PRODUCTION OF RADIOACTIVE IODINE

David J. Schlyer

Iodine-123

Probably the most widely used cyclotron produced radiohalogen is I-123. It has gradually replaced I-131 as the isotope of choice for diagnostic radiopharmaceuticals containing radioiodine. It gives a much lower radiation dose to the patient and the gamma ray energy of 159 keV is ideally suited for use in a gamma camera. The gamma ray will penetrate tissue very effectively without excessive radiation dose. For this reason, it has in many instances replaced the reactor produced iodine-131 (Lambrecht and Wolf 1973). A great number of radiopharmaceuticals have been labeled using I-123 and the number is increasing.

One of the most promising uses of I-123 is in the imaging of monoclonal antibodies to localize and visualize tumors. However, preclinical and clinical experiences with radiolabeled antibodies have not realized the expectations regarding specificity and sensitivity of tumor localization with these agents. It appears that much of the administered activity is not associated with the tumor site and only a small fraction actually accumulates there. Work continues in this area and tumor-associated antigens can be targets for specific antibody reagents.

Another area of active research in radioiodine labeled compounds is in the area of receptor binding. This area, at the moment, is an area of basic research with only a few clinical applications. The strides mad in this area will probably bring clinical diagnostic tests in the future. Receptor specific ligands have been synthesized with I-123 for SPECT imaging and now with I-124 for PET imaging. Ligands have also been synthesized for reuptake sites.

Production Reactions

The major reactions for the production of iodine-123 are given in the following table. As can be seen from this table there are two major routes to I-123. The first is the direct route and the second is through the Xenon-123 precursor. The advantage of going through the Xe-123 is that the xenon can be separated from the original target material and allowed to decay in isolation which gives an I-123 with very little contamination from other radioisotopes of iodine.

Nuclear Reaction	Useful Energy Range (MeV)	% Natural Abundance	References
$^{127}I(p,5n)^{123}Xe : {}^{123}I$	55 +	100	Adilbish et al 1980, Cuninghame et al 1976, Jungerman and Lagunas-Solar 1981, Zaitseva et al 1991. Lagunas-Solar et al 1986
$^{127}I(d,6n)^{123}Xe : {}^{123}I$	83	100	Weinreich et al 1976

$^{122}Te(d,n)^{123}I$	14 to 8	2.4	Zaidi et al 1983
$^{123}Te(p,n)^{123}I$	15 to 8	0.87	Barral et al 1981
$^{124}Te(p,2n)^{123}I$	26 to 20	4.6	Dahl and Tilbury 1972, Clem and Lambrecht 1991, Hupf et al 1968
$^{122}Te(^{4}He,3n)^{123}Xe$: ^{123}I			Lambrecht and Wolf 1972, Silvester et al 1969
$^{124}Xe(p,pn)^{123}Xe$: ^{123}I	15 to 30	0.10	Graham et al 1985, Witsenboer et al 1986, Firouzbakht et al 1987, Tárkányi et al 1991, Kurenkov et al 1989
$^{121}Sb(^{4}He,2n)^{123}I$	15 to 25	57.4	Watson et al 1973
$^{123}Sb(^{3}He,3n)^{123}I$	20 to 30	42.6	Watson et al 1973

The most common reaction for the production of I-123 in the recent past has been the $^{124}Te(p,2n)^{123}I$ reaction on highly enriched Te-124. The high enrichment is necessary since there is a second source of I-124 contamination and this comes from the $^{125}Te(p,2n)^{124}I$ nuclear reaction on any Te-125 which may be present in the target material (Guillaume et al 1975, Kondo et al 1977a).

This leads to one of the basic facts of life in radioisotope production. It is not always possible to eliminate the radionulidic impurities even with the highest isotopic enrichment and the widest energy selection. An example of this is given below in Figure 3 for the production of Iodine-123 with a minimum of I-124 impurity (Guillaume 1975, Lambrecht and Wolf 1973, Clem and Lambrecht 1991, Qaim and Stöcklin 1983).

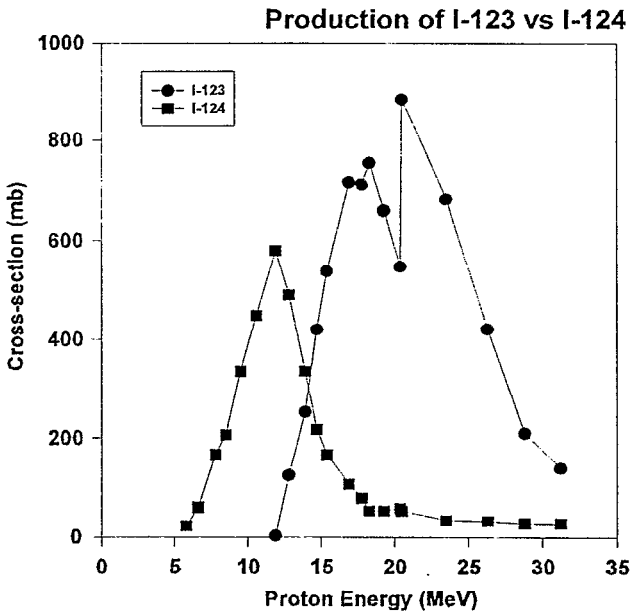

Figure 1 - Cross-sections of the $^{124}Te(p,2n)^{123}I$ and the $^{124}Te(p,n)^{124}I$ reactions

As can be seen from this graph, it is not possible to eliminate the I-124 impurity from the I-123 because the I-124 is being made at the same energy. All that can be done is to minimize the I-124 impurity by choosing an energy where the production of I-124 is near a minimum. In this case a proton energy higher than about 20 MeV will give a minimum of I-124 impurity.

As an example of how the impurity level can be calculated, the following equation can be written which allows calculation at any energy as long as the relevant cross sections are known (Barrall et al 1981). The percentage of I-124 in I-123 is given by:

$$\%I-124 = \frac{\sigma^{**}\frac{N^*}{N'} + \sigma^*}{\frac{S}{S'}\left(\sigma\frac{N}{N'} + \sigma'\right) + \left(\sigma^{**}\frac{N^*}{N'} + \sigma^*\right)} x100$$

Where:

$\sigma = {}^{123}Te(p,n)^{123}I$
$\sigma' = {}^{124}Te(p,2n)^{123}I$
$\sigma^* = {}^{124}Te(p,n)^{124}I$
$\sigma^{**} = {}^{125}Te(p,2n)^{124}I$
N = %Te-123
N′ = %Te-124
N* = %Te-125
$S = (1-e^{-\lambda 1t})$ (λ1- decay constant for I-123, t is time of irradiation)
$S' = (1-e^{-\lambda 2t})$ (λ2- decay constant for I-124, t is time of irradiation)

The reaction on tellurium has been gradually replaced by the $^{124}Xe(p,pn)^{123}Xe : {}^{123}I$ reaction since this gives I-123 with greatly reduced I-124 contamination. The dose to the patient is therefore reduced and the image is somewhat clearer.

In general, the production of I-123 through the Xe-123 precursor has replaced the direct production methods for those who can carry out the indirect production. There are two factors which limit the production of I-123 by the indirect methods. If the $^{124}Xe(p,pn)^{123}Xe : {}^{123}I$ method is used, the cost of the highly enriched Xe-124 is a factor. At the time of this writing, the cost of 1 liter of 99% enriched Xe-124 is about US$70,000 and a typical target takes between one to two liters of gas. This results in a substantial investment and although the gas can usually be quantitatively recovered after irradiation, the accidental loss of the gas could be a severe loss to a isotope production program. If the $^{127}I(p,5n)^{123}Xe : {}^{123}I$ reaction is used, a cyclotron energy of greater than 55 MeV is required and cyclotrons of this energy are becoming quite rare.

There is still some controversy as to the correct cross-section values for the production of

I-123 from enriched xenon-124. Several studies have been published and there has been a considerable amount of discussion in the amount of I-123 which can be produced from this reaction (Tarkanyi et al 1991, Kurenkov et al.1989, Firouzbakht 1992a, Firouzbakht et al 1992b). The conclusion is the same in both cases. One can produce quite large amounts of very high purity I-123 from these reactions. A comparison of the cross-sections as measured by Tarkanyi et al (Tarkanyi et al 1991) and by Kurenkov et al. (Kurenkov et al.1989) shows that the agreement for the $^{124}Xe(p,2n)^{123}I$ is quite good, but the $^{124}Xe(p,pn)^{123}Xe$ reaction shows some differences.

Targetry

The targets used for production of I-123 can be grouped into three classifications. These are solid targets, liquid or molten targets and gaseous targets. I-123 is commonly produced in all three types of targets depending on the energy of the cyclotron being used and on the availability of enriched Xe-124 as a target material. Each type of target has its own advantages and disadvantages. There have been a set of criteria first proposed by Van den Bosch and Tertoolen (Van den Bosch et al 1977, Tertoolen et al 1977) which serve as guidelines for I-123 target construction. These criteria are:

a) Thermal and radiation stability of the target and target support under irradiation, combined with adequate thermal conductivity and heat dissipation

b) Simple and almost complete separation of iodine from the tellurium within a short time period, preferably in less than half an hour.

c) Simple and almost complete reprocessing of the target; the loss of expensive enriched tellurium should be kept below 1% per irradiation and separation.

d) The chemical state of the iodine produced should not handicap any *in vivo* application or labeling procedure.

These criteria, although applied to solid tellurium targets serve as good guidelines for all iodine targets. Similar guidelines were reiterated by Qaim (Qaim 1989) who emphasized the power dissipation of the targets and that efficient heat transfer is one of the prime requirements in target construction. He also emphasized the need for accurate nuclear data in order to design targets efficiently.

Solid Targets: One of the most common targets for the production of I-123 is the reaction of tellurium. The typical targets are of two different materials. The first is elemental tellurium and the second is tellurium oxide (Kondo et al 1977a, Qaim 1989). A typical target would be tellurium electrodeposited onto a copper plate which was then irradiated internally in the cyclotron. An example of this type of target is shown in Figure 2.

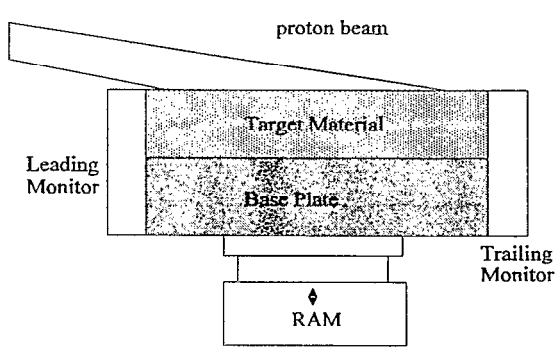

Figure 2.- Internal cyclotron target for grazing incidence. The target material is usually electrodeposited on the surface of the plate

The major advantage of this type of target is that higher beam currents can be used as a result of the low angle on incidence of the beam to the target. This general type of solid target can be used as an external target also with a somewhat higher angle of incidence and therefore at a somewhat lower beam current.

The inclined plane target may also be used as an external target. An example of this is shown in Figure 3. The target has the advantage of being easy to handle after irradiation. The disadvantage is that the beam current which can be put onto external targets are less that those for internal inclined plane targets. The main reason is that the angle of incidence of the external target is, in general, greater than that of the internal target. This results in a much higher heat load per unit area and a thicker target material layer.

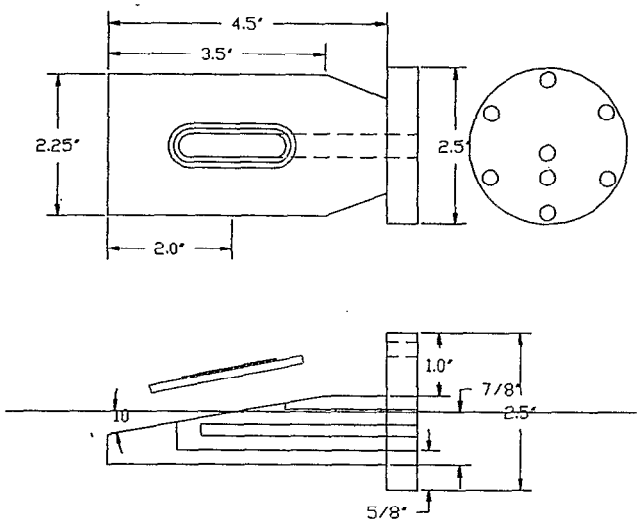

Figure 3. Inclined plane target for external beam. The powdered target material is pressed into a plate with or without grooves for irradiation.

Solid targets made from powdered tellurium have also been widely used for the production of I-123 (Acerbi et al 1976, Barral et al 1981, Clem and Lambrecht 1991, Dahl and Tilbury 1972, Guillaume et al 1975, Hupf et al 1968, Kondo et al 1977b, Mahunka et al 1996, Michael et al 1981, Sodd et al 1973, Weinreich et al 1976). The tellurium powder has often been mixed with aluminum powder to increase the heat transfer characteristics of the target. A common problem with these targets is melting of the elemental tellurium and consequent loss of the radioiodine from the matrix.

An internal powder target has been developed and used with the $^{122}Te(d,n)^{123}I$ reaction (Zaidi et al 1983). This target has a flow through design to extract the iodine-123 during the irradiation.

Other types of alloy targets have been used for production of I-123 such as a tellurium-gold alloy (Lambrecht et al 1977). This technique has been used extensively when the thermal

conductivity of the primary material is low and/or the melting point is low. Tellurium oxide has been used for the production of I-123. The oxide has the advantage of a high melting point and therefore a low loss of the iodine from the matrix during irradiation.

A final type of solid target is the cryogenic target for the production if I-123 from enriched xenon-124 (Firouzbakht et al 1992). This type of target has the advantage of being failsafe in the sense that the xenon is frozen and therefore won't be lost in the case of a foil rupture. The disadvantage is that the target must be kept supplied with liquid nitrogen during irradiation.

Liquid targets: There were three types of liquid targets used for the production of I-123. These were the molten salt target used for production of I-123 from sodium iodide salt in a high energy beam (Jungerman et al 1981, Mausner et al 1986). A picture of this "hockey puck" target is shown in Figure 4.

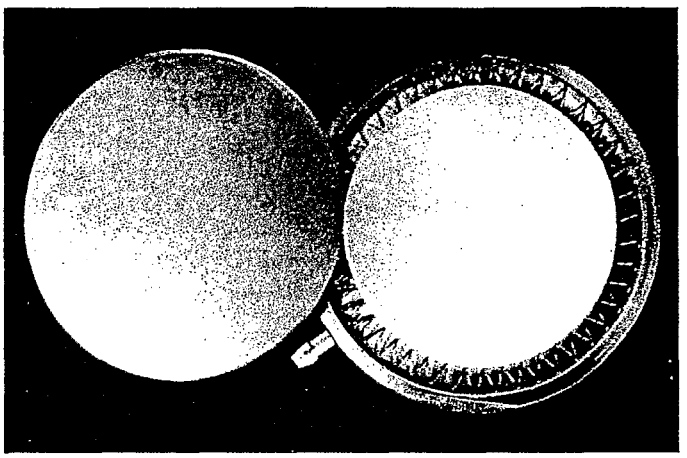

Figure 4 - Sodium iodide salt target for high energy irradiations. Target shown is from the BLIP facility at Brookhaven National Laboratory

This has been used by itself or as the first target of several for isotope production (Suzuki and Iwata 1977). A liquid iodine target has been used for routine production at low beam intensities with a sweep gas to remove the Xe-123 as it is made (Godart et al 1977). The last was the use of a liquid such as methylene iodide in a recirculating flowing target (Cuninghame et al 1976). This target had some problems with polymerization of the target material and was not a popular target.

Gaseous targets: More and more of I-123 is being made from the reaction of protons on enriched Xe-124 gas. This target has the advantage of producing very high purity I-123 with easy recovery of the target material. These targets typically contain one to two liters of gas at elevated pressure. The real danger here is the possibility of losing a foil which may result in the loss of the target gas into the cyclotron and then into the atmosphere. Several designs have been published to reduce or eliminate the possibility of such a loss (Firouzbakht et al 1996). In most cases the xenon gas is trapped in a loop contained at liquid nitrogen temperatures. These loops, if properly constructed, can trap more than 99% of the xenon gas in the targets This type of target has been tested extensively and has proven to be reliable in routine operation. An example of this type of target is shown in Figure 5.

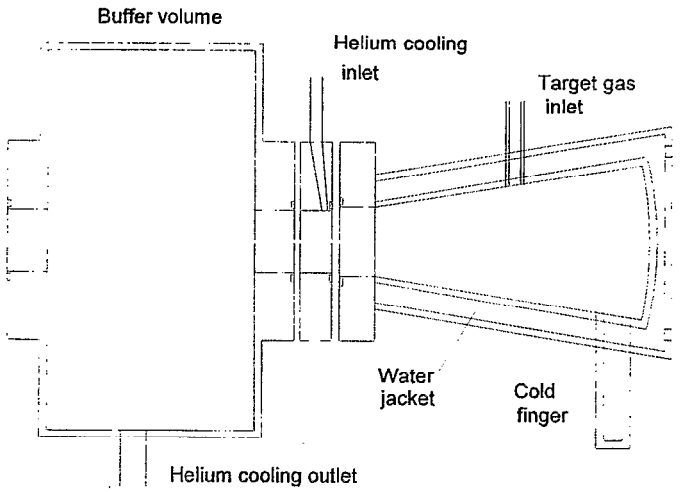

Figure 5. "No-fail" gaseous xenon target for the production of I-123. The buffer volume is attached to several loops of tubing submerged in liquid nitrogen. A flow of helium is pumped through the tubing after being used to cool the front foil.

Radioisotope Separation

The separation of the radioiodine from the target matrix is accomplished in two different ways depending on whether the I-123 is made from the direct method or from the indirect method. In the indirect method, the xenon-123 is isolated from the matrix and then allowed to decay to I-123 in a separate vessel. This separation is usually not a difficult one since the xenon is very unreactive and can usually be extracted from the target readily. In the case of the direct production from tellurium, the problem is slightly more difficult.

A common method of extraction is the use of dry distillation. In this method, the tellurium powder or tellurium oxide powder is heated to near the melting point with a flow of gas over the plate. The iodine-123 is distilled out of the matrix and carried by the sweep gas to a receiver vessel where it is trapped. This vessel usually contains a base solution and the iodine is in the chemical form of iodide. A wet chemical method can also be used dissolving the Te powder and then oxidizing the iodide to iodine and distilling it out of the solution (Acerbi et al 1976).

Iodine-124

Although I-124 has often been considered as an impurity in preparations of I-123, it does have attractive attributes for use in some PET radiopharmaceuticals (Frey et al 1986, Lambrecht et al 1988b, Weinreich et al 1997). The half-life of 4.2 days is long enough for localization with monoclonal antibodies and the 23% positron decay allows imaging with PET. The use of I-124 is becoming more widespread. Iodine-124 has potential as both a diagnostic and therapeutic radionuclide (Weinreich et al 1997, Sheh et al 2000). The primary problem with I-124 is the extra dose resulting from the high energy gamma rays associated with the isotope.

Production Reactions

There are several reactions which can be used to produce I-124 depending on the cyclotron particles and energy available to carry out the irradiations. A list of the potential reactions is shown below.

Nuclear Reaction	Useful Energy Range (MeV)	% Natural Abundance	References
$^{124}Te(p,n)^{124}I$	10 to 20	4.8	Kondo et al 1977a,b, Scholten et al 1995
$^{124}Te(d,2n)^{124}I$		4.8	Lambrecht et al 1988a, Firouzbakht et al 1993, Sharma et al 1988
$^{124}Te(d,3n)^{124}I$	15 to 30	4.8	Firouzbakht et al 1993
$^{121}Sb(^{4}He,n)^{124}I$	15 to 25	57.4	Silvester et al 1969
$^{123}Sb(^{3}He,2n)^{124}I$		42.6	Silvester et al 1969

The most common of these is either the proton reaction or the deuteron reaction on enriched tellurium-124. The deuteron reaction gives a higher yield of I-124 if deuterons are available. The yield for the proton reaction is about 0.09 mCi/μAhr (Kondo et al 1977b) while the deuteron reaction produces 0.55 mCi/μAhr (Lambrecht et al 1988). The reaction on antimony also results in a low yield of about 1 mCi/μAhr (Silvester et al 1969).

Targetry

The targetry for the production of I-124 is limited to solid targets. The target is either elemental tellurium or tellurium oxide (Stevenson et al 1995, Qaim 1989). The targets are identical to those used for the production of I-123 from tellurium. The target plates can be made from either platinum or tantalum. Elemental tellurium can be electrodeposited on the target plate. Tellurium oxide is usually melted into a cavity on the target plate. In some cases, small amounts of aluminum oxide are added to the tellurium to add in adhesion of the oxide to the surface of the plate (Sheh et al 2000).

Radioisotope Separation

The separation of the iodine from the tellurium can be accomplished by distillation of the iodine-124 from the tellurium oxide matrix. This is usually done at temperatures of about 750°C. The iodine is carried away from the target with a sweep of either oxygen or helium. The oxygen tends to keep the tellurium in the oxide form and reduces the loss from distillation of the elemental tellurium (Knust et al 2000, Sheh et al 2000, Michael et al 1981).

CONCLUSIONS

Radioisotopes of Iodine have played a fundamental role in biomedical research and in clinical nuclear medicine. The wide variety of decay characteristics and half-lives available with these isotopes have made them useful for diagnostic imaging as well as therapy. Iodine-123 has been a staple in diagnostic imaging and continues to be a valuable isotope for research in receptor binding assays and metabolism. Iodine-124 has recently gained new prominence in PET imaging

with a 4 day half-life, it is compatible with quantitative imaging of labeled monoclonal antibodies. The future seems active for these radioisotopes and research on their production and separation will continue.

ACKNOWLEDGEMENT

This research was supported at Brookhaven National Laboratory under contract DE-AC02-98CH10886 with the U.S. Department of Energy and its Office of Biological and Environmental Research and by the National Institutes of Health (National Institutes of Neurological Diseases and Stroke NS-15380).

References:

Acerbi, E., Birattari, C., Castiglioni, M., Resmini, F. (1975), Produciton of ^{123}I for Merdical Purposes at the Milan AVF Cyclotron Int. J. Appl. Radiat, Isot. **26**:741-747.

Adilbish, M., Chumin, V.G., Khalkin, V.A., Knotek, O., Kuznetsova, M, JA., Norseev, V., Fominykh, V.I., and Zaitseva, N.G. (1980), ^{123}I Production from Radioxenon Formed in Spallation Reactions by 660 MeV Protons for Medical Research, Int. J. Applied Radiat. Isot. **31**:163-167,.

Barrall, R.C., Beaver, J.E., Hupf, H.B., Rubio, F.F. (1981), Production of Curie Quantities of High Purity I-123 with 15 MeV Protons. Eur. J. Nucl. Med **6**:411-415.

Clem, R.G., and Lambrecht, R.M. (1991), Enriched ^{124}Te Targets for Production of ^{123}I and ^{124}I, Nucl Instr Methods **A303** 115-118.

Cuninghame, J.G., Morris, B., Nichols, A.L., Taylor, N.K. (1976), Large Scale Production of ^{123}I from a Flowing Liquid Target Using the (p, 5n) Reaction. Int. Jour. Appl Radiat Isot. **27**:597-603.

Dahl, J.R., and Tilbury, R.S., The Use of a Compact Multiparticle Cyclotron for the Production of ^{52}Fe, ^{67}Ga, ^{111}In and ^{123}I for Medical Purposes (1972), Int. J. Appl. Radiat Isot. **23**:431-437.

Firouzbakht, M.L., Teng, R.R., Schlyer, D.J., and Wolf, A.P. (1987), Production of High Purity Iodine-123 from Xenon-124 at Energies Between 15 and 34 MeV Radiochimica Acta, **41**:1-4.

Firouzbakht, ML, Schlyer, DJ, Wolf, AP (1992) Production of Iodine-123 from Xenon-124: Cross-sections and Yields Radiochimica Acta, **56**:167-171.

Firouzbakht ML, Schlyer DJ, Wolf AP (1992), Effect of Foil Material on the Apparent Yield of the $^{124}Xe(p,x)^{123}I$ Reaction. Appl. Radiat. Isot. **43**:741-745.

Firouzbahkt, M. L., Schlyer, D. J., and Wolf, A. P. (1992), A Solid Xenon Ice Target for the Production of I-123 Proceedings IXth International Symposium on Radiopharmaceutical Chemistry. Paris, France 6-10 April 1992.

Firouzbakht, M.L., Schlyer, D.J., Finn, R.D., Laguzzi, G. and Wolf, A.P. (1993), Iodine-124 Production: Excitation Function for the $^{124}Te(d,2n)^{124}I$ and the $^{124}Te(d,3n)^{123}I$ Reactions from 7 to 24 MeV. Nucl. Instru. Meth. in Phy Res. **B79**:909-910.

Firouzbakht, ML, Schlyer, DJ, Wolf, AP (1995) "Failsafe" gas target for the production of I-123 from Xe-124, Proceedings of the Sixth Workshop on Targetry and Target Chemistry, Aug. 17-19 Vancouver, B.C. Canada, 1995, p. 79-81.

Frey, P.E., Townsend D.W., Flattet, A., De Gautarrd, R., Widgren, S., Jeavons, A., Christin, A., Smith A., Long, A., Donath, A.(1986), Tomographic imaging of the human thyroid using ^{124}I, J. Clin. Endocrnol. Metab. **63**:918-927.

Godart, J., Barat, J.L, Menthe, A., (1978), In Beam Collection of ^{123}Xe for Carrier-free ^{123}I Production, Int. J. Appl. Radiat. Isot. **28**:967-969.

Graham, D., Trevena, I.C., Webster, B., and Williams, D. (1985), Production of High Purity Iodine-123 Using Xenon-124. J. Nucl. Med. **26**:105.

Guillaume, M., Lambrecht, R.M., and Wolf, A.P. (1975), Cyclotron Production of ^{123}Xe and High Purity ^{123}I: A Comparison of Tellurium Targets. Int. J. Appl. Radiat. Isot. **26**:703-707.

Hupf, H.B., Eldridge, J.S., and Beaver, J.E. (1968), Production of Iodine-123 for Medical Applications, Int. J. Appl. Radiat. Isot. **19**:345-351.

Jungerman, J.A., Lagunas-Solar, M.C. (1981), Cyclotron Production of High Purity Iodine-123 for Medical Applications, J. Radioanalytical Chemistry, **65**:31-45.

Kondo, K., Lambrecht, R.M., Norton, E.F., and Wolf, A.P. (1977b), Improved Target and Chemistry for the Production of ^{123}I and ^{124}I Int. J. Appl. Radiat. Isot. **28**:765-771, 1977b.

Kondo, K., Lambrecht, R.M., and Wolf, A.P. (1977a), Iodine-123 Production for Radiopharmaceuticals XX* Excitation Functions for the $^{124}Te(p,2n)^{123}I$ and $^{124}Te(p,n)^{124}I$ Reactions and the Effect of Target Enrichment on Radionuclidic Purity. Int. J. Appl Radiat. Isot. **28**:395-401.

Knust, E.J., Dutschka, K., Weinreich, R. (2000), Preparation of ^{124}I Solutions After Thermodistillation of Irradiated $^{124}TeO_2$ Targets, Appl. Radiat. Isot. **52**:181-184.

Kurenkov, N.V., Malinin, A.B., Sebyakin, A.A., Venikov, N.I. (1989), Excitation Functions of Proton-Induced Nuclear Reactions on ^{124}Xe: Production of ^{123}I, J. Radioanal. Nucl. Chem. Lett. **135**:39-50.

Lagunas-Solar, M.C., Carvacho, O.F., Liu, B-L, Jin, Y., Sun, Z.X. (1986), Cyclotron Production of High Purity ^{123}I I. A Revision of Excitation Functions, Thin-Target and Cumulative Yields for $^{127}I(p,xn)$ Reactions, Appl. Radiat. Isot. **37**:823-833.

Lambrecht, R.M., and Wolf, A.P. (1973), Cyclotron and Short-Lived Halogen Isotopes for Radiopharmaceutical Applications. In New Developments in Radiopharmaceuticals and Labelled Compounds. Vol. 1, IAEA Vienna, 1973, pp. 275-290.

Lambrecht, R.M., Wolf, A.P. (1972), The $^{122}Te(^{4}He, 3n)^{123}Xe \rightarrow ^{123}I$ Generator, Radiat. Res. **52**:32-46.

Lambrecht, R.M., Mantescu, C., Redvanly, C., and Wolf, A.P. (1972), Preparation of High Purity Carrier-free ^{123}I-Iodine Monochloride as Iodination Reagent for Synthesis of Radiopharmaceuticals, IV. J. Nucl. Med. **13**:266-273.

Lambrecht, R.M., Ritter, E., Becker, R., and Wolf, A.P. (1977), Cyclotron Isotopes and Radiopharmaceuticals- XXI. Fabrication of ^{122}Te-Au Targets for Isotope Production. Int. J. Appl. Radiat Isot. **28**:567-571.

Lambrecht, R.M., Sajjad, M., Qureshi, M.A., and Al-Yanbawi, S.J. (1988a), Production of Iodine-124. J. Radioanal. Nucl. Chem Letters, **127**:143-151.

Lambrecht, R.M., Woodhouse, N., Phillips, R., Wolczak, D., Qureshi, A., Delos Reyes, E., Graser, C., Al-Yanbawi, S., Al-Rabiah, A., Meyer, W., Marlais, W., Syed, R., Banjar, F., Rifai, A., Miliebari, S. (1988b), Investigational Study of Iodine-124 with a Positron Camera, Am J. Physiol. Imaging, 3:197-200.

Mahunka, I., Ando, L., Mikecz, P., Tcheltsov, A.N., and Suvorov, I.A. (1996), Iodine-123 Production at a Small Cyclotron fro Medical Use. J. Radioanal. Nucl. Chem. Letters **213**:135-142.

Mausner, L.F., Srivastrava, S.C., Mirzadeh, S., Meinken, G.E., Prach, T. (1986), ^{123}I Research and Production at Brookhaven National Laboratory, Appl. Radiat. Isot **37**:843-851.

Michael, H., Rosezin, H., Apelt, H., Blessing, G., Knieper, J., Qaim, S.M. (1981), Some Technical Improvements in the Production of ^{123}I via the $^{124}Te(p,2n)^{123}I$ Reaction at a Compact Cyclotron, Int. J. Appl. Radiat. Isot. **32**:581-587.

Qaim, S.M., and Stocklin, G., Production of Some Medically Important Short-Lived Neutron Deficient Radioisotopes of Halogens. (1983), Radiochimica Acta, **34**:25-40.

Qaim, S.M., (1989) Target Development for Medical Radioisotope Production at a Cyclotron. Nuc. Instr. Methods in Phys. Research. **A282** 289-295.

Scholten, B., Kovacs, Z., Tarkanyi, F., Qaim, S.M. (1995), Excitation Functions of the $^{124}Te(p,xn)^{124,123}I$ Reactions from 6 to 31 MeV with Special Reference to the Production of ^{124}I at a Small Cyclotron. Appl. Radiat. Isot. **46**:255-259.

Sharma, H.L., Zweit, J., Downey, S., Smith, A.M., and Smith, A.G. (1988), Production of ^{124}I for Positron Emission Tomography, J. Labelled Cmpds Radiopahrm. **26**:165-167.

Sheh, Y., Koziorowski, J., Balatoni, J., Lom, C., Dahl, D.R., and Finn, R.D. (2000), Low Energy Cyclotron Production and Chemical Separation of "no carrier added" Iodine-124 from a Reusable, Enriched Tellurium-124 Dioxide/Aluminum Oxide Solid Solution Target. Radiochim. Acta, **88**:169-173.

Silvester, D.J., Sugden, J., Watson, I.A., Preparation of Iodine-123 by Alpha Particle Bombardment of Natural Antimony, (1969), Radiochem. Radioanal. Letters **2**:17-20.

Sodd, VJ, Blue, JW, Scholz, KL, Oselka, MC, (1973) A gas-flow powder target for the cyclotron production of pure ^{123}I. International Journal of Applied Radiation Isotopes **24**, 171-177.

Stevenson, N.R., Buckley, K., Gelbart, W.Z., Hurtado, E.T., Johnson, R.R., Ruth, T.J., and Zeisler, S.K. (1995), On-Line Production of Radioiodines with Low Energy Accelerators. Proceedings of the Sixth Workshop on Targetry and Target Chemistry, Aug. 17-19, 1995 Vancouver, B.C., Canada, p 82-83.

Suzuki, K., Iwata, R. (1977), A Multi-Target Assembly in an Irradiation with High Energy Particles. Simultaneous Production of ^{123}I, ^{62}Zn and $^{13}NH_3$, Int. J. Appl. Radiat. Isot. **28**:663-665.

Tárkányi, F., Qaim, S.M., Stöcklin, G., Sajjad, M., Lambrecht, R.M., Schweickert, H. (1991), Excitation Functions of (p,2n) and (p,pn) Reactions and Differential and Integral Yields of ^{123}I in Proton Induced Nuclear Reactions on Highly Enriched ^{124}Xe. Appl. Radiat. Isot. **42**:221-228.

Tertoolen, J.F.W., van den Bosch, R., Goeij, J.J.M., van der Heide, J.A., Theelen, H.M.J., Zegers, C. (1977), A New Approach to Target Chemistry for the Iodine-123 Production via the ^{124}Te(p,2n)^{123}I Reaction. J. Label Comp. Radiopharm. **13**:232.

Van den Bosch, R., De Goeij, J.J.M., Van der Heide, J.J. et al. (1977), A New Approach to Target Chemistry for the Iodine-123 Production via the ^{124}Te(p,2n)^{123}I Reaction. Int. J. Appl. Radiat. Isot. **28**:255-261.

Watson, I.A., Waters, S.L., and Silvester, D.J. (1973), Excitation Functions for the Reactions Producing ^{121}I, ^{123}I and ^{124}I from Irradiation of Natural Antimony with ^{3}He and ^{4}He Particles with Energies up to 30 MeV, J. Inorg. Nucl. Chem. **35**:3047-3053.

Weinreich, R., Qaim, S.M., Michael, H., Stocklin, G. (1976), Production of ^{123}I and ^{28}Mg by High Energy Nuclear Reactions for Applications in Life Sciences. J. Radioanal. Chem. **30**:53-66.

Weinreich, R., Wyer, L., Crompton, N., Gunther, I., Roelcke, U., Leenders, K.L., Knust, E.J., Finn, R.D., and Blasberg, R.G. (1977), Production and Quality Assurance of 5-[^{124}I]Iodo-2'-deoxyuridine for Functional Imaging of Cell Proliferation in vivo. J. Labelled Cmpds Radiopahrm **40**:346-347.

Witsenboer, A.J., De Goeij, J.J.M., Reiffers, S. (1986), Production of Iodine-123 via Proton Irradiation of 99.8% Enriched Xenon-124, Proceedings of the Sixth International Symposium of Radiopharmaceutical Chemistry, Boston, MA June 29-July 3, 1986, p. 259.

Zaidi, J.H., Qaim, S.M., and Stocklin, G. (1983), Excitation Functions of Deuteron Induced Nuclear Reactions on Natural Tellurium and Enriched 122Te: Production of ^{123}I via the ^{122}Te(d,n)^{123}I-Process. Int. J. Appl. Radiat. Isot. **34**:1425-1430.

Zaitseva, N.G., Deptula, C., Knotek, O., Khan, K.S., Mikolaewski, S., Mikeć, P., Rurarz, E., Khalkin, V.A., Konov, V.A., Popinenkova, L.M. (1991), Cross Sections for the 100 MeV Proton-Induced Nuclear Reactions and Yields of some Radionuclides Used in Nuclear Medicine, Radiochim. Acta **54**:57-72.