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PROSPECTS FOR THE METHODS OF RADIONUCLIDE PRODUCTION

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Перспективы методов получения радиоактивных ядер

Описаны методы получения радионуклидов для медицинских целей. Применение ускорителей на низкие энергии предпочтительно в отношении экономии бюджетных средств. Высокий выход изотопов в реакциях может быть достигнут с помощью интенсивного тормозного излучения на ускорителях электронов или высокоинтенсивных пучков альфа-частиц на циклотронах. Выбор материала мишени и энергии частиц позволяет варьировать условия для получения заранее заданного продукта. Предложены новые возможности для оптимизации методов синтеза изотопов, в частности, применение мишеней из благородных газов для производства и транспорта активностей. В дополнение к известным, обсуждаются новые варианты «генераторной» схемы и отобрано большое число изотопов, перспективных в контексте их применения в медицине. Среди них: изотопы/изомеры, излучающие мягкую радиацию для селективного и щадящего воздействия на организм, а также позитронные эмиттеры для PET и радиоактивные изотопы элементов, удобных для химического выделения, таких как галогены и щелочные металлы.

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Prospects for the Methods of Radionuclide Production

Methods of radionuclide production for the nuclear-medicine purposes are described. In a budget approach, the application of low-energy accelerators is especially advantageous. Intense flux of bremsstrahlung at electron accelerators or high-current cyclotron beams of alpha particles must supply a great yield for many isotopes. The choice of a target material and of the projectile energy provides enough variation for concrete species formation. The innovating procedures are here proposed for optimizing of methods, for instance, application of the noble-gas target for production and transport of activities. The known and new variants of the «generator» scheme are discussed. Many isotopes are listed as promising in the context of the therapeutic and theragnostic applications. Among them are isotopes/isomers emitting soft radiation for the selective and careful body treatment, also the positron emitters for PET, and the halogen and alkali-metal species convenient for chemical separation.

The investigation has been performed at the Flerov Laboratory of Nuclear Reactions, JINR.

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1. INTRODUCTION

Over recent decades, the nuclear medicine is formed as a separate branch of the nuclear science. Among a variety of methods, the treatment of oncology events with proton and heavy-ion beams seems the most efficient way, but too expensive for the wide application as well. Production and use of the radionuclide sources of radiation is definitely more economic, much lower in expenses compared to the proton-synchrotron therapy. That is accounting the costs both for the basic machine construction and for the services in operation. A great number of radionuclides are known and that allows a flexible choice of the concrete isotope and its production method individually for each treatment task. In literature, there are typically distinguished the therapeutic and theragnostic sources: the first ones serve for elimination of tumors mostly due to the internal irradiation and second ones for the tomography diagnosis. The radionuclides suitable for application in both modes are listed and characterized in the Brookhaven and Dubna publications: the review chapter [1] and the book [2]. Various scientific and practical issues are addressed there to the production methods, to the chemical processing of the active materials, and to the pharmaceutical preparations. Some cases of the «dual-purpose» isotopes and isotope pairs are described in [1]. Unlike to that, the isotope production with commonly used low-energy accelerators is under the scope in the present work. The facilities constructed at JINR, Dubna could be useful for the studies of the definite production methods without a great-fund investment and the corresponding isotopes are listed here. Clearly, practical application of them is possible only at much higher beam intensities for the necessary activity supply. Enough funds are required for the construction of such an accelerator facility combined to the clinical hospital for patients. But on today, we discuss only the studies aimed to the quantitative characterization of the methods including new variants and possibilities. In general, this report is mostly addressed to the nuclear research and lower to the medical issues. The isotopes useful for the oncology treatment, for the positron-emission tomography PET, and for the single-photon-emission computer tomography SPECT are of interest.

2. NEW POSSIBILITIES

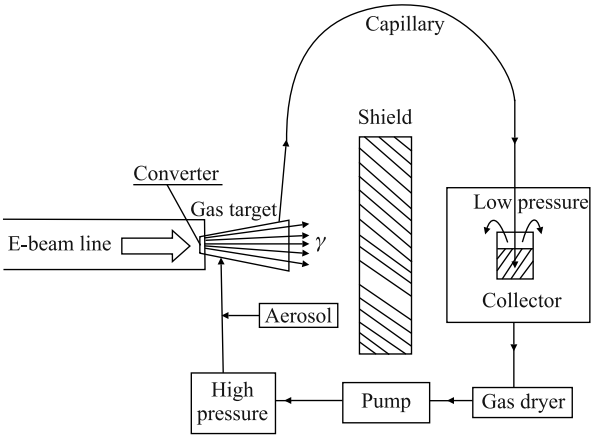
Historically, the radioisotope therapy had been started since many decades applying the radium/radon therapy and external gamma irradiations by high-intensity ^{60}Co «cannon». Then, it was realized that ^{60}Co and many other sources are not

the best for therapy because they generate the damage of healthy tissues and even of a whole body by the great dose. It becomes clear that the specified choice of the radiation source is crucial and it must precede the medical application. Searching for the new variants, nuclear scientists have distinguished some species promising for nuclear medicine, but unfortunately, produced at modern high-power facilities and required great expenses. For instance, such sort proposals are described on the production of the ^{195m}Pt isomer [3] and of the ^{149,152,155}Tb nuclides [4]. The isomer of ^{195m}Pt is really attractive and it is producible due to double-neutron capture by the ^{193}Ir target followed with the β^-decay of ^{195m}Ir. This method could be feasible only using a great neutron flux as in the Oak Ridge high-flux reactor*. Another example [4] supposes the isotope production with 1.4 GeV protons at the accelerator in Switzerland and the application of the ISOLDE facility for the mass separation of Tb isotopes. Both mentioned facilities in Oak Ridge and in Geneva are of a high-power class being extremely expensive even for services and exploit. The idea of innovation contradicts thus to the efficient use in practice.

In the present work, the options provided by the regular nuclear reactions at low energy machines are reviewed and characterized. Some of them appear as a new and promising for medical applications. The isotopes are selected by several criteria: a) short-range radiation emitters including the isomers allowing the treatment of a narrow area in the body; b) the nuclides useful for PET, or SPECT, or dual-purpose application; c) the isotopes ensuring enough specific activity after simple chemical isolation. The variants are commented in more detail below in the following subsections and in the presented Tables. The attractive properties are mentioned in the last column of Tables as «Remark». Strictly speaking, the majority of β, γ-emitters could be used for SPECT after some adjustment and the positron emitters are in major suitable for PET, or as dual-purpose agents.

2.1. Noble-Gas Targets Exposed to the Bremsstrahlung. The gas-jet method was originally developed for transport of the radioactive products recoiled from a solid target in reactions with charged particles. The recoil atoms are collected in a gas volume and transported with the gas flow through the capillary to the spectroscopy station [5]. Nothing prevents the use of a gas volume as the target for exposure it with bremsstrahlung flux in both variants of the static gas target and in the gas-jet configuration. The production of the ^{123}I therapeutic nuclide was developed in [6]. The wider possibilities for the gas-target application are not yet explored and some available schemes are described in the present paper. The lay-out of setup for the activity production and accumulation is displayed in the Figure. The electron beam from accelerator generates the bremsstrahlung in

*More details on the possibilities for production of ^{195m}Pt are discussed in [11].



Draft diagram of the gas-transport setup. Arrows define the gas-flow direction

the tungsten converter serving also as a wall of the tiny camera filled with the gas needed for the experiment. The noble gas is preferential to avoid the corrosion of constructive materials. Typically, the He-jet was popular.

The camera is filled from outside under selected pressure. The gas leaves it permanently through the little-diameter hole to the capillary. The fast transport is arranged for the products of activation together with the gas flow into the area where the products are collected. The used gas must be directed to the recirculation system as shown in the Figure. The parameters of camera volume, pressure, and the capillary diameter must be tuned for optimizing of the transport time. Sometimes, even the sonic jet could be arranged at optimum tuning. Transmitted through the capillary gas is filtered in the liquid collector. The halogen or alkaline element products are successfully dissolved in the physiology-saline content of the collector. For better efficiency, the NaCl aerosols could be added in the gas. The halogen products are successfully produced in photon induced (γ, p) reaction with the noble-gas targets. This reaction is one of the most abundant with light targets, unlike to the heavy-element targets where (γ, n) strongly dominates. The irradiation of Ne and Ar targets must be well productive for F and Cl radionuclides. The bromine products are achievable with Kr gas irradiation and iodine — with the Xe target. In the latter case, the increased photon flux may meet the requirement of a suitable yield for the products of (γ, p) reactions despite reduced cross sections.

A permanent renovation of gas in the target volume does not reduce the total activity yield over long irradiation. In the described gas-jet scheme, the pressure is chosen providing the optimum transport efficiency. A static target may allow high pressure of the gas if it is needed for special great-productivity irra-

diations. The mentioned Dubna facility involves the MT-25 microtron operating regularly for acceleration of electrons up to 23 MeV with a beam power of about 0.3 kW. In real activation experiments, the products were typically detected by the γ-spectroscopy method. It was shown in [7] that the power of Dubna microtron is enough to observe the reactions characterized with as low yield as 10^{-6} of the total dipole-resonance photoabsorption yield. Such a great productivity may not yet be enough for the medical isotopes with required specific activity. However, there are known over the world the high-power electron machines supplying the Megawatt beam power, more than enough for radioisotope production. The radiation safety problem is typical for the high-power nuclear facilities. The discussed here bremsstrahlung irradiations of noble-gas targets in combo with the gas transport create softer problems compared to those successfully resolved at high-flux reactors and at high-energy, high-power proton synchrotrons. In any case, for medical applications, the special facility must be constructed and the requirements to the beam intensity must be quantitatively optimized. The experiments in Dubna may supply the data for preliminary estimates.

The radionuclides achievable in this scheme are listed in Table 1. We comment now some details on the example of the Ar gas irradiation. The convenient β, γ-emitter ^{39}Cl ($T_{1/2} = 56$ min), is produced in the ^{40}Ar(γ, p) reaction. Within the scheme shown in the Figure, the final product is accumulated in a form of the

Table 1. Products generated at noble-gas targets exposed to bremsstrahlung

Reaction	Product	Halflife	Radiation*	Remark
^{20}Ne (γ, d)	^{18}F	110 min	β^+ 100%	For PET
^{40}Ar (γ, p)	^{39}Cl	56 min	β^-, γ	—
^{80}Kr (γ, n)	^{79}Kr	34.9 h	$\varepsilon, \gamma, \beta^+$ 7%	For PET
^{82}Kr (γ, d)	^{80m}Br	4.42 h	e^-, γ 37 keV	Soft radiation
^{83}Kr (γ, p)	^{82}Br	35.3 h	β^-, γ	—
^{84}Kr (γ, n)	^{83m}Kr	1.83 h	e^-, γ 9 keV	Soft radiation
^{86}Kr (γ, n)	^{85m}Kr	4.48 h	β^-, γ 151 keV	Soft radiation
^{124}Xe (γ, n)	^{123}Xe$\rightarrow^{123}$I	2.1 h $\rightarrow$ 13.2 h	γ 159 keV	Generator, soft radiation
^{130}Xe (γ, n)	^{129m}Xe	8.89 d	e^-, γ 40 keV	Soft radiation
^{132}Xe (γ, n)	^{131m}Xe	11.9 d	e^-, γ 164 keV	Soft radiation
^{134}Xe (γ, n)	^{133m}Xe	2.19 d	e^-, γ 233 keV	Soft radiation
^{136}Xe (γ, n)	^{135m}Xe	15.3 min	Pure γ 527 keV	For SPECT
$^{\mathrm{nat}}$Xe (γ, p)	Series of I isotopes	Minutes to days	Different β, γ energies	For combinatory treatments

*Electron capture is indicated with ε, while emission of conversion and Auger electrons — with e^-.

physiological saline due to the adding of NaCl salt in the aerosol supply and in the water collector. The system can work continuously supplying the solution for injections. Relatively short-lived ^{39}Cl therapeutic agent provides enough specific activity of the solution and also prevents the radioactive pollution of the patient body after the treatment. The practically stable ^{39}Ar ($T_{1/2} = 269$ years) is the only product of ^{39}Cl decay and it creates a negligible activity. The required quantitative parameters could be regulated by tuning of the beam intensity, of the time for a gas renewal, and of the collector volume.

Other isotopes — the products of Ne, Kr, and Xe targets irradiation are also listed in Table 1. The radioactive properties of the nuclides are taken from Nuclear Data Sheets [8] and from Tables [9]. The ^{18}F positron emitter is attractive for PET tomography, while ^{80m}Br and ^{82}Br activities are promising in the mode of therapeutic agents, the same as described above ^{39}Cl. The noble-gas nuclides are produced in the (γ, n) reactions and they must be useful for therapy of breathing organs. Especially interesting looks a group of isomers emitting short-range radiation, as e^- and soft γ radiation. This is crucial for careful therapy avoiding the damage of healthy tissues. The production of a valuable ^{123}I radionuclide was earlier explored in [6] applying the «generator» mode. In practical sense, even simplified irradiation of the Xe gas of natural isotopic composition could be useful. The iodine products of a great specific activity could be obtained by separation of I from Xe gas. The sample will contain many isotopes characterized with different halflives from minutes to days and with different energies of the emitted radiation. It could be used for SPECT diagnosis or for the heavy-duty therapy of patients suffered from the late-stage oncology. The great activity and different halflives of isotopes allow a flexible variation of the time-protocol for the treatment of different patients.

2.2. Noble-Gas Targets Exposed to α-Particle Beams. The method of gas jet is also ready for transport of the products generated with cyclotron beams of α-particles. The scheme of irradiations is similar to that shown in the Figure. The entrance wall of the camera must be made of thin foil for penetration of the moderate-energy alphas in the gas volume. There are known the vacuum-dense foils resistive to the charged particle beams. Typically, the metal foils are used, as Be, Al, Ti, Zr foils and even the kapton organics. Higher cross sections compared to the photon irradiations are expected in the case of reactions induced by alphas. The beam current required for reasonable productivity must be safe for the entrance-foil stability.

The promising isotopes producible in this way are listed in Table 2. The alkaline elements of the first group are created past emission of protons/deuterons from the compound nucleus and elements of the second group due to (α, xn) reactions. Such chemical properties are convenient for sorption of them from the gas flow in water solutions of the suitable salt. Respectively, the methods

Table 2. Products generated at the noble-gas targets exposed to the ^{4}He ion beam

Reaction	Product	Halflife	Radiation	Remark
^{4}He (α, n)	^{7}Be	53.3 d	ε, γ 478 keV	For SPECT
^{22}Ne (α, d)	^{24}Na	15 h	β^-, γ	For SPECT
^{40}Ar (α, d)	^{42}K	12.4 h	β^-, γ	For SPECT
^{80}Kr (α, d)	^{82m}Rb	6.3 h	γ, β^+ 100%	For PET
^{129}Xe $(\alpha, 2n)$	^{131}Ba	11.5 d	ε, γ	—
^{132}Xe (α, p)	^{135m}Cs	53 min	γ	Pure γ, for SPECT
^{132}Xe (α, d)	^{134m}Cs	2.9 h	e^-, γ 127 keV	Soft radiation
^{134}Xe (α, d)	^{136}Cs	13.2 d	β^-, γ	—
^{136}Xe (α, n)	^{139}Ba	83 min	β^-, γ	For SPECT

described above in Subsec. 2.1 for the activity processing are actual in this case as well.

2.3. Radionuclides Produced with Different Targets. The reactions generated by the bremsstrahlung and α-particle beams in different, typically solid materials, are listed in Table 3. Some of them could be the best for medical applications. Even the method of helium-jet remains applicable for transport of the products of α-particle irradiation. The entrance foil in this case must be replaced with the thin target of necessary isotope faced to the gas volume. For the target backing, the resistive foil must be used, the same as above. An impact momentum due to the α-particle collision must be enough for the recoil product move into the helium gas volume. The alpha-induced reactions are especially advantageous because the product activity could be separated from the target-bulk material by chemical methods, even independently on the gas-transport use. For products of the (γ, n) reactions, the chemical purification of the product of interest is only possible in the «generator» scheme when it is accumulated past β decay of the reaction product, see below in Table 4. The ^{75}Br and ^{76}Br positron emitters supply interesting possibilities for PET, as is indicated in Table 3. The generator scheme may be applied for their production but low-abundance ^{74}Se isotope is required as a target. Suitable reactions are visible at higher energy of projectiles which requires greater expenses for ^{75,76}Br production.

Many isotopes listed in Table 3 are potentially promising not only for medical treatments but also in research programs for studies of the many-elements metabolism «in vivo» using the radioactive «markers» taken in the nanogram amounts without carrier. Some isotopes were successfully produced with the higher energy proton beams at iThemba facility in South Africa [10]. Dubna cyclotrons are also productive. The reactions with alphas at an energy $\leqslant 40$ MeV may provide the better-purity activities because of selective production of the needed species under suppressed yields of the background nuclides.

Table 3. Medical radionuclides achievable with different targets exposed to bremsstrahlung and α-particle beams

Reaction	Product	Halflife	Radiation	Remark
^{59}Co (γ, n)	^{58m}Co	9 h	e^-	Soft radiation
^{66}Zn (γ, n)	^{65}Zn	244 d	ε, γ	For SPECT
^{76}Se (γ, n)	^{75}Se	119 d	ε, γ	—
^{90}Zr(γ, n)	^{89}Zr	78 h	$\varepsilon, \gamma, \beta^+$ 23%	For PET
^{156}Dy (γ, p)	^{155}Tb	5.32 d	ε, γ	For SPECT [4]
^{204}Hg (γ, n)	^{203}Hg	46.6 d	β^-, γ 279 keV	Medium energy
^{204}Pb (γ, n)	^{203}Pb	51.9 h	ε, γ 279 keV	Medium energy
^{25}Mg $(\alpha, \alpha' p)$	^{24}Na	15 h	β^-, γ	For SPECT
^{64}Ni (α, n)	^{67}Cu	61.9 h	β^-, γ	Dual purpose [1]
^{65}Cu $(\alpha, 2n)$	^{67}Ga	78.3 h	β^-, γ	Dual purpose [1]
^{74}Se $(\alpha, 2n)$	^{76}Kr$\rightarrow^{76}$Br	14.6 h $\rightarrow$ 16 h	γ, β^+57%	Generator, for PET
^{74}Se $(\alpha, 3n)$	^{75}Kr$\rightarrow^{75}$Br	4.5 min $\rightarrow$ 1.6 h	γ, β^+ 72%	Generator, for PET
^{78}Se (α, d)	^{80m}Br	4.42 h	e^-, γ 37 keV	Soft radiation
^{79}Br (α, n)	^{82m}Rb	6.3 h	γ, β^+ 100%	For PET
^{80}Se (α, d)	^{82}Br	35.3 h	β^-, γ	—
^{80}Se (α, n)	^{83m}Kr	1.83 h	e^-, 9 keV	Soft radiation
^{103}Rh (α, n)	^{106m}Ag	8.3 d	ε, γ	—
^{103}Rh $(\alpha, 2n)$	^{105}Ag	41.3 d	ε, γ	—
^{116}Cd $(\alpha, 3n)$	^{117m}Sn	13.6 d	e^-, γ 159 keV	Dual purpose [1]
^{121}Sb $(\alpha, 2n)$	^{123}I	13.2 h	ε, γ 159 keV	Soft radiation
^{127}I $(\alpha, 2n)$	^{129}Cs	32 h	ε, γ	—
^{201}Hg $(\alpha, 2n)$	^{203}Pb	51.9 h	ε, γ 279 keV	Medium energy

2.4. New Options for the Generator Scheme. The generator method was proposed for chemical isolation of the reaction products from a bulk target materials. Productive reactions with neutral projectiles, like (n, γ), (n, n'), $(n, 2n)$ and (γ, n), remain the atomic number Z of a product without changes, same as Z of the target. The chemical isolation is therefore impossible. Some attempts to use physical methods for separation were fragmentary successful, for instance, in the case of the well-known Scillard–Chalmers experiments. But chemical methods could not be replaced with some operations exploiting the recoil momentum of reaction products. The only exclusion is the method of gas transport for the recoiled nuclei, as is described above. Today, the sophisticated methods are developed for the acceleration, deflection of produced beam and focusing, deceleration, charge exchange, and final separation of the reaction products. But they are hardly applicable for operations with a great activity. Chemistry remains of importance for the processing of radioactive species prepared for the medical purposes. In the

generator scheme, the activity of interest is accumulated past β/ε decay of the primary reaction product. Changed atomic number allows the selective isolation of the decay products from the bulk target material. For example, the ^{99}Mo $\rightarrow$ ^{99m}Tc generator has been successfully operated at clinics since the decades.

Inspecting the nuclide chart, we have distinguished the promising variants for realization of the generator method and they are listed in Table 4. Many of them were already mentioned in publications, for instance, in [1, 2, 10]. Some newer decay chains and reactions are added. Strictly speaking, the classical generator scheme implies that the mother activity is longer lived than the final product of interest. In this version, the activity produced in the reaction serves as a source for supply of the daughter nuclides and they could be chemically extracted several times over the decay time. Some of listed in Table 4 cases do not meet this classical requirement. But at least, single chemical isolation is possible and this may be crucial for practical use. So, we include such cases in the list of generators, despite the long-lasting supply of the final activity is restricted.

Now, it would be worth to stress on our proposal for production of In radionuclides within the generator method: ^{116}Cd$(\gamma, n)^{115}$Cd, 53.5 h $\rightarrow$ ^{115m}In,

Table 4. Generator method options

Reaction	Product	Halflife	Radiation	Remark
^{46}Ti $(\gamma, 2n)$	^{44}Ti $\rightarrow$ ^{44}Sc	60.4 y $\rightarrow$ 3.92 h	γ, β^+ 95%	For PET
^{50}Cr $(\gamma, 2n)$	^{52}Fe $\rightarrow$ ^{52m}Mn	8.3 h $\rightarrow$ 21 min	γ, β^+ 98%	For PET
^{58}Ni (γ, n)	^{57}Ni $\rightarrow$ ^{57}Co	36 h $\rightarrow$ 272 d	ε, γ	Soft radiation
^{66}Zn $(\alpha, 2n)$	^{68}Ge $\rightarrow$ ^{68}Ga	271 d $\rightarrow$ 68 min	γ, β^+ 89%	For PET
^{74}Se (γ, n)	$^{73g/m}$Se $\rightarrow$ ^{73}As	7.1 h/39 m $\rightarrow$ 80.3 d	e^-, γ 53 keV	Soft radiation
^{74}Se $(\alpha, 2n)$	^{76}Kr $\rightarrow$ ^{76}Br	14.6 h $\rightarrow$ 16 h	γ, β^+57%	For PET
^{79}Br $(\alpha, 2n)$	^{81}Rb $\rightarrow$ ^{81m}Kr	4.6 h $\rightarrow$ 13 s	Pure γ 190 keV	Soft radiation
^{96}Zr(α, n) ^{98}Mo(n, γ) ^{100}Mo(γ, n)	^{99}Mo $\rightarrow$ ^{99m}Tc	66 h $\rightarrow$ 6 h	e^-, γ 141 keV	Soft radiation
^{104}Pd (γ, n)	^{103}Pd $\rightarrow$ ^{103m}Rh	17 d $\rightarrow$ 56 min	e^-, γ 40 keV	Soft radiation
^{114}Cd(n, γ) ^{116}Cd(γ, n)	^{115}Cd $\rightarrow$ ^{115m}In	53.5 h $\rightarrow$ 4.49 h	γ 336 keV	Medium energy
^{116}Cd (n, γ)	$^{117g/m}$C$\rightarrow^{117m/g}$In	2.5/3.4 h $\rightarrow$ 1.9/0.7 h	β, γ	For SPECT
^{124}Xe (γ, n)	^{123}Xe $\rightarrow$ ^{123}I	2.1 h $\rightarrow$ 13.2 h	ε, γ 159 keV	Soft radiation
^{120}Te (γ, n)	^{119}Te $\rightarrow$ ^{119}Sb	16.1 h $\rightarrow$ 38.2 h	ε, e^-, γ 24 keV	Soft radiation
^{130}Ba $(\gamma, 2n)$	^{128}Ba $\rightarrow$ ^{128}Cs	2.43 d $\rightarrow$ 38 min	γ, β^+ 61%	For PET
^{176}Hf $(\alpha, 2n)$	^{178}W $\rightarrow$ ^{178}Ta	22 d $\rightarrow$ 9.3 min	ε, γ	—
^{226}Ra (γ, n)	^{225}Ra $\rightarrow$ ^{225}Ac	14.9 d $\rightarrow$ 10.0 d	α, β, γ set of Ac $\rightarrow$ Bi chain	For heavy-duty cases

4.49 h and ^{116}Cd$(n,\gamma)^{117g/m}$Cd, 2.5/3.4 h $\rightarrow$ $^{117m/g}$In, 1.9/0.7 h. As known from the nuclide decay data, the feeding of daughter products in the indicated chains takes place and is characterized by a great probability, near 100%. The mother/daughter lifetimes are especially convenient for $A = 115$ isobars and the scheme looks very similar to the mentioned production of ^{99m}Tc. Therefore, it must be advantageous in practical application, though the test experiments are yet necessary. Until now, in irradiations by 23-MeV bremsstrahlung we have succeeded in Dubna to observe the production of ^{115}Cd with high yield and practically 100% conversion of it to ^{115m}In. Several other, not yet explored options are contained in Table 4, among them the production of ^{57}Co, ^{73}As, ^{76}Br, and ^{119}Sb. Unfortunately, the low-abundance ^{74}Se and ^{120}Te isotopes must be used as targets. Similar disadvantage restricts the application of the discussed in literature variants, for instance, production of ^{128}Cs with the ^{130}Ba target. It was remarked above that some isotopes could be preferentially produced with charged particles at higher energies. That means the greater expenses for constructing and operating of such machines. We discuss here only the possibilities with accelerators supplying the beams of electrons and α-particles at energies of $E_e \sim 25$ and $E_\alpha \sim 40$ MeV, correspondingly.

3. CONCLUSION

New possibilities for production of the radioactive isotopes at the modest-energy accelerators are proposed and discussed. The supply of both therapeutic and theragnostic isotope species is requested by the needs of nuclear medicine. The development of new methods must involve the series of extensive experimental studies to clarify the principles and practical details, despite a massive bulk of information is available in literature. Concrete recommendations are issued in the present work for some cases. The high-efficiency production and separation of purified isotopic species is of importance to minimize the damaging effects under treatment of patients. The radioecology requirements are also essential when the methods and the facilities for radionuclide production are worked out.

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