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THE CYCLOTRON TR-FLEX AT THE CENTER FOR RADIOPHARMACEUTICAL CANCER RESEARCH AT HELMHOLTZ-ZENTRUM DRESDEN-ROSSENDORF

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Abstract

The new Center for Radiopharmaceutical Cancer Research was established at Helmholtz-Zentrum Dresden-Rossendorf e.V. to centralize the main units: a high current proton cyclotron, a radiopharmaceutical production – GMP unit including quality control, laboratories for PET-radiochemistry, chemical laboratories, laboratories for biochemical investigation, laboratories for small animal imaging and an animal keeping facility.

The cyclotron TR-Flex was put into operation in 2017 and it is equipped with two extraction ports. Both are movable to adjust the energy of the extracted proton beam in the range from 15 MeV up to 30 MeV. One extraction port is coupled with a combination magnet and two beam lines. A [^{123}I]-iodine gas target station is installed at the first beam line and a four-port target selector is installed at the end of beamline two. The second extraction port has no beamlines but is equipped with a four-port target selector. Two [^{18}F]- water targets, one [^{18}F]F_2 gas target, one [^{11}C]CH_4 gas target, one [^{11}C]CO_2 gas target, one 30° and one 90° solid state target are mounted on two target selectors.

In our contribution we report our experience of the new cyclotron TR-Flex during the first two operation years. Typical beam parameters, saturation yields and the reliability of the TR-Flex are presented. Furthermore we describe the new home-built Radionuclide Distribution System.

INTRODUCTION

Radiopharmaceutical research and the production of radiopharmaceuticals have a long history at the Research Center in Rossendorf. The production of radiopharmaceuticals started in 1958. The basis were a nuclear research reactor (10 MW) and the Cyclotron U-120 (Leningrad). A broad scale of radiolabeled products based on ^{14}C, ^{131}I, ^{123}I, ^{32}P, ^{75}Se, ^{67}Ga, ^{85}Sr, ^{111}In, ^{211}At and fission radionuclides such as ^{90}Sr/ ^{90}Y, ^{99}Mo were provided. Furthermore, the Research Center was the second producer of fission ^{99}Mo/ ^{99m}Tc-generators with an amount of 20 TBq ^{99}Mo per week. A wide-spread research to ^{99m}Tc coordination chemistry and radiopharmacology and ^{99m}Tc-kits was established including a wide range of labelled compounds for human use.

The Cyclotron U-120, Leningrad (1958 - 1999) was used for routine production of ^{67}Ga, ^{85}Sr, ^{111}In, ^{123}I, ^{211}At and the corresponding labelled compounds for human use. The start for research for PET was in 1982. The first [^{18}F]FDG (electrophil) production was in 1983.

1997 marked the official opening of Rossendorf PET-Center for research and application including the manufacturing authorization for PET drugs. The marketing authorization includes [^{18}F]FDG (GlucoRos), [^{18}F]Fluoride (NaFRos) and [^{18}F]FDOPA (DOPARos). Furthermore, there are 15 different radiopharmaceuticals available on demand.

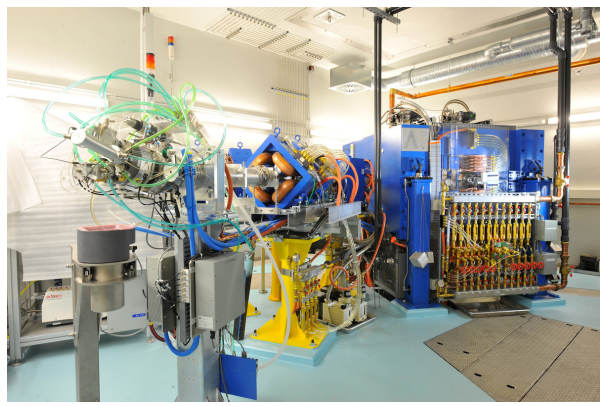

Figure 1: The TR-Flex cyclotron at the HZDR. The beamline 1B with a 4-port target selector is shown in the foreground. The second 4-port target selector is at the opposite side of the Cyclotron. Picture: HZDR/Frank Bierstedt

The former cyclotron of the HZDR, an IBA Cyclone 18/9, was put in operation in autumn 1996. After 18 years of routine operation comprehensive upgrades would have to be necessary to fulfill the new demands in the second decade of the 21th century. On the other hand HZDR could not forego the RN production with the Cyclone 18/9 during the ZRT building phase. Thus, HZDR decided to install a new cyclotron with higher ion energy and higher ion bean current.

THE TR-FLEX CYCLOTRON

The TR-Flex cyclotron, shown in Fig. 1, from Advanced Cyclotron Systems Inc. (ACSI, Canada) [1] was put into operation in 2017. The cyclotron is equipped with two extraction ports. Both extraction foils are radially movable to adjust the energy of the extracted proton beam in the range of 15 MeV up to 30 MeV. Two beamlines are connected behind a combo magnet on the extraction port 1. Two 4 port

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target selectors are installed at one beamline and the second extraction port. The following targets are installed:

- two [^{18}F]F$^-$ water targets and one [^{18}F]F_2 gas target
- one [^{11}C]CH_4 gas target and one [^{11}C]CO_2 gas target
- one 30° and one 90° solid state target
- one [^{123}I]I$^-$ gas target

ION ENERGY

The cyclotron is designed to extract ions in the range of 18 MeV up to 30 MeV. But it is of real interest to extract ions at lower ion energies. The reaction cross section for a lot of radionuclides are higher and the impurities are lower for lower ion energies. Hence, experiments were done to determine the lowest possible ion extraction energy. Autoradiography measurements at ion beam energies of 14 MeV and 30 MeV were executed to determine the profile of the proton beam hitting the solid target installed at the beamline target selector. The Autoradiographic measurement of a 30 µA beam current with an energy of 30 MeV is shown in Fig. 2.

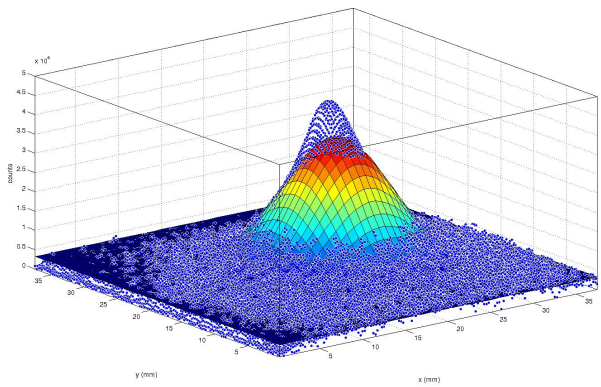

Figure 2: Autoradiographic measurement of an irradiated gold disk at the 90°-solid state target, beam energy 30 MeV. (blue dots: measured values, colored surface: fitted curve)

A two dimensional Gaussian function was fitted to the measured profile to determine the beam size in x- and y-direction.

$$I(x,y) = I_0 \cdot e^{-\left(\frac{(x-\mu_x)^2}{2\cdot\sigma_x^2}+\frac{(y-\mu_y)^2}{2\cdot\sigma_y^2}\right)} \quad (1)$$

We measured a pretty well shaped beam profile for lower and higher energies at the target selector at the end of the beamline. The FWHM value in x- and y-direction was for low and high energies in the range of 13(1) mm. We extract the beam at an energy above 15 MeV because of a higher beam loss in the beamline for lower energies.

ENERGY DEGRADER

A 700 µm thick Al-disk was installed at the 90° solid state target instead of the vacuum foil to reduce the energy below 15 MeV. SRIM-calculations shows an energy loss within the Al-disk in in the range of 3.0 MeV to 4.5 MeV depending on the initial beam energy.

The Al-disk is manufactured produced from one piece and a water cooling is installed. A schematic view of the energy degrader is shown in Fig. 3. It is an Al-flange with a diameter of 40 mm and a beam window with a diameter of 16 mm with a thickness of 700 µm. The flange is directly water cooled. FEM simulations show an maximum temperature of 500 °C in the center of the beam window at an ion current of 80 µA.

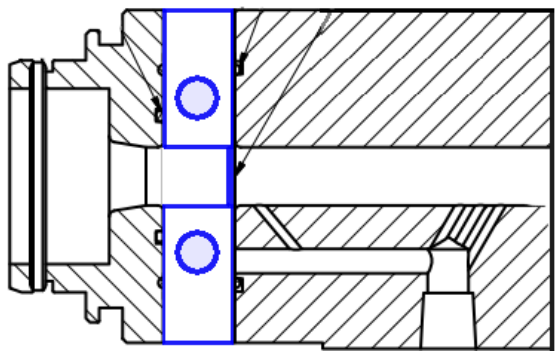

Figure 3: The energy degrader (blue part) is installed instead of the vacuum foil in front of the solid target system.

The energy degrader was tested for the ^{64}Cu production using 13 MeV protons for the ^{64}Ni(p,n)^{64}Cu reaction [2, 3] were carried out and evaluated. Typical irradiation parameters for the copper production are an ion current of 70 µA and an irradiation time of 90 min. The molar activity of the ^{64}Cu is about 1 TBq µmol^{-1}. We achieved an activity of 18 GBq that is corresponding to a saturation yield of 4.0 GBq µA^{-1} strongly depending on the ^{64}Ni mass on the gold disk.

PRODUCED RADIONUCLIDES

The following radionuclides are produced reliably with the TR-Flex since the beginning of 2018. Typical production parameters of the new TR-Flex and the achieved activities are presented in Table 1.

Table 1: Typical Production Parameters of the TR-Flex

Isotope	Chem. Form	Typ. Current	Irr. Time	Actitvity
^{18}F	F^-	80 µA	20 min	95 GBq
^{18}F	F_-	105 µA	70 min	355 GBq
^{18}F	F_2	30 µA	60 min	20 GBq
^{11}C	CO_2	40 µA	35 min	155 GBq
^{11}C	CH_4	30 µA	40 min	55 GBq
^{64}Cu	Cu	70 µA	90 min	16 GBq
^{123}I	I^-	150 µA	360 min	350 GBq

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THE RADIONUCLIDE DISTRIBUTION SYSTEM

A new Radionuclide Distribution System was developed and installed by the Department of Research Technology at HZDR. The liquid and gas targets are unloaded through capillaries to a central hot cell. Henceforward the radionuclides can be distributed automatically to the 25 hot cells in the whole Center for Radiopharmaceutical Cancer Research.

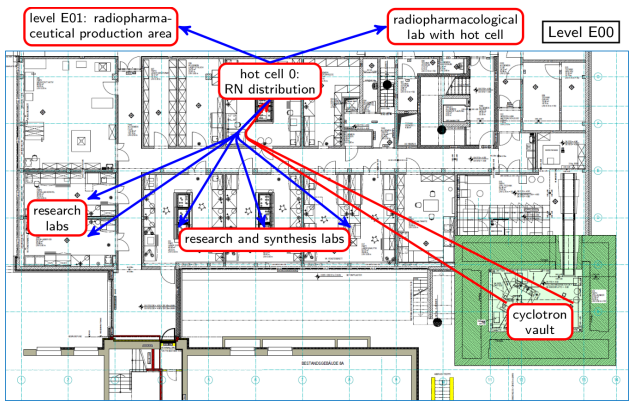

Figure 4: Schematic view of the radionuclide distribution in the building. red lines: unload the targets to the hot cell "0", blue lines: radionuclide distribution within the ZRT building.

The system controls the target unload and the transport to the hot cells within the whole building. The gas is transported by stainless steel capillaries with an inner diameter of 1.4 mm and the liquid is transported by PTFE capillaries with an inner diameter of 0.8 mm. The transport distances can reach up to 100 m. The supervision of the relevant parameters and interlock system for the radiation protection (shielding of the hot cells, correct transportation path, correct ventilation system) and generation of the target unload clearance signal sent to the cyclotron is done automatically by the Radionuclide Distribution System.

Normally this is an automatic transport but also an manual operation and a so-called emergency mode, that allows to abrogate the interlock system, is possible. A schematic view of the distribution is shown in Fig. 4. Solid targets are unloaded to a transport container on a hand cart. An unload clearance signal is generated when the hand cart is docked at the solid target system and the cooling water blow out as well as the unload process is done by the control system of the cyclotron. Also the iodine target is unloaded into a transport container. The container is docked the a hot cell and the target is washed out through PTFE capillaries into the container.

CONCLUSIONS

In our contribution we introduced the new cyclotron TR-Flex including first results of the radionuclide production and beam characterization measurements. We presented the energy degrader to reduce the energy of the solid targt system. The Al-flange was dismounted and checked after more than 40 production runs with a total amount of about 3800 µA h deposited charge. A very slight plastic deformation was seen. The integration of the Al-flange was successful. The production of further radionuclides will be started in the future step by step.

REFERENCES

[1] R. Watt, W. Gyles, and A. Zyuzin, "Building on TR-24 success: Advanced cyclotron systems Inc. launches a new cyclotron model", *J. Radioanal. Nucl. Chem*, vol. 305, pp. 93–98, Jul. 2015. doi:10.1007/s10967-015-4048-y

[2] D. W. McCarthy, R. E. Shefer, R. E. Klinkowstein, L. A. Bass, W. H. Margeneau, C. S. Cutler, C J. Anderson, and M. J. Welch, "Efficient production of high specific activity ^{64}Cu using a biomedical cyclotron", *Nucl. Med. Biol.*, vol. 24, pp. 35–43, Jan. 1997. doi:10.1016/S0969-8051(96)00157-6

[3] S. Thieme, M. Walther, H.-J. Pietzsch, J. Henniger, S. Preusche, P. Maeding, and J. Steinbach, "Module-assisted preparation of ^{64}Cu with high specific activity", *Applied Radiation and Isotopes*, vol. 70, pp. 602–608, Apr. 2012. doi:10.1016/j.apradiso.2012.01.019