HIGH PURITY IODINE-123 PRODUCED VIA P,N REACTION

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Studies on radionuclide purity of iodine-123 produced during irradiation of targets with different degree of ^{123}Te enrichment by protons from MGC-20 cyclotron have been carried out. The best result is obtained for the target containing 0.6% of ^{122}Te, 99.3% of ^{123}Te and 0.06% of ^{124}Te (the other isotopes altogether <0.04%). The final product contained as the only impurity <0.03% of ^{124}I by the end of bombardment (1 hour). The greater part of this impurity seems to be caused by the reaction of ^{123}Te(p,γ)^{124}I.

1 Introduction

^{123}I radionuclide is one of the most promising isotopes in nuclear medicine [1]. This is explained by its ability for substituting the hydrogen atoms virtually in all the compounds. The iodine-labeled compounds are more natural for human organism, than many other radiopharmaceuticals. However, the high production cost of iodine-123 by means of cyclotrons limits the possibilities of its application, so technetium-99m is used in most cases. It is not surprising, that over twenty nuclear reactions for ^{123}I production have been investigated. However, only four nuclear reactions are used for commercial production of ^{123}I (table 1).

Table 1: Nuclear reactions used for commercial production of ^{123}I.

	Reaction	E_p, MeV	Ref.
1	^{127}I(p,5n)^{123}Xe(e,β$^+$)^{123}I	≈ 70	[2]
2	^{124}Xe(p,2n)^{123}Cs(β$^+$)^{123}Xe(e,β$^+$)^{123}I	≈ 30	[3,4]
3	^{124}Te(p,2n)^{123}I	25-30	[5,6,7]
4	^{123}Te(p,n)^{123}I	12-17	[8,9]

Any radiopharmaceutical preparation in nuclear medical diagnostics is characterized by radionuclide purity determined by the content of radionuclide impurities. Emission of impurities may deteriorate the image contrast in diagnostics and increase the exposure dose of patient. Higher requirements on radionuclide purity meet the modern trends of nuclear medicine. Up to now, iodine-123 of the highest quality is produced using ^{124}Xe. However this way involves the use of 30 MeV accelerator, ^{124}Xe - very expensive gas for target and complicated process equipment. In the first and third reactions (table 1) the impurities arise from the interaction of protons with the basic target material; thus there are the principal limitations on radionuclide purity. In the first case ^{125}I is produced by ^{127}I(p,5n), in the third case it is impossible to obtain the ^{124}I content <0,6% (by activity) because of ^{124}Te(p,n) reaction.

The production of ^{123}I by ^{123}Te(p,n)^{123}I reaction is attractive because the small-size cyclotron with 14-15 MeV protons can be used. (As a target, tellurium oxide TeO_2 is applied). Iodine-123 being produced in the target is separated by a rather simple method of dry distillation in the chemical form, which is convenient for subsequent synthesis. There are no principal limitations on the achievement of radionuclide purity close to 100%. Therefore, the main goal of this work is to study the possibility of production of ^{123}I with high radionuclide purity by ^{123}Te(p,n)^{123}I reaction.

2 Analysis of results of the previous studies.

In most works on the use of ^{123}Te(p,n)^{123}I reaction, the attempts to achieve the high radionuclide purity have failed. The impurities arising on proton irradiation of target are formed, as a rule, in reactions on tellurium isotopes. Such impurities constitute isotopes of iodine; among them the most dangerous ones are ^{124}I (half-life 4 days, gamma ray 603 keV and β+-emission), ^{125}I (half-life 60 days, gamma ray 35.5 keV), ^{126}I (half-life - 13 days, hard gamma rays and β$^-$-emission) and ^{130}I (half-life 12.4 hours, hard gamma rays and β$^-$-emission). The higher is the target enrichment by ^{123}Te the lower is the value of impurities. Table 2 presents data on impurity content in final product by the end of bombardment (EOB) for different composition of targets. As it is seen from table 2, with increase of the target enrichment by ^{123}Te up to 91%, only the impurity of ^{124}I remains significant. For diagnostic purposes the impurity of ^{124}I in preparation should be, by various estimates, below 5% [6], 3-4% [10] or 2-3% [7]. Nevertheless, in recent years there is a trend to make the impurity content decrease for more prolonged application time of preparation and better quality of images when using such preparations as MIBG or fatty acids.

Table 2 : Isotope composition of tellurium targets in % and content of iodine impurities in final product as a percentage of activity.

Mass number of tellurium	Isotope composition of targets			
	[8] target 1	[8] target 2	[9] target 1	[9] target 2
120		0.01	0.3	
122	2.3	1.77	1.17	1.60
123	67.3	70.1	85.4	91.0
124	11.7	10.54	5.12	2.70
125	3.9	3.24	1.69	0.70
126	5.7	5.07	2.56	1.30
128	5.0	4.78	2.27	1.40
130	4.1	4.49	1.80	1.30
Impurities by the end of bombardment				
^{124}I	2.3	2.7	0.93	0.66
^{125}I	0.04			
^{126}I	0.26	0.18	0.11	0.02
^{130}I	2.1	4.00	<0.5	0.26

3 Measurements of ^{124}I impurity.

At the Radium Institute works have been carried out recently on improving the quality of radiopharmaceuticals labeled ^{123}I due to decrease of ^{124}I impurity. Table 3 presents data obtained at 15 MeV protons from MGC-20 cyclotron at different times for targets used in the production of ^{123}I-labeled radiopharmaceuticals. ^{124}I impurity was determined by measurements of gamma-spectra by a standard procedure with the use of Ge(Li) detector (other impurities of iodine with hard gamma rays were not detected).

Table 3: Isotope composition of targets used at the Radium Institute and ^{124}I content in final product.

Mass number	Isotope composition of tellurium targets in %			
	1990 target 1	1994 target 2	1996 target 3	1997 target 4
120	<0.1	<0.1	<0.1	<0.01
122	1.6	0.5	8	0.6
123	95.6	98.5	91.5	99.3
124	2.7	0.9	0.5	0.06
125	<0.1	<0.1	<0.1	<0.01
126	<0.1	<0.1	<0.1	<0.01
128	<0.1	<0.1	<0.1	<0.01
130	<0.1	<0.1	<0.1	<0.01
^{124}I impurities in % of activity for 1 hour irradiation				
	0.37	0.16	0.11	0.024

The target 1 enriched by 95,6% of ^{123}Te enabled us to obtain ^{123}I with 0.5-0.6% of ^{124}I impurity at EOB, what made it possible to use the radiopharmaceutical not only on the date of its production, but also the day after. In 1994 [11] target 2 with 98,5% enrichment was used; the impurity activity of ^{124}I was reduced by half. It turned out that better results could be obtained when using the target 3 with lower enrichment by ^{123}Te, decreasing the ^{124}I impurity and increasing the ^{122}I impurity. The formation of ^{122}I as a result of $^{122}Te(p,n)$ reaction dos not influence radionuclide purity, because the half-life of ^{122}I is 3,6 min. ^{121}I, resulting from $^{122}Te(p,2n)$ reaction (half-life 2,1 hours, main energy of gamma ray - 212,5 keV) dos not deteriorate the preparation quality as well. The highest radionuclide purity of the preparation was achieved in 1997 with the use of the target 4 enriched by 99.3% of ^{123}Te. However, as it can be seen from the estimates given below, the value of ^{124}I impurity proved to be higher than it could be expected from the isotope composition of target.

Actually, the activity value obtained as a result of nuclear reaction is proportional to number of target nuclei (N), reaction yield (Y) and depends on irradiation time (t). The value of ^{124}I impurity activity in % would be as following

$$\eta^*_{124}=100*N_{124}*Y_{124}*(1-\exp(\ln 2*t/T_{1/2(124)}))/ N_{123}*Y_{123}*(1-\exp(\ln 2*t/T_{1/2(123)})) \quad (1)$$

Where t is irradiation time, Y_{123} and Y_{124} are yields of $^{123}Te(p,n)^{123}I$ and $^{124}Te(p,n)^{124}I$ reactions, respectively; $T_{1/2(123)}$ and $T_{1/2(124)}$ - half-lives of ^{123}I and ^{124}I, respectively. ^{123}I and ^{124}I yields of p,n-reactions with 15 MeV protons on ^{123}Te [9] and ^{124}Te [6] are rather alike in size. We assume that these values are the same, then

$$\eta^*_{124}=100*N_{124}*(1-\exp(\ln 2*t/T_{1/2(124)}))/ N_{123}*(1-\exp(\ln 2*t/T_{1/2(123)})) \quad (2)$$

The ratio N_{124}/N_{123} is determined by the content of tellurium isotopes in the target. Table 4 presents the estimated values of impurity ^{124}I with the use of targets of various isotope composition and value of impurity measured experimentally for t = 1 hour. It is evident that the ratio between the measured values and the estimates approaches 1, i.e. the assumption about the similarity of isotope reaction yields is valid. The exception is the value for the target 4 containing 99,3% of ^{123}Te.

In the case of 0,06% ^{124}Te, the value of ^{124}I impurity is three times greater than the expected one. This discrepancy can be explained by the occurrence of $^{123}Te(p,\gamma)^{124}I$ reaction. For eliminating this discrepancy it is sufficient that the yield of p,γ reaction for 1 hour of bombardment be equal to $1,6*10^{-4}$ of the yield of p,n reaction. If this is so, there is a principal limitation on radionuclide purity - 99,984 % for $^{123}Te(p,n)^{123}I$ reaction.

Table 4: Estimated and measured values of ^{124}I impurity in % normalized to irradiation time 1 hour.

Content in %		Ref.	η^*_{124}	η_{124}	$\frac{\eta_{124}}{\eta^*_{124}}$
Te-123	Te-124				
67,3	11,7	[8]	2,36	2,13	0,90
70,1	10,5	[8]	2,03	1,92	0,95
85,4	5,12	[9]	0,81	0,93	1,15
91	2,7	[9]	0,40	0,66	1,65
95,6	2,7		0,38	0,37	0,97
98,5	0,9		0,12(1)	0,16(1)	1,33
91,5	0,5		0,07(1)	0,11(1)	1,57
99,3	0,06		0,008(1)	0,024(3)	3,00

4 Assessment of ^{125}I impurity

Along with the formation of ^{124}I, it seems quite plausible that ^{125}I is formed through p,n reaction on ^{125}Te in the target. Therefore, special studies have been conducted for determination of ^{125}I in radiopharmaceutical sodium iodide. For determination of ^{125}I yield by intensity of its gamma ray 35.5 keV, a series of factors should be taken into account:

- intense absorption of soft gamma-rays;
- volatility of iodine;
- possible presence of ^{125m}Te, emitting gamma-quanta with the energy as ^{125}I.

To eliminate absorption, the sample being measured was prepared by multiple dropping and drying of sodium iodide solution on filter paper. The diameter of radioactive spot was no more than two centimeters.

The volatility of iodine was checked by several measurements of one sample at prolonged period of time. The intensity of 35.5 keV line remained constant within the error with allowance for ^{125}I decay in all the performed measurements.

For determining the presence of ^{125m}Te isomer, the solution of sodium iodide was evaporated, and the glass bottle, which contained it, was heated on an electric stove up to complete removal of ^{125}I. Gamma-line 35.5 keV was not observed on the measured spectrum, what permits to draw a conclusion about the absence of detectable ^{125m}Te quantity.

The value of ^{125}I impurity for the targets enriched by 95.6% (target 1), 98.5% (target 2) and 99.3% (target 4), normalized to an irradiation time 1 hour constitute - $2,1(1)*10^{-3}$%, $3,6(2)*10^{-4}$% and $1,4(1)*10^{-4}$ %, respectively.

5 Conclusion

The studies performed at the Radium Institute on the radionuclide purity of radiopharmaceuticals labeled by ^{123}I arising from proton irradiation of tellurium oxide targets with various enrichment degree have given the following results. ^{124}I is practically the sole significant impurity of the final product. The value of this impurity decreases with the decrease of ^{124}Te content in the target. For all the targets under investigation the impurity of ^{124}I in the final product does not affect the image quality, and the ^{124}I radiation exposure on the production date was considerably less than those of ^{123}I. Clearly within 30 hours after irradiation the contribution of ^{124}I increases. Table 5 presents data on the effect of ^{124}I content (different targets) on the increase of radiation exposure to the patient. The data are given for the case of thyroid diagnostics with 35% uptake [12].

Table 5 : ^{124}I contribution into radiation exposure with the use of different targets in 30 hours after irradiation

Target	^{124}Te content in target (%)	^{124}I content by activity (%)	Ratio between dose of ^{124}I and ^{123}I
№1	2,7	2,0	1,30
№2	0,9	0,8	0,56
№4	0,06	0,12	0,08

It is seen from the Table 5 that the radiation exposure in 30 hours after irradiation for the targets with ^{124}Te content below 0,9% makes a contribution from ^{124}I below the half of patient's exposure dose from ^{123}I. The doses caused by the presence of ^{125}I in the quantity $<3.10^{-3}$% at the EOB are negligible. Thus, using the radiopharmaceuticals for two days after EOB, ^{123}I produced by proton irradiation of tellurium target with ^{124}Te content <0.9% has about the same quality as iodine obtained from ^{124}Xe(p,2n) reaction.

In order to attain the high radionuclide purity, there is no need for high enrichment by ^{123}Te; it is sufficient to decrease ^{124}Te content in target (with the increase of ^{122}Te content to 8-10%).

The highest radionuclide purity 99.976% was obtained for the target containing 0.06% of ^{124}Te. The tellurium of this target was produced by the technology for centrifugal separation of stable isotopes. The peculiarities of enrichment are considered in [13]. One of the advantages of this technology for production of high-pure ^{123}I is the lower cost of starting isotope of ^{123}Te comparing to the highly enriched ^{124}Xe-isotope.

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