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Dependence of quality of thallium-201 on irradiation data

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ABSTRACT

Backgrounds: Thallium-201 is produced through ^{203}Tl *(p, 3n)* ^{201}pb ^{201}Tl reaction by cyclotron. This radioisotope has known as one of the cyclotron radioisotopes which is used for myocardial perfusion in the coronary artery disease, Tl-201 after chemical purification and quality control in the form of ^{201}Tl-chlorid is ready to send to the hospitals.
Materials and methods: In this work the effect of the proton energy on quality of Tl-201, was studied. Radionucleidic purity was determined by high purity Ge (HPGe) detector Gamma spectrometer, in production time and after one half-life (73h). The targets were coated with Enriched Thallium-203 (97%).
Results: The Variation of thickness of targets was 18.3±1.3µm. The different energies of bombardment on quality of Tl-201 and Tl-200, Tl-202, and Pb-203 (as impurity) were studied. The results have shown that optimum energy for proton was 28.5 MeV.
Conclusion: The variation energy of bombardment can change the purity of Tl-201 but all results were in the standard range according to the United States Pharmacopoeia (USP) and European Pharmacopoeia. *Iran. J. Radiat. Res.; 2003; 1(1): 51 - 54.*

Keywords: *Quality control of thallium chloride, quality of* ^{201}Tl*, radionuclide purity, thallium 201.*

INTRODUCTION

Thallium-201, has known as one of the cyclotron radioisotopes which is used for myocardial perfusion in the coronary artery disease, this radioisotope is obtained by proton irradiation of an enriched Thallium-203 target in cyclotron involving with the threshold reaction; ^{203}Tl (p 3n) ^{201}pb. This reaction is followed by the decay of the parent nuclide ^{201}pb (half-life 9.4h) into the Tl-201 by electron capture. Naturally occurring thallium consist of two main isotopes, thallium-203 (natural abundance 29.5%) and thallium-205 (natural abundance70.5%) the initial raw material for cyclotron targets is the enriched stable -thallium-203 (Lewis and Dewitt 1994, Kurenkov 1995, US Pharmacope 1995).

The overall production of this isotope will include preparation of the target, bombardment by a 26-30-cyclotron proton beam and chemistry of production.

Radiochemical procedure for Tl-201 implies three steps:

1- First one, the formed ^{201}pb is separated from the enriched Tl-203 after isolation of the irradiated target.

2- after a suitable decay time (32 hours) more than 90% of the ^{201}pb decay into Tl-201. The second step is separation of non-carrier added ^{201}Tl from remaining ^{201}pb.

3- after purification, the final solution is used as a pharmaceutical production of the sterile,

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radioactive injectable thallous chloride (Kuzlova 1987, Winkel 1995).

Specification of thallous chloride (^{201}Tl) is summarized in table 1.

Table 1. Specification of ^{201}Tl

Half-life	73.1 hours
Energy of Gamma	0.135, 0.166, 0.167 MeV
X-rays	0.068 to 0.082 MeV
Radionuclid Impurity	Tl-202<1.9% Tl-200<1.0% Pb-203<0.25%
Specific Activity	>3,7GBq. μg (100mCi/μg)
Chemical form	Sterile, Isotonic solution
Energy of bombardment	28-30MeV
Average Beam Current	180-200μA per target

MATERIALS AND METHODS

Target preparation: Enriched thallium-203 (99.7%) was coated by electro-deposition on a copper -baking target. Copper was chosen as the substrate due to its suitable heat condition; in this process the targets are plated from alkaline EDTA solution containing an anodic depolarizer (hydrazine hydrate) and a Wetting agent applying a bipolar chopped saw tooth plating voltage. Four targets are plated simultaneously with a current yield better than 98% in less than 5 hours. The thickness of targets was 18.3±1.3 μm.

Target Irradiation:The copper-plated Thallium targets situated on special shuttle were sent through the cyclotron solid target room by rabbit system. The shuttle geometry was designed such that the targets could see the beam at the angle of 6°. Then the targets were bombarded with the intensity of 200μA protons current integrator, which was connected, and measured the beam current to faraday cap. Afterwards, the target cooling system was shut off and target was guided through to the hot cell by rabbit system. To setup a series irradiation of identical enriched ^{201}Tl-target bombardment during irradiation time 8±0.4 hours for the energy on increasing ^{201}Pb yield were absorbed. The energy of the proton beam was reduced during passage through the target and elastic collisions, atomic excitation and ionization lost energy. Indicating peak energies for the reactions (p, n), (p, 2n) and (p, 3n) etc. In addition, similar production cross sections existed for protons bombarding thallium-205 indicating that even a trace impurity level of thallium-205 within the target material thallium-203 would lead to bombarding thallium-205 indicating that even a trace impurity level of thallium-205 within the target material thallium-203 would lead to radionuclide impurity species in the final product. The competition reactions are given in table 2. And elastic collisions, atomic excitation and ionization lose energy. Indicating peak energies for the reactions (p, n), (p, 2n), and (p, 3n) etc. In addition, similar production cross sections existed for protons bombarding thallium-205 indicating that even a trace impurity level of thallium-205 within the target material thallium-203 would lead to radionuclide impurity species in the final product. The competition reactions are given in table 2.

Table 2. Competing Reactions Thallium bombardment

Reaction	Initial material	Radioactive products	Half life
(p, 4n)	Tl-203	Pb-200	21.58 h
		↓	
		Tl-200	26.1 h
(p, 3n)	Tl-203	Pb-201	9.4 h
		↓	
(p, 5n)	Tl-205	Tl201	73.1 h
(p, 2n)	Tl-203	Pb-202m	3.62 h
		↓	
(p, 4n)	Tl-205	Tl-202	12.32 d
(p, n)	Tl-203	Pb-203	51.9 h
		↓	
(p, 3n)	Tl-205	Tl-203	Stable
(p, 2n)	Tl-205	Pb-204m	1.1 h
		↓	
		Pb-204	$>1.4\times1o^{17}$y
(p, n)	Tl-205	Pb-205	1.5×10^{7} y

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RESULTS

Maximum $^{200}Pb/^{201}Pb$ activity ratio at the end of chemistry-1If A (^{200}Pb) and A (^{201}Pb) represent the lead activities of the bulk at EOC-1, and A (^{200}Tl) and A (^{201}Tl) represents the thallium activities at calibration time, the maximum A (^{200}pb)/A (^{201}Pb) lead ratio can be calculated from equation (1):

$$\frac{A(^{200}Tl)}{A(^{201}Tl)} = \frac{2}{95} = \frac{A(^{200}Pb)}{A(^{201}Pb)} \times \frac{G(^{200}Tl)}{G(^{201}Tl)} \times \frac{D(^{200}Tl)}{D(^{201}Tl)} \qquad (1)$$

Where: G (^{200}Tl) and G (^{201}Tl) are the growing factors of ^{200}Tl and ^{201}Tl for a decay time of 32hrs.ie.Chemistry –2 is performed 32hours after EOC-1, the time for maximum ^{201}Tl yield. These factors can be easily calculated by means of MDEQ.BAS code. It follows that, G (^{200}Tl) =0.332 and G (^{201}Tl) =0.095 D (^{200}Tl) and D (^{201}Tl) are the decay factors of associated with the pre calibration time (72hrs). From the half-life it readily follows that, D (^{200}Tl) =0.148 and D (^{201}Tl) =0.505.

By substituting these numerical values into equation (Dewitt 1994) one obtains:

$$R = \frac{A(^{200}Pb)}{A(^{201}Pb)} = 0.02 \qquad (2)$$

The maximum ^{200}pb decay at EOC-1 must be less than or equal to2% of the ^{201}pb activity. The curve for the ^{203}Tl (p, 3n) ^{201}pb reactions shows a maximum at 29 MeV.
While the threshold energy of the ^{203}Tl(p, 4n) ^{200}pb reaction is located at about 28.0 MeV. This suggests that, to meet the USP xxII requirements R≤2; equation (Dewitt 1994) the energy of the impinging protons may be more than 28 MeV resulting in an increase of the ^{201}pb yield (US Pharmacope 1995).

The excitations cross-section for proton bombardment of enriched thallium-203 with cyclotron (cyclone-30 IBA) in NRCAM is given in figure 1. From this graph it is possible to determine the maximum bombardment energy for the proton beam by ^{200}Pb as a radionuclide impurity that is created via the reaction (p, 4n), consequently the maximum proton energy should be fixed at 28.5 MeV. The minimum bombardment energy or exit energy of the proton beam is similarly constrained buy the impurity Pb-200m created by the reaction (p, 2n). Regarding the minimum energy at the exit of the enriched Tl-201 material similarly fixed at 22.5 MeV.

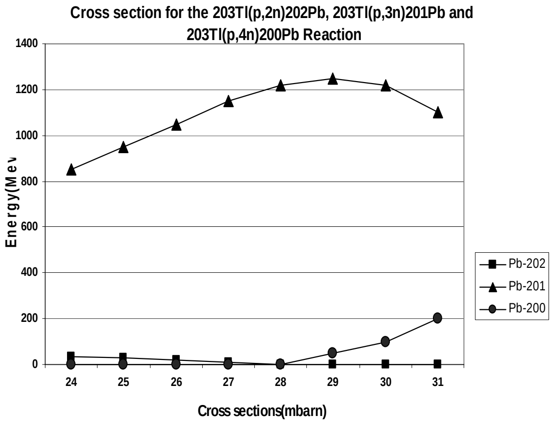

Figure 1. Cross section for the 203 TI (p, 2n) 202pb, 203T(p, 3n) 201 pb and 203TI(p, 4n, 200 pb reaction

Influence of the proton energy on ^{201}pb yield:

From the excitation graph, the energy loss of protons per μm Tl, an effective thickness of the Tl-layer (thickness in beam direction =773μm), can be calculated easily. The input and output energies of the protons and the ^{201}Pb yield that is proportional to the surface area under the excitation curve between input and output energy of the particles (SRIM 2001). This area can be fairly estimated by planimetry. Some results are summarized in Table 3.

Table 3. Influence of proton energy on the ^{201}Pb yield

Proton Energy (MeV)		**Surface area (mm)**	**^{201}pb yield (Arbitrary unit)**
Ein	Eout		
28,0	20,0	0,6781	1
28.5	21.0	0.6319	1,08
29.0	21,5	0,6407	1,13
29.5	22	0.6508	1,18
30,0	22,5	0,665	1,22

Bombardment is done during the same irradiation time (standard 10 hours), for which

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the energy set differs by for example 0.5 MeV (28.0, 28.5, 29.0, 29.5 and 30.0). By setting up a series of irradiation of identical thallium targets (enriched or natural), in products, the highest energy still meeting the USP requirement (R≤ 2) is selected.

Radionuclidic quality control: Calibrated HPGe spectrometry revealed the following radionuclidic composition of the ^{201}Tl batch:

^{201}Tl ≤ 99.5%
^{200}Tl ≤ 0.1%
^{202}Tl ≤ 0.3%
^{201}pb ≤ 0.003%
^{203}pb ≤ 0.05%

DISCUSSION

The maximum bombardment energy for the proton beam- in this case it was determined by the impurity radionuclide Pb-200 created via the reaction (p, 4n), resulting in a doughtier product Tl-200 that has a half-life of 26 hours and a high-energy gamma ray. This would increase the patient dose considerably if the percentage impurity was allowed to be greater than 1%. Consequently this fixes the maximum bombardment energy for thallium production at 28.5 MeV. The minimum bombardment energy or exit of the proton beam is similarly constrained by the impurity radionuclide Pb-202 resulting ^{202}Tl has a half-life of 12 days and a gamma emission of 1.0 MeV. The minimum energy at the exit of the enriched Tl-203 material is similar fixed at 24 MeV.

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