PHOTONUCLEAR PRODUCTION OF F-18

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^{18}F is one of the most important positron emitters which are routinely used in the positron emission tomography (PET). The recoil nuclei method in the ^{19}F(γ,n)^{18}F reaction was used for the production of ^{18}F free carrier. The sufficiently high energy of recoil nuclei in this reaction can be up to 200 keV. The mixture of 180 nanometer CaF_2 nanoparticles and an acceptor in the form of a nanoparticle of food salt was irradiated with bremsstrahlung with a maximum energy of 13.5 MeV. Irradiated samples were placed in distilled water to dissolve the sodium chloride. The yield of the ^{18}F isotope in the solution was 30.2% of the total activity of the sample. The estimation of the ^{18}F production on an electron accelerator with a power of 10 kW and an energy of 35 MeV can be up to 1 Ci for 4 hours.

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INTRODUCTION

The advantage of the PET method, in comparison with other methods of instrumental medical diagnostics, is the possibility of obtaining information about the fate of radionuclides in the body that correspond to the basic elements-organogenes included in the composition of biologically significant molecules. Positron emitters are used to label various radiopharmaceuticals. The significant advantages of PET are realized in the study of cerebral blood flow and cerebral blood volume, regional metabolism of carbohydrates and oxygen, in neurochemical studies – to obtain data on the density of individual receptors and their functioning in the healthy and diseased brain of man [1].

To detect abnormalities in the metabolism of oxygen, a positron emitter of ^{15}O is used. This is important in the treatment of epilepsy, brain tumors, ischemic lesions, etc.

To evaluate the neurotransmitter systems, in particular dopamine, a number of radiotracers are used, among which L-DOPA, and its radiofluorinated analogue ^{18}F-6-fluorideDOPA. To assess the activity of various receptor systems, their antagonists are most often used, which are capable of more or less irreversibly binding to them. As radio raisers, isotope analogs of known radiopharmaceuticals are often used: phenothiazines (chlorpramazine), benzamides (raclopride), as well as various benzodiazepines, opiates, acetylcholine derivatives, etc.

In cardiology, the most popular positron radiators are ^{13}N in the form of NH_3, and ^{82}Rb in the form of RbCl (for evaluating regional perfusion of the heart muscle) and fatty acids labeled with carbon-11 (for evaluating the regional metabolism of fatty acids) [1].

The most widely used in PET are ^{11}C, ^{13}N, ^{15}O, and ^{18}F. An important circumstance is that the listed isotopes, except for ^{18}F, are isotopes of biogenic elements. Various biomolecules (including simple alcohols, sugars, amino acids, steroids, alcaloids and host drugs) can be carried with positron emitters without altering their bio-chemical and physiological activities. We note that the close Van der Waals radii of H and F allow us, with some reservations, to introduce ^{18}F into labeled compounds instead of hydrogen without major disturbances in the geometry of the radiotracer.

In addition to widely used isotopes ^{11}C, ^{13}N, ^{15}O, and ^{18}F, other isotopes are also used, which significantly expands PET capabilities for diagnosis of various diseases (Tabl). The maximum spatial resolution that can be obtained by the PET method is limited to the range of positrons in the object under study. The values of the positron ranges in water are given in table. As follows from the data in the table, the values of the positron ranges are significantly different, which introduces an error in determining the place of the event, which in principle cannot be corrected. It can be seen that the minimum value of the positron range is realized for ^{18}F. However, for some applications, these isotopes have significant advantages (for example, cardiac studies using ^{82}Rb).

Although ^{18}F is not a significant element in living organisms, its nuclear properties make its use in labelling of significant value. At present, in the overwhelming majority of PET centers, the ^{18}O(p,n)^{18}F reaction is used to produce fluorine-18 in the form of a fluoride ion, which occurs when protons irradiated with water enriched with oxygen-18.

Most PET use ^{18}F, which is obtained in the reaction ^{18}O(p,n)^{18}F. Nevertheless, other methods of obtaining ^{18}F are being developed. Using brake gamma radiation of 140 MeV electrons with an intensity of 80 μA, Brinkman and Wyand [2] attempted to use the ^{18}F photonuclear reaction of ^{19}F(γ,n)^{18}F in targets filled with liquid fluorinated hydrocarbons. Depending on the type of hydrocarbon, the activity extracted by water ranged from 11 to 68%. Of the total induced activity. Given the correct choice of the irradiated material, it was possible to achieve activities of ^{18}F-up to 100 mCi. At the same time, it was shown that the extractable fluoride contains an admixture of radioactive organic fluorinated compounds, both used for irradiation, and products of reactions of recoil atoms. Due to the strong radioactive decomposition, the mole activity of fluoride did not exceed 0.25 Ci/mmol.

In [3], attempts were made to obtain ^{18}F on a linear electron accelerator, which is used to irradiate cancer patients. The high cost of obtaining ^{18}F on cyclotrons prompted the appearance of work [4], where studies were made of its production on a linear accelerator of electrons with an energy of 55 MeV.

Isotope	$T_{1/2}$, hours	Mean and maximum energy β-particles, keV (intensity, %)	E_γ, keV (intensity, %)	R_{90} of β^+, mm
^{11}C	20.96	385.7, 960.4 (99.77)	511 (199.5)	1.68
^{13}N	9.97	491.8, 1198.5 (99.80)	511 (199.6)	2.26
^{15}O	2.037	735.28, 1735.0 (99.9)	511 (199.8)	3.61
^{18}F	109.77	249.8, 633.5 (96.73)	511 (193.4)	0.94
^{62}Cu	9.673	772.1, 1763.9 (0.138); 1320.7, 2936.9 (97.60)	511 (196); 1172.7 (0.35)	7.26
^{64}Cu	12.7	278.2, 653 (17.6); 188.85, 573 (38)	511 (35.2); 1347 (0.55)	1.04
^{62}Zn	9.255	255.4, 597.5 (8.2)	511 (15.8); 40.8 (22.6); 507.6 (14.8); 548.35 (15.3); 596.6 (26)	0.96
^{68}Ga	67.71	352.6, 821.7 (1.19); 836.0, 1899 (87.7)	511 (178.4); 1077.3 (3.2)	3.94
^{75}Br	96.7	514, 1181 (3.6); 601.4, 1376 (3.3); 708.1, 1612 (4.9); 772, 1753 (53); 904, 2040 (4)	511 (150.8); 141.2 (6.6); 286.5 (88); 431.8 (3.97)	3.78
^{76}Br	16.2	336, 781 (6.3); 427.2, 990 (5.2); 1532, 3382 (25.8); 1800, 3941 (6)	511 (109); 559.2 (74); 657 (15.9); 1853.7 (14.7)	8.35
^{82}Rb	1.2575	527.7, 1206.7 (0.32); 843.2, 1903 (0.12); 1167.6, 2601 (13.1); 1534.6, 3378 (81.8)	511 (189); 777 (12.5); 1395 (0.47)	7.65
^{86}Y	14.74	535.4, 1221 (11.9); 681.1, 1545 (5.6); 883.3, 1988 (3.6); 1436.8, 3141 (2.0)	511 (64); 443.1 (16.9); 627.7 (32.6); 703.3 (15.4); 777.4 (23); 1076.6 (82.5); 1153 (31.3); 1920.7 (21.3)	3.34
^{89}Zr	78.41	395.5, 902.3 (22.74)	511 (45.89); 909.1 (99.86); 1712 (0.86)	1.72
^{82}Rb	1.2575	527.7, 1206.7 (0.32); 843.2, 1903 (0.12); 1167.6, 2601 (13.1); 1534.6, 3378 (81.8)	511 (189); 777 (12.5); 1395 (0.47)	7.65
^{94m}Tc	52	404.5, 917 (0.92); 639.3, 1446 (0.93); 1094.2, 2439 (67.6)	511 (140.3); 871 (94.2); 1522 (4.5); 1868.7 (5.7)	5.79
^{110}In	69.1	1014.7, 2260 (60.7)	511 (122.5); 657.75 (97.7)	5.37
^{124}I	4.176	687.04, 1534.9 (11.7); 974.7, 2137.6 (10.7)	511 (45); 602.7 (62.9); 722.8 (10.36); 1591 (11.15)	4.24
^{134}La	6.45	946.9, 2104 (1.56); 1224.4, 2709, (62)	511, (127.2); 604.7 (5.04)	6.44

Also note the work of the Polish group, which are developing alternative methods for obtaining ^{18}F on neutrons [6] and protons [6]. Works on a production of ^{18}F and neutrons [7, 8] are known.

The purpose of the present article is the production of a high specific activity ^{18}F on the basis of nanoparticles of calcium fluoride and the effect of Szilard-Chalmers.

RESULTS AND DISCUSSION

For the production of ^{18}F with high specific activity was used Szilard-Chalmers method [9]. Nanoparticles CaF_2 and white salt were used as donor and acceptor, respectively. For the concentration of recoil nuclei in among donor (white salt), nanoparticle sizes CaF_2, containing an activatable element, must be less than or equal to the range of the recoil nuclei (Fig. 1).

The evaporation model for compound nuclei predicts that the emitted neutron energy distribution approaches the form of a Maxwell distribution [10, 11]:

$$w(E_n) = const\,\frac{E_n}{\theta^2}\exp(-\frac{E_n}{\theta}),$$

where $\theta = [(E_\gamma - B_n)/a]^{1/2}$; B_n – separation energy of neutron; E_γ – bremsstrahlung energy. The constant a definition of the speed of ascending of a density of levels of a nucleus at increasing of energy. The experimental estimate of this constant is a ≈ A/15 МэВ$^{-1}$.

However, in light nuclei, a structure is observed in the cross section of the photonuclear reaction (Fig. 2). The cross section for the ^{19}F(γ,n)^{18}F reaction up to a photon energy of 26 MeV is realized due to a small number of single-particle dipole transitions, which can take place in this nucleus [12]. These properties also appear in the spectra of emitted neutrons. In Fig. 3 shows the spectra of neutrons from the ^{19}F(γ,n)^{18}F reaction, which correspond to transitions in the ^{18}F nucleus to the ground, excited, and solid states [14 - 16]. It can be seen that the neutron spectrum has a structure that is related to the discrete states of the final nucleus.

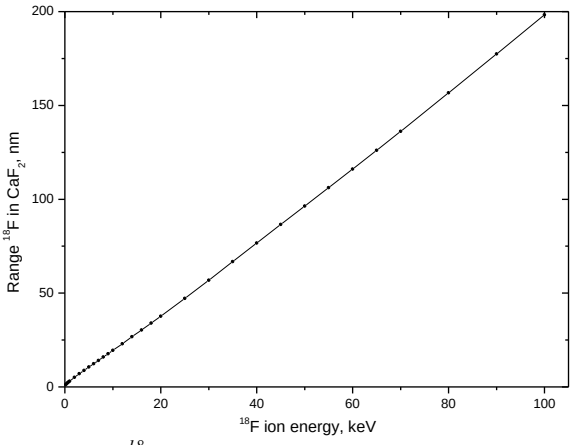

Fig. 1. ^{18}F ranges in natural calcium fluoride

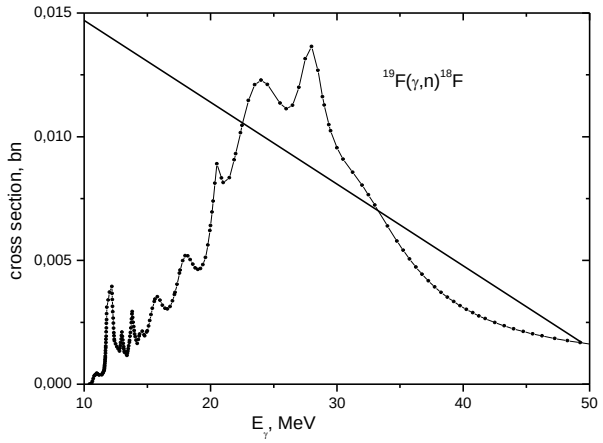

Fig. 2. Cross section of reaction $^{19}F(\gamma,n)^{18}F$ [13]

Procedure of deriving calcium fluoride in nanosize state was the following: the grinding of calcium fluoride in an agate mortar for a long time, the precipitation of powder in the distilled water. The velocity of subsidence of calcium fluoride particles was being determined out of the equation:

$$V = \frac{2g(\rho - \rho_o)r^2}{9\eta},$$

where ρ, ρ_o – density of calcium fluoride particles and water, accordingly; g – acceleration of free falling; r – particle radius; η – dynamic viscosity of water. After 3.5 hours of precipitation the solution was decanted. A solution of calcium fluoride particles was then precipitated for 85 hours. In the obtained sediment were nanoparticles of calcium fluoride in the size from 0.5 to 2.5 μm. In the second case, a solution of calcium fluoride precipitated in the cylinder 434 hours. The supernatant of a solution of calcium fluoride was then evaporated. This allowed obtaining nanoparticles of calcium fluoride with an average size of 180 nm.

The mixture of CaF_2 nanoparticles and an acceptor in the form of nanoparticles of a food salt was irradiated with bremsstrahlung with a maximum energy of 13.5 MeV.

After activation of samples and standards the activity of radioisotopes obtained in reactions $^{19}F(\gamma,n)^{18}F$ has been measured by Ge(Li)-detector with volume 50 cm^3 and with energy resolution 3.2 keV in the area of 1332 keV (Fig. 4).

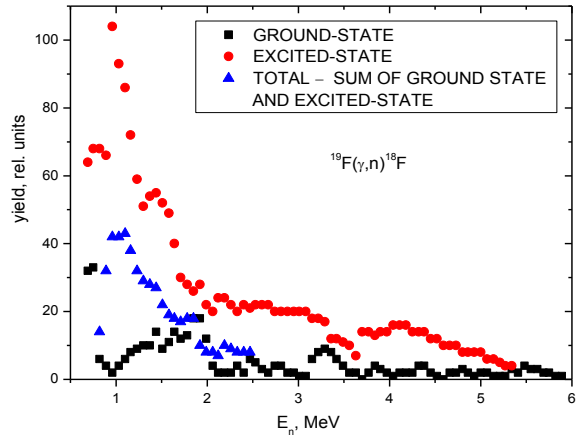

Fig. 3. Photoneutrons from Teflon; pulse height spectra (E_γ(max) = 21 MeV) [16]

The estimate of the average energy of neutrons for a gamma radiation with the maximum energy of 13.5 MeV of reaction reaches 3 MeV. Therefore, the average energy of recoil nuclei of ^{18}F is equal 80 keV. Recoil nuclei ^{18}F can leave nanoparticles of CaF_2 from a depth of 150 nm (see Fig. 1). For the average radius of CaF_2 nanoparticles 1.5 μm the part of recoil nuclei, which can go out into a solution, is 4.75%. The yield of ^{18}F out of extractable phase amounted ~ 3.03%.

For the average radius of CaF_2 nanoparticles 180 nm the part of recoil nuclei, which can go out into a solution, is ~30%. Yield of ^{18}F out of extractable phase amounted 30.2%.

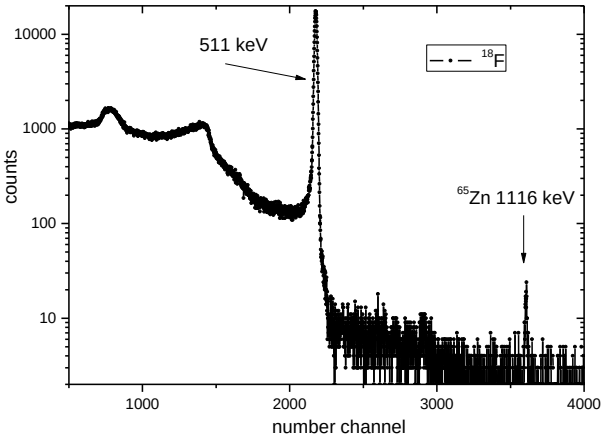

Fig. 4. The spectrum of ^{18}F, $E_{\gamma max}$ = 13.5 MeV

The estimation of the ^{18}F production on an electron accelerator with a power of 10 kW and an energy of 35 MeV can be up to 1 Ci for 4 hours.

CONCLUSIONS

1. The possibility of photonuclear production of carrier free ^{18}F by using recoil nuclei of calcium fluoride nanoparticles that produced by reaction $^{19}F(\gamma,n)^{18}F$ has been found.

2. The mixture of CaF_2 nanoparticles and an acceptor in the form of a nanoparticle of a food salt was irradiated by bremsstrahlung with a maximum energy of 13.5 MeV. Irradiated samples were placed in a distilled water to dissolve the sodium chloride.

3. The maximum yield of the ^{18}F isotope in the solution was 30.2% of the total activity of the sample.

4. The estimation of the ^{18}F production on an electron accelerator with a power of 10 kW and an energy of 35 MeV can be up to 1 Ci for 4 hours.

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ФОТОЯДЕРНЫЙ МЕТОД ПРОИЗВОДСТВА F-18

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^{18}F один из самых важных позитронных излучателей, который обычно используется в позитронной эмиссионной томографии (ПЭТ). Цель нашего исследования состояла в том, чтобы развить метод ядер отдачи в реакции ^{19}F(γ,n)^{18}F для производства свободного ^{18}F. Достаточно высокая энергия ядер отдачи в этой реакции может достигать 200 кэВ. При подготовке получения ^{18}F использовалась смесь наночастиц CaF_2, а также хлорат натрия или клиноптилолита как донор и акцептор соответственно, которые были облучены тормозным излучением с максимальной энергией 13,5 МэВ. Выход изотопа ^{18}F в растворе составлял 30,2% от общей активности образца. Оценка производства ^{18}F на электронном ускорителе мощностью 10 кВт и энергией 25 МэВ может составлять до 1 Ки в течение 4 часов. Показано, что фотоядерный метод производства ^{18}F более эффективен, чем получение ^{18}F на циклотронах.

ФОТОЯДЕРНИЙ МЕТОД ВИРОБНИЦТВА F-18

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^{18}F є один з найважливіших позитронних випромінювачів, який зазвичай використовується в позитронній емісійній томографії (ПЕТ). Мета нашого дослідження полягала в тому, щоб розвинути метод ядер віддачі в реакції ^{19}F(γ,n)^{18}F для виробництва вільного ^{18}F. Досить висока енергія ядер віддачі в цій реакції може досягати 200 кеВ. При підготовці отримання ^{18}F використовувалася суміш наночастинок CaF_2, а також хлорат натрію чи кліноптілоліту як донор і акцептор, відповідно, які були опромінені гальмівним випромінюванням з максимальною енергією 13,5 МеВ. Вихід ізотопу ^{18}F в розчині становив 30,2% від загальної активності зразка. Оцінка виробництва ^{18}F на електронному прискорювачі потужністю 10 кВт і енергією 25 МеВ може становити до 1 Кі протягом 4 годин. Показано, що фотоядерний метод виробництва ^{18}F більш ефективний, ніж отримання ^{18}F на циклотронах.