POSSIBILITY OF PRODUCING SOME RADIONUCLIDES FOR MEDICINE USING JINR ACCELERATORS

S.N.Dmitriev, V.A.Khalkin, R.Ts.Oganessian, G.G.Gulbekyan,
L.M.Onishchenko, G.Ya.Starodub, N.G.Zaitseva
Joint Institute for Nuclear Research, Dubna, Moscow reg., 141980, Russia

ABSTRACT

Prospects of using the JINR accelerators (the microtron MT–25, the cyclotron U–200 and the phasotron) for the production of some medical radioisotopes from various targets at different energies of accelerated ions are considered. Methods of producing the high-purity ^{123}I on the MT–25 and the isotopically ultra pure ^{237}Pu on the U–200 are described. A project of a proton cyclotron dedicated to the production of radioisotopes is discussed.

1. INTRODUCTION

The application of radionuclides for the diagnostics of different diseases and, to a lesser extent, for the radiotherapy has a tendency to growth. A significant part of radionuclides for nuclear medicine are obtained in the nuclear reactions with accelerated ions. The widely used radionuclides are:

1. The gamma-emitters used in cardiology, oncology, pulmonology: ^{67}Ga, ^{111}In, ^{123}I, ^{127}Xe, ^{201}Tl.
2. The short-lived β^+ emitters for PET:^{11}C, ^{13}N, ^{15}O, ^{18}F.
3. Generator isotopes including: the gamma-emitters ^{81}Rb–^{81m}Kr, ^{195m}Hg–^{195m}Au and β^+ emitters ^{68}Ge–^{68}Ga, ^{82}Sr–^{82}Rb, etc.
4. The potentially important nuclides investigated with the aim of introducing them for regular application: ^{52}Fe, ^{73}Se, ^{75}Br, ^{97}Ru, ^{178}Ta, ^{211}At, etc.

The greatest volumes of production and application characterize such nuclides as ^{67}Ga, ^{111}In, ^{123}I, ^{201}Ta, the generators ^{81}Rb–^{81m}Kr, ^{82}Sr–^{82}Rb.

Along with the progress in the creation and wide application in the clinical practice of new efficient electron devices (scintillation chambers, tomographs and etc.) which recreate quickly and in detail the picture of radionuclides distribution in the body, there goes on continuously the search for new promising radiopharmaceuticals.

Active investigations are going on with such radionuclides as ^{97}Ru, ^{211}At, ^{237}Pu, the generators ^{68}Ge–^{68}Ga, ^{178}W–^{178}Ta for which methods of producing the amount required for the routine work are studied. Thus, the ^{97}Ru is regarded as a nuclide possessing greater diagnostic potential than ^{99m}Tc and also as a chemical therapeutic agent for oncology.[1] The ^{68}Ge–^{68}Ga generator is an extremely convenient source for a positron emitter and ^{68}Ga has the same importance for the PET investigations as ^{99m}Tc in gamma-chamber research.[2] The ^{178}Ta becomes important both for the radionuclidic angiography using low energy detectors and for the PET investigations.[1]

2. PRODUCTION OF RADIONUCLIDES AT THE JINR

The possibility of obtaining a number of radionuclides for nuclear medicine on the accelerators of the JINR such as the U–200 cyclotron, the MT–25 microtron, the phasotron and a special high current proton accelerator which can be specially created (U-120I)[3] is considered in the Table. It contains the data referring to the production mode, estimates of the expected yields and of the probable volumes of radionuclides which could be obtained.

The data presented in the Table demonstrate that a large scale production of ^{97}Ru, ^{68}Ge and ^{178}W may be organized on the U–120I proton accelerator (in case it is built).

The table presents methods of producing radionuclides which are most widely used in medicine. There is also a possibility to produce on the JINR accelerators sufficient quantities of other more rare but not less important radionuclides for nuclear-medical investigations such as, ^{26}Al, ^{143}Pm, ^{144}Pm, ^{145}Pm, ^{175}Hf.

As an example, the tecnique of producing isotopically ultra-pure plutonium-237 (for metabolic research *in vivo*) on the U–200 accelerator and short-lived iodine-123 on the MT–25 microtron is described in brief below.

TABLE

JINR Accelerators and production of some radionuclides

A — the U–200 cyclotron, 36 MeV, ^{4}He, 100 μA; FLNR
B — the phasotron, 660 ÷ 20 MeV, proton, 6 μA (internal beam)*; LNP
C — the U–120I proton cyclotron, 35–40 MeV, 100 μA (projected)[3)]
D — the MT–25 microtron, 25 MeV e^-, 20 μA; FLNR

nuclide ($T_{1/2}$)	accele-rator	nuclear reaction	energy range, MeV	yield(EOB) mCi/μA-hr	exposi-tion, hr	production yield, mCi
^{68}Ge–^{68}Ga	A	^{66,67}Zn(^{4}He,xn)	35–15	0,001	200	20
(288d/68m)	B	^{nat}Ga(p,xn)	60–15	0,057	100	35
	C	^{69}Ga(p,2n)	35–15	0,044	100	440
^{81}Rb–^{81m}Kr	C	^{82}Kr(p,2n)	35–15	6,5	5	2750
(4,6h/13s)						
^{82}Sr–^{82}Rb	B	^{85}Rb(p,4n)	60–30	0,4	100	220
(25d/78s)						
^{97}Ru (2,9d)	A	^{nat}Mo(^{4}He,xn)	36–14	0,1	20	180
	B	^{99}Tc(p,3n)	50–20	7,0	20	760
	C	^{99}Tc(p,3n)	35–20	3,7	20	6700
^{111}In(2,83d)	A	^{109}Ag(^{4}He,2n)	35–10	0,7	20	1280
	C	^{112}Cd(p,2n)	30–20	6,0	20	10900
	C	^{113}Cd(p,3n)	35–25	9,45	20	17000
^{123}I(13,3h)	C	^{124}Xe(p,2n)+(p,pn)	30–25	10	4(+7)**	4000
	D	^{124}Xe(γ,n)	25	0,1/1g^{124}Xe	10(+2)	200
^{127}Xe(36,4d)	B	^{133}Cs(p,7n)	100–60	0,47	50	140
	C	^{127}I(p,n)	35–10	0,015	100	145
^{178}W–^{178}Ta	A	^{176,177}Hf(^{4}He,xn)	35–18	0,07	100	625
(22d/9,3m)	B	^{181}Ta(p,4n)	60–30	1,3	50	370
	C	^{181}Ta(p,4n)	35–30	0,3	20	580
^{195m}Hg–^{195m}Au	B	^{197}Au(p,3n)	50–20	10	5	290
(40h/30s)	C	^{197}Au(p,3n)	35–20	6	10	5600
^{201}Tl(3,06d)	C	^{203}Tl(p,3n)	30–22	0,7	10(+32)	700
^{211}At(7,2h)	A	^{209}Bi(^{4}He,2n)	30–10	0,5	10	335
^{237}Pu(45,3d)	A	^{235}U(^{4}He,2n)	32–21	0,0003	100	3
			25–24	0,00005	100	0,5***

* practically, only 70% of the proton beam intensity are used;
** decay time;
*** isotopically ultra-pure ^{237}Pu for the metabolism research *in vivo*.

3. PRODUCTION OF I–123 ON THE MT–25 ELECTRON BEAM

The method of producing ^{123}I in photonuclear reactions from enriched ^{124}Xe(γ,n)^{123}Xe$\longrightarrow$^{123}I using a small size electron accelerator was suggested and developed at the FLNR, JINR.[4–6] Though in this case the yield of ^{123}I is lower as compared with that of the proton irradiated ^{124}Xe, compact electron accelerators can complete with more expensive cyclotrons. An important advantage of this method is the possibility of creating a wide enough net of regional centers producing ^{123}I on these facilities. The researches carried out on the microtron MT–22, MT–25[5–7] and including the designing of a target assembly and of the radiochemical procedure have allowed to suggest a method of producing a high-purity ^{123}I preparation with the following characteristics: specific activity ~200 mCi/ml (~7.4 GBq/ml), radionuclidic admixtures $<10^{-6}$(Bq/Bq), content of I^- $\geq$95%, pH of the solution 7—9, admixtures of stable elements <0.05 μg/ml.

At the corresponding organization of the work on the MT–25 microtron there could be produced during a year at the irradiation of ^{124}Xe weighting 10 g (250 runs of 10 hr each) up to 50 Ci of iodine-123.

4. PRODUCTION OF ISOTOPICALLY ULTRA PURE ^{237}Pu

The ^{237}Pu ($T_{1/2}$=45,3 d, EC 99,9%) is the only Pu isotope which answers the medical requirements to metabolism research *in vivo*. However, a ^{237}Pu preparation used for injection to humans must be nearly free from α-emitting Pu isotopes. The method of producing isotopically ultra pure ^{237}Pu was developed.[7] Plutonium-237 was obtained in the reaction ^{235}U(^{4}He,2n) on the U–200 cyclotron of the FLNR. ^{235}U of 99,99% isotopic purity was used as a target. The dependence of the yields of ^{237}Pu, ^{236}Pu and ^{238}Pu on the energy of the ion beam was studied. Plutonium was separated from uranium and fission products (after dissolving the irradiated target in nitric acid) by using the anion exchange chromatography. An additional isotopic enrichment of ^{237}Pu was carried out with the electromagnetic mass-separator of the YASNAPP–facility. The preparation obtained with the ^{236}Pu:^{237}Pu:^{238}Pu ratio equal to 2.10^{-7}:1:$\leq 3.10^{-7}$ (Bq/Bq) is the purest among the preparations reported to date by different laboratories.

5. REFERENCES

1) Proc. 33th Annual Meeting Soc. Nucl. Med., Washington 1986, J. Nucl. Med.**27**, Abstr. 142, 687, 691, pp.911, 1043, 1044(1986).
2) Guillaume,M. and Brihaye,C.,"Generators of ultrashort lived radionuclides for routine clinical aplications,"Radiochim. Acta **41**,119(1987).
3) Glazov, A.A., Denisov, Yu.N., Dmitrievskij, V.P. et al. "Cyclotron for medical isotopes production (U–120I)," 2nd Int. Conf. on Cycl. and their Appl., Bechine ČSSR 1989 (JINR, Dubna 1989), D9-89-708, pp.87-95.
4) Zvara,I.,"Possibility of ^{123}I production for radiodiagnostics using electron accelerators," Comm. JINR 18-82-20, Dubna 1982.
5) Flerov,G.N., Oganessian,Yu.Ts., Belov,A.G., Starodub,G.Ja., "Production of short-lived ^{123}I isotope at the microtron MT–25," Preprint JINR 18-85-75, Dubna 1 1985.
6) Oganessian, Yu.Ts., Starodub, G.Ja., Buklanov, G.V., Korotkin, Yu.S., Belov, A.G.,"Production of ^{123}I radiobiological specimen on 25 MeV electron beam," Preprint JINR 18-88-758, Dubna 1988.
7) Dmitriev, S.N., Oganessian, Yu.Ts., Buklanov, G.V. et al., "Production of radiochemically ultra pure Plutonium-237 for metabolism research in human body," presented at the 3rd Int.Conf. on Nuclear and Radiochemistry, Vienna, Austr.,Sept.1992.