INNOVATORY PRODUCTION OF RADIOISOTOPES ^{117m}Sn, ^{186}Re AND ^{188}Re FOR LABORATORY TESTS AND THE FUTURE APPLICATION IN NUCLEAR MEDICINE*

Natalia Młyńczyk[a], Adam Konefał[a], Andrzej Orlef[b]
Maria Sokół[b], Justyna Rostocka[a], Wioletta Lniak[a]
Bartłomiej Gawełczyk[a]

[a]Institute of Physics, University of Silesia in Katowice, Poland
[b]Department of Medical Physics
Maria Skłodowska-Curie Memorial Cancer Centre and Institute of Oncology
Gliwice, Poland

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In this work, innovatory production of three radioisotopes ^{117m}Sn, ^{186}Re and ^{188}Re, which can be used in nuclear medicine, is described. The natural tin and rhenium targets were irradiated by a high-energy 20 MV X-ray therapeutic beam from a medical linear accelerator. Additionally, the targets were in the photoneutron field. The radioisotopes were obtained in photonuclear and neutron reactions. A special lead-PMMA system was used to increase the slowed-down neutron flux in the target volume. The specific activities of ^{117m}Sn, ^{186}Re and ^{188}Re are 11 kBq/g, 2.6 MBq/g and 0.26 MBq/g in the saturation state, respectively. The produced amounts of the radioisotopes of tin and rhenium are sufficient for various laboratory tests in nuclear medicine.

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1. Introduction

In the last decade, several independent reactor shutdowns and outage extensions have significantly disrupted global radioisotope supplies [1]. Therefore, new methods of production of radioisotopes for nuclear medicine applications are required. The goal of this work was to extend our previous studies [2, 3] and to test a possibility of production of three prospective medical radionuclides: ^{117m}Sn, ^{186}Re and ^{188}Re, using medical linacs.

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^{117m}Sn is a diagnostically promising radioisotope, because it emits γ rays of 158.6 keV, which is close to the energy of ^{99m}Tc. The half-life ($T_{1/2}$) of 13.6 days and the γ decay to the stable state with a some amount of conversion electrons make this tin isomer an ideal alternative to ^{99m}Tc, especially considering the fact that the latter is contaminated with ^{99}Mo and when used in radio-pharmaceutical injections provides an unnecessary radiation dose to the patients [4, 5]. Until now, ^{117m}Sn was only suggested as an effective agent for the palliation of pain from bone metastases [6–8]. However, it is absent in the list of diagnostic radioisotopes because of its inefficient production in nuclear reactors.

^{186}Re ($T_{1/2}$ = 90.64 h) disintegrates by electron capture (EC) and β^+ (6.9%) and β^- (93.1%) decays. It emits γ rays with energies of 122.58 keV and 137.16 keV. Another rhenium radioisotope, ^{188}Re, ($T_{1/2}$ = 16.98 h) disintegrates by β^- decay and emits γ rays of 155.0 keV. The rhenium radioisotopes are used in the radiation therapy of elbow, hip and ankle joints of the youth [9]. The possibility of their production in medical linear accelerators installed almost in each oncology centre certainly contributes to studies on new applications of these radioisotopes in nuclear medicine.

2. Materials and methods

2.1. Characteristics of targets and reactions

Targets of natural tin and rhenium were irradiated at the Oncology Centre in Gliwice (Poland) using high-energy 20 MV X-ray therapeutic beams from two Varian medical linear accelerators: Clinac-2300 and TrueBeam. These radiotherapy systems are often equipped with such high-energetic photon beams. The high-energy photons induce photonuclear reactions (γ, n) in which radioisotopes as well as neutrons contaminating a therapeutic beam are produced [10–16]. These neutrons may induce some secondary reactions. The targets were mounted on the accelerator window in the therapeutic beam. Thus, they were activated both by high-energy photons and by neutrons. For rhenium, the targets were in a film form (57–60 mg/cm^2), whereas in the case of tin, they were small plastic containers filled with a tin powder (1.048–1.143 g/cm^2).

Three of ten natural stable tin isotopes were used for production of ^{117m}Sn *i.e.* ^{116}Sn (abundance of 14.54%), ^{117}Sn (7.68%) and ^{118}Sn (24.23%). ^{117m}Sn originated from the photonuclear reaction ^{118}Sn$(\gamma, n)^{117m}$Sn and from two reactions induced by neutrons: ^{116}Sn$(n, \gamma)^{117m}$Sn and ^{117}Sn$(n, n')^{117m}$Sn. The maximum photonuclear cross section of 290 mb corresponds to the photon energy of 15 MeV [17]. The neutron capture cross section does not exceed 6 mb [18]. The cross section for production of ^{117m}Sn in the neutron inelastic scattering reaction does not exceed 0.1 b [18] and a neutron energy over 317.2 keV is required.

Two natural stable rhenium isotopes: ^{185}Re (37.4%) and ^{187}Re (62.6%), were activated in the following reactions: $^{187}\mathrm{Re}(\gamma,n)^{186}\mathrm{Re}$, $^{185}\mathrm{Re}(n,\gamma)^{186}\mathrm{Re}$ and $^{187}\mathrm{Re}(n,\gamma)^{188}\mathrm{Re}$. The maximum photonuclear cross section is about 420 mb at 13 MeV [17] for ^{187}Re. The cross sections of the thermal neutron capture reactions are 120 b and 80 b [18, 19] for ^{185}Re and ^{187}Re, respectively. Moreover, these isotopes have many very large resonances for neutron capture, reaching even several tens of thousands barns in the energy range from 2 eV to about 1 keV [19]. Additionally, the fast neutron reaction $^{187}\mathrm{Re}(n,2n)^{186}\mathrm{Re}$ occurs for energies higher than 7.75 MeV (the maximum cross section of 2.24 b at 14.25 MeV) [20].

2.2. Experimental system and determination of the obtained activities

The location of a target during its irradiation is presented in Fig. 1. The lead-PMMA system located on the beam path was applied to increase the slowed-down neutron flux in the target. The 5 cm thick lead block was an additional neutron source, whereas the 10 cm PMMA layer was a neutron moderator and enhanced the neutron scattering.

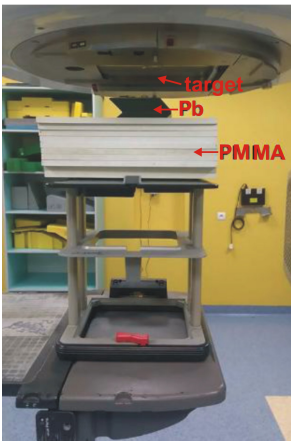

Fig. 1. A target located on the accelerator window and the lead-PMMA system.

The activities of the produced radioisotopes were determined from the measured γ-ray spectra of the radioactive decays. The spectra were acquired by means of two similar HPGe semiconductor detectors. The detection efficiency was $\varepsilon = 0.5\%$ at 1332 keV (^{60}Co) for a source located in the centre of the upper surface of the aluminum detector shield ($\varepsilon = N_{\mathrm{meas}}/N_{\mathrm{emit}}$ in %, N_{meas} — the number of counts (photons) observed by the detector, N_{emit} — the number of photons emitted by the source). The resolution of the detection setup was 1.2 keV at 1332 keV. The multiple samples were

measured separately in singles mode in two HPGe detectors. The energy and efficiency calibrations of the detectors were carried out with commercial sources of ^{152}Eu, ^{133}Ba and ^{60}Co. The summing effect was corrected by means of Monte Carlo simulation (Geant4 [21]). Each detector was connected to a multichannel analyser controlled by the Tukan8k software [22], also applied to calculate the photopeaks' net areas and, susequently, the activities of the radiosotopes produced in the targets.

3. Results and discussion

The γ-ray spectra representing the produced radioisotopes of tin and rhenium are presented in Fig. 2 (irradiation time: 15 minutes, beam rate: 600 monitor units per minute, which corresponds to 10^{12} photons per cm^2 per second on the surface of the accelerator window). The slowed-down neutron flux was 10^5 per cm^2 per second in the target volume [15].

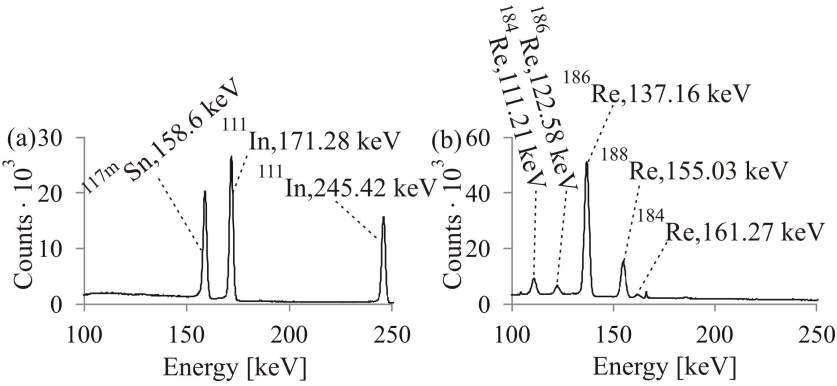

Fig. 2. The HPGe γ-ray spectra of the radioisotopes produced using targets of natural tin (a) and rhenium (b). A contamination by the radioisotopes of ^{111}In ($T_{1/2} = 2.81$ d) and ^{184}Re (139 h) is visible.

Employing the targets with a natural composition of tin and rhenium leads to the appearance of contaminations with the radioisotopes such as of ^{111}In and ^{184}Re. ^{111}In is a result of the radioactive decay of ^{111}Sn originating from the photonuclear reaction ^{112}Sn(γ, n) ^{111}Sn. The maximum cross section of this reaction is only 290 mb, the abundance of ^{112}Sn is only 0.97% and the half-life of ^{111}Sn (35.3 minutes) is relatively short. In consequence of the latter, it is easy to remove ^{111}In from the target, because the half-life of ^{117m}Sn is almost five times longer than the half-life of the undesirable indium radioisotope ($T_{1/2} = 2.81$ d). In the case of the Re target, such separation of radioisotopes is impossible, because ^{184}Re (resulting from ^{185}Re$(\gamma, n)^{184}$Re, 420 b at 15 MeV) has a half-life of 169 h, thus being longer than the half-lives

of the radioisotopes of ^{186}Re and ^{188}Re. The specific activity increased by using enriched tin with only the isotopes involved in the reactions of interest ensure that no ^{111}Sn is produced. The use of a target enriched in the heaviest rhenium isotopes limits the production of ^{184}Re.

The saturation curves for the produced radioisotopes are shown in Fig. 3. The saturation of activity of ^{186}Re is reached after about 400 hours of irradiation, whereas in the case of ^{188}Re, it is observed after about 120 hours. For ^{117m}Sn the longest irradiation time of about 2000 hours is needed to reach the saturation state, because this isomer of tin has the half-life much longer than the rhenium radioisotopes. The highest specific activity was obtained for ^{186}Re, being 2600 kBq/g in the saturation state, whereas the lowest one of 11 kBq/g was measured for ^{117m}Sn, which is far less than for the other rhenium isotope, ^{188}Re (260 kBq/g). The specific activities differ, because contrary to ^{117m}Sn, the produced rhenium radioisotopes have many high resonances for the neutron-capture reaction. Moreover, ^{186}Re can also be produced in the $(n, 2n)$ reaction induced by fast neutrons. The surfaces of the beam windows (13.5 cm × 13.5 cm) in typical medical accelerators are large enough to irradiate large targets and to get higher activities. The activities of the considered radioisotopes obtained for the accelerator window fully covered by the target and estimated for an irradiation time of 1 hour are shown in Table I.

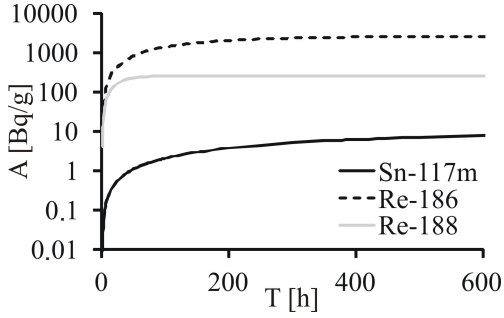

Fig. 3. The saturation curves for the activated targets located on the accelerator window. Irradiation was performed with the use of the lead-PMMA system. The curves were calculated on the base of a measurement lasting 15 minutes.

TABLE I

Estimated activity of produced radioisotopes for large 13.5 cm × 13.5 cm targets activated in a 20 MV therapeutic beam for 1 h.

Target	^{117m}Sn	^{186}Re	^{188}Re
Activity	4.2 kBq	3.6 MBq	2.1 MBq

4. Conclusions

The obtained specific activities, particularly those of ^{117m}Sn and ^{186}Re, are relatively low, which is mainly due to a relatively small neutron flux and mismatching of the therapeutic photon spectrum and the photonuclear cross sections. For the produced radioisotopes of tin and rhenium, the maximum cross sections for photonuclear reactions fall within the energy range of 13–15 MeV, while the photon energy spectrum of the 20 MV therapeutic beam applied in this study has its maximum at about 4.5 MeV. This problem was explained in details by Bzymek *et al.* [2]. When more massive targets are used (*e.g.* the irradiated mother isotope covers the whole surface of an accelerator window), the radioisotope yield can be increased. Such an approach is effective because the photon and neutron fluences are almost constant on the whole surface of the accelerator window. The radioisotopes of tin and rhenium of increased activity can be applied in various laboratory tests in nuclear medicine.

REFERENCES

[1] C. Ross *et al.*, *Physics in Canada* **66**, 19 (2010).
[2] E. Bzymek *et al.*, *Acta Phys. Pol. B* **47**, 777 (2016).
[3] E. Bzymek *et al.*, *Acta Phys. Pol. B* **48**, 671 (2017).
[4] D.R. Shearer *et al.*, *J. Nucl. Med.* **29**, 695 (1988).
[5] B.M. Dantas *et al.*, *Braz. Arch. Biol. Technol.* **48**, 2015 (2008).
[6] J. Vucina *et al.*, Fifth Yugoslav Nuclear Society Conference YUNSC — 2004, pp. 325–328.
[7] I. Martinez-Rovira, Y. Prezado, *Med. Phys.* **42**, 6703 (2015).
[8] B. Ponsard *et al.*, *Appl. Radiat. Isot.* **67**, 1158 (2009).
[9] J.B. Ćwikła *et al.*, *J. Ultrason.* **14**, 241 (2014).
[10] A. Konefał *et al.*, *Radiat. Prot. Dosim.* **128**, 133 (2008).
[11] A. Konefał *et al.*, *Phys. Med.* **24**, 212 (2008).
[12] K. Polaczek-Grelik *et al.*, *Appl. Radiat. Isot.* **70**, 2332 (2012).
[13] M. Janiszewska *et al.*, *Strahlenther Onkol.* **190**, 459 (2014).
[14] A. Konefał *et al.*, *Radiat. Prot. Dosim.* **162**, 197 (2014).
[15] A. Konefał *et al.*, *Rad. Meas.* **86**, 8 (2016).
[16] M. Bieniasiewicz *et al.*, *Acta Phys. Pol. B* **47**, 771 (2016).
[17] S.S. Dietrich, B.L. Berman, *At. Data Nucl. Data Tables* **38**, 199 (1998).
[18] Manual for reactor produced radioisotopes, IAEA-TECDOC-1340, 2003.
[19] B.V. Carlson *et al.*, *AIP Conf. Proc.* **769**, 1676 (2005).
[20] N. Jovančević, *Eur. Phys. J. A* **52**, 148 (2016).
[21] https://geant4.web.cern.ch/
[22] http://tukan.ncbj.gov.pl/?sLang=en