



You have downloaded a document from  
**RE-BUŚ**  
repository of the University of Silesia in Katowice

**Title:** Medical Radioisotopes Produced with Cyclotron Beams in Warsaw

**Author:** J. Choiński, J. Jastrzębski, P. J. Napiorkowski, M. Sitarz, A. Stolarz, Katarzyna Szkliniarz, A. Trzcńska, J. Wojtkowska, Wiktor Zipper

**Citation style:** Choiński J., Jastrzębski J., Napiorkowski P. J., Sitarz M., Stolarz A., Szkliniarz Katarzyna, Trzcńska A., Wojtkowska J., Zipper Wiktor. (2017). Medical Radioisotopes Produced with Cyclotron Beams in Warsaw. „Annals Radiation Therapy and Oncology” (Vol. 1, iss. 1 (2017), art. no 1005)



Uznanie autorstwa - Licencja ta pozwala na kopiowanie, zmienianie, rozprowadzanie, przedstawianie i wykonywanie utworu jedynie pod warunkiem oznaczenia autorstwa.



UNIwersYTET ŚLĄSKI  
W KATOWICACH



Biblioteka  
Uniwersytetu Śląskiego



Ministerstwo Nauki  
i Szkolnictwa Wyższego



# Medical Radioisotopes Produced with Cyclotron Beams in Warsaw

Jarosław Choiński<sup>1</sup>, Jerzy Jastrzębski<sup>1\*</sup>, Paweł J Napiorkowski<sup>1</sup>, Mateusz Sitarz<sup>1,2</sup>, Anna Stolarz<sup>1</sup>, Katarzyna Szkliniarz<sup>3</sup>, Agnieszka Trzcińska<sup>1</sup>, Jolanta Wojtkowska<sup>4</sup> and Wiktor Zipper<sup>3</sup>

<sup>1</sup>Heavy Ion Laboratory, University of Warsaw, Poland

<sup>2</sup>Faculty of Physics, University of Warsaw, Poland

<sup>3</sup>Department of Nuclear Physics, Institute of Physics, University of Silesia, Poland

<sup>4</sup>National Centre for Nuclear Research, Poland

## Abstract

The various production routes of the prospective medical radioisotopes <sup>43</sup>Sc, <sup>44g</sup>Sc, <sup>44m</sup>Sc, <sup>47</sup>Sc, <sup>44</sup>Ti/<sup>44g</sup>Sc, <sup>99m</sup>Tc, <sup>72</sup>Se/<sup>72</sup>As and <sup>211</sup>At were investigated by a team from the Heavy Ion Laboratory, University of Warsaw (HIL-UW), the University of Silesia (US) and the National Centre for Nuclear Research (NCNR). Three cyclotrons were employed: the K=160 heavy-ion cyclotron with an internal 32 MeV alpha particle beam and the p/d PETtrace medical cyclotron at HIL and the C30 proton cyclotron at NCNR in Świerk, near Warsaw. The Thick Target Yields, activity at the End of Bombardment (EOB) and the impurities produced in addition to the main isotope are reported. The possible medical applications of these radioisotopes are briefly discussed.

## Introduction

In 2012 a new unit, the Radiopharmaceuticals Production and Research Centre (RPRC) [1-4], devoted to the production of and research into innovative radioisotopes for medical diagnostics and therapy, was inaugurated at the Heavy Ion Laboratory of the University of Warsaw (HIL-UW). The unit is equipped with a PETtrace medical cyclotron (produced by the General Electric Company) providing proton and deuteron beams of 16.5 MeV and 8.4 MeV respectively. A range of chemical equipment for the synthesis and quality control of radiopharmaceuticals is also installed. In addition to the regular production of FDG for commercial use in Positron Emission Tomography the new unit enabled the laboratory team to enter a new research field in the applications of radioisotopes in medical diagnosis and therapy.

In parallel the K=160 heavy ion cyclotron [5], already in operation for almost two decades for basic research in nuclear physics and heavy ion applications, is employed to produce research quantities of medically interesting radioisotopes. In this work samples are irradiated by the internal alpha particle beam.

Additionally, the home made C30 cyclotron [6,7] operating at the National Centre for Nuclear Research in Świerk, near Warsaw, although with relatively low beam current, enables us to extend the available proton energy range up to 28 MeV. A proton beam with similar energy but with higher intensity will be available soon from a new machine accelerating protons, deuterons and alpha particles, currently under construction at Świerk.

## The Heavy Ion Laboratory of the University of Warsaw

The Heavy Ion Laboratory (Figure 1) is a "User Facility" with around 100 national and foreign users per year. The isochronous K<sub>max</sub>=160 cyclotron (Figure 2) delivers around 3000 h of gaseous or metallic heavy ion beams per year with energies between 2 MeV/nucleon and 10 MeV/nucleon and masses up to 40. The current HIL research programme comprises nuclear physics, atomic physics, materials science, solid state physics, biology, particle detector development and testing, and recently production of research quantities of medical radioisotopes. The last mentioned subject is discussed in the present paper.

A second proton-deuteron cyclotron (Figure 3) is devoted to the commercial production of radiopharmaceuticals for Positron Emission Tomography (PET) and research into innovative medical radioisotopes.

## OPEN ACCESS

### \*Correspondence:

Jerzy Jastrzębski, Heavy Ion Laboratory, University of Warsaw, Poland,

E-mail: jastj@slcj.uw.edu.pl

Received Date: 26 May 2017

Accepted Date: 04 Sep 2017

Published Date: 12 Sep 2017

### Citation:

Choiński J, Jastrzębski J, Napiorkowski PJ, Sitarz M, Stolarz A, Szkliniarz K, et al. Medical Radioisotopes Produced with Cyclotron Beams in Warsaw. *Ann Radiat Ther Oncol.* 2017; 1(1): 1005.

Copyright © 2017 Jerzy Jastrzębski.

This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.





Figure 1: The Heavy Ion Laboratory building, North side.



Figure 2: The K=160 heavy ion cyclotron, accelerating gaseous and metallic ions with masses up to 40 and energies up to about 10 MeV/nucleon.



Figure 4: The layout of the Radiopharmaceuticals Production and Research Centre. The radioisotopes produced by the proton or deuteron beam from the PETtrace cyclotron (left of the figure) are transferred to one of the chemistry laboratories: L1 serving for the routine production of Fluoro-Deoxy-Glucose (FDG) or L2 devoted to research activity with  $^{11}\text{C}$ ,  $^{15}\text{O}$  or  $^{18}\text{F}$  radioisotopes. The quality control area (right of the figure) is also divided into two parts: for testing regularly produced FDG and for radiopharmaceuticals in the research stage.



Figure 5: The PETtrace p/d cyclotron installed in its cave.

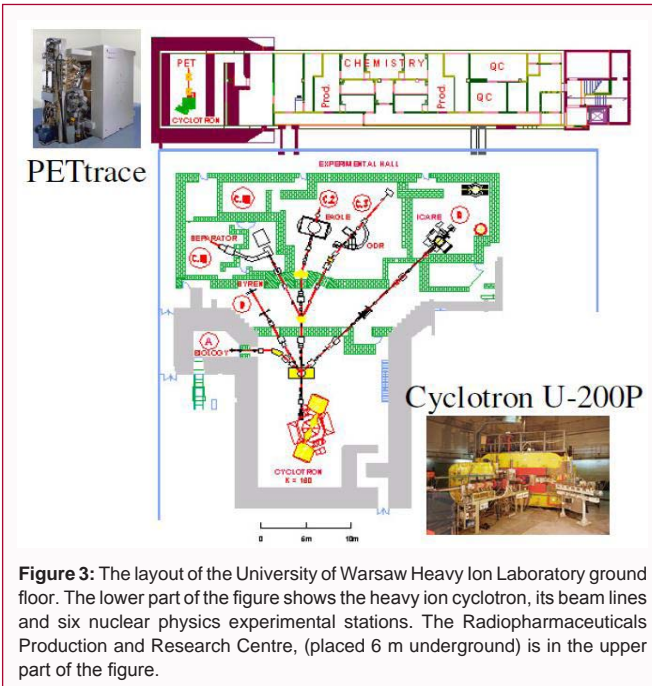


Figure 3: The layout of the University of Warsaw Heavy Ion Laboratory ground floor. The lower part of the figure shows the heavy ion cyclotron, its beam lines and six nuclear physics experimental stations. The Radiopharmaceuticals Production and Research Centre, (placed 6 m underground) is in the upper part of the figure.

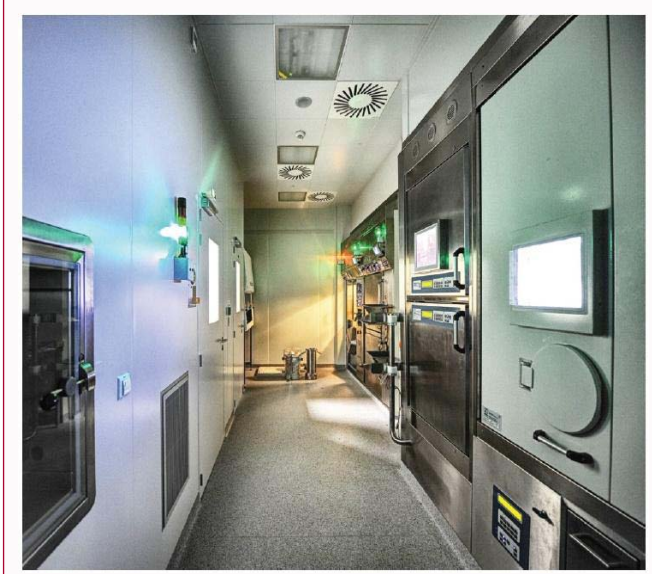
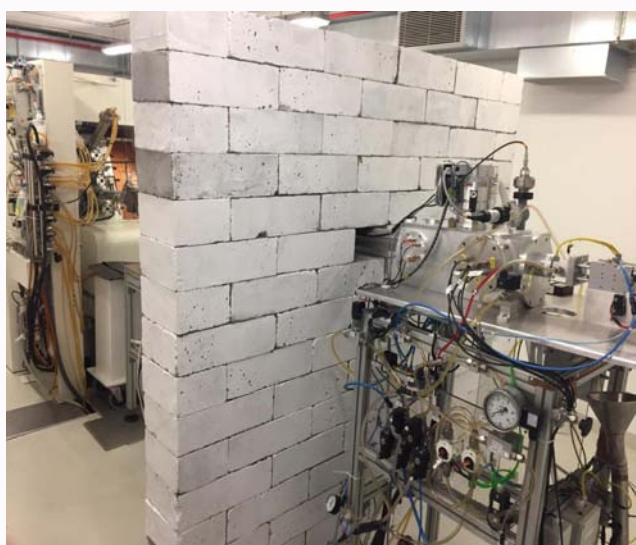


Figure 6: Hot cells in the research laboratory.

The convenient position of the HIL at the heart of the Scientific Campus Ochota where the scientific departments of the University of Warsaw, the Polish Academy of Sciences and Warsaw Medical University are located opens up possibilities for large interdisciplinary

collaborations. The Institute of Nuclear Chemistry and Technology, located about 15 km from HIL, is also closely involved in the research



**Figure 7:** The external beam line installed on the PETtrace cyclotron for the irradiation of solid samples.

part of this project.

## Radiopharmaceuticals Production and Research Centre

A 3D representation of the layout of the RPRC is given in Figure 4. The PETtrace cyclotron and one of the chemistry rooms are shown in Figure 5 and 6. An external beam line for the irradiation of solid samples was recently designed and constructed [8] in the laboratory and is presented in Figure 7. The specially developed cooling system allows rather high proton and deuteron beam intensities to be used for the irradiation of these samples.

## Characteristics of Proton, Deuteron and Alpha Particle Production Routes of the Investigated Radioisotopes

Tables 1-3 present the investigated radioisotopes and some characteristics of the production routes employed for the three projectiles. All our experimental data presented in these tables and obtained with carbonate, chloride or oxide targets (with the

exception of metallic and natural ones) are recalculated to the highest commercially available target isotope enrichment. Short comments on a few of them are given below.

<sup>43</sup>Sc. This radioisotope [9,10], with prospective Positron Emission Tomography (PET) applications, has a substantially longer half-life ( $T_{1/2}=3.89$  h) than the currently employed <sup>18</sup>F ( $T_{1/2}=1.8$  h) or <sup>68</sup>Ga ( $T_{1/2}=68$  min) and a strong  $\beta^+$  branch. It can, therefore, be delivered to hospital PET scanners from much more distant production centers. <sup>43</sup>Sc is also an ideal theranostic partner for the therapeutic <sup>47</sup>Sc. We produced <sup>43</sup>Sc using four different nuclear reactions: (p,n), (d,n) and ( $\alpha$ ,p)+( $\alpha$ ,n). The latter reactions produce very pure <sup>43</sup>Sc using a natural Ca target and are therefore preferred for centre's equipped with cyclotrons accelerating alpha particle beams to energies of 20 MeV or higher. The (d,n) route also gives a rather pure product, but with the currently employed medical accelerators the thick target efficiency for this reaction is rather low (it would be about a factor of two higher with 15 MeV deuterons). Finally, the (p,n) reaction has a good yield using medical accelerators but the resulting product is contaminated with <sup>44</sup>Sc.

<sup>44</sup>Sc. A second Sc radioisotope [11,12] of a similar half-life ( $T_{1/2}=3.97$  h) to <sup>43</sup>Sc with a strong positron branch. It decays almost completely to an excited state at 1157 keV. Also, an isomeric state of 271 keV above the ground state has a half-life of 2.4 d and decays to the ground state. These two properties of <sup>44</sup>Sc allow applications of this radioisotope to be extended to more sophisticated uses besides its classic use in PET techniques. Firstly, it was proposed a few years ago [13] to develop a new technique, the so called-three photon PET, in which the high energy gamma ray in coincidence with the two 511 keV annihilation quanta substantially improves the PET spatial resolution, caused by the non-negligible range of the annihilating positrons (the 1157 keV gamma line is emitted from the place where the radiopharmaceutical is absorbed). It was also shown [14] that this technique substantially decreases the PET patient dose. Secondly, the other particularity of <sup>44</sup>Sc, the existence of a much longer lived isomeric state, led to a proposal [15-17] for the synthesis of an *in vivo* <sup>44m</sup>Sc/<sup>44g</sup>Sc generator for PET studies of long biological processes. In the present study two isomers of <sup>44</sup>Sc were produced by the (p,n) and ( $\alpha$ ,np+pn+d) reactions on CaCO<sub>3</sub> targets. The proton induced reaction gives a very high activity at EOB for the

**Table 1:** The prospective medical radioisotopes investigated using a proton beam. The column TTY/TY denotes the Thick Target Yield or Target Yield in MBq/ $\mu$ Ah.

Isotope and $T_{1/2}$	Projectile energy (MeV)	Target	TTY / TY (MBq/ $\mu$ Ah)	Activity after 4 h irradiation with 1 $\mu$ A beam		Reference
				$A_{EOB}$ (MBq)	Largest impurity (%)	
<sup>99m</sup> Tc, 6 h	16-8, 26-8	<sup>100</sup> Mo (99.815%)	404 (21), 910 (30)	1294 (67), 2914 (96)	1.26 (8) <sup>100</sup> Tc, 1.82 (7) <sup>100</sup> Tc	[30]
<sup>43</sup> Sc, 3.89 h	17-4	<sup>43</sup> CaCO <sub>3</sub> (90%)	320 (20)	930 (70)	11.0 (1.0) <sup>44g</sup> Sc	[18]
<sup>44g</sup> Sc, 3.97 h	12-4	<sup>44</sup> CaCO <sub>3</sub> (94.8%)	350 (50)	10.0 (1.4) E+2	0.42 (8) <sup>44m</sup> Sc	[18]
<sup>44m</sup> Sc/ <sup>44g</sup> Sc, 2.4 d	12-4	<sup>44</sup> CaCO <sub>3</sub> (94.8%)	1.08 (13)	4.2 (5)	2.7 (4) <sup>48</sup> Sc, apart from <sup>44g</sup> Sc	[18]
<sup>44g</sup> Sc, 3.97 h	16-4	<sup>44</sup> CaCO <sub>3</sub> (94.8%)	670 (80)	1.9 (2) E+3	0.66 (13) <sup>44m</sup> Sc	[18]
<sup>44m</sup> Sc/ <sup>44g</sup> Sc, 2.4 d	16-4	<sup>44</sup> CaCO <sub>3</sub> (94.8%)	3.2 (5)	13 (2)	1.3 (3) <sup>48</sup> Sc, apart from <sup>44g</sup> Sc	[18]
<sup>44g</sup> Sc, 3.97 h	22-6	<sup>44</sup> CaCO <sub>3</sub> (94.8%)	870 (80)	2.5 (2) E+3	11.5 (1.4) <sup>43</sup> Sc	[18]
<sup>44m</sup> Sc/ <sup>44g</sup> Sc, 2.4 d	22-6	<sup>44</sup> CaCO <sub>3</sub> (94.8%)	7.3 (6)	28 (2)	10.0 (1.2) E+2 <sup>43</sup> Sc, apart from <sup>44g</sup> Sc	[18]
<sup>47</sup> Sc, 3.35 d	16-10	<sup>48</sup> CaCO <sub>3</sub> (97.1%)	21 (2)	83 (8)	150 (20) <sup>48</sup> Sc	[18]
<sup>47</sup> Sc, 3.35 d	22-17	<sup>48</sup> CaCO <sub>3</sub> (97.1%)	49 (4)	193 (12)	35 (4) <sup>48</sup> Sc	[18]
<sup>47</sup> Sc, 3.35 d	28-16	<sup>48</sup> CaCO <sub>3</sub> (97.1%)	85 (5)	334 (16)	27 (2) <sup>48</sup> Sc	[18]
<sup>47</sup> Sc, 3.35 d	28-18	<sup>48</sup> TiO <sub>2</sub> (99.6%)	2.0 (1)	7.7 (3)	20.0 (1.1) E+2 <sup>44g</sup> Sc, 57 (3) <sup>44m</sup> Sc	[18]



**Table 2:** The prospective medical radioisotopes investigated using a deuteron beam. The column TTY denotes the Thick Target Yield in MBq/μAh.

Isotope and T <sub>1/2</sub>	Projectile energy (MeV)	Target	TTY (MBq/μAh)	Activity after 4 h irradiation with 1 μA beam		Reference
				A <sub>EOB</sub> (MBq)	Largest impurity (%)	
<sup>43</sup> Sc, 3.89 h	7-0	<sup>42</sup> CaCO <sub>3</sub> (95.9%)	35 (2)	99 (7)	0.22 (3) <sup>44g</sup> Sc	[18]

**Table 3:** The prospective medical radioisotopes investigated using an alpha particle beam. The column TTY/TY denotes the Thick Target Yield or Target Yield in MBq/μAh.

Isotope and T <sub>1/2</sub>	Projectile energy (MeV)	Target	TTY / TY (MBq/μAh)	Activity after 4 h irradiation with 1 μA beam		Reference
				A <sub>EOB</sub> (MBq)	Largest impurity (%) at EOB	
<sup>211</sup> At, 7.2 h	29-19	<sup>nat</sup> Bi	37 (6)	123 (20)	0.025 (6) <sup>210</sup> At	[29]
<sup>72</sup> As, 26 h	29-16	<sup>70</sup> GeO <sub>2</sub> (95.3%)	11.7 (9)	44 (3)	220 (10) <sup>73g</sup> Sc	
<sup>72</sup> Se/ <sup>72</sup> As, 8.5 d	29-16	<sup>70</sup> GeO <sub>2</sub> (95.3%)	0.84 (0.14)	3.3 (6)	2950 (40) <sup>73g</sup> Se	
<sup>43</sup> Sc, 3.89 h	20-0	<sup>nat</sup> CaCO <sub>3</sub>	84 (4)	240 (11)	0.034 (5) <sup>47</sup> Sc	[31]
<sup>43</sup> Sc, 3.89 h	20-0	<sup>nat</sup> Ca (metal)	210 (30)	600 (86)	0.035 (7) <sup>47</sup> Sc	[31]
<sup>43</sup> Sc, 3.89 h	20-0	<sup>40</sup> CaCO <sub>3</sub> (99.99%)	88 (13)	252 (37)	2.5 (1) E-4 <sup>47</sup> Sc	[31]
<sup>43</sup> Sc, 3.89 h	31-0	<sup>nat</sup> CaO	98 (10)	280 (28)	0.75 (9) <sup>44g</sup> Sc	[29]
<sup>43</sup> Sc, 3.89 h	29-19	<sup>41</sup> KCl (95.4%)	60 (9)	172 (26)	13 (1) <sup>44g</sup> Sc	[31]
<sup>44g</sup> Sc, 3.97 h	29-12	<sup>42</sup> CaCO <sub>3</sub> (95.9%)	44 (7)	127 (20)	13.7 (8) <sup>44m</sup> Sc	[31]
<sup>44m</sup> Sc/ <sup>44g</sup> Sc, 2.4 d	29-12	<sup>42</sup> CaCO <sub>3</sub> (95.9%)	4.7 (8)	18 (3)	40.6 (9) <sup>43</sup> Sc, apart from <sup>44g</sup> Sc	[31]
<sup>44g</sup> Sc, 3.97 h	20-2	<sup>41</sup> KCl (95.4%)	61 (10)	176 (29)	15.9 (7) <sup>43</sup> Sc	[31]
<sup>44m</sup> Sc/ <sup>44g</sup> Sc, 2.4 d	20-2	<sup>41</sup> KCl (95.4%)	3.0 (6)	12 (2)	233 (15) <sup>43</sup> Sc, apart from <sup>44g</sup> Sc	[31]
<sup>47</sup> Sc, 3.35 d	20-0	<sup>44</sup> CaCO <sub>3</sub> (99.2%)	1.0 (1)	3.7 (4)	51 (3) <sup>43</sup> Sc	[18]
<sup>44</sup> Ti/ <sup>44g</sup> Sc, 60 y	29-12	<sup>42</sup> CaCO <sub>3</sub> (95.9%)	3.2 (8) E-5	1.3 (3) E-4	70 (20) <sup>46</sup> Sc	

for this very long-lived radioisotope the impurity at 1 y after EOB is indicated.

ground state formation and a more than 150 times lower one for the isomer after 4 h of the irradiation with 16 MeV protons. The isomer/ground state activity ratio at EOB substantially increases for the alpha particle route. However, due to the much larger range of protons than alpha particles in the CaCO<sub>3</sub> target, the isomer activity is only 1.5 lower than the ground state one for protons than for alpha particles of the same beam intensity and for the appropriate beam energies. Evidently, due to much larger <sup>44g</sup>Sc production a much longer cooling time is necessary for proton irradiation in order to obtain a pure <sup>44m</sup>Sc. All these aspects should be considered if an *in vivo* generator is to be synthesized [18].

<sup>47</sup>Sc. This therapeutic radioisotope, with a low energy β-decay, is the theranostic partner of Sc positron emitters and was previously produced using slow or fast neutrons from nuclear reactors [19-21]. The alternative accelerator routes are currently being investigated in a number of research centre's under the Cooperative Research Programme of the IAEA [22]. The (p,2n) reaction for the formation of this isotope was recently proposed [10,22] and was investigated in detail by our group [18]. It was shown that only a rather limited proton energy range can be used to produce relatively pure <sup>47</sup>Sc and even then a long cooling time of the irradiated sample is necessary to avoid the presence of <sup>48</sup>Sc, a radioisotope emitting a few high energy gamma lines, strongly increasing the patient dose (for 10 hours irradiation time, 150 hours after EOB the <sup>48</sup>Sc activity is 10% of the <sup>47</sup>Sc one and 420 hours are necessary to reach 1% contamination). Assuming that an activity of 2 GBq of <sup>47</sup>Sc is necessary for one therapeutic application, that the irradiation time is 10 hours and that the proton beam current is 100 μA, one irradiation leads to one patient application containing 1% contamination of the injected sample with <sup>48</sup>Sc.

The (p,2p) reaction on the rather cheap <sup>48</sup>Ti oxide was also investigated [18]. The reaction yield obtained at 28 MeV to 18 MeV

was, however, 12 times smaller than with the (p,2n) reaction and a substantial cooling time was also necessary.

<sup>44</sup>Ti/<sup>44g</sup>Sc. This 60 y half-life generator was previously produced by the Mainz team [23] using a 200 mA proton beam at 25 MeV on a thick <sup>45</sup>Sc target. As the half-life of the mother isotope is very long, the irradiation time was 200 days in order to obtain 185 MBq of <sup>44</sup>Ti activity. We have produced this isotope by the (α,2n) reaction on a thick <sup>42</sup>Ca target using a 29 MeV alpha particle beam. In Table 3, we present the TTY of <sup>44</sup>Ti production for an alpha particle beam within the investigated energy range. However, a substantial cross section for this reaction extends up to much higher energies. Therefore, using JANIS library, we also calculated the TTY value for the energy range 56 MeV to 12 MeV, the upper energy value corresponding to the expected alpha particle energy of the future high current SPIRAL2 linear accelerator [24]. The value obtained was 76 MBq/μAh. Assuming e.g. the future SPIRAL2 alpha particle beam intensity to be 3.6 pA the production of <sup>44</sup>Ti/<sup>44g</sup>Sc with equivalent strength to the Mainz generator would need about 20 days of irradiation time of maximum enriched, commercially available target material. Evidently, the question of whether the target can sustain such a high current should be resolved first.

<sup>211</sup>At. This prospective therapeutic alpha emitter has been studied at a number of places around the world [25-27]. The main problem encountered is the stability of the injected radiopharmaceuticals. Within our programme this radioisotope was and is currently produced by irradiation of a natural, mono-isotopic Bi target with a He<sup>+</sup> internal cyclotron beam [28,29]. The various ways of forming radiopharmaceuticals with it are being studied by our collaborators from the Institute of Nuclear Chemistry and Technology in Warsaw. The production efficiency as a function of the He<sup>+</sup> bombarding energy and the level of contamination by the very dangerous <sup>210</sup>At

was determined [29].

## Summary and Conclusions

Research into the production of prospective medical radioisotopes conducted at the Heavy Ion Laboratory of the University of Warsaw was begun a few years ago and is being actively pursued. In this paper a list of the targets and nuclear reactions investigated up to the present time was presented. Research on the synthesis of radiopharmaceuticals is performed at the Institute of Nuclear Chemistry and Technology in Warsaw and the POLATOM Department of the National Centre for Nuclear Research in Świerk, near Warsaw using the radioisotopes thus produced. The location of HIL in the Warsaw University scientific campus opens possibilities for large-scale interdisciplinary activity using the produced medical radioisotopes.

## Acknowledgments

The installation of the Radiopharmaceuticals Production and Research Centre at HIL-UW was supported by grants from the Polish Ministry of Sciences (project 4974/IA-IB/115/2004), Polish Ministry of Health (contract No. 4/7/2/2007/1834/3195), the International Atomic Energy Agency (Technical Cooperation Programme projects POL/04/016 and POL/04/018), Sectorial Operational Programme ICE (contract No. 1/1.4.3/2/2005/24/144/447/2007/U) and The Programme Innovative Economy under National Strategic Reference Framework (contract No. POIG.02.02.00-14-024/08-00). We thank M. Kisieliński for running the C30 cyclotron at Świerk, A. Jakubowski for his help in the sample irradiations and B. Radomyski and N. Keeley for editorial help. Part of this work was performed within the framework of the EU Horizon 2020 project RIA-ENSAR2 (654 002) and by the Polish Funding Agency NCBiR grant No. DZP/PBS3/2319/2014. This research is conducted in close collaboration with the Institute of Nuclear Chemistry and Technology in Warsaw. We warmly thank Aleksander Bilewicz and his team for their participation in this interdisciplinary research programme.

## References

- Jastrzębski J, Chojiński J, Cydzik I, Hechner D, Kilian K, Napiorkowski PJ, et al. Radiopharmaceuticals Production and Research Centre at the University of Warsaw. Proceedings of 5th International Conference on Imaging Technologies in Biomedical Sciences; 2009 Sep 13-16; Milos Island, Greece.
- Jastrzębski J. Radioactive nuclei for medical applications. *Acta Phys Pol B*. 2012;43:193-207.
- Choiński J, Jastrzębski J. The opening ceremony of the Radiopharmaceuticals Production and Research Centre at the Heavy Ion Laboratory of the University of Warsaw, May 15, 2012. Followed by an International Conference PETRAD2012. *Nucl Med Rev Cent East Eur*. 2012;15(2):163-4.
- Choiński J, Jastrzębski J, Kilian K, Mazur I, Napiorkowski PJ, Pekal A, et al. The Radiopharmaceuticals Production and Research Centre established by the Heavy Ion Laboratory of the University of Warsaw. *EPJ Web of Conferences*. 2014;66:10003.
- Choiński J, Czosnyka T, Dworski J, Jastrzębski J, Kownacki J, Kulczycka E, et al. Warsaw cyclotron: present status and plans of development. *Nukleonika*. 2013;48(2):S109-15.
- Sura J, Wejchert CZ, Kulinski S, Getka S. The C30 cyclotron for the production of the short-lived medical and industrial isotopes. A. Soltan Institute for Nuclear Studies (currently: National Centre for Nuclear Research) 1982/ZDAJ/PL/B internal report (1982), in polish.
- Marti F, editor. Proceedings from Sixteenth International Conference: Cyclotrons and their applications. AIP Conference Proceedings. Vol. 600; 2001. p. 513.
- Choiński J, Bracha T, Radomyski B, Swiatek L, Antczak M, Jakubowski A, et al. Accelerator production of  $^{99m}\text{Tc}$ - an external, well cooled, target holder for the PETtrace cyclotron. Annual Report HIL Warsaw; 2015.
- Walczak R, Krajewski S, Szkliniarz K, Sitarz M, Abbas K, Choiński J, et al. Cyclotron production of  $(43)\text{Sc}$  for PET imaging. *EJNMMI Phys*. 2015;2(1):33.
- Bilewicz A, Walczak R, Majkowska A, Misiak R, Choiński J, Sitarz M, et al. Cyclotron production of theranostic pair  $^{43}\text{Sc}$ - $^{47}\text{Sc}$  on calcium targets. *Eur J Nucl Med Mol Imaging*. 2016;43(1):S135.
- Severin GW, Engle JW, Valdovinos HF, Barnhart TE, Nickles RJ. Cyclotron produced  $^{44g}\text{Sc}$  from natural calcium. *Appl Radiat Isot*. 2012;70(8):1526-30.
- Valdovinos HF, Hernandez R, Barnhart TE, Graves S, Cai W, Nickles RJ. Separation of cyclotron-produced  $^{44}\text{Sc}$  from a natural calcium target using a dipentyl pentylphosphonate functionalized extraction resin. *Appl Radiat Isot*. 2014;95C:23-9.
- Grignon C, Barbet J, Bardiès M, Carlier T, Chatal JF, Couturier O, et al. Nuclear medical imaging using  $\beta+\gamma$  coincidence from  $^{44}\text{Sc}$  radio-nuclide with liquid xenon as detection medium. *Nucl Instrum Methods Phys Res A*. 2007;571(1-2):142-5.
- Lang C, Habs D, Parodi K, Thierolf PG. Sub-millimeter nuclear medical imaging with reduced dose application in positron emission tomography using  $\beta-\gamma$  coincidences. *J Inst*. 2013;0:1-19.
- Alliot C, Audouin N, Barbet J, Bonraisin AC, Bossé V, Bourdeau C, et al. Is there an interest to use deuteron beams to produce non-conventional radionuclides? *Front Med (Lausanne)*. 2015;2:31.
- Alliot C, Kerdjoudj R, Michel N, Haddad F, Huclier-Markai S. Cyclotron production of high purity ( $^{44m,44}\text{Sc}$ ) with deuterons from ( $^{44}\text{CaCO}_3$ ) targets. *Nucl Med Biol*. 2015;42(6):524-9.
- Duchemin C, Guertin A, Haddad F, Michel N, Métivier V. Production of scandium-44 m and scandium-44 g with deuterons on calcium-44: cross section measurements and production yield calculations. *Phys Med Biol*. 2015;60(17):6847-64.
- Sitarz M, Szkliniarz K, Jastrzębski J, Choiński J, Jakubowski A, Kapinos K, et al. Production of Sc medical radioisotopes with proton and deuteron beams. [preliminary data].
- Mausner LF, Kolsky KL, Joshi V, Srivastava SC. Radionuclide development at BNL for nuclear medicine therapy. *Appl Radiat Isot*. 1998;49(4):285-94.
- Müller C, Bunka M, Haller S, Köster U, Groehn V, Bernhardt P, et al. Promising prospects for  $^{44}\text{Sc}$ -/ $^{47}\text{Sc}$ -based theragnostics: application of  $^{47}\text{Sc}$  for radionuclide tumor therapy in mice. *J Nucl Med*. 2014;55(10):1658-64.
- [http://cra.iaea.org/cra/stories/2015-09-30-F22053-New\\_Emerging\\_Radionuclides.html](http://cra.iaea.org/cra/stories/2015-09-30-F22053-New_Emerging_Radionuclides.html)
- Report on the 1st Research Coordination Meeting on Therapeutic Radiopharmaceuticals Labelled with New Emerging Radionuclides ( $^{67}\text{Cu}$ ,  $^{186}\text{Re}$ ,  $^{47}\text{Sc}$ ). Vienna: IAEA; 2016.
- Roesch F. Scandium-44: benefits of a long-lived PET radionuclide available from the ( $^{44}\text{Ti}$ )/( $^{44}\text{Sc}$ ) generator system. *Curr Radiopharm*. 2012;5(3):187-201.
- Ferdinand R, Bernaudin PE, Di Giacomo M, Bosland P, Olry G, Gómez Martínez Y. Status and challenges of spiral2 SRF linac. Proceedings of 16th International Conference on RF Superconductivity (SRF2013), 2013 Sep; Paris, France. Joint Accelerator Conferences Website, SRF13, 2014.
- Zalutsky MR, Pruszyński M. Astatine-211: production and availability. *Curr Radiopharm*. 2011;4(3):177-85.

26. Wilbur DS, Hadley SW, Hines JJ, Atcher RW. Assessment of dry distillation methods for improving protein labeling yields with astatine-211. *J Labelled Compd Rad.* 1991;30:214-5.
27. Guerard F, Gestin JF, Brechbiel MW. Production of [211At]-astatinated radiopharmaceuticals and applications in targeted  $\alpha$ -particle therapy. *Cancer Biother Radiopharm.* 2013;28(1):1-20.
28. Cedrowska E, Łyczko M, Piotrowska A, Bilewicz A, Stolarz A, Trzcińska A, et al. Silver impregnated nanoparticles of titanium dioxide as carriers for 211At. *Radiochim Acta.* 2016;104(4):267.
29. Szkliniarz K, Jastrzębski J, Bilewicz A, Chajduk E, Choiński J, Jakubowski A, et al. Medical radioisotopes produced using the alpha particle beam from the Warsaw heavy ion cyclotron. *Acta Phys Pol A.* 2015;127:1471-4.
30. Szkliniarz K, Sitarz M, Jastrzębski J, Choiński J, Jakubowski A, Kapinos K, et al. Production efficiency and radioisotopic purity of 99mTc formed using the (p,2n) reaction on a highly enriched 100Mo target. *Mod Phys Lett A.* 2017;32(17):1740012.
31. Szkliniarz K, Sitarz M, Walczak R, Jastrzębski J, Bilewicz A, Choiński J, et al. Production of medical Sc radioisotopes with an alpha particle beam. *Appl Radiat Isot.* 2016;118:182-9.