PHOTONUCLEAR PRODUCTION OF Pm-149

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^{153}Sm is successfully used for palliative treatment of patients with bone metastases and pain. ^{153}Sm is being produced in the reactors by means of irradiating of ^{152}Sm. In radio-labelled radiopharmaceuticals per each isotope of ^{153}Sm contained about 1000 atoms of the ^{152}Sm, which greatly influence the kinetics of its transport into the tumor. Production of ^{149}Pm isotopes that do not contain impurities of other isotopes, it was implemented using photonuclear reactions. The characteristics ^{149}Pm is practically coincides with the parameters of ^{153}Sm. The irradiation of neodymium of natural isotopic composition was carried out by means of bremsstrahlung with a maximum energy of 12.5 MeV. For production of ^{149}Pm the reaction $^{150}Nd(\gamma,n)^{149}Nd$ ($T_{1/2}$=1.73 hours) $\rightarrow$ ^{149}Pm was used. Reaction $^{148}Nd(\gamma,n)^{147}Nd$ ($T_{1/2}$=10.93 days) $\rightarrow$ ^{147}Pm ($T_{1/2}$=2.62 years) will lead to low activity ^{147}Pm provided daily extraction ^{149}Pm. The rare earth elements of cerium group successfully are separated in a multistage extraction column using a normal tributyl ester of phosphoric acid.

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INTRODUCTION

The metastatic bone lesions develop in various cancers and are accompanied by persistent pain. For the palliative treatment of patients with bone metastases and pain successfully used isotopes. Intensively used for this purpose ^{153}Sm, which is produced in the reactors by irradiating isotope ^{152}Sm. Despite the large capture cross section of thermal neutrons per each isotope of ^{153}Sm contains about 1000 atoms of the ^{152}Sm, which greatly influence the kinetics of its transport into the tumor.

Targeted tumor radiotherapy requires radioisotopes with high specific activity, high LET particle emissions, photon emissions for monitoring therapy with imaging and follow-up as well as adsorbed dose distribution and half-lives long enough to allow the preparation and distribution of radiopharmaceuticals. Encouraging clinical results have been achieved with ^{177}Lu-DOTATATE and [^{177}Lu-DOTA^{0}-Tyr^{3}]-octreotide (^{177}Lu-DOTATOC) in the treatment of neuroendocrine tumors [1 - 3]. Because all lanthanides have similar chemical properties, they should have similar labeling procedures, and ^{177}Lu might easily be replaced by other radiolanthanides (Table).

Decay Data for the ^{153}Sm, ^{149}Pm and ^{177}Lu

Isotope	Decay period, hours	Energy β-particles (intensity), keV (%)	Energy γ-radiation, keV, (intensity, %)
^{153}Sm	46.44	640 (32), 710 (49), 810 (19)	103.2 (29,2)
^{149}Pm	53.08	1072 (97)	285.6 (2,9)
^{177}Lu	160.8	497 (90)	208.3 (7.4)
^{169}Er	223.2	322 (15), 330 (85)	–

Depending on the production route, either no-carrier-added (nca) or carrier-added (ca) radionuclides are obtained. High specific activity is necessary for systemic radionuclide therapy [4], especially when using peptides with pharmacological side effects [5].

An important criterion for therapeutic use radiolanthanides is their energy deposition in tumors and in a normal tissue. The absorbed dose to a normal tissue, and especially to the organs concentrating a certain isotope, should be maintained so low as far as possible. These radionuclides with low emission of a gamma radiation should be used. On Fig. 1 the qualities of medical isotopes of lanthanoids are given at use for radiotheraphy of tumours [6]. It is possible to see that ^{149}Pm insignificantly yields at the use of therapy of tumors of a smaller size of ^{177}Lu and ^{153}Sm. Merit of ^{149}Pm is presented of gamma radiation with energy 208 keV.

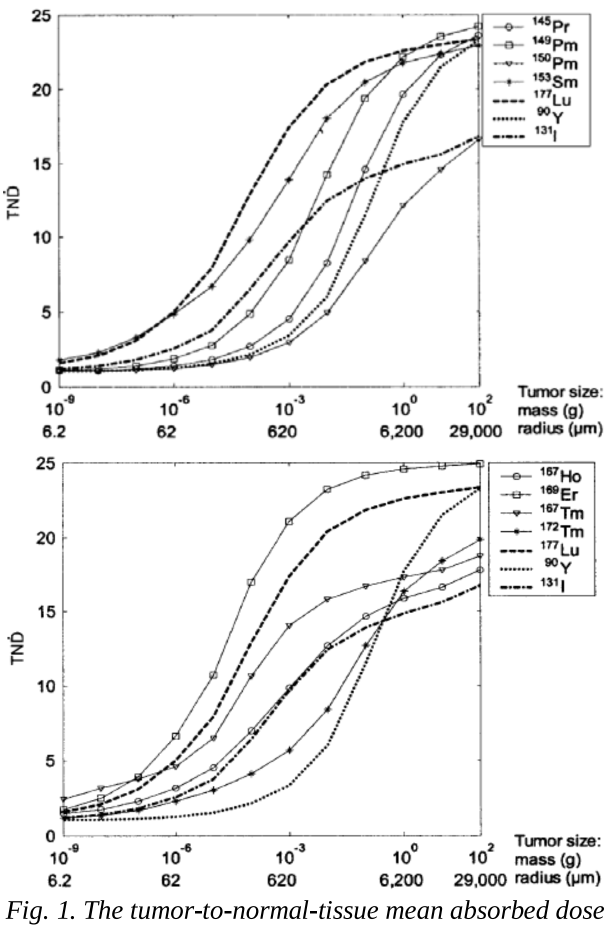

Fig. 1. The tumor-to-normal-tissue mean absorbed dose rate ratio ($TN\dot{D}$) [6]

The essential issue in the palliative treatment of disseminated bone metastases is action of radiation of isotopes by a marrow. Therefore, for therapy of osteal metastases the best properties possess of ^{169}Er isotopes (Fig. 1). However, absence of the gamma radiation impedes diagnostic of deposition of ^{169}Er in a tumor and in normal tissue during treatment.

The carrier free ^{149}Pm can be efficiently produced and isolated from an enriched ^{148}Nd target after irradiating in reactor [7]. The aim of this paper is realize of technology of carrier free ^{149}Pm by means of photonuclear reaction. The characteristics of ^{149}Pm is practically coincide with parameters of ^{153}Sm (see Table).

RESULTS AND DISCUSSION

The irradiation of neodymium of natural isotopic composition and weighing 50 mg was carried out by means of bremsstrahlung with a maximum energy of 12.5 MeV. Prevalence of isotopes ^{148}Nd and ^{150}Nd is 5.73% and 5.62%, respectively. The reaction cross section $^{150}Nd(\gamma,n)^{149}Nd$ ($T_{1/2}$=1.73 hours) $\rightarrow$ ^{149}Pm at the maximum at 12.5 MeV is 220 mb (Fig. 3). After activation of samples and standards the activity of radioisotopes obtained in reactions $^{150}Nd(\gamma,n)^{149}Nd$ 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. 2).

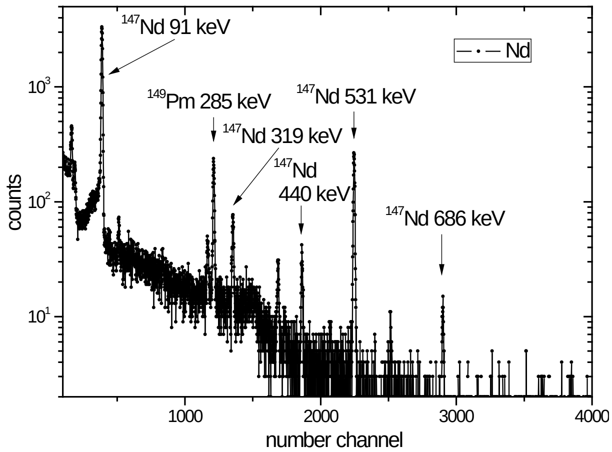

Fig. 2. The spectrum of Nd after irradiated bremsstrahlung with E_{max} = 12 MeV

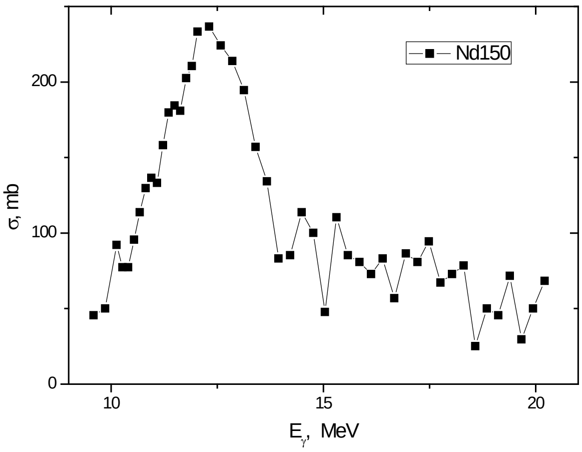

Fig. 3. Cross section of reaction $^{150}Nd(\gamma,n)^{149}Nd$ [9]

Reaction $^{148}Nd(\gamma,n)^{147}Nd$ ($T_{1/2}$=10.93 days) $\rightarrow$ ^{147}Pm ($T_{1/2}$=2.62 years) (Fig. 4) will lead to low activity ^{149}Pm provided daily extraction ^{149}Pm. The rare earth elements of cerium group successfully are separated in a multistage extraction column using a normal tributyl ester of phosphoric acid [8].

The cross section of the thermal neutron capture of daughter isotopes ^{149}Pm is 40140 b. Therefore, use of ^{149}Pm of a neutron capture therapy is possible.

On the linear accelerator of electrons of NSC KIPT with an energy of 36 MeV and a current 260 μA it is possible to produce 0.5 Ci ^{149}Pm during the day with using of neodymium (30 g) with a natural isotopic composition [10, 11]. In the targets of similar masses, but enriched in ^{150}Nd, the daily yield can attain 10 Ci for ^{149}Pm.

Let's notice that obtaining of ^{153}Sm with a high specific activity by means of a magnetic separation are undertaken [12].

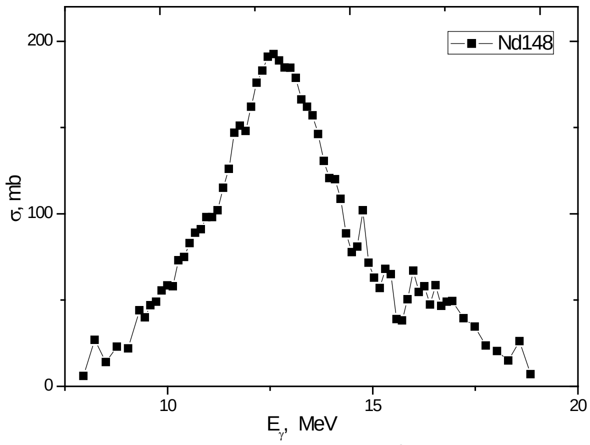

Fig. 4. Cross section of reaction $^{148}Nd(\gamma,n)^{147}Nd$ [9]

CONCLUSIONS

The possibility of photonuclear production of ^{149}Pm medical radioisotopes produced by reaction $^{150}Nd(\gamma,n)^{149}Nd$ ($T_{1/2}$=1.73 hours) $\rightarrow$ ^{149}Pm was investigated. As a result, there is prepared with high specific activity of ^{149}Pm 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=36 MeV and a current 260 μA it is possible to produce 0.5 Ci ^{149}Pm during the day by using of neodymium (30 g) of natural isotope composition.

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ФОТОЯДЕРНЫЙ МЕТОД ПРОИЗВОДСТВА Pm-149

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Для паллиативной терапии больных с метастазами в кости и болевым синдромом успешно используется ^{153}Sm, который производится на реакторах при облучении изотопа ^{152}Sm. В используемом радиопрепарате на каждый изотоп ^{153}Sm приходится около 1000 атомов изотопа ^{152}Sm, что существенно влияет на кинетику его поступления в опухоль. Производство изотопов, не содержащих примесей других изотопов, предполагается реализовать при помощи фотоядерного производства ^{149}Pm, который по своим характеристикам практически совпадает с параметрами ^{153}Sm. Проведено облучение неодима естественного изотопного состава тормозным излучением с максимальной энергией 12,5 МэВ. Для производства ^{149}Pm использовалась реакция $^{150}Nd(\gamma,n)^{149}Nd$ ($T_{1/2}$=1,73 часа) $\rightarrow$ ^{149}Pm. Реакция $^{148}Nd(\gamma,n)^{147}Nd$ ($T_{1/2}$=10,93 дня) $\rightarrow$ ^{147}Pm ($T_{1/2}$=2,62 года) будет создавать малую активность ^{147}Pm при условии ежедневного выделения ^{149}Pm. Редкоземельные элементы цериевой группы успешно разделяются в многоступенчатых экстракционных колоннах с использованием нормального трибутилового эфира ортофосфорной кислоты.

ФОТОЯДЕРНИЙ МЕТОД ВИРОБНИЦТВА Pm-149

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Для паліативної терапії хворих з метастазами в кістках і болісному синдромі успішно використовується ^{153}Sm, що виробляється на реакторах при опроміненні ізотопу ^{152}Sm. У радіопрепараті, який використовується, на кожен ізотоп ^{153}Sm приходиться близько 1000 атомів ізотопу ^{152}Sm, що істотно впливає на кінетику його надходження в пухлину. Виробництво ізотопів, що не містять домішок інших ізотопів, передбачається реалізувати з використанням фотоядерного виробництва ^{149}Pm, що за своїми характеристиками практично збігається з параметрами ^{153}Sm. Проведено опромінення неодиму природного ізотопного складу гальмівним випромінюванням з максимальною енергією 12,5 МеВ. Для виробництва ^{149}Pm використовувалася реакція $^{150}Nd(\gamma,n)^{149}Nd$ ($T_{1/2}$=1,73 год.) $\rightarrow$ ^{149}Pm. Реакція $^{148}Nd(\gamma,n)^{147}Nd$ ($T_{1/2}$=10,93 дня) $\rightarrow$ ^{147}Pm ($T_{1/2}$=2,62 роки) буде утворювати малу активність ^{147}Pm за умови щоденного виділення ^{149}Pm. Рідкоземельні елементи церієвої групи успішно розділяються в багатоступінчастих екстракційних колонах з використанням нормального трибутилового ефіру ортофосфорної кислоти.