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Research Article

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Laser-accelerated Proton Beams from a Solid Hydrogen Target as a Future Source of Radionuclides for Positron Emission Tomography

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Abstract The production of radionuclides for positron emission tomography through future laser-accelerated proton beams is an interesting perspective. We evaluated the production yields that can be expected according to a new source term based on three-dimensional particle-in-cell (PIC) simulations of the laser available at ELI-Beamlines interacting with an innovative cryogenic hydrogen target. Results indicate that 370 MBq activity can be reached within a few minutes of irradiation for the four conventional PET nuclides ^{18}F, ^{11}C, ^{13}N and ^{15}O, and for several heavier positron emitters, such as ^{60}Cu, ^{62}Cu, ^{63}Zn, ^{68}Ga and ^{73}Se, currently used in pre-clinical and clinical studies.

Keywords Laser, particle acceleration, positron emission tomography, Extreme Laser Infrastructure

Introduction

Currently the availability of efficient, compact and cost-effective systems for producing radioactive isotopes to be employed in diagnostic and therapeutic procedures of nuclear medicine is a challenge which can be potentially overcome thanks to emerging laser-acceleration technologies, due to their compactness and flexibility.

As a matter of fact, PW-class laser facilities are being built within the ELI (Extreme Light Infrastructure) pan-European project, such as the ELI-Beamlines facility in the Czech Republic which will deliver intense pulsed beams of protons and other light hadrons for various multidisciplinary applications based on the availability of a PW-class, 10-Hz laser system [1]. The potential use of laser accelerated proton/ion beams for medical applications grew in these last years, in particular for the development of laser-based hadrontherapy which would benefit in terms of cost-effectiveness (compact accelerator and beam transport, reduced shielding) as well as flexibility since, in principle, the same "laser accelerator" can produce different secondary sources (ions, electrons, X-rays, neutrons) with controllable energy spectra, thus potentially paving the way towards a hybrid cancer treatment and diagnostic setups. Furthermore, due to the possibility to distribute the same laser beam in different locations just using light optical mirrors instead of heavy magnetic device, additional "end-stations" can be developed, for instance for the generation of radionuclides that can be used "in place" for positron emission tomography (PET) applications.

The concept of laser-based production of PET nuclides has been preliminary investigated in some experiments, [2-4] and also quantitative estimates in terms of production yield for given radioisotopes were given through theoretical studies [5-7]. Such theoretical estimations were based on proton source terms experimentally

measured at the APRI-GIST facility (0.1-1 PW, 30 fs, 0.1 Hz) in South Korea and also based on numerical prediction in the so-called Target Normal Sheath Acceleration (TNSA) regime [8-9]. Such laser acceleration regime can be realized experimentally at moderate intensities (>10^{18} W/cm^2) and with ~μm thick foils used as targets [10].

Further theoretical estimates have been recently proposed for the production of some of the most common radionuclides employed in PET [6-7], assuming a laser intensity of 7E+20 Wcm^{-2}, linearly (p-)polarized laser beam of 4 μm (FWHM) width, with a number of protons/pulse of 1.6E+11 and maximum proton energy of 40 MeV and also for a laser intensity of 5E+21 Wcm^{-2}, number of protons/pulse of 6.5E+11 and maximum proton energy of 100 MeV impinging on a nanostructured target.

More recently, a new source term has been proposed based on three-dimensional particle-in-cell (PIC) simulations of the laser available at ELI-Beamlines (PW-class, 10 Hz) interacting with an innovative cryogenic hydrogen target (continuous flow of a solid-H ribbon) recently tested with a kJ-class laser [11]. In optimal conditions, in terms of laser intensity on target, our PIC simulations show that the proton spectrum can be controlled by tuning the laser fluence and polarization (keeping constant the laser pulse energy) both in terms of proton energy and proton fluxes, the latter being very high at relatively low proton energies. Such configuration is ideal for PET since the cross sections for typically produced radionuclides present maxima at moderate proton energies (around 10-20 MeV).

Materials and Methods

In this work we show how new perspectives arise from the adoption of the new source term simulated by 3D-PIC proton spectrum (laser intensity =2E+21 Wcm^{-2}, circularly polarized light, 5 μm FWHM focal spot diameter, 2.5E+13 total number of protons per pulse and 20.6 MeV maximum proton energy for a solid-H target). Based on such new data, reported in Fig. 1, we evaluated the production yields for a large set of radioisotopes by means of the TALYS code (rel. 1.8) and a suitably adapted approach, [5,12] assuming an irradiation time of T_{irr} = 1 h, and laser repetition rates of 1, 5 and 10 Hz.

As in our previous study, concerning irradiation geometry, the target surface area was considered large enough to intercept the whole proton flux, and the target thickness large enough to fully absorb the projectiles.

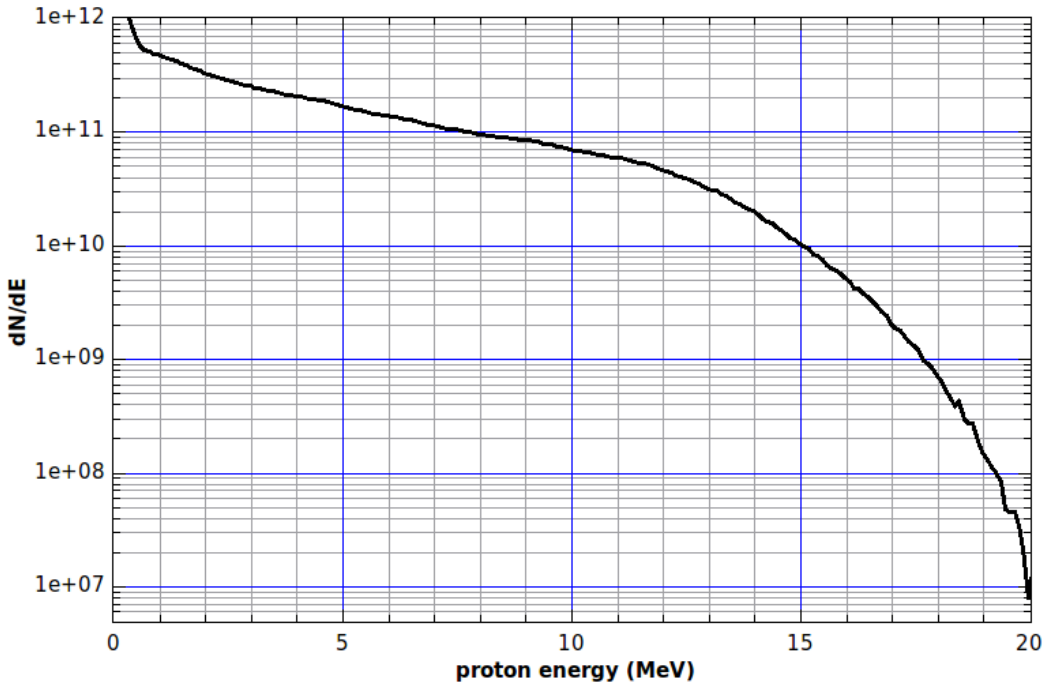

Figure 1: The new source term simulated by 3D-PIC proton spectrum

In our calculations we extended the set of radionuclides already investigated in Refs. [5-7], to a wider range of nuclides, in order to study most of the positron emitters currently employed or proposed as suitable candidates for clinical applications [13].

Results and Discussion

Table 1 reports the yields for the proton spectra produced from the solid-H target.

Bearing in mind that the PW-class laser available at ELI-Beamlines is expected to operate up to 10 Hz, and assuming that the innovative cryogenic H-target delivery system can, in principle, also operate with 10 Hz repetition rate, high production yields could be achieved and the resulting estimates appear realistic. Consequently, the production of a 10 mCi (370 MBq) activity needed in average to prepare a single clinical dose of a PET radiopharmaceutical, can be reached abundantly within a few minutes of irradiation both for the four *conventional* PET nuclides ^{18}F, ^{11}C, ^{13}N and ^{15}O, and also for several heavier positron emitters, such as ^{60}Cu, ^{62}Cu, ^{63}Zn, ^{68}Ga and ^{73}Se, that are currently being used both in pre-clinical and clinical studies.

Our theoretical estimations clearly show that the optimization of laser-generated proton sources in terms of advanced target development and acceleration regimes can lead to potential applications in clinical settings such as PET. This is a very promising perspective, especially in view of the possibility to feed alternatively, at the same facility, radionuclide production beamlines for radiopharmaceutical preparation and a hadrontherapy beamline for cancer treatments using a cost-effective approach based on peculiarities and flexibility of laser driven secondary sources.

Conclusions

The calculations presented in this study demonstrate that the optimization of solid hydrogen targetry improves significantly the production of positron emitting radionuclides useful for the preparation of PET radiopharmaceuticals, and that clinically-relevant amounts of activity will be obtainable with fast irradiation times.

The feasibility of exploiting the laser-accelerated proton beams expected at the ELI-Beamlines facility, which will offer the unique capability of ultrahigh peak power (PW) ad high repetition rate (10 Hz), for in-line preparation of single doses of radiopharmaceuticals is thus confirmed and further encouraged.

Finally, considering that such laser-driven proton sources are being proposed as alternative compact sources for hadrontherapy applications, the potential interest towards these facilities is improved by the potentiality to exploit a single compact accelerator (laser-plasma) for the two-fold aim of producing radionuclides for PET diagnostics, and supplying the hadrontherapy treatment unit.

Table 1: Production yields at 10 Hz repetition rate for the selected positron emitting nuclides, using the new source term for proton spectra assuming an irradiation time T_{irr} = 1 h.

Reaction	**$T_{1/2}$**	**E_{th}**	**Yield (solid-H)**
	(min)	(MeV)	(MBq)
^{14}N(p,α)^{11}C	20	3.13	3130.0
^{16}O(p,α)^{13}N	10	5.55	1290.0
^{15}N(p,n)^{15}O	2	3.77	2570.0
^{18}O(p,n)^{18}F	110	2.57	2180.0
^{52}Mn(p,n)^{52}Fe	497	3.22	180.0
^{60}Ni(p,n)^{60}Cu	24	7.03	966.0
^{61}Ni(p,n)^{61}Cu	200	3.07	512.0

^{62}Ni(p,n)^{62}Cu	10	4.82	3690.0
^{64}Ni(p,n)^{64}Cu	762	2.50	261.0
^{63}Cu(p,n)^{63}Zn	38	4.21	1410.0
^{68}Zn(p,n)^{68}Ga	68	3.76	4040.0
^{86}Sr(p,n)^{86}Y	1.483	6.09	99.0
^{89}Y(p,n)^{89}Zr	4.709	3.66	24.0
^{73}As(p,n)^{73}Se	438	3.56	2940.0
^{77}Se(p,n)^{77}Br	3.427	2.18	39.0
^{124}Te(p,n)^{124}I	6.048	3.97	44.0

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