PHOTONUCLEAR PRODUCTION OF Yb-175

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The use of photonuclear nanotechnology makes it possible to obtain the ^{175}Yb isotope with acceptable characteristics without the content of impurities of other isotopes. Irradiation of Yb_2O_3 nanoparticles of a natural isotope composition weight`s 123.5 mg in a mixture with clinoptilolite nanoparticles by bremsstrahlung with an E_{max}=13.5 MeV was carried out. The prevalence of ^{176}Yb isotopes is 12.6%. The reaction cross section of ^{176}Yb(γ,n)^{175}Yb ($T_{1/2}$=100.8 hours) have two maximums at 12.5 and 16 MeV about 350 mbn. After separation of the clinoptilolite particles, the activity of ^{175}Yb in the theirs was 3.2% of the total activity of the sample for the size of Yb_2O_3 nanoparticles of the 180 nm.

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INTRODUCTION

Metastatic bone damage is the most common manifestation of progression in many cancers. The frequency of bone metastases in breast cancer varies from 47 to 85% according to different authors, from 33 to 85% in prostate cancer, from 28 to 60% in the thyroid gland, from 33 to 40% in the kidneys, from 30 to 55%. In many cases, pain syndrome is the dominant factor that worsens the patient's quality of life. Sometimes this is the only complaint of the patient [1].

Isotopes ^{153}Sm and ^{177}Lu are successfully used for carrying out of palliative therapy of patients with metastasises in a bone and a painful syndrome. These isotopes are produced in reactors upon irradiation of ^{152}Sm and ^{176}Lu isotopes. Despite the large thermal neutron capture cross sections (206 bn for ^{152}Sm and 2097 bn for ^{176}Lu), each isotope ^{153}Sm and ^{177}Lu account for a significant number of impurity atoms that affect the kinetics of their uptake by a tumor. Also in the production of ^{177}Lu, an impurity of ^{177m}Lu forms on the reactors. More preferably, the ^{176}Yb(n,γ)^{177}Yb → ^{177}Lu reaction is, but it has a low cross section (about 1 bn). At present, no producer of high specific activity ^{177}Lu exists in Europe and clinics are dependent on the supplies from the U.S.A., Canada and Russia. Unfortunately, the quality of ^{177}Lu preparations decreases with the time needed for delivery and the price increases [1].

More acceptable nuclear characteristics of ^{175}Yb (Table) allow reducing the influence of β-particles on the bone marrow. Therefore, intensive research is being conducted on the production of this isotope [2 - 5]. The use of photonuclear nanotechnology makes it possible to obtain the ^{175}Yb isotope with better characteristics (Table) without the content of impurities of other isotopes.

With used of reactors highly enriched ^{174}Yb targets are needed for the production ^{175}Yb in order to obtain high radio-nuclidic purity. If natural ytterbium is used as target, ^{169}Yb and ^{177}Yb will also be produced. The cross-section of ^{168}Yb(n,γ)^{169}Yb is very large (2300 barns) but the percent abundance is small (0.13%); and being a long-lived isotope the amount formed will be relatively low at short irradiation times. ^{169}Yb ($T_{1/2}$ = 32.018 days) decays by electron capture process (100% K electron capture) followed by the emission of Auger electrons of low yield and the principle γ photons are of reasonably low energy (177 keV (22.5%), 197 keV (35.9%)). Though considered as a radionuclidic impurity, the presence of small amounts of ^{169}Yb will not cause any serious problem in the in vivo application of ^{175}Yb. ^{176}Yb present in the natural target (natural abundance 12.62%) will get activated to ^{177}Yb which decays with a $T_{1/2}$ of 1.5 hours to ^{177}Lu. The specifi c activity of ^{175}Yb produced by direct (n,γ) reaction is adequate for therapeutic applications such as bone pain palliation and small joint synovectomy, however, is not adequate for radiolabeling peptides and antibodies [2].

Decay Data for the ^{153}Sm, ^{177}Lu and ^{175,169}Yb

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)
^{177}Lu	160.8	177 (11.6); 385.3 (9); 498.3 (79.4)	55.8 (2.77); 112.9 (6.17); 208.4 (10.36)
^{175}Yb	100.8	73.8 (20.4); 356.3 (6.7); 470.1 (72.9)	54.1 (3.74); 113.8 (3.87); 282.5 (6.13); 396.3 (13.2)
^{169}Yb	768.4	50.4 (34.3); 71.1 (6.2); 99.7 (5.5); 117.8 (10.9); 120.4 (5.2); 138.6 (12.9); 187.8 (2.1)	63.1 (43.6); 109.8 (17.4); 130.5 (11.4); 177.2 (22.3); 197.8 (35.9); 307.7 (10)

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 [6], especially when using peptides with pharmacological side effects [7].

The essential issue at 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. However, absence of the gamma radiation impedes diagnostic of deposition of ^{169}Er in a tumor and in normal tissue during treatment.

The aim of this paper is realize of technology of carrier free ^{175}Yb by means of photonuclear reaction. The characteristics of ^{175}Yb is practically coincide with parameters of ^{153}Sm and ^{177}Lu (Table).

RESULTS AND DISCUSSION

Irradiation of Yb_2O_3 nanoparticles of a natural isotope composition weight`s 123.5 mg in a mixture with clinoptilolite nanoparticles (265.4 mg) by bremsstrahlung with an E_{max}=13.5 MeV was carried out. The prevalence of ^{176}Yb isotope is 12.6%. The reaction cross section of ^{176}Yb(γ,n)^{175}Yb ($T_{1/2}$=100.8 hours) have two maximums at 12.5 and 16 MeV about 350 mbn (Fig. 1). Also, nuclear reactions take place on the isotopes ^{170,168}Yb during the irradiation by bremsstrahlung of ytterbium with natural isotopic composition. The prevalence of ^{170,168}Yb isotopes are 3.14% and 0.135%, respectively. The reaction cross section of ^{170}Yb(γ,n)^{169}Yb ($T_{1/2}$=32.018 days) also has two maximums at 12.5 and 16 MeV about 350 mbn (Fig. 2). Therefore, the ^{169}Yb impurity, when using ytterbium with a natural isotopic composition, may amount to about 3% of the activity. And as mentioned above, the presence of small amounts of ^{169}Yb will not cause any serious problem in the "in vivo" application of ^{175}Yb. The use of the enriched ^{176}Yb allows a significant reduction in the ^{169}Yb impurity.

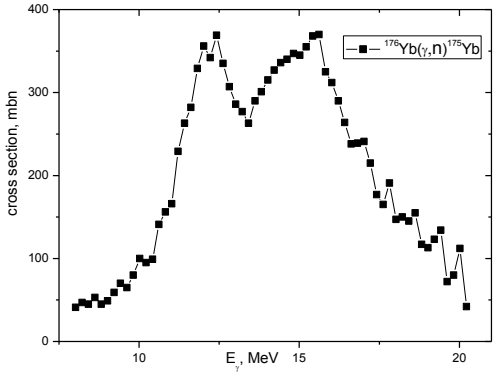

Fig. 1. Cross section of reaction $^{176}Yb(\gamma,n)^{175}Yb$ [8]

Also, nuclear reactions take place on the isotopes ^{170,168}Yb during of the irradiation by bremsstrahlung of ytterbium of a natural isotopic composition. The prevalence of ^{170,168}Yb isotopes are 3.14% and 0.135%, respectively. The reaction cross section of ^{170}Yb(γ,n)^{169}Yb ($T_{1/2}$=32.018 days) also has two maximums at 12.5 and 16 MeV about 350 mbn (Fig. 2). Therefore, the ^{169}Yb impurity, when using ytterbium with a natural isotopic composition, may amount to about 3% of the activity. Using enriched ^{176}Yb allows to significantly reduce the impurity of ^{169}Yb.

Procedure of deriving Yb_2O_3 in nanosize state was the following: the grinding of ytterbium oxide in an agate mortar for a long time, the precipitation of powder in the distilled water. The velocity of subsidence of of ytterbium oxide particles was being determined out of the equation:

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

where ρ, ρ_o – density of ytterbium oxide particles and water, accordingly; g – acceleration of free falling; r – particle radius; η – dynamic viscosity of water. The powder of yttrium oxide was placed in a cylinder with distilled water 12 cm high. A solution of ytterbium oxide particles was then precipitated for 735 hours. The supernatant of a solution of ytterbium oxide was then evaporated. This allowed obtaining nanoparticles of ytterbium oxide with an average size of 180 nm.

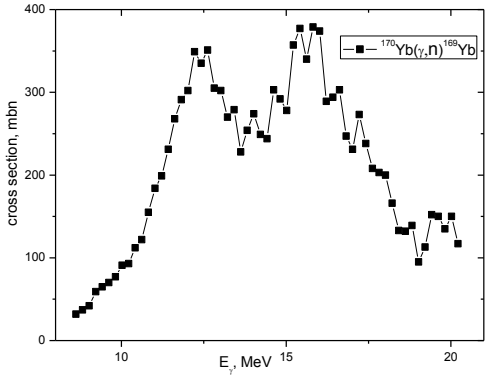

Fig. 2. Cross section of reaction $^{170}Yb(\gamma,n)^{169}Yb$ [8]

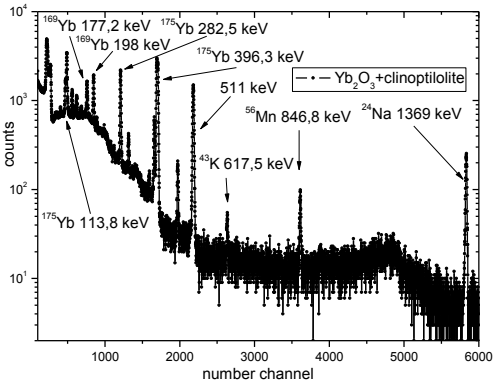

Fig. 3. The spectrum of Yb_2O_3+clinoptilolite after irradiated bremsstrahlung with E_{max} = 13.5 MeV

The particles of clinoptilolite were obtained by the following method: grinding in an agate mortar, deposition in a cylinder with distilled water 10 cm high for 1 hour, reprecipitation of the supernatant in the cylinder (H = 10 cm) for 4.5 hours. After decantation, the precipitate was evaporated on a water bath. This made it possible to obtain clinoptilolite particles 2.5 μm in size.

After activation of samples and standards the activity of radioisotopes obtained in reactions ^{176}Yb(γ,n)^{175}Yb 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. In Fig. 3 shows the spectrum of a mixture of ytterbium nanoparticles of natural isotopic composition (180 nm) and of clinoptilolite particles (2.5 μm) (see Fig. 3) after irradiation with bremsstrahlung.

The estimate of the average energy of neutrons for a gamma radiation with the energy of 13.5 MeV of reaction ^{176}Yb(γ,n)^{175}Yb is equal 980 keV [9, 10]. Therefore, the average energy of recoil nuclei of ^{175}Yb is equal 5.6 keV. For this energy recoil nuclei, ^{175}Yb can leave nanoparticles of Yb_2O_3 from a depth of 3.8 nm (Fig. 4).

The procedure for the isolation of the particles clinoptilolite was the following: a mixture of ytterbium nanoparticles and clinoptilolite particles was mixed in of magnetic stirrer; the precipitation of powder in a cylinder with the distilled water 12 cm high for 4.5 hours; drying the sediment in a water bath. This procedure was carried out twice. The spectrum of the precipitate of clinoptilolite particles with implanted atoms ^{169,175}Yb is

shown in Fig. 5. The yield of ^{175}Yb was 1.7% of the total activity of the mixture of ytterbium nanoparticles and clinoptilolite particles. The given value of an yield practically coincides with settlement value of 1.53%.

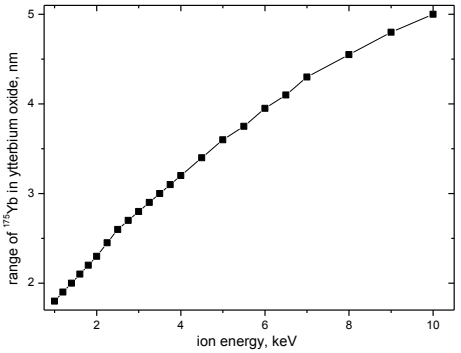

Fig. 4. ^{175}Yb ranges in ytterbium oxide

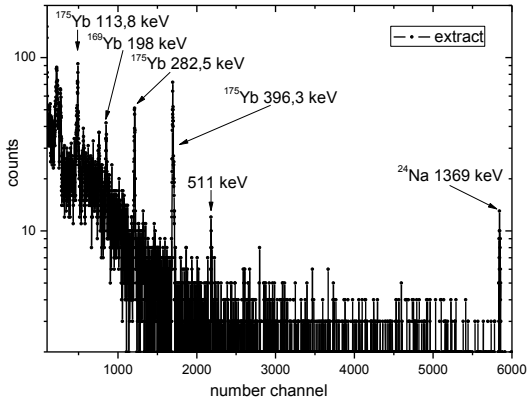

Fig. 5. The spectrum of separated clinoptilolite particles after irradiated bremsstrahlung with E_{max}=13.5 MeV

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 1.2 Ci ^{175}Yb during the day with using of ytterbium (30 g) with a natural isotopic composition [4]. In the targets of similar masses, but enriched in ^{176}Yb, the daily yield can attain 8 Ci for ^{175}Yb.

CONCLUSIONS

The possibility of photonuclear production of ^{175}Yb medical radioisotopes produced by reaction ^{176}Yb(γ,n)^{175}Yb ($T_{1/2}$=100.8 hours) was investigated. As a result there is preparation with high specific activity of ^{175}Yb 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 1.2 Ci ^{175}Yb during the day by using of ytterbium (30 g) of natural isotope composition.

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ФОТОЯДЕРНЫЙ МЕТОД ПРОИЗВОДСТВА Yb-175

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Использование фотоядерных нанотехнологий позволяет получить изотоп ^{175}Yb с лучшими характеристиками без содержания примесей других изотопов. Проведено облучение наночастиц Yb_2O_3 с массой естественного изотопного состава 123,5 мг в смеси с наночастицами клиноптилолита с помощью тормозного излучения с E_{max}=13,5 МэВ. Распространенность изотопов ^{176}Yb составляет 12,6%. Сечение реакции ^{176}Yb(γ,n)^{175}Yb ($T_{1/2}$=100,8 ч) имеет два максимума при 12,5 и 16 МэВ около 350 мбн. После отделения частиц клиноптилолита активность ^{175}Yb в них составляла 3,2% от общей активности образца для размеров наночастиц Yb_2O_3 180 нм.

ФОТОЯДЕРНИЙ МЕТОД ВИРОБНИЦТВА Yb-175

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Використання фотоядерних нанотехнологій дозволяє отримати ізотоп ^{175}Yb з кращими характеристиками без вмісту домішок інших ізотопів. Проведено опромінення наночастинок Yb_2O_3 з масою природного ізотопного складу 123,5 мг у суміші з наночастинками кліноптілоліта за допомогою гальмівного випромінювання з E_{max}=13,5 МеВ. Поширеність ізотопів ^{176}Yb становить 12,6%. Перетин реакції ^{176}Yb(γ,n)^{175}Yb ($T_{1/2}$=100,8 год.) має два максимуми при 12,5 і 16 МеВ близько 350 мбн. Після відділення частинок кліноптілоліта активність ^{176}Yb у них становила 3,2% від загальної активності зразка для розмірів наночастинок Yb_2O_3 180 нм.