THE PRODUCTION OF RADIONUCLIDES ^{123}I, ^{77}BR FOR NUCLEAR MEDICINE WITH HIGH ENERGETIC ^{4}HE PARTICLES.

F.Helus, W.Maier-Borst
Deutsches Krebsforschungszentrum, Institut für Nuklearmedizin, 69 Heidelberg, Germany.

R.M.Lambrecht, A.P.Wolf
Brookhaven National Laboratory, Chemistry Department, Upton, New York 11973, USA.

Abstract

The feasibility of using 50-102 MeV alpha particles to produce the $^{123}Xe \longrightarrow {}^{123}I$ and $^{77}Kr \longrightarrow {}^{77}Br$ generators were evaluated using targets of natural sodium iodide and sodium bromide. Thick target yields of direct and indirect produced ^{123}I and ^{77}Br have been measured. Production rates for other resulted radionuclides were also measured, and the level of indirectly produced ^{125}I impurity were determined.

Introduction

The desirable physical characteristics of iodine-123 that make the nuclide, if used in high radionuclidic purity, nearly ideal for radiopharmaceutical applications are well known. The highest purity ^{123}I available is produced from the $^{123}Xe \xrightarrow{2,1hr} {}^{123}I$ generator, since the radiohalogens produced by direct nuclear reactions can be removed from ^{123}Xe parent before it decays to ^{123}I 1,11). The radioiodine of consequence is then ^{125}I, which arises from the concurrent production of ^{125}Xe with ^{123}Xe and the decay of ^{125}Xe ($^{125}Xe \xrightarrow{16,8hr} {}^{125}I$) simultaneously with the decay of the ^{123}Xe. A compilation of some in literature described reactions for direct production of iodine-123 is listed in table 1.

TABLE 1

Reported methods of ^{123}I production - Direct reactions

Reaction	Incident beam energy (MeV)	Target material (natural-enriched %)	Thick Target yield (mCi/µAh)	Reference
$^{121}Sb\ (^{4}He,2n)^{123}I$	25	Sb - nat.	0,150	(2)
$^{123}Sb(^{3}He,3n)^{123}I$	23	Sb - nat.	0,024	(3)
$^{122}Te\ (d,n)^{123}I$	7	Te - 95,4	0,100	(1)
$^{123}\ (p,n)^{123}I$	19	Te - 79,0	0,440	(1)
$^{125}Te\ (p,2n)^{123}I$	28	Te - 96,2	0,54	(1)
$^{125}Te\ (p,3n)^{123}I$	36	Te - 95,5	0,85	(1)

Most of the cyclotron production methods producing ^{123}Xe have been evaluated and are shown in table 2.

TABLE 2

Reported methods of ^{123}I production -
Generator systems $^{123}Xe \xrightarrow{\beta^{+},EC} {}^{123}I$.

Reaction	Incident beam energy (MeV)	Target material (natural-enriched %)	Thick target yield (mCi/µAh)	Reference
$^{122}Te\ (\alpha,3n)^{123}Xe$	46	Te - 95,0	0,200	(4)
$^{122}Te(^{3}He,2n)^{123}Xe$	27	Te - 90,9	0,530	(1)
$123Te(^{3}He,3n)^{123}Xe$	30	Te - 76,5	1,10	(1)
$^{127}I\ (p,5n)^{123}Xe$	57,5	I_2 - nat.	3,0	(5)
$^{127}I\ (d,6n)^{123}Xe$	78	NaI- nat.	8,o	(6)
$^{124}Te\ (\alpha,5n)^{123}Xe$	85	Te - nat.	0,250	(7)
$^{127}I\ (\alpha,8n)^{127}Cs$	102	NaI- nat.		this work

The alpha reaction with 46 MeV alpha's has been in routine production4) as a source of ^{123}I for clinical use. The proton5) and deuteron6) spallation reactions $^{123}I(p,5n)^{123}Xe$, E_H= 50-65 MeV and $^{127}I(d,6n)^{123}Xe$, E_D= 65-69 MeV result in ^{123}I of nearly comparable purity. Certain accelerators such as the Karlsruhe cyclotron have 102 MeV alphas, but protons and deuterons too low energy to produce ^{123}Xe by either reaction.

In this study we have tested the feasibility of using high energy alpha reactions to produce $^{123}Xe \longrightarrow {}^{123}I$ generator. Alpha reactions on ^{127}I (100% natural abundance) were tested. The reactions concerned are shown in table 3. Nuclear reactions with high energy particles are more complicated than lower energy reactions. From our preliminary experiments it followed that ^{123}I is produced in two different ways - either by the direct reaction or indirectly via ^{123}Cs or ^{123}Xe. When we consider only very simple reaction mechanism then last two reactions in table 3 described directly produced ^{123}I. For indirectly produced ^{123}I we assume the reactions $^{127}I\ (^{4}He,8n)\ ^{123}Cs$ and $^{127}I\ (^{4}He,p7n)\ ^{123}Xe$.

Proc. 7th Int. Conf. on Cyclotrons and their Applications (Birkhäuser, Basel, 1975), p. 474-477

TABLE 3

Reaction	Q (MeV)
$^{127}I\ (^{4}He,4n)^{127}Cs \longrightarrow {}^{127}Xe \longrightarrow {}^{127}I$ (stab.)	- 32,61
$^{127}I\ (^{4}He,5n)^{126}Cs \longrightarrow {}^{126}Xe$ (stab.)	- 42,75
$^{127}I\ (^{4}He,6n)^{125}Cs \longrightarrow {}^{125}Xe \longrightarrow {}^{125}I$	- 50,91
$^{127}I\ (^{4}He,7n)^{124}Cs \longrightarrow {}^{124}Xe$ (stab.)	- 61,50
$^{127}I\ (^{4}He,8n)^{123}Cs \longrightarrow {}^{123}Xe \longrightarrow {}^{123}I$	- 70,04
$^{127}I\ (^{4}He,{}^{4}He\ n)^{126}I$	- 9,14
$^{127}I\ (^{4}He,{}^{4}He2n)^{125}I$	- 16,24
$^{127}I\ (^{4}He,{}^{4}He3n)^{124}I$	- 25,84
$^{127}I\ (^{4}He,{}^{4}He4n)^{123}I$	- 33,30
$^{127}I\ (^{4}He,2p\ 6n)^{123}I$	- 61,60

Reactions (α,8n) and (α,6n) have been studied previously[12], but the objective of that study was the identification and nuclear decay properties of ^{123}Cs and ^{125}Cs. Cross-section and yield data have not been reported. Xenon was separated from the target material by using two different techniques - generator method of Sodd[1] and chemical method.

Bromine-77 appears to be the best bromine nuclide, because it has a 56hr half-life and lower energy gamma radiation than either ^{76}Br or ^{82}Br. The published production methods and potential production reactions are shown in table 4.

TABLE 4

Radionuclides produced by 100 MeV alpha bombardment of sodium iodide

Nuclide	Half-life	E_γ (keV)	Analyzed gamma-lines abundance %	Thick target yield $\mu Ci/_{\mu Ah}$ EOB
^{121}I	2,12 h	212,5	84,3	1359,4
^{121}Te	17,0 d	573,08	79,1	5,6
^{123}Xe	2,08 h	148,70	50,0	541,6
^{123}I	13,3 h	159,10	83,0	684,0
^{124}I	4,17 d	602,71	62,0	34,2
^{125}Xe	16,8 h	188,43	55,0	1022,9
^{125}I	60,14 d	calculated from ^{125}Xe		12,1
^{126}I	12,8 d	388,47	35,4	24,9
^{127}Cs	6,25 h	411,1	63,0	1812,9
^{127}Xe	36,406 d	202,84	58,2	22,0
^{24}Na	15,0 h	1368,55	100,0	403,1

Production of ^{77}Br by the alpha particle bombardement of arsenic pentoxide has been made on routine basis for clinical use[9,13]. In future ^{77}Br may find use in generator systems[10] as a label for bromine compounds and as an alternative to iodine when preparing radiopharmaceuticals[14]. Advantage in producing ^{77}Br by means of ^{77}Kr decay is the possibility of excitation labeling. In the production method described here, natural sodium bromide is bombarded with alpha particles in the energy range 50-102 MeV.

Experimental

The irradiations were performed at the Kernforschungszentrum cyclotron at Karlsruhe[15]. Energy selection was made by placing the internal target at the appropriate radius in the cyclotron. The integrated dose was measured only by the integration of the cyclotron beam current. For the yield figures the irradiation dose was 150 uAsec at a beam current of 0,5uA. The salt targets were pressed at 10kp/cm^2 and mounted in an Al target holder (5mmx7mmx11mm) and sealed with a 0,020mm Al foil of 99,99% purity. The sodium iodide and bromide (Merck) salt targets varied from 150 to 160 mg/cm^2. Identification and assay of gamma-ray emitting radionuclides were done on a 4096-channel Ge(Li) Intertechnique spectrometer combined with a Multi-20 small computer. The computer provided photopeak integration, a spectral plot and half-life information. Because of the transportation distance between Karlsruhe and Heidelberg, it was not possible to assay radionuclides with very short half-lives.

Results and Discussion

TABLE 5

Production rates of direct and indirect ^{123}I produced by 60 - 102 MeV alpha bombardment of sodium iodide.

E_α	Thick target yield of ^{123}I		
	Direct produced	Indirect produced	
MeV	$\mu Ci/\mu Ah$ ^{123}I	$\mu Ci/\mu Ah$ ^{123}Xe	$\mu Ci/\mu Ah$ ^{123}I
60	9,0	—	—
70	84,8	—	—
80	204,1	—	—
85	254,2	11,4	3,1
90	328,4	65,2	17,4
95	415,2	225,2	60,1
100	539,3	541,6	144,7
102	526,9	626,8	167,1

The thick target yield of radionuclides produced by 100 MeV alpha bombardement of sodium iodide were determined and are listed in table 5.

^{124}I and ^{126}I nuclides can be produced only by direct reactions, because ^{124}Xe and ^{126}Xe are stable isotopes. The most probable reactions to produce ^{124}I and ^{126}I directly are shown in table 3. Presence of all directly produced radioiodines does not affect the radionuclidic purity of the ^{123}I if the radioxenons are separated from the NaI either during or immediately after the irradiation.

Table 6 summarizes the thick target yield measurements for the production of ^{123}Xe by bombardement of NaI with 60-102 MeV alphas.

TABLE 6

Methods of ^{77}Br production

Direct reaction	Q (MeV)	Reference
$^{75}\mathrm{As}\ (^{4}\mathrm{He},2n)^{77}\mathrm{Br}$	-13,51	(9)
$^{76}\mathrm{Se}\ (d,n)^{77}\mathrm{Br}$	- 3,04	—
$^{78}\mathrm{Se}\ (p,2n)^{77}\mathrm{Br}$	-12,64	—
Indirect reaction		
$^{76}\mathrm{Se}\ (^{4}\mathrm{He},3n)^{77}\mathrm{Kr} \rightarrow {}^{77}\mathrm{Br}$	-26,81	(10)
$^{76}\mathrm{Se}\ (^{3}\mathrm{He},2n)^{77}\mathrm{Kr} \rightarrow {}^{77}\mathrm{Br}$	- 6,23	—
$^{79}\mathrm{Br}\ (p,3n)^{77}\mathrm{Kr} \rightarrow {}^{77}\mathrm{Br}$	-22,76	—
$^{79}\mathrm{Br}\ (^{4}\mathrm{He},6n)^{77}\mathrm{Rb} \rightarrow {}^{77}\mathrm{Kr} \rightarrow {}^{77}\mathrm{Br}$	-48,44	this work

The data indicate that the production rate of ^{123}Xe increases from 11,4 to 626,8 μCi/μAh between 85 and 102 MeV. ^{123}Xe was not observed at $E_\alpha < 85$ MeV.

The yield of ^{123}Xe and its corresponding yield of ^{123}I is too low, and the production rate of ^{125}I too high (as follows from table 4), to make the alpha reactions on ^{127}I of practical value at these energies.

Similar work has been done to investigate the possibility to produce $^{77}\mathrm{Kr} \longrightarrow {}^{77}\mathrm{Br}$ generator. The production rates obtained for directly and indirectly produced ^{77}Br with 60-102 MeV alphas are given in table 7.

TABLE 7

Production rates of direct and indirect ^{77}Br produced by 50 - 102 MeV alpha bombardment of sodium bromide.

E_α	Thick target yield of ^{77}Br		
	Direct produced	Indirect produced	
MeV	μCi/μAh ^{77}Br	μCi/μAh ^{77}Kr	μCi/μAh ^{77}Br
60	30,50	—	—
65	53,90	—	—
70	76,46	34,20	0,77
75	89,21	87,52	1,98
80	81,87	254,14	5,75
85	123,53	513,72	11,63
90	172,90	624,20	14,13
95	238,25	1298,30	29,40
100	281,28	1784,50	40,41

^{77}Kr yield increases very rapidly from 34 to 1784 μCi/μAh with alpha energy from 70 to 102 MeV. From yield figures at 100 MeV alpha energy it follows that only about 12% of the obtained ^{77}Br is produced via ^{77}Kr. The nuclear reaction leading to ^{77}Br and ^{77}Kr are expected to occur more favorably for routine production of ^{77}Br only when higher beam currents or higher alpha energy are available.

Table 8 summarizes production rates of radionuclides produced by 100 MeV alphas.

TABLE 8

Radionuclides produced by 100 MeV alpha bombardment of sodium bromide

Nuclide	Half-life	Analyzed gamma-lines		Thick target yield
		E_γ (keV)	abundance (%)	μCi/μAh EOB
^{74}As	17,7 d	595,7	59,5	2,32
^{75}As	120 d	135,9	58,0	3,74
^{75}Br	100 m	286,5	80,0	748,56
^{76}Br	15,9 h	559,0	65,7	380,40
^{77}Kr	1,24h	129,7	84,0	1784,50
^{77}Br	56 h	238,9	26,0	321,70
^{79}Kr	34,9 h	261,3	11,0	265,13
^{81}Rb	4,7 h	446,3	23,5	1631,06
^{82m}Rb	6,4 h	776,8	83,0	236,77
^{83}Rb	83 d	529,6	30,4	2,66

The most important impurity is ^{76}Br from the decay of ^{76}Kr. This can be limited by allowing the ^{77}Kr to decay only for three half-lives. By using the gas flow system

^{77}Kr can be separated from directly produced radiobromines and other contaminants. This is the first report of the use of 70-102 MeV alpha bombardement to produce $^{77}\text{Kr} \longrightarrow {}^{77}\text{Br}$ generator.

Acknowledgment

We are indebted to the cyclotron staff of the Kernforschungszentrum Karlsruhe for their active cooperation and H.ASMUS and H.SCHULTZ for the continuous help.

References

1) Sodd,V.J., Blue,J.W., and Wellman,H.N., U.S.Department of Health, Education and Welfare Publication BRH/DMRE 70-4 (1970)

2) Silvester,D.J., Sugden,J., and Watson,I. A., Radiochem.Radioanal Letters 2, 17 (1969)

3) Dahl,J.R., and Tilbury,R.S., Int.J.Appl. Rad.Isotopes 23, 431 (1972)

4) Lambrecht,R.M., Wolf,A.P., Radiation Research 52, 32 (1972)

5) Fusco,M.A., et al., J.Nucl.Med., 13, 729 (1972)

6) Weinreich,R., Schult,O., and Stöcklin, G., Int.J.Appl.Rad.Isotopes 25, 535 (1974)

7) Lambrecht,R.M., et al., (in press)

8) Erdtmann,G., Soyka,W., Die -Linien der Radionuklide, KFA JÜL-1003-AC, Apr.1974

9) Helus,F., Radiochem.Radioanal.Letters 3, 45 (1970)

10) Blue,J.W., Benjamin,P.P., J.Nucl.Med.12, 416 (1971)

11) Lambrecht,R.M., et al., J.Nucl.Med.13, 266 (1972)

12) Mathur,H.B., Hyde,E.K., Phys.Rev.96, 126 (1954)

13) Nunn,A.D., Nucl.Instruments and Methods 99, 251 (1972)

14) Sargent,T., et al., J.Nucl.Med.16, 243 (1975)

15) Schulz F., and Bellman H., KFK Report, Karlsruhe 685, Dec. (1967)