

# HISTORY OF THE DEVELOPMENT OF RADIOTHERAPY AS AN EXACT SCIENCE

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## Abstract

The development of radiation therapy technologies in oncology from its origins to the present day is associated with the desire to ensure high accuracy of dose delivery to the tumor for receipt the greatest effect with minimal toxicity. The development of radiobiology has determined the possibilities of choosing optimal irradiation schemes and modes, taking into account the radiobiological characteristics of neoplasms. Achievements modern radiotherapy - This result perennial works, research and discoveries, result implementations brave ideas several generations scientists and engineers, physicists and doctors. IN article reflected most significant events in the history of the use of various types of ionizing radiation that became fundamental For formations modern remote And contact radiation therapy.

**Keywords:** Radiotherapy, linear accelerator, brachytherapy, dose fractionation schedules.

## Introduction

History radiotherapy started 8 November 1895 g. V this day William Conrad X-ray exposed mysterious X-rays, outgoing from the cathode ray tube. Immediately preceding to study properties these rays, V.K. X-ray already 28 December 1895 G. did first message "ABOUT new view rays" at a meeting of the Physical-Medical Society of Würzburg. Scientist, became V overnight worldwide famous, refused the patent and the greatest discovery of the century became the property of all mankind. All in all, 7 months later 5 magazine "Medical Record» In 1986, Victor Despaigne, a French physician, reported about the first successful experience of irradiating a patient in France With cancer stomach. Other sources they attribute championship V treatment cancer X-rays medical student from Chicago Emil Grubbe. The subsequent history of radiotherapy is closely linked to the history of particle physics. In 1896, Antoine Henri Becquerel, professor physicists V Paris, discovers the phenomenon of natural radioactivity of uranium salts, and in 1898 the spouses Marie Sklodowska-Curie and Pierre Curie reported a new radioactive element, radium, became first radioactive element used to treat cancer in the early 20th century. There was still a long road of trial and error, victories and defeats, before how radiotherapy turned into from empirical method V accurate science. The history of radiation therapy is described in numerous publications, But With positions today's days It is important to trace how the basic principles emerged and technologies of modern high-precision and high-tech radiotherapy.



**Evolution technologies ray therapy**

Tube Crooks, applied V.K. X-ray for physical research, was improved by the American physicist William Coolidge V 1913 g. Later, the Coolidge tube with a "hot" cathode found wide application V treatment And diagnostics until the 1950s. But the low energy of the photons of the first X-ray installations, limiting the depth of their penetration into tissues, did not allow for effective irradiate tumors internal localizations. Efforts undertaken in the early 20th century to increase the energy of X-rays to 200 keV, and later to 700 keV and more, multi-field irradiation and grid filters allowed improve distribution doses, but did not solve the problem of precise dose delivery to the tumor in principle. At the same time, the desire to increase the energy of photons led to the emergence of a new principle of particle acceleration using a high-frequency alternating potential, proposed V 1929 G. Ernest Lawrence V Californian university V Berkeley, What made it possible to test the first linear accelerator already in 1930. Then followed invention new generations of cyclic accelerators electrons, based on induction in principle acceleration. IN 1940 G. Donald Kerst builds the first reliably functioning betatron, Soviet physicist Vladimir Wexler V USSR and Edwin Macmillan V Los Alamos national laboratories USA invent synchrotron. Betatrons were the first accelerators adapted For medical goals, But significant dimensions and heavy weight of the installations, as well as low intensity radiation steel reason Togo, what's wrong development technologies linear acceleration Betatrons were superseded by linear electron accelerators (LEAs). Microwave technology and principle running waves, applied V radars in time Second World wars V Great Britain, were used V linear accelerators, and the first one LUE With energy 8 MeV was installed at Hammersmith Hospital (London) in 1953. In 1954, a linear accelerator with a power of 6 MeV; To 1989 G. V USA was functioning already around 1000 LUE. Improvement LUE determined all subsequent progress in remote irradiation, but it took several decades before how succeeded create modern high-tech generation installations. More V at the end 1940 g. group scientists Stanford university was formed company "Varian Associates». Among founders companies were brothers Russell And Sigurd Variants are the inventors of the klystron, a microwave generator, the main element of modern medical LUE [9]. WITH end 1960s gg. company "Varian" established the production of medical LUEs, which gradually replaced gamma-therapeutic devices. Gamma therapy originated in the early 20th century, when the isotope radium-226 was first used for so-called "telerradium therapy," but only with the production of an artificial isotope Co-60, which emits photons with average energy 1.26 MeV, it became possible to effectively irradiate tumors internal localizations With limitation doses in the skin. The first gamma-therapeutic device with Co-60 was created V Canada V 1952 G. The relative cheapness of cobalt units, the simplicity of the design, and the fundamental advantages over kilovoltage X-ray therapy contributed to the fact that gamma therapy with Co-60 became the most widely used method of remote irradiation in oncology for several decades, filling the historical gap between X-ray therapy and conformal RT with high-energy photons LUE. New era high precision ray therapy began with equipping accelerators with a multi-leaf collimator (MLK). Today difficult say, who first proposed using multiple, separately controlled plates to collimate the beam, capable of regardless move And forming homogeneous volume irradiation, corresponding to the shape and size of the tumor, but further improvement of the MLC allowed the implementation of the most precise RT technologies. The development of radiation therapy is directly related to the emergence and



improvement of such visualization methods as computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET). CT with volumetric visualization, which became available in 1982, in combination with the MLC provided qualitative transition from two-dimensional to 3D conformal radiation therapy. Rapidly developing computer technologies have made it possible to effectively control radiation parameters to create an optimal dose distribution and ensure protection of normal tissues.

More one direction high precision LT is based on the change in radiation intensity over check movements petals collimator V beam. Swedish medical physicist Anders Bråne in 1982 G. became pioneer modulated by intensity ray therapy (Intensity Modulated Radiation Therapy (IMRT), but to implement this idea And to provide wide availability technology succeeded only To the end past centuries. Today, intensity modulated irradiation in static (IMRT) or rotary variant (Volumetric modulated arc therapy, VMAT) has reached a high level of sophistication and has become the most widely used technology LT V treatment tumors various localizations. Systems visualizations provisions of the patient and the tumor during the irradiation session, based on scanning with a conical kilovolt or megavolt beam, breathing control systems during irradiation of formations that move with breathing have become a mandatory component of modern accelerators complexes.

### Story stereotactic radiation therapy

The search for ever more precise technologies has accompanied the entire history of radiation therapy. The founders of radiosurgery - non-invasive, But comparable by efficiency And accuracy With operation LT technology, - steel neurosurgeons, first appreciated the possibilities of high-dose and high-precision irradiation of brain formations. In 1951, Lars Lexell, Swedish professor neurosurgery, proposed the principle of irradiation of brain tumors brain With high precision With using developed them same stereotactic frame, guide radiation X-ray tubes, and introduced the concept of stereotactic radiosurgery (SRS). The principle of precise energy delivery was based on achieving a maximum dose with a high gradient at the periphery by crossing a large number of radiation beams at the isocenter; while precise positioning of the patient's head And, respectively, irradiated neoplasms relatively source radiation was provided stereotactic frame. This idea was implemented Lexell together With physicist Larsson on basis Co-60, because energy photons of the X-ray tube was too small. The first model of the Gamma Knife had 179 Co-60 sources and was installed in 1967 at Sophiahemmet Hospital V Stockholm.

In 1989 G. neurosurgeon from Buenos Aires Osvaldo Betti published results his own experience conducting radiosurgery on accelerator at 66 patients with arteriovenous malformations. On whether linear accelerators instead of stereotactic frames were used various systems of X-ray navigation For visual control. Such The approach has allowed us to expand the capabilities of radiosurgery for irradiation extracranial neoplasms And conduct some sessions hypofractional stereo taxi LT. American neurosurgeon John Adler proposed stereotactic irradiation in 1990 compact accelerator With energy 6 MeV installed on robotic hand, directing radiant energy in any direction, to any part of the body under continuous control of the position tumors two X-ray cameras. This technology was called "CyberKnife". In 2002, R. Timmerman and his co-authors first used stereotaxic ablative irradiation early lung cancer, which later became an alternative to surgery at



inoperable patients. Striving for uniformity in terminology among specialists, B.V. Lou With co-authors suggested V 2011 G. the concept of stereotactic ablative radiotherapy (Stereotactic ablative radiotherapy, SABR), including high-dose irradiation intracranial pathologies (stereotactic radiosurgery, SRS) and stereotactic irradiation extracranial formations (stereotactic body radiotherapy, SBRT). For latest 20 years together With technical improvement endured significant changes And efficiency LT. SABR with a high dose per fraction allows for biological effect, unattainable at fractional, fractionally extended irradiation, thanks to which stereotactic technologies find All wider application V oncology. Together with the aim of achieving a high dose gradient at the target edge at all high precision photonic technologies irradiation accompanied by increase in volume fabrics, receiving small doses, What carries in yourself risks occurrence second tumors And other late complications. These consequences more remains to be assessed as experience accumulates.

### Story brachytherapy

The beginning of contact irradiation or brachytherapy was laid by the spouses Marie and Pierre Curie, who transmitted V 1901 test tube With radium V St. Louis Hospital (Paris, France). Radium was initially used for contact irradiation of skin lesions. One of the first successful irradiations of two patients with basal cell skin cancer was performed in St. Petersburg in 1903. 1903 G. American doctor Margaret Cleave was the first to use 700 mg of radium bromide placed in a test tube for contact irradiation of a patient with inoperable cancer necks uterus. IN 1909 g. on congress urologists V Paris for the first time reported the treatment of prostate cancer with radium sealed in V tube And implantable through urethra. In first half XX V. Ra-226, open the Curies, was the only radioactive isotope for contact irradiation, but a number of physical properties this isotope made it difficult his practical application. Due to the low specific activity Ra-226 irradiation sessions were long, and V connections With accompanying alpha radiation Ensuring security required significant efforts. After discoveries V 1934 G. spouses Irene Joliot- Curie And Frederick Joliot phenomena artificial radioactivity in the history of radiation therapy began a new period. Was received whole row artificial isotopes, application which For remote and contact irradiation proved more successful. Thus, in the 1950s, artificial radiation replaced radium . isotopes Co-60, Cs-137 And Ir-192, used in modern brachytherapy systems. A revolutionary event in the history of brachytherapy was the afterloading\* technology with the sequential introduction of hollow endostats and a radiation source into the tumor or lumen of the affected organ, proposed in 1960 by W.K. Henschke and co-authors. Initially, the radioactive source was introduced into an installed and secured V tumors endostat manually, But already V 1960s installations for automatic introduction of a radiation source appeared . The technology of automated afterloading (remote afterloading) eliminated irradiation medical staff, A Volumetric CT or MRI visualization of endostat position and software dosimetric planning ensure conformal dose distribution in the target.

### Story terms And concepts

In 1922, at the International Oncology Congress in Paris, RT was first identified as a new independent medical clinical discipline. In 1925, the International Congress of Radiology established the



International Commission on Radiation units and measurements (ICRE). In 1928 G. on Second international congress radiologists in Stockholm officially adopted a unit of measurement for ionizing radiation in the air - X-ray (R), What gave opportunity quantify radiation exposure. In 1953, the ICRU replaced the Roentgen unit of dose measurement with the Absorbed Depth Dose, or “Rad” (radiation absorbed dose, rad), which was used until 1985. Subsequently, the Gray (Gy), equivalent to 100 rads and named after the English physicist Lewis Gray, became the main system unit of absorbed depth dose measurement.

Development technologies radiotherapy required the unification of efforts of specialists from different fields And different countries, What allowed To the end XX c. to create conditions for conducting multicenter randomized studies. The era of evidence-based medicine began, and radiotherapy was recognized as an exact science.

### **Evolution ideas about fractionation doses in stories radiobiology**

The concept of radiation dose fractionation has fundamental meaning For the magnitude of the dose and its distribution over time are closely related to the technologies of delivery of radiation energy, have undergone significant changes over the course of their development. At the beginning of the last century, treatment typically consisted of a single, prolonged exposure to radiation from a cathode ray tube or radium placed in a test tube. Such irradiation was accompanied by severe skin damage, and the effectiveness its dose remained low. In 1911, Claude Regault, a French physician and biologist, discovered that skin damage could be avoided if the dose was administered not in a single dose but in several sessions over several days. Henry Coutard, who worked under him at the Paris Radium Institute in the 1920s, gg., developed concept fractional irradiation lasting several weeks, fractional irradiation at treatment tumors are you naked And necks And in every possible way contributed dissemination of this concepts among international scientific community. In 1934 G. Henry Coutard suggested fractionation scheme With dose 200 X-ray for fraction c 5 fractions 5 week. Such conventional fractionation With summing up 25–35 fractions for 5–7 weeks remains to real time basis radical radial treatments various neoplasms, allowing to achieve the greatest damage tumors With low risk complications from healthy tissues.

Early clinical observations demonstrated advantage fractional irradiation over a single one, but it was only in 1975 that H.R. Withers formulated "rule 4R» (reoxygenation, redistribution, repair, repopulation), which has become the cornerstone of the rationale for the biological advantage of fractional irradiation. At the same time, fractional-extended irradiation is prolonged in time, which can reduce the effectiveness of treatment due to the radioresistance of surviving tumor cells. The latter circumstance predetermined interest in the use of hypofractionation regimens with enlarged one-time in doses, became possible with the advent of modern technologies of intensity modulated irradiation and stereotactic RT, providing a high level of protection adjacent To tumors critical structures and leveling risk complications at increasing the dose.

### **Conclusion**

Today radiotherapy has V in his own arsenal various types of radiation, has modern technologies that provide various methods of precise dose delivery to the tumor. The success of modern radiotherapy was predetermined by the efforts of many specialists over decades. Story radiotherapy



became example of how ideas, expressed more V beginning past centuries, succeeded implement Today V result technical progress and development of radiobiology. IN one article difficult embrace All aspects ray therapy. Radionuclide therapy - analogue drug therapy, - since its inception in 1920s gg. becomes All more directed thanks to new isotopes and radiopharmaceuticals. Its rich story There is And at methods radiomodifications, among which the main place is occupied by systemic therapy. Simultaneous chemoradiotherapy has become the standard treatment for tumors of a number of localizations , there are Prospects combinations ray therapy With targeted therapy and immunotherapy.

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