

THE HISTORY OF RADIATION THERAPY (PART I)

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Abstract

In 1903, on the basis of Morozov Institute of the Moscow Imperial University (currently, P. Herzen Moscow Oncology Research Center, a branch of the National Medical Research Radiological Center, Ministry of Health of the Russian Federation), the first specialized unit in Russia was opened – department of radiation therapy of oncological diseases, in which scientific research in the field of medical radiology was officially launched in our country for the first time. The first studies in the field of radiation therapy can be attributed to this period.

The article presents a brief summary of the historical development of radiotherapy in the world and in Russia; provides information on the achievements of global importance, fundamental for this scientific field. The activities of leading Russian organizations in the field of radiation therapy are reviewed; names of scientists, doctors and other specialists who have made a significant contribution to its development are provided. The main literature sources relevant to the field are given.

The data in this article may be of interest and be useful for biomedical scientists, practicing radiologists and radiotherapists, oncologists, medical and graduate students, interns and other specialists.

Key words: history of medicine, development of radiation therapy, radiotherapy, medical radiology, therapeutic radiology, X-ray radiology, X-ray therapy, treatment of malignant neoplasms, radiological methods in oncology, radiation therapy in oncology, radioactivity.

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К ИСТОРИИ РАЗВИТИЯ ЛУЧЕВОЙ ТЕРАПИИ (ЧАСТЬ I)

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Резюме

В 1903 г. на базе Института им. Морозовых Императорского Московского университета (ныне Московский научно-исследовательский онкологический институт имени П.А. Герцена – филиал ФГБУ «Национального медицинского исследовательского центра радиологии» Минздрава России) открыли первое в России специализированное подразделение – отдел лучевой терапии онкологических заболеваний, в котором впервые в нашей стране были официально начаты научные исследования в области медицинской радиологии. К этому же периоду можно отнести первые исследования в области лучевой терапии.

В работе освещены основные этапы развития лучевой терапии в нашей стране и в мире; приведена информация о важнейших научных достижениях, имеющих общемировое значение и являющихся основополагающими для данного научного направления. Рассмотрена деятельность ведущих российских организаций в области лучевой терапии; названы имена ученых, врачей и других специалистов, внесших значительный вклад в ее развитие. Приведены основные литературные источники, актуальные в рассматриваемой области.

Данные статьи могут представлять интерес и быть полезными в работе ученых медико-биологического профиля, практикующих врачей-радиологов и радиотерапевтов, онкологов, слушателей факультетов последипломного образования, студентов медицинских факультетов, аспирантов, ординаторов и других специалистов.

Ключевые слова: история медицины, развитие лучевой терапии, радиотерапия, медицинская радиология, терапевтическая радиология, рентгенорадиология, рентгенотерапия, лечение злокачественных новообразований, радиологические методы в онкологии, лучевая терапия в онкологии, радиоактивность.

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Introduction

2018 marked the 115th anniversary of the beginning of Russia's first research in the field of medical radiology on the basis of the Morozovs Institute of the Imperial Moscow University. Since 2014, this medical institution has been called P. A. Herzen Moscow Oncology Research Center (P. A. Herzen MORC), a Branch of the National Medical Radiology Research Center of the Ministry of Health of the Russian Federation (FSBI NMRC of Radiology of the Ministry of Health of the Russian Federation). In 1903, the first specialized radiological unit in our country, the department of radiation therapy of oncological diseases, was opened at the Morozovs Institute. To date, P. A. Herzen MORC, together with other two leading medical scientific organizations of Russia, A. F. Tsyb MRRC and O. N. Lopatkin Research Institute of Urology and Interventional Radiology, operate as a part of the FSBI NMRC of Radiology of the Ministry of Health of the Russian Federation.

The history of the formation and development of radiation therapy in the world dates back to the end of the 19th century, when the effects of ionizing radiation on the body were first studied. They were initiated by a number of fateful historical events connected with the discovery of artificial and natural radioactivity which caused a real revolution in science, including in the fields of physics, medicine, biology, etc., and predetermined its further development in various spheres of human activ-

ity. The history of radiation therapy will always keep the names of the scientists who were at the forefront of the discovery of radioactivity: Wilhelm Conrad Roentgen, Maria and Pierre Curie, Henri Becquerel and their followers [1].

A comprehensive study of the properties of X-rays was started immediately after they were discovered by K. Roentgen on November 8, 1895; it involved the determination of their physical properties, as well as their effects on various biological objects [2-4]. These processes were accelerated by the discovery of natural radioactivity in 1896 [5].

As early as 1896, Russian scientist I. R. Tarkhanov, who was one of the first to substantiate the ability of ionizing radiation to cause functional and structural changes in cells, tissues, organs and throughout the body, foresaw the widespread use of radiological methods in medicine [6].

In the same year, J. Gillman (USA) and V. Despeignes (France) made attempts to treat malignant neoplasms with X-rays [7]. In the same period, several more cases of treatment of cancer patients with X-rays were described.

In 1897, L. Freund (Austria) published data on the use of fractionated radiotherapy for the treatment of extensive pigmented nevus in a child [8]. This message and this date are often referred to as the beginning of radiation therapy, which is currently widely used in foreign and Russian medical practice [9-11].

Radiation therapy received a significant impetus after H. Becquerel described natural radioactivity, followed by radium and polonium discovery by Maria and Pierre Curie [5, 12]. In 1902, radium was successfully used in Vienna for the treatment of pharyngeal cancer, and in 1904 in New York, radium tubes were implanted directly into the tumor [13, 14].

In the Russian Empire, the works of the founder of radiation therapy of malignant tumors, D. F. Reshetillo, were published: the "X-ray Treatment" manual in 1906 [15] and later, in 1910, the monograph "Radium and its use for the treatment of skin diseases, malignant neoplasms and certain diseases of internal organs", which can be considered the first fundamental work published on this topic.

In 1911, Cl. Regaud (France) conducted experiments on the sterilization of a ram with three fractions of ionizing radiation with an interval of 15 days between them. The work by L. Freund and Cl. Regaud's series of experiments formed the basis of fractionated distance radiation therapy [8,16]. In the same period, in 1910, in the USA, O. Pasteau and P. Degrais proposed a brachytherapy method by delivering a radium ampoule through the urethra to the prostate [17, 18].

Cl. Regaud, in collaboration with other scientists at the Radium Institute of Paris, developed various techniques for using radium sources, including as an alternative to surgical resections and for intracavitary therapy of cervical tumors and tumors with other localisations [19].

In the same institute in 1920, H. Coutard successfully used fractional remote radiation therapy to treat a variety of head and neck tumors. The dose rate guidelines were the reactions to radiation of the skin and mucous membranes. H. Coutard proposed collimation in the formation of beams and the use of metal filters for the formation of monochrome radiation [20].

An important contribution to the development of the phenomenon of the time-dose-effect relationship in radiation therapy was made by the work of E. Quimby and M. Strandquist (USA) [21, 22]. Within this framework, F. Ellis (England) proposed using the concept and formula of a nominal standard dose, which compared different treatment regimens based on the total dose, the number of fractions and the total treatment time [23]. The work performed in this direction in respect of individual types of tumors and normal tissues remains relevant to this day, as well as the linear quadratic model used, which takes into account the ratio of unreparable and reparable radiation damage for various cell types.

The energy of the first X-ray therapy installations did not exceed 100 keV, which limited their practical application. In 1913, W. Coolidge (USA) developed X-ray tubes

with energy of about 200 keV. Later, the therapy with their use was called orthovoltage. The improvement took place in the direction of monochromization of the beam. Filters and a method of multi-field irradiation were widely used to produce harder X-ray irradiation and improve the dose distribution. In the early 1920s, devices were developed which could rotate beams around the tumor, which significantly expanded the possibilities and efficiency of radiation therapy in oncology. Significant optimization of radiotherapy was achieved after the development of a "cascade" tube, which was installed at the Memorial Hospital in New York, by W. Coolidge in 1926 [24, 25].

After E. Lawrence and D. Sloan (USA) created a linear accelerator in 1930 and the betatron was invented by D. Kerst (USA) in 1940, and synchrotron was produced by V. I. Wexler (USSR) and E. McMillan (USA), radiation therapy received a new impulse for further improvement.

The progress of radiation therapy accelerated sharply in 1950s-1960s. As early as in 1956, H. Kaplan treated patients at Stanford University with 6 MeV photons [26]. In the early 1960s, compact linear accelerators with the possibility of rotational irradiation were created. However, the development of radiation therapy during this period was mainly associated with the use of remote gamma therapy with cobalt-60 (^{60}Co) sources [27].

The next stage in the development of radiation therapy (early 1990s) is associated with the widespread use of high-energy linear accelerators, normally up to 20 MeV [28, 29]. The introduction of this technique significantly improved the technical parameters of radiation therapy and its tolerance by patients.

Further optimization of radiation therapy is associated with the improvement of diagnostic equipment, the widespread use of computerized (CT), magnetic resonance (MRI), positron emission (PET) tomographs, which allowed to develop the systems of three-dimensional planning of conformal radiation therapy [30]. At the same time, improvements were made to some additional options accompanying radiation therapy: fixing devices, systems forming irradiation fields with a complex configuration, etc. have appeared. The use of optimized conformal planning systems for radiation therapy, which implies maximum dose uniformity in the target and minimal radiation load on the tissues surrounding the tumor, was a qualitatively new step in the improvement of radiation therapy.

In 1978, it became possible, for the first time, to vary the intensity of the beams over the area of exposure, which provided more opportunities for further optimization of the spatial distribution of the dose during the implementation of intensity-modulated radiation therapy (IMRT). In the recent years (2000–2018), it became possible to perform radiation therapy with due account for the changes in the position of the tumor during ir-

radiation, the so-called image-guided radiation therapy (IGRT) [31, 32]

The main sources of radiation in modern radiation therapy are still the photon and electron radiation of accelerators. Today, the most interesting area, from the scientific and practical points of view and the perspectives of the method development, is hadron therapy (proton, ion, neutron) [33]. Protons, carbon ions, due to the presence of the Bragg peak, have better possibilities than photon radiation for optimizing the spatial distribution of the dose, which is especially important when the tumor is close to structures which are critical in terms of radiosensitivity [34].

Ion and neutron radiation have numerous radiobiological advantages compared with sparsely ionizing (photon, electron) radiation as it makes it possible to target more effectively slow-growing, hypoxic, recurrent and radioresistant tumors.

R. Stone (USA), who began his research in 1938, six years after the discovery of neutrons, became a pioneer in the use of a fast neutron beam for the treatment of malignant neoplasms [35]. At that time, it was not known that the same absorbed doses of different types of radiation create significantly different effects. Traditional regimes of neutron irradiation of patients resulted in severe radiation damage, and after a series of failures in 1942, the use of neutron radiation was discontinued for a long time.

The revival of interest in neutron therapy occurred after the research performed by the radiologist M. Catterall (UK), who, in cooperation with the physicist D. Bewley (USA) in the 1970s in Hammersmith, performed clinical trials on a cyclotron with an energy of fast neutrons of 8 MeV; the outcome of this work was a manual on the use of fast neutrons in oncology therapy [36]. At the end of the twentieth century, neutron therapy began to develop in our country [37]. It was proved that it is most effective in the treatment of tumors that are resistant to sparsely ionizing radiation.

The first positive experience of neutron capture therapy (NCT) is associated with the name of H. Hatanaka (Japan), who received very promising results in the treatment of brain gliomas in 1968 [38].

R. Wilson (USA) reported the possibility of using protons for radiation therapy for the first time in an article published in 1946 [39], and proton therapy was carried out on accelerators in the Berkeley Radiation Laboratory in 1954 and at Uppsala University (Sweden) in 1957.

Practical development of radiation therapy applications began in Japan in 1994, in the city of Chiba. The first hospital in the world specialized in ionic therapy was created at the National Institute of Radiological Sciences (NIRS) [40].

It should be noted that the main factor restricting wider clinical use of these technologies was their high

cost and a limited number of specialized medical sources of hadrons.

The history of the development of radiation therapy in our country is inextricably linked with the history of this discipline in the rest of the world.

An important role in the development of Russian radiology was played by P. A. Herzen MORC [41], where, as it has been already mentioned, the first specialized subdivision of this type in Russia, the department of radiation therapy of oncological diseases, was opened in 1903. That was the beginning of the first official research in this field in Russia. The department was headed by D. F. Reshetillo, a prominent scientist who was at the beginning of the research on the possibilities of radiation therapy for the treatment of malignant tumors. Under the leadership of D. F. Reshetillo, as early as in the very first stages of the development of the radiation therapy method in oncology, the effectiveness of the fractional irradiation method was studied [15].

The radiologists of the institute were at the origin of the creation of the first gamma-therapeutic units with radium and radium-mesothorium sources and took an active part in the development and testing of new models of these devices.

In the 1920s-1930s, radiologists investigated the effectiveness of extensive fractional method of radiation therapy, various aspects of the overall effect of radiation on the patient's body during local irradiation of a tumor, dose distribution over time, the best options for combining radiation of different energies with different tumor localizations (M. P. Astrakhan, M. P. Domshlak, D. B. Nevo-rozhkin, S. R. Frenkel and others).

P. A. Herzen MORC began the development of methods of concomitant and combined radiation treatment of breast and cervix cancer, as well as cancer with other localisations (P. A. Herzen, M. P. Domshlak, L. M. Nisnevich, A. I. Savitsky, S. R. Frenkel).

In 1939, the first teleradium unit in the USSR was installed at the institute; the source used in the unit was 4 g of radium. In that time, there were no installations with a greater activity in other countries.

After the war, P. A. Herzen MORC resumed its research aimed at the development and enhancement of radiation therapy. Special attention was paid to the development of the concomitant method with the use of various sources, dose levels and volumes of exposure. The combination of close-focus radiotherapy and remote radiotherapy was tested for the treatment of cancer of the oral cavity, vulva, and cervix (Astrakhan, D. B., Volkova, M. A., Kiseleva, E. S.).

In the 1960s – 1970s, studies were conducted at the institute with the use of ^{198}Au , ^{90}Y , ^{32}P , ^{131}I , as well as testing of brachytherapy devices of AGAT series, ROKUS series remote radiation therapy devices, the first domestic

MICROTRONE type spiral accelerator (V. A. Kvasov, Yu. A. Rakhmanin and others.). A significant contribution to the solution of the problem of tumor radioresistance during radiation therapy was made by the research conducted by A. V. Boyko, S. L. Daryalova, A. V. Chernichenko.

In the years that followed, the areas of work of P. A. Herzen MORC in the field of radiation therapy were the following:

- the development and introduction into a wide clinical practice of a complex of automated methods and means of radical radiation therapy;
- development of radiomodifiers to increase the effectiveness of radiotherapy of malignant tumors;
- development and introduction into clinical practice of laser facilities for the treatment of cancer patients.

In 2014, P. A. Herzen MORC became a part of FSBI of the National Medical Radiology Research Center of the Ministry of Health of the Russian Federation, and Academician A. D. Caprin was appointed as the head of the institution.

The Roentgenologic and Radiologic Institute founded in St. Petersburg in 1918 (later known as the State Roentgenologic and Radiologic Institute and CRIRRI; and now called FSBI Russian Scientific Center of Radiology and Surgical Technologies named after Academician A. M. Granov) of the Ministry of Health of the Russian Federation was the world's first institution of this kind [42]. Later, it became a model for roentgen radiological institutes established in Kharkov (1920), Moscow (1924) and other cities of the USSR.

The founder of the world's first Roentgenologic and Radiologic Institute was professor M. I. Nemenov. In the beginning of the activities of the institute, some of its specialists were the most significant representatives of Russian physics, clinical and theoretical medicine: I. V. Kurchatov, N. N. Anichkov, V. G. Garshin, A. A. Zavarzin, N. S. Kupalov, E. S. London, G. V. Mor, G. A. Nadson, V. A. Oppel, N. N. Petrov, P. V. Troitsky, N. Ya. Chistovich and others, whose works laid the foundations of Russian X-ray radiology.

For the first time in our country, treatment methods based on the use of X-rays and radium for various tumors and non-neoplastic diseases were developed in the Roentgenology and Radiology Institute, and in 1937 the first Russian manual on the clinical use of radium for therapeutic purposes was published.

In this period, as well as later on, the achievements of the Institute in the field of radiation therapy were also associated with the names of I. N. Grekov, F. S. Grossmann, L. I. Korytova, B. A. Konov, N. N. Petrov, A. S. Strashinin, L. P. Simbirtseva, V. A. Shaak, A. M. Yugenbyrg and many others.

In 1966, the medical and biological department was created at the phasotron of A. F. Ioffe Physicotechni-

cal Institute for the purpose of developing methods of hadron (proton) therapy of tumor and non-tumor diseases that cannot be cured with traditional methods of radiation therapy. The successful introduction of this method into clinical is associated with the name of Professor B. A. Konov.

As mentioned above, in January 1924, by the decision of the Council of People's Commissars, Roentgen Institute was established (later, Moscow Research Institute of Roentgenology and Radiology; Moscow Research Institute of Diagnostics and Surgery), which is now the Federal State Institution «Russian Research Center of Roentgenology and Radiology» of the Ministry of Health of the Russian Federation (RRCRR) [43].

The first director of the institute was academician P. P. Lazarev, the founder of domestic biophysics, a pioneer in the study of the biological effects of ionizing radiation and the creator of the world's first rotational x-ray machines.

Since the establishment of the institution, a significant place in its work has belonged to the issues of improving radiation therapy for tumor and non-tumor diseases, including gynecological diseases. (Ivanitskaya, E.P., Karlin, M.I., Kolosov, M.A., Shaposhnikova, N.E., and others), thoracic and abdominal diseases (Kornev, N.I., Panshin, G.A., Pavlov, A.S., Podlyaschuk, L.D., Pereslegin, I.A., Ruderman, A.I., Sarkisyan, Y. K., Tsybulsky, I. B., and others).

Much attention was paid to the development of rational methods of radiation therapy, evaluation of the effectiveness of radiation treatment and the development of measures to prevent complications after radiation therapy (Panshin, G.A., Titova, V.A., Khmelevsky, E.V. and others).

The Institute is one of the pioneers in the development of modern methods of combined and complex treatment of malignant tumors of the main localizations, which have a significant economic effect.

At the Research Institute of Oncology opened on the basis of I. I. Mechnikov Leningrad Multidisciplinary Hospital, now FSBI N. N. Petrov National Medical Research Center of Oncology of the Ministry of Health of Russia (N. N. Petrov NMRC for Oncology), [44] radiation therapy of malignant tumors has been used since its foundation in 1927, when professor N.N. Petrov ordered radium preparations and needles to be made in Paris.

During the establishment of the institute, radiation treatment was carried out by the employees of one X-ray department which had two, and later three, radiotherapy devices.

In 1945, a special radium laboratory was organized at the institute, which was headed by N. D. Perumov. Under her leadership, a method of photodosimetry of radium gamma rays was developed and the suitability of this

method for photodosimetry of ^{60}Co rays was tested. This technique made it possible to measure doses and investigate the homogeneity of radiation in any planes of the irradiated tissue volume.

In 1967, a high-energy laboratory was opened, with powerful megavolt installations for remote radiation therapy; its head was A.P. Kozlov. The laboratory has developed computer programs for optimal dosimetry planning of megavolt radiotherapy, which are used in all Russian-made radiotherapy units (gamma devices like ROKUS, Agat C, Agat R, accelerators of B5M-25, LUE-25 types, etc., AGAT-B, AGAT-VU devices for intracavitary radiation).

In the late 1960s, the personnel of the former Radium Laboratory worked in the Radiology Department: L. E. Pakulina, N. D. Perumova, A. A. Stankevich, V. M. Uglova and others. The main scientific direction of the radiological department was the improvement and development of remote and contact radiation therapy for malignant tumors. In 1965–1966, a device for autoloading intracavitary gamma therapy was developed.

Currently, the department has a 40-bed in-patient ward, where intensive research is successfully conducted aimed at improving the treatment of common tumors of the esophagus, trachea and bronchi with the use of the methods of endoscopic surgery, argon plasma coagulation and intraluminal brachytherapy. A new medical technology has been created for the treatment of locally advanced malignant tumors of the central bronchi and trachea, and various types of intensive, large-scale preoperative irradiation in breast, lung, esophagus, cardiac stomach and rectum cancers are undergoing intensive testing.

Due to the creation of new specialized institutes and departments and oncological dispensaries in the USSR, there was a rapid development of technical, radiobiological and methodological aspects of radiation therapy.

Significant contribution to the development of radiation therapy in our country in the previous and the subsequent years was made by N. N. Azhigaliev, B.M. Aliev, S. B. Balmukhanov, L. M. Goldstein, Ya. G. Dillon, M. P. Domshlak, K. I. Zholkiver, A. N. Kishkovsky, A. V. Kozlova, G. V. Muravskaya, M.P. Pobedinsky, A.D. Podliashchuk, A. S. Pavlov, I. A. Pereslegin, A. I. Ruderman, S. F. Frenkel and many other scientists.

Successes in the development of domestic radiotherapy are also associated with the activities of the FSBI N.N. Blokhin National Medical Research Center of Oncology of the Ministry of Health of the Russian Federation [45, 46].

In 1959, it was decided to build the Institute of Experimental and Clinical Oncology of the Academy of Medical Sciences of the USSR (IE&CO of MSA of the USSR), which later became N.N. Blokhin Russian Oncological Research Center (N.N. Blokhin RORC). The first head of the entire radiotherapy section was A. I. Ruderman, and the spe-

cialists who worked under his leadership included B. M. Aliyev, E. M. Ivanova, M. M. Nevinskaya, M. S. Starichikov and others.

An important contribution to the successful development of radiation therapy in N. N. Blokhin RORC was the creation of the Department of Medical Physics and the Radiobiology Laboratory headed by professor S. P. Yarmonenko.

From 1980 to 1995, the Department of Clinical Radiation Therapy was headed by Professor B. M. Aliyev. His students became heads of radiotherapy departments in various parts of the USSR: in N. N. Blokhin RORC, S. I. Tkachev, T. V. Yuriev, in Lithuania, E. A. Aleknavichus, in Kyrgyzstan, R. A. Aralbayev.

From 1982 to 2001, the Radiation Therapy Department of N. N. Blokhin RORC was headed by Professor G. V. Goldobenko, the first President of the Russian Association of Therapeutic Radiation Oncologists (RATRO), an enthusiastic and talented scientist, an excellent doctor and teacher. Under his leadership, research in the field of optimization of dose fractionation modes was greatly expanded, as well as research related to the use of radioprotectors (hypoxic gas mixtures) and radiosensitizers (local hyperthermia, artificial hyperglycemia, and cryo-radiation therapy), and much broader opportunities were provided for the use of radiation therapy in pediatric oncology.

In 2001, professor S. I. Tkachev was appointed to the position of the head of the department.

The department of radiation therapy included the section of proton radiation therapy headed by professor A. I. Ruderman (1976–1984), where B.V. Astrakhan, G. D. Monzul, G. V. Makarova and others worked. The core assets of the department were the technical proton accelerators of A. I. Alikhanov Institute of Theoretical and Experimental Physics in Moscow and the Joint Institute for Nuclear Research in Dubna, Moscow Region, where proton radiation therapy was administered to more than 3,000 cancer patients.

As early as in 2001, the department of radiation therapy of N. N. Blokhin RORC became the first center in Russia to use 3D volumetric planning and conformal (3D CRT) radiation therapy and its more advanced options: intensity-modulated radiation therapy (IMRT), Volumetric Intensity Modulated Arc Therapy (VIMAT), image-guided radiation therapy (IGRT), radiation therapy with tumor movement control, stereotactic radiosurgery (SRS) and stereotactic radiotherapy (SRT). The study of the effectiveness of the use of radioprotectors and radiosensitizers continued, and the use of various types of the sequences of radiation and pharmaceutical treatment of cancer was enhanced and expanded.

The department of radiosurgery, established in 1980 and led by N.S. Androsoy until 1995, and then by M. I.

Nechushkin, improved the methods of contact and concomitant radiation therapy in gynecological oncology (O. A. Kravets), oncoproctology (I. A. Gladilina), oncurology (A. V. Petrovsky), hematology (E. S. Makarov).

Since 2003, ESTRO educational schools for radiologists from Russia and the CIS countries have been held regularly on the basis of the Department of Radiotherapy of N.N. Blokhin RORC.

Since 2006, the Department of Radiotherapy and the Association of Medical Physicists of Russia (whose president is professor V. A. Kostylev) have organized and conducted educational courses for radiologists and medical physicists in Russia and the CIS countries. V. A. Kostylev and G. V. Goldobenko also organized the Russian Association of Therapeutic Radiation Oncologists (RATRO) and led it in the early stages of its formation. In the following years, RATRO presidents were Yu. S. Mardynsky, A. V. Chernichenko, and now it is led by A. D. Caprin.

Well-known scientists S. B. Aliyev, T. N. Borisova, S. M. Ivanov, S. V. Medvedev, O.P. Trofimova work in the radiation department. In 2015, the department of radiation therapy was headed by A.V. Nazarenko, and it continued to develop and improve the use of radiotherapy in the complex treatment of cancer patients.

An active part in the development of new methods of radiation, combination and complex therapy of malignant neoplasms and the improvement of existing ones is taken by oncology institutes and large oncological dispensaries in Arkhangelsk, Volgograd, Irkutsk, Kazan, Rostov-on-Don, Tomsk, Ufa, Chelyabinsk, Chita, etc.

As it is well-known, the foundation of radiation therapy is physical/technical, radiobiological and medical knowledge. Therefore, the main specialists in this field are, respectively, medical physicists, radiobiologists, radiotherapists, as well as representatives of engineering and technical field, without whose participation the creation and operation of modern radiotherapy equipment would be unthinkable.

When we recall the scientists and engineers who developed and improved the equipment for radiation therapy, we have to mention, first of all, three main organizations: Leningrad Research Institute of Electrophysical Equipment named after D.V. Efremov, now AO RIEPE (creation and production of accelerator technology and LUE-15, LUER 20, LUER 20M), Snezhin All-Union Research Institute of Instrument Engineering, now FSUE Russian Federal Nuclear Center E. I. Zababakhin All-Russian Scientific Research Institute of Technical Physics (creation and production of gamma-therapeutic equipment based on ^{60}Co and other radioactive elements), and RPA Agat (production of Rokus gamma-therapeutic units and Microtron accelerator).

Well-known researchers who worked in these institutions made a significant contribution to the development and production of Russian radiation therapy units. They include V. M. Aleshin, E. A. Zhukovsky, S.P. Kapitsa, V. A. Komar, A.R. Mirzoyan, A.F. Rimman, A. G. Sulkin, A. S. Shtan, M. V. Kheteev and many others.

Modern radiation therapy is also impossible without medical physicists. The contribution of Soviet and Russian physicists to ensuring the quality of radiation therapy in the 2nd half of the twentieth century is in no way inferior to the achievements of their American and European colleagues. This applies primarily to the emergence and implementation of mathematical methods for optimizing the distribution of the absorbed dose, multi-leaf collimation, matrix detectors for analyzing the dose distribution of photon and electron radiation, conformal radiation therapy, physico-technical substantiation and improvement of hadron (proton and neutron) therapy [47].

A significant contribution to the development of Soviet/Russian medical physics was made by S. M. Vatinitsky, I. A. Ermakov, R. V. Sinitsyn, A. M. Chervyakov, O. A. Shtukovsky (TsRRRI); A. I. Krongauz, R. S. Milstein, E. G. Chikirdin (MRRRI); E. B. Bozhanov, A. P. Kozlov (N. N. Petrov Institute of Oncology); V. A. Kvasov (P. A. Herzen Research Institute); O. N. Denisenko (MRRC, Obninsk); M. A. Weinberg, V.A. Kostylev, N. A. Lutova, N. N. Lebedenko, T. G. Ratner (N. N. Blokhin RORC); I. G. Tarutin, A. G. Strakh (N. N. Alexandrov Institute of Oncology, Belarus); B. K. Nikishin (KRRROI, Ukraine) and many others.

It was these specialists who suggested most of the technical solutions and provided their implementation, and their developments corresponded to the advanced trends in the development of therapeutic techniques. Unfortunately, for objective reasons, Russian manufacturers failed to maintain a high level and scope of radiotherapy equipment production.

We are currently witnessing a revival of attention to the Russian medical instrument-making industry and a rapidly reviving interest in the use of ionizing and non-ionizing radiation in various branches of science and technology, and especially in medicine.

The unique experience of cooperation of A. F. Tsyb MRRC and AO Research Institute for Technical Physics with leading physico-technical institutions of Russia served as the basis for the implementation of a pilot project on the creation and conduct of clinical trials of the first sample of a domestic specialized medical import-substituting radiotherapy complex based on innovative equipment, 6 MeV accelerator and a cone-beam tomograph, in Obninsk.

The work is implemented in the framework of the agreement between the Ministry of Education and Science of the Russian Federation and AO Research Institute of Technical Physics and Automation on the provision

of a subsidy dated 03.10.2017 No. 14.582.21.0011 "The Creation and Transfer for Clinical Trials of a Sample of an Import-Substituting Radiotherapy Complex Based on Innovative Equipment (6 MeV accelerator and a cone-beam tomograph)". The unique identifier of the agreement is RFMEFI58217X0011.

The results of the work of A. F. Tsyb MRRC, a branch of the NMRC of Radiology of the Ministry of Health of the Russian Federation and AO Research Institute of Technical Physics and Automation confirm the relevance and practical significance of the research conducted in the institution. They are the evidence of the effective use of the synthesis of fundamental and applied research for the development of new medical radiological technologies and their introduction into medical practice.

The Institute of Medical Radiology of the Academy of Medical Sciences of the USSR, the largest institute of radiological profile, was established in Obninsk in 1962, and, with its powerful experimental base and clinic, it became the country's leading institution for the development of high-tech medical radiological methods for diagnosing and treating patients and the basic institution for the research on the problems of Medical Radiology and Radiation Medicine. Its founder and first director was academician G. A. Zedgenidze [48, 49]. Today it is A. F. Tsyb Medical Radiological Research Center (director: professor of RAS S. A. Ivanov), which since 2014 has been a branch of FSBI «National Medical Research Center of Radiology» of the Ministry of Health of the Russian Federation (Director General: Academician of RAS A. D. Kaprin), including also P. A. Herzen Moscow Research Institute of Oncology. (director: Academician of RAS A. D. Kaprin) and N. A. Lopatkin Research Institute of Urology and Interventional Radiology (director: corr. member of RAS O. I. Apolikhin).

The inclusion of the MRRC into the united Center, the Federal Research Center for Radiology of the Ministry of Health of the Russian Federation, provided broader opportunities for introducing the results of the center's own basic research into clinical practice, opening up new ways to successfully solve current development problems and create high-quality practical applications of therapeutic radiology [50].

Continuing research in the field of medical radiology, radiation biology and radiation epidemiology will undoubtedly contribute to the reinforcement of national security in the field of public health and improve the health of Russian citizens.

Part II of this article will present a more detailed review of the achievements of the A.F. Tsyb MRRC and its place in the history of the development of radiation therapy.

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