APPLICATION OF NUCLEAR METHODS

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WORLD TRENDS IN THE APPLICATION OF ACCELERATORS FOR THE PRODUCTION OF BASIC ISOTOPES FOR NUCLEAR MEDICINE

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The basic isotopes of nuclear medicine presently are ^{99}Mo and ^{18}F. For the production of these isotopes, there was a need to create accelerators to satisfy the needs for isotopes for large countries. For these purposes, electron accelerators are developed using warm and superconducting accelerating structures. It is also assumed to use neutron generators and cyclotrons.

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INTRODUCTION

The development of new directions in the physics and technology of accelerators is associated with the creation of unique installations designed to receive answers to studies of the fundamental properties of matter and the evolution of the Universe. Modern new accelerator technologies arise in connection with the practical problems of fight against cancer and cardiovascular illnesses of man. Nuclear medicine has played a leading role in resolving these issues over the past twenty years. Nuclear medicine is industry of medicine, using radionuclidess for diagnostics and treatment of illnesses. The use of radioactive isotopes for the diagnosis and treatment of cancer and other diseases is widely used in modern medical practice [1-7].

Vast studies of properties of radio-nuclidess are presently undertaken, the most effective application of every investigational isotope domains are certain for the use, both in diagnostics of diseases and at affecting different new formations in the organism of man [8-10]. In most developed countries (USA, Europe, Japan), the use of radio-nuclidess carries mass character. An equipment and medical preparations are worked out and certificated, procedures of application of radioactive preparations are standartized for diagnostics and treatment of certain types of diseases [11]. Preparation of specialists is conducted for this industry of medicine. The stable production of all necessary nomenclature of isotopes is created, both within the limits of separate regional centers of nuclear medicine and in the scales of whole countries. The market of medical radioisotopes in 2016 made an about 7.7 milliard of dollars of the USA, and a to 13.6 milliard can increase to 2021 [7, 12]. Leading firms can provide delivery of necessary radiopharmaceuticals practically in any point of the world [13, 14].

The stability of the production and supply of isotopes is one of the main requirements for nuclear medicine, since people are constantly sick, and most isotopes cannot be manufactured for future use. This is due to the peculiarities of the physics of production of some of the most commonly used isotopes.

It should be noted that about 10% of procedures with radioactive isotopes (mainly for cancers) are used for treatment, 90% of procedures are used to diagnose various diseases [7].

At the use of isotopes most attention is spared to the methods of early diagnostics of diseases. In this case probability of positive effect from further treatment of disease is most.

Single-photon emission computed tomography (SPECT) and positron emission tomography (PET) are two most widespread methods of diagnostics in nuclear medicine, based on the use of isotopes that emit gamma quanta and positrons [15, 16].

We will consider the methods of production of the main isotopes used by these techniques and the prospects for using electron accelerators for these purposes.

The international database of isotopes that can be used in nuclear medicine contains more than 76 isotopes [8, 9]. However the use only a few from them caused the necessity of search and development of the new accelerating systems for their production.

The most widespread radioisotope used in diagnostics is technetium-99 (^{99m}Tc), with approximately 40 million procedures in a year, on that is near 80% procedures of nuclear medicine and 85% diagnostic scan-outs in nuclear medicine in the whole world [7]. By other isotope, on the production of that the modern PET tomography is based, there is ^{18}F.

1. ISOTOPES PRODUCTION FOR SPECT TOMOGRAPHY

SPECT is based on the use of isotopes that emit gamma quanta. With the help of pharmaceuticals, the isotope is introduced into the body and accumulates in certain organs. The emitted gamma quanta are recorded using an ionization chamber. Based on the data obtained, a two-dimensional or three-dimensional distribution of the isotope is constructed, which makes it possible to obtain information about negative changes in the organ. SPECT is currently the most widespread scanning technology for diagnostics and monitoring of a wide range of diseases [7, 15].

The widespread use of the ^{99m}Tc isotope in diagnostics is due to a number of properties that meet the requirements of the technique [15].

The ^{99m}Tc radionuclide has a half-life of 6.01 h. When ^{99m}Tc decays, it emits gamma quanta with energy of 0.1405 MeV. These photons are efficiently detected by the ionization chamber and have low absorption in the human body. Sodium pertechnetat ^{99m}Tc can be easi-

ly combined for the preparation of various radiopharmaceuticals. An additional advantage is the fact that the isotope can be obtained from the parent ^{99}Mo isotope by decay with a lifetime of 66.02 h. A compact ^{99m}Tc generator from this isotope has been developed, which can be delivered practically anywhere on earth in a very short time [5-8, 10, 15].

Isotopes ^{201}Tl, ^{123}I, ^{111}In are also used for SPECT tomography, but their application is limited [5, 8, 15].

From 95 to 98% of all ^{99}Mo in the world is obtained from the weapons-grade fission ^{235}U [1, 7, 15, 17-19] (75% [7]). Reactors are used with thermal neutron fluxes at the level of $10^{14}…10^{15}$ neutrons/(cm^2 s) due to the fission of the ^{235}U nucleus in the reaction – ^{235}U (n, F) ^{99}Mo. The cross-section for fission of uranium-235 by thermal neutrons is 582.6 barn. The share of ^{99}Mo in decomposition products is 6.1% [17, 18].

This process for obtaining ^{99}Mo is currently considered the cheapest. The use of targets with low uranium enrichment leads to an increase in the price of the product yield by 20 percent [7].

For the production of ^{99}Mo in reactors, the neutron capture reaction ^{98}Mo (n, γ) ^{99}Mo can be used. However, the cross section for this reaction is 0.136 barn for thermal neutrons is two orders of magnitude lower than the cross section for production from ^{235}U [5, 15-17]. The production of ^{99}Mo by this method turned out to be less effective for obtaining large amounts of the isotope [18-21].

The widespread use of the ^{99}Mo isotope causes constant and close attention to the methods and problems of its production [7, 10, 12, 22]. In connection with the closure of reactors, all greater attention is spared to methods for producing an isotope using accelerators protons, deuterons and electrons [7, 17, 18, 23, 24].

With the help of cyclotrons, using the reaction ^{100}Mo (p, 2n) ^{99m}Tc, it is possible to obtain sufficient amounts of the isotope, but for this it is necessary to completely change the entire system for obtaining ^{99m}Tc, based on the use of ^{99}Mo [24, 25].

With the help of electron accelerators, the reconstruction of the existing methods of obtaining ^{99}Mo can be carried out with much lower costs. Quite a lot of works have been devoted to the development of isotope production technology [6, 10, 17-19, 26-35]. The production of an isotope using electron accelerators is possible only using the reactions ^{238}U (γ, F) ^{99}Mo and ^{100}Mo (γ, n) ^{99}Mo. These reactions make it possible to obtain the required amount of the isotope to meet the needs of entire countries with the modern development of electron accelerator technologies [17-19].

The United States consumes about half of the world's ^{99}Mo. However, most of this isotope is produced in other countries, which poses a number of supply stability issues. Therefore, several projects for the production of the isotope are financed in the USA, based on existing and new developments of electron and deuteron accelerators [32]. They must completely solve the problem of producing the required amount of the isotope without using weapons-grade uranium.

The NorthStar Medical Radioisotopes company, based on its developments, has created a ^{99m}Tc technetium generator from ^{99}Mo, produced without the use of uranium [33, 34].

A generator corresponds to all standards of Pharmacopoeia for ^{99}Mo that allows using him together with existent generators.

The ^{99}Mo isotope will be produced at a specially designed electron accelerator. The target will be ^{100}Mo with 95 percent enrichment. Obtaining an isotope in this way is 30% more efficient than obtaining it by irradiation of enriched ^{98}Mo in a reactor [33].

In early 2019, NorthStar announced the signing of a contract for the purchase of eight Rhodotron® TT300 HE electron beam accelerators manufactured by IBA [35]. The Rhodotron® TT300 HE accelerator has been specially designed to meet this challenge (Fig. 1). NorthStar has placed purchase orders for the first pair of accelerators and completed building of new productive complex by an area 30 000 apt. feet in September, 2019. It is expected that the first pair of accelerating will arrive in USA during the fourth quarter of 2020.

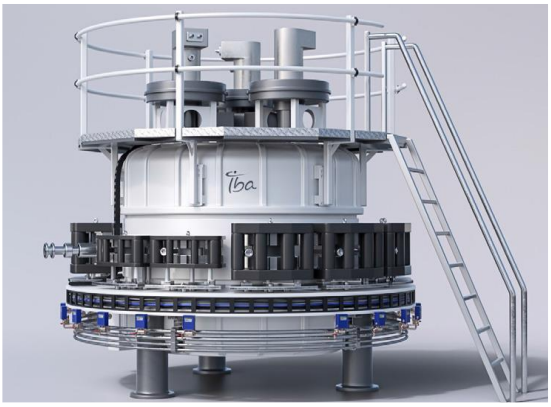

Fig. 1. Accelerator Rhodotron® TT300 HE [35]

Beam parameters – 125 kW, 40 MeV, 3.1 mA, 107.5 MHz, energy spread ~ 5%. The accelerator provides continuous 24/7 operation.

Company "Niowave" (state Michigan) [36-38] has demonstrated the production of molybdenum-99 at its Lansing R&D facility and hopes to produce up to 25 percent of the molybdenum-99 used in the United States within the next six years. The company produces medical isotopes without nuclear reactors or highly enriched uranium, instead using superconducting linear accelerators to separate natural uranium. Now "Niowave" produces a superconducting electronic Linac of 40 MeV and a power of 100 kW for the production of medical radioisotopes [37] (Fig. 2).

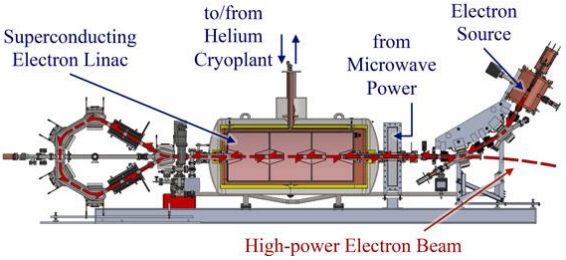

Fig. 2. Commercial Superconducting Electron Linac [36]

A company "SHINE Medical Isotopes" began on May, 9, 2019 building of complex on the production of medical isotopes in Janesville (Wisconsin, USA) [39]. The company may start commercial production of ^{99}Mo

in 2021, after the construction of the plant is completed. The proposed method is the production of isotopes by fission in a target with LEU dissolved in an aqueous solution [40, 41].

In 2015 of SHINE and GE Healthcare declared, that successfully got the pharmaceutical class of ^{99m}Tc from Drytec™ (producer of generators Technetium ^{99m}Tc) of company GE Healthcare for the production of sodium pertechnetate for the injections of ^{99m}Tc, using ^{99}Mo, producible the innovative process of SHINE. The positive results of this dough confirm that ^{99}Mo, produced by means of process of SHINE, can be plugged in existing chain of supplying with ^{99}Mo.

The source of neutrons in this production is a deuteron accelerator and a tritium target. In cooperation with Phoenix, SHINE managed to achieve the highest neutron flux in such an accelerator-target system – 4.6×10^{13} neutrons per second. The results obtained indicate that this scheme can become a powerful competitor to the use of superconducting electron accelerators.

The sectional diagram of the installation is shown in Fig. 3.

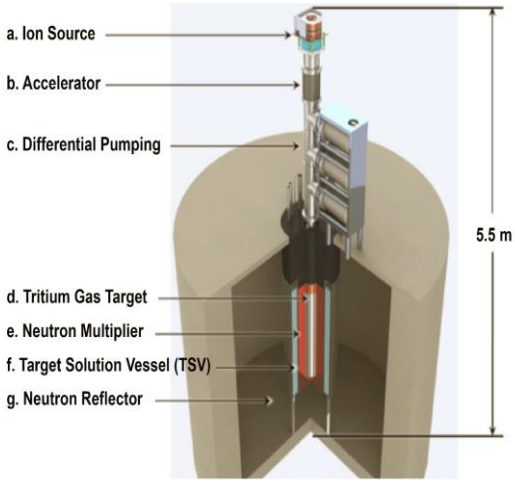

Fig. 3. Isotope production scheme

Fig. 4. The deuteron accelerator

The appearance of the deuteron accelerator is shown in Fig. 4.

In the complex with a total area of about 4 thousand square meters, eight accelerating systems for the production of isotopes will be installed. For molybdenum-99, their productivity will be about a third of the world's demand for this isotope.

2. ISOTOPES PRODUCTION FOR PET DIAGNOSTICS

As indicated above, in the cost measurement of using ^{99}Mo, in nuclear medicine, a significant place is occupied by the use of positron emitters, which are used in PET diagnostics [7-9].

Comprehensive data on the cross sections of reactions, with the help of which they can be obtained, are contained in the international database [8]. Of a fairly large range of isotopes that emit positrons as a result of nuclear transformations, four are currently used: ^{15}O (half-life 2.04 min), ^{13}N (9.96 min), ^{11}C (20.4 min), ^{18}F (110 min). The most commonly used pharmaceutical in clinical PET scanning is fluorodeoxyglucose, a glucose analogue labeled with the ^{18}F isotope. Fluorodeoxyglucose is used in almost all scans for oncology and in most cases in neurology, which accounts for more than 95% of all PET scans [16].

For many years, the possibility of obtaining the above diagnostic isotopes for PET diagnostics using electron accelerators has been studied [17, 30, 42-53]. Some advantages of using electron accelerators for the production of PET isotopes have been demonstrated.

But the analysis of the modern world production of these isotopes showed that only a few reactions involving protons and deuterons are actually used for production [7, 16].

This is due to the fact that at the beginning of the development of PET centers, which include an accelerator, the cheapest was the cyclotron. Last models of PET centers are used fully automated accelerators equipped with superconducting magnets that operate at nitrogen temperatures. This is, for example, the iMiTRACE cyclotron [54, 55] (Fig. 5).

Fig. 5. iMiTRACE Cyclotron

iMiTRACE Cyclotron accelerates protons to 12 MeV with a current of up to 50 μA and requires 65 kW of power to operate. With the help of this cyclotron, it is possible to obtain isotopes ^{18}F, ^{11}C with productivity for ^{18}F more 60 GBq after 2 h 30 min of bombardment.

Since the cost of the accelerator is an essential part of the equipment of the PET center and their renewal can be expected only with the payback of previous investments, one should not expect the use of electron technological accelerators in the next decade, provided their cost competition in comparison with other types of accelerators.

Thus, despite some advantages, electron accelerators, including superconducting ones, will not be used in PET centers in the near future.

CONCLUSIONS

The production of other isotopes that can be used in modern nuclear medicine [6, 36, 50], taking into account a small part of their production in terms of cost to the isotopes discussed above, does not currently require the use of specially designed accelerating systems. Therefore, it makes no sense to discuss the advantages of using one or another accelerator for their production. As the world practice shows, the most profitable for their production is the use of any operating options.

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СВІТОВІ ТЕНДЕНЦІЇ У ВИКОРИСТАННІ ПРИСКОРЮВАЧІВ ДЛЯ ВИРОБНИЦТВА ОСНОВНИХ ІЗОТОПІВ ДЛЯ ЯДЕРНОЇ МЕДИЦИНИ

І.С. Гук

Основними ізотопами ядерної медицини сьогодні є ^{99}Mo і ^{18}F. Для виробництва цих ізотопів виникла необхідність створення прискорювачів, що дозволяють задовольнити потреби в ізотопах для великих країн. З цією метою розроблені електронні прискорювачі, що використовують теплі і надпровідні прискорюючі структури. Також передбачається використовувати нейтронні генератори і циклотрони.

МИРОВЫЕ ТЕНДЕНЦИИ В ПРИМЕНЕНИИ УСКОРИТЕЛЕЙ ДЛЯ ПРОИЗВОДСТВА ОСНОВНЫХ ИЗОТОПОВ ДЛЯ ЯДЕРНОЙ МЕДИЦИНЫ

И.С. Гук

Основными изотопами ядерной медицины в настоящее время являются ^{99}Mo и ^{18}F. Для производства этих изотопов возникла необходимость создания ускорителей, позволяющих удовлетворить потребности в изотопах для больших стран. Для этих целей разработаны электронные ускорители, использующие теплые и сверхпроводящие ускоряющие структуры. Также предполагается использовать нейтронные генераторы и циклотроны.