# PRODUCTION OF THE SHORT-LIVED RADIONUCLIDES FOR POSITRON-EMISSION TOMOGRAPHY: CYCLOTRON OR LINEAR ELECTRON ACCELERATOR

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Analysis of the methods of the short-lived positron emitting radionuclides production on linear electron accelerators for positron-emission tomography (PET) was performed. Methods of extraction of short-lived isotopes from the irradiated samples are considered. It is shown that specific activity of radionuclides produced on linear electron accelerators is sufficient for the gamma-camera and PET diagnostic.

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## INTRODUCTION

In last years the use of the radionuclides in nuclear medicine, biology, for the estimation of the environment state and other areas was widely adopted. Practically in all nuclear centres, having reactors or accelerators, there are the programs on the development and research of the production methods of the different radionuclides.

Nuclear tracers produced on the basis of these radionuclides after introduction of them to the patient organism allow obtaining the information about the pathological changes in the various human organs.

The production of the radionuclides for medical purposes is based, mainly on the use of nuclear reactors. However, their production in this case is accompanied by the accumulation of the plenty of long-living isotopes.

Other ecologically cleaner and economically expedient methods of the radionuclides productions are based on the use of the charged particles accelerators, mainly, cyclotrons [1 - 6] and also the linear accelerators [7 - 10].

The analysis of the problem state of the radionuclides production on the cyclotrons for nuclear medicine is list to the papers [11 - 13].

In this paper the evaluation of the radionuclides production possibility for PET on the linear electrons accelerators (linacs) is performed. For this the experimental data about the value of the specific activity of the short-lived radionuclides $^{11}C$, $^{13}N$, $^{15}O$, $^{18}F$ were obtained on the linear electrons accelerator LUE-20 NSC KIPT (Kharkov) [14]. Basic estimation of the production possibility of the short-lived radionuclides on the linacs, suitable for the clinical application in the PET diagnostic were listen in paper [15].

## TECHNOLOGY OF THE USE OF THE LINEAR ELECTRON ACCELERATORS

The number of the linear electron accelerators (linacs), manufactured in the Soviet years, exceeded many times the number of the manufactured cyclotrons. It is explained by that linear electron accelerators found the extensive use in the national economy and medicine [16].

Linacs began to manufacture intensively in post-war years. So, in KIPT (Kharkov) as the result of the performed theoretical investigations on the steady motion of the electrons in accelerating structures were created the linear electron accelerators on the energy 0.7 MeV (1952) and 3 MeV (1954). Then the linacs on the energy of 40 and 90 MeV were manufactured. Multisectional 300 MeV linac (1964) became by the prototype of 2 GeV linac (1965) at that time largest in Europe [18]. Kharkov experience on the creation of the linear electron accelerators was used by the Research Institute of Electrophysics Apparatus the name of V.D. Efremov (Leningrad) that organized the linacs manufacturing of the different function. This institute created also the cyclotrons U-120 and U-240 (120 and 240 cm is the electromagnets diameter), that worked in the nuclear centres of the of the FSU and beyond. These cyclotrons were used for the radionuclides producing and the performing of the fundamental investigations. These cyclotrons were large-tonnage large-dimension machines, consuming the megawatts of the electric power.

Physicists of CERN in 70-th years developed the method of the positron emission tomography. First PET began to work in the Geneva hospital. Physicians estimated quickly this method as reliable diagnostics in oncology, cardiology, neurology etc. PET is perspective direction of the nuclear medicine in which are used the nuclear tracers – subtracts of the metabolism [19].

For the production of the short-living radionuclides $^{11}C$, $^{13}N$, $^{15}O$, $^{18}F$ (positron emitters) the specially engineered small-size cyclotrons with the diameter of poles 50…70 cm which allowed to spread widely the method of PET are used now. A cyclotron accelerates protons to energy 18 MeV and deuterons to energy 9 MeV.

The current of the accelerated particles arrive at 20…40 μA. The protons run in the water are about 3.5 mm; the heat generation in the target arrives at 200…400 W. To shut out the target overheating in the irradiation process, it is blown by gaseous helium. As result of the irradiation the short-living radionuclides with activity a few Curie units are produced. For the inspection of one patient it is necessary to produce about $10^9$ Bq. Principal physics of PET is given in various publications [3, 19 - 22].

The alternative to the cyclotron method of the production of the positron emitters is the irradiation on commercially available linacs with the electron energy 20…50 MeV [16, 17]. Accelerated electrons at the passing through targets with large Z (tantalum, tungsten, gold, platinum, uranium,) generate bremsstrahlung gamma-quanta. Spectrum these gamma-quanta are continuous and their maximal energy is equal to energy of the accelerated electrons.

The nuclear reactions $^{12}C(\gamma,n)^{11}C$, $^{14}N(\gamma,n)^{13}N$, $^{16}O(\gamma,n)^{15}O$, $^{19}F(\gamma,n)^{18}F$ are proceeded under the action

of the gamma-quanta with the high energy (10…30 MeV). In earlier published papers the yield of these short-lived radionuclides were experimentally determined at the different irradiation modes and it is shown, that their activity can arrive of the value necessary for PET diagnostics.

In given paper we will consider the most essential publications that were found in the database of INIS. The papers in which the extraction methods of the short-lived radionuclides from the irradiated targets for the subsequent realization of the nuclear tracers synthesis are described was chosen. Author of the article [23] used for the production of $^{15}O$ the electron linear accelerator manufactured by Varian Co. with maximal electrons energy 26 MeV and current 200 μA. The idea of author consists in separating of $^{15}O$ from some parent matrix, using reactions with the recoil nuclei $^{15}O$ (Szilard-Chalmers – the phenomenon of the nucleus recoil in some nuclear reactions).

In this case as the result of the photonuclear reaction $^{16}O(\gamma,n)^{15}O$ the considerable kinetic energy of the nucleus $^{15}O$ results in the break of molecule $H_2O$. The free atom $^{15}O$ is appearing. The atoms $^{15}O$ after can be separated from the $H_2O$ matrix by the different methods. In particular, it is possible to use the method in which 50% $^{15}O$ can be allocated from water by boiling. It is also possible to use targets in the form of $H_2O$ or mixture of $H_2O$ and 10% $H_2O_2$ with the blowing out by helium.

The target was the cylindrical polyethylene container of 500 $cm^3$ volume, 6 cm diameter and 8 cm long filled with water.

The production possibility of $^{15}O$ due to the photonuclear reaction $^{16}O(\gamma,n)^{15}O$ is facilitated by the availability of the photonuclear data contained in National Bureau of Standards Handbook. The yield estimation of the short-lived radionuclides for the reactions given above is listed in the papers [24, 25]. In particular, it is shown that specific activity $^{15}O$ 2.75 mCi/g can be produced at the electrons current 100 μA, thick converter and at the location of the target in the 3 cm distance from the converter at 10 minute irradiation.

In the experiments with the extraction of $^{15}O$ the container irradiation was performed at the electron energy of 26 MeV and current 76 μA during 4 min. After the irradiation the container was placed in the dosimeter for the activity measuring. Then water was poured out from the container and the container activity was again measured for the estimate of the contribution of $^{11}C$ to the total activity. Then this procedure was repeated at the energy of 23.5 MeV.

The target with the boiling water for the obtaining of $^{15}O$ was the glass vaporizer filled with the distilled water on 3/4 volume, the heater for the water boiling, the condenser for the collection of the water vapour and the return of the condensed water back in the vessel. Remaining mixture of water vapour and $^{15}O$ passed through the trap at -76°C (dry ice) in which condensed most of the remaining water vapour. All system was blown by helium (0.88 l/min) that served as the carrier of the water vapour and oxygen $^{15}O$.

Remaining mixture of helium and $O_2$ was then transported on the cooper tubing to the experimental area for realization of radio-chemistry synthesis. Here in the trap at the cooling by the liquid nitrogen (-196°C) there was the cryocondensation of $O_2$. For the effective catching of $O_2$ the trap was filled with the molecular sieve material. It was found that the molecular sieve is necessary for efficient capture due to the very close value of condensing temperature (-183ºC) to the temperature -196°C.

As a result of the performed studies it was defined that at the 23.5 MeV electron energy and current 100 μA in the polyethylene bottle with 6 cm diameter, 18 cm long filled by the water, at the irradiation within 4 min apart of the 9 cm from the converter the activity of $^{15}O$ by time of the irradiation end was 39 mCi. The same target irradiated at the electron energy of 26 MeV and current 100 μA gives approximately 184 mCi $^{15}O$ on the irradiation end.

The experiments on the production of nuclide $^{11}C$ are described in paper [26]. Linac similar to paper [23] was used. The bremsstrahlung target was platinum 2 mm thickness. For producing of $^{11}C$ in form $^{11}CO$ liquid carbon dioxide ($CO_2$), cyclohexane (hexamethylene) ($C_6H_2$) and glacial acetic acid ($C_2H_4O_2$) were used as target materials. These substances contain the significant amount of carbon and have no impurity.

As a result of irradiation on the bremsstrahlung beam of the linac the (γ,n)-reaction with formation of $^{11}C$ is occurred. The target chamber for $CO_2$ consisted of the stainless steel cylinder of 15 cm in length and 5 cm in diameter and condenser above it 10 cm long and 5 cm in diameter.

The photonuclear target was located approximately 5 cm from the bremsstrahlung target and was filled approximately with 260 g of $CO_2$. The cylinder was cooled by the water at the 20°C temperature. It was made for the prevention of the temperature increase of $CO_2$ above its critical temperature (31°C), that can result in the pressure increase in the target chamber. For the vapours liquefaction of $CO_2$ and their returns as the liquid to the target chamber the cooling water (8°C) was circulated on the heat-exchanger of the condenser.

The product gas was then passed by the helium stream through the a trap of the copper heat exchanger at the temperature -196°C to remove $CO_2$ vapors, and then through the molecular sieve trap at -196°C for cryoprecipitation of $^{11}CO$. The separated activity in two last traps was measured.

In the same conditions the liquid cyclohexane and glacial acetic acid in glass vessels of 20 cm long and 10 cm in diameter, located in 5 cm from the bremsstrahlung target was irradiated. The $C^{11}$ – hydrocarbons product is appearing at the disintegration of the cyclohexane molecule at the irradiation.

The data of the experiment on the production of the nuclide $^{13}N$ as well depending on the radiation angle of the gamma quanta was listening in the paper [27]. Linac similar to paper [23] was used. As the material of the nitrogen specimens was used $NH_4NO_3$. The specimens contained (0.55±0.0055) g of the nitrogen as solution of $NH_4NO_3$ in $H_2O$ in polypropylene test tubes of 30 mm long with the internal diameter 9.5 mm and external 12 mm. They were *i*nstalled in the line from the lucute holder that was located in the field of the bremsstrah-

lung normally to the photon beam axis apart of 28.5 cm from the bremsstrahlung target. The angle between nitrogen specimens was changed from 3.06 to 2.33° in the range of the gamma radiation angle from 0 to 30.51°.

After the irradiation the nitrogen specimens with $^{13}N$ were moved in the non-irradiated test tubes before the radiometry for the estimation of the contribution of the radionuclide $^{11}C$ from the containers. Measuring was delayed approximately on 20 min after the irradiation end to allow $^{15}O$ to disintegrate to very small level. Weighing of the specimens containers before and after the transfer of the contents showed, that less than 0.5% of the contents was remained after transfer.

The investigations on the evaluation of the production of radionuclide $^{18}F$ were performed on the linear electron accelerator LUE-20 NSC KIPT [14]. For the production of the nuclides $^{18}F$ the fluoroplastic film ($C_2F_4$) in the glass vessel with the distilled water and crystalline LiF were used. The targets irradiation was performed at the electrons energy of 25 MeV and the beam current 10 μA for the duration from one to three hours. Radiometry of the produced $F^{18}$ was delayed approximately on two hours after the irradiation end for the decreasing of the $^{11}C$ activity.

Extraction of the active $^{18}F$ isotope from the matrix is possible due to the Szilard-Chalmers reaction. Recoil energy of the nucleus $^{18}F$ exceeds of the chemical bond energy it in the molecule. Thus, the atom $^{18}F$ leaves its place in the matrix and braked in the matter. At the irradiation of fluoroplastic in water, due to the presence of large surface contacting with water, part active $^{18}F$ passes to water as an ion $^{18}F$.

The part of $^{18}F$ that passed into the aqueous phase was 7…11% that agrees with data of paper [28]. The some understated yield value of the radionuclide $^{18}F$ in water can be explained by the adsorption of ion $^{18}F$ on the surface of the glass vessels. In case of the using of LiF (20 mg) was obtained considerably larger specific production of $^{18}F$. At the recalculation on the irradiation time up to the saturation the specific activity $^{18}F$ was $3 \cdot 10^9$ Bq/g/μA.

## CONCLUSIONS

Thus, the analysis of the performed investigations showed that on linear electron accelerator with the electron energy about 30 MeV and average current 100 μA can be produce clinically necessary amounts of the radionuclides – positron emitters. Present linacs can exchange cyclotrons in the PET complexes that can allow the expenses shortening on the creation of the PET complexes.

The use of the target system with boiling water can provide the method for the production of sufficient amount relatively high activity radionuclides ($^{15}O$-$O_2$,) suitable for the use in nuclear medicine.

The yield of (γ,n)-reactions for the production of $^{11}C$, $^{13}N$, and $^{15}O$ substantially depends on the electrons energy and angular distribution of the gamma quanta on the target. Data can be useful to the calculation of the radionuclides yield at creation of the photonuclear target systems, in particular, at the estimation of the electrons energy for the generation of the photons beam at the use of the target systems similar to described in the mentioned papers.

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## НАРАБОТКА КОРОТКОЖИВУЩИХ РАДИОНУКЛИДОВ ДЛЯ ПОЗИТРОННОЙ ЭМИССИОННОЙ ТОМОГРАФИИ: ЦИКЛОТРОН ИЛИ ЛИНЕЙНЫЙ УСКОРИТЕЛЬ ЭЛЕКТРОНОВ

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Проведен анализ методов наработки короткоживущих радионуклидов на линейных ускорителях электронов для позитронной эмиссионной томографии. Рассмотрены методы извлечения короткоживущих изотопов из облученных образцов. Показано, что удельная активность радионуклидов, полученных на линейных ускорителях электронов, может быть достаточной для диагностики на гамма-камерах и для позитронной эмиссионной томографии.

## НАПРАЦЮВАННЯ НЕДОВГОЖИВУЧИХ РАДІОНУКЛІДІВ ДЛЯ ПОЗИТРОННОЇ ЕМІСІЙНОЇ ТОМОГРАФІЇ: ЦИКЛОТРОН АБО ЛІНІЙНИЙ ПРИСКОРЮВАЧ ЕЛЕКТРОНІВ

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Проведено аналіз методів напрацювання недовгоживучих радіонуклідів на лінійних прискорювачах електронів для позитронної емісійної томографії. Розглянуто методи здобування недовгоживучих ізотопів із опромінених зразків. Показано, що питома активність радіонуклідів, одержаних на лінійних прискорювачах електронів, може бути достатньою для діагностики на гамма-камерах та для позитронної емісійної томографії.