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Radiochemical methods in production of radionuclides at a cyclotron

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Abstract
Extensive use of radiochemical methods has been made over decades in radionuclide development work at different cyclotrons at the Forschungszentrum Jülich. In this article, a brief overview of the methods used in investigations on nuclear data, high-current targetry, chemical processing, etc. is given, with some typical examples in each area. The large and clinical scale productions of some standard and non-standard positron emitters, respectively, using the proton and deuteron beams at a small cyclotron are elaborated. Furthermore, some ongoing development work on two therapeutic radionuclides of great current interest, namely ^{193m}Pt and ^{211}At, using the α-particle beam at the new medium-sized cyclotron, is described.

Keywords Radiochemical methods · Nuclear data · High current targetry and chemical processing · Standard and non-standard positron emitters · Therapeutic radionuclides

Introduction

Radiochemical methods play an important role in production of radionuclides at a cyclotron. At the Forschungszentrum Jülich (FZJ) many of those methods have been applied over decades on a very broad basis (for periodic reviews cf. [1–3]), i.e. in nuclear data measurements, development of high-current targetry, chemical processing of the irradiated target material, quality control of the radioactive product, and recovery of the target material, especially if it is isotopically enriched. All those areas of investigation are rather challenging and demand skilful applications of radioanalytical techniques. Most of the older works were performed using four cyclotrons (JULIC, CV28, BC1710 and PETtrace) at FZJ, but the present emphasis is on a newly installed Cyclone 30XP cyclotron (supplied by IBA, Belgium).

In this article we give an overview of radiochemical techniques used in various areas of investigations related to medical radionuclide development work, then describe in some detail the production of several standard and novel radionuclides at the FZJ, and finally outline our recent efforts to produce the important α-emitting radionuclide ^{211}At for clinical application.

Overview of radiochemical techniques used in different areas of work

Nuclear data studies

Nuclear reaction cross sections are important for optimisation of production routes of radionuclides, i.e. to maximise the yield of the desired radionuclide and to minimise the level of radioactive impurities. The measurement of cross sections of charged-particle induced reactions at a cyclotron via the stacked-sample technique demands preparation of thin solid samples for irradiations. Over the last two decades extensive cross-section measurements have been done in a large number of laboratories, but mostly using target elements of natural isotopic composition, generally available in the form of thin foils. The results obtained, however, have been only of limited use because the levels of impurities could not be accurately estimated. For obtaining more suitable data, measurements on isotopically enriched targets were necessary. They involved preparation of thin targets using different physico-chemical methods. In this direction extensive studies have been performed in our laboratory (for detailed references [cf. 3, 4]). Electrolytic deposition was found to be an effective method. Using a small-volume

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electrolytic cell with a rotating electrode [5] and different electrolytic solutions, thin solid samples of rather expensive, highly enriched target isotopes (e.g. ^{18}O, ^{50}Cr, ^{54}Fe, ^{58}Ni, ^{61}Ni, ^{62}Ni, ^{64}Ni, ^{68}Zn, ^{70}Zn, ^{70}Ge, ^{74}Se, ^{76}Se, ^{77}Se, ^{120}Te, ^{122}Te, ^{123}Te, ^{124}Te, ^{125}Te, ^{126}Te, ^{192}Os, etc.) were prepared to measure cross sections of proton, deuteron, ^{3}He- and α-particle induced reactions. The major emphasis was on low-energy reactions up to 20 MeV to produce a large number of non-standard positron emitters (e.g. ^{51}Mn, ^{55}Co, ^{61}Cu, ^{64}Cu, ^{86}Y, ^{120}I, ^{124}I, etc.) at a small medical cyclotron. But higher energy range up to 100 MeV was also investigated to determine suitable conditions to produce other positron emitters (e.g. ^{73}Se, ^{75}Br, ^{77}Kr, ^{83}Sr, ^{124}I, etc.) as well as several therapeutic radionuclides (e.g. ^{67}Cu, ^{77}Br, ^{193m}Pt, etc.). Another commonly used and relatively simple technique, also employed when handling enriched material, was sedimentation, and the products investigated included ^{72}As, ^{86}Y, ^{94m}Tc and ^{99m}Tc. Though the spread of the material on the backing was occasionally not uniform, through proper care good uniformity could be achieved. As an example, we describe a recent new measurement of the excitation function of the ^{86}Sr(p,n)^{86}Y reaction carried out under an international cooperation [6]. The enriched material ^{86}SrCO$_3$ was sedimented on an Al-backing under very well optimised conditions. Thereafter each sample was examined under a microscope, and only the homogeneous and mechanically stable samples were selected for stack irradiations. The cross-section results obtained are shown in Fig. 1 and are quite different from the older literature data which were rather discrepant. The new data are reproduced well by the nuclear model calculation. Furthermore, the calculated integral yield of ^{86}Y from the new excitation function is very close to the experimentally reported batch yields of this radionuclide. The discrepancy in the data is thus solved by a careful new measurement.

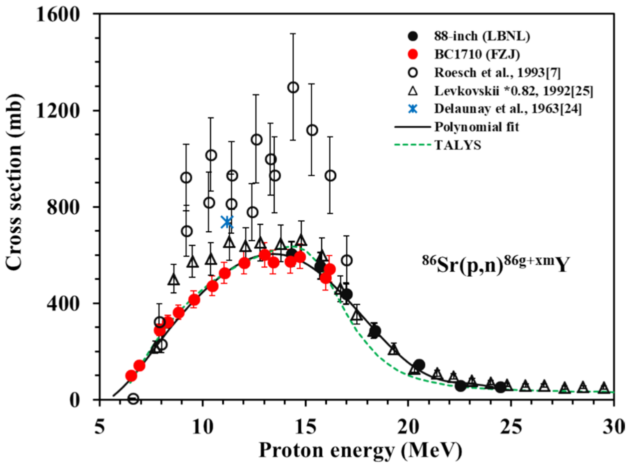

Fig. 1 Excitation function for the formation of the radionuclide ^{86}Y in proton irradiation of an enriched ^{86}Sr target (after [Ref. 6], where full references to discrepant literature data are also given)

It is worth pointing out that the use of well-prepared thin samples of enriched target materials in stack irradiations generally led to rather clean γ-ray spectra. Therefore, in most of the investigations discussed above, the radioactivity of the desired product could be accurately determined via standard non-destructive high-resolution γ-ray spectroscopy. In a few special cases, however, use of somewhat versatile radiochemical techniques was necessary to characterize the product. We give a few examples: (i) While investigating the ^{64}Ni(p,n)^{64}Cu reaction, due to the occurrence of only a single γ-ray of energy 1346 keV of weak intensity (0.54%), the product ^{64}Cu was counted in a gas flow beta proportional counter (to measure the positrons) as well as via γγ-coincidence counting (to measure the annihilation photons); (ii) While investigating the ^{68}Zn(p,2p)^{67}Cu reaction at energies > 50 MeV, besides ^{67}Cu, a strong matrix activity due to ^{67}Ga formed via the ^{68}Zn(p,2n)-reaction also occurred. Since the half-lives and γ-ray energies of both ^{67}Ga and ^{67}Cu are similar, we resorted to a radiochemical separation of radiocopper prior to high-resolution γ-ray spectroscopy; (iii) While studying the production of ^{103}Pd via ^{103}Rh(p,n)^{103}Pd and ^{102}Ru(^{3}He,2n)^{103}Pd reactions, we did not rely on standard γ-ray spectroscopy because of the very weak intensity of the 357 keV γ-ray (0.0221%) emitted by ^{103}Pd. Instead, we performed X-ray spectroscopy utilizing a Si(Li) and a low-energy pure Ge detector (with a thin Be window); (iv) In studies on the formation of ^{193m}Pt via the ^{192}Os(α,3n)-reaction, a radiochemical separation of the radioplatinum was performed to obtain it free from osmium and iridium isotopes. Thereafter, the radioplatinum was subjected to X-ray spectroscopy, as in the case of ^{103}Pd mentioned above. These examples should demonstrate the versatility of the use of radiochemical techniques in the determination of nuclear data for cyclotron production of radionuclides at FZJ.

It may be mentioned that in recent years, besides our laboratory, several other groups have also initiated cross-section measurements using thin solid targets of enriched materials (e.g. Nantes, Legnaro, Saitama, Seoul, Madison, etc.).

To date, no cross-section measurements have been done using liquid targets. For measurements on gas targets, however, a cryogenic technique was developed to handle highly-enriched gases (^{18}O$_2$, ^{38}Ar, ^{78}Kr, ^{82}Kr, ^{83}Kr, ^{124}Xe, etc.) and transfer them to thin-walled cylinders for use as thin targets (for original references [cf. 2]). After the irradiation the enriched gas was cryogenically recovered and the produced non-gaseous radionuclide rinsed/washed out for further use.

Development of high-current targetry

The physico-chemical aspect of high-current targetry consists of developing heat-resistant thick targets, mostly in solid form. This often involves the preparation of a relatively thick layer (up to a few hundred µm) of the target material via electrolytic deposition on a metal backing, using specially designed large cells, and performing irradiations with slanting charged-particle beams. A typical example is the deposition of enriched ^{64}Ni on a gold foil to produce ^{64}Cu [cf. 7], enriched ^{68}Ge on a Pt disc to produce ^{68}Ga [cf. 8] and enriched ^{70}Zn on a Au foil to produce ^{67}Cu [cf. 9, 10]. In many other cases, suitably prepared alloys or intermetallic compounds are also applied (e.g. Cu_3As alloy for production of ^{77}Br in α-particle induced reaction on ^{75}As [cf. 2] or NiSe alloy for production of radiobromine in proton induced reaction on ^{nat}Se [11]). Occasionally, the target material oxide is spread on another metal, melted or sintered, and then used as an irradiation target (e.g. $^{120}TeO_2$ and $^{124}TeO_2$ on Pt to produce ^{120}I and ^{124}I, respectively [cf. 12]). Spark plasma sintering was used for preparation of ^{70}ZnO targets for ^{67}Cu production [cf. 13]. In special cases, high-pressure gas targetry is also employed, e.g. for ^{82m}Rb production via the ^{82}Kr(p,n)-reaction, ^{75}Br production via the ^{78}Kr(p,α)-reaction or ^{123}I production via the ^{124}Xe(p,x)-reaction [cf. 2, 3].

Besides the solid and gas targetry mentioned above, an elegant and very effective method has been developed for worldwide application for production of ^{18}F via a pressurised $H_2{}^{18}O$ liquid target [cf. 2]. Furthermore, over the last few years, a new targetry concept has been developed in many laboratories to produce non-standard positron emitters in small quantities at medical cyclotrons. It involves irradiation of a metal salt dissolved in a suitable solvent ("solution target"). The radionuclides produced so far via the (p,n)-reaction include ^{44g}Sc, ^{64}Cu, ^{68}Ga, ^{89}Zr, etc. (for typical reviews [cf. 14, 15]). As expected, chemistry plays a very important role here, both with regard to the choice of the chemical compound for use as target material as well as in the chemical purification of the desired radionuclide formed in the irradiation.

Chemical processing of the irradiated target material

This is a crucial step in the development of a production route of a radionuclide, whereby the desired product should be obtained in a pure form and the target material should be recovered for reuse. Many laboratories have been working in this direction. As mentioned above, for production of non-standard positron emitters and novel therapeutic radionuclides at an accelerator, mostly solid targets are utilized. In those cases both dry and wet chemical separation methods have been developed [cf. 2, 3]. The dry method involves distillation or thermochromatography. The best example of the dry distillation technique is furnished by separation of the increasingly important radioiodines, especially ^{120g}I and ^{124}I, from irradiated $^{120}TeO_2$ and $^{124}TeO_2$ targets, respectively, at 755 °C [cf. 12]. Radioiodine is collected almost quantitatively in iodide form and the target is regenerated (without much loss) for the next production run. Thermochromatography, on the other hand, involves the formation of a chemical species of the radioactive product, enabling its separation from the irradiated target. However, due to insufficient vapor pressure, the activity condenses in the cooler section of the thermochromatographic tube, from which it is typically removed by rinsing. The method has been successfully used in our laboratory in the separation of ^{73}Se, ^{75}Br, ^{76}Br, ^{77}Br, ^{94m}Tc, etc. (for review [cf. 2, 3]).

Wet chemical processing of the irradiated solid is more commonly applied than the dry method. In general, one step solvent extraction and ion-exchange techniques are extensively used in the separation of novel positron emitters produced via low-energy reactions. Occasionally a radiolytic method is developed, for example for separation of ^{55}Co formed via the ^{58}Ni(p,α)-process [16] and ^{86}Y produced through the ^{86}Sr(p,n)-reaction [17]. In a few cases, a prior concentration of the radionuclide is carried out via co-precipitation or adsorption, followed by its specific separation by one of the above-mentioned methods. For example, ^{86}Y formed through the ^{86}Sr(p,n)-reaction is first co-precipitated with $La(OH)_3$, and then purified via ion-exchange chromatography [18, 19].

In recent years, extensive efforts have been devoted to utilize both ion-exchange and solvent extraction techniques more effectively [cf. 20]. Thus, a large number of new ion-exchange resins have been commercially developed and conditions for separation have been improved. With regard to solvent extraction, new chelating agents have been introduced [cf. 21]. These novel developments have led to higher separation yields with less extraction cycles.

In contrast to production of novel radionuclides using low-energy nuclear reactions (mostly positron emitters), where a one-step chemical separation may be adequate, the production of radionuclides using an intermediate energy reaction (positron emitters or therapeutic radionuclides) demands a combination of several separation techniques. Typical examples are the production of ^{67}Cu, ^{72}Se, ^{117m}Sn, ^{225}Ac, etc. Extensive work in this direction is ongoing in our institute as well as in several other laboratories.

Quality control of the product

The final step in the development of a medical radionuclide at a cyclotron consists of quality control of the obtained product, and again here the role of radiochemistry is very important. We invariably consider the following four aspects [cf. 3]:

- Radionuclidic purity. It is achieved via the choice of a suitable nuclear process and energy range, combined with a clean chemical separation. It is analysed by γ-ray spectroscopy.
- Radiochemical purity. It implies that the separated product exists in the form of one major chemical species. It is tested by radio-chromatographic methods, such as high performance liquid chromatography (HPLC), ion-exchange chromatography, etc.
- Chemical purity. It stipulates the absence of non-radioactive impurities which are analysed by one or more of the standard techniques like ultraviolet (UV) or infrared (IR) detection, inductively coupled plasma mass spectroscopy (ICP-MS), etc.
- Specific activity. It is defined as the radioactivity per unit mass of the product. For estimating the specific activity of a product, generally the radioactivity of the whole batch is measured in an ionisation chamber and the mass is determined after the decay of the radionuclide via a sensitive detection method, such as UV, IR, refractive index or conductivity measurement.

Production of radionuclides at FZJ

Large scale production of standard PET-radionuclides

The production of the short-lived standard positron emitters, namely ^{11}C ($T_{1/2}=20.4$ min), ^{15}O ($T_{1/2}=2.0$ min) and ^{18}F ($T_{1/2}=110$ min), is routinely carried out for patient care diagnostic investigations via positron emission tomography (PET). The nuclear routes used are ^{14}N(p,α)^{11}C, ^{14}N(d,n)^{15}O and ^{18}O(p,n)^{18}F, respectively. The two old small cyclotrons (JSW BC 1710 and PETtrace GE Health Care [General Electric]) are adequate for their production and the technology has been standardised [cf. 2, 3]. For ^{11}C and ^{15}O production, a high-pressure batch target filled with N_2 gas is employed. For ^{11}C production, the irradiation is done with protons and for ^{15}O with deuterons. For ^{18}F production via the ^{18}O(p,n)^{18}F reaction, on the other hand, a pressurised liquid target filled with $H_2{}^{18}O$ is used. All three positron emitters are made available in the desired chemical forms in 150–200 GBq quantities.

Clinical scale production of non-standard PET radionuclides

With growing significance of PET in diagnostic nuclear medicine, the need for novel positron emitters, also termed as non-standard positron emitters, has been increasing, especially for studying slow metabolic processes and for quantification of targeted therapy. Over the years about 20 non-standard positron emitters have evolved and the subject has been treated in several review articles [cf. 22, 23]. The common route for production of each radionuclide is the low-energy (p,n)-reaction on an enriched target isotope. In a few cases, other low-energy reactions, such as (d,n) and (p,α) have also been employed. Four novel positron emitters, namely ^{64}Cu, ^{86}Y, ^{89}Zr and ^{124}I, have reached the stage of clinical scale production. We discuss briefly the production of ^{64}Cu, ^{86}Y and ^{124}I, which were mainly developed at FZJ.

The radionuclide **^{64}Cu** emits low-energy positrons, has no disturbing γ-ray, has a suitable half-life of 12.7 h and forms interesting stable coordination compounds. It is thus very suitable for studying slow metabolic processes. It also forms a theranostic pair with the β^--emitting therapeutic radionuclide ^{67}Cu ($T_{1/2}=2.6$ d) [cf. 24]. For its production, a large number of reactions have been studied [cf. 25], but the production route ^{64}Ni(p,n)^{64}Cu, originally suggested by us [7], was most successfully utilized. It involves the use of the rather expensive highly enriched target material electroplated on a gold surface. The separation of $^{64}CuCl_2$ is done via anion-exchange chromatography and the technology is well developed for production of > 99% pure ^{64}Cu in batches of about 40 GBq and recovery of the enriched target material. Based on that technology, commercial scale production of this radionuclide is being developed by several companies and institutions.

The radionuclide **^{86}Y** ($T_{1/2}=14.7$ h) is a positron emitting partner of the β^--emitting radionuclide ^{90}Y ($T_{1/2}=2.7$ d) in theranostic studies [cf. 24]. For its production, several routes have been investigated [cf. 26], However, the ^{86}Sr(p,n)-reaction on an enriched $^{86}SrCO_3$ target originally developed at FZJ [18] was found to be the best. There has been some discrepancy in the cross-section data but as described above, this has recently been resolved through a more accurate measurement [6]. The chemical separation is done by coprecipitation of ^{86}Y with $La(OH)_3$, followed by ion-exchange isolation of radioyttrium from the bulk lanthanum [18, 19]. An alternative electrolytic separation method has also been developed [17, 27, 28]. The technology for clinical scale production of ^{86}Y is fairly well advanced and this radionuclide is commonly obtained in batch yields of about 2 GBq. It is now being commercialised.

The radionuclide **^{124}I** ($T_{1/2}=4.18$ d) is somewhat longer lived, and so the radiation dose from this radionuclide is higher compared to standard PET radionuclides. It is used in tumour targeting and for radiation dosimetry of thyroid treatment. Furthermore, it is the diagnostic partner of the β^--emitting ^{131}I ($T_{1/2}=8.0$ d) in theranostic studies [cf. 24]. For its production, a large number of reactions have been studied [cf. 29] but the route ^{124}Te(p,n)^{124}I on a highly enriched target suggested by us [30] proved to be the best. As mentioned above, it commonly involves irradiation of a $^{124}TeO_2$ target and removal of radioiodine by a distillation process, whereby the irradiated enriched target is regenerated for reuse [cf. 12]. The yield of ^{124}I via the $^{124}Te(p,n)$-reaction is rather low, with batch yields amounting to about 0.5 GBq, so the product is somewhat expensive. However, it is of 99.9% radionuclidic purity [cf. 12]. Due to increasing demands for this radionuclide, intensified efforts are underway in several laboratories to produce it in larger quantities.

Development of some promising PET and SPECT radionuclides

Our efforts towards development of some further potentially useful diagnostic radionuclides are continuing and the present emphasis is on ^{45}Ti ($T_{1/2}=3.1$ h), ^{72}As ($T_{1/2}=1.1$ d) and ^{203}Pb ($T_{1/2}=51.9$ h), the first two for PET studies and the latter for investigations using single-photon emission computed tomography (SPECT). With regard to ^{72}As, experimental and theoretical studies on the $^{72}Ge(p,xn)^{71,72}As$ reactions using an enriched ^{72}Ge target have been completed [31], and development work on targetry and chemical separation is continuing. Similarly, for production of ^{203}Pb, excitation function measurement of the $^{205}Tl(p,3n)^{203}Pb$ reaction on a highly-enriched target material, electrolytic preparation of the target for high-current irradiations, and an extraction chromatographic separation method for the desired product, are reaching completion. In this article we limit ourselves to a description of investigations on the radionuclide ^{45}Ti, which are more complete.

Titanium (IV) complexes, especially titanocene complexes, exhibit high antitumour-activity. The radionuclide **^{45}Ti** is thus of potential interest in tumour research. Its production via the $^{45}Sc(p,n)^{45}Ti$ reaction was reported rather early [32]. Later, the chemical separation was done using cation-exchange chromatography or solvent extraction, and the product was obtained with good radionuclidic purity [33–38]. We measured accurately the excitation functions of the $^{45}Sc(p,xn)^{44,45}Ti$ reactions up to 30 MeV and showed that the suitable energy range to produce ^{45}Ti is $E_p=12\rightarrow7$ MeV [39]. Furthermore, for tracer experiments, a pellet of Sc_2O_3 was irradiated and the separation of ^{45}Ti was carried out via two methods: (a) thermochromatography, (b) ion chromatography. The apparatus developed for thermochromatography [40] is shown in Fig. 2. The irradiated target was placed on a ceramic support and introduced in an oven. A flow of Cl_2 gas was started and the oven temperature raised to 900 °C. The radionuclide ^{45}Ti was removed from the target as $[^{45}Ti]TiCl_4$ and collected in a cooling bath at −78 °C. The recovery of ^{45}Ti amounted to 76 ± 5% and the radionuclidic purity was determined as > 99%. After trapping, the $[^{45}Ti]TiCl_4$ could be directly used for ^{45}Ti-radiolabelling at the no-carrier-added (nca) level.

The separation via ion chromatography [41] is illustrated in Fig. 3. The irradiated target is dissolved in 10 M HCl and the solution is loaded on a column filled with ZR-Resin™ (in hydroxamate form). The column is eluted at first with 5 mL of 10 M HCl and then with 5 mL of H_2O, whereby Sc^{3+} is removed from the column (recovery of the target material). Thereafter the column is flushed with 2.5 mL of 0.1 M oxalic acid (at pH = 2.8) whereby radioactive $^{45}Ti^{4+}$ is eluted. Under optimised conditions, this method enables ^{45}Ti-recovery of 61 ± 8% within 7 min. The radionuclidic purity is > 99% and the radiochemical purity amounts to > 98% Ti^{4+}. The resulting ^{45}Ti-solution could be directly used for complexation with model chelators.

Both dry and wet chemical separations are completed within 15 min. In typical experiments with a beam current of 2 μA and irradiation time of 30 min, the ^{45}Ti production batch yield achieved is 0.5 GBq and the level of the chemical impurity Sc amounts to 3.0 ± 1.8 μg/mL of the radioactive solution. Thus, the quantity and quality of the ^{45}Ti produced are adequate for preparing radioactive tracers for preclinical

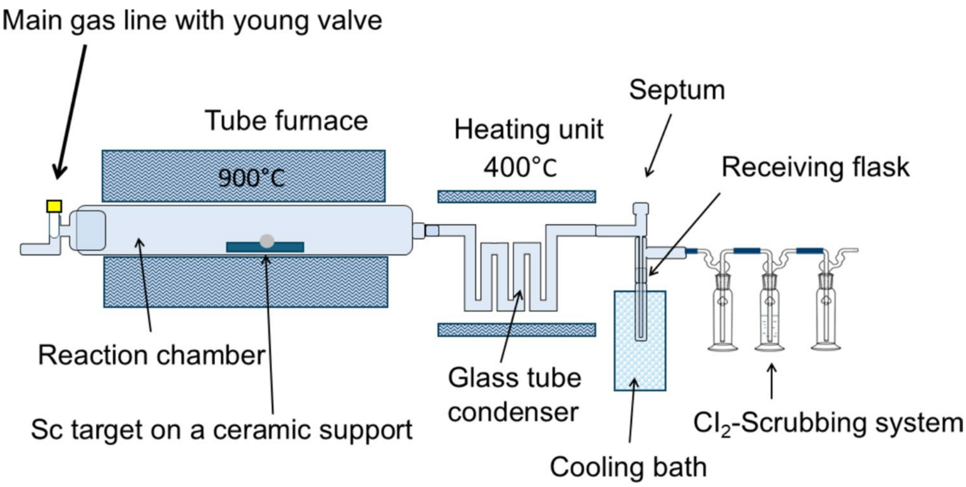

Fig. 2 Schematic representation of the dry-distillation separation setup (after [Ref. 40])

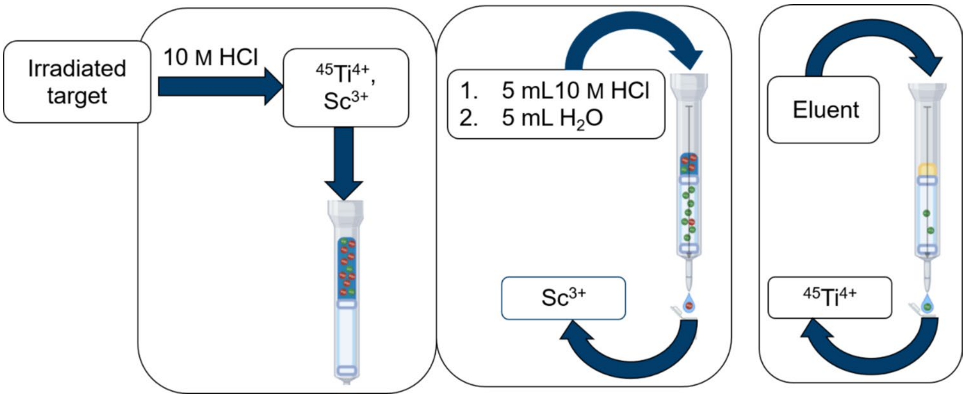

Fig. 3 Scheme of the wet-chemical ^{45}Ti/Sc separation method (after [Ref. 41])

studies. Efforts are underway to upgrade the technology to clinical scale production of this radionuclide.

Development of therapeutic radionuclides using the α-particle beam

Among the therapeutic radionuclides, the present emphasis at FZJ is on ^{193m}Pt and ^{211}At. The radionuclide ^{193m}Pt ($T_{1/2} = 4.3$ d) decays via a highly converted isomeric transition to the ground state, whereby up to 33 Auger electrons are emitted. This radionuclide is therefore of great interest in Auger therapy, provided a high-specific activity product could be made available. This is not possible via the generally used ^{192}Pt(n,γ)^{193m}Pt process. In our laboratory, the excitation function of the ^{192}Os(α,3n)^{193m}Pt reaction was measured up to 38 MeV using a highly enriched target [42]. For small scale production, highly enriched ^{192}Os was electroplated on a Ni foil and, after irradiation, radioplatinum was separated via distillation and solvent extraction techniques [43]. The batch yield of ^{193m}Pt was about 10 MBq [43]. Presently, the production procedure is being upgraded using the 30 MeV α-particle beam available at our cyclotron. An elaborate liquid–liquid extraction procedure for separation of ^{193m}Pt and recovery of the target material has been developed and the results will be separately reported.

A second therapeutic radionuclide of current interest is the α-emitting ^{211}At ($T_{1/2} = 7.2$ h). It decays by direct α-particle emission (42%) to ^{207}Bi ($T_{1/2} = 31.6$ a) and by EC (58%) to ^{211}Po ($T_{1/2} = 0.5$ s), followed by α-emission to ^{207}Pb (stable). Thus, each decay of ^{211}At is associated with the emission of an α-particle. The recently enhanced interest in this radionuclide is due to the high therapeutic value of α-particles that is based on their short range and high linear energy transfer (LET), amounting to about 100 keV μm^{-1}, which is close to ideal values for biological effectiveness. Several methods for ^{211}At production have been reported (for reviews [cf. 44, 45]. But the most suitable method has been found to be the ^{209}Bi(α,2n)-reaction. Its cross-section database is well standardised [cf. 46], and the production methodology has been rather well developed. Most commonly, a solid bismuth target has been used, and the chemical separation of ^{211}At was achieved via dry distillation [cf. 47–50]. In recent years, however, wet chemical procedures have also been developed for isolation of ^{211}At [cf. 51–55]. Yet there is still scope of optimisation work because of great demand for this radionuclide. Furthermore, due to its rather short half-life, new partnerships, alliances and collaborative networks of ^{211}At producers are being established across the USA, Europe and Japan. The FZJ has also become a partner in the European collaboration and we describe very briefly some of our efforts in this direction.

We perform a stringent control of the energy of the α-particle extracted from the cyclotron via determination of the ratio of two activities [5] generated in a thin Cu-foil in front of the main target to minimise the formation of ^{210}At ($T_{1/2} = 8.3$ h), which decays to the undesired long-lived ^{210}Po ($T_{1/2} = 138.4$ d). The target developed can withstand beam currents of up to 50 μA. The typical ^{211}At production yield after separation amounts to 30–35 MBq / μAh and the level of the ^{210}At impurity to 0.01%. Both dry distillation and wet chemical separation methods are being automated with the aim to establish its clinical scale production.

Concluding remarks

In this short overview of the radiochemical methods used at the Forschungszentrum Jülich, we have tried to highlight their significance in investigations on various areas of development work (i.e. nuclear data, high-current targetry, chemical processing, etc.). Cyclotron-based production technology of standard positron-emitting radionuclides (^{11}C, ^{15}O and ^{18}F) is well established, and large scale production is routinely done. The production technology of novel radionuclides is rapidly progressing. For production of non-standard positron emitters at small medical cyclotrons, application of highly-enriched targets, and accurate knowledge of nuclear data are absolutely necessary. Thus, hard-core nuclear data research is mandatory for meeting quality control demands. Most of those measurements were carried out at FZJ using radiochemical techniques. A brief account is given of three important non-standard positron emitters, viz. ^{64}Cu, ^{86}Y and ^{124}I, which were mainly developed in our laboratory. Furthermore, some recent results related to the development of the non-standard positron emitter ^{45}Ti and the therapeutic radionuclides ^{193m}Pt and ^{211}At are also elaborated. Our present focus is on the α-emitting ^{211}At in the framework of a European Collaboration. The great interest aroused in recent years in radionuclide research substantiates the notion that this area of work is advancing the frontiers of medical science.

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