REVIEW OF CYCLOTRON PRODUCTION AND QUALITY CONTROL OF "HIGH SPECIFIC ACTIVITY" RADIONUCLIDES FOR BIOMEDICAL, BIOLOGICAL, INDUSTRIAL AND ENVIRONMENTAL APPLICATIONS AT INFN-LASA*

C. Birattari, M. Bonardi*, F. Groppi, L. Gini, Universita' degli Studi and INFN-Milano, LASA, I-20090 Segrate (Milano), E. Menapace, ENEA, I-40128 Bologna, Italy

Abstract

At the "Radiochemistry Laboratory" of Accelerators and Applied Superconductivity Laboratory, LASA, a wide range of high specific activity radionuclides, RNs, have been produced in No Carrier Added form, for both basic research and application purposes. Use was made of the AVF proton cyclotron (K=45) of Milan University (up to 1987). More recently, the irradiations were carried out at the Scanditronix MC40 cyclotron (K=38; p, d, He-4 and He-3) of JRC-Ispra, Italy, of the European Community. In order to optimize the irradiation conditions for radioisotope production, a series of thin- and thick-target excitation functions have been experimentally determined. For each RN, a specific radiochemical separation has been developed in order to obtain GBq (mCi) amounts of the radiotracers in "high specific activity" No Carrier Added form (NCA).

1 INTRODUCTION

Radionuclides of very High Specific Activity are of great relevance in many applications: Nuclear Medicine imaging and systemic radionuclide therapy, metallo-toxicological and environmental studies, industrial applications. In order to obtain a high SA, it is necessary separating the accelerator-produced RN from the irradiated target, without addition of isotopic carrier. This kind of RNs are named No Carrier Added (NCA) and their specific activity can reach values close to the theoretical "carrier-free" one (CF) (see Table 1).

2 DEFINITIONS AND METHODS

2.1 Specific Activity and Isotopic Dilution Factor

Specific activity (SA), is defined as the "activity of a well stated RN to the total mass of isotopic carrier" present in the sample. It is measured in Bq/g in the SI. In practice, even without the "voluntary addition" of isotopic carrier during the radiochemical processing, the RN produced, is always diluted in a variable amount of both stable and radioactive isotopes of same element (i.e. same Z). This means that in most cases, a CF-SA is not achievable, and the RN of interest is always isotopically diluted. The isotopic dilution factor, IDF, is defined as the ratio between the total number of atoms of a stated element to the number of atoms of RN of interest.

Thus, the IDF is the ratio between CF-SA to real SA; it is a non-dimensional quantity. Both stable and radioactive isotopes of the RNs are produced by both side nuclear reactions and decay. Furthermore, any target material or chemicals, contains normally ultra-trace amounts of isotopic carrier. The term CF RN, must by used carefully as stressed several times [1,2]. The real SA, even if obtained in NCA condition, must by measured experimentally by either analytical or radioanalytical "elemental analysis" techniques [1,3,4,5]. Only when no other isotopes are present, a RN can be defined CF.

Moreover the CF-SA is a physical constant, an intensive parameter defined as: $N_a \lambda$ / a.m., where N_a is the Avogadro constant, λ is the decay constant of the RN and a.m. is the atomic mass of RN itself. A similar definition can be given for Molar SA (Bq/mol). Conversely, the NCA-SA is not a constant, but decays with time with the half-life of the RN, as well as the IDF increases with time with the same law. Finally, the longer is the time elapsed from EOB and the EOCP, the lower is the SA achievable.

We found experimentally, that IDF values ranging from 10 to some thousands are common for most NCA RNs even if extra-pure chemicals, targets and radiochemical processing equipment are used [1-12].

Table 1: Useful Definitions

Symbol	Parameter	unit
SA	Specific Activity	Bq/g
CF-SA	Carrier Free-SA	Bq/g
NCA-SA	No Carrier Added-SA	Bq/g
CA-SA	Carrier Added-SA	Bq/g
NCF-SA	Nearly Carrier Free-SA	Bq/g
AC	Activity Concentration	Bq/g
MSA	Molar Specific Activity	Bq/mol
IDF	Isotopic Dilution Factor	adim
EOB	End Of Bombardment	
EOIB	End Of an Instantaneous Bombardment (i.e: $\tau \rightarrow 0$)	
EOCP	End Of Chemical Processing	

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*Mauro.Bonardi@MI.INFN.IT

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2.2 Methods to achieve a" very high" SA-RN

In order to produce very high SA RNs, it is necessary inducing nuclear reactions, whose product has atomic number different from target one. Even using of the Szilard-Chalmers hot-atom method, leads to large IDFs.

Amongst the various possible methods, the use of light ion accelerators (mainly cyclotrons), presents several advantages. The RN produced, belongs to the "neutron poor" side of beta stability valley. Thus, its beta decay mode is either Electron Capture or positron emission. The half-life of such RNs is normally short, thus they are suitable tracers for applications envisaged. In case of positron emitters, the annihilation radiation is efficiently detected by Positron Emission Tomographs. In case of simple γ de-excitation, both high-resolution γ-spectrometry and Single Photon Computerized Tomographs, are effective for both detection and image reconstruction. Amongst the possible nuclear reaction induced by fast ions (Cp), those of (Cp,xn) kind, present significant cross-sections in the energy range up to some tens MeV/nucleon. Moreover, the cross-section of single reaction channels, are higher for light ions in the compound nucleus energy region. Finally, due to the lower stopping power of light ions in materials, ion beam from protons up to alpha particle are normally preferred.

Finally, the beam current, normally available in a light ion accelerator, is larger than for heavier ions. To day, proton-cyclotron beam currents of several milliA are available, even if the power density reaches values of several kW per g of irradiated material, even with fraction of milliA beams of some tens MeV/nucleon:

$$P\ (watt) = I\ (\mu A)\ \Delta E\ (MeV) / \gamma z \qquad (1)$$

where, ΔE is the "average" energy loss of beam into the target, γz is the "average" beam charge into the target (1 for protons) and I is the beam current itself.

Thus, since 25 years we pointed our main attention to this kind of light projectiles, for RN production purposes.

2.3 Thin-target excitation functions

In order to optimize production of a specific RN, minimizing at the same time the production of radioisotopic impurities, the "accurate" knowledge of behavior of cross-sections of each reaction, as a function of beam energy is mandatory. The off-line technique we used to measure the "effective" cross-section of nuclear reactions, was the irradiation of "thin-targets", followed by off-line high resolution HPGe γ-spectrometry.

This method allows measuring direct nuclear reaction cross-sections of single reaction channels, only when the target is of mono-isotopic composition or is isotopically enriched. In other cases the thin-target yield gives an information on the "effective " reaction cross-section σ*(E), that is barely the weighted summation of different reaction channel cross-section concerned $\sigma_i(E)$, on different isotopes present in the target, as per eq. 2:

$$\sigma^*(E) = \Sigma\ w_i\ \sigma_i\ (E) \qquad (2)$$

Nevertheless, even this information is relevant for RN production purposes. For radioisotope production, the "thin-target" yield *y(E)* is defined, at the EOIB, as the slope at the origin to the growing curve vs. irradiation time τ, of the activity A of a given RN per unit beam current and per unit energy loss, that is (in Bq / C MeV):

$$y(E)_{EIOB} = y(E,0) = \left(\frac{\partial(\partial[A/I])}{\partial E\ \partial \tau} \right) \tau \to 0 \qquad (3)$$

$$y(E) = \frac{\sigma^*(E)\ N_A\ \lambda}{a.m.\ \gamma z\ e\ \left(\frac{dE}{dx}(E) \right)} \qquad (4)$$

2.4 Thick-Target excitation functions and Yield

Whenever, the effective cross-sections σ*(E) of all reactions concerned are known, the thick-target yield *Y(E,ΔE)* for each RN produced, can be calculated by either numerical or analytical integration of *y(E)*, as a function of both incident projectile energy E and energy loss ΔE of beam in target itself, that is in (Bq / C):

$$Y(E,\Delta E) = \int_{E-\Delta E}^{E} y(x)\ dx$$

This definition holds in the raw approximation of a *monochromatic beam* of energy E, *not affected by either intrinsic energy spread or straggling*, in which, the integrand *y(x)* represents the thin-target excitation functions of eqs. (3,4). In case of total particle energy absorption in the target (i.e: energy loss ΔE = E), the function *Y(E,ΔE)* reaches a value $Y(E,E-E_{th})$, for ΔE = E-Eth, that represents mathematically the *envelope* of the *Y(E,ΔE) family of curves*. This *envelope* is a *monotonically increasing* curve, never reaching either a maximum or a saturation value, even if its slope becomes negligible for high particle energies and energy losses. Eq. (5) states obviously that the production yield of a thick-target does not increase further, if the residual energy in the target is lower then the nuclear reaction energy threshold, E_{th}. In practice, the use of a target thickness larger than "effective" one, is unsuitable from technological point of view, due to the larger power density Pd (watt / g) deposited by the beam in target material itself, instead of target cooling system [6,7,8].

Figure 1, showing the calculated thick-target yields for (p,xn) nuclear reaction on Mo target of natural isotopic composition to produce technetium-95m, was obtained by analytical integration of experimental thin-target excitation functions. In the same pictures, the first and second calculated loci of the maxima of thick-target yield are represented. These maxima correspond to couples of optimized values (E,ΔE), having different values for each different RN. This set of thick-target yields allows calculating the optimum irradiation conditions [6-12].

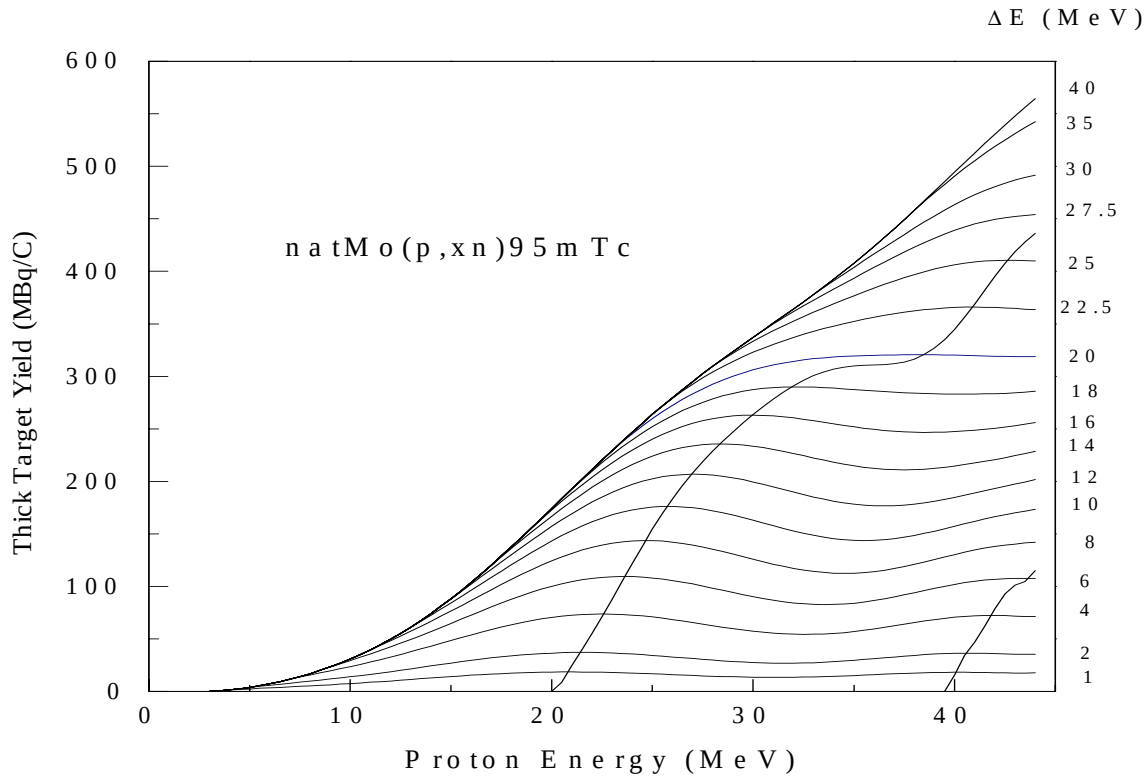

Figure 1: Calculated "thick-target yield" from experimental "thin-target" excitation functions of $^{nat}Mo(p,xn)^{95m}Tc$ nuclear reactions, as a function of both proton energy E and energy loss ΔE, in target itself.

2.5 Specific Activity Optimization

Whenever, the thick-target yield of a RN is optimized, a selective radiochemical separation of the RN of interest, executed in No Carrier Added conditions, leads to the higher specific activity that is possible gaining, through that chosen nuclear route [9-12]. A real CF-SA is achievable with artificial short-lived RNs only. The minimization of IDF is achieved also, with this method.

As an example, even if, in case of technetium radiotracers the NCA-SA was very high, nevertheless an IDF of not less than 10-100 was obtained due to the presence to other medium and long-lived technetium radioisotopes produced by side reactions, together with technetium-95m, like technetium-96g,97(m+g),98,99g.

3 CONCLUSIONS

The "accurate" knowledge of the behavior of thin-target excitation functions for nuclear reaction leading to cyclotron production of relevant RNs, allows increasing both radionuclidic purity and specific activity of RN itself, by use of very selective radiochemical separations.

Several thin-target excitation functions of RNs of widespread use in Nuclear Medicine, have been measured by the LASA-INFN group and are presently "recommended" by an IAEA-TECDOC document [13].

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