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Decay data and production yields of some non-standard positron emitters used in PET

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The increasing significance of non-standard positron emission tomography (PET) nuclides in medicine is briefly outlined. The decay data of those radionuclides are generally well known, except for the positron emission intensity ($I_{\beta+}$) in a few cases. The recent precise measurements on the $I_{\beta+}$ values for ^{64}Cu, ^{76}Br, ^{120}I and ^{124}I are described. Some general aspects of cyclotron production of radionuclides are discussed. The need of some fundamental nuclear chemistry research with regard to the development of a new production route is demonstrated. An accurate knowledge of the excitation function of a nuclear reaction is essential to optimize the production route. The yield of a product calculated from the excitation function of a reaction gives the maximum achievable yield. Such yields are given for 24 radionuclides presently attracting attention. The experimental yields are always lower than the theoretical values, calling upon constant improvements in targetry and chemical processing procedures. Many of the non-standard PET nuclides, like ^{64}Cu, ^{86}Y, ^{94m}Tc, ^{124}I, etc. are produced in good yields at low energy cyclotrons while for production of some other radionuclides (e.g. ^{52}Fe, ^{73}Se, ^{83}Sr, etc.) an intermediate energy cyclotron is required.

KEY WORDS: Tomography, emission computed - Radiopharmaceuticals - Production, data.

In positron emission tomography (PET) the so-called "organic" positron emitters ^{11}C ($T_{?}$=20.3 min), ^{13}N ($T_{1/2}$=10 min), ^{15}O ($T_{1/2}$=2 min) and ^{18}F ($T_{1/2}$=110 min) are commonly used. All of them are almost pure positron emitters. The first three radionuclides being very short-lived are generally used on site of production. The fourth radionuclide, *i.e.* ^{18}F, is somewhat longer lived and can be transported to appreciable distances. Due to this reason as well as due to low positron energy and ease of production, ^{18}F has become the most commonly used PET nuclide. Two other widely used short-lived positron emitters are produced *via* generator systems. They are ^{68}Ge ($T_{1/2}$ =270.8 d)/^{68}Ga($T_{1/2}$=67.6 min) and ^{82}Sr($T_{1/2}$=25.3 d)/^{82}Rb($T_{1/2}$=1.3 min). Due to relatively long half-lives of the parents, the two generator systems are very useful for routine clinical applications. Furthermore, in recent years some new interest has developed in gallium chemistry. The generator produced ^{68}Ga is thus being increasingly used in those investigations.

In view of enhancing significance of PET in diagnostic nuclear medicine, considerable efforts have been devoted over the last 25 years towards development of a large number of non-conventional positron emitters. Some of the early works dealt with ^{30}P ($T_{1/2}$=2.5 min), ^{38}K ($T_{1/2}$=7.5 min), ^{62}Cu ($T_{1/2}$=10 min), ^{75}Br ($T_{1/2}$=1.6 h), ^{122}I ($T_{1/2}$=3.6 min), etc. Whereas ^{30}P, ^{38}K and ^{75}Br were produced directly *via* suitable nuclear reactions, ^{62}Cu and especially ^{122}I were obtained in a generator mode from their respective parents ^{62}Zn ($T_{1/2}$=9.1 h) and ^{122}Xe ($T_{1/2}$=20.1 h).

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Although those radionuclides are still used in some special cases, the trend has somewhat shifted towards more purpose oriented longer-lived positron emitters.

Today, there are two major directions in which non-standard, *i.e.* non-conventional, positron emitters are used. The first one concerns the study of slow metabolic processes, like protein synthesis, cell proliferation, etc. where relatively long-lived positron emitters are required. The second one relates to quantitation aspects, both in diagnosis *via* single photon emission tomography (SPECT) and dosimetry in internal open source radiotherapy. If the SPECT radioisotope in a pharmaceutical could be substituted by a positron emitting homologue, the distribution kinetics could be determined quantitatively *via* PET. The results would then be of immediate use in quantification of the SPECT pharmaceutical. In internal radiotherapy, generally a pure β^- emitter like ^{89}Sr or ^{90}Y is preferred, but since the distribution of the radioactivity cannot be measured accurately from outside of the body, the dosimetry is rather empirical. On the other hand, if the radiotherapeutical could be mixed with a small amount of a positron emitting homologue, the distribution of the radioactivity could be easily determined *via* PET and the dose calculation would then be on a more firm footing.

In this article, the author is dwelling on the development of non-standard PET radionuclides with the above mentioned two motivations in mind. Several aspects of development work deserve attention. This contribution, however, deals with the basic nuclear data for production and application of some of the non-standard positron emitters.

Decay data

Decay data are the major criterion for the choice of a radionuclide for medical application. In general, the decay data are fairly well known.[1] A problem with many of the non-standard relatively long-lived positron emitters, however, is that the positron emission intensity is often rather low and not exactly known, thereby causing some uncertainty in the quantitation of tomographic scans. For the more promising radionuclides it is therefore imperative to determine some of the relevant decay data with higher accuracy.

The decay data of most of the non-standard positron emitters were determined in the context of nuclear structure studies; the recent related works deal more with evaluations[1] of older data rather than with new measurements. Since many of the radioactive samples used in older measurements were prepared without radiochemical separations, they were radionuclidically not pure. Furthermore, β-ray spectroscopy has not attained the same precision as high-resolution γ-ray spectroscopy. The X-ray component, which is related to electron capture (EC) decay, was determined in older works generally using a gas counter. It appears, therefore, worthwhile to perform new measurements on some important radionuclides, especially on positron emission intensities, in cases where they appear to be rather uncertain.

The modern methodology of determination of positron emission intensity consists of preparation of a very clean thin source, accurate measurement of annihilation radiation (using both HPGe detector γ-ray spectroscopy and $\gamma\gamma$-coincidence counting) and determination of EC component *via* high-resolution X-ray spectroscopy using a thin Ge or Si(Li) detector.

The measurement of decay data of ^{64}Cu ($T_{1/2}$ =12.7 h) constitutes a typical case. This radionuclide decays by three modes, *viz.* β^- emission, EC and β^+ emission. According to the latest evaluation[1] the positron emission intensity corresponds to 17.4%. The experimentally reported I_{β^+} values, however, range between 17.4% and 19%. With EC a very weak γ-transition of energy 1 346 keV has also been reported. Its intensity could range between 0.47% and 0.6%. In a recent work,[2] the radionuclide was produced either *via* the ^{64}Ni(p,n)^{64}Cu or the ^{66}Zn(d,α)^{64}Cu reaction using highly enriched (>99%) target material. The radiocopper was chemically separated and a thin sample on filter paper was prepared for radioactivity measurement *via* β counting, $\gamma\gamma$-coincidence counting, and X-ray and γ-ray spectroscopy. From all the counting results and the literature knowledge a decay scheme of ^{64}Cu was developed which is reproduced in Figure 1. The β^- branching intensity of 38.4% deduced in that experiment is very close to the value of 38.1±0.3% measured *via* mass spectrometry.[3] The β^+ emission intensity was found to be 17.8±0.4%.

Similar to ^{64}Cu, work on a few other important non-standard PET nuclides has also been performed in recent years.[2, 4-6] The results on β^+ emission intensities are summarized in Table I. It is suggested that for the four investigated radionuclides, *viz.* ^{64}Cu, ^{76}Br, ^{120}I and ^{124}I the given I_{β^+} values should be adopted as

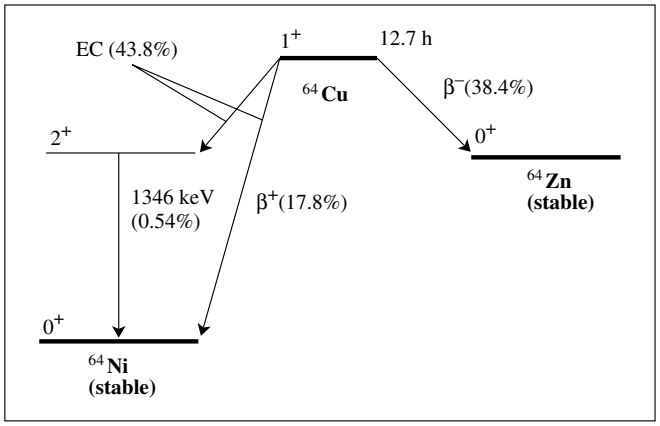

Figure 1.—Decay scheme of ^{64}Cu with intensities of emitted radiations. [From Qaim *et al.*[2]].

standard values. Regarding other non-standard PET nuclides, such measurements also need to be done.

Production data

General considerations

Production data are primarily related to the formation of a desired radionuclide under optimum conditions. In the choice of a production process for a non-standard PET nuclide, therefore, following points need to be given due attention.

Availability of a cyclotron

The desire to develop non-standard PET nuclides is generally prevalent at PET centers with low-energy cyclotrons ($E_p \leq 18$ MeV, $E_d \leq 10$ MeV). The nuclear reactions which could be applied are low-energy processes, *e.g.* (p,n), (p,α), (d,n), (d,α), etc. Occasionally a higher energy two particle cyclotron (with $E_p \leq 30$ MeV, $E_d \leq 15$ MeV) or a multiparticle intermediate energy cyclotron (accelerating p, d, ^{3}He and α-particles) with $E_p \leq 70$ MeV may be available. In those cases, several nuclear reactions, like (p,xn), (^{3}He,xn), etc. may be suitable for production purposes.

Availability of highly enriched target material

Since many of the radionuclides can be produced *via* low-energy nuclear reactions only on isotopically enriched targets, the availability of suitable target material, which is usually rather expensive, may be absolutely necessary.

Table I.—*Recently determined $I_{\beta+}$ values of some non-standard PET nuclides.*

Radionuclide	$T_{1/2}$	Positron emission intensity (%)	
		Literature values [1]	Precise value
^{64}Cu	12.7 h	17.4-19	17.8±0.4 [2]
^{76}Br	16.2 h	56-62.5	58.2±1.9 [2]
^{120}I	1.35 h	39-81	56.1±3.2 [4]
^{124}I	4.18 d	21.6-26	22±0.5 [2, 6]
			21.6±0.4 [5]

High current targetry

In order to be able to produce sufficiently large amounts of the desired radionuclide, it is absolutely necessary to develop target materials and target holders which would withstand high beam fluxes of charged particles. Furthermore, the radioactive product should be relatively easily separated from the matrix activity.

Efficient chemical processing

It is imperative that from the irradiated target material not only the desired radionuclide is separated in a clean form, but also the target material is efficiently recovered for reuse. Thus, the chemical processing may demand very skilful radiochemical work.

During all the above-mentioned considerations, the major criteria are the yield and the purity. Utmost attempts need to be made to get the product in high yield and with the highest possible purity.

Excitation functions

The probability of a nuclear reaction leading to the formation of a radionuclide is expressed in terms of "cross section", and its energy dependence is called an "excitation function". An accurate knowledge of the excitation function allows to calculate the production yield of a radionuclide *via* the well-known activation equation, provided the number of target nuclei and the projectile flux are exactly known.

Cross section data near reaction thresholds

As discussed above, many of the PET centers equipped with small cyclotrons have considerable

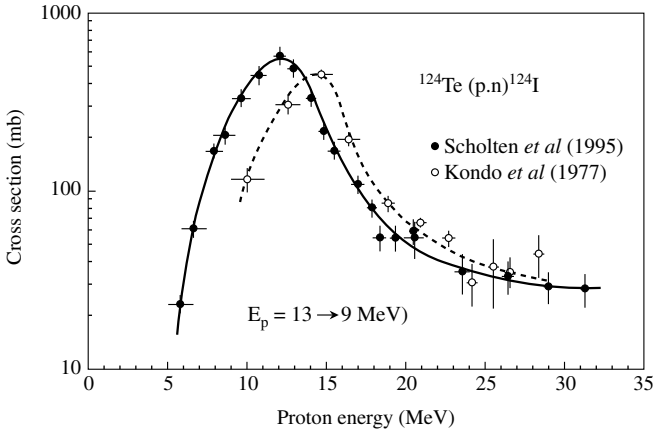

Figure 2.—Excitation function of the ^{124}Te(p,n)^{124}I reaction. The high precision measurements near the reaction threshold done by Scholten *et al.*[7] are now the basis of yield calculations for the production of ^{124}I.

interest in producing non-standard positron emitters. For the very decision whether an available low-energy cyclotron is suitable for production, an accurate knowledge of the excitation function of the nuclear reaction near the threshold is necessary. In the higher energy region, the cross section data help to optimize the production route. As an example, the cross section data for the production of ^{124}I *via* the ^{124}Te(p,n)^{124}I reaction are shown in Figure 2. An early measurement[8] was limited to proton energies >10 MeV. As a consequence this reaction was considered to be unsuitable for production of ^{124}I, and resort was made to the ^{124}Te(d,2n)^{124}I reaction.[9-11] The latter reaction needs higher deuteron energies than those available at PET centers: the production was therefore limited. After the publication of a more thorough study near the threshold,[7] it became evident that the (p,n) process is quite suitable for use at a low-energy cyclotron. Thereafter, most of the laboratories shifted over to this reaction[6, 12-14] and today even some commercial companies are utilizing this method for ^{124}I production. The accurate cross section database near the threshold allows the optimum use of even a very small cyclotron (E≤11 MeV) for production of ^{124}I on a limited scale.[15]

Regarding other nuclides, a recent accurate measurement of the ^{76}Se(p,n)^{76}Br reaction cross section near the threshold[16] confirmed that this radionuclide can be conveniently produced at a low-energy cyclotron. Other important radionuclides which are generated *via* the (p,n) reaction and whose excitation functions have been accurately measured [17-20] near the thresholds are ^{64}Cu , ^{86}Y, ^{94m}Tc and ^{120}I. All those radionuclides can be produced using a low-energy cyclotron available at a PET center.

Two other low-energy nuclear reactions which occasionally find application in the production of some non-standard PET nuclides are (p,α) and (d,n). They are generally used when a (p,n) reaction is not possible (due to non-availability of a suitable target material). Some of the examples are:[21-24] ^{58}Ni(p,α)^{55}Co, ^{54}Fe(d,n)^{55}Co and ^{74}Se(d,n)^{75}Br. For proper application of each method, the respective database near the threshold was strengthened through accurate measurements.

Competing reaction channels

At projectile energies >20 MeV, several intermediate energy reactions like (p,xn), (p,pxn), etc. start competing and the demand on the needed nuclear data information increases. Several radionuclides can be produced only *via* such reactions because of lack of suitable target nuclides on which low-energy reactions could be induced. Another motivation for using an intermediate energy reaction may be to obtain higher yield of a product. However, the level of radionuclidic impurities is then also higher. The radionuclide ^{73}Se, for example, is produced almost exclusively *via* the ^{75}As(p,3n)^{73}Se reaction since no low-energy reaction is possible.[25] The target window (or thickness), however, has then to be chosen such that the yield of the desired product is high and the levels of the long-lived impurities are low. If the range E_p=40 → 30 MeV is chosen, then the yield of ^{73}Se is 1406 MBq/μA·h and the levels of ^{72}Se and ^{75}Se impurities are limited to <0.2%.

In an attempt to increase the yield of ^{124}I the ^{125}Te(p,xn)-reactions were investigated in detail[26] and the results are shown in Figure 3. The suitable energy range for ^{124}I production *via* the ^{125}Te(p,2n)^{124}I reaction is E_p=21 → 15 MeV. The integral yield is about 5 times higher than that *via* the ^{124}Te(p,n)^{124}I reaction, but the level of the ^{125}I impurity is also considerably higher.

For production of nuclides in the intermediate energy region mostly proton beams are utilized. However, in certain special cases deuteron, ^{3}He- and α-particle beams have also proven to be useful. This is particularly true if targetry involving (p,xn) or (d,xn) reactions is difficult. The radionuclides ^{30}P ($T_{1/2}$=2.5 min) and

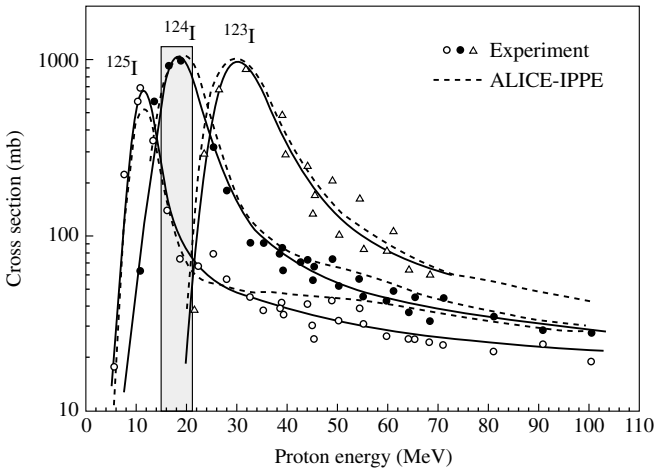

Figure 3.—Excitation functions of ^{125}Te(p,xn)^{123,124,125}I reactions. The shaded area gives a suitable energy range (E_p=21→15 MeV) for the production of ^{124}I. [From Hohn *et al.*[26]].

^{38}K ($T_{1/2}$ =7.5 min), for example, are advantageously produced *via* the ^{27}Al(α,n)^{30}P and ^{35}Cl(α,n)^{38}K reactions, respectively. Similarly, the radionuclide ^{75}Br ($T_{1/2}$ =1.6 h) had been produced for a long time *via* the ^{75}As(^{3}He,3n)^{75}Br reaction.

In order to demonstrate the variety of nuclear processes which could be used for the production of a radionuclide, the case of ^{64}Cu, one of the most important non-standard PET radionuclides, is considered in detail. Table II gives a summary of the methods suggested for its production in a no-carrier-added form. Originally the ^{64}Zn(n,p)^{64}Cu reaction was used[27] which, however, does not have a high yield. Furthermore, the product is contaminated with ^{67}Cu, unless enriched ^{64}Zn is used as target material. The ^{64}Ni(d,2n)^{64}Cu reaction has a high yield,[28] but the deuteron energy needed for production is not available at cyclotrons in PET centers. The ^{64}Ni(p,n)^{64}Cu reaction gives high yield[17] and can be utilized at a small-sized cyclotron. The ^{66}Zn(d,α)^{64}Cu reaction has a relatively low yield[29] and is thus not attractive. The ^{nat}Zn(d,x)^{64}Cu process is, however, interesting[30, 31] if about 25 MeV deuterons are available. The ^{68}Zn(p,αn)^{64}Cu reaction has a good yield,[29, 32] but the upper energy limit is 35 MeV since at higher energies considerable amount of ^{67}Cu is also formed as impurity.

As far as practical production of ^{64}Cu is concerned, small amounts have been generated *via* the reactions ^{68}Zn(p,αn)^{64}Cu[33] and ^{nat}Zn(d,x)^{64}Cu.[34, 35] The reaction ^{64}Ni(p,n)^{64}Cu, originally suggested by the Jülich group,[17] has, however, become the method of choice, although the highly enriched ^{64}Ni used as target material is rather expensive. The method has been developed to almost perfection at St. Louis[36] and is also successfully used at Bethesda.[37] This example demonstrates that the successful use of a suggested method is dependent on many factors, which are given above.

TABLE II.—*Routes for production of ^{64}Cu.*

Production route	Suitable energy range (MeV)	Calculated integral yield (MBq/μA·h)	Reference
^{64}Zn(n,p)^{64}Cu	Fission spectrum	14.5*	27
^{64}Ni(d,2n)^{64}Cu	19 → 15	389	28
^{64}Ni(p,n)^{64}Cu	12 → 9	241	17
^{66}Zn(d,α)^{64}Cu	13 → 7	6.6	29
^{nat}Zn(d,x)^{64}Cu	25 → 10	50	30, 31
^{68}Zn(p,αn)^{64}Cu	35 → 20	~100	32

*Activity/mg Zn at Φ_n=8.7×10^{13} n cm^{-2} s^{-2} for 150 h.

FORMATION OF ISOMERIC STATES

A new feature of the non-standard PET nuclides in comparison to the standard PET nuclides is the occasional occurrence of isomeric states. In practice, one of the isomeric states is of interest and the other is merely an impurity. The ratio of their cross sections depends on the type of reaction through which they are produced. The production of ^{94m}Tc ($T_{1/2}$ =52 min) in the interaction of protons with enriched ^{94}Mo constitutes a typical case. The excitation functions for the formation of various radionuclides[19] are shown in Figure 4. Through adjustment of the energy range in the target the products ^{93m,g}Tc are easily removed. However, the amount of undesired ^{94g}Tc in the desired ^{94m}Tc cannot be altogether eliminated. Over the energy range of E_p=13 → 7 MeV, the ^{94g}Tc impurity in ^{94m}Tc amounts to 6%. In an attempt to decrease the level of the impurity, two other processes, namely ^{93}Nb(^{3}He,2n)^{94m,g}Tc and ^{92}Mo(α,pn)^{94m,g}Tc, were also investigated. The level of the ^{94g}Tc impurity found was, however, 25% and 30%, respectively. Thus the ^{94}Mo(p,n)^{94m,g}Tc reaction is the best choice. It may be emphasized here that this type of fundamental nuclear investigations are mandatory to find the reaction giving the lowest level of the isomeric impurity, since the isomeric cross section ratio is difficult to

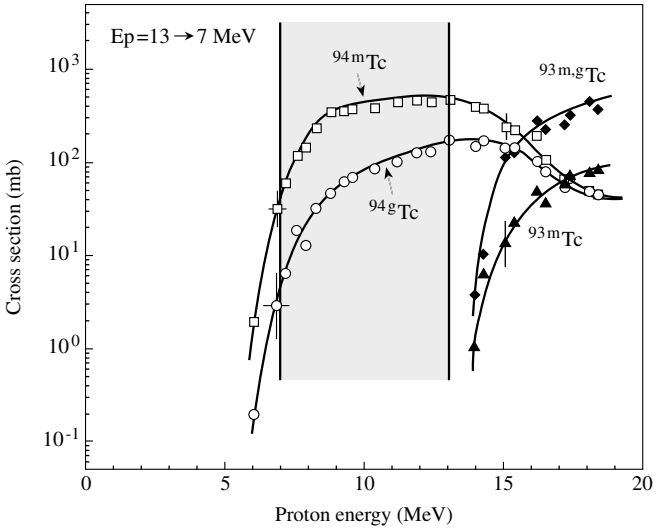

Figure 4.—Excitation functions of ^{94}Mo(p,xn)^{93m,93g,94m,94g}Tc reactions. For production of ^{94m}Tc the suitable energy range is E_p=13→7 MeV where the level of the ^{94g}Tc impurity amounts to 6%. [From Rösch and Quaim [19]].

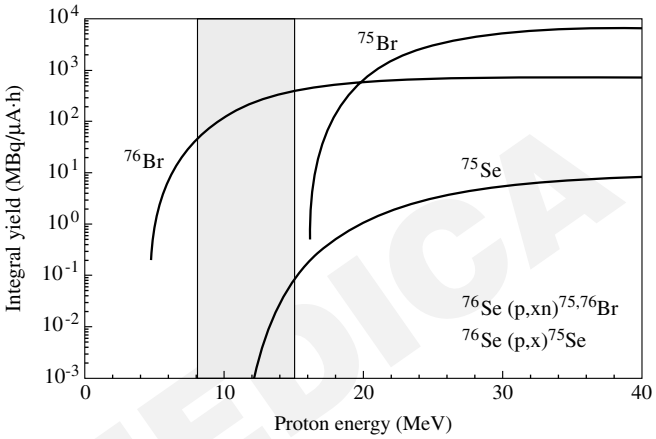

Figure 5.—Integral yields of ^{75,76}Br and ^{75}Se (calculated from the measured excitation functions) plotted as a function of projectile energy. The shaded area gives the optimum energy range (E_p=15→8 MeV) for the production of ^{76}Br. [From Hassan *et al.*[16]].

predict. Often even the most sophisticated nuclear model calculations reproduce the experimental data after considerable input parameter adjustments.[38-40] Some of the important non-standard PET nuclides where isomeric states occur are ^{52m,g}Mn, ^{82m,g}Rb, ^{86m,g}Y, ^{94m,g}Tc, ^{120m,g}I, etc.

Integral yields

The integral yield of a nuclear reaction product denotes the radioactivity achieved at the end of an irradiation. In charged particle induced reactions, it always refers to a definite projectile energy range effective within the target.

The integral yield can be calculated from the excitation function of a reaction. It can also be determined experimentally under production conditions. A comparison of the two values (*i.e.* calculated and experimental yields) then reflects the quality of targetry and chemical processing related to large scale production of the radionuclide.

Calculation of integral yield

From a given excitation function, the expected yield of a product for a certain energy range, *i.e.* target thickness, can be calculated[41] using the expression:

$$Y = \frac{N_L H}{M} I(1-e^{-\lambda t}) \int_{E_1}^{E_2} \left(\frac{dE}{d(\rho x)}\right)^{-1} \sigma(E)dE$$

where Y is the activity (in Bq) of the product, N_L is the Avogadro number, H is the enrichment (or isotopic abundance) of the target nuclide, M is the mass number of the target element, I is the projectile current, $dE/d(\rho x)$ is the stopping power, $\sigma(E)$ is the cross section at energy E, λ the decay constant of the product and t the time of irradiation. The limits of the integration give the energy range of the projectile effective in the target, and the yield is then valid for that energy range. The calculated yield value represents the maximum yield which can be expected from a given nuclear process. Such calculations are often done in radionuclide development programs. The assumptions made include: 1) specific energy range; 2) beam current of 1 μA; 3) irradiation time of 1 h.

Thus the calculated yield is given in the units MBq/μA·h.

As a typical example, the integral yields of ^{76}Br, ^{75}Br and ^{75}Se calculated from the recently measured[16] excitation functions of the reactions ^{76}Se(p,n)^{76}Br, ^{76}Se(p,2n)^{75}Br and ^{76}Se(p,pn)^{75}Se, respectively, are shown in Figure 5 as a function of proton energy. The shaded area gives the optimum energy range (E_p=15 → 8 MeV) for the production of ^{76}Br: the ^{75}Br is completely avoided and small amount of ^{75}Se formed is removed chemically. The integral yield of ^{76}Br over this energy range amounts to 360 MBq/μA·h

TABLE III.—*Short-lived non-standard PET nuclides ($T_{1/2}$≤2 h).*

Nuclide	$T_{1/2}$	Common production route	Energy range (MeV)	Calculated yield (MBq/μAh)	Radionuclidic impurity (%)	Reference
^{30}P	2.5 min	^{27}Al(α,n)	28 → 10	740	—	42
^{38}K	7.5 min	^{35}Cl(α,n)	22 → 7	270	^{34m}Cl (0.2)	43
		^{38}Ar(p,n)*	16 → 12	777		44
^{51}Mn	46.2 min	^{50}Cr(d,n)*	10 → 4	700	^{52m}Mn (<4)	45
^{62}Cu**	9.7 min	^{62}Ni(p,n)*	14 → 10	13×10^3	$^{61, 64}$Cu (0.8)	46
^{75}Br	1.6 h	^{75}As(^{3}He,3n)	36 → 25	278	^{76}Br (1.7)	47
		^{76}Se(p,2n)	24 → 21	1.2×10^3	^{76}Br (2)	48, 49
^{77}Kr	1.2 h	^{77}Se(3He,3n)*	36 → 15	425	$^{76, 79}$Kr (0.7)	50
^{94m}Tc	52 min	^{94}Mo(p,n)	13 → 7	2×10^3	^{94g}Tc (6)	19
^{110g}In	1.1 h	^{111}Cd(p,2n)*	23 → 16	6×10^3	^{110m}In (10)	51
^{120g}I	1.3 h	^{120}Te(p,n)	15 → 9	2×10^3	^{120m}I (4.8)	20
		^{122}Te(p,3n)	37 → 32	3.6×10^3	^{120m}I (25)	52

*Using highly enriched target isotope; **the preferred method of production of this radionuclide is the ^{62}Zn-^{62}Cu generator route. The parent nuclide is produced via the ^{63}Cu(p,2n)^{62}Zn reaction.

and is obtained by subtracting the yield at 8 MeV from that at 15 MeV.

CALCULATED YIELDS OF NON-STANDARD POSITRON EMISSION TOMOGRAPHY NUCLIDES

The excitation functions of most of the non-standard PET nuclides have been relatively well investigated and, in general, therefrom the integral yields have been calculated. For the formation of some nuclides, a large number of reactions have been studied. For practical reasons, however, discussed above, only one or two nuclear routes have been developed for each nuclide to be produced in sufficient quantity and good quality. The production is done using an optimum energy range, *i.e.* a range giving the maximum yield of the product and the minimum amount of radionuclidic impurities.

An exhaustive documentation of calculated yields of various non-standard PET nuclides produced *via* all the routes is beyond the scope of this article. Instead attention was directed to one or two most commonly used production reactions [42-61] for each radionuclide. For those reactions, then, the reported optimum energy range was adopted and the calculated yield of the radionuclide under study was deduced. Similarly, the major impurities and their magnitudes were estimated. The results are given in two tables. The short-lived radionuclides (with $T_{1/2}$≤2 h) are given in Table III. Those radionuclides have found only some limited applications. In Table IV are listed the longer lived non-standard PET nuclides which have been used in one way or the other for many years. It, however, does not include a few radionuclides like ^{45}Sc and ^{74}As for which (according to the judgement of this author) accurate excitation functions are not available, although those radionuclides have been practically produced in small quantities and used in a few studies.

A few PET nuclides used as analogues of some therapeutic or SPECT-diagnostic radionuclides are also given in Tables III and IV. They constitute the useful analogue pairs ^{86}Y-^{90}Y, ^{83}Sr-^{89}Sr and ^{124}I-^{131}I where PET is combined with therapy, and the pairs ^{66}Ga-^{67}Ga, ^{94m}Tc-^{99m}Tc, ^{110m}In-^{111}In, and ^{120}I-^{123}I in which the PET radionuclide can be used to quantify the biodistribution of a radiopharmaceutical which is normally labeled with the corresponding SPECT nuclide.

COMPARISON OF THEORETICAL AND PRACTICAL YIELDS OF NON-STANDARD POSITRON EMISSION TOMOGRAPHY NUCLIDES

In order to demonstrate the feasibility of medical application of a radionuclide it has to be produced in sufficient quantity. This involves irradiation of a relatively thick target at a high beam current for a sufficiently long period, followed by its chemical processing to isolate the desired radionuclide from the matrix activity. The radionuclide activity extrapolated to the end of bombardment is called the "batch yield". It is then normalized to beam current and time of irradiation. The result is then in units of MBq/μA·h and is denoted as "experimental thick target yield". If now it is compared with the yield calculated from the exci-

TABLE IV.—*Non standard PET nuclides with intermediate half-lives ($T_{1/2} \geq 2$ h).*

Nuclide	$T_{1/2}$	Common production route	Energy range (MeV)	Calculated yield (MBq/μAh)	Radionuclidic impurity (%)	Reference
^{52}Mn	5.6 d	^{nat}Cr(p,xn)	20 → 10	0.4	^{54}Mn (<0.5)	45
		^{52}Cr(^{3}He,t)	36 → 10	5.6	^{54}Mn (0.8)	53
^{52}Fe	8.3 h	^{55}Mn(p,4n)	100 → 60	22	^{55}Fe (<2)	54
		^{52}Cr(^{3}He,3n)	36 → 17	1.3	^{55}Fe (<0.01)	53
^{55}Co	17.6 h	^{58}Ni(p,n)α*	15 → 7	14	^{57}Co (0.5)	21
		^{54}Fe(d,n)*	10 → 5	32	$^{56, 57}$Co (<0.1)	22, 23
^{61}Cu	3.4 h	^{61}Ni(p,n)*	12 → 9	647	^{60}Cu (14.6)	17
^{64}Cu	12.7 h	^{64}Ni(p,n)*	12 → 9	236	^{61}Cu (0.4)	17
^{66}Ga	9.4 h	^{66}Zn(p,n)*	13 → 8	433	—	55
^{72}As	26 h	^{nat}Ge(p,xn)	18 → 8	93	^{71}As (<10)	56
^{73}Se	7.1 h	^{75}As(p,3n)	40 → 30	1.4×10^{3}	$^{72, 75}$Se (<0.2)	25
^{76}Br	16 h	^{76}Se(p,n)	15 → 8	360	—	16
		^{75}As(3He,2n)	18 → 10	11	^{77}Br (1.6)	47
^{82m}Rb	6.2 h	^{82}Kr(p,n)*	14.5 → 10	370	^{81}Rb (0.01)	57
^{83}Sr	32.4 h	^{85}Rb(p,3n)	37 → 30	160	^{85}Sr (0.24)	58
^{86}Y	14.7 h	^{86}Sr(p,n)*	14 → 10	400	^{87}m,gY (3)	18
^{89}Zr	78.4 h	^{89}Y(p,n)	12 → 6	43	^{88}Zr (<0.1)	59
^{90}Nb	14.6 h	^{90}Zr(p,n)	15 → 8	423	$^{92, 95, 96}$Nb (3)	60
^{124}I	4.18 d	^{124}Te(p,n)*	12 → 8	16	^{125}I (0.1)	11
		^{124}Te(d,2n)*	14 → 10	17.5	^{125}I (1.7)	61

*Using highly enriched isotope as target material.

tation function over the same energy range as for the thick target, the ratio reflects the efficiency of the applied production methodology.

For all the non-standard PET nuclides listed in Tables III and IV both theoretical and experimental yields are available. The general result is that the experimental yield is always lower than the theoretical value. Some of the reasons may be: a) uncertainty in the thickness of the irradiated sample; b) inhomogeneity of the target; c) undefined chemical composition of the target; d) lower enrichment of the target. The theoretical yield calculation is generally for a 100% enriched metallic/element target; e) uncertainty in the projectile beam intensity. In production runs often defocused and wobbled beams are used, resulting in deflection of part of the beam from the target (which is not separately recorded to be able to introduce a correction); f) materials damage due to high current; g) loss of the product during irradiation; h) loss of the radioactive product during chemical processing.

The experimental yield is thus strongly dependent on high current targetry and chemical processing of the irradiated material. The yields often vary between 20% and 80 % of the theoretical values. In the methodological development of a radionuclide, a relatively low yield may be sufficient to perform the feasibility tests. However, when real applications increase, the demands on the availability of the radionuclide increase. Out of all the non-standard PET nuclides listed in Tables III and IV, 7 of them, *viz.* ^{64}Cu, ^{72}As, ^{73}Se, ^{76}Br, ^{86}Y, ^{94m}Tc and ^{124}I, have been receiving enhanced attention. The basic cross section data and calculated yields are available as standard data. Several laboratories around the world, and even a few commercial companies, are spending lot of efforts to enhance the batch yields as well as the thick target yields. The latter involves optimization work to obtain the experimental value as close to the theoretical value as possible.

Conclusions

The decay data of most of the non-standard PET nuclides are generally well known, except for the positron emission intensity in a few cases. Using very pure radioactive samples and modern techniques of X-ray and γ-ray spectroscopy, it is possible to determine the $I_{\beta+}$ values accurately. The development of a non-standard PET nuclide for applications demands some fundamental nuclear chemistry research.

Measurement of the excitation function of a nuclear reaction allows optimization of the production route. The theoretical yield of a radioactive product calculated from the excitation function gives always the maximum achievable yield. Efforts related to targetry and chemical processing are then constantly under improvement to get the experimental yield value as close to the theoretical value as possible. Many of the important non-standard PET nuclides (^{64}Cu, ^{72}As, ^{76}Br, ^{86}Y, ^{94m}Tc, ^{124}I, etc.) can be produced in good yields at low energy cyclotrons ($E_p \leq 18$ MeV), using highly enriched target materials. For production of some other radionuclides, *e.g.* ^{52}Fe, ^{73}Se, ^{83}Sr and ^{124}I (in large quantities), an intermediate energy cyclotron is required.

References

1. Evaluated Nuclear Structure Data File (ENSDF), National Nuclear Data Center (NNDC), Brookhaven, USA, and International Energy Agency (IAEA). Vienna: February, 2006.
2. Qaim SM, Bisinger T, Hilgers K, Nayak D, Coenen HH. Positron emission intensities in the decay of ^{64}Cu, ^{76}Br and ^{124}I. Radiochim Acta 2007;95:67-73.
3. Wermann G, Alber D, Pritzkow W, Riebe G, Vogl J, Görner W. Determination of the β^- branching ratio of ^{64}Cu by mass spectrometric investigations of the decay products in neutron transmuted copper. Appl Radiat Isot 2002;56:145-151.
4. Hohn A, Coenen HH, Qaim SM. Positron emission intensity in the decay of ^{120g}I. Radiochim Acta 2000;88:139-41.
5. Woods DH, Woods SA, Woods MJ, Makepeace JL, Downey CWA, Smith D *et al.* The standardization and measurement of decay scheme data of ^{124}I. Appl Radiat Isot 1992;43:551-60.
6. Qaim SM, Hohn A, Bastian T, El-Azoney KM, Blessing G, Spellerberg S *et al.* Some optimization studies relevant to the production of high-purity ^{124}I and ^{120g}I at a small-sized cyclotron. Appl Radiat Isot 2003;58:69-78.
7. Scholten B, Kovács Z, Tárkányi F, Qaim SM. Excitation functions of ^{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 1995;46:255-9.
8. Kondo K, Lambrecht RM, Wolf AP. Excitation functions of the ^{124}Te(p,2n)^{123}I and ^{124}Te(p,n)^{124}I reactions and the effect of target enrichment on radionuclidic purity. J Appl Radiat Isot 1977;28:395-401.
9. Lambrecht RM, Sajjad M, Qureshi MA, Al-Yanbawi SJ. Production of ^{124}I. J Radioanalyt Nucl Chem Lett 1988;127:143-50.
10. Sharma HL, Zweit J, Downey S, Smith AM, Smith AG. Production of ^{124}I for positron emission tomography. J Labelled Compd Radiopharm 1988;26:165-7.
11. Knust EJ, Dutschka K, Weinreich R. Preparation of ^{124}I solutions after thermodistillation of irradiated $^{124}TeO_2$ targets. Appl Radiat Isot 2000;52:181-4.
12. McCarthy TJ, editor. Proceedings of the 8th International Workshop on Targetry and Target Chemistry. St. Louis, USA: 24-26 June 1999.
13. Sheh Y, Koziorowski J, Balatoni J, Lom C, Dahl JR, Finn RD. Low energy cyclotron production and chemical separation of no-carrier-added ^{124}I from a reusable, enriched Te-124 dioxide/aluminium dioxide solid solution target. Radiochim Acta 2000;88:169-73.
14. Glaser M, Mackay DB, Ranicar ASO, Waters SL, Brady F, Luthra SK. Improved targetry and production of ^{124}I for PET studies. Radiochim Acta 2004;92:951-6.
15. Nye JA, Avila-Rodrigues MA, Nickles RJ. Production of [^{124}I]-iodine on an 11 MeV cyclotron. Radiochim Acta 2006;94:213-6.
16. Hassan HE, Qaim SM, Shubin Y, Azzam A, Morsy M, Coenen HH *et al.* Experimental studies and nuclear model calculations on proton-induced reactions on ^{nat}Se, ^{76}Se and ^{77}Se with particular reference to the production of the medically interesting radionuclides ^{76}Br and ^{77}Br. Appl Radiat Isot 2004;60:899-909.
17. Szelecsényi F, Blessing G, Qaim SM. Excitation functions of proton induced nuclear reactions on enriched ^{61}Ni and ^{64}Ni: possibility or production of no-carrier added ^{61}Cu and ^{64}Cu at a small cyclotron. Appl Radiat Isot 1993;44:575-80.
18. Rösch F, Qaim SM, Stöcklin G. Nuclear data relevant to the production of the positron emitting radioisotope ^{86}Y *via* the ^{86}Sr(p,n)- and ^{nat}Rb(^{3}He,xn)-processes. Radiochim Acta 1993;61:1-8.
19. Rösch F, Qaim SM. Nuclear data relevant to the production of the positron emitting technetium isotope ^{94m}Tc *via* the ^{94}Mo(p,n)-reaction. Radiochim Acta 1993;62:115-21.
20. Hohn A, Coenen HH, Qaim SM. Nuclear data relevant to the production of ^{120g}I *via* the ^{120}Te(p,n)-process at a small cyclotron. Appl Radiat Isot 1998;49:1493-6.
21. Reimer P, Qaim SM. Excitation functions of proton induced reactions on highly enriched ^{58}Ni with special relevance to the production of ^{55}Co and ^{57}Co. Radiochim Acta 1998;80:113-20.
22. Sharma H, Zweit J, Smith AM, Downey S. Production of ^{55}Co, a short-lived, positron emitting radiolabel for bleomycin. Appl Radiat Isot 1986;37:105-9.
23. Zaman MR, Qaim SM. Excitation functions of (d,n) and (d,α) reactions on ^{54}Fe: relevance to the production of high purity ^{55}Co at a small cyclotron. Radiochim Acta 1996;75:59-63.
24. Qaim SM, Stöcklin G. Excitation functions of ^{74}Se(d,xn)^{75,74m}Br reactions: comparative evaluation of possible routes for the production of ^{75}Br at a small cyclotron. Appl Radiat Isot 1993;44:1443-7.
25. Mushtaq A, Qaim SM, Stöcklin G. Production of ^{73}Se *via* (p,3n) and (d,4n) reactions on arsenic. Appl Radiat Isot 1988;39:1085-91.
26. Hohn A, Nortier FM, Scholten B, van der Walt TN, Coenen HH, Qaim SM. Excitation functions of ^{125}Te(p,xn)-reactions from their respective thresholds up to 100 MeV with special reference to the production of ^{124}I. Appl Radiat Isotope 2001;55:149-56.
27. Mirzadeh S, Knapp FF. In "Manual for Reactor Produced Radioisotopes", IAEA, Vienna, 2003, TECDOC-1340.p.51-7.
28. Zweit J, Smith AM, Downey S, Sharma HL. Excitation functions for deuteron induced reactions in natural nickel-production of no-carrier-added ^{64}Cu from enriched ^{64}Ni targets for positron emission tomography. Appl Radiat Isot 1991;42:193-7.
29. Hilgers K, Stoll T, Skakun Ye, Coenen HH, Qaim SM. Cross section measurements of the nuclear reactions ^{nat}Zn(d,x)^{64}Cu, ^{66}Zn(d,α)^{64}Cu and ^{68}Zn(p,αn)^{64}Cu for production of ^{64}Cu and technical developments for small scale production of ^{67}Cu *via* the ^{70}Zn(p,α)^{67}Cu process. Appl Radiat Isot 2003;59:343-51.
30. Groppi F, Bonradi ML, Gini L, Mainardi C, Menapace E, Abbas K *et al.* Thin-target excitation functions and optimisation of nca ^{64}Cu and ^{66,67}Ga production by deuteron induced nuclear reactions on natural zinc target, for radiometabolic therapy and for PET. Nucl Instr Meth 2004;B213:373-7.
31. Tárkányi F, Takacs S, Ditroi F, Hermanne A, Sonck M, Shubin Y. Excitation functions of deuteron induced nuclear reactions on natural zinc up to 50 MeV. Nucl Instr Meth 2004;B217:531-50.
32. Szelecsényi F, Steyn GF, Kovács F, Vermeulen C, van der Meulen NP, Dolley SG *et al.* Investigation on the ^{66}Zn(p,2pn)^{64}Cu and ^{68}Zn(p,x)^{64}Cu nuclear processes up to 100 MeV: production of ^{64}Cu. Nucl Instrum Methods 2005;240:625-37.
33. Smith SV, Waters DJ, Di Bartolo N. Separation of ^{64}Cu from ^{67}Ga waste products using anion exchange and low acid aqueous/organic mixtures. Radiochim Acta 1996;75:65-8.
34. Bonardi ML, Groppi F, Birattari C, Gini L, Mainardi C, Ghioni A *et al.* Thin-target excitation functions and optimization of simulta-

neous production of NCA copper-64 and gallium-66,67 by deuteron induced nuclear reactions on a natural zinc target. J Radioanal Nucl Chem 2003;257:229-41.
35. Kozempel J, Abbas K, Simonelli F, Zampese M, Holzwart U, Gibson N *et al.* A novel method for nca ^{64}Cu by the ^{64}Zn(d,2p)^{64}Cu reaction and dual ion-exchange column separation. Radiochim Acta 2007;95:75-80.
36. McCarthy DW, Shefer RE, Klinkowstein RE, Bass LA, Margeneau WH, Cutler CS *et al.* Efficient production of high specific activity ^{64}Cu using a biomedical cyclotron. Nucl Med Biol 1997;24:35-43.
37. Szajek LP, Meyer W, Plascjak P, Eckelman WC. Semiremote production of [^{64}Cu]$CuCl_2$ and preparation of high specific activity [^{64}Cu]Cu-ATSM for PET studies. Radiochim Acta 2005;93:239-44.
38. Qaim SM, Mushtaq A, Uhl M. Isomeric cross-section ratio for the formation of ^{73m,g}Se in various nuclear reactions. Phys Rev C 1988;38:645-50.
39. Strohmaier B, Faßbender M, Qaim SM. Production cross sections of ground and isomeric states in the reaction systems ^{93}Nb+^{3}He, ^{92}Mo+α and ^{94,95}Mo+p. Phys Rev C 1997;56:2654-65.
40. Sudár S, Hohn A, Qaim SM. Nuclear model calculations on proton and deuteron induced reactions on ^{122}Te and ^{120}Te with particular reference to the formation of the isomeric states ^{120m,g}I. Appl Radiat Isot 2000;52:937-41.
41. Qaim SM. Cyclotron production of medical radionuclides. In: Rösch F, editor. Handbook of nuclear chemistry. Dordrecht, The Netherlands: Kluwer; 2003;4:47-79.
42. Sahakundu SM, Qaim SM, Stöcklin G. Cyclotron production of short-lived ^{30}P. Int J Appl Radiat Isot 1979;30:3-5.
43. Qaim SM, Sutisna MS, Ollig H. Production of ^{38}K *via* the ^{35}Cl(α,n)-process at a compact cyclotron. Appl Radiat Isot 1988;39:479-82.
44. Tárkányi F, Kovács Z, Qaim SM, Stöcklin G. Production of ^{38}K *via* the ^{38}Ar(p,n)-process at a small cyclotron. Appl Radiat Isot 1992;43:503-7.
45. Klein ATJ, Rösch F, Qaim SM. Investigation of ^{50}Cr(d,n)^{51}Mn and ^{nat}Cr(p,x)^{51}Mn processes with respect to the production of the positron emitter ^{51}Mn. Radiochim Acta 2000;88:253-64.
46. Piel H, Qaim SM, Stöcklin G. Excitation functions of (p,xn)-reactions on ^{nat}Ni and highly enriched ^{62}Ni: possibility of production of medically important radioisotope ^{62}Cu at a small cyclotron 1992;57:1-5.
47. Alfassi ZB, Weinreich R. The production of positron emitters ^{75}Br and ^{76}Br: excitation functions and yields for ^{3}He and α-particle induced reactions on arsenic. Radiochim Acta 1982;30:67-71.
48. Paans AJM, Welleweerd J, Vaalburg W, Reiffers S, Woldring MG. Excitation functions for the production of bromine-75: a potential nuclide for the labeling of radiopharmaceuticals. Int J Radiat Isot 1980;31:267-73.
49. Kovács Z, Blessing G, Qaim SM, Stöcklin G. Production of ^{75}Br *via* the ^{76}Se(p,2n)^{75}Br reaction at a compact cyclotron. Int J Appl Radiat Isot 1985;36:635-42.
50. Youfeng He, Qaim SM, Stöcklin G. Excitation functions for ^{3}He-particle induced nuclear reactions on ^{76}Se, ^{77}Se and ^{nat}Se: possibilities of production of ^{77}Kr. Int J Appl Radiat Isot 1982;33:13-9.
51. Tárkányi F, Szelecsényi F, Kopecky P, Molnar T, Ando L, Mikecz P *et al.* Cross sections of proton induced nuclear reactions on enriched ^{111}Cd and ^{112}Cd for the production of ^{111}In for use in nuclear medicine. Appl Radiat Isot 1994;45:239-49.
52. Hohn A, Scholten B, Coenen HH, Qaim SM. Excitation functions of (p,xn) reactions on highly enriched ^{122}Te: relevance to the production of ^{120g}I. J Appl Radiat Isot 1998;49:93-8.
53. Fessler A, Alfassi ZB, Qaim SM. Excitation functions of ^{3}He induced reactions on natural chromium: possibilities of production of ^{52}Fe, ^{53}Fe and ^{52}Mn for medical use. Radiochim Acta 1994;65:207-13.
54. Steyn GF, Mills SJ, Nortier FM, Simpson BRS, Meyer BR. Production of ^{52}Fe *via* proton induced reactions on manganese and nickel. Appl Radiat Isot 1990;41:315-25.
55. Szelecsényi F, Boothe TE, Tavano E, Plitnikas ME, Tárkányi F. Compilation of cross sections/thick target yields for ^{66}Ga, ^{67}Ga and ^{68}Ga production using Zn targets up to 30 MeV proton energy. Appl Radiat Isot 1994;45:473-500.
56. Spahn I, Steyn G, Nortier FM, Coenen HH, Qaim SM. Excitation functions of ^{nat}Ge(p,xn)^{71,72,73,74}As reactions up to 100 MeV with a focus on the production of ^{72}As for medical and ^{73}As for environmental studies. Appl Radiat Isot 2007;65:1057-64.
57. Kovács Z, Tárkányi F, Qaim SM, Stöcklin G. Production of 6.5 h ^{82m}Rb *via* the ^{82}Kr(p,n)-process at a low-energy cyclotron. A potential substitute for ^{82}Rb. Appl Radiat Isot 1991;42:831-4.
58. Kastleiner S, Qaim SM, Nortier FM, Blessing G, van der Walt TN, Coenen HH. Excitation functions of ^{85}Rb(p,xn)^{85m,g,83,82,81}Sr reactions up to 100 MeV: integral tests of cross section data, comparison of production routes of ^{83}Sr and thick target yield of ^{82}Sr. Appl Radiat Isot 2002;56:685-95.
59. Mustafa MG, West Jr. HI, O'Brien H., Lanier RG, Benhamou M, Tamura T. Measurements and a direct-reaction-plus-Hauser-Feshbach analysis of ^{89}Y(p,n)^{89}Zr, ^{89}Y(p,2n)^{88}Zr and ^{89}Y(p,pn)^{88}Y reactions up to 40 MeV. Phys Rev 1988;C38:1624-37.
60. Busse S, Rösch F, Qaim SM. Cross section data for the production of the positron emitting niobium isotope ^{90}Nb *via* the ^{90}Zr(p,n)-reaction. Radiochim Acta 2002;90:1-5.
61. Bastian T, Coenen HH, Qaim SM. Excitation functions of ^{124}Te(d,xn)^{124,125}I reactions from threshold up to 14 MeV: comparative evaluation of nuclear routes for the production of ^{124}I. Appl Radiat Isot 2001;55:303-8.