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PRODUCTION OF ^{68}Ge, ^{64}Cu, ^{86}Y, ^{89}Zr, ^{73}Se, ^{77}Br AND ^{124}I POSITRON EMITTING RADIONUCLIDES THROUGH FUTURE LASER-ACCELERATED PROTON BEAMS AT ELI-BEAMLINES FOR INNOVATIVE PET DIAGNOSTICS

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ABSTRACT. The development of innovative production pathways for high-Z positron emitters is of great interest to enlarge the applicability of PET diagnostics, especially in view of the continuous development of new radiopharmaceuticals. We evaluated the theoretical yields of ^{64}Cu, ^{86}Y, ^{89}Zr, ^{73}Se, ^{77}Br and ^{124}I PET isotopes, plus the ^{68}Ge isotope, parent of the ^{68}Ga positron emitter, in the hypothesis of production through laser-accelerated proton sources expected at the ELI-Beamlines facility. By means of the TALYS software we simulated the nuclear reactions leading to the above radionuclides, hypothesizing three possible scenarios of broad proton spectra, with maximum energies of about 9, 40 and 100 MeV. The production yields of the studied radionuclides, within the expected fluences, appear to be suitable for pre-clinical applications.

1. Introduction

The Extreme Light Infrastructure (ELI) project will build three large-scale laser facilities. Among these, ELI-Beamlines, currently in commissioning phase in Prague (Czech Republic), is planned to deliver intense sources of multi-MeV proton beams potentially applicable to several bio-medical purposes (Bulanov *et al.* 2014; Macchi, Borghesi, and Passoni 2013; Masood *et al.* 2014; Torrisi *et al.* 2015), among which nuclear medicine applications are of our particular interest (Amato *et al.* 2013, 2011, 2012). Positron emitter radionuclides to be used in PET diagnostics are usually obtained by inducing nuclear reactions through cyclotron accelerated proton beams on several targets (IAEA 2008). In this field, laser-accelerated proton or deuteron beams were proposed as potential sources (Fritzler *et al.* 2003; Kimura and Bonasera 2011; Ledingham *et al.* 2004; Spencer *et al.* 2001). The ELI-Beamlines fully diode-pumped PW laser system will operate up to 10 Hz to get intensities in the order of 10^{22} W cm^{-2} (Margarone *et al.* 2015, 2012) and proton fluences around 10^{11} p/pulse, corresponding to a current of 160 nA, when operating at 10 Hz. In this work we aim to study the feasibility to produce high-Z PET nuclides by using the laser-accelerated proton sources planned at the ELI-Beamlines facility. In particular, we

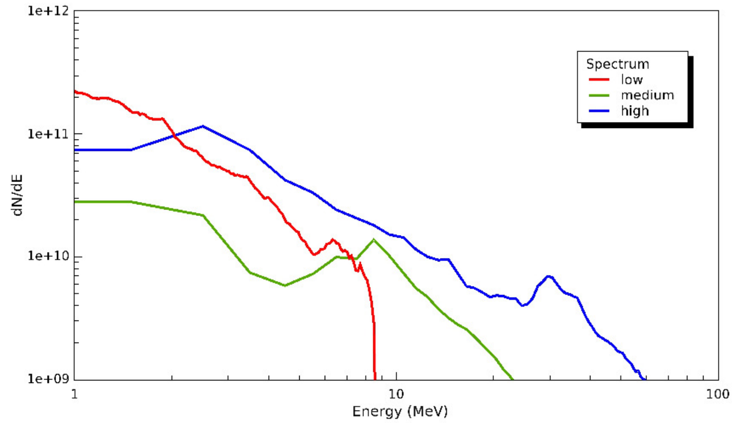

FIGURE 1. Proton spectra expected at the ELI-Beamlines facility in the three energy ranges considered.

devote our attention to six among the most promising positron emitting nuclides to be used for PET diagnostics and theranostics, i.e., ^{64}Cu, ^{86}Y, ^{89}Zr, ^{73}Se, ^{77}Br and ^{124}I, plus the ^{68}Ge isotope, which is the parent nucleus of the positron emitter ^{68}Ga. Recent studies have shown the increasing interest for these nuclides in PET diagnostics (Anderson and Ferdani 2009; Braad *et al.* 2015; Rangacharyulu and Roh 2015; Zhang, Hong, and Cai 2011), that pushed forward the development of experimental techniques of production (Braghirolli *et al.* 2014; Holland, Sheh, and Lewis 2009; Obata *et al.* 2003; Sadeghi *et al.* 2009).

2. Materials and methods

The design of ELI-Beamlines plant forecasts a set of proton beams, with their respective energy spectra and fluences, that can in principle be employed for our purposes. In particular, we considered low-, medium- and high-energy spectra, corresponding to $5 \cdot 10^{19}$, $7 \cdot 10^{20}$ and $5 \cdot 10^{21}$ W cm^{-2} laser intensity in the "Target Normal Sheath Acceleration" (TNSA) regime. In TNSA regime, ions can be accelerated due to different physical processes, depending on the region of the target. Generally speaking, ions acceleration is due to intense electric fields, originating by strong charge separations created by laser-matter interactions. The two main mechanisms of concurrent charge displacement are: the laser ponderomotive force acting on electrons at the front surface, and the partial conversion of the laser radiation into kinetic energy of relativistic electrons. These electrons give rise to an extremely intense longitudinal electric field, which is responsible for the efficient ion acceleration (Passoni, Bertagna, and Zani 2010). Figure 1 reports the hypothesized energy spectra employed for our simulations and Table 1 summarizes the main features assumed in the three irradiation regimes. Low- and medium-energy spectra come from experimental measurements performed at APRI-GIST facility (South Korea), that is equipped with a 0.1-1 PW, 30-fs, 0.1 Hz laser, while the high-energy spectrum is obtained by numerical simulations assuming the expected PW, 30 fs, 10 Hz laser system at ELI-Beamlines (Margarone *et al.* 2015, 2012).

TABLE 1. Proton source terms adopted.

Reference	laser intensity (W cm^{-2})	rep. rate (Hz)	proton E_{max} (MeV)	charge (p/pulse)	current (nA)
Low	$5 \cdot 10^{19}$	1-10	9	$4.7 \cdot 10^{11}$	75.2 - 752
Medium	$7 \cdot 10^{20}$	1-10	40	$1.6 \cdot 10^{11}$	25.6 - 256
High	$5 \cdot 10^{21}$	1-10	100	$6.5 \cdot 10^{11}$	104 - 1040

The production yields of ^{68}Ge, ^{64}Cu, ^{86}Y, ^{89}Zr, ^{73}Se, ^{77}Br and ^{124}I were calculated from the nuclear reaction channels listed below:

$$^{69}Ga + p \rightarrow {}^{68}Ge + 2n \quad (1)$$
$$^{64}Ni + p \rightarrow {}^{64}Cu + n \quad (2)$$
$$^{86}Sr + p \rightarrow {}^{86}Y + n \quad (3)$$
$$^{89}Y + p \rightarrow {}^{89}Zr + n \quad (4)$$
$$^{73}As + p \rightarrow {}^{73}Se + n \quad (5)$$
$$^{77}Se + p \rightarrow {}^{77}Br + n \qquad (a) \quad (6)$$
$$^{78}Se + p \rightarrow {}^{77}Br + 2n \qquad (b) \quad (7)$$
$$^{124}Te + p \rightarrow {}^{124}I + n \quad (8)$$

We considered the (p,n) or $(p,2n)$ reactions on several targets, and we selected the most efficient channel for each desired nuclide. All considered targets (^{69}Ga, ^{64}Ni, ^{86}Sr, ^{89}Y, ^{73}As, $^{77,78}Se$, ^{124}Te) are in solid state and in pure isotopic form. Due to the wide proton energy spectra assumed, in conjunction with the possible presence of contaminant elements and isotopes in target materials, several competing nuclear reactions can in principle arise, alongside with the desired channels of production. They would act as sources of undesired isotopes, which can lower the purity and specific activity of products. As an example, ^{64}Cu production via channel (2) requests a ^{64}Ni solid enriched target. IAEA (2009) reports that ^{64}Ni enriched more than 95% leads to a ^{64}Cu production with purity higher than 99%. In particular, the contaminant nuclides ^{60}Cu, ^{61}Cu, ^{55}Co, ^{61}Co and ^{57}Ni are produced. While ^{55}Co, ^{61}Co and ^{57}Ni can be chemically separated from Cu isotopes, ^{60}Cu ($T_{1/2} = 24\,\text{min}$) and ^{61}Cu ($T_{1/2} = 3.3\,\text{hrs}$), having half-lives shorter than ^{64}Cu ($T_{1/2} = 12.7\,\text{hrs}$), become negligible after a suitably chosen cooling time. Obata *et al.* (2003), using low energy protons, have shown that the Cu contaminants are not detectable at three hours from EOB.

A different scenario is encountered for ^{124}I production through proton bombardment of ^{124}Te, where an overlap between the cross sections for ^{124}I and ^{123}I production occurs between about 12 and 30 MeV. For this reason, IAEA TRS 468 recommends to use proton beams in $(9 \div 13)$ MeV energy interval. However, a separation between ^{124}I and ^{123}I isotopes is feasible exploiting the faster decay of ^{123}I ($T_{1/2} = 13\,\text{hrs}$) with respect to ^{124}I ($T_{1/2} = 4.2$ days). In our calculations, we assumed that the surface area and thickness of the target are large enough to absorb the whole proton beam. Considering that the incident particle flux follows a broad spectrum, the rate of radionuclide production, R, can be evaluated as:

$$R = n\chi \left(1 - e^{-\lambda t}\right) \int_{E_0}^{0} \frac{\phi(E)\cdot\sigma(E)}{dE/dx} dE \tag{9}$$

where n is the target thickness in nuclei per cm^2, χ is the chemical target purity, $\phi(E)$ is the differential incident particle flux, λ is the decay constant of the produced nuclide in s^{-1}, t is the irradiation time in seconds, σ is the reaction cross-section in cm^2, E_0 is the initial energy of the incident particles in MeV and dE/dx is the energy loss by the projectile per unit path length (IAEA 2008).

The total production yields of each nuclide for the three proton spectra were calculated through TALYS software, rel. 1.6 (Koning, Hilaire, and Duijvestijn 2005). TALYS is a code simulating nuclear reactions that can calculate, in a wide range of projectile energies (from 1 keV to several hundred MeV), many nuclear quantities. This code includes the so-called *medical isotope production* option which provides, from a pre-loaded database of nuclear cross-sections, the total activity of a given nuclide produced in the chosen channel, for a set value of energy (MeV) and beam current (mA). In this modality, TALYS allows to set the residual energy of projectiles after traversing the target. By setting this parameter to zero, we ensured that the target thickness was considered large enough to fully stop the beam. After dividing each proton spectrum into a number of energy bins, TALYS was cyclically run by means of an *ad-hoc* written script, and the total production yields were obtained by summation over the whole energy spectrum. In detail, the low-energy spectrum was divided in 80 energy bins, while 40 and 100 bins were adopted for the medium-energy and high-energy spectra, respectively.

3. Results and discussion

The production yields of the seven positron emitting radionuclides under consideration, for low- medium- and high-energy regimes, are reported in Figs. 2, 3 and 4, respectively, assuming an End Of Bombardment (EOB) of 60 min with 1 Hz of repetition rate. The production yields Y were evaluated for a typical irradiation time T_{irr} = 1 h with a pulse repetition rate ν = 1 Hz and then re-scaled for a generic irradiation time T_{irr} and repetition rate ν according to the following equation:

$$Y(T_{irr},\nu) = Y(1h,1Hz)\cdot\nu\cdot\frac{1-e^{-\lambda T_{irr}}}{1-e^{-\lambda 1h}}. \tag{10}$$

The next step consisted in the integration of the production yields, for each radionuclide, over the whole energy interval, as reported in Table 2 for two hypotheses of irradiation times (60 and 120 min) and three repetition rates (1, 5 and 10 Hz), as results from the application of Eq. 9. To keep into account the performances offered by cyclotron production methods, in the same table we compare our results with the experimental yields obtainable by means of low and medium energy cyclotrons, as reported by literature.

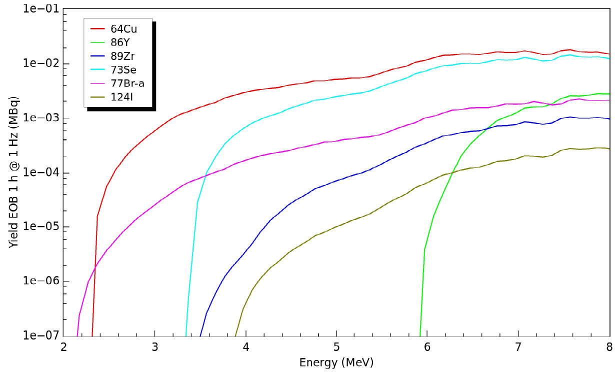

FIGURE 2. Radionuclide production yields vs. proton energy in the low-energy regime.

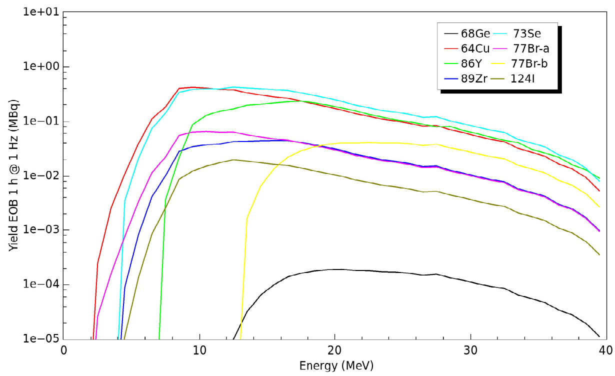

FIGURE 3. Radionuclide production yields vs. proton energy in the medium-energy regime.

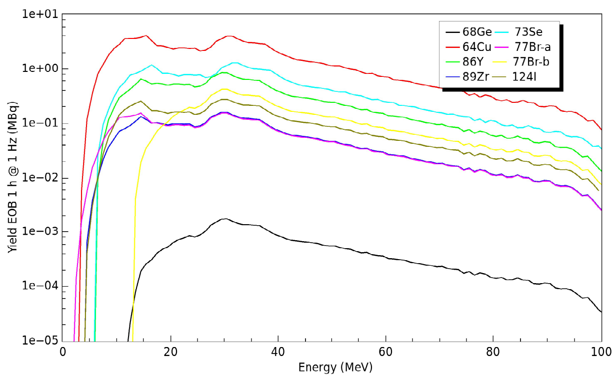

FIGURE 4. Radionuclide production yields vs. proton energy in the high-energy regime.

TABLE 2. Total production yields in the three proton energy regimes for different irradiation times (min) and repetition rates (Hz). A comparison with medical cyclotron production yields (Y^{cycl}, in MBq/μAh units) at given proton energies (E^{cycl}, in MeV units) is reported from literature.

Nuclide	$T_{1/2}$(min)	Y^{cycl}	E^{cycl}	Ref.	ν	1	1	5	5	10	10
					T_{irr}	60	120	60	120	60	120
					spectrum			Y(MBq)			
^{68}Ge	389980.8	3.4	50	(A)	low	0.000	0.000	0.000	0.000	0.000	0.000
					medium	0.003	0.006	0.016	0.031	0.031	0.062
					high	0.044	0.088	0.219	0.438	0.438	0.876
^{64}Cu	762	70	13	(B)	low	0.5	1.0	2.5	4.8	4.9	9.5
					medium	5.5	10.6	27.3	53.1	54.6	106.3
					high	133.6	260.1	668.1	1300.7	1336.2	2601.4
^{86}Y	1483.2	100	22	(A)	low	0.0	0.1	0.2	0.4	0.4	0.8
					medium	3.5	6.9	17.5	34.5	35.0	69.0
					high	25.1	49.5	125.6	247.6	251.1	495.3
^{89}Zr	4708.8	56	15	(C)	low	0.0	0.0	0.1	0.2	0.2	0.4
					medium	0.7	1.4	3.6	7.2	7.2	14.3
					high	4.9	9.7	24.5	48.7	48.9	97.4
^{73}Se	432				low	0.3	0.6	1.7	3.1	3.3	6.3
					medium	6.5	12.5	32.7	62.3	65.3	124.6
					high	39.6	75.6	198.2	378.1	396.3	756.2
$^{77}Br^{(a)}$	3427.2	100	15	(D)	low	0.1	0.1	0.3	0.5	0.5	1.0
					medium	0.9	1.7	4.4	8.7	8.8	17.5
					high	5.0	9.9	24.9	49.5	49.8	99.0
$^{77}Br^{(b)}$	3427.2	200	30	(E)	low	0.0	0.0	0.0	0.0	0.0	0.0
					medium	0.7	1.3	3.3	6.5	6.5	12.9
					high	9.7	19.3	48.7	96.7	97.3	193.4
^{124}I	6048	13	12.6	(F)	low	0.0	0.0	0.0	0.0	0.0	0.0
					medium	0.3	0.5	1.3	2.6	2.6	5.2
					high	8.8	17.6	44.1	87.9	88.2	175.8

(A) IAEA (2009); (B) Obata *et al.* (2003); (C) Holland, Sheh, and Lewis (2009);
(D) Hassan and Qaim (2011); (E) Spahn *et al.* (2011); (F) Schmitz (2011).

Figure 5 describes a comparison between the activities obtained for each radionuclide in the three energy regimes in the original calculation conditions of EOB = 60 min at 1 Hz. A detailed analysis of the production yields for the different radionuclides leads to observe that potential clinically relevant amounts of activities (hundreds of MBq) can be achieved for ^{64}Cu, ^{86}Y and ^{73}Se nuclides at repetition rates higher than 5 Hz. ^{64}Cu presents the highest yield among all nuclides, with about 1.3 GBq attainable, with the high-energy proton spectrum, at EOB 120 min and 5 Hz or 60 min and 10 Hz. However, the use of high-energy protons can lead to lower specific activities with respect to the ones obtainable at low

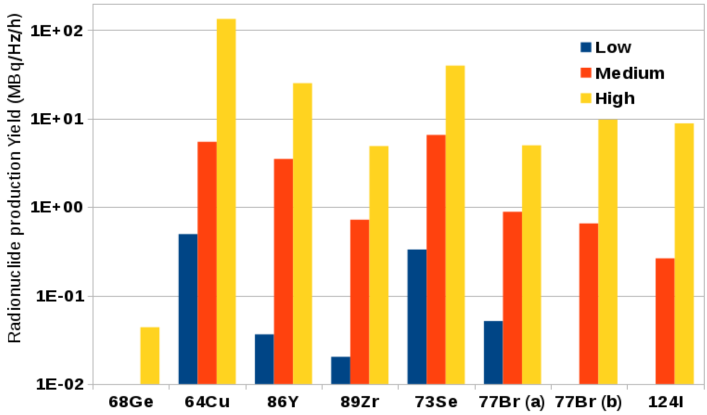

FIGURE 5. Comparison between the total radionuclide production yields for EOB= 60 min at 1 Hz, in the three proton energy regimes considered.

energy. Lower values of final activity can be produced for other nuclides. In particular, all radionuclides but ^{68}Ge show production yields from tens to hundreds of MBq, that can be useful for pre-clinical applications. The medium-energy proton spectrum, above 5 Hz, can produce such quantities of ^{64}Cu, ^{86}Y and ^{73}Se, while the high-energy regime is requested to yield comparable activities for ^{89}Zr, ^{77}Br and ^{124}I. From a comparison with the low-Z radionuclide production yields reported in a previous work (Amato *et al.* 2016a,b), one can infer that most of the high-Z nuclides studied in the present work show lower yields, no matter the energy regime employed, due also to the shorter half-lives of ^{18}F, ^{11}C, ^{15}O and ^{13}N with respect to the nuclides analysed in the present study.

4. Conclusions

The innovative production techniques for high-Z PET radionuclides, recently proposed as an alternative to conventional cyclotrons, represent a powerful challenge for the application of laser-accelerated particle beams inducing nuclear reactions. The research of more efficient preparation methods for these novel positron emitters is particulaly relevant, in view of the continuous development of new radiopharmaceuticals. Through the TALYS software, an evaluation of the theoretical yields of ^{68}Ge, ^{64}Cu, ^{86}Y, ^{89}Zr, ^{73}Se, ^{77}Br and ^{124}I isotopes was performed.

Our study suggests that, with the proton fluences expected at the ELI-Beamlines facility, a proper combination of irradiation time and repetition rate, can in principle yield relevant activity amounts for several radionuclides, useful in pre-clinical applications. The possibility to get clinically relevant levels of activity with laser beam techniques requires further studies and experimental development, regarding beam intensities, target systems and activity recovery methods. In particular, in order to compete with traditional medical cyclotrons, these innovative acceleration techniques should evolve towards narrower energy spectra characterized by higher fluences, while the traditional technological issues about targetry and radiochemical methods of separation must be studied, as well as for accelerator-based facilities, to minimize the use of expensive enriched target materials and post bombardment chemical pathways of purification.

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References

Amato, E., Italiano, A., Margarone, D., Pagano, B., Baldari, S., and Korn, G. (2016a). “Future laser-accelerated proton beams at ELI-Beamlines as potential source of positron emitters for PET”. *Journal of Instrumentation* **11**. DOI: 10.1088/1748-0221/11/04/C04007.

Amato, E., Italiano, A., Margarone, D., Pagano, B., Baldari, S., and Korn, G. (2016b). “Study of the production yields of ^{18}F, ^{11}C, ^{13}N and ^{15}O positron emitters from plasma-laser proton sources at ELI-Beamlines for labeling of PET radiopharmaceuticals”. *Nuclear Instruments and Methods in Physics Research, Section A: Accelerators, Spectrometers, Detectors and Associated Equipment* **811**, 1–5. DOI: 10.1016/j.nima.2015.12.011.

Amato, E., Italiano, A., Minutoli, F., and Baldari, S. (2013). “Use of the GEANT4 Monte Carlo to determine three-dimensional dose factors for radionuclide dosimetry”. *Nuclear Instruments and Methods in Physics Research, Section A: Accelerators, Spectrometers, Detectors and Associated Equipment* **708**, 15–18. DOI: 10.1016/j.nima.2013.01.014.

Amato, E., Lizio, D., Ruggeri, R., Raniolo, M., Campennì, A., and Baldari, S. (2011). “An analytical model for improving absorbed dose calculation accuracy in non spherical autonomous functioning thyroid nodule”. *Quarterly Journal of Nuclear Medicine and Molecular Imaging* **55**(5), 560–566.

Amato, E., Minutoli, F., Pacilio, M., Campennì, A., and Baldari, S. (2012). “An analytical method for computing voxel S values for electrons and photons”. *Medical Physics* **39**(11), 6808–6817. DOI: 10.1118/1.4757912.

Anderson, C. and Ferdani, R. (2009). “Copper-64 radiopharmaceuticals for PET imaging of cancer: Advances in preclinical and clinical research”. *Cancer Biotherapy and Radiopharmaceuticals* **24**(4), 379–393. DOI: 10.1089/cbr.2009.0674.

Braad, P., Hansen, S., Thisgaard, H., and Høilund-Carlsen, P. (2015). “PET imaging with the non-pure positron emitters: ^{55}Co, ^{86}Y and ^{124}I”. *Physics in Medicine and Biology* **60**(9), 3479–3497. DOI: 10.1088/0031-9155/60/9/3479.

Braghirolli, A., Waissmann, W., Da Silva, J., and Dos Santos, G. (2014). “Production of iodine-124 and its applications in nuclear medicine”. *Applied Radiation and Isotopes* **90**, 138–148. DOI: 10.1016/j.apradiso.2014.03.026.

Bulanov, S., Wilkens, J., Esirkepov, T., Korn, G., Kraft, G., Kraft, S., Molls, M., and Khoroshkov, V. (2014). “Laser ion acceleration for hadron therapy”. *Physics-Uspekhi* **57**(12), 1149–1179. DOI: 10.3367/UFNe.0184.201412a.1265.

Fritzler, S., Malka, V., Grillon, G., Rousseau, J. P., Burgy, F., Lefebvre, E., *et al.* (2003). “Proton beams generated with high-intensity lasers: Applications to medical isotope production”. *Applied Physics Letters* **83**, 3039–3041. DOI: 10.1063/1.1616661.

Hassan, H. and Qaim, S. (2011). “A critical survey of experimental cross section data, comparison with nuclear model calculations and estimation of production yields of ^{77}Br and ^{77}Kr in no-carrier-added form via various nuclear processes”. *Nuclear Instruments and Methods in Physics*

Research, Section B: Beam Interactions with Materials and Atoms **269**(10), 1121–1129. DOI: 10.1016/j.nimb.2011.02.080.

Holland, J., Sheh, Y., and Lewis, J. (2009). “Standardized methods for the production of high specific-activity zirconium-89”. *Nuclear Medicine and Biology* **36**(7), 729–739. DOI: 10.1016/j.nucmedbio.2009.05.007.

International Atomic Energy Association (2008). *Cyclotron produced radionuclides: principles and practice*. No. 465. Technical Reports Series.

International Atomic Energy Association (2009). *Cyclotron produced radionuclides: physical characteristics and production methods*. No. 468. Technical Reports Series.

Kimura, S. and Bonasera, A. (2011). “Deuteron-induced reactions generated by intense lasers for PET isotope production”. *Nuclear Instruments and Methods in Physics Research, Section A: Accelerators, Spectrometers, Detectors and Associated Equipment* **637**, 164–170. DOI: 10.1016/j.nima.2011.02.043.

Koning, A., Hilaire, S., and Duijvestijn, M. (2005). “TALYS: Comprehensive nuclear reaction modeling”. *AIP Conference Proceedings* **769**, 1154–1159. DOI: 10.1063/1.1945212.

Ledingham, K. W. D., McKenna, P., McCanny, T., Shimizu, S., Yang, J. M., Robson, L., *et al.* (2004). “High power laser production of short-lived isotopes for positron emission tomography”. *Journal of Physics D: Applied Physics* **37**, 2341–2345. DOI: 10.1088/0022-3727/37/16/019.

Macchi, A., Borghesi, M., and Passoni, M. (2013). “Ion acceleration by superintense laser-plasma interaction”. *Reviews of Modern Physics* **85**(2), 751–793. DOI: 10.1103/RevModPhys.85.751.

Margarone, D., Kim, I., Psikal, J., Kaufman, J., Mocek, T., Choi, I., Stolcova, L., Proska, J., Choukourov, A., Melnichuk, I., Klimo, O., Limpouch, J., Sung, J., Lee, S., Korn, G., and Jeong, T. (2015). “Laser-driven high-energy proton beam with homogeneous spatial profile from a nanosphere target”. *Physical Review Special Topics - Accelerators and Beams* **18**(7). DOI: 10.1103/PhysRevSTAB.18.071304.

Margarone, D., Klimo, O., Kim, I., Prokůpek, J., Limpouch, J., Jeong, T., Mocek, T., Pkal, J., Kim, H., Proka, J., Nam, K., Tolcová, L., Choi, I., Lee, S., Sung, J., Yu, T., and Korn, G. (2012). “Laser-driven proton acceleration enhancement by nanostructured foils”. *Physical Review Letters* **109**(23). DOI: 10.1103/PhysRevLett.109.234801.

Masood, U., Bussmann, M., Cowan, T., Enghardt, W., Karsch, L., Kroll, F., Schramm, U., and Pawelke, J. (2014). “A compact solution for ion beam therapy with laser accelerated protons”. *Applied Physics B: Lasers and Optics* **117**(1), 41–52. DOI: 10.1007/s00340-014-5796-z.

Obata, A., Kasamatsu, S., McCarthy, D., Welch, M., Saji, H., Yonekura, Y., and Fujibayashi, Y. (2003). “Production of therapeutic quantities of ^{64}Cu using a 12 MeV cyclotron”. *Nuclear Medicine and Biology* **30**(5), 535–539. DOI: 10.1016/S0969-8051(03)00024-6.

Passoni, M., Bertagna, L., and Zani, A. (2010). “Target normal sheath acceleration: Theory, comparison with experiments and future perspectives”. *New Journal of Physics* **12**. DOI: 10.1088/1367-2630/12/4/045012.

Rangacharyulu, C. and Roh, C. (2015). “Isotopes for combined PET/SPECT imaging”. *Journal of Radioanalytical and Nuclear Chemistry* **305**(1), 87–92. DOI: 10.1007/s10967-015-3945-4.

Sadeghi, M., Aboudzadeh, M., Zali, A., and Zeinali, B. (2009). “^{86}Y production via ^{86}Sr(p,n) for PET imaging at a cyclotron”. *Applied Radiation and Isotopes* **67**(7-8), 1392–1396. DOI: 10.1016/j.apradiso.2009.02.038.

Schmitz, J. (2011). “The production of [^{124}I]iodine and [^{86}Y]yttrium”. *European Journal of Nuclear Medicine and Molecular Imaging* **38**(SUPPL. 1), S4–S9. DOI: 10.1007/s00259-011-1782-4.

Spahn, I., Shehata, M., Spellerberg, S., Scholten, B., Coenen, H., Qaim, S., Steyn, G., Vermeulen, C., Kovács, Z., and Szelecsényi, F. (2011). “Investigation of production possibilities of radiobromines for diagnostic and therapeutic applications”. *Journal of the Korean Physical Society* **59**(23), 1983–1986. DOI: 10.3938/jkps.59.1983.

Spencer, I., Ledingham, K. W. D., Singhal, R. P., McCanny, T., McKenna, P., Clark, E. L., *et al.* (2001). "Laser generation of proton beams for the production of short-lived positron emitting radioisotopes". *Nuclear Instruments and Methods in Physics Research, Section B: Beam Interactions with Materials and Atoms* **183**, 449–458. DOI: 10.1016/S0168-583X(01)00771-6.

Torrisi, L., Calcagno, L., Giulietti, D., Cutroneo, M., Zimbone, M., and Skala, J. (2015). "Laser irradiations of advanced targets promoting absorption resonance for ion acceleration in TNSA regime". *Nuclear Instruments and Methods in Physics Research, Section B: Beam Interactions with Materials and Atoms* **355**, 221–226. DOI: 10.1016/j.nimb.2015.01.019.

Zhang, Y., Hong, H., and Cai, W. (2011). "PET tracers based on zirconium-89". *Current Radiopharmaceuticals* **4**(2), 131–139. DOI: 10.2174/1874471011104020131.

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