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POSSIBILITES OF ISOTOPES PRODUCTION OF ^{153}Sm, ^{175}Yb, ^{186}Re AT THE ELECTRONIC ACCELERATOR

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Photonuclear technology for producing osteotropic isotopes ^{153}Sm ($T_{1/2}$ = 1.9 days, E_β = 0.8 MeV, E_γ = 103.2 keV), ^{175}Yb ($T_{1/2}$ = 4.2 days, E_β = 0.5 MeV, E_γ = 396.3 keV) and ^{186}Re ($T_{1/2}$ = 3.8 days, E_β = 1.1 MeV, E_γ = 137.2 keV) with using nanoparticles (50…80 nm) of oxides of these elements and the Szilard-Chalmers reaction to increase specific activity have been developed at the NSC KIPT electron accelerator. Such medical isotopes are not produced in Ukraine. The overall electron accelerator isotope yield when bremsstrahlung irradiated these samples with a maximum energy of 40 MeV and a current of 250 μA for ^{186}Re and 13.5 MeV and a current of 500 μA for ^{153}Sm and ^{175}Yb has been shown to have the advantages of higher specific activity, negligible the content of impurities and does not require immobilization of radioactive waste in comparison with a reactor and a cyclotron.

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INTRODUCTION

Bone metastases are a frequent complication in various tumors such as prostate, breast, lung often causing progressive pain [1]. Bone metastases in the skeleton occur in many patients with solid malignant tumors.

For the treatment of patients with bone metastases, various methods of treatment are used: surgical treatment, chemotherapy, external beam radiation therapy and radionuclide therapy [2, 3].

Recently, in various countries, in the treatment of patients with multiple metastases, radionuclide therapy has been actively used. The method is based on the ability of β-emitting drugs to accumulate in bone metastases. In world practice, for the palliative therapy of bone metastases, radiopharmaceuticals based on ^{153}Sm, ^{175}Yb, ^{89}Sr, ^{186,188}Re, ^{177}Lu, ^{90}Y, ^{32,33}P are now used. These radionuclides are delivered to pathological localization by various transport compounds based on bisphosphonate. In bisphosphonate the groups attached to central carbon atom determine their potency as anti-resorption drugs. There is a relationship between bisphosphonate`s molecular structure and hydroxyapatite – $Ca_{10}(PO_4)_6(OH)_2$ – the main bone mineral component. These compounds are fixed in the bone matrix instead of calcium.

The main optimal properties of radiopharmaceuticals for radionuclide therapy in bone metastases are as follows: 1 – high selective accumulation in metastases; 2 – rapid elimination from healthy tissue; 3 – maximum energy of β-radiation from 0.5 to 2.0 MeV; 4 – path length of β-particles in tissues – up to 1 cm; 5 – the possibility of outpatient use; 6 – easy of production; 7 – convenience and stability of delivery.

A positive feature of radiopharmaceuticals with ^{153}Sm, ^{175}Yb, ^{186}Re isotopes is the presence of γ-radiation in their spectrum. The presence of γ-radiation makes it possible to obtain a scintigraphic image on a gamma camera and accurately determine the accumulation of the drug in metastases after the administration of the drug.

The physical characteristic of the isotopes ^{153}Sm, ^{175}Yb, ^{186}Re are as follows: ^{153}Sm ($T_{1/2}$ = 1.9 days, E_β = 0.8 MeV, E_γ = 103.2 keV), ^{175}Yb ($T_{1/2}$ = 4.2 days, E_β = 0.5 MeV, E_γ = 396.3 keV) and ^{186}Re ($T_{1/2}$ = 3.8 days, E_β = 1.1 MeV, E_γ = 137.2 keV). These isotopes decay with the release of Auger electrons. The most intense internal conversion electrons are due to L-Auger electrons. There are L-Auger electrons with energy and intensity for ^{153}Sm E = 4.69 keV – 53.2%, ^{175}Yb E = 6.02 keV – 6.34%, and ^{186}Re E = 6.88 keV – 6.48%. In other words, a synergistic effect of the action of Auger electrons and γ-radiation is possible.

1. NUCLEAR REACTIONS

Samarium is being used of natural isotopic distribution. Prevalence of isotopes ^{147}Sm, ^{152}Sm, ^{154}Sm is 15.0, 26.7, 22.7%, respectively. The reaction ^{152}Sm(γ,n) causes the production of ^{151}Sm ($T_{1/2}$ = 90 years) with low radiation. The reaction ^{147}Sm(γ,n) leads to producing ^{146}Sm isotope with a half-life of $1.03\cdot10^8$ years through α-decay. Reaction ^{144}Sm(γ,n)^{143}Sm ($T_{1/2}$ = 8.83 min) –> ^{143}Pm ($T_{1/2}$ = 265 days) results by isotopes with low levels of radiation due to their $T_{1/2}$. Only ^{153}Sm from reaction ^{154}Sm(γ,n) will significantly reduce the side effect of cancer therapy.

Along with ^{175}Yb the γ-activation of natural Yb produces other radionuclides (Table). In (γ,p) reactions ^{173}Tm with quickly decay, and ^{172}Tm with weak low-energy gamma radiation form. Radionuclide ^{167}Tm which is formed from ^{168}Yb(0.13%) is very not much. Noticeable ^{169}Yb can be suppressed using a ^{176}Yb enriched target.

The medium activity ^{175}Yb isotope can be produced using thermal neutrons that bombard a natural target by the reaction ^{174}Yb(n,γ) or charged particles d ore ^{3}He from reactions ^{174}Yb(d,p), ^{176}Yb(d,t), and ^{176}Yb(^{3}He,α).

It was also found that ^{175}Yb (31 Ci/g) or (1145 GBq) can be produced with 95% radionuclide purity (with a content of 3%) by irradiating a Yb_2O_3 target with thermal neutrons $3\cdot10^{13}$ n/cm^2/s during 5 days [4]. Also, ^{175}Yb can be obtained on the basis of photonuclear reactions when an ytterbium target is irradiated during 1 h with a bremsstrahlung gamma radiation at an electron

accelerator with an energy of 20 MeV [5]. In this case, the radiation of gamma photons ^{175}Yb is low-energy and has a low distribution.

The rather long lifetime of ^{175}Yb makes it possible to carry out transportation, labeling, and purification without a possible loss of isotope activity. β-emitter ^{175}Yb is able to selectively accumulate in the localization of metastases with increased mineralization and increased bone tissue metabolism.

Natural rhenium consists of two isotopes ^{185}Re(37.4%) and ^{187}Re(62.6%). The production of ^{186}Re is carried out at an electron accelerator using nuclear reaction ^{187}Re(γ,n)^{186}Re.

At the same time, the ^{184}Re radionuclide, which has significant activity, in the reaction ^{185}Re(γ,n) is also produced. The use of a target highly enriched in ^{187}Re is required to prevent ^{184}Re. It is also possible to use the neutron generator which would lead to the production of not only ^{186}Re, but also ^{188}Re.

Isotope ^{188}Re gamma radiation has the most intense transition – 155.0 keV with a quantum yield of 14.9%. The most important future of preparation ^{188}Re based on them is the possibility by their generation production. The ^{188}W/^{188}Re generator has the advantage that the ^{188}Re isotope can be generated over a fairly long period due to $T_{1/2}$ = 69.4 days isotope ^{188}W.

For the production of the generator isotope ^{188}W the reactors on the base of double neutron capture with a neutron density of ~ $3\cdot10^{15}$ cm$^{-2}\cdot$c^{-1}, and ^{186}W target with enrichment of up to 99.95% is used. As a result, for example, commercial generator ORNL (USA) ^{188}W/^{188}Re uses ~ 25 g tungsten and this causes difficulty to receivering ^{188}Re from chromatography columns. The specific activity ^{188}W in such a generator is 100…200 MBq/mg of tungsten. To do this, a silver-based cation/anion column is introduced into the generator, to reduce the volume of the mobile phase to 10…15 ml. The problems of using low concentrations of the specific activity tungsten, lead to the need to create new ^{188}W/^{188}Re generators, whish simplify the design of the generator and its operation. A feature of the production of the ^{188}W/^{188}Re generator at electron accelerators is that the production of ^{188}W from reaction ^{192}Os(γ,α) with a high specific activity can reach a theoretical specific activity of ~ 36.9 GBq/mg of tungsten [6].

The radiation of ^{186}Re β-particles is the most effective for targeted radiotherapy. Low-energy photons make it possible to simultaneously perform scintigraphy and dosimetric studies without the introduction of other isotopes, such as ^{99m}Tc.

To date, the production of isotopes of samarium, ytterbium and rhenium has not been established in Ukraine, despite the fact that each of these isotopes has proven itself in clinical practice as effective and safe. These isotopes have certain physiological properties, and specific biochemical and pharmacological advantages, which are of considerable interest for radionuclide diagnostics and therapy.

The purpose of that study was to evaluate the feasibility of producing the isotopes ^{153}Sm, ^{175}Yb, and ^{186}Re with high specific activity on an electron accelerator.

2. MATERIALS AND METHODS

Nanoparticles (50…80 nm) of Sm_2O_3, Yb_2O_3, and ReO_2 oxides were used as targets. Activation by bremsstrahlung radiation with energy of 13.5 MeV and current of 500 μA on liner electron accelerator was carried out for Sm_2O_3 and Yb_2O_3 nanoparticles. ReO_2 nanoparticles were activated at energy of 40 MeV and current 250 μA. After each exposure the targets were cooled for 24 h to get rid of the activity of short-lived impurities.

A classic method for increasing the specific radioactivity of accelerator-produced isotopes is the Szilard-Chalmers reactions [7]. Nanoparticles Sm_2O, Yb_2O_3, ReO_2 and nanoparticles clinoptilolite used as donor and acceptor, respectively.

The activity of isotopes obtained in reactions ^{154}Sm(γ,n)^{153}Sm, ^{176}Yb((γ,n)^{175}Yb, and ^{187}Re(γ,n)^{186}Re in nanoparticles clinoptilolite measured by Ge(Li)-detector with volume 50 cm^3 and with energy resolution 3.2 keV in the area of 1332 [8].

To reduce the influence of the background, the detector is equipped with three-layer Pb-Cu-Al protection. Standard amplitude spectrum processing programs processed the spectra obtained from the samples. The detection limit of the elements was 10^{-4}…10^{-7}% of the mass. Prior to analysis, the samples were prepared according to International Atomic Energy Agency (IAEA) Instruction [9].

3. RESULTS AND DISCUSSION

The spectrums of targets Sm, Yb, and Re are shown in the following figures. The lines registered on the spectrums are in table. The lines of gamma radiation of ^{153}Sm are observed in the spectrum (Fig. 1).

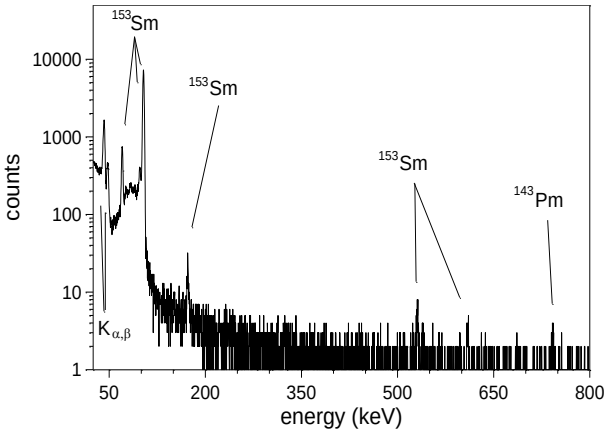

Fig. 1. The spectrum of Sm after irradiated bremsstrahlung with E_{max} = 13.5 MeV

On the accelerator of electrons with energy 13.5 MeV and a current 500 μA isotope ^{153}Sm can be produced ~ 1 Ci during the day by using a 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.

In the presents of the same parameters, the isotopes ^{175}Yb can be produced ~ 1.2 Ci during the day by using ytterbium ~ 30 g with a natural isotopic composition (Figs. 2, 3).

Table Lines registered on the spectrums

Radionuclide $T_{1/2}$	Basic reactions	γ-lines keV (n_i %)
Sm (Z=62)	Stable A(%)	144(3.1), 147(15.0), 148(11.3), 149(13.8), 150(7.4), 152(26.7), 154(22.7)
^{143}Pm 265D	^{144}Sm(γ,n)-^{143}Sm(8.83M)->^{144}Sm(γ,p)	742.(38.5)
^{153}Sm 46.27H	^{154}Sm(γ,n)	69.7(4.85), 75.4(0.35), 83.4(0.20), 89.5(0.18), 97.4(0.85), 103.2(31.43), 172.9(0.08), 531.4(0.07), 533.3(0.04), 609.2(0.01)
Yb (Z=70)	Stable A(%):	168(0.13), 170(3.05), 171(14.3), 172(21.9), 173(16.1), 174(31.8), 176(12.7)
^{167}Tm 9.25 D	^{168}Yb(γ,n)-^{167}Yb(17.5M)->^{168}Yb(γ,p)	57.1(4.69), 207.8(41.02)
^{169}Yb 32.026 D	^{170}Yb(γ,n)	63.1(44.21), 93.6(2.61), 109.8(17.47), 118.2(1.87), 130.5(11.31), 177.2(22.16), 198.0(35.8), 261.1(1.72), 307.7(10.06)
^{172}Tm 63.6 H	^{173}Yb(γ,p)	78.8(6.54)
^{173}Tm 8.24 H	^{174}Yb(γ,p)	398.9(87.9), 461.4(6.86)
^{175}Yb 4.185 D	^{176}Yb(γ,n)	113.8(3.87), 137.7(0.235), 144.9(0.672), 251.5(0.17), 282.5(6.13), 396.3(13.2)
Clinoptilolite – $(NaK)_4CaAl_6Si_{30}O_{72}•24H_2O$		
^{24}Na 14.96H	^{27}Al(100%)(n,α) ^{23}Na(100%)(n,γ)	1369.(100.), 2754.(99.9) – 1022.->1732.
^{43}K 22.3H	^{44}Ca(2.086%)(γ,p)	372.8(86.8), 617.5(79.2)
^{47}Sc 3.345D	^{48}Ca(0.185%)(γ,n)-^{47}Ca(4.546D)->	159.4(67.9)
^{56}Mn 2.58H	^{55}Mn(100%)(n,γ) ^{57}Fe(2.2%)(γ,p)	846.8(98.9)
^{87m}Sr 2.803H	^{87}Sr(7.0%)(γ,γ') ^{88}Sr(82.58%)(γ,n)	388.5(82.1)
Re (Z=75)	Stable A(%): 185(37.4), 187(62.6)	
^{183}Re 70.0D	^{185}Re(γ,2n)	162.3(23.3)
^{184}Re 38.0D	^{185}Re(γ,n)	111.2(17.14), 252.8(3.02), 641.9(1.94), 769.8(0.67), 792.1(37.5), 894.8(15.6) 903.3(37.9), 1023.(0.52), 1275.(0.12)
^{186}Re 90.64H	^{187}Re(γ,n)	122.6(0.56), 137.2(8.22)
^{188}Re 16.98H	^{187}Re(n,γ)	155.0(14.95)
Al cover foil and others		
^{24}Na 14.96H	^{27}Al(100%)(n,α)	1369.(100.)
511	$e^+ + e^- \rightarrow$	511.
^{40}K 1.28E+9Y	^{40}K -> ^{40}Ar+β^+	1461.(10.7)

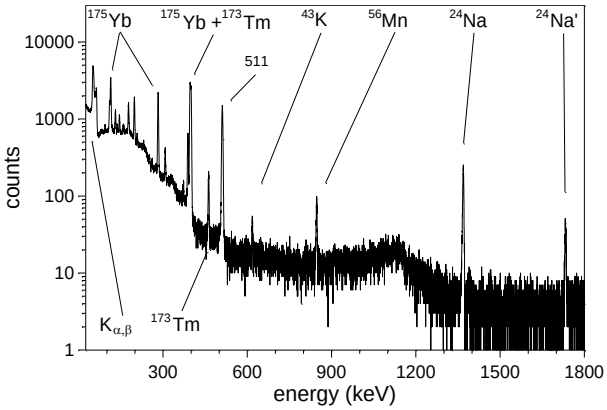

Fig. 2. The spectrum of Yb after irradiated bremsstrahlung with E_{max} = 13.5 MeV

In the target of similar mass, but enriched in ^{176}Yb the daily yield can attain 8 Ci for ^{175}Yb.

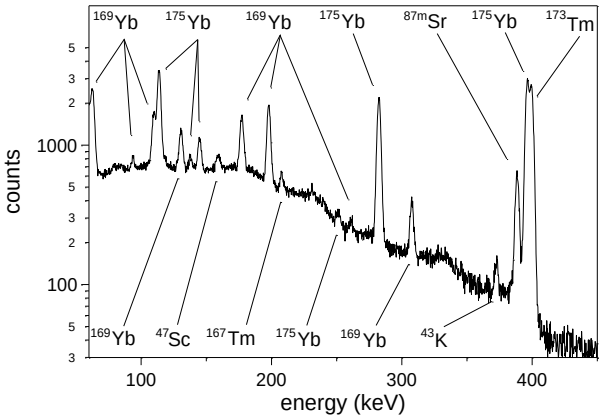

Fig. 3. The fragment of the low-energy of the same Yb spectrum

On a linear accelerator, it is possible to produce up to 30…40 Ci/day ^{186}Re with high specific activity at energy 40 MeV and current 250 μA (Figs. 4, 5).

Note that recoil nuclei are stopped in the acceptor-clinoptilolite from all these reactions ^{154}Sm(γ,n)^{153}Sm, ^{176}Yb((γ,n)^{175}Yb and ^{187}Re(γ,n)^{186}Re.

With an electron accelerator, it is possible to achieve a yield of isotopes ^{153}Sm, ^{175}Yb, and ^{186}Re higher activity and without impurities than with reactors and cyclotrons. For example, the total yield of the production ^{186}Re at the electron accelerator is 60 μCi/μA year to the

reactor – 7.5 μCi/μA year [10] and the cyclotron – 20 μCi/μA year [11].

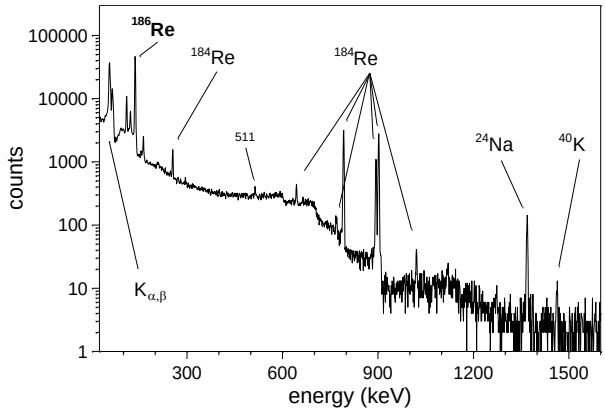

Fig. 4. The spectrum of Re after irradiated bremsstrahlung with E_{max} = 40 MeV

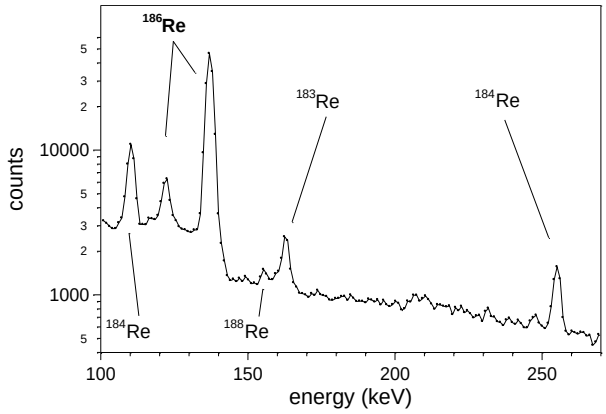

Fig. 5. The fragment of the same spectrum in the region ^{186}Re lines

CONCLUSIONS

The possibilities of the photonuclear production of isotopes ^{153}Sm, ^{175}Yb, and ^{186}Re as medical radioisotopes produced by the reactions ^{154}Sm(γ,n)^{153}Sm, ^{176}Yb((γ,n)^{175}Yb, and ^{187}Re(γ,n)^{186}Re with using Szilard-Chalmers reaction was investigated. The nanoparticles Sm_2O_3, Yb_2O_3, ReO_2 and clinoptilolite nanoparticles were used the output of isotopes ^{153}Sm, ^{175}Yb, and ^{186}Re.

In NSC KIPT on the linear accelerator of electrons, the product of isotopes ^{153}Sm, ^{175}Yb, and ^{186}Re properties suggest for efficient use for pain palliation. These isotopes have been used for more than a decade around the world.

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МОЖЛИВОСТІ ВИРОБНИЦТВА ІЗОТОПІВ ^{153}Sm, ^{175}Yb, ^{186}Re НА ЕЛЕКТРОННОМУ ПРИСКОРЮВАЧІ

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

На електронному прискорювачі ННЦ ХФТІ розроблені фотоядерні технології одержання остеотропних ізотопів ^{153}Sm ($T_{1/2}$ = 1,9 доби, E_β = 0,8 МеВ, E_γ = 103,2 кеВ), ^{175}Yb ($T_{1/2}$ = 4,2 доби, E_β = 0,5 МеВ, E_γ = 396,3 кеВ) та ^{186}Re ($T_{1/2}$ = 3,8 доби, E_β = 1,1 МеВ, E_γ = 137,2 кеВ) з використанням наночастинок (50…80 нм) оксидів цих елементів та реакції Сциларда-Чалмерса для підвищення питомої активності. В Україні такі медичні ізотопи не виробляються. Показано, що загальний вихід ізотопів на прискорювачі електронів при опроміненні цих зразків гальмівним випромінюванням з максимальною енергією 40 МеВ і струмом 250 μА для ^{186}Re та 13,5 МеВ і струмом 500 μА для ^{153}Sm та ^{175}Yb має такі переваги, як більш високу питому активність, незначний вміст домішок і не потребує іммобілізації радіоактивних відходів у порівнянні з реактором та циклотроном.