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Review Article

Application of therapeutic linear accelerators for the production of radioisotopes used in nuclear medicine

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Abstract

This review paper summarizes the possibilities of the use of therapeutic linear electron accelerators for the production of radioisotopes for nuclear medicine. This work is based on our published results and the thematically similar papers by other authors, directly related to five medical radioisotopes as ^{99}Mo/^{99m}Tc, ^{198}Au, ^{186}Re, ^{188}Re, ^{117m}Sn, produced using therapeutic linacs. Our unpublished data relating to the issues discussed have also been used here. In the experiments, two types of radiation were included in the analysis of the radioisotope production process, i.e. the therapeutic twenty-megavolt (20 MV) X-rays generated by Varian linacs and neutron radiation contaminating the therapeutic beam. Thus, the debated radioisotopes are produced in the photonuclear reactions and in the neutron ones. Linear therapeutic accelerators do not allow the production of radioisotopes with high specific activities, but the massive targets can be used instead. Thus, the amount of the produced radioisotopes may be increased. Apart from linear accelerators, more and more often, the production of radioisotopes is carried out in small medical cyclotrons. More such cyclotrons are developed, built, and sold commercially than for scientific research. The radioisotopes produced with the use of therapeutic linacs or cyclotrons can be successfully applied in various laboratory tests and in research.

Keywords: nuclear medicine; radioisotopes; therapeutic linacs.

Introduction

The interest in the development of medical radioisotopes used for noninvasive nuclear medicine imaging of disease and cancer therapy is growing.[1] Currently, the most medical radionuclides are produced in research nuclear reactors by irradiation of the uranium disks (fission reactions) or the targets enriched in the parent isotope (neutron capture reactions, (n,γ)).[1,2] However, over the past decade, several independent shutdowns and downtimes of the research reactors have significantly disrupted the global supply of radioisotopes,[3] which destroyed the current supply chain of the reactor product ^{99}Mo.[4]

With the advent of PET technology, the need for a more reliable supply of radionuclides with short half-lives drove the industry to develop small medical cyclotrons for the production of the primary radiopharmaceutical, fluorine-18-fluorodeoxyglucose (FDG). Today, there are literally thousands of small cyclotrons operating daily around the world for medical applications. More such cyclotrons are developed, built, and sold commercially than for scientific research; however, beyond FDG production, these accelerators are also used in research and in the production of various diagnostics and theranostic radionuclides, replacing the nuclear reactors. More than 80% of all diagnostic procedures in the world are carried out using ^{99m}Tc obtained from a ^{99}Mo/^{99m}Tc generator. ^{99m}Tc is a basic radioisotope used in nuclear medicine for diagnostics of the liver, lungs and bones.[5-8] The alternative accelerator-based production methods[9] of both ^{99}Mo and ^{99m}Tc include ^{238}U photofission,[10] phototransmutation of ^{100}Mo via the ^{100}Mo(γ,n)^{99}Mo channel[11] or the direct production of ^{99m}Tc via the ^{100}Mo(p,2n) transformation.[12] ^{99m}Tc can be produced in small medical cyclotrons, as reveals from the theoretical studies,[13] and the IAEA recommendations.[14] IAEA recommends using medical cyclotrons with proton energy of 18 MeV close the maximum cross section for production of ^{99m}Tc in the ^{100}Mo(p,2n)^{99m}Tc reaction on the highly ^{100}Mo-enriched target material.[14] The ^{99}Mo/^{99m}Tc complex used in the generators of technetium-99m is increasingly produced in the ^{100}Mo(γ,n)^{99}Mo photonuclear reaction,[15,16] using the linear electron accelerator by Mevex[17] with a nominal potential of 35 MV. This method of production of the ^{99m}Tc radioisotope is dominant in Canada. New methods of the production of ^{99m}Tc and other radioisotopes

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Authors' contribution: A – Research concept and design, B – Collection and/or assembly of data, C – Data analysis and interpretation, D – Writing the article, E – Critical revision of the article, F – Final approval of the article.

used in diagnostics and medical therapy are constantly being sought.[18-20]

The aim of this review is to present the "state of the art" of the research aimed at testing of the production of the selected medical radionuclides by means of therapeutic linear accelerators.[21-23] Our results on the production of five medical radioisotopes as ^{99}Mo/^{99m}Tc, ^{198}Au, ^{186}Re, ^{188}Re, and ^{117m}Sn using therapeutic linacs are summarized here, and the details of the nuclear reactions leading to the formation of these nuclei are discussed. Due to the interaction of high-energy electrons and photons with the accessories of the LINAC head, different secondary particles might be created.[24-30] The neutrons constitute one of the most important contamination of the therapeutic beams and cause extra doses to the patients during treatment.[31,32] However, the fluence rate of neutrons produced by the reactions with electrons is more than two orders of magnitude lower than that of the high-energy photons from the X-ray beams. Moreover, it strongly depends on the energy of the X-rays.[33-35] The neutron field generated around the therapeutic linear electron accelerator has a broad energy spectrum ranging from thermal and resonance neutrons to fast neutrons with energies of several MeV.[36-38] Particularly efficient production of radioisotopes occurs under the influence of slowed-down neutrons. In general, the slower the neutron, the greater the probability of the nuclear reaction. Due to the cross sections of nuclear reactions leading to the formation of radioisotopes, the high-energy X-rays and the therapeutically undesirable neutrons can be used to produce radioactive isotopes.[21-23]

Method

Characteristics of the X-ray and neutron fields

The field of high-energy X-rays occurs within a therapeutic beam. Outside a therapeutic beam, the fluence rate of the field drops sharply. The scheme of a therapeutic beam profile is presented in **Figure 1**. The simulations carried out by the Monte Carlo method using the GEANT4 code for the Clinac 2300 medical accelerator showed that the X-ray fluence rate reaches the values of 10^{10} - 10^{11} photons per second per unit area.[39]

As indicated in a number of works, the neutron field appears during the emission of the therapeutic beam throughout the treatment room. Its greatest intensity occurs in the immediate vicinity of the accelerator head. The thermal and resonance neutron fluence rates in the treatment room are depicted in **Figure 2**. The maximum neutron fluence rate reaches the value of 10^5 neutrons per second per unit area.[25,34]

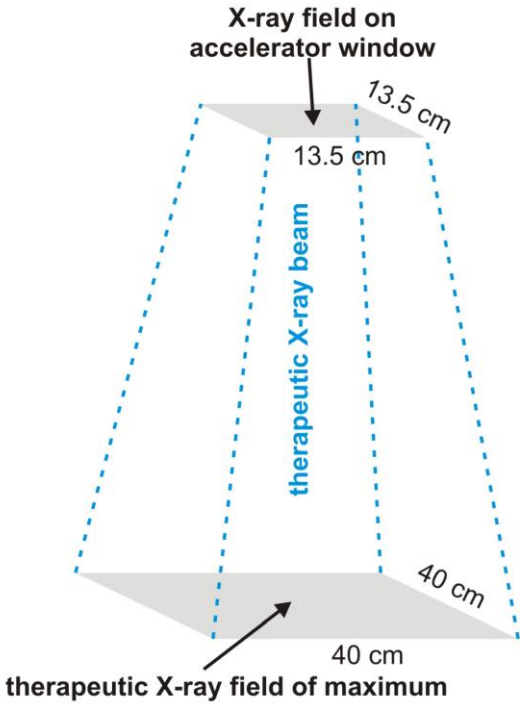


Figure 1. Schematic presentation of the area of the therapeutic X-ray beam in Varian linear accelerators for the 40 cm x 40 cm radiation at SSD (source - surface distance) = 100 cm. Outside the beam area, there is only scattered radiation dominated by lower-energy photons if therapeutic X-rays are used.

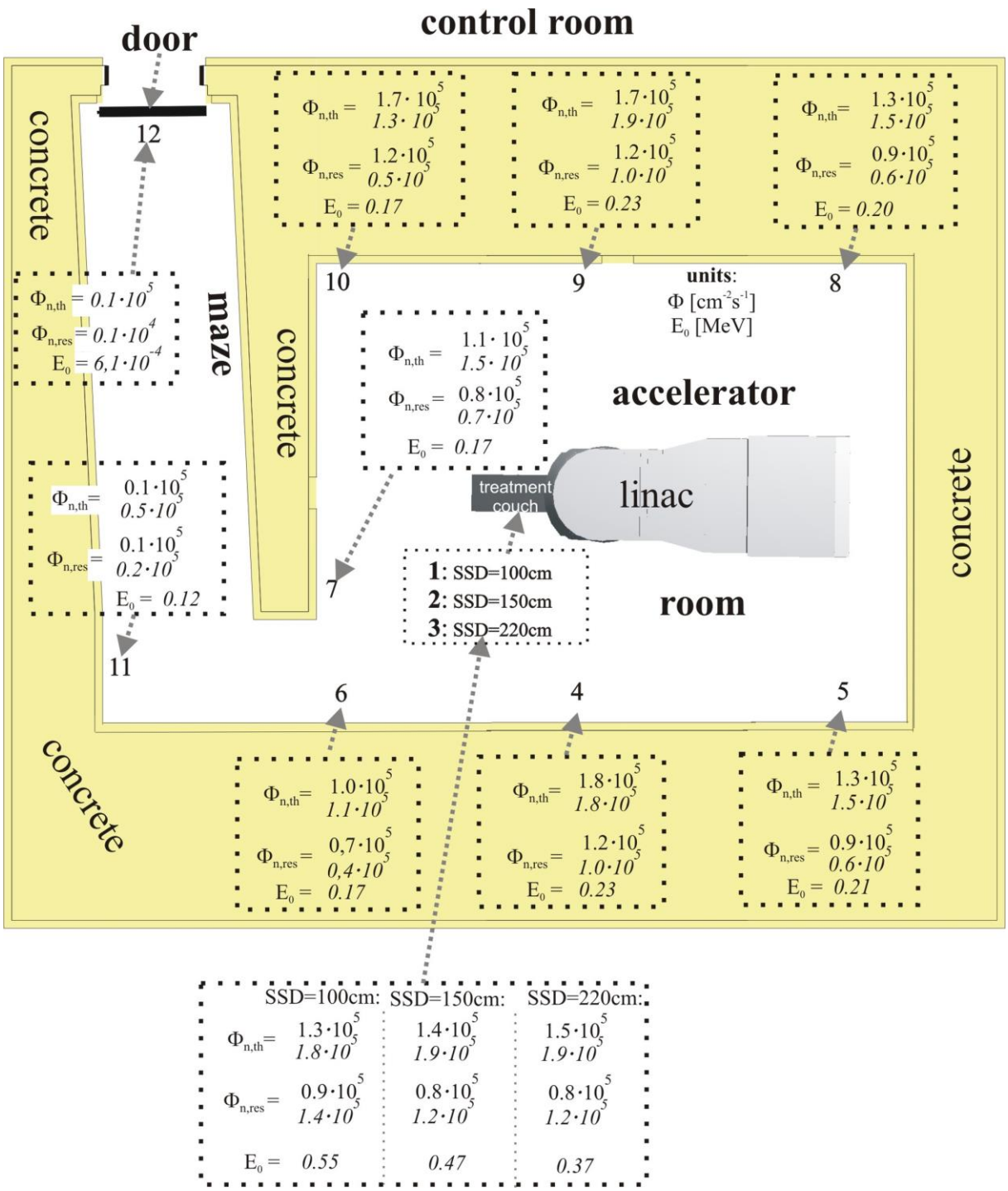


Figure 2. The scheme of the Clinac 2300 EX accelerator treatment room (maze + accelerator room): the distribution of the thermal neutron fluence rate $\Phi_{n,th}$, the resonance neutron fluence rate $\Phi_{n,res}$ and the average energies E_0 of neutrons during the emission of the 20 MV X-ray beam. The values in italics were obtained in the Monte Carlo (GEANT4) simulations, and the values in regular font were measured by the excited activity method with indium foil. The values of the fluence rate marked with the numbers 1-3 were determined on the surface of the treatment couch for three different SSD values. The values from 4 to 11 were determined on the wall surface at a distance of 1 m from the floor. The values marked with 12 correspond to the area of the door in the maze.

Thus, in order to produce a radioisotope in a photonuclear reaction, the irradiated material (target) must be placed within the therapeutic beam, while the neutron reactions can take place effectively anywhere in the accelerator room. Most often, however, the target is placed on the surface of the accelerator window (**Figure 3**), where both the X-ray fluence rate and the neutron one are the highest.[28]

To increase the neutron fluence rate, a lead-moderator system is often placed directly under the accelerator window (**Figure 4**). The moderator material is usually poly-methyl-methacrylate (PMMA) or other plastic. The photonuclear reactions take place in the lead layer, which makes lead an additional source of neutrons. Neutrons from lead are additionally slowed down in a layer of a moderator, enriching a field of slow neutrons. With longer exposure times, the lead becomes so radioactive that this fact cannot be ignored from a radiation protection point of view. Three radioisotopes: ^{209}Pb, ^{205}Pb, and ^{203}Pb, produced in the photonuclear and neutron capture reactions, contribute to this radioactivity. The first one is a β^- emitter with a half-life ($T_{1/2}$) of 2.3 h, emitting electrons with the maximum energy of 644 keV, which are converted to X-rays in lead. The next two radioisotopes disintegrate by electron capture (EC) and β^+ processes. The half-life of ^{205}Pb is long ($1.5 \cdot 10^7$ y), whereas that of ^{203}Pb is 51.9 h. Additionally, the latter radioisotope is a γ emitter emitting γ rays of energies of 279.2 keV and 680.5 keV. Therefore, after longer exposures, a lead-moderator system should be treated as radioactive waste.

Characteristics of nuclear reactions used for the radioisotope production

A medical linear accelerator (LINAC) customizes high energy X-rays or electrons as the therapeutic beams, as well as non-therapeutic neutron radiation. Therefore, the production of various radioisotopes is possible via three types of nuclear reactions: electronuclear, photonuclear and neutron ones. However, in practice, the electron beams are not effective, because, in the range of the therapeutic energies, the maximum cross sections for electronuclear reactions are 2-3 orders of magnitude smaller than those for photonuclear ones.

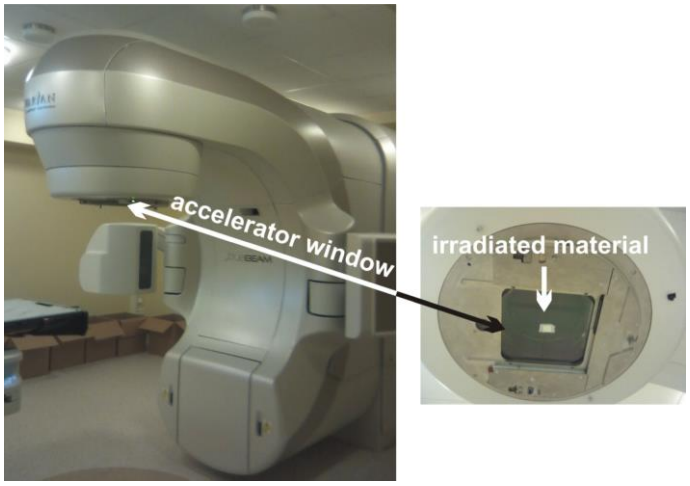


Figure 3. View of a medical linac and an accelerator window with an irradiated material (target).

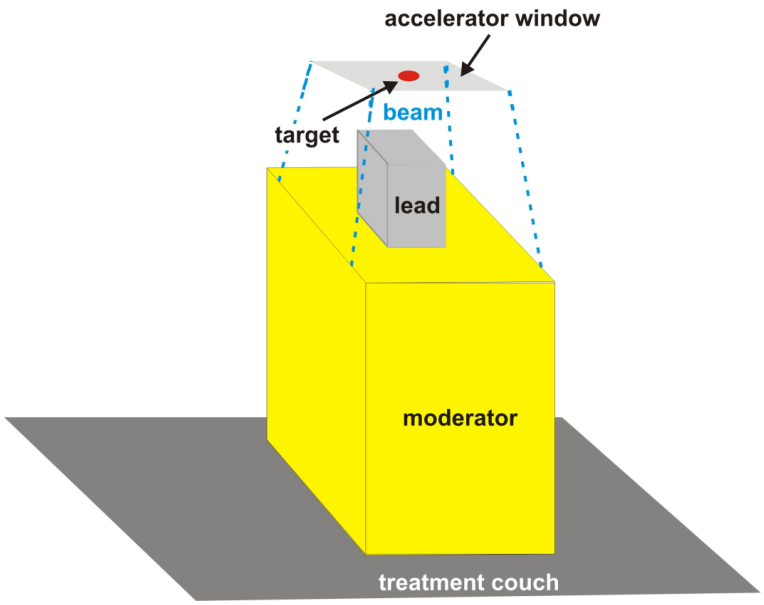


Figure 4. Scheme of the lead-moderator system used to increase the fluence rate of slowed-down neutrons. Neutrons created and slowed down in the lead-moderator system undergo further interactions, including elastic ones, which results in their further energy loss and increases the fluence rate of thermal and resonance neutrons also in the area of the irradiated material (target) on the surface of the accelerator window.

Photonuclear reactions

Due to the energy range of the therapeutic high-energy X-ray beams (being up to about 20 MeV), only photonuclear (photoneutron) reactions (γ,n) and (γ,2n) are used for the production of radioisotopes. Both the (γ,3n) reaction and the reactions in which the charged particles are produced, require higher energies. The photonuclear reactions are resonant in nature. The half-width of the resonance can reach even several MeV.[40,41] For this reason, these reactions are often referred to as a giant resonance. For heavy nuclei, the maximum cross section for the photonuclear reactions falls close to 12 MeV, and it shifts towards higher energies, up to 23 - 24 MeV, with the decreasing mass of the nucleus. For most isotopes, the threshold energies for the reactions (γ,n) are ca. 8 - 10 MeV. **Figure 5** presents the energy spectrum of a 20 MV therapeutic X-ray beam, juxtaposed with the cross sections for the photonuclear reactions for two isotopes of significantly different atomic numbers.

The energy spectrum of the 20 MV high-energy X-ray beam covers the energy range of the photonuclear reactions occurring for heavy nuclei, whereas that for the light nuclei reactions is only partially consistent with this spectrum. Moreover, in case of the isotopes with higher mass numbers, the cross-sections for the photonuclear reactions are larger by an order of magnitude. Therefore, the photonuclear reactions induced by the therapeutic X-ray beams are only used to produce the radioisotopes with a relatively large mass number.

Neutron reactions

Neutron capture reactions (n,γ) play an essential role in the production of radioisotopes, as their cross sections are high in the range of thermal and resonance energies. For many isotopes, the cross section values reach several tens of thousands of barns. Such example of a neutron capture reaction is shown in **Figure 6**. The inelastic neutron scattering reactions (n,n'), (n,γn') etc. are used less frequently.

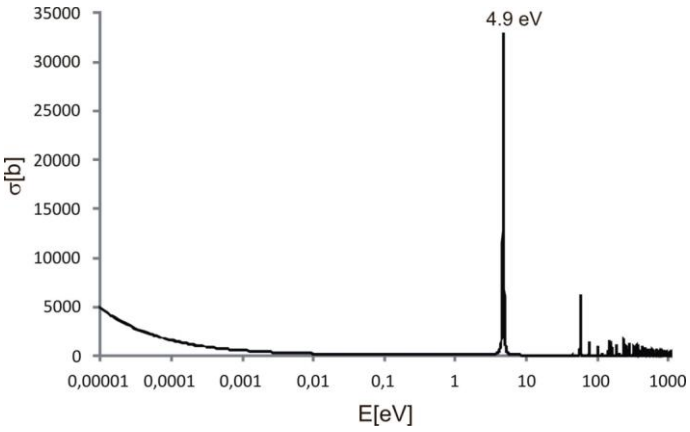


Figure 6. The cross section of the ^{197}Au(n,γ)^{198}Au reaction with a high resonance of 32910 b at 4.9 eV and several smaller resonances (drawn on the base of the ENDF data).

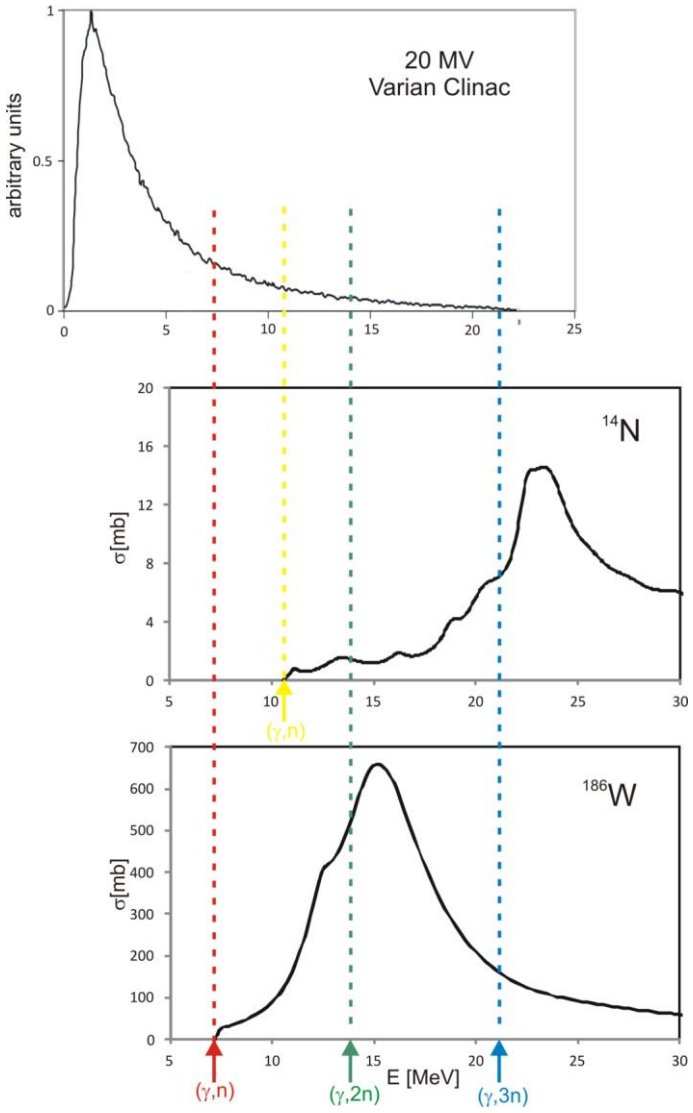


Figure 5. The energy spectrum of the therapeutic 20 MV X-ray beam from Clinac-2300 EX and the cross sections for the photonuclear reactions for two isotopes of significantly different mass numbers. The spectrum was obtained via the Monte Carlo simulation, and the cross sections were drawn on the basis of the IAEA's Evaluated Nuclear Data File (ENDF) data being consistent with the Atlas of Photoneutron Cross Sections.[40]

Determination of the activity of the generated radioisotopes

The activity of the produced radioisotopes is usually determined from the energy spectra of γ rays emitted by the disintegrating atomic nuclei of these radioisotopes. High-purity germanium (HPGe) detectors are most often used for gamma spectroscopy.

Results

The presented results were obtained using the therapeutic 20 MV beam of Varian medical linear accelerators (Clinac-2300 EX and TrueBeam). Five radioisotopes used in nuclear medicine, such as ^{99m}Tc, ^{198}Au, ^{186}Re, ^{188}Re and ^{117m}Sn were produced.

^{99m}Tc

The 1 mm thick natural molybdenum square-shaped (1 cm x 1 cm) targets were used by Bzymek at al. for production of ^{99m}Tc [21] using the radiation generated by the medical linacs. Three nuclear reactions (**Figure 7**) are of importance: ^{98}Mo(n,γ)^{99}Mo, ^{100}Mo(n,2n)^{99}Mo and ^{100}Mo(γ,n)^{99}Mo, the latter, a photonuclear reaction being the dominant. ^{99}Mo produced in this reaction, with a half-life of 65.94 h, decomposes to ^{99m}Tc ($T_{1/2}$ = 6.01 h). The cross section for the neutron capture reaction ^{98}Mo(n,γ)^{99}Mo (**Figure 7a**) that may take place in the neutron field is much smaller than that for the above-mentioned photonuclear reaction (**Figure 7b**). Moreover, on the surface of the accelerator window, where the targets are usually irradiated, the photon fluence rate at the target is about five orders of magnitude greater than the neutron one.

Though, the cross section of the ^{100}Mo(n,2n)^{99}Mo reaction is ~1.5 b in the neutron energy range from 12 to 17 MeV (**Figure 7b**), being 10-times larger than the thermal-neutron capture cross section of ^{98}Mo (**Figure 7a**), however, the former reaction is of minor importance, because at the target only 0.4% of all neutrons have energy greater than 8 MeV, as reveals from the Monte Carlo calculations.[21]

The specific activities A_s in the saturation state, obtained by Bzymek at al.[21], fall in the range from 155.4 to 163.2 kBq/g and their uncertainties are less than 1%.

^{196}Au and ^{198}Au

The thin targets made of natural gold (i.e. ^{197}Au, abundance of 100%) were used by Bzymek at al. for the production of the ^{196}Au ($T_{1/2}$ = 6.18 d) and ^{198}Au (2.70 d) radioisotopes.[22] ^{196}Au has yet to find its applications in nuclear medicine, while ^{198}A is used to treat cancer of the uterus, bladder, cervix, prostate, melanoma, breast, and skin. The targets were circle-shaped foils of 5 mm in diameter and 0.1 mm thick. They were irradiated with the therapeutic 20 MV X-ray beam from the Clinac-2300 EX accelerator.

The neutron capture reaction ^{197}Au(n,γ)^{198}Au was the main source of ^{198}Au, whereas ^{196}Au was obtained in the photonuclear ^{197}Au(γ,n)^{196}Au reaction. The energy dependence of the cross sections of the (γ,n) and (n,2n) reactions is presented in **Figure 8**, whereas that for the (n,γ) is available in **Figure 6**: apart from the high resonances, in the range of the thermal energies the value of 96 barns for the ^{197}Au(n,γ)^{198}Au reaction is seen.[41]

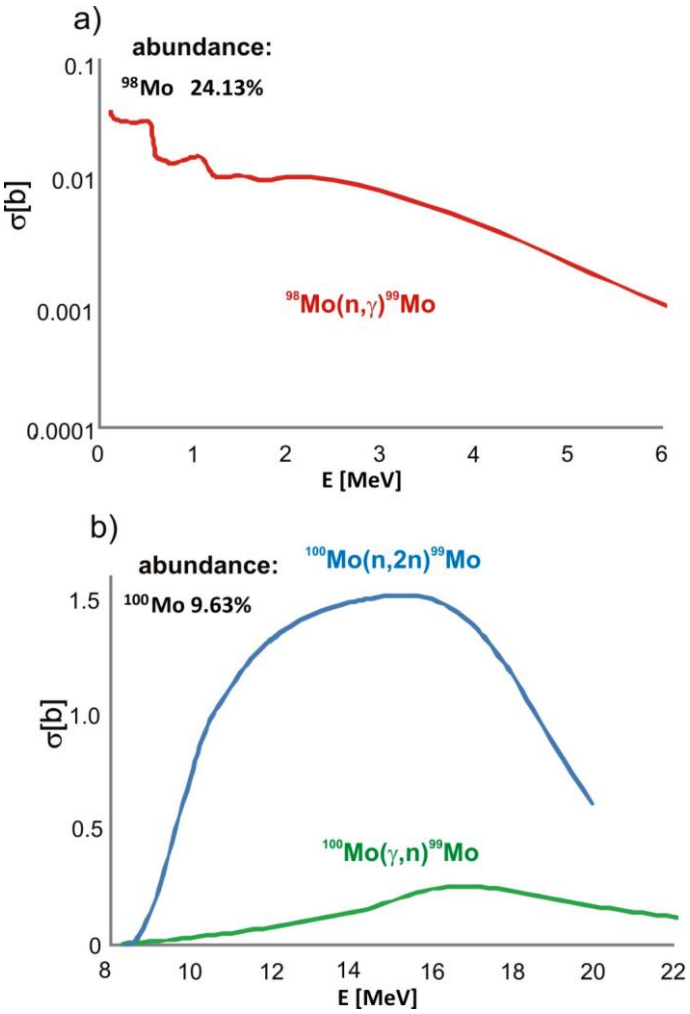


Figure 7. The cross sections of the following reactions: a) ^{99}Mo and ^{98}Mo(n,γ)^{99}Mo and b) ^{100}Mo(γ,n)^{99}Mo, ^{110}Mo(n,2n) considered as possible ways of production of ^{99}Mo, drawn on the base of the ENDF data.

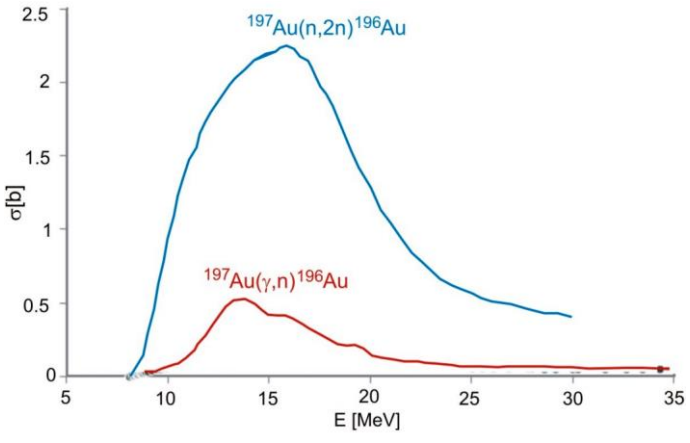


Figure 8. The cross sections of the following reactions: ^{197}Au(γ,n)^{196}Au and ^{197}Au(n,2n)^{196}Au considered as the possible ways of production of ^{196}Au (drawn on the base of the ENDF data).

The second gold radioisotope, ^{196}Au, was produced in the photonuclear reaction.[22] The (n,2n) reaction, despite of its cross section being higher than that of the (γ,n) reaction (**Figure 8**), does not play a role in this production, because of similar reasons as in the case of the ^{99}Mo production. ^{196}Au can also be produced in the proton cyclotrons in the (p,p'n) reaction. The cross section for this reaction reaches the maximum of 0.2 b at 45 MeV.[42] The cyclotrons used in proton therapy are well suited to carry out this reaction.

The irradiation conditions and activities of the ^{198}Au radioisotope obtained by Bzymek et al.[22] with the 20 MV X-ray beam from Clinac-2300 EX are collected in **Table 1**. The authors showed a relationship between the obtained activities and the size of the radiation field. The obtained maximum specific activity A_s of the ^{196}Au radioisotope was 1.5 MBq, the value being significantly higher than that of ^{198}Au. It was obtained when the target was irradiated on the surface of the accelerator window.

As revealed in **Table 1** the lead-PMMA system influences the obtained activities of the gold radioisotopes.

^{186}Re, ^{188}Re and ^{184}Re

Rhenium is composed of two naturally abundant isotopes ^{187}Re (abundance: 62.6%) and ^{185}Re (abundance: 37.4%). Using a medical linear accelerator and natural rhenium targets it is possible to produce ^{186}Re and ^{188}Re – two radioisotopes used in nuclear medicine.[23,51,52] These radioisotopes are obtained in the following nuclear reactions: ^{187}Re(γ,n)^{186}Re, ^{185}Re(n,γ)^{186}Re and ^{187}Re(n,γ)^{188}Re. The natural rhenium targets in the form of the 5 mm × 5 mm square-shaped foils (57-60 mg/cm^2) were used by Młyńczyk et al.[23] for the production of the rhenium radioisotopes. The targets were irradiated with 20 MV X-ray therapeutic beam from the Clinac 2300-EX medical linac. For ^{187}Re the maximum photonuclear cross section is about 420 mb at 13 MeV.[43] For ^{185}Re and ^{187}Re the cross sections of the thermal neutron capture reactions are 120 b and 80 b, respectively.[44,45] Moreover, these isotopes have many high resonances for the neutron capture, reaching even several tens of thousands of barns in the energy range from 2 eV to about 1 keV.[45] Additionally, the fast neutron reaction ^{187}Re(n,2n)^{186}Re occurs for energies higher than 7.75 MeV (the maximum cross section of 2.24 b at 14.25 MeV).[43] Rhenium-186 ($T_{1/2}$ = 90.64 h) disintegrates by electron capture and by the β^+ (6.9%) as well as β^- (93.1%) decays, emitting γ rays with the energies of 122.58 keV and 137.16 keV. The second rhenium radioisotope, rhenium-188 ($T_{1/2}$ = 16.98 h), disintegrates by a β^- decay and emits γ rays of 155.03 keV. In addition to rhenium-186 and rhenium-188, the rhenium-184 radioisotope with a half-life of 38 d is also produced. It originates from the photonuclear reaction ^{185}Re(γ,n)^{184}Re (420 b at 15 MeV) and decays by electron capture and a β^+ decay, emitting, among others, 111.21 keV γ rays. Currently, this radioisotope has not found yet any application in nuclear medicine, similarly as gold-196. However, it can be a calibration source, due to its relatively long half-life. The use of a target enriched in the heavier natural rhenium isotope limits the production of ^{184}Re. The obtained activities of ^{186}Re and ^{188}Re in the saturation state for various radiation conditions are presented in **Table 2**.

Table 1. The obtained specific activities of gold-198 in the saturation state A_s for the various radiation field sizes and target locations. The radiation fields related to the therapeutic 20 MV X-ray beam were determined on the accelerator window, i.e. in a horizontal plane perpendicular to the main axis of the used therapeutic beam at SSD = 67.5 cm. The target was located on the surface of the accelerator window or on a wall of the treatment room.[22]

Target location	Radiation field size	A_s [kBq/g]
Wall of accelerator room	1 cm × 1 cm	96.6 ± 1.0
Window of accelerator	1 cm × 1 cm	145.0 ± 1.5
Wall of accelerator room	13.5 cm × 13.5 cm	82.2 ± 0.8
Window of accelerator	13.5 cm × 13.5 cm	97.7 ± 1.0
Window of accelerator *	13.5 cm × 13.5 cm	510.4 ± 5.1

** With the PMMA – lead system.*

Table 2. The obtained specific activities of rhenium-186 and rhenium-188 in the saturation state A_s for various irradiation conditions. The radiation fields were specified as described in Table 1.[23]

Radioisotope	Target location	Radiation field size	A_s [kBq/g]
rhenium-186	Window of accelerator	3.5 cm × 3.5 cm	2359.3 ± 1.7
	Window of accelerator *	3.5 cm × 3.5 cm	2394.8 ± 4.7
	Window of accelerator	13.5 cm × 13.5 cm	1603.0 ± 2.9
	Window of accelerator *	13.5 cm × 13.5 cm	2618.9 ± 7.8
	Outside the beam **	13.5 cm × 13.5 cm	147.1 ± 18.4
rhenium-188	Window of accelerator	0.5 cm × 3.5 cm	83.1 ± 0.9
	Window of accelerator *	3.5 cm × 3.5 cm	263.9 ± 0.6
	Window of accelerator	13.5 cm × 13.5 cm	71.3 ± 0.2
	Window of accelerator *	13.5 cm × 13.5 cm	287.9 ± 1.0
	Outside the beam **	13.5 cm × 13.5 cm	62.0 ± 10.9

** With the PMMA-lead system, ** on the wall of the accelerator room.*

The activities of ^{186}Re are significantly greater than those of ^{188}Re. This is due to the fact that the lighter radioisotope is produced in three nuclear reactions, while the heavier one is produced only in the neutron capture reaction. As in the case of the gold radioisotopes (**Table 1**) the influence of the radiation field on the obtained activities of rhenium radioisotopes is visible. The presence of the lead-PMMA system, which increases the fluence rate of the neutrons slowed down in the target on the accelerator window, causes a strong increase in the obtained activities.

^{117m}Sn

^{117m}Sn (nuclear isomer) is a diagnostically promising radioisotope, because it emits γ rays of 158.6 keV, which is close to the energy of ^{99m}Tc.[47] Its half-life is $T_{1/2}$ = 13.6 d, and its decay to a stable state is accompanied by the emission of conversion electrons of discrete energies and range, which make this tin isomer an ideal alternative to ^{99m}Tc,[48] 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.[49,50] Until now, ^{117m}Sn was only suggested as an effective agent for the palliation of pain from bone metastases.[47,48] However, it is absent in the list of diagnostic radioisotopes because of its inefficient production in research nuclear reactors.

Młyńczyk et al.[23] produced ^{117m}Sn using the targets of natural tin in the form of small plastic containers filled with tin powder (1.048-1.143 g/cm^2). The targets were irradiated using the 20 MV X-ray beam generated by the TrueBeam medical linear accelerator. Three of ten natural stable tin isotopes reveal to be suitable for the ^{117m}Sn production: ^{116}Sn (abundance of 14.54%), ^{117}Sn (7.68%) and ^{118}Sn (24.23%). ^{117m}Sn originates from the photonuclear reaction ^{118}Sn(γ,n)^{117m}Sn and from two reactions induced by neutrons: ^{116}Sn(n,γ)^{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.[40] The neutron capture cross section does not exceed 6 mb.[44] The cross section for the production of ^{117m}Sn in the neutron inelastic scattering reaction does not exceed 0.1 b[44] and neutron energy over 317.2 keV is required. In their experiment, Młyńczyk et al. obtained ^{117m}Sn with a specific activity of 11 kBq/g in the saturation state.[23] However, when employing the targets with a natural mixture of tin isotopes, some contaminations with ^{111}In must be expected. ^{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 ^{111}Sn has a relatively short half-life of 35.3 minutes. Thus, 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).

Discussion and conclusions

The specific activities of all obtained radioisotopes are low compared with those reached in the research nuclear reactors or cyclotrons, which is mainly due to a relatively small neutron fluence rate as well as mismatching of the used therapeutic beam spectrum and the photonuclear cross sections. In the case of all considered radioisotopes used in nuclear medicine, the maximum cross sections of the photonuclear reactions fall within the energy range of 13-17 MeV, while the energy spectra of the therapeutic 20 MV X-ray beams applied in the studies reviewed in this paper have their maximum at about 2.5 MeV.

A serious limitation in the production of the considered radioisotopes is the long irradiation time needed to obtain the saturation state of activity. **Table 3** shows the irradiation times necessary to achieve 97% activity at a radioactive equilibrium for the main produced radioisotopes. In practice, such long emissions of the therapeutic beams are impossible, because the medical accelerators are intended for use in radiotherapy. Therefore, **Table 3** also presents the specific activities of the produced radioisotopes after one hour of irradiation (A_{1h}) for the targets and the irradiation conditions used in the presented studies.

Table 3. Irradiation times, t, of the targets necessary to reach 0.97 A_s, i.e. $t \approx 5T_{1/2}$, and the specific activities A_{1h} of the produced radioisotopes after one hour of irradiation for the targets irradiated with the 20 MV X-ray beams from the Varian medical linear accelerators.

Radioisotope	t [h]	A_{1h} [kBq/g]
^{99}Mo	330	1.7
^{198}Au	324	5.4
^{186}Re	453	19.9
^{188}Re	85	11.6
^{117m}Sn	1632	below 0.1

The obtained activities of the produced radioisotopes are appropriate for laboratory tests, for example, for testing new pharmaceuticals, etc. However, it should be noted that in the presented experiments, the small-sized targets were used. Medical accelerators allow placing in the high-energy X-rays or neutron fields the targets containing large masses of the materials intended for the production of radioisotopes. When using massive targets, larger amounts of radioisotopes can be produced, despite a low specific activity. Thus, the use of medical accelerators, commonly available devices, for the production of radioisotopes will contribute to the dissemination of the laboratory research on medical radioisotopes, which will certainly entail the development of nuclear medicine.

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