Journal of Physics: Conference
Series

PAPER • **OPEN ACCESS**

Instruments and methods for theranostic radioisotope production at the Bern medical cyclotron

To cite this article: G Dellepiane *et al* 2022 *J. Phys.: Conf. Ser.* **2374** 012179

International Conference on Technology and Instrumentation in Particle Physics IOP Publishing
Journal of Physics: Conference Series **2374** (2022) 012179 doi:10.1088/1742-6596/2374/1/012179

Instruments and methods for theranostic radioisotope production at the Bern medical cyclotron

G Dellepiane[1], P Casolaro[1], P D Häffner[1], I Mateu[1], P Scampoli[1,2], N Voeten[1], E Zyaee[1] and S Braccini[1]

[1] Albert Einstein Center for Fundamental Physics (AEC), Laboratory of High Energy Physics (LHEP), University of Bern, Switzerland
[2] Department of Physics ’Ettore Pancini’, University of Naples Federico II, Complesso Universitario di Monte S. Angelo, Napoli, Italy

E-mail: `gaia.dellepiane@lhep.unibe.ch`

Abstract. Radioisotopes for theranostics are essential for nuclear medicine developments. Their production using solid target stations is challenging and new instruments and methods derived from particle physics are needed. A research program is ongoing at the 18 MeV Bern medical cyclotron, equipped with a solid target station and a 6 m long beam transfer line ending in a separate bunker. To irradiate 6 mm diameter compressed powder pellets, novel target ”coins” were conceived and realized together with methods to assess the beam energy and the production cross sections. To measure the activity at End of Beam (EoB) a system based on a CdZnTe detector was installed. To accurately assess the properties of the beam, novel non-destructive one- and two-dimensional beam monitoring detectors were developed. An ultra-compact active irradiation system based on a novel magnetic lens and two-dimensional beam detectors was conceived and tested with the beamline and recently installed in an outport of the cyclotron.

1. Introduction

The concept of theranostics in nuclear medicine is based on the use of a pair of radioisotopes with very similar or identical chemical properties, one for diagnostics and one for therapy. They are used to label biomolecules that undergo the same metabolic processess within the patient body, allowing at the same time to treat the disease and to follow the therapy evolution. For this reason, novel medical radioisotopes are essential for the development of personalized nuclear medicine. The most widely used technique for the production of standard radioisotopes such as ^{18}F is the irradiation of liquid targets. However, many of the most interesting radionuclides, such as radiometals, are produced from rare and expensive materials available as powders and the use of solid target stations represents a possible but challenging solution. A research program aimed at optimizing the production of new radioisotopes from solid targets is ongoing at the Bern University Hospital (Inselspital), thanks to new developments in accelerator and detector physics as well as new methods for measuring the beam energy and the production cross sections.

2. Materials and Methods

The Bern University Hospital (Inselspital) cyclotron laboratory [1] features an IBA Cyclone 18/18 cyclotron (18 MeV, max. 150 μA extracted current, 8 out ports), equipped with 4 liquid targets for routine ^{18}F production, an IBA Nirta Solid Target Station (STS) and a 6 m long Beam Transfer Line (BTL). The BTL brings the beam in a second bunker with independent access, allowing carrying out both multidisciplinary research activities and routine industrial production of ^{18}F labeled PET tracers, performed by the spin-off company SWAN Isotopen AG. To enhance the cyclotron performance, an ultra compact Automatic Focalization System (AFS) based on a novel magnet lens and a two-dimensional beam detector was recently conceived, constructed and tested [2].

3. Solid target developments

The solid target station (STS) is installed on one out port of the cyclotron and allows to produce novel radioisotopes by irradiating solid materials. It was designed to irradiate a disk (24 mm in diameter, 2 mm thick), on which the target material is electroplated. The back and the front side of the disk are respectively water-cooled and helium-cooled, to avoid overheating during the irradiation. To irradiate materials in form of compressed powder pellets or solid foils, a new target coin was conceived and realized by our group (Fig. 1). The coin is composed of two halves kept together by small permanent magnets. The thickness of the front part is used to adjust the energy of protons reaching the target material, in order to optimize the produced activity and the radionuclidic purity. The back part hosts the 6 mm diameter target and an O-ring to prevent the escape of molten material or any gas produced during the irradiation. It is also necessary to completely stop the protons in order not to activate the water cooling. To minimize the dose to the personnel, a mechanical transfer system (named Hyperloop, Fig. 2-a) was developed and installed by our group to load the target station without entering the cyclotron bunker. The STS was customized with a pneumatic transfer system (STTS) by TEMA Sinergie (Fig. 2-b) that allows to send the shuttle containing the irradiated target either to one hot cell in the nearby GMP radio-pharmacy, or to a receiving station located in the BTL bunker (Fig. 2-c). To assess the activity at end of beam (EOB) by means of gamma spectroscopy, a system based on a 1 cm^3 CdZnTe (CZT) crystal was installed in the receiving station. The detector was experimentally calibrated with a High Purity Germanium (HPGe) detector, considering that the target always has the same size and lands with the same orientation. The system allows measuring the produced activity with an accuracy of a few percent [3].

Being the beam extracted from the cyclotron ~12 mm FWHM at STS, about only 25% of the

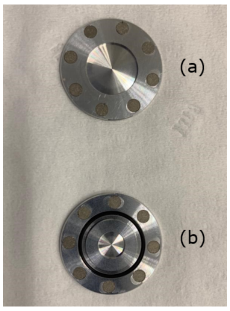

Figure 1. The front cover (a) and the back part (b) of the coin target (24 mm diameter, 2 mm thick).

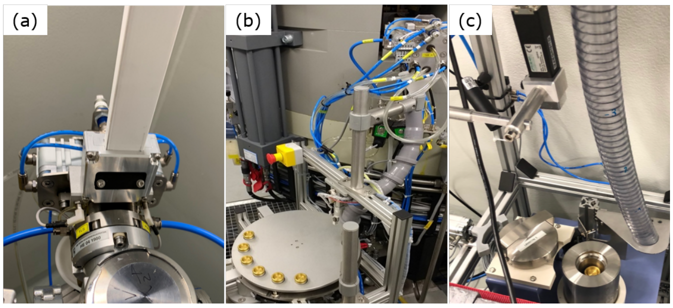

Figure 2. (a) The Hyperloop connected to the STS. (b) The IBA Nirta solid target station and the solid target transfer system by TEMA Sinergie installed on the Bern medical cyclotron. (c) The receiving station located in the BTL bunker.

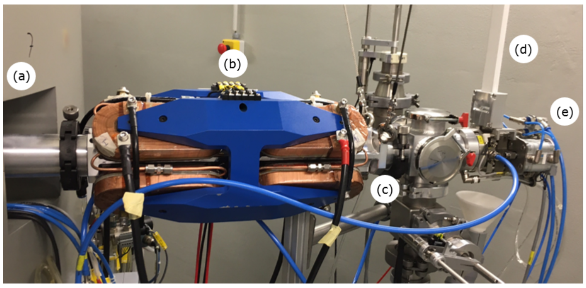

Figure 3. (a) Out port 7 of the Bern medical cyclotron; (b) Mini-PET BeamLine; (c) UniBEaM detector; (d) Hyperloop; (e) IBA Nirta STS.

protons are effectively used to produce the desired isotope if a 6 mm pellet is used. This fact produce unwanted residual activity in the coin, giving rise to specific radiation protection issues. To optimize the irradiation performance, the Automatic Focusing System (AFS) was conceived, constructed and recently tested [2]. The AFS is made of the Mini-PET BeamLine (MBL) by the company D-Pace [4], an innovative compact (∼50 cm) magnet embedding two quadrupoles and two steering magnets, and of the UniBEaM [5], a non-destructive two-dimensional beam profiler based on scintillating silica doped fibers passing through the beam. This detector was developed by our group to measure the beam profile in a wide range of currents; a commercial version of the UniBEaM is manufactured by D-Pace [6]. The system steers the beam on target and focuses it down to the diameter of the pellet, controls its size and position and corrects its characteristics if necessary. The AFS will likely improve the production yield and minimize unwanted radiation protection and handling issues; being compact, it can be installed in any medical cyclotron facility. Thanks to these developments, several radionuclides (^{44}Sc, ^{48}V, ^{61}Cu, ^{64}Cu, ^{68}Ga, ^{155}Tb, ^{165}Er and ^{165}Tm) have been produced at the Bern medical cyclotron. In particular, the production of about 15 GBq of ^{44}Sc represents a very promising result in view of theranostic clinical applications [7].

4. Beam energy and cross sections measurement

To optimize the radioisotope production, precise knowledge of the beam energy and of the cross sections is crucial. The measurement of the beam energy extracted on the STS is ongoing with a method based on the stacked-foils technique, using the well known monitor reaction ^{48}Ti(p,n)^{48}V. Two stacks composed of natural Ti thin foils, separated by an energy degrader of Nb, are positioned in the coin and irradiated. The resulting activities of ^{48}V are measured by the HPGe detector. The detector efficiency was assessed using a multi-gamma source, the activity of which is known with an uncertainty below 1%. The method has been validated in the BTL, where the extracted beam energy was measured also with others methods and found to be (18.3±0.3) MeV [8][9]. To measure cross sections from materials in form of powder, a novel method was developed by our group [10]. It is based on the irradiation of the full mass of the target material by means of a proton beam with a flat profile (Fig. 4) instead of the usual procedure relying on the irradiation of a uniformly thick target. The beam is flattened by the optical elements of the BTL and monitored on-line with the UniBEaM detector (Fig. 5). To measure the beam current hitting the target material, a custom target station was designed and built (Fig. 5, Fig. 6). The station is composed of a 6 mm diameter collimator, an electron suppressor ring and a target holder. The holder is connected to an ammeter (B2985A Keysight) for current measurements on target. The collimator is connected to ground and provides a beam of controlled diameter. The electron suppressor ring is connected to a negative bias voltage in order to repel secondary electrons produced during the irradiation that would lead to an artificial

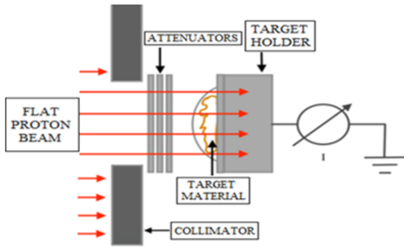

Figure 4. New cross section measurements procedure based on a flat beam current surface density developed by our group.

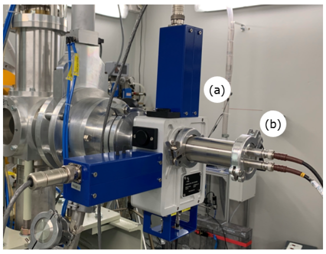

Figure 5. Experimental set-up for cross section measurements: the UniBEaM detector (a) and the target station (b).

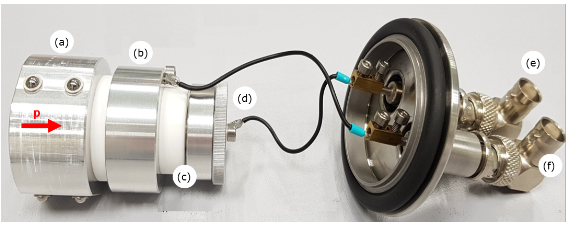

Figure 6. Target station for cross section measurements: (a) grounded collimator; (b) electron suppressor ring; (c) attenuators holder; (d) target holder; (e) beam current signal; (f) bias voltage.

increase in the measured beam current. The beam energy is degraded by means of aluminum attenuator discs placed in front of the target and is determined using the SRIM Monte Carlo code [11]. The obtained activity is assessed with the HPGe detector, allowing to measure the cross section at the given energy. With this method, the production cross section of several radioisotopes (^{47}Ca [12], ^{43}Sc, ^{44}Sc [10][13], ^{44m}Sc, ^{47}Sc, ^{48}Sc, ^{48}V [10], ^{61}Cu, ^{66}Ga, ^{67}Ga, ^{68}Ga, ^{154}Tb, ^{155}Tb, ^{156}Tb, ^{165}Tm, ^{166}Tm, ^{167}Tm) was measured.

5. Conclusion and outlook

In the framework of the research program on the production of theranostic and non standard radioisotopes ongoing at the Bern medical cyclotron laboratory, new instruments and methods were developed. A new target coin to irradiate solid materials in form of compressed powders was conceived, constructed and tested, together with a novel automatic focusing system capable of focusing the beam on small targets. This apparatus allows to enhance the production performance and minimizes the activation of the material outside the target. New procedures to measure the nuclear cross sections, the beam energy and the produced activity at EoB were also developed. The promising results obtained up to now represent an important milestone in view of the use of medical cyclotrons for theranostics and personalized nuclear medicine.

Acknowledgments

We acknowledge contributions from LHEP engineering and technical staff (Roger Hänni and Jan Christen, in particular). We are thankful to the SWAN Isotopen AG maintenance team (Riccardo Bosi and Michel Eggemann, in particular) for the collaboration in the set-up and operation of the solid target system. This research was partially funded by the Swiss National Science Foundation (SNSF). Grants: 200021_175749 and CRSII5_180352.

References

[1] Braccini S *et al.* 2019 *Proceedings of Cyclotrons2019* (Cape Town: JACoW) p 127
[2] Häffner P D *et al.* 2021 *Applied Sciences* **11(6)** 2452
[3] Dellepiane G *et al.* 2021 *IL NUOVO CIMENTO* **44 C** 130
[4] Dehnel M P *et al.* 2013 *Proceedings of Cyclotrons2013* (Vancouver: JACoW) p 251
[5] Auger M *et al.* 2016 *Journal of Instrumentation* **11** P03027
[6] Potkins D E *et al.* 2017 *Physics Procedia* **90** 215
[7] van der Meulen N *et al.* 2020 *Molecules* **25(20)** 4706
[8] Häffner P D *et al.* 2019 *Instruments* **3** 63
[9] Nesteruk K P *et al.* 2018 *Journal of Instrumentation* **13** P01011
[10] Carzaniga T S *et al.* 2017 *Applied Radiation and Isotopes* **129** 96
[11] Ziegler J and Manoyan J 1988 *Nuclear Instruments and Methods* **B35** 215
[12] Carzaniga T S and Braccini S 2019 *Applied Radiation and Isotopes* **143** 18
[13] Carzaniga T S *et al.* 2019 *Applied Radiation and Isotopes* **145** 205