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Editorial

Special Issue "Instruments and Methods for Cyclotron Produced Radioisotopes"

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Abstract: The 17th Workshop on Targets and Target Chemistry (WTTC17) was held in Coimbra (Portugal) on 27–31 August 2018. A few months before, the 13th Workshop of the European Cyclotron Network (CYCLEUR) took place in Lisbon (Portugal) on 23–24 November 2017. These two events reassembled major experts in the field of radioisotope production, targets, target chemistry and cyclotrons. In the last few years, significant advances have been obtained in these fields with direct implications for science and society. Instruments and methods, originally developed for nuclear and particle physics, played a crucial role and remarkable developments are on-going. The production of novel radioisotopes for both diagnostics and therapy is expected to produce a breakthrough in nuclear medicine in the next years, paving the way towards theranostics and personalized medicine. This Special Issue presents a collection of original scientific contributions on the latest developments on instruments and methods for medical and research cyclotrons as well as on target and target chemistry for the production of radioisotopes.

Keywords: cyclotrons; targets; target chemistry; radioisotopes; theranostics

1. Introduction

Translational research is fundamental for the development of modern medicine. On the basis of the findings of basic science and of the technology developed to obtain them, novel medical applications can be conceived and put into practice with a direct benefit for the society. A sound example of this virtuous process is represented by cyclotrons. Originally conceived for nuclear and particle physics, they are nowadays fundamental for the supply of medical radioisotopes.

In the last ten years, the number of facilities based on compact medical cyclotrons largely increased, mainly to match the constantly growing demand of radioisotopes for Positron Emission Tomography (PET) imaging. These accelerators are often in operation in hospitals and provide proton beams in the energy range 15–25 MeV and in the intensity range 10–500 μA. Deuteron beams are sometimes also available. The production of radioisotopes is performed also with larger cyclotrons providing 30 MeV proton beams with intesities of the order of 1 mA. They are mostly installed in laboratories or radio-pharmaceutical industries. Furthermore, a few large research facilities operate 70 MeV proton cyclotrons. 30 MeV and 70 MeV proton cyclotrons are in some cases able to accelerate also α particles or other ions.

Compact medical cyclotrons are mainly used for the production of ^{18}F, which is presently the most common PET radioisotope. In the recent years, several novel PET radioisotopes are studied to widen the portfolio of radio-labelled bio-molecules to investigate specific diseases. Along this line, positron emitting radio-metals have a prominent role since some of them could be used in combination with with a beta-minus emitting partner to label the same molecule for therapeutic purposes. These two radioisotopes form a so-called theranostic pair which allows the combination of therapy and diagnostics, paving the way towards personalized medicine.

The path towards novel radio-labelled tracers and therapeutic agents is like a relay race, where physics plays a crucial role in optimizing the irradiation methodologies and in developing novel targets and chemistry is essential to provide effective methods to manipulate the irradiated target material and label the compounds. More in general, this field joins multi-disciplinary efforts not only from physics and chemistry but also from engineering, pharmacy and medicine. Furthermore, a close connection with industry is essential to bring the results of scientific research to the patients.

This special issue collects 15 research papers, 4 communications, 2 technical notes and one review. It represents a comprehensive summary of the most recent advances in the fields of medical cyclotrons, targets, radio-chemistry and non-convectional medical radioisotopes.

2. Cyclotrons and Related Developments

Medical cyclotrons are usually installed in hospitals and research centres. Some of them are operated by radio-pharmaceutical companies, that have sometimes their own production facilities. These accelerators are characterized by a large scientific potential that may extend beyond radioisotope production, especially if they are equipped with external beam transfer lines. A large number of new facilities are under construction or planned worldwide. It is important to remark that an accurate planning phase is crucial to reach the goals of such complex installations. An excellent example of a state-of-the art facility for the production of medical radioisoptopes is the new Center for Radiopharmaceutical Cancer Research at the Helmholtz-Zentrum Dresden-Rossendorf [1], where a variable energy (18–30 MeV) cyclotron was recently installed. This cyclotron is equipped with two beamlines, two target selectors and several liquid, gas and solid target stations to produce a very large variety of research radioisotopes.

For an optimal production of radioisotopes either in quality or in quantity, an accurate knowledge of the production cross-sections and of the features of the accelerator are mandatory. In particular, the energy of the pristine beam is crucial if solid targets are bombarded. Methods for the measurement of the beam energy of a medical cyclotron were developed by the University of Bern [2] using a multi-leaf Faraday cup and by the University of Coimbra [3] using stacks of natural titanium foils interleaved by niobium degraders.

For an efficient use of a medical cyclotron, regular preventive maintenance is of paramount importance. The wear and the lifetime of components of the accelerator, as the ion source, are key features. Along this line, a new kind of ion source filament was studied and tested at TRIUMF [4].

3. Targets and Related Developments

Targets can be classified according to the form of the bombarded material: Gas, liquid or solid. Commercial solutions are available for compact medical cyclotrons, although research is ongoing especially on solid target stations. For an efficient exploitation of large high-energy and high-power cyclotrons, specific targets have to be developed. This is the case of the 70 MeV cyclotron in operation at iThemba LABS in South Africa [5] or of the thorium metal target for the production of ^{225}Ac developed at TRIUMF [6].

The control of the temperature of both the target and of the cooling system is of paramount importance to avoid problems that may cause damage to the target and to the equipment with potential radiation protection implications. For this purpose, a system to measure the temperature in the cyclotron targets cooling water during bombardment was developed at the University of Coimbra [7].

Solid targets are used to produce non-conventional radioisotopes, radio-metals in particular. They present several critical issues as the release of the irradiated target followed by the transfer into a radio-chemistry laboratory. This is accomplished using different methodologies which are the subject of continuous improvements. A novel quick-release target system aimed at decreasing the retrieval time of the irradiated target to less than one minute was developed at TRIUMF [8], allowing to reduce the radiation dose to the operators. The bombardment of a solid target is followed by target dissolution and chemical separation, often implying complex logistics and potential radiation protection hazards. To simplify this process, W.Z. Gelbart and R.R. Johnson [9] proposed a system encompassing a solid target with in-situ dissolution. Cost-effective methods for solid target construction were developed. In particular, 3D printing was used at the Cyclotron Facility in Perth [10].

^{11}C is a PET radioisotope that, due to its short half-life of about 20 minutes, cannot be transported far away from the production site and is of interest only for hospital based facilities where the PET scanner and the cyclotron are located at very short distance. Despite this disadvantage, ^{11}C is used to label relevant medical compounds and novel targets are under study, as the one presented in the paper by J. Peeples et al. [11] based on boron nitride nanotubes (BNNTs).

^{68}Ga is an emerging PET radioisotope that is usually produced by means of Ge/Ga generators. Cyclotron production is challenging and several research groups are focusing on liquid or solid target irradiation techniques. A novel method based on a fused zinc target was investigated at TRIUMF [12].

In the last years, accelerator production of ^{99m}Tc was investigated to cope with the potential crisis of the production of Mo/Tc generators. The preparation of ^{100}Mo targets is difficult since molybdenum metal cannot be electroplated. To overcome this difficulty, W.Z. Gelbart and R.R. Johnson [13] proposed a method to prepare targets that uses a specific cladding process. To realize ^{100}Mo and ^{nat}Y solid targets for cyclotron production of ^{99m}Tc and ^{89}Zr, magnetron sputtering was proposed by H. Skliarova et al. [14]. Novel ideas were also put forward, as the powder-in-gas target proposed by G. Lange [15].

4. Radio Chemistry Developments

The availability of radio-metals is fundamental for the development of theranostics in nuclear medicine. Reliable and efficient methods for the separation and the purification are under study. The University of Coimbra [16] developed an automated process based on a commercially available module suitable for ^{68}Ga, ^{64}Cu and ^{61}Cu obtained through irradiation of liquid targets.

The production of medical radioisotopes is very often performed by irradiating rare and expensive isotope-enriched target materials that have to be recovered and reused. Although quite standardized, the production processes of ^{18}F can be improved. In particular, the ^{18}O enriched water has to be recovered and recycled. A method for optimized treatment and recovery of ^{18}O enriched irradiated water was developed by the Ruhr University Bochum [17]. For recycling highly ^{100}Mo-enriched target material for cyclotron production of ^{99m}Tc, a closed-loop solution was developed, as reported in the paper by H. Skliarova et al. [18].

5. Non-Conventional Medical Radioisotopes

Non-conventional medical radioisotopes are the focus of research activities by several groups worldwide. In particular, radio-metals can be used to label peptides and proteins. Scandium is an interesting case, since ^{43}Sc/^{47}Sc and ^{44}Sc/^{47}Sc represent promising theranostic pairs. For an optimal production of scandium isotopes with the desired purity, accurate knowledge of the production cross-sections is mandatory. The measurement of the cross-sections is a complex process and the possibility to derive them from Thick Target Yield (TTY) measurements in the case of scandium was studied by M. Sitarz et al. [19]. Other radio-metals of interest are ^{52}Mn and ^{165}Er studied in Orleans [20] and ^{45}Ti, which was proposed for PET, as reported in the review by P. Costa et al. [21].

Although not commonly available, α particle beams can be used for the production of medical radioisotopes. This is the case of ^{97}Ru, which is a potential radioisotope for Single Photon Emission Computed Tomography (SPECT). Its production was studied with the ARRONAX [22] multi-particle cyclotron via the reaction ^{nat}Mo(α,X).

6. Outlook

The production of radio-isotopes by means of cyclotrons is an expanding field of scientific research. Some of the most recent developments—such as theranostics in nuclear medicine—are still in their infancy and a large number of findings and advances is expected in the near future. This Special Issue represents a summary for experts active in the field as well as a guideline for students and young scientists.

Conflicts of Interest: The authors declare no conflict of interest.

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