness is measured in  $\text{g}/\text{cm}^2$  (Table 3).

**Table 3. Equivalent thickness of some of the most commonly used absorbers of  $\alpha$ -particles with an energy of 7 MeV,  $\text{mg}/\text{cm}^2$**

Air	Mica	Aluminum	Copper	Silver	Gold
1.2	1.4	1.62	2.26	2.86	3.96

### 1.3.2. Interaction of $\beta$ -radiation with the matter

Like  $\alpha$ -particles,  $\beta$ -particles dissipate their energy mainly in the processes of ionization and excitation of the atoms which they interact with. The type of interaction of light particles, in which the direction of their movement rather than energy is practically changed, is sometimes called *elastic scattering*, unlike *inelastic scattering* (drag), which is observed when a very high energy electron passes near the nucleus. At the same time, there is one more type of energy loss – during deceleration of high-energy  $\beta$ -particles in the Coulomb field of atomic nuclei, electromagnetic radiation is emitted with the wavelengths corresponding to X-ray. This process is called *bremsstrahlung*. Consequently, during the passage of high-energy electrons through matter, *the formation of electromagnetic radiation* also occurs.

$\beta$ -track is very winding. For  $\beta$ -particles, specific ionization decreases rapidly as their energy increases. At the end of the path of a  $\beta$ -particle, when its energy decreases to several keV, the ionization and, consequently, the energy loss per unit path increases.

The  $\beta$ -particle range is expressed in the equivalent thickness. Most often aluminum is used as an absorber.

### 1.3.3. Interaction of neutrons with the matter

Unlike charged particles, neutrons don't have an electric charge, which allows them to freely penetrate deep into atoms, and reaching nuclei, they are either absorbed by them or scattered on them.

**Elastic neutron scattering.** As a result of the elastic neutron scattering (n, n) on the nucleus, the energy of the primary neutron  $E_n$  is distributed between the scattered neutron and the recoil nucleus (Table 4).

*Table 4. Relative fractions of neutron energy  $\delta_E$ , transferred to the nuclei of some elements during elastic scattering*

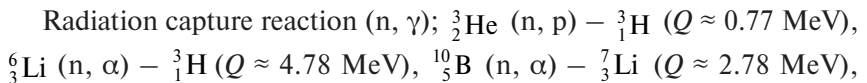
Element	H	C	O	Pb
Mass number	1	12	16	208
$\delta_E$	0.5	0.142	0.111	0.0096

As a result of the elastic neutron scattering, *highly ionizing protons* are formed. When neutrons are absorbed, the atomic nuclei become unstable and in decaying, generate protons;  $\alpha$ -particles and photons of  $\gamma$ -radiation are also capable of producing ionization. In such *nuclear reactions*, radioactive isotopes of elements can form and cause the induced radioactivity, which can also cause ionization. The substance and the recoil nuclei that occur during nuclear transformations are ionized.

With elastic scattering on nuclei of carbon, nitrogen, oxygen and other elements that make up tissues, a neutron loses only 10–15% of energy, and when colliding with hydrogen nuclei – protons – that are almost equal in mass with them, the neutron energy decreases on average twice being transferred to the recoil proton (Fig. 5). Therefore, substances containing a large number of hydrogen atoms (water, paraffin) are used *to protect against neutron radiation* because neutrons quickly waste their energy in these substances and slow down.

In this case, part of the neutron energy is transferred to the recoil proton as kinetic. The neutron scattering deviates from the previous direction and has less energy. Thus, in neutron irradiation, the final biological effect is associated with ionization producing indirectly by secondary particles or photons. Consequently, the predominant contribution of one or another kind of nuclear interaction of neutrons depends on their energy, as well as on the composition of the irradiated substance.

**Neutron inelastic interaction.** It occurs as a reaction of inelastic neutron scattering ( $n, n'\gamma$ ), all kinds of nuclear reactions: ( $n, \gamma$ ); ( $n, p$ ); ( $n, \alpha$ ); ( $n, \alpha$ ); ( $n, np$ ); ( $n, 2n$ ) and others, as well as the induced fission reactions of atomic nuclei ( $n, f$ ). Nuclear reactions under the action of neutrons can take place as direct ones or through a compound nucleus. Depending on the energy balance, reactions can be exoenergetic (passing at any neutron energy), for example:



nuclear fission reactions ( $n, f$ ) with isotopes  ${}^{235}_{92}\text{U}$  and  ${}^{239}_{94}\text{Pu}$  or others, or threshold reactions ( $n, 2n$ ) at  $E_n > 8$  MeV and others.

## 1.4. Ionization potential, linear energy transfer

The same amount of energy can be transferred to a biological object when irradiated with various types of ionizing particles. The absorbed energy is spent on the excitation and ionization of atoms and molecules. The final radiobiological effect is based on the physicochemical transformations of excited and ionized molecular structures. The biological effect of ionizing radiation is associated not only with the amount of the absorbed energy, but largely depends on the nature of the spatial micro distribution of the absorbed energy as well. Absorption of the same dose of radiation leads to different effects.

The energy transferred by a charged particle per unit of its range in a substance is called *linear energy transfer* (LET).

The value of the energy loss per unit of the range (linear energy transfer – LET) is inversely proportional to the kinetic energy of the particle and is related to the density of the distribution of ionization events along the particle track. LET is measured in keV per 1  $\mu\text{m}$  of water. Most of the energy of ionizing radiation is absorbed by reducing the energy of an ionizing particle or photon quantum.

This is the criterion of “quality” of radiation, the effectiveness of its biological action. In mathematical expressions, LET is denoted by the symbol  $L$ :

$$L = \frac{\text{energy transferred by a particle to a substance, keV}}{\text{distance travelled by particle, } \mu\text{m}}.$$

The concept of LET was introduced by R. Zirklem in 1954. The unit of LET is 1 keV/ $\mu\text{m}$  of tissue (1 keV/ $\mu\text{m}$  = 62 J/m).

Typical levels of LET for the most common types of radiation are the following:  $\alpha$ -radiation of  ${}^{60}\text{Co}$  and X-rays with the wavelength of  $\sim 20$  nm (250 keV) have LET of about 0.3 and 2 keV/ $\mu\text{m}$ , respectively, neutrons with the energy of 14 MeV – 12, and heavy charged nuclear particles – from 100 to 2,000 keV/ $\mu\text{m}$ . However, such a division is rather arbitrary, since LET is associated not only with the physical nature of radiation but also depends on the speed of a particle’s flight.

In modern powerful accelerators, heavy particles accelerate to such high energies that their speed approaches the speed of light. In this case, LET of all particles is reduced to the minimum value, which is typical to rarely ionizing light particles (for example, electrons) with the energy of 1 MeV. Therefore, at a very high speed of the movement, fast protons and electrons have the same LET since they have the equal charge.

Depending on the value of LET, all types of ionizing radiation are divided into *rarely and densely ionizing types*.

- Usually all types of radiation are referred to *rarely ionizing radiation* (regardless of their physical nature), with  $LET < 10 \text{ keV}/\mu\text{m}$ ,

- *Densely ionizing types of radiation* are those for which the LET exceeds this value. Neutrons are classified as densely ionizing radiation, since the recoil protons formed by them strongly ionize the matter. However, their occurrence is at great depth due to the high penetrating power of neutrons.

The boundary between them is the conventionally accepted value of  $LET = 10 \text{ keV}/\mu\text{m}$ . As the velocity of charged particles decreases, LET increases.

So, all types of ionizing radiation directly or indirectly cause either excitation or ionization of atoms or molecules of biosystems. However, when objects are irradiated with different types of ionizing radiation at equal doses, quantitative and sometimes qualitatively different biological effects occur, which is associated with the spatial distribution of the energy released during the interaction in the irradiated microvolume – with LET.

LET of charged particles increases with a decrease in their speed; therefore, at the end of the range the energy output by any charged particle is maximum. This feature of the interaction of heavy nuclear particles is used in the tumor treatment as it allows concentrating the significant amount of energy at the depth of the affected tissue with minimal scattering in healthy tissues along the beam.

It has been established that LET is proportional to the square of the charge: the  $\alpha$ -particle, which is formed during a radioactive decay and has a charge of +2, causes the appearance of ions four times more often. In air,  $\alpha$ -particles, depending on the initial energy, form 40,000–100,000 ion pairs and  $\beta$ -particles – 30–300. The mean range of particles increases with increase of their energy. At present, the relationship between these parameters for each particle is precisely defined.

The value of LET in  $\text{keV}/\mu\text{m}$  depends on the density of the substance. When LET is divided into a substance density  $p$ , we obtain the value  $L/p$ , which doesn't depend on the density. This value is also called LET I, or the



braking power of the substance, which is measured in  $\text{MeV} / \text{cm}^2\text{g}^{-1}$ . As follows from the definition, the LET value characterizes the distribution of the energy transferred to the substance along the particle track. Knowing LET, it is easy to determine the average number of ions formed per unit of a particle track. An average of 34–36 eV is spent on one pair of ions. If to divide LET into energy to form one pair of ions, we obtain the linear ionization density (LID):  $\text{LID} = \text{LET} / 34$  (number of ion pairs per  $\mu\text{m}$  range).

The higher the LET value, the more energy the particle leaves per unit of the range and the more densely the ions generated by it are distributed along the track.

LID is a quantitative value of the ionizing ability of ionizing radiation and is equal to the number of ion pairs created by a particle (quantum) per unit of the range in a substance, and LID depends on many factors such as speed, mass and charge of the particle, the energy of quanta, properties of the matter, etc. To avoid uncertainty because of the properties of the substance, and to characterize only the properties of ionizing radiation, the LID is determined in the standard substance – dry air (Table 5).

*Table 5. Average values of LID in the air*

The type of the radiation	LID (pairs of ions · $\text{cm}^{-1}$ )
$\alpha$ -particles	40,000
$\beta$ -particles	400
X-rays and $\gamma$ -quanta	5
protons	10,000

It is obvious that in other substances with the different density, the values of the LID will be different. Practical interest of LID measured under standard conditions (in air) and in human tissues is of practical interest. It should be noted that it is more reasonable to predict the development of the reaction in biological tissues, realizing the degree of its ionization, but not the air. It is empirically found that the LID, which is contained in human tissues, is about 800 times higher than the LID measured in air:  $\text{LID}_{\text{tissue}} \geq 800 \text{LID}_{\text{air}}$ . The greatest damaging effect on living tissues is caused by radiation, which creates a large LID since each pair of ions is a destroyed biomolecule.

Ionization density is increased at the end of the particle track. With an equal particle velocity, the level of ionization is proportional to the square of the particle charge; also, with equal energy, the ionization density increases with a larger particle mass.

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