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BIOPHYSICS AND MEDICAL PHYSICS (REVIEW)

Radiation Technology in Medicine: Part 2. Using Isotopes in Nuclear Medicine

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Abstract—In this article, we discuss the role of radionuclide technologies among other nuclear methods used in medicine. We analyze the condition and perspectives of the development of nuclear technology with regard to using radionuclides in medicine, for brachytherapy in particular. We review the modern use of radionuclide facilities in medicine.

Keywords: radionuclides, radionuclide diagnostics, radionuclide therapy, brachytherapy, stereotactic surgery.

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INTRODUCTION: RADIOACTIVE ISOTOPES IN MEDICINE

Radiation technologies began to be used after several fundamental discoveries. In 1895 W. Röntgen detected X-ray radiation. In 1896, A. Becquerel discovered the radioactivity of certain types of matter. In 1897, D. Thomson determined that cathode beams consist of elementary particles, viz., electrons. E. Rutherford in 1899 and P. Villard in 1900 then found that radioactive elements emit alpha and beta particles, as well as gamma rays. In early 1896 scientists discovered the damaging effects of X-rays on the skin; in November of that year Freund carried out a scheduled exposure of a hairy nevus to radiation [1]. In 1901, A. Danlos used radioactive isotopes for tuberculosis treatment and in 1903 A. Bell started placing radium sources inside or near tumors.

In the late 1920s to the early 1930s the first charged-particle accelerators were built: the cascade accelerator, the cyclotron, and the linear-particle accelerator. They were used to manage nuclear reactions for transforming chemical elements and producing first artificial radioactive isotopes. These and further discoveries became the basis for the development of nuclear technologies in various sectors, including medical applications.

Today, there are over 100 000 medical devices that use ionizing radiation, aside from the millions of X-ray machines.

Nuclear technologies in medicine are applied in the area of radiation therapy and nuclear medicine, which traditionally incorporates radionuclide diagnostics and therapy [3–7]. Radiation therapy is either performed on the distant basis (electron and photon beams from electron accelerators, proton and ion beams from proton accelerators, neutron beams from neutron generators or nuclear reactors, photons from cobalt machines, etc.), or on the contact basis (the ionizing radiation source is located in direct contact with the exposed volume. The latter method involves placing the radiation source near the treated region or inside it. This is a boundary-type method, which can be categorized as either radiation therapy or a nuclear medicine method. During the last decade, a new independent line of technology development has been evolving from radiation therapy, viz., stereotactic surgery [8, 9], which uses such unique machines as the Gamma Knife and Cyber Knife and specifically modified linear accelerators.

The structure of nuclear technologies in medicine is given in Fig. 1. Among them, radioactive isotope technologies have become especially important. Approximately 100 radionuclides are either used or can be potentially applied in nuclear medicine (out of ~3000 isotopes that are known). This field consumes over 50% of the isotopes produced in the entire world [10].

The main sources of medical radionuclides production are reactors and charged particle accelerators (various kinds of cyclotrons with energies of 4–

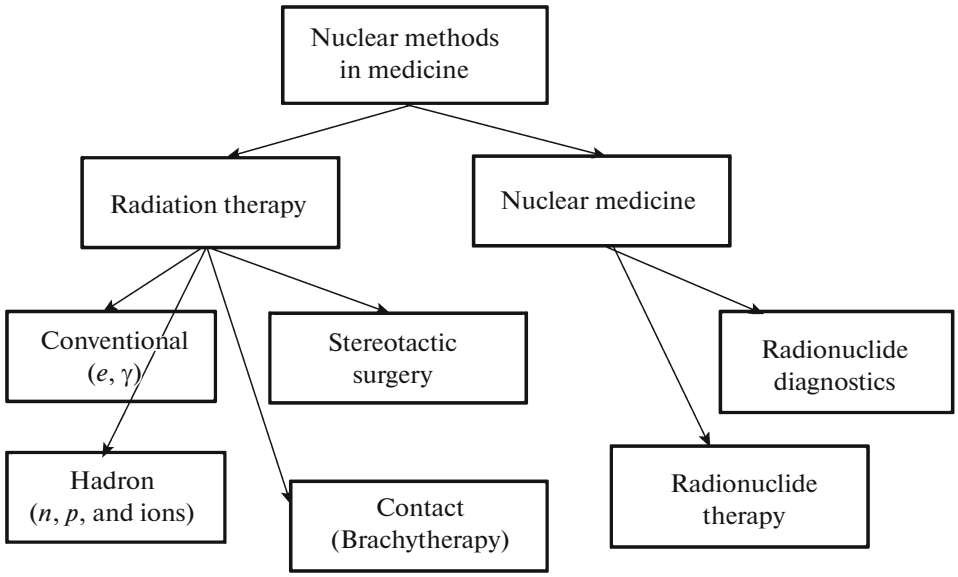

Fig. 1. The structure of nuclear technologies in medicine.

30 MeV). Currently, over 45 types of radionuclides are produced for medical purposes, which include approximately 27 types of radionuclides used in diagnostics and approximately 37 types of radionuclides used in therapy. The group of radionuclides that are produced by the generator method, which emerge from the decay of β^+ and β^- and as a result of electron capture and isomeric transitions, contains approximately 20 radionuclides [11].

This article presents a review of the current state and perspectives of the development of nuclear technology for the use of radionuclides in medicine in Russia and in the world. It covers the state of development in radionuclide technologies and the change in the number of machines for this purpose in Russia relative to the world, in comparison with other countries.

THE PHYSICS OF RADIONUCLIDE TECHNOLOGIES IN MEDICINE

After X-radiation achieved widespread application in diagnostics and therapy, physicists suggested using other types of penetrating radiation in medicine.

In the first third of the 20th century, a number of radiation technologies emerged in medical practice on the basis of the radioactivity phenomenon that is present in some types of matter. Those included contact radiation therapy and external-beam radiation therapy, as well as nuclear medicine, which consist of radionuclide diagnostics and therapy.

Radiation Therapy with Radioactive Sources

Historically, the idea of using radionuclides in medicine was first expressed in contact-radiation therapy, or brachytherapy.

Brachytherapy. In this type of radiation therapy a small, hermetically sealed radiation source is placed inside the body tissue or near a zone that requires treatment. Radioactive material in this case does not directly enter the body; the surrounding tissues are exposed through the walls of the capsule.

The concept of using radiation in cancer treatment was first proposed early in 1901 by the French physical scientist P. Curie. In 1910, the American scientists D. Pasto and P. Degre developed a treatment methodology that provided the delivery of the required dose of radioactive material to the prostate. Later, in 1917, B. Barringer suggested a method for introducing radioactive microsources into a tumor using special hollow needles.

The idea of using isotopes in contact radiation therapy consists of placing a radionuclide inside or in close proximity to a tumor. The isotopes are placed in a manner so that when the cancer–healthy tissue boundary is reached, the dose of radiation declines. In this case, the effect of ionizing radiation (IR) on cancer cells results in their death, while healthy tissues receive a significantly lower dose of radiation and thus preserve their function. It is known that cancer cells are prone to uncontrolled division (proliferation) and are more sensitive to radiation than other tissues [32]. Thus, ionizing radiation is more likely to damage tumor cells than healthy tissues. This causes a decrease in the number of tumor cells after each session of radiation therapy. In the so-called therapeutic dose interval ionizing radiation beams damage tumor cells but

Table 1. The characteristics of main isotopes used in brachytherapy

Radionuclide	Method of production	Half-life	Type of radiation	*E*, MeV
^{226}Ra	*U*-ore treatment	1620 years	γ	2.45
^{137}Cs	Product of decay	30.17 years	γ	0.662
^{60}Co	Neutron activation	5.26 years	γ	1.17; 1.33
^{192}Ir	Neutron activation	74 days	γ	0.38
^{125}I	Product of decay	59.6 days	γ	0.027; 0.0314; 0.0355
^{169}Yb	Neutron activation	31 days	γ	0.09
^{103}Pd	Neutron activation	17 days	γ	0.021
^{106}Ru	Product of decay	1.02 years	β	3.54
^{90}Sr	Product of decay	28.7 years	β	2.27

do not damage healthy tissue cells to the same extent. In this case it is important that specialists select the dose that does not damage healthy tissues (the dose that healthy tissues can endure).

The introduced source, to a good approximation, can be considered as a point source, which allows one to expose a certain volume of tumor tissue that is necessary. One of the advantages that brachytherapy offers, in comparison with external-beam radiation therapy, is the rapid decline of the radiation dose away from the radioactive source; thus, a smaller volume of healthy tissue is exposed to radiation. This enables using higher doses of radiation in treating tumors without the risk of exceeding the dose limit for healthy tissue. Thus, a target can receive a dose of up to 160 Gy, which is approximately two times higher than in external-beam radiation therapy.

The main requirements for a radionuclide used in brachytherapy are its half-life, activity, type of emitted particles, and cost-efficiency of the production. Low-energy photons or electrons are usually used. Energy of photons is selected in the manner such that the dose that is transferred to the tissues is concentrated near the source and the dose absorbed by healthy tissues is minimal; the energy of photons in this case is within the range of several keV. Electrons can have an energy of up to several MeV, because their mean path is approximately 0.5–1.0 cm. Due to their small path, alpha particles are virtually not used in brachytherapy; for example, the path of particles with energy of approximately 10 MeV in biological tissue composes approximately a hundred μm.

Throughout the entire history of brachytherapy, approximately 150 radionuclides have been used [12–19]. The following sources are in clinical use for the purpose of brachytherapy: ^{125}I, ^{103}Pd, ^{131}Cs, ^{60}Co, and ^{192}Ir. Much less frequently, the radionuclides ^{198}Au, ^{106}Ru, and ^{252}Cf are used. During the long period since the 1930s, the ^{226}Ra and ^{222}Rn isotopes had been used in brachytherapy; however, due to radiation safety reasons, their actual usage has been discontinued. From the practical viewpoint, considering the above requirements, the ^{125}I, ^{103}Pd, ^{131}Cs, ^{60}Co isotopes are most convenient for clinical use.

Depending on the application specifics, the produced sources are shaped as capsules, which usually have double walls; however, there are also non-capsule methods. Such capsules are shaped like needles, tubes, grains, wire, pills, etc., which are placed directly in a patient's body.

Isotopes are usually categorized by the type of emitted radiation. Table 1 shows the characteristics of isotopes that decay emitting photons and electrons used in different periods of brachytherapy. According to the energy of the emitted photons, isotopes are divided into low-energy and high-energy isotopes. The first group includes isotopes that emit photons with an energy of several tens of keV (^{125}I, ^{103}Pd and ^{169}Yb), and the other group includes isotopes that emit photons with an energy of several hundreds of keV up to MeV. As well, brachytherapy experimentally uses the ^{252}Cf, ^{32}P, ^{145}Sm, ^{182}Ta, ^{177}Lu, and ^{188}Re radioactive isotopes [32].

External-beam radiation therapy. Since 1950s, radionuclides have also been widely used in external-beam radiation therapy. These machines used the ^{60}Co radioactive isotopes, which emit photons with energies of 1.17 and 1.33 MeV.

The first radiation therapy machine with ^{60}Co as a source was commissioned in 1951 in Canada [8] by a company that is now called MDS Nordion; it is the leading supplier of gamma therapy devices. The use of radioactive sources was especially developed in the oncology institute in Toronto [9]. As well, ^{137}Cs sources were used in this institute; there were attempts to use ^{192}Ir, which has a half-life of only 74.5 days. The first two isotopes were easily processed in the reactor and had longer half-lives, viz., ^{60}Co, 5 years and ^{137}Cs, 30 years.

The concept of using the ^{60}Co isotope relied on the fact that the energy and intensity of the beams that

evolve upon the decay of the ^{60}Co isotope were comparable with the energy and intensity using accelerators; however, the cobalt machine was smaller in size. In this context, the principles of photon-beam action from ^{60}Co upon matter are the same as that of a bremsstrahlung photon beam from an electron accelerator. They are based on the radiotherapeutic interval, i.e., the difference in sensitivity to radiation between the tumor and the surrounding tissues. This means that when tissues are exposed to ionizing radiation, there is a difference between the dose that is admissible for normal tissues and the dose that is required to kill tumor cells. The survivability of healthy tissue cells upon exposure to radiation appears to be higher than that of a tumor due to the difference in sensitivity to radiation; the beam action results in the death of tumor cells while preserving the functionality and ability to recover in cells of healthy tissue. For various types of tissue, the value of the therapeutic interval is different and radiation doses must be calculated for each particular case with consideration of the maximum admissible dose for surrounding and healthy tissues and high-risk organs. So-called critical organs and tissues are damaged more easily than cancer cells.

Stereotactic surgery. The use of the ^{60}Co isotope was the basis of stereotactic surgical devices. From the physics standpoint, the concept was that the distribution of the dose from the ^{60}Co source decreases with depth. This allowed the successful treatment of tumors located several centimeters from the surface with radiation. Deeply situated tumors were difficult to expose using cobalt machines, because surface tissues received an excessive radiation dose. If one point becomes the target of several cobalt sources at the same time, the dose at that point will exceed the dose in surface tissues by several times. This idea was the basis for stereotactic surgery devices, which were later called the Gamma Knife.

In 1951, L. Leksell proposed the concept of stereotactic surgery that does not require cephalotomy using radioactive sources ^{60}Co [19, 20]. This concept was implemented in cooperation with the radiobiologist B. Larson, which resulted in the creation of the device called the Gamma Knife. The first surgery with the use of such a device was completed in Stockholm in 1968.

The advantage of this method is that many beams (there were 179 of them in the first device and 192 to 201 in further models) from radioactive sources are aimed in one point where the absorbed dose greatly exceeds the dose on the surface of a human body. In this case, a dose of up to 10 Gy is delivered directly to the tumor, causing its death, and healthy tissues receive a negligible radiation dose. The gamma Knife allows the treatment of vascular tissue neoplasms and brain tumors, including metastases, without surgical intervention and many weeks of exposure of the brain to radiation. Globally, the number of such units is growing; today, there are 300 of them.

Neutron capture therapy. As a result of research by Goldhaber (1934), it was determined that some isotopes have a larger cross section of thermal neutron capture. This property found use for neutron capture therapy [20].

The essence of this method is that before exposing tumor cells to a thermal neutron beam, an agent that contains the boron isotope ^{10}B or the gadolinium isotope ^{157}Gd is injected. Neutrons are captured by the isotope, and a nuclear reaction occurs producing a large amount of energy in the cell, resulting in the increase in tumor's sensitivity to the radiation flux. In the cancerous cell, secondary radiation emerges that produces sufficient energy to kill it. In this manner, for example, after capturing a thermal neutron, the natural isotope ^{10}B transitions into ^{11}B and then decays, forming alpha particles and the recoil ion ^{7}Li. The agent introduced in cells is designed to only accumulate in the tumor and paths of alpha particles and the recoil ion present in the tissue are comparable with the actual sizes of cells (up to 12–13 μm); thus, the surrounding healthy tissues are virtually unaffected by the radiation. The neutron capture therapy method allows the treatment of large, multiple, and radio-resistant malignant tumors; it is used for exposing deeply located tumors and brain tumors, which at times cannot be treated by surgical intervention [21].

Nuclear Medicine

The date of the advent of nuclear medicine historically belongs to mid-1940s. However, as mentioned above, medical specialties such as brachytherapy and radionuclide diagnostics emerged much earlier.

Radionuclide diagnostics. Radiation diagnostics involves X-ray, ultrasound, and isotope studies; a broad range of X-ray studies play a major role. These are followed by the methods of ultrasound diagnostics, which are used in the majority of medical institutions. Radionuclide diagnostics (RND), which is the functional imaging of inner organs, is a small but developing branch of radiation diagnostics.

In the mid-1920s, J. Hevesi performed the first experiments on diagnosing metabolism in mice using radionuclides ^{210}Bi and registering photons using a Geiger-Müller counter. Such methods of diagnostics were first applied in 1927 by Blumgart and Weiss. They used radon gas to estimate the hemodynamics in patients with heart failure. The radioisotope ^{131}I was first applied for diagnosing thyroid gland diseases by Herz in the late 1930s [20].

After E. Lawrence invented the cyclotron, artificial radionuclides were developed [23]. The first ^{99m}Tc radionuclide was synthesized in 1938 at the cyclotron in Berkeley.

The advancement of nuclear and radiation physics resulted in the creation of a number of impressive machines, viz., the magnetic resonance imaging (MRI) scanner, gamma camera (GC), single-photon emission computed tomography (SPECT) scanner, positron emission tomography (PET) scanner, computed tomography (CT) scanner, tomotherapy systems, and others. Each type of tomography has its own special advantages. A great number of physical, chemical, and medical scientists have been awarded the Nobel prize for their inventions. Experience has proven that the best results are achieved when these technologies are used in combination.

Generally, the methods of radiation diagnostics are divided in two major lines of development. The first line is diagnostics that uses external sources of ionizing and non-ionizing radiation. In this case, the photographic method is used, with various kinds of radiation (X-rays, gamma rays, radio-frequency radiation, etc.) to study tissue structure. Devices that work on the basis of this concept include X-ray, CT, and MRI scanners. The second line is studying the dynamics of organ functioning. Radionuclide markers are introduced in tissues; organ functioning is monitored according to the location and movement of these markers. Such studies are carried out with via radionuclide diagnostic methods (GC, SPECT, and PET).

The principle of radionuclide diagnostics using GC, SPECT, and PET is based on measuring the density of radionuclide distribution in pathological areas. Various types of radionuclides are absorbed differently by organs and tissues. For the purposes of diagnostics, isotopes are selected depending on the ability of the tissue to accumulate the specific type of isotope. The half-life of the radionuclide is also taken into account; it must be longer than the time of its distribution in a certain organ or tissue area and sufficient for studies by a doctor. Moreover, when cancer patients are examined, it is necessary to select a radionuclide that has a higher concentration in a tumor than in healthy tissue. Then, using diagnostic equipment, the shape and volume of the tumor can be seen. If the half-life of the radionuclide is too long, the patient's healthy tissues will absorb an excessive dose of radiation. That is the reason that it is important that the radionuclide decays rapidly after the examination and is easily and fully removed from the body. In this context, the activity of radionuclides must be low in order to decrease the dose absorbed by healthy tissues.

In practice, various chemical compounds are used, viz., radiopharmaceutical agents (RPA), that contain a certain radionuclide. They deliver the radionuclide to the abnormal focus and after the examination is completed they remove it from the body in a manner such that the remaining amount of radioactive material is minimal, i.e., poses no threat to the patient. A great number of radiopharmaceutical agents for diagnostics can be created on the basis of the same radionuclide.

The density of a radionuclide's distribution in scanners is determined according to the number of photons emitted by the radionuclide during decay, which are registered by special detectors. In GC and SPECT scanners, separate photons are detected; in PET, pairs of photons that move in the opposite direction are detected. By the distribution of photons in various depths of tissue, the isotope distribution is determined and the structure of the tissue is visualized on a computer display by mathematical software.

The first device of this kind was the *gamma camera*.

The concept of the gamma camera (a principally new diagnostic device) was proposed by Copeland and Benjamin in 1949 [26]. The main contribution to the scanning method and the creation of gamma cameras was made by Anger and Mallard starting from 1952. The first gamma camera was created by the American engineer, Anger, in 1966.

Isotopes introduced in an organ emit one photon at a time, which is registered by a scintillation detector. The design of a gamma camera includes a detector and electronic circuits; computer analysis locates the tumor and draws a two-dimensional image of the organs.

With the improvement of computing technology, more precise diagnostic means were created on the basis of the gamma camera principles, viz., single-photon emission computed tomography (SPECT); their development started in 1963–1964. SPECT provided the ability to obtain images from many directions, on which a three-dimensional view of an object was based.

To diagnose the whole body, either a mobile detector is used, which moves along the patient's body, or a mobile table, which moves under a stationary detector. In SPECT systems, a mobile unit is used, which is called a gantry, a device that rotates the radiation source and/or detector around the patient's body.

In the gantry device, the detector and collimators rotate following the path of a circle, ellipse, or the patient's body contour. Since SPECT provides section views of the examined organs, the resulting reconstructed image is not distorted by image overlays of other organs above the organ of interest, which is critical in diagnostics and represents a major advantage in comparison with studies performed using the gamma camera. The radionuclides used in radiation diagnostics are listed in Table 2.

Another example of using nuclear physics in medicine is a *positron emission tomography* (PET) scanner. PET uses radionuclides ^{11}C, ^{13}N, ^{15}O, and ^{18}F, which decay emitting positrons.

The first application of the ^{131}I radioisotope in diagnosing thyroid diseases occurred in the late 1930s. The early imaging devices of the 1950s were scanners

Table 2. Isotopes used in diagnostics

Radionuclide	$T_{1/2}$	Energy of β-radiation or γ-quanta, MeV
^{51}Cr	27.7 days	0.32
^{57}Co	267 days	0.122
^{62}Cu	9.7 min	1.173
^{67}Ga	61.8 h	0.185
^{75}Se	120 days	0.136
^{81m}Kr	13 s	0.19
^{81}Rb	4.6 h	0.19
^{85}Sr	64.8 days	0.514
^{95}Tc	20 h	0.766
^{97m}Tc	89 days	0.965
^{99m}Tc	6 h	0.141
^{111}In	2.8 days	0.171
^{113m}In	99.5 min	0.392
^{123}I	13.3 h	0.159
^{131}I	8.1 days	0.365
^{132}I	2.3 h	0.668
^{127}Xe	36.4 days	0.203
^{133}Xe	5.3 days	0.081
^{199}Tl	7.4 h	0.455
^{201}Tl	72.9 h	0.167

with two-coordinate scanning technology and scintillation cameras. In clinical practice, these kinds of devices started to be widely used in mid-1960s. Since that period, the Anger camera (or gamma camera) has become one of the basic technical means of imaging using isotopes.

In the 1970s and 1980s, experiments dealing with the consumption of glucose marked with β^+ radioactive isotopes of carbon and fluorine by tumors led to the idea of diagnosing pathologies by registering two coinciding photons emitted when positrons annihilate. These studies became the underlying principle of the positron emission tomography (PET) method. The American researchers M. Ter-Pogossian, M. Phelps, and E. Hoffman designed the *positron emission tomography* (PET) scanner.

In order to visualize tissues using PET, an agent containing a radioactive isotope that emits a positron when it decays, is delivered to organs. The positron passes a distance of up to 3 mm in tissue, loses energy upon encountering molecules and atoms, annihilates with an electron at the moment it stops, and turns into two photons with the energy of 0.511 MeV, which fly apart in opposite directions. These photons are registered by scintillation detectors. Further, following the coincidence patterns, pairs of photons whose signals were delivered at the same time are selected. When a set of such detectors is placed around a radiation source (the patient's body) the direction of the path along which the annihilation occurs can be determined; by measuring the time interval between the scintillation at the first and second paired detectors, the precise location of the source can be found.

Special complex scanners combine two types of tomography, viz., SPECT + CT, SPECT + MRI, PET + CT, PET + MRI, and PET + SPECT, which allow carrying out radioisotope, X-ray, and computed tomography studies at the same time for cardiology, oncology, and neurology. They also provide more detailed anatomic information when performing radionuclide diagnostics.

Radionuclide therapy. Synthesizing radionuclides by accelerators led to the possibility to use them in medicine, which marked the beginning of an important nuclear medicine specialty, viz., radionuclide therapy (RNT).

The basis for the development of nuclear medicine was the first CR-1 nuclear reactor, which was opened in 1942 [27]. It allowed for intense processing of various radioactive isotopes and their further supply to consumers. The time at which isotope supply was initiated in 1946 is considered as the date when nuclear medicine using radioactive isotopes in diagnostics and therapy began.

The physical principles of RNT are similar to the principles of radionuclide diagnostic (RND) system formation. Preliminary dosimetric planning for RNT is performed in the same manner as that for RND. First, an optimal RPA is selected; its activity is computed on the basis of the data on its distribution in biological tissues, in pathologic neoplasms, and in the surrounding tissues of the patient's body.

The main criterion for RPA selection in radionuclide therapy is the ratio of the amount of accumulated radionuclide in the tumor to the amount in healthy tissues. The higher this ratio is, the higher the radiation dose is in the inner abnormal focus compared to the dose absorbed by the surrounding tissues. Unlike RND, where isotopes that emit photons when decaying are used, RNT uses radionuclides that emit β^- and, much more rarely, α radiation, which are absorbed and leave all the energy in the tissues where it was accumulated.

The energy of electrons and α-particles in RNT can have practically any value; the half-life of the radionuclide must not be long, as this may lead to undesired exposure of normal organs and tissues in which the radionuclide can occur after introduction into the body. However, the half-life of the radionuclide must not be too short. In this case, the radiation would be uneven, which may impair the therapeutic effect of RNT. The optimal radionuclides have a half-life of several hours to several days.

Table 3. Isotopes used in radionuclide therapy

Radionuclide	$T_{1/2}$	Type of decay	Average energy of β radiation and energies of the most intense α and γ radiations, MeV
^{32}P	14.3 days	β^-	0.6952
^{67}Cu	61.8 h	β^-	0.1475; γ0.1846
^{77}Br	56 h	EC; β^+	γ0.239; 0.521
^{90}Y	64.3 h	β^-	0.928
^{89}Sr	50.6 days	β^-	0.583
^{111}In	2.8 days	EC	γ0.1713; 0.2454
^{117m}Sn	13.6 days	IT	γ0.1586
^{124}I	4.2 days	EC; β^+	γ0.6027; 1.691
^{125}I	60 days	EC	γ0.0355
^{131}I	8.1 days	β^-	0.1914; γ0.3645
^{186}Re	90.6 days	β^-; EC	0.342; γ0.1372
^{188}Re	16.9 h	β^-	0.7539; γ0.155
^{212}Bi	60.6 min	β^-	0.665; α6.054; γ0.7273
^{211}At	7.2 h	α	α5.870; γ0.0687
^{225}Ac	10 days	α	α5.830
^{153}Sm	46.7 h	β^-	0.2232; γ0.1032
^{149}Tb	4.2 h	EC; β^+; α	α3.967; γ0.165; 0.3623
^{166}Ho	26.8 h	β^-	0.668; 1.850; γ0.0806
^{169}Er	9.4 days	β^-	0.0991
^{177}Lu	6.7 days	β^-	0.1368; γ0.2884

When radionuclides for RNT are selected, physicians take another issue into account, which is the presence of low-intensity radiation along with electron and γ particle fluxes. This enables additional visual control of RPA distribution in the patient's body using radionuclide diagnostic methods, regulation of radiation doses in abnormal focuses and their adjustment following the dynamics. Despite the fact that the entire body receives a small amount of additional radiation, this condition is important in selecting nuclides for RNT. An important requirement for an RPA used in therapy is chemical non-toxicity, sterility, and the reliability of fixation of the radioactive marker in the agent's molecules [39–42].

In the 20th century, the most widely applied treatment methods were methods using isotopes ^{32}P, ^{198}Au, ^{131}I, ^{90}Y and ^{89}Sr. The list of nuclides used for medical purposes has notably enlarged. Table 3 shows the characteristics of the isotopes that are already used and studied in medicine. Today, ^{131}I, ^{153}Sm, ^{89}Sr, ^{32}P, ^{186}Re, ^{188}Re, ^{90}Y, ^{117m}Sn, ^{177}Lu, ^{169}Er, and other isotopes are successfully used in clinical practice. Research has also been continuing regarding the use of agents based on ^{67}Cu, ^{124}I, ^{149}Tb, ^{166}Ho, ^{211}At, ^{212}Bi, ^{225}Ac, ^{213}Bi, and other isotopes.

CONCLUSIONS

The advancement of nuclear technology in medicine led to a wide distribution of devices using radionuclides, viz., cobalt machines, radiosurgical units such as the Gamma Knife, and diagnostic and research means. In order to produce isotopes, a large number of nuclear reactors and accelerators are used. This article described the amount, types, and regions for such facilities in Russia and in the world. The total numbers of types of medical equipment that operate on the basis of inventions of nuclear physics and its distribution by type are given in Fig. 2. Devices that operate on the basis of radionuclides are approximately 25% of the total units of medical equipment; the major proportion of this is used in radionuclide diagnostics (85%) and in contact radiation therapy and external-beam radiation therapy (15%) [28–31].

Due to the diagnostic and therapeutic possibilities that are provided by devices that operate on the basis of exposing biological tissues to ionizing radiation, such devices are in demand in medical centers. Thus,

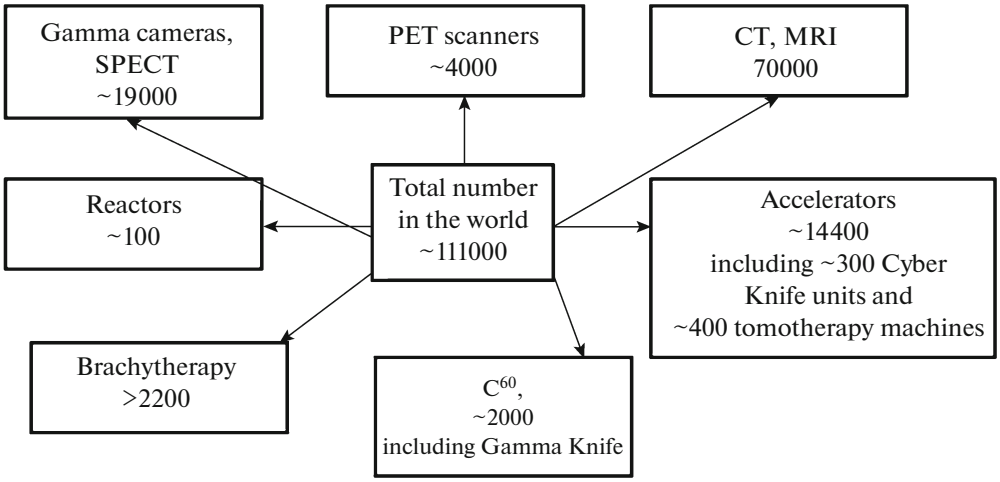

Fig. 2. Nuclear facilities in the world.

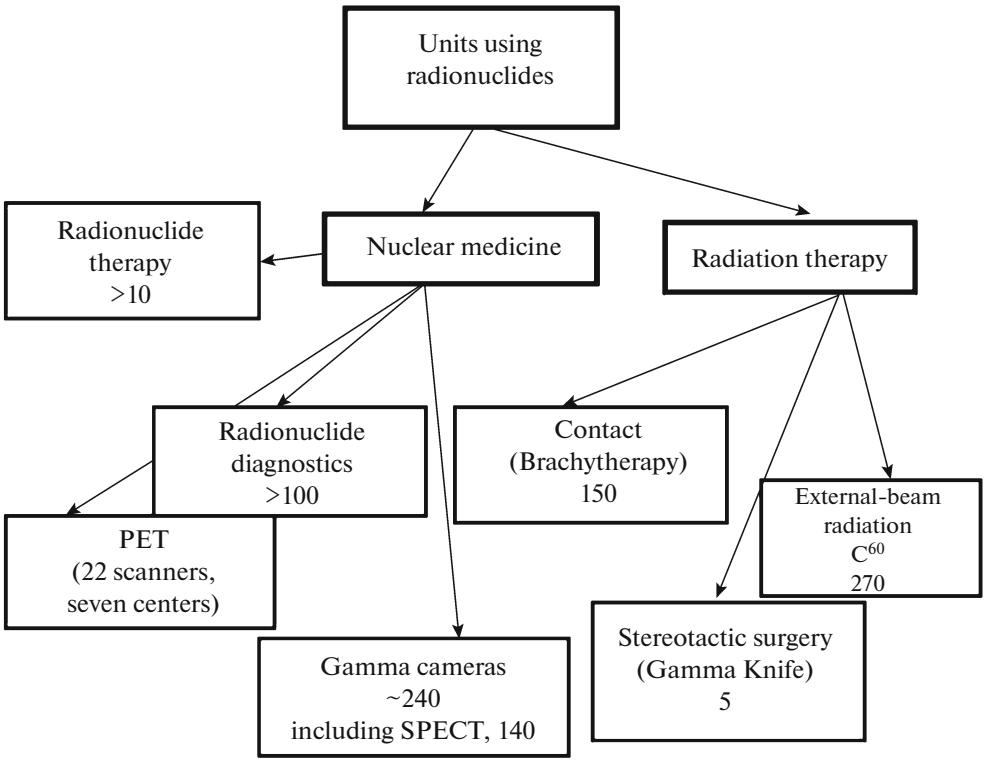

Fig. 3. Facilities using radionuclides that operate in Russian medical centers.

in Russia there are more than 420 units for external-beam radiation therapy [33–38]: 150 electron accelerators, three centers of proton and ion therapy (two more centers are currently under construction), seven stereotactic devices (Cyber Knives), 270 sources of γ radiation and five Gamma Knife units (Fig. 3). The fleet of diagnostic facilities in Russia consists of the following units: 240 gamma cameras (including 140 SPECT scanners), 100 computed tomography scanners, 22 PET scanners (including seven fully equipped PET centers), and 450 MRI scanners. There are more than ten centers for radionuclide therapy and over 100 centers for radionuclide diagnostics.

Globally, there are over 800 brachytherapy centers, in which at least 2200 contact beam therapy units operate. The most popular manufacturers of brachytherapy equipment are GammaMed, Varian BrachyTherapy (United States), and Nucletron (Hol-

land). Currently, there are at least 150 cobalt machines that operate in 19 brachytherapy centers and oncology hospitals in Russia; however, most of them are outdated. In the recent decades, the pace of upgrading the units and their growth in number has been improving [44].

The significant portion of medical equipment using radionuclide technologies in Russia (~40%) is CT and MRI scanners. There are approximately 700 medical devices that use radioactive isotopes in Russia, i.e., 30% of the total amount of medical equipment. Approximately 12% of this equipment is used for external-beam radiation therapy, 7% is used in contact radiation therapy, and 11% is used in radionuclide diagnostics.

Approximately ten reactors and twenty proton accelerators are used in Russia to produce isotopes for medical purposes.

Over 200 radiopharmaceutical agents are produced in the entire world. In Russian medicine, 22 radiopharmaceutical agents are used for isotope-based diagnostics and 20 imported sets are used for radioimmunoassay and more than 5 are used in PET scanning.

In Russian clinics, the majority of the medical equipment that uses nuclear technologies is imported from abroad. However, scientific institutions, in cooperation with state and commercial organizations, are currently designing facilities for radiation diagnostics, contact radiation therapy, and external-beam radiation therapy and developing technologies for producing radionuclides that are at the global level [45].

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