APPLICATION OF THE INR PROTON LINAC FOR DEVELOPMENT OF METHODS OF RADIOTHERAPY AND NUCLEAR MEDICINE

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The review of the results of researches in the field of proton therapy and contact radiotherapy (high-dose-rate brachytherapy) is presented. Medical beam formation elements for a wide range of proton energies were calculated, elaborated and tested with proton beams. These therapeutic beams cover most sizes and localizations of tumors. Researches of a new source for high-dose-rate brachytherapy with Yb-169 were carried out. This source has several important advantages compared to conventional sources. Experiments of activation of the new source at the INR Neutron complex were performed and therapeutic properties of the new source were confirmed. We also present in this paper the current status of the new target assembly for producing of some PET isotopes with 20 MeV protons.

PACS: 87.56

1. FORMATION OF THERAPEUTIC PROTON BEAM

The present results are the further development of earlier results of the Laboratory of medical physics (LMP) of INR. The parameters of double scattering system were calculated with the help of the program NEU4, based on multiple scattering model for Highland Gauss distribution. As input data we used measured Bragg distributions. Design of the beam formation system is shown on Fig. 1. The Al membrane thickness is 1.045 mm, the graphite collimator has the diameter of 100 mm and the thickness of 180 mm.

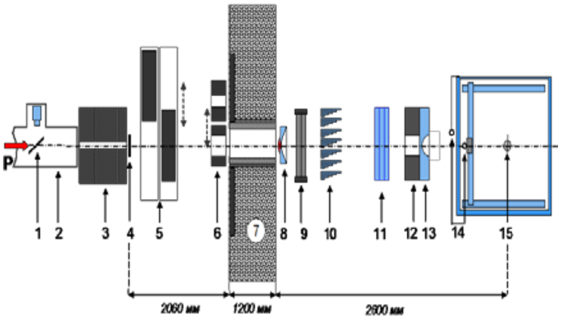


Fig. 1. Formation system of medical proton beam. 1 – luminofore with TV-camera; 2 – proton channel; 3 – graphite collimator; 4 – the primary scatterer (S1); 5 – beam stop; 6 – beam aperture collimators of 40 and 70 mm; 7 – shielding; 8 – secondary scatterer (S2); 9 – ion chamber; 10 – ridge filter; 11 – energy degrader; 12 – individual collimator; 13 – bolus; 14 – ion chambers in a water phantom; 15 – system isocenter

For the scatterer S1 we used copper foils of 400 µm at 209 MeV and of 100 µm at 160 MeV. At 127 MeV the aluminum membrane works well for S1. The room shielding thickness is 120 cm. The scatterer S2, containing copper foil with a shaped plexiglass retarder, allows to achieve the same energy loss of protons across the beam cross section. Then the proton beam passes through the plane-parallel ionization chamber monitor model 786 (PTW Freiburg), which performs the function of measuring the intensity of the generated beam and the reference monitor units. Afterwards, the beam passes through the ridge filter, individual collimator and individual bolus intended for the final formation of the beam before it is fed to the phantom (the patient).

Measurements of the absorbed dose in water were executed by means of the Wellhofer WP600 analyzer, consisting of the water phantom with the dimensions 600×600×300 mm, two ionization chambers: the reference IC-10 of 0.14 cm^3 and the field plane-parallel Scanditronix PPC05 chamber of 0.05 cm^3, system of its three-dimensional movement, the two-channel electrometer for measurement of ionization current of chambers and the operating computer.

The field camera was installed in the position for scanning of power of the dose in various points in the water phantom, and the reference was fixed on a lateral wall of the phantom within a beam area. The relation of signals of the field and the reference chamber was registered, compensating essential instability of the beam intensity. The axis of the ionization camera was directed parallel to a beam line, scanning of depth doses and profiles was carried out relative to the isocenter. Detector positioning in the phantom was carried out with an accuracy of 0.1 mm, movement speed was 7 mm/sec. Prior to the measurements of the beam generated by a system of double scattering, we performed the beam adjustment and measurement without the scatters S1 and S2 both for 160 and for 209 MeV. For example, Fig. 2 shows the configuration of the beam profiles for energy level of 160 MeV.

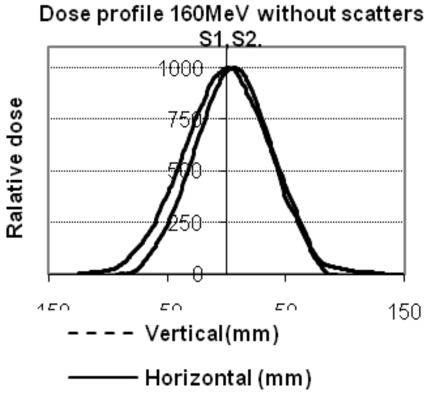


Fig. 2. The beam profiles without scatters S1, S2

After setting up the beam, the scatters S1, S2 were introduced and profiles and depth dose distribution were measured. Figs. 3, 4 show the vertical and horizontal beam profiles at different depths in the water phantom for energy levels of 160 and 209 MeV.

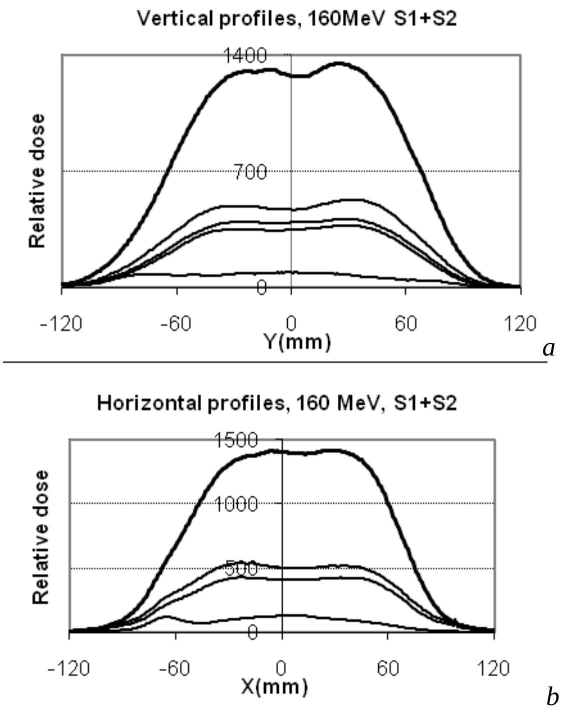


Fig. 3. Vertical (a) and horizontal (b) profiles of the proton beam 160 MeV with scatterers S1, S2

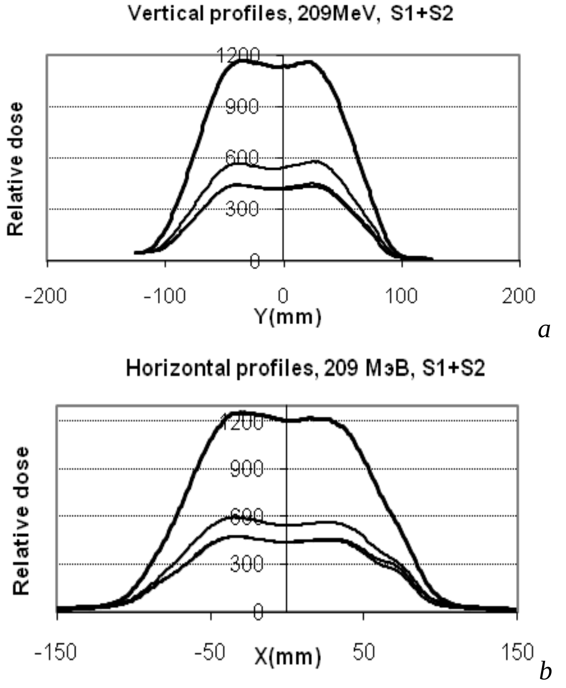


Fig. 4. Vertical(a) and horizontal(b) profiles of the proton beam 209 MeV with scatterers S1, S2

Unevenness of plateau profiles ranged from 3% to 8.5% (between the maximum and minimum values on the plateau). The resulting profiles can be considered acceptable in view of the further impact of incremental forming tool leading to its alignment.

Then we measured the depth dose distribution for 160 MeV (Fig. 5) and for 209 MeV (Fig. 6) proton energy.

The measured Bragg curves are in a good agreement with each other, the average spread of corresponding values (standard deviation) is in the range 1…2%. For proton energy of 160 MeV, the average value range of the protons in the approximation of continuous deceleration equals to 156.2 ± 0.07 mm. According to the ICRU49, the average energy of the beam is equal to 149.25 MeV. The energy loss of protons achieved in the secondary scatter-moderator was 4.93 MeV.

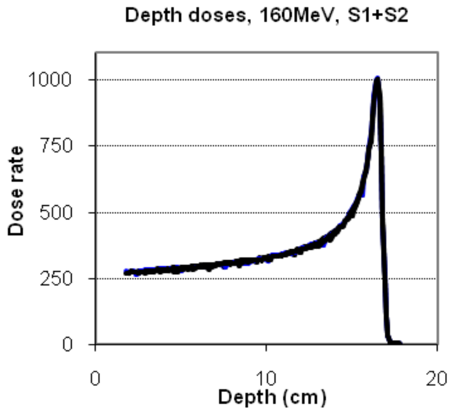


Fig. 5. Depth-dose distribution on the beam axis in the water phantom after the installation of the S1+S2 scatterers, E = 160 MeV

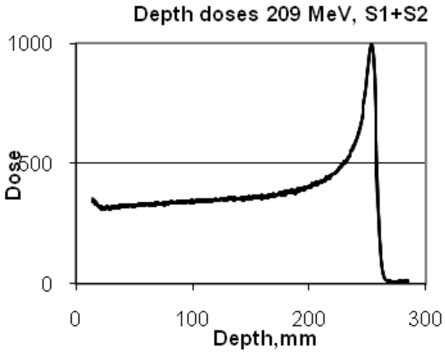


Fig. 6. Depth-dose distribution on the beam axis in the water phantom after the installation of the S1+S2 scatterers, E = 209 MeV

For 209 MeV energy, the range of protons after passage of the double scattering was equal to 256.2 ± 0.1 mm. According to NIST this corresponds to the energy 198.6 MeV. Thus, the loss of energy after passing through the secondary scatter S2 was 7.5 MeV.

The next step in the set up of a therapeutic proton beam was the formation of a plateau of the depth dose distributions (SOBP).

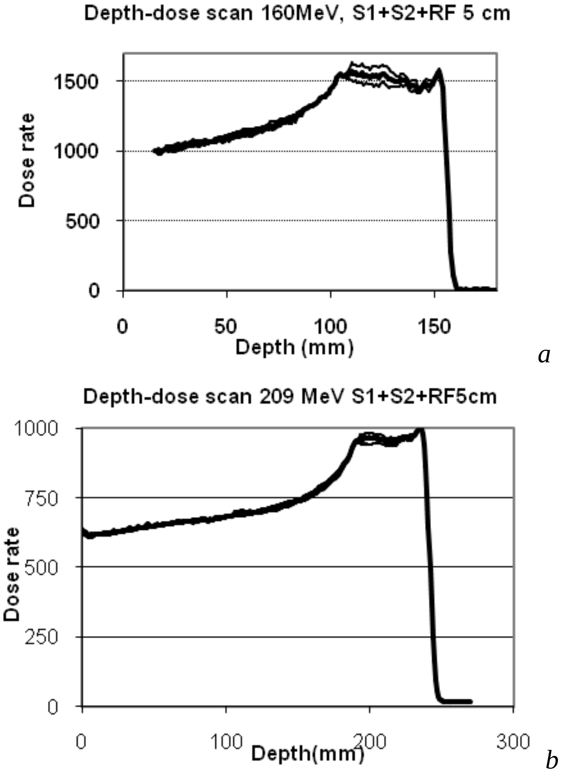
For the designing of the filter the program “Ridge Filter” was developed. For a given modulation depth, this program allows to calculate the weight of each component of energy entering the material and the relative widths of each step of the filter. The program also allows to control the energy profile of each component at an entrance to the phantom to ensure sufficient "mixing" of all the components and to choose the size of gap between ridges in the filter. At the open areas of the filter diffuser a copper foil was installed with the thickness of 200 microns. This was done in order to provide that the components, passed through the filter without energy loss, would then distributed across the beam.

Multiple scattering of protons in the filter was described by the Highland model. Integration of a stream of scattered protons on elements (steps) of each crest was carried out with the use of the program of two-dimensional adaptive integration.

Several ridge filters have been designed, manufactured and tested with a calculated width modulation of 3, 5 and 7 cm with the initial beam energy of 160 MeV and of 5 cm with the energy of 209 MeV.

Each filter consisted of ten ridges, the gap between the ridges was 10 mm, the length of the active part of the ridge was 100 mm in the assembly was allowed to cover the work filter area of 100×100 mm.

Fig. 7 show the results of the scan depth doses for energy 160 and 209 MeV.



a

b

Fig. 7. The dose distribution in the depth of modulation of the ridges filters with 5 cm for energies 160 MeV (a) and 209 MeV (b)

For the filter for energy 160 MeV non-uniformity of a dose on a plateau is 10%. For the filter on energy 209 MeV small overestimate of the contribution of the basic components of a proton beam is present, but uniformity of a dose on a plateau within the limits of 6% is provided. Other filters have shown an increase appreciable up to 20% of high-energy components and require insignificant adjustment.

These results of formation of the therapeutic proton beams provided the possibility of an individual formation of beams with the help of individual collimators and boluses in order to measure the uniformity of the dose distribution in a given volume of the target.

Along with ionization methods of dosimetry for measurements of distribution of the absorbed dose at depth, the radiochromic film Gafchromic MD-55 was placed inside a solid phantom made from the water equivalent material Plastic Water DT and Plastic Water LR with transverse and longitudinal positions of film. A beam energy of 160 and 209 MeV was formed by means of the individual collimator with a diameter of 30 mm and bolus, providing a hemispherical back isodose surface. As an example, the measured beam penumbra at different depths for 160 MeV is shown in Fig. 8.

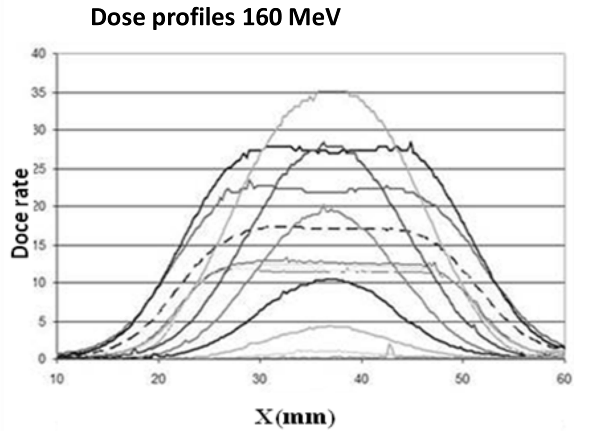


Fig. 8. Dose profiles at different depths of water equivalent phantom at a beam energy of 160 MeV, the film Gafchromic MD-55, 30 mm collimator

Despite the complexity of the method, it is the most accurate for the study of basic parameters of the penumbra of the proton beams (and thus, the parameters of multiple scattering of protons) with high spatial resolution.

2. RADIOACTIVITY SOURCE WITH Yb-169 FOR HIGH-DOSE-RATE BRACHYTHERAPY

The high-dose brachytherapy (HDB) – is a version of contact radiotherapy, in which the closed source with activity 1…10 Ci repeatedly enters through a catheter into tumor volume and can be used for several patients. Today the sources Ir-192 and Co-60 are used for this purpose. The new perspective isotope is Yb-169. Advantages of this isotope for HDB are related to the rather soft range of radiation (average energy ~ 93 keV) and high specific activity. The source on base Yb-169 allows to carry out medical procedures repeatedly, reducing requirements for biological protection of the treatment room and allowing to expand a scope of application HDB.

In our institute the source was obtained by irradiating a stream with thermal neutrons upon a sample with oxide of stable isotope Yb-168 in a sealed cylindrical titanium shell, with diameter of 0.7 mm and a length of 2.7 mm. Enrichment of an isotope Yb-168 to 20% was carried out by a method of laser division of stable isotopes on the AVLIS installation of the firm "Medical Sterilizing Systems". The sample with an isotope Yb-168, with the weigh of about 3 mg, was activated within 5 days by thermal neutrons in the vertical channel of the RADEX installation of INR. Fast neutrons, produced in a tungsten target, created the thermal neutron flux in a plastic container, and thermal neutrons activated the isotope Yb-168. With an average proton beam current of about 30 mA and energy of 209 MeV, the flux density of fast neutrons, with energy of about 500 keV, was ~ 10^{10} neutron·s^{-1}. The dose rate, from ytterbium activated sample after irradiation, was about 1 mSv/h. Photon radiation spectrum of the activated sample was measured with a Ge detector during 10 days after the activation and is shown in Fig. 9.

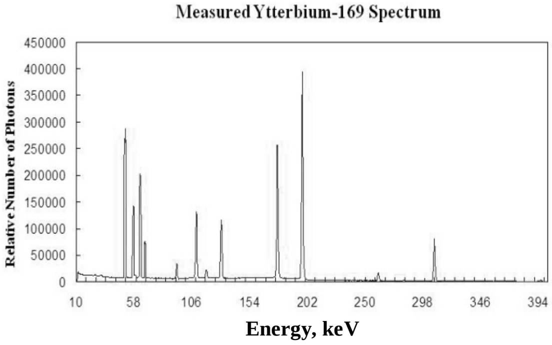


Fig. 9. The measured spectrum of photons from the source of ytterbium-169

In the spectrum of the main emission lines of the radionuclide Yb-169, contributions from other radio nuclides are small, as the intensity of the lines of the radio nuclide Yb-175 is 25 times less than Yb-169. Also, an insignificant contribution of radionuclide Sc-46, which could be produced in the titanium shell due to the reaction Ti-46 (n, p) Sc-46, was observed.

Thus, the activation conditions ytterbium samples at the facility RADEX INR can get interstitial sources based on Yb-169, with a low contribution of the high-energy component of the radiation.

To investigate the source of the radiation, dose distribution with Yb-169 was placed in the phantom in the form of a cube 10×10×10 cm (see Fig. 2), made of the Plastic Water LR. This material has the same cross sections as water (within the accuracy of 0.5%) for photons in the energy range 15 keV…8 MeV. Between the phantom plates we placed radiochromic film sheets of Gafchromic MD-55. These films were calibrated with the help of radiotherapeutic apparatus RTA-02 model at 100 kV, with a filter of 1.8 mm Al. The source was inside the phantom for a time comparable to a half-life of the radionuclide Yb-169 (32 days).

After the end of the exposure, the films were delayed for 2 weeks for the stabilization of level of contrast, and scanned. The red channel, as the most informative for this type of film, was allocated, pixel brightness was measured and transformed into the dose distribution by means of a calibration curve (Fig. 10).

An anisotropy of the dose distribution source at the level of 20% was determined. It is caused by self-absorption of photons in the active part of it and the shell. Two months after irradiation, Yb-169 activity was about 0.1 mCi.

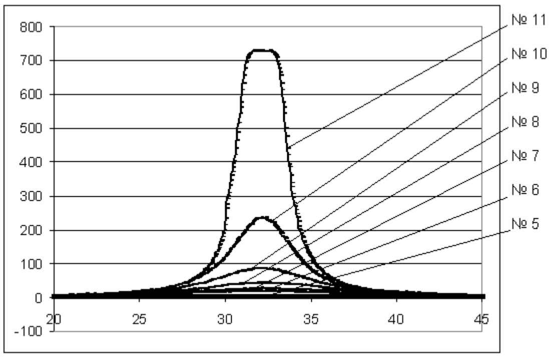


Fig. 10. Dose profiles measured by the film at the center of the projection of the Yb-169 source

This source has used titanium capsule and pressing technology with ytterbium oxide sintering. However, a significant amount of source material was titanium tube, which also distorted the spectrum of the radiation source after neutron activation. To overcome these drawbacks with IHPP developed a unique technology for manufacturing high-density ceramic-rich sources of ytterbium oxide. Ceramics density reaches the limit of the theoretical value (9.1 g/cm^3 for the cubic phase ytterbium oxide and 10 g/cm^3 for the monoclinic phase), sources have high mechanical characteristics and a glassy surface. Using superdense ceramics of this type has the following advantages:

a) It is possible to abandon the titanium container for one made of a ceramic core and glass-like surface, creating sealed radioactive source;

b) Failure of the titanium container allows to increase the diameter of the active core up to 0.6 mm and bring its volume up to 1 mm^3 (with length 3.5 mm) with increasing weight to 10 mg, when using ytterbium oxide enriched with Yb-168 at 20%, the activity of the core (depending on the neutron irradiation) is 15-18 Cu. When using ytterbium oxide enriched in Yb - 168 at a level of 40…45 % the activity of the source may not exceed 30Ci (irradiation neutron flux density of $4{\cdot}10^{14}$ n/cm^{2}s).

3. THE TARGET FOR FDG PRODUCTION

At the INR linac the target station is developed for the production of the isotope fluorine-18 for the subsequent synthesis of FDG (fluoro-deoxy-glucose). It is a most common radiopharmaceutical, used in nuclear medicine for positron emission tomography for imaging of malignant tumors. F-18 is prepared by irradiating isotopically enriched ^{18}O to 95% water protons reaction $H_2{}^{18}O$ (p, n)^{18}F.

One of the main requirements is the effective removal of the heat produced by proton beams in the target camera. For example, for a beam current of 30 mkA and energy of 20 MeV, the power, generated in the small target volume of 0.3…3 ml, is 600 W! Other requirements are defined by physical and chemical properties of a material of the target. The material has to be chemically inert and produce a minimum of radioactivity after the session. In world practice, target is usually made of niobium, which meets the basic requirements. In order to avoid technical problems, we produced the test version of a target from the stainless steel (Fig. 11).

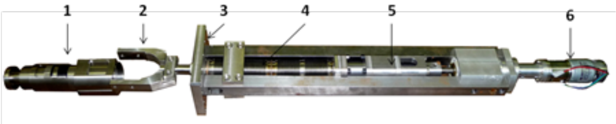


Fig. 11. Target node: 1 – target in unassembled form; 2 – target holder; 3 – mounting flange to the vacuum chamber; 4 – bellows; 5 – swinging target mechanism; 6 – electric motor

Fig. 12 shows the vacuum chamber with ports for attaching target node.

In the chamber there are sensors for measuring a vacuum, a current proton beam, and a target temperature. Loading and unloading of the target and its water cooling is done using electromagnetic valves controlled by the computer.

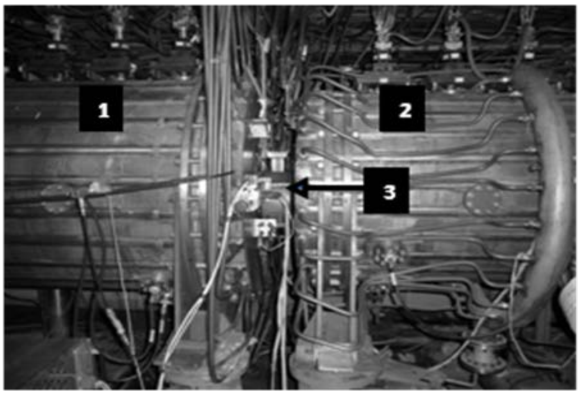


Fig. 12. 1, 2 – section of the accelerator cavities;
3 – vacuum chamber with three ports fixing targets

The possibility to use another port of the camera for the production of the isotope of iodine 124, which is formed in reaction $^{124}Te(p, n)^{124}I$, is now considered.

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Article received 04.10.2013

ПРИМЕНЕНИЕ ЛИНЕЙНОГО УСКОРИТЕЛЯ ПРОТОНОВ ИЯИ РАН ДЛЯ РАЗВИТИЯ МЕТОДОВ ЛУЧЕВОЙ ТЕРАПИИ И ЯДЕРНОЙ МЕДИЦИНЫ

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Проведен обзор результатов исследований в области протонной терапии и контактной радиотерапии (высокодозовой брахитерапии). На основании расчетов были изготовлены и испытаны на протонном пучке элементы системы формирования базовых терапевтических пучков КПТ ИЯИ РАН в широком диапазоне энергий протонов. Эти пучки позволяют проводить протонную терапию для новообразований практически любой локализации. Были проведены исследования нового источника для высокодозовой брахитерапии на основе изотопа Yb-169, имеющего ряд принципиальных преимуществ по сравнению с другими источниками. Проводились эксперименты по активации нового источника на нейтронном комплексе ИЯИ РАН, подтвердившие его терапевтические свойства. Показано состояние дел по сборке мишени для наработки ПЭТ изотопов на пучке протонов с энергией 20 МэВ.

ЗАСТОСУВАННЯ ЛІНІЙНОГО ПРИСКОРЮВАЧА ПРОТОНІВ ІЯД РАН ДЛЯ РОЗВИТКУ МЕТОДІВ ПРОМЕНЕВОЇ ТЕРАПІЇ ТА ЯДЕРНОЇ МЕДИЦИНИ

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Проведено огляд результатів досліджень в області протонної терапії та контактної радіотерапії (високодозової брахітерапії). На підставі розрахунків були виготовлені і випробувані на протонному пучку елементи системи формування базових терапевтичних пучків КПТ ІЯД РАН в широкому діапазоні енергій протонів. Ці пучки дозволяють проводити протонну терапію для новоутворень практично будь-якої локалізації. Були проведені дослідження нового джерела для високодозової брахітерапії на основі ізотопу Yb-169, що має ряд принципових переваг порівняно з іншими джерелами. Проводилися експерименти з активації нового джерела на нейтронному комплексі ІЯД РАН, які підтвердили його терапевтичні властивості. Показано стан справ зі збирання мішені для напрацювання ПЕТ ізотопів на пучку протонів з енергією 20 МеВ.