

CYCLOTRON PRODUCTION OF “VERY HIGH SPECIFIC ACTIVITY” PLATINUM RADIOTRACERS IN NO CARRIER ADDED FORM*

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Abstract

At the "Radiochemistry Laboratory" of Accelerators and Applied Superconductivity Laboratory, LASA, several production and quality assurance methods for short-lived and high specific activity radionuclides, have been developed. Presently, the irradiations are carried out at the Scanditronix MC40 cyclotron ($K=38$; p, d, He-4 and He-3) of JRC-Ispra, Italy, of the European Community, while both chemical purity and specific activity determination are carried out at the TRIGA MARK II research reactor of University of Pavia and at LASA itself. In order to optimize the irradiation conditions for platinum radiotracer production, both thin- and thick-target excitation function of $^{nat}\text{Os}(\alpha, xn)$ nuclear reactions were measured.

A very selective radiochemical separation to obtain Pt radiotracers in No Carrier Added form, has been developed. Both real specific activity and chemical purity of radiotracer, have been determined by neutron activation analysis and atomic absorption spectrometry. An Isotopic Dilution Factor (IDF) of the order of 50 is achieved.

1 INTRODUCTION

Platinum, is a very rare element, that is presently introduced into the echo-systems, mainly by the catalytic converters of motor-vehicles. Furthermore, Pt organo-metallic compounds (ex: cis-Pt and carbo-Pt) are used extensively for tumor chemo-therapy [1].

Amongst the “neutron poor” radionuclides (RN) of platinum: platinum-188,189,191 are suitable tracers for short- and medium-term metallo-toxicological studies on cell cultures. These RNs can be efficiently produced by either proton irradiation on iridium target [2] or alpha induced reactions on osmium target of natural isotopic composition, in the α energy range up to 38 MeV, as shown in previous report [2].

2 DEFINITIONS AND METHODS

2.1 Specific Activity, Isotopic Dilution Factor and Chemical Purity

Specific activity (SA), is defined as the “activity of one 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” of the target, the RN produced is always diluted in a variable amount of both stable and radioactive isotopes of same element [3].

After the experimental measurement of both thick- and thin-target excitation functions of these reactions, it is possible optimizing irradiation conditions and to radiochemically separating the platinum RNs from both irradiated target and other “non-isotopic” contaminants, without addition of isotopic carrier. The “very high specific activity” platinum radiotracers obtained, are used to simulate the exposure of living organisms to very small amounts of this element, like those present today in the industrialized countries [1]. Some RNs of osmium and iridium are produced by both “several” side reactions and decay charging (D), and are then radiochemically separated from platinum radiotracer itself (Table 1).

Moreover, stable impurities of platino-ferrous metals like: Fe, Ru, Pd, Ir and Au are present even in the extra-pure Os target used for irradiation. Radionuclidic, radiochemical and chemical purity tests have been carried out on the platinum radiotracer obtained [3]. The data base we used for γ -emission energy and intensity is Reus 1983 [4], while both mass defects and half-lives used for calculating Q values and SA are taken from Browne 1986 [5]. The γ -spectrometer was calibrated by a ^{152}Eu source.

Table 1: Main RN produced, calculated energy threshold (MeV) and Carrier Free Specific Activity (GBq/ μg)

RN	T1/2	main	Eth	ICB	CF-SA
188Pt	10.2 d	$\alpha, 2n$	19.3	22.5	2.52
189Pt	10.89 h	α, n	12.4	22.5	56.3
191Pt	2.9 d	α, n	11.3	22.3	8.72
188Ir	1.729 d	α, X	?+D	22.5	14.9
189Ir	13.2 d	α, X	?+D	22.4	1.94
190gIr	11.78 d	α, d	15.1	22.4	2.16
192gIr	73.831 d	α, d	14.6	22.3	0.32
194mIr	171 d	α, d	14.5	22.3	0.15
183mOs	9.9 h	α, X	?+D	22.5	64.0
185Os	93.6 d	α, X	?+D	22.5	0.28

2.2 Thin-target excitation functions

The relevance of the “accurate “ knowledge of “cross-section” data is stressed by a recent IAEA-TECDOC publication [6]. In fact, in order to optimize production of a specific RN, minimizing at the same time production of

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radioisotopic impurities, the “accurate” knowledge of behavior of excitation function $y(E)$ of each reaction, at the End Of an Instantaneous Bombardment, EOIB (i.e: irradiation time $\tau \rightarrow 0$), 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.

Experimentally, the excitation function $y(E)_{EOIB}$ in (Bq/C MeV), is calculated by the following equation, that holds for a RN produced by direct nuclear reaction only, without any decay charging (and for very low dead counting times):

$$y(E)_{EOIB} = \frac{C_{\gamma}}{(\varepsilon_{\gamma} \alpha_{\gamma} LT) Q \Delta E} D(RT) G(\tau) e^{\lambda WT}$$

where: Q = integrated proton charge (C) (obtained either from Faraday cup read-out or beam monitor reactions), C_{γ} = net photo-peak counts at energy E_{γ} above background continuum, α_{γ} = γ -emission absolute intensity, ε_{γ} = experimental efficiency at the γ -energy considered, $\lambda = \ln 2/T_{1/2}$ = decay constant (s^{-1}), LT = Live counting Time (s), DT = Dead counting Time (s), RT = Real counting Time (s) = $LT + DT$, WT = Waiting Time from the EOIB (s), τ = Irradiation Time (s), ΔE = non-dimensional quantities $D(RT)$ = “decay factor” to “average” beam energy loss in the target (MeV) and the correct decay during counting time and $G(\tau)$ = “growing

factor” to correct decay during irradiation, are defined as:

$$D(RT) = \frac{\lambda RT}{1 - e^{-\lambda RT}} \quad ; \quad G(\tau) = \frac{\lambda \tau}{1 - e^{-\lambda \tau}}$$

2.3 Thick-Target excitation functions and Yields

Figure 1, shows the “calculated” thick-target yields for $^{nat}\text{Os}(\alpha, xn)^{*}\text{Pt}$ nuclear reactions on Os target of natural isotopic composition, with total projectile energy absorption. The data were obtained by analytical integration of “experimental” thin-target excitation functions [8]. Moreover, the calculated values are compared with the “experimental” ones, presented in another paper [7]. The results obtained are in agreement within 10-20 %. As expected, the thick-target yield of ^{189}Pt is higher than those of ^{191}Pt and ^{188}Pt in the high-energy region. At 33 MeV, the thick-target yield of ^{191}Pt is about 50 times that of ^{188}Pt . Even if the reaction Q values, are of a few MeV, the yield becomes significant beyond the Coulomb barrier of incoming projectile only, that is of the order of 22 MeV (Table 1).

In present case, “under barrier” reactions, presented cross-section too low to be measured for all RNs with our experimental set up.

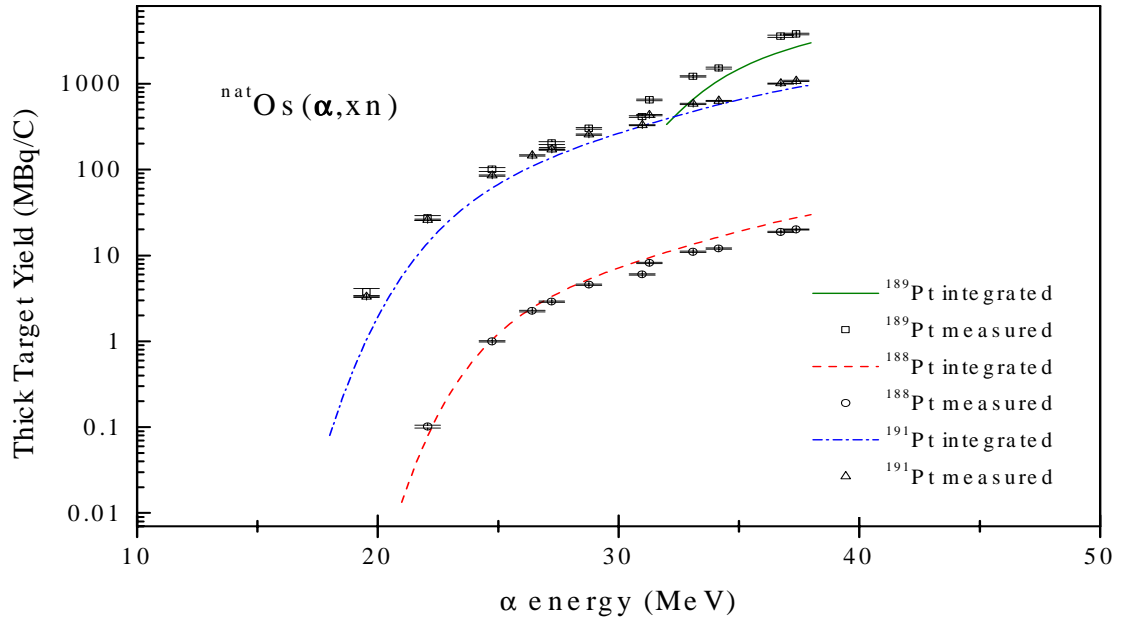


Figure 1: Calculated “thick-target yield” by integration of experimental “thin-target” excitation functions of $^{nat}\text{Os}(\alpha, xn)^{*}\text{Pt}$ nuclear reactions [8], compared with the experimental thick-target yields [7].

2.4 NCA Radiochemical Separation

Two very selective and effective radiochemical separations of Pt radiotracers by both irradiated Os target and other chemical and radiochemical impurities, were set up. The details have been published elsewhere [8]. One is: the irradiated Os target was dissolved in *aqua regia*; the solution was brought to conc. nitric acid and volatile osmium tetra-oxide was boiled off. The dried residue, was re-dissolved in conc. HCl, than dried again and re-dissolved in high-purity water at pH 7. Hydroxylamine chloride solution was added as a reductant at 65 °C. After addition of a slight excess of didentate chelating agent [9], diphenyl-thiocarbazon (i.e: dithizone)[10], the Pt(II) dithizonate, was extracted almost selectively in carbon tetrachloride. The Pt was then back-extracted from organic phase, by washing with ammonia at pH 9. To destroy dithizone, the final solution was mineralized by *aqua regia*, with addition of drops of hydrogen peroxide.

2.5 Radiochemical Purity

The radiochemical purity [3] of NCA Pt radiotracer was tested by ion exchange radio-chromatography [8]. As expected, the Pt was present as anionic chloro-complexes, [^{*}Pt][PtCl₄]²⁻ and [^{*}Pt][PtCl₆]²⁻, in its two more stable oxidation states Pt(II) and Pt(IV) respectively [1]. The ¹⁸⁸Ir charged by decay of its parent ¹⁸⁸Pt [5], was easily eluted as aquo-cation by a strong anion exchange resin.

2.6 Radionuclidic Purity

Actually, at the EOB and even at the EOCP, a mixture of ¹⁸⁹,¹⁸⁸,¹⁹¹Pt is present. After a proper cooling time ¹⁸⁸,¹⁹¹Pt are present only. It is relevant to stress that the medium-lived ¹⁸⁸Pt, even if is present in smaller amounts than ¹⁹¹Pt, as can be calculated by Fig. 1, it is always at transient equilibrium with its daughter RN ¹⁸⁸Ir [5].

2.7 Chemical Purity and Specific Activity Determination

Whenever, the thick-target yield of a RN is optimized [11], 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 chosen nuclear route. The minimization of IDF is achieved also with this method. The Pd(II) impurities follows the chemistry of Pt(II) [1], while all the other relevant metals, were efficiently decontaminated. In the final solution, the main impurity present was Fe(II), that is isomorphous with both Pt(II) and Pd(II) [1,10].

In present case, we measured the real NCA-SA at the EOCP by means of Graphite Furnace Atomic Absorption Spectrometry (GF-AAS). Other metal impurities, were determined by either GF-AAS or Instrumental Neutron Activation Analysis (INAA), by re-irradiation of decayed samples [12-16]. The results are reported in Table 2. The

NCA-SA of ¹⁹¹Pt was of the order of 179 MBq/μg at the end of a ten hours bombardment, with 3 μA alpha beam at 33 MeV energy. The final decontamination factor from Os target was larger than 10⁶. The IDF reached is about 48. Just in principle, using higher beam currents could lead to a proportional increase of specific activity up to a real Nearly Carrier Free (NCF) condition. A very low Pt concentration of less than 80 ng/ml and GBq ^{*}Pt radiotracer activities are obtained.

Table 2: Elemental composition of solution after osmium distillation (11 ml) and final radio-Pt solution (5 ml).

Element	μg / 11 ml	ng / 5 ml	Technique
Pt	0.69 ± 0.05	440 ± 50	GFAAS
Au	0.10 ± 0.01	45 ± 5	INAA
Fe		≈ 30000	GFAAS
Ir	1.16 ± 0.04	< 25	GFAAS, INAA
Pd		60 ± 7	GFAAS
Ru	0.30 ± 0.05	< 35	INAA
Os	4.50 ± 0.35	< 50	INAA

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, obviously by use of very selective radiochemical separations, without the addition of isotopic carrier.

In present case, medium-lived Pt radiotracers have been produced very selectively. The elemental impurities present in the final solution were of the order of ng per ml (ppb), apart iron, whose content was of the order of μg (ppm). A very low IDF of the order of 48 was obtained for ¹⁹¹Pt radiotracer, even it could be decreased further.

4 REFERENCES

- [1] Hartley ed., Chemistry of the Platinum Group Metals, Elsevier, Amsterdam, The Netherland, 1991.
- [2] Arginelli, Bonardi et al. Report INFN/TC-95/20, 1995
- [3] Bonardi et al. Sci. Total Environ. 17 (1981) 257.
- [4] Reus, Westmeier ADNDT 29 (1983) 194.
- [5] Browne, Firestone Table of Radioactive Isotopes, John Wiley & Sons, New York, 1986.
- [6] <http://www-NDS.IAEA.org/medical/>.
- [7] Groppi et al. J. Radioanal. Nucl. Chem. 249 (2001).
- [8] Bonardi al. J. Radioanal. Nucl. Chem. 236 (1998) 159.
- [9] Leight, Nomenclature of Inorganic Chemistry, Recommendations 1990, Blackwell Sci. Publ., Oxford.
- [10] Pribil, Analytical Applications of EDTA and Related Compounds, Pergamon Press, Oxford, UK, 1972.
- [11] Bonardi, Birattari J. Radioanal. Chem. 76 (1983) 311
- [12] Bonardi al. J. Radioanal. Nucl. Chem. 134 (1989) 199
- [13] Birattari al. J. Radioanal. Nucl. Chem. 160 (1992) 493
- [14] Bonardi al. J. Radioanal. Nucl. Chem. 193 (1995) 39.
- [15] Bonardi al. J. Radioanal. Nucl. Chem. 195 (1995) 227
- [16] Bonardi et al. Microchem. J. 51 (1995) 278.