Spallation Produced Radioisotopes for Nuclear Medical Application*)

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Spallation reaction opens new additional possibilities for production of a number of medical useful isotopes. In some cases all the present world demand is produced through spallation. Because of the high transmission of target materials for medium or high energy protons lower cross-sections may be more than compensated by using massive targets. The unspecific nuclear reaction as well as the radiochemical processing of such massive targets lead to several difficulties. New ways for processing of large spallation targets are required. The possibilities of modern ISOL-techniques (ISOL = Isotope Separator On-Line) for the production of medical useful radio-isotopes will be discussed in some detail. Corresponding cross-section data are reviewed and discussed in relation to physico-chemical data requirements. In detail the following radio-isotopes will be discussed: 81-Rb, 82-Sr, 123-I, 167-Tm and 211-At.


Keywords
astatine 211; iodine 123; nuclear medicine; rubidium 81; spallation; spallation fragments; strontium 82; thulium 167

1. Introduction

It is well known, that spallation reaction is the most convenient way to produce very neutron-deficient nuclei far from the line of beta-stability [1—3]. The use of intense beams of high energy protons has been also recognized and exploited for some time for the production of neutron deficient radioisotopes for practical application [4—11]. The main advantage of beams in the 0.5 to 1 GeV range lies at present in high product output through an ability to penetrate and induce nuclear reactions in target materials having thicknesses on the order of hundreds grammes per cm². The large number of target atoms can more than compensate for the generally low reaction cross sections (order of 10⁻³⁻² m² or 10 mb) compared to the cross sections often associated with lower energy reactions used in more conventional ways for isotope production.

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In interactions of high energy protons with heavy target elements three main types of nuclear reactions occur: spallation, fission and fragmentation (see Fig. 1 taken from [16]). For crosssection or yield calculations for the spallation and fragmentation methods basing on the work of Rudstam [12] are used. Rudstam observed, that the cross-section for isodisliperic nuclei grow with increasing mass-number or opacity decreases homogeneously with growing mass deficit. Consequently he proposed an empirical exponential equation, which was than modified for special applications [13—15].

Cross-sections for spallation reaction products have been discussed at the IAEA Consultants Meeting in Vienna, April 13—15, 1981 [20]. In general measurements of spallation cross-sections fall within a factor of approximately 2 of the value predicted by Rudstam's empirical systematics [12] which seems to be sufficient for the moment. Optimization of target and separation techniques are of similar importance. It is the aim of this paper to discuss the production of medical isotopes via spallation as a complex prob-
It is our suggestion, that new separation techniques could solve some of the problems and open possibilities to produce valuable spallation radioisotopes in a more sufficient way.

Today new rapid separation methods based on thermochemical and physical principles allow radioactive nuclei of almost all elements to be continuously transferred from an accelerator irradiated target into an ion beam. These techniques often referred to as target ion-source system have in the last 20 years turned on-line mass separators into the most efficient tool for production and study not only of nuclei far from stability but radioactive nuclei in general [23]. The principle of such an ISOL-system is shown in Fig. 2. For more general information see [1 - 3].

The production, transport and separation processes in such an integrated ISOL-system can be divided into the following main steps:

i. Formation of the products in interaction of an intense proton beam of around 700 MeV
ii. Diffusion of the product nuclei from the interior to the target surface
iii. Desorption from the surface
iv. Transport of the product to an ion-source
v. Ionization of the product
vi. Mass-separation of the products.

For a complete description of the processes we need to know about the following data (others than nuclear data):

- Diffusion coefficients
- Adsorption enthalpies
- Ionization behaviour.

2. High temperature diffusion

The solution of the second Fick law

$$\frac{dc}{dt} = D \frac{d^2c}{dx^2}$$

$$F(\%) = 100 - \sum_{n=0}^{\infty} \frac{1}{\sqrt{\pi^2}} \frac{d}{dx} \left( \frac{(2n+1)^2 \pi^2 D c}{D} \right)$$

THE PRINCIPLE OF ON-LINE MASS SEPARATION
describes the relation of fractional release \( F \) of a given nuclear reaction product, the diffusion coefficient \( D \) and the target-foil thickness \( d \) [24]. This equation (2) is applicable for the special sample conditions: foiles or plates where the foil-thickness \( d \) is small compared to the length and width \( (d \ll a \approx b) \) and with homogeneous distribution of the diffusing particles throughout the matrix. The experimental value \( F \) can be transformed into diffusion coefficients using the tables of Zimen [25]. The activation energy \( E_A \) for the diffusion process can be obtained from an Arrhenius plot according eqn. (3).

\[
D = D_0 \exp \left( \frac{E_A}{RT} \right)
\]

where \( R \) is the gas-constant.

Systematical studies have been performed in the following manner: target foils of refractory metals were labelled homogeneously with radio tracers by irradiating them with 660 MeV protons. Samples of the irradiated foils were annealed in high vacuum at high temperatures. The samples were analyzed before and after heating by means of gamma-spectroscopy for determination of the fractional release of spallation reaction products. The results are published for the following target elements: Ti [26, 33], Zr [20, 27], Nb [28], Mo [29], Hf [30], Ta [31], W [32], Re [33], Ir [33], Th [33]. For illustration a few results are presented in Figs. 3–6.

The diffusion release studies may be summarized in the following way:

i. In a given host metal of the IV B, V B or VI B group of the periodic table the diffusion coefficients for trace elements grow in the following sequence:

\[
D_{\text{IA}} < D_{\text{IIA}} < D_{\text{IIIA}}
\]

For example Y diffuses faster than Sr, which is faster than Rb (see Fig. 3). The reason for this sequence is the decreasing radius of the diffusing particles.

ii. The diffusion coefficient for a given trace element decreases for different host metals in the following sequence:

\[
D_{\text{IVB}} < D_{\text{VB}} < D_{\text{VIB}}
\]
1. Diffusion coefficients of spallation reaction products in polycrystalline Ta (lower part) in comparison with the atomic and ionic radii of the diffusing particles (upper part). Ta-foils of 83 µm thickness were irradiated with 660 MeV protons. The diffusion coefficients were determined for the indicated elements simultaneously from release studies, the annealing temperature was 2750 K, annealing time 300 s. No significant difference in the diffusion behaviour of the rare earth elements has been observed, they all diffuse faster than Sr and Ba.

For example, Y diffuses fastest in Zr and in Nb faster than in Mo. Compare Figs. 3 and 5. The reason for this effect is the growing lattice density of the host metals.

iii. In a given host metal the elements of one group of the periodic table diffuse according to growing atomic masses: Sr diffuses faster than Ba in Ta (see Fig. 6).

iv. From the systematical study one can evaluate, that all rare earth elements diffuse in metal matrices as $M^{2+}$-particles, the II A-elements as $M^{3+}$, the alkaline earth elements as $M^+$ and the noble gases as neutrals (see Fig. 6 and Fig. 3).

In general one can conclude that solid phase diffusion processes very often are fast in order to use refractory metals as high temperature targets. A large number of other refractory materials such as metalloids, borides, carbides as well as molten metals and alloys has been investigated to develop suitable targetsystems for ISOLDE (review papers see [61, 60, 44]).

3. Surface effects

In our release studies we found that in Ta the diffusion of the rare earth elements is more rapid than of Ba followed by Cs. For the desorption from the surface the sequence is reverse with Cs being fastest followed by Ba, lanthanides and Hf. Thus in a Ta-powder target the rare earth elements will be delayed compared to Cs and Ba due to the large total surface. Consequently from a Ta-foil target with optimized foil thickness the rare earth elements will be released more rapidly because the surface is diminished. The surface adsorption behaviour or in other terms the adsorption enthalpies play an important role in the release of nuclear reaction products from a target as well as for the transport of the products in the gas phase.

Desorption studies for rare earth elements have been performed in a similar way as the release studies [34]. Fig. 7 illustrates the possibilities to use differences in the adsorption enthalpies for thermochromatographic separations.

A systematical study of the adsorption of trace metals at metallic surfaces has recently been published by Roesch.
and Eichler [35]. The wide variation of the surface material, the composition of the used carrier gases, variation of the gas pressure and temperature opens the wide range of separation techniques starting from gaschromatography over gasthermochromatography and thermochromatography to vacuum thermochromatography.

4. Ionization

A selective ionization is a modern radiochemical separation technique. For the production of radioisotopes via spallation the following ion-source principles are suitable to be operated in an integrated target ion-source system:

i. Positive surface ionization ion-source with Ta-ionizer kept at 1300 K for selective ionization of the alkaline elements K, Rb, Cs and Fr [36]. The ionization efficiency is of the order of 90%.

ii. Positive surface ionization ion-source with W-ionizer (or Re) at high temperatures (2700 ... 3000 K) for ionizing the lanthanoids, In, Sn, Ge, Al, Ca, Sr, Ba, Li, Na and Ti. The ionization efficiency varies from a few % up to 80% [36, 37, 38].

iii. Negative surface ionization ion-source with LaB6-ionizer for selective ionization of Cl, Br, I and At. Ionization efficiencies of up to 40% have been obtained [36, 39].

iv. The plasma discharge ion-source with cooled line at 300 K and ionization temperatures around 1300 K is used for selective ionization of noble gases. Efficiencies achieved for He, Ar, Kr, Xe and Rn are 0.5%, 2%, 5%, 15%, 30% and 40% respectively [36]. A similar source with a cooled line kept at 700 K is used to ionize the volatile elements of the group IIIB Zn, Cd and Hg with efficiencies of 10 ... 60% [36].

v. A high temperature version of the plasma discharge ion-source (line at 220 K) is intended to ionize the less volatile elements from group IIB, III, IV and V. This ion-source can be used in conjunction with CF3 to form volatile fluorides of the mentioned elements [36].

5. Chemical selectivity

As mentioned the product mixture of a massive target irradiated with protons with $E_p = 0.5$ GeV is rather complex. The difficulties to handle such targets and product mixtures can be compared with the fission product mixture in isotope production plants only. Nevertheless chemical selectivity can be obtained using the above mentioned techniques by one or several of the following means:

i. Selective release from the target (Sr from Zr [40]).

ii. Selective adsorption of unwanted species at suitable surfaces (selective release of Yb from Ta-powder [33]) or selective transport of the required product (39Fe from Ni [41]).

iii. Selective ionization.

iv. Mass-separation of molecular side bands (iodine as AI+ particles [36]). Isobaric separations using differences in the adsorption enthalpies [42].

6. ISOL-technique for production of medical isotopes via spallation

In this chapter we like to illustrate the possibilities of the discussed techniques for the production of some of the most important medical radioisotopes via spallation route.

6.1. 81-Rb

Because of the short half-life there is no much sense to produce 81-Rb via spallation, but the isotope separator opens the way to produce a new type of 81-Rb-81m-Kr-generator. 81-Rb is best produced at ISOLDE using a Nb-powder target with yields of 3.8 - 10^10 atoms per second for 1 pA proton beam current (Figs. 8, 9 [44]). This production rate corresponds to 1.0 MBq/µAs (or 20 mCi in 7.7 min collection time for 1 pA proton beam current). By implanting the 81-Rb+-ions into mylar foils (or other plastic material like polyethylene etc.) an implantation type of 81-Rb-81m-Kr-generator is obtained. The 81m-Kr can be eluted nearly quantitatively by blowing air over the implanted Rb-source as well as by elution with isotonic saline solution suitable for direct infusion [43]. No 81m-Kr-elution will be achieved by using metallic foils as implantation backing. The 81-Rb break through is as low as in conventional 81m-Kr-generator systems. The implantation type generator could be realized of extremely small size since for an implantation density of 10^14 atoms/cm^2 less than 0.5 cm^2 foil area is required to make a 800 MBq (20 mCi) generator.
6.2. 82-Sr

Recently the complete problems about 82-Sr-82-Rb-generator have been published [45]. The cross-section for the formation of 82-Sr in Mo irradiated with 800 MeV protons is \((2.3 \pm 0.1) \cdot 10^{-23} \text{m}^2\) (23 mb) and for 85-Sr \((4.8 \pm 0.7) \cdot 10^{-22} \text{m}^2\) (43 mb) [46] (Tab. 1). The radiochemical procedure has been modified several times [47, 48, 49]. High dose rates of the irradiated targets \((10^7 \text{R/h} \text{in} 1 \text{cm distance})\) [48], large amounts of process solutions and unsatisfied purity of the final 82-Sr-preparation were the main problems in the wet radiochemical process [48, 49]. The isotopic byproduct 85-Sr remains still a serious problem. At EOB an average isotopic ratio 82/85-Sr of only 1.0 to 1.2 is obtained depending on irradiation time. During the clinical use of the generator the 85-Sr grows up to an excess of a few 100% compared to the 82-Sr activity. It was already proposed to solve this problem by using an isotope separator [48].

We recommend to use additional ISOL-target technique. From a 50 g/cm² Zr-foil target (foil-thickness up to 0.5 mm) the Sr is released rather selective at 1750 K (Fig. 3). A high temperature surface ionization ion-source could give an ionization yield of better than 50%. At the collector of an isotope separator pure 82-Sr and 85-Sr could be collected. The cross-contamination for routine practical use is almost less than 0.1% in this mass region. Recent studies at CERN demonstrated, that a Zr-foil target could withstand a well focussed proton beam of 100 µA [50]. It is expected to obtain 10⁵ atoms 82-Sr per 1 µAs or 10¹⁴ Bg/1000 µAh (10 h, 100 µA). The advantage of this technology is first the high isotopic purity; secondly practically no liquid waste is produced. The disadvantage is that no other product as 77-Br or 88-Y are available simultaneously from the same target.

6.3. 123-I

Special interest was directed to the production of radioxenon via spallation [18, 20, 51]. It has been demonstrated, that by optimized choice of irradiation and decay periods rather pure 123-I could be obtained. Also important was the possibility to produce 125-I and 127-Xe simultaneously. From a 175 g CsCl-target after 4 h irradiation and 4 h grow up period for 123-I via 123-Xe decay 850 mCi 123-I with 0.4% 125-I contamination is obtained [52]. The 127-Xe produced via spallation at TRIUMF from 0.8 cm thick CsCl-pellet contains 15% of 129m-Xe and 12% of 131m-Xe [11]. Cross-section data are summarized in Tab. 1.
The 125-I contamination in spallation produced 123-I preparations presently is higher than those for the (p, 5n)-production route. One possibility to solve this problem is the application of ISOL-technique. From a molten La-target kept at 1770 K Cs is released fast and transported to a surface ionization ion source [57, 36]. This combination is highly selective for Cs. The total efficiency is of the order of 80...90%. The Cs-yield curve is shown in Fig. 10 [44]. The yield as well as the activity of the corresponding products are as follows:

<table>
<thead>
<tr>
<th>Cs-isotope</th>
<th>yield [atoms/μA]</th>
<th>product</th>
<th>yield [Bq/sl]</th>
<th>activity [mCi/l]</th>
</tr>
</thead>
<tbody>
<tr>
<td>122-Cs</td>
<td>5.0 \times 10^6</td>
<td>123-I</td>
<td>7.3 \times 10^4</td>
<td>71</td>
</tr>
<tr>
<td>123-Cs</td>
<td>1.1 \times 10^4</td>
<td>125-I</td>
<td>1.4 \times 10^4</td>
<td>1.5</td>
</tr>
<tr>
<td>127-Cs</td>
<td>1.3 \times 10^3</td>
<td>127-Xe</td>
<td>2.9 \times 10^2</td>
<td>2.8</td>
</tr>
</tbody>
</table>

Note that these activities are obtained for 1 μA proton beam intensity only. The molten La-target of the given design could withstand a beam current of 50 μA [50]. From this figures one can easy estimate: the system is able to produce multi-Ci quantities of 123-I and allmost Ci-quantities of 125-I and 127-Xe simultaneously within a few hours. The isotopic impurities are determined from the mass-resolution of the isotope separator. The 125-I contamination in the final 123-I preparation will be of the order of 10⁻³%.

6.4. 167-Tm

The isotope 167-Tm is suitable for scintigraphic in vivo studies [59]. The best way to produce 167-Tm is via spallation reaction [58, 59]. The most elegant way would be the application of ISOL-technique. As already mentioned a Ta-powder target give highly selective Yb-isotopes [60], the other rare earth elements are discriminated by surface effects. A Ta-foil target connected to the same ion-source produces isobars of the rare earth elements [33] (Fig. 11).
The production rate for 167-Yb is $1.1 \times 10^{10}$ atoms/μA proton beam intensity. This gives a practical production yield for 167-Tm of approximately 1 mCi/μA h. The Ta-foil target of the given design could be irradiated with 100 μA proton beam current [50].

6.5. 211-At

In similarity to 123-I the medical important 211-At (radionuclide therapy) can be produced with satisfied isotopic purity via the 211-Rn [62]. The cross-sections for the formation of 211-Rn as well as for 211-At from uranium are significant smaller than for thorium as target [65] (Tab. 1). ISOL-technique can be used to produce 211-At via the mother-nuclide in a very elegant way. ThO₂ or ThC₂ targets [61] are connected to a plasma discharge ion source with cold line [36]. Practical yield of nearly $10^{10}$ 211-At atoms per second and μA proton beam intensity have been obtained [61, 36].

7. Conclusions

i. Spallation reaction is a very suitable route for production of some medical radioisotopes. Because of the limited number of corresponding accelerators as well as because of the priority of experiments at such facilities a regular supply of short-lived isotopes like 81-Rb or 123-I produced in this way seems to be unrealistical. For long-lived isotopes however a few production runs per year will be sufficient to organize a regular supply.

ii. Stable impurities in the target material, isotopic impurities due to the lack of reaction selectivity, waste problems and others are the main complicating factors in radiochemical processing of large spallation targets. ISOL-techniques open new ways in spallation radioisotope production and application. Isotope separation technique itself is also useful to be applied in "classical" RI-production to improve the isotopic purity. iii. Modern physico-chemical data are of same relevance as nuclear data in radioisotope production. By knowing data for release, surface adsorption and ionization ISOL-technique is a suitable tool to determine simultaneously cross-sections.

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Beyer et al. : Spallation Produced Radioisotopes
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1. Introduction

The nuclear structure of light nuclei have been shown as one of the important tools for extracting some static properties of these nuclei. The nuclear shell model has been extensively used in an attempt to explain certain features of light nuclei. The shell model calculations lead to the result that both of the L-S and J-J coupling schemes do not give an adequate explanation of the relevant experimental data. The intermediate coupling in the p-shell for all nuclei has been extensively calculated and have been shown that the energies of almost all known low-lying levels are related to their applications, Los Alamos, Aug. 18 – 22, 1986.

Keywords
beryllium 9; cluster model; facldev equations; generator-coordinate method; lippmann-schwinger equation; nuclear models; nuclear structure; three-body problem