PHOTONUCLEAR METHOD OF PRODUCTION OF FREE ^{153}Sm BY USE OF NANOPARTICLES OF SAMARIUM OXIDE AND CLINOTILOLITE

N.P. Dikiy[1], A.N. Dovbnya[1], N.V. Krasnoselskiy[2], Yu.V. Lyashko[1], E.P. Medvedeva[1], D.V. Medvedev[1], V.L. Uvarov[1]

[1]National Science Center "Kharkov Institute of Physics and Technology", Kharkov, Ukraine;
[2]S.P. Grigoriev Institute for Medical Radiology, Kharkov, Ukraine
E-mail: ndikiy@kipt.kharkov.ua

Nanoparticles of Sm_2O_3 and clinoptilolite were used for obtaining ^{153}Sm with a high specific activity by means of using recoil nuclei from reaction $^{154}Sm(\gamma,n)^{153}Sm$ in clinoptilolite. After an irradiating nanoparticle mixture by means of bremsstrahlung of electron accelerator, the Sm_2O_3 removed by dissolution in a hydrochloric acid. The part of recoil atoms of ^{153}Sm in clinoptilolite nanoparticles in case use of a bremsstrahlung with the maximum energy of 12.5 MeV is 12.3%. Paths of augmentation of a specific activity and yield ^{153}Sm are considered for use of photonuclear reactions.

PACS: 28.60.+s; 87.53.Jw

INTRODUCTION

All lanthanides have similar chemical properties, they should have similar labeling procedures, and ^{153}Sm might easily be replaced by other radiolanthanides. An important measure of therapeutic use radiolanthanides is their energy deposition in tumors and in normal tissue. The absorbed dose to normal tissue, and especially to critical organs, needs to be kept as low as possible [1 - 3]. ^{153}Sm widely used for the palliative treatment of bone metastases.

Metastatic bone disease is the most frequent manifestation of progression of many cancer diseases. The frequency of bone metastasis in breast cancer varies according to different authors, from 47 to 85% of prostate cancer – from 33 to 85%, thyroid – from 28 to 60%. The pain is the most common symptom of the metastatic bone disease. For example, in breast cancer patients with bone metastases, the bone pain is found in 70…80%. In many cases, pain is the dominant factor in worsening the quality of life of the patient. In this context, the deliverance of the pain or, at least, decrease its intensity is one of the most important factors in improving the quality of life of cancer patients with bone metastases. Different methods used during the treatment of patients with the metastatic bone disease: external beam radiation therapy, chemotherapy, hormone therapy, bisphosphonates, surgical treatment, symptomatic medication, radionuclide therapy.

Radiation therapy is a traditional and one of the most effective methods. The method is based on the possibilities of some β-emitting products accumulate in the bone metastases. «Internal» β-irradiation of metastatic tissue allows achieve reduction of tumor infiltration and ensure prolonged analgesia. In the last 20 years, the use of this type of treatment has become common in many radiological and oncology clinics around the world. The use radiopharmaceuticals spectrum is increasing.

Range R_{90} for β-particles from ^{153}Sm in water, with the energy of 810 keV is 1.45 mm. This causes noticeable damage to bone marrow. Ranges R_{90} of high-energy β-particles of ^{169}Er, ^{175}Yb, and ^{177}Lu in water are 0.6, 0.8, and 0.85 mm, respectively. Therefore, isotopes of ^{169}Er, ^{175}Yb, and ^{177}Lu significantly less are damaging bone marrow. As a result, more acceptable characteristics are for ^{169}Er, ^{175}Yb, ^{177}Lu, with average energy β-particles 100, 127, and 133 keV, respectively:

Decay Data for the ^{153}Sm, ^{175}Yb, and ^{169}Er

Isotope	Decay period, hours	Mean and maximum energy β-particles (intensity), keV (%)	E_{γ}, keV (intensity, %)
^{153}Sm	46.44	199.5, 634.7 (31.3), 225.3, 704.4 (49.4), 264.3, 807.6 (18.4)	103.2 (29.2)
^{169}Er	223.2	98.3, 342.9 (45), 101.0, 351 (55)	–
^{175}Yb	100.6	19.0, 73.8 (20.4) 102.4, 356.3 (6.7) 139.9, 470.1 (72.9)	114 (3.9) 146 (0.67) 282 (6.1) 396 (13.2)
^{177}Lu	160.8	47.7, 177.0 (11.6) 111.7, 385.3 (9.0) 149.35, 498.3 (79.4)	54.6 (1.6) 55.8 (2.8) 113 (6.17) 208 (10.4)

The production of ^{153}Sm is based on the radiative capture of neutrons by isotope ^{152}Sm (206 barns). For neutron flux in the reactor $5\cdot10^{13}$ n/cm^2·s and irradiation during 2 days the ^{153}Sm specific activity 345 mCi/mg achieved (one atom ^{153}Sm on ^{152}Sm 1280 atoms) [4]. The maximum specific activity of ^{153}Sm is 436 Ci/mg. However, in the production of ^{153}Sm in a nuclear reactor, unavoidable presence ^{152}Sm occur, which causes problems when using monoclonal anti-bodies, fragments or small peptides in cancer therapy. Also, ^{153}Sm flow into the tumor is limited because of the large amount of the impurity isotope ^{152}Sm. This causes problems of palliative therapy of bone metastases with certain primary cancers. Use free ^{153}Sm will significantly reduce the side effects of cancer therapy.

^{153}Sm free production is possible using charged particles [5]. The yield of thick ^{153}Sm target is up to 500 GBq/K using deuterons with the energy of 40 MeV. However the economic characteristics of the production of free ^{153}Sm led to the appearance of the project of its production using magnetic separation of ^{152,153}Sm mixture of isotopes, which are obtained, for a reactor [6]. Methods production of free isotopes for palliative

treatment of bone metastases were implemented and by means of reactors. For example, for the production of ^{177}Lu the nuclear reaction ^{176}Yb(n,γ)^{177}Yb → ^{177}Lu used, in which the cross-section of radiative thermal neutron capture is only 2.4 bn. The ^{176}Yb abundance is 12.73%. Therefore, the laser enrichment of ^{176}Yb [7] is used to increase the yield of free ^{177}Lu.

The aim of the present article was to investigate the feasibility of producing the free radionuclide ^{153}Sm by use of recoil nuclei out of Sm_2O_3 nanoparticles from ^{154}Sm(γ,n)^{153}Sm reaction.

RESULTS AND DISCUSSION

For the production of ^{153}Sm with high specific activity was used Szilard-Chalmers method [8]. Nanoparticles Sm_2O_3 and clinoptilolite were used as donor and acceptor, respectively. For the concentration of recoil nuclei in among donor (clinoptilolite), nanoparticle sizes Sm_2O_3, containing an activatable element, must be less than or equal to the range of the recoil nuclei (Fig. 1).

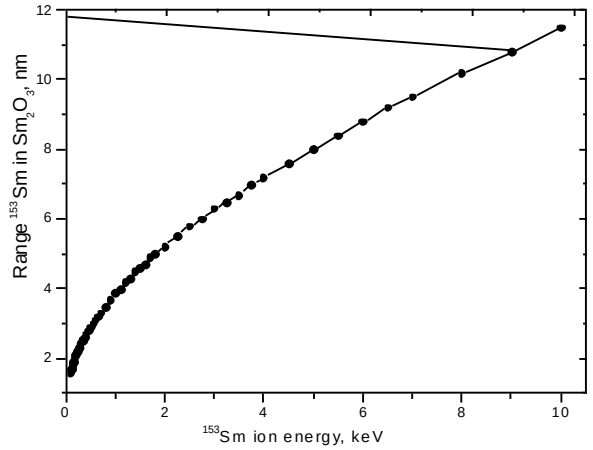

Fig. 1. ^{153}Sm ranges in natural samarium oxide

The energy of the recoil nucleus depends on the pulse gamma ray, neutron pulse emitted, the angle between the direction of doing these pulses, where E_r – recoil energy samarium atom, the M is the mass of samarium atom, m – mass of the neutron, the Q – energy nuclear reaction, c – the speed of light, θ – the angle between the directions of the neutron is-started-up and the incident photon, and has the following form:

$$E_r = \frac{ME_\gamma^2}{2(M+m)^2c^2} + \frac{m^2}{2(M+m)^2}\left\{(E_\gamma + Q)2(M+m) - \frac{E_\gamma^2}{c^2}\right\} -$$

$$-\frac{E_\gamma Mm\cos\theta}{2c(M+m)^2}\left\{\frac{(E_\gamma + Q)2(M+m) - \frac{E_\gamma^2}{c^2}}{Mm}\right\}^{1/2}. \qquad (1)$$

The energy spectrum of neutrons depends on the incident bremsstrahlung, target material. The evaporation model for compound nuclei predicts that the emitted neutron energy distribution approaches the form of a Maxwell distribution [9, 10]:

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

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

The estimate of the average energy of neutrons for a gamma radiation with the energy of 12 MeV of reaction ^{154}Sm(γ,n)^{153}Sm is equal 628 keV [9, 10]. Therefore, the average energy of recoil nuclei of ^{153}Sm is equal 4.1 keV. For this energy recoil nuclei, ^{153}Sm can leave nanoparticles of Sm_2O_3 from a depth of 7.25 mm (see Fig. 1).

The procedure of transforming clinoptilolite in the nanosize state was the following: the grinding of clinoptilolite in an agate mortar for a long time, the precipitation of powder in the distilled water with the subsequent centrifugation. Sm_2O_3 and clinoptilolite samples weighing 300 mg were ground in an agate mortar. After vigorous mechanical stirring Sm_2O_3 and clinoptilolite, sample was irradiated for 3 hours with a maximum bremsstrahlung energy 12.5 MeV. Samarium is being used of natural isotopic distribution. Prevalence of isotopes ^{154}Sm, ^{152}Sm, ^{147}Sm and ^{144}Nd is 22.4, 26.6, 15.09, and 3.15%, respectively. The reaction cross section ^{154}Sm(γ,n)^{153}Sm ($T_{1/2}$=46.44 hours) at the maximum at 12.5 MeV is 260 mb (Fig. 2).

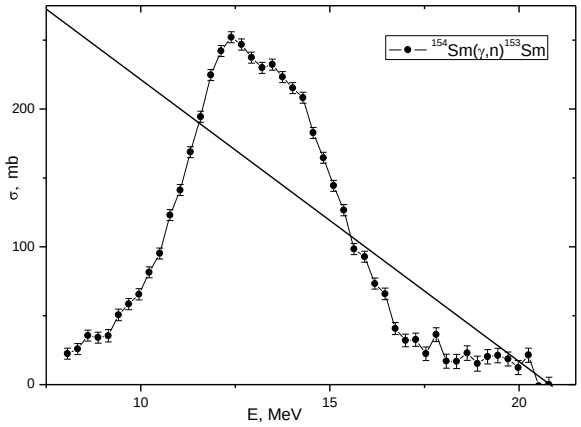

Fig. 2. Cross section of reaction ^{154}Sm(γ,n)^{153}Sm [11]

The reaction of ^{152}Sm(γ,n)^{151}Sm causes the production of ^{151}Sm isotopes with a half-life of 90 years with low radiation. Reaction ^{147}Sm(γ,n)^{146}Sm leads to producing ^{146}Sm isotope with a half-life of $5\cdot10^7$ years through alpha decay. Reactions ^{144}Sm(γ,n)^{143}Sm ($T_{1/2}$=8.83 min) → ^{143}Pm ($T_{1/2}$=265 days) is implemented by hours of isotopes with low levels of radiation.

The activity of radioisotopes obtained in reactions ^{154}Sm(γ,n)^{153}Sm in clinoptilolite and solution Sm_2O_3 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. 3). Only lines of gamma radiation of ^{153}Sm are observed in the spectrum. Note, that recoil nuclei are stopped in the clinoptilolite from all these reactions. Therefore, to obtain 100% of the ^{153}Sm recoil atoms must be used enriched isotope ^{154}Sm.

The sample of Sm_2O_3 and clinoptilolite after an irradiating has been placed into hydrochloric acid (1 ml) for dissolution Sm_2O_3. After a wash in distilled waters, the rest of clinoptilolite has been subjected centrifugation. Have again added the distilled water in clinoptilolite and

have spent centrifugation. After first and second centrifugation the activity of solution Sm_2O_3 was 74.6% and 13.6% of initial, accordingly. The activity clinoptilolite with recoil nuclei of ^{153}Sm was 12.3% from the initial.

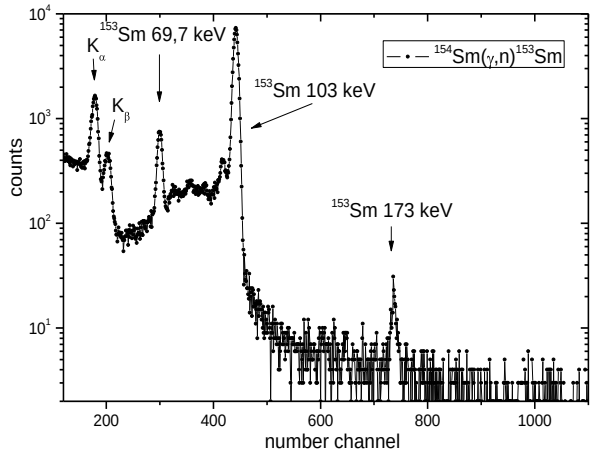

Fig. 3. The spectrum of Sm after irradiated bremsstrahlung with E_{max} = 12.5 MeV

The 1 ml of a hydrochloric acid was added in clinoptilolite for excision of Sm_2O_3 sediment again. Then, the distilled water was added in clinoptilolite and was spent a centrifugation. In this case, clinoptilolite activity with recoil nuclei of ^{153}Sm was 3.09% from the initial. The estimate of a part of atoms ^{153}Sm in clinoptilolite for the average diameter of 150 nanometers equaled 6.4%.

At centrifugation the velocity of subsidence of clinoptilolite particles was being determined out of the equation:

$$V = \frac{3g(\rho - \rho_0)r^2}{9\eta}, \qquad (2)$$

where ρ, ρ_0 – density of clinoptilolite particles and water, accordingly, g – acceleration of free falling, r – particle radius, η – dynamic viscosity of water. The velocity of turnovers of the centrifuge was 12 thousand/s. In this case, the sedimentation at a centrifugation was accomplished for the diameter of clinoptilolite particles from 60 nanometers.

Therefore, the part nanoparticles clinoptilolite is less in the dimension 60 nanometers can get in decant solution Sm_2O_3. More effective are use nanoparticles Sm_2O_3 as it is possible the smaller dimensioning (∅ 10…20 nanometers). It will allow enlarging an amount of recoil nuclei ^{153}Sm which will abandon nanoparticles Sm_2O_3 (to 20% for ∅ 20 nanometers). Diameter nanoparticles clinoptilolite should compound about 100 nanometers [12].

For the mixture of Sm_2O_3 nanoparticles and clinoptilolite on the linear accelerator of electrons of NSC KIPT with the energy 23 MeV and a current 700 μA is possible to produce 1 Ci ^{153}Sm during the day by using of samarium (40 g) with a natural isotopic composition. In the target of similar mass, but enriched in ^{154}Sm, the daily yield can attain 5 Ci for ^{153}Sm.

CONCLUSIONS

The possibility of photonuclear production of free ^{153}Sm medical radioisotopes produced by the reaction $^{154}Sm(\gamma,n)^{153}Sm$ ($T_{1/2}$=46.44 hours) by Szilard-Chalmers method was investigated. In this case, the nanoparticle composition of Sm_2O_3 and clinoptilolite was used. As a result, there is prepared with high specific activity of ^{153}Sm which is necessary for systemic radionuclide therapy, especially when using peptides with pharmacological side effects.

In NSC KIPT on the linear accelerator of electrons with E=23 MeV and a current 700 μA it is possible to produce 1 Ci ^{153}Sm during the day by using of samarium oxide nanoparticles (40 g) of natural isotope composition.

REFERENCES

1. H. Uusijarvi, P. Bernhardt, F. Rosch, et al. Electron- and Positron-Emitting Radiolanthanides for Therapy: Aspects of Dosimetry and Production // *J. Nucl. Med.* 2006, v. 47, p. 807-814.
2. F. Monroy-Guzman, F.J. Barreiro, E.J. Salinas, et al. Radiolanthanides Device Production // *World J. Nucl. Sci. Tech*. 2015, v. 5, p. 111-119.
3. N.P. Dikiy, Yu.V. Lyashko, E.P. Medvedeva, et al. Kinetics of ^{153}Sm oxabiphor in the blood of cancer patients undergoing complex therapy for bone metastasis // *Problems of Atomic Science and Technology. Series "Nuclear Physics Investigations"*. 2015, № 3, p. 73-75.
4. A. Bahrami-Samani, M. Ghannadi-Maragheh, Z. Naseri, et al. Production, quality control and biological evaluation of ^{153}Sm-TTHMP as a possible bone palliation agent // *Iran J. Nucl. Med.* 2011, v. 19(2), p. 60-68.
5. F. Tarkanyi, S. Takacs, A. Hermanne, et al. Cross sections of deuteron induced reactions on natSm for production of the therapeutic radionuclide ^{145}Sm and ^{153}Sm // *Appl. Rad. Isot.* 2014, v. 91, p. 31-37.
6. J.M. D'Auriaa, K. Franka, A. Ketringb, et al. Production of high specific activity of ^{153}Sm by isotope separation following neutron irradiation // *Abs. 8-th Inter. Conf. on Isotopes.* 2014, Omnipress, Chicago, USA, p. 115.
7. H. Park, D.H. Kwon, Y. Cha, et al. Laser Isotope Separation of Yb-176 for the Production of Lu-177 // *Proced. of the KNS spring meeting*. 2005, 2 p.
8. L. Szilard, T.A. Chalmers. Detection of neutrons liberated from beryllium by gamma-rays: a new technique for inducing radioactivity // *Nature.* 1934, v. 134, p. 494-495.
9. V.V. Varlamov, B.S. Ishhanov, I.M. Kapitonov. *Photonuclear reactions. Modern status experimenttal data.* M.: "University book", 2008, 304 p.
10. B.S. Ishkhanov, I.M. Kapitonov. *The interaction of electromagnetic radiation with atomic nuclei.* M.: "MGU", 1979, 216 p.
11. P. Carlos, H. Beil, R. Bergere, et al. The giant dipole resonance in the transition region of the samarium // *Nucl. Phys.* 1974, v. 225A, p. 171-175.
12. N.P. Dikiy, A.N. Dovbnya, Yu.V. Lyashko, et al. Radiative stability and sorption ability of clinoptilolite nanoparticles // *Problems of Atomic Science and Technology. Series "Nuclear Physics Investigations"*. 2015, № 3, p. 76-78.

Article received 14.03.2016

ФОТОЯДЕРНЫЙ МЕТОД ПРОИЗВОДСТВА СВОБОДНОГО ^{153}Sm ПРИ ИСПОЛЬЗОВАНИИ НАНОЧАСТИЦ ОКСИДА САМАРИЯ И КЛИНОПТИЛОЛИТА

Н.П. Дикий, А.Н. Довбня, Н.В. Красносельский, Ю.В. Ляшко, Е.П. Медведева, Д.В. Медведев, В.Л. Уваров

Наночастицы Sm_2O_3 и клиноптилолита использовались для получения ^{153}Sm с высокой удельной активностью посредством торможения ядер отдачи из реакции $^{154}Sm(\gamma,n)^{153}Sm$ в клиноптилолите. После облучения тормозным излучением электронного ускорителя Sm_2O_3 удалялся растворением в соляной кислоте. Доля атомов отдачи ^{153}Sm в наночастицах клиноптилолита при использовании тормозного излучения с максимальной энергией 12,5 МэВ составила 12,3%. Обсуждаются пути увеличения удельной активности и выхода ^{153}Sm при использовании фотоядерных реакций.

ФОТОЯДЕРНИЙ МЕТОД ВИРОБНИЦТВА ВІЛЬНОГО ^{153}Sm ПРИ ВИКОРИСТАННІ НАНОЧАСТИНОК ОКСИДУ САМАРІЮ І КЛИНОПТИЛОЛІТУ

М.П. Дикий, А.М. Довбня, М.В. Красносельський, Ю.В. Ляшко, О.П. Медведєва, Д.В. Медведєв, В.Л. Уваров

Наночастинки Sm_2O_3 і клиноптилоліту використовувалися для одержання ^{153}Sm з високою питомою активністю за допомогою гальмування ядер віддачі з реакції $^{154}Sm(\gamma,n)^{153}Sm$ у клиноптилоліті. Після опромінення гальмовим випромінюванням електронного прискорювача Sm_2O_3 видалявся розчиненням у соляній кислоті. Доля атомів віддачі ^{153}Sm у наночастинках клиноптилоліту при використанні гальмового випромінювання з максимальною енергією 12,5 МеВ склала 12,3%. Обговорюються шляхи збільшення питомої активності і виходу ^{153}Sm при використанні фотоядерних реакцій.