

LINACS FOR MEDICAL ISOTOPE PRODUCTION^{*)}

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ABSTRACT

LINACS FOR MEDICAL ISOTOPE PRODUCTION. This paper reviews efforts on using high energy (25 – 30 MeV) and high power (10-20 kW) electron linacs and lower energy (7 MeV) proton linacs for medical radioisotope production. Using high energy x-rays from the electron linacs, PET (Positron Emission Tomography) radioisotopes are produced through photonuclear reactions such as $^{19}\text{F}(\gamma, n)^{18}\text{F}$, which also allow production of other PET radionuclides ^{11}C , ^{13}N , and ^{15}O . Other mostly used medical radionuclides $^{99\text{m}}\text{Tc}$ can also be obtained by using the electron linacs, through photofission or photonuclear reactions. Proton linacs for PET have also been recently developed and the product has been available in the market since 2005. The linacs have been tested for ^{18}F production. As a proton accelerator, the target systems and nuclear reactions are similar to the ones used in PET cyclotrons.

Keywords: electron linacs, proton linacs, photonuclear, photofission, medical radioisotopes

INTRODUCTION

In the medical world, linear accelerators (linacs) particularly electron linacs, are mostly used to generate high energy electron beam to be used directly or converted to high energy photon for gamma therapy, mostly for cancer treatment. Medical isotope production for diagnostics such as $^{99\text{m}}\text{Tc}$ is carried out by neutron irradiation in nuclear reactors, or in the case of short-lived isotopes such as ^{18}F for PET (Positron Emission Tomography) by using cyclotrons.

However some studies on using high energy (25-30 MeV) and high power (10-20 kW) electron linacs for medical isotope production through photonuclear reactions such as $^{19}\text{F}(\gamma, n)^{18}\text{F}$, which can use ^{19}F of natural (100%) abundance as target, had been carried out. This is in contrast with $^{18}\text{O}(p, n)^{18}\text{F}$ of proton reactions which require expensive gas targets enriched with isotopes ^{18}O in production using cyclotrons. Similar photonuclear reactions also allow production of other PET radionuclides ^{11}C , ^{13}N , and ^{15}O . Other medical radionuclides such as $^{99\text{m}}\text{Tc}$ can also be obtained on electron accelerators, which cannot be obtained by using cyclotrons. Due to this reason the use of electron linacs is not only for gamma therapy, but also as a tool of production of radionuclides for diagnostics [1].

Ion linacs for PET has also been recently developed by Hitachi, Ltd. and AccSys Technology, Inc. (Hitachi's subsidiary company) and the product has been available in the market since 2005. The AccSys PULSAR -7 is a radiofrequency linear proton (H^+) accelerator for PET radionuclide

production consisting of 30 keV duoplasmatron ion source, 3.5 MeV RFQ (radiofrequency quadrupole) first stage accelerator, 7 MeV DTL (drift tube linac) second stage accelerator, shielded PET radionuclide target system, and PC-based control system [2]. The accelerator, with the beam transport line, is approximately 6.1 m long, weighs approximately 3 tons and the target system shield weighs approximately 9 tons. All of these units are mounted in a medical coaches 16 m semi-trailer. As a proton accelerator, the target system is similar to the one in PET cyclotron. However, as a linear proton accelerator it saves the weight and complexity of cyclotron magnet (minimum weight of about 14 tons of magnet and its mechanical design for optimum focusing and relativistic correction) [3].

ELECTRON LINACS

PET Radionuclides

Photonuclear cross sections yielding PET radionuclides ^{15}O , ^{13}N , ^{11}C from respectively natural abundant isotopes all peaks at about 25 MeV of photon energy (Fig. 1). A neutron knocked off from a stable isotope yields a proton rich or positron emitter isotope which is applicable for PET. Experiments using photons from linacs at this energy had been carried out by Mac Gregor (1957)[4], Lutz (1969)[5], and Dovbnya *et al.* (1999) [1]. The result is resumed in Table 1. The most popular PET radionuclide ^{18}F was obtained at specific activities in the order of 10^6 Bq/g or 10^2 μCi per μA of linac electron beam current by using photonuclear reactions at 25 MeV [1].

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Data on production of ¹⁵O at various electron linacs are given in Table 2.

Target for photon irradiations is simpler in preparation as it is not subjected to direct beam heating as in the case of proton or deuteron irradiations. The beam heating is mostly borne by the heavy metal target (tungsten) converting the

electron beam energy into photons at up to about 50% efficiency.

Because target nuclides are composed of naturally abundant isotopes, isotopic enrichment is therefore not required. The design of the target can also take into account the high penetrability of photons.

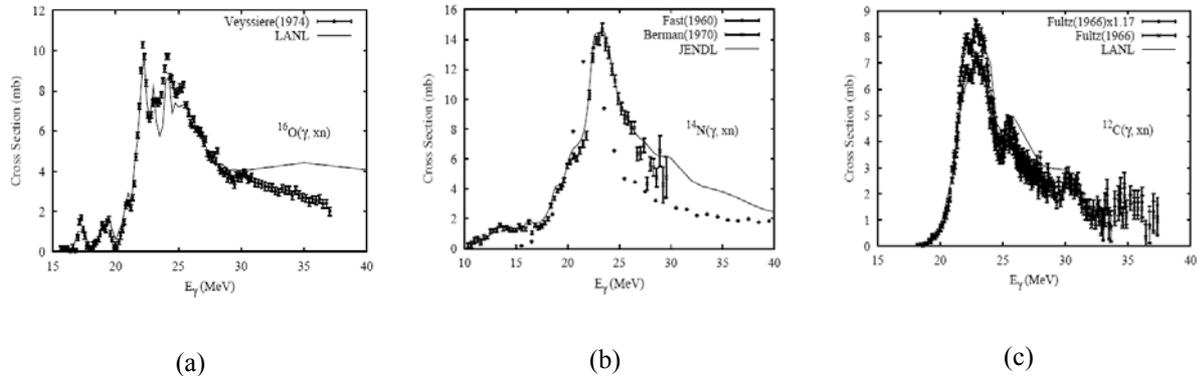


Figure 1. Photonuclear cross sections for ¹⁶O, ¹⁴N, ¹²C yielding PET radionuclides, all peaks at about 25 MeV of photon energy [6].

Table 1. Specific activities (in Bq/g per μA of linac electron beam current) of some PET radionuclides obtained by using photonuclear reactions at 25 MeV [1].

Radionuclide	Mac Gregor (1957)	Lutz (1969)	Dovbnya <i>et al.</i> (1999)
¹¹ C	9.25×10 ⁶	5.30×10 ⁶	1.90×10 ⁶
¹³ N	3.76×10 ⁶	1.04×10 ⁶	1.67×10 ⁶
¹⁵ O	3.20×10 ⁶	8.40×10 ⁶	2.50×10 ⁶
¹⁸ F	2.04×10 ⁶	2.12×10 ⁶	1.70×10 ⁶

Table 2. Comparative data on production of ¹⁵O at various electron linacs [1].

Data on	Center of Nuclear Medicine, Cincinnati, USA (1982)[7]	Kurchatov, IAE, Moscow (1985)[8]	NSC KIPT, Kharkov (1999)[1]
	$E_0 = 26$ MeV	$E_0 = 30$ MeV	$E_0 = 25$ MeV
Irradiation conditions	$I_{av} = 100$ μA	$I_{av} = 100$ μA	$I_{av} = 300$ μA
	$T_{irr} = 4$ min	$T_{irr} = 7$ min	$T_{irr} = 10$ min
	$V = 500$ cm ³	$V = 200$ cm ³	$V = 200$ cm ³
Integral activity	184 mCi	700 mCi	130 mCi
	(6.8×10 ⁹ Bq)	(25.9×10 ⁹ Bq)	(4.8×10 ⁹ Bq)

The only drawbacks of photonuclear processes are the cross sections which are one to two orders smaller than those of nuclear reactions of proton or deuteron. Figure 1 shows cross sections in the order of millibarn, as compared to hundreds of millibarn cross sections of proton or deuteron irradiations at lower energy thresholds in Fig. 2 and Fig. 3.

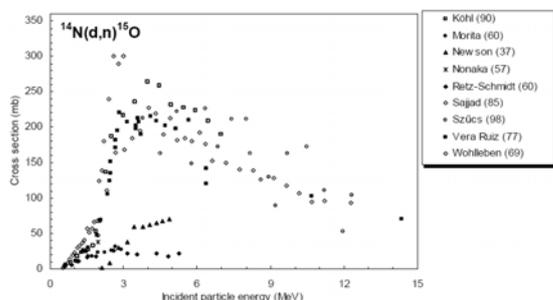
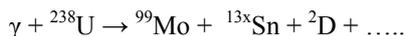


Figure 2. Deuteron cross sections on ^{14}N yielding PET radionuclide ^{15}O [9].

Non-PET Medical Radionuclides

Currently about 80% of the yearly worldwide 40 million nuclear medicine procedures use ^{99}Mo . The ^{99}Mo isotope has been traditionally manufactured using nuclear reactors to irradiate highly enriched uranium targets. The Canada's National Research Universal (NRU) reactor at Chalk River, which produces about half of the world's supply, has been operating since 1957 and suffered from age-related shutdowns. The advances in accelerators enable high beam power to produce medical isotopes [10, 11].

One favored approach uses photons from a high-power electron linear accelerator to produce ^{99}Mo from natural uranium through photonuclear reaction



The radiochemistry to recover and refine the ^{99}Mo generated through photofission from natural uranium target is similar to that which is currently in use for reactors using highly enriched uranium targets. Canada's five-year plan (2010–2015) for TRIUMF includes the construction and operation of a high-power (5 MW) electron linear accelerator. A single multimegawatt machine could supply the entire Canadian market or 5–7% of the total North American market [10, 12].

Another approach at Yerevan Physics Institute (YerPhi) in Armenia is to use ^{100}Mo target through photonuclear reaction $\gamma + {}^{100}\text{Mo} \rightarrow {}^{99}\text{Mo} + \text{n}$, ^{99}Mo ($T_{1/2} = 67$ hours) \rightarrow $^{99\text{m}}\text{Tc}$ ($T_{1/2} = 6$ hours) with threshold of reaction at 9.1 MeV. Unlike uranium target, this approach gives high purity isotopes and free from other radioisotopes which

otherwise should be removed as wastes. The project was started at 2006 with collaborators from University of British Columbia/TRIUMF, Canada [13].

To produce $^{99\text{m}}\text{Tc}$, the existing linear high current electron accelerator ($I = 250 \mu\text{A}$ and $E = 20$ MeV) at YerPhi was used to irradiate a 20 g target of enriched ^{100}Mo for 100 hours to produce approximately 20–40 Ci of $^{99\text{m}}\text{Tc}$ isotope, which correspond to about 5 Ci or 1.85×10^{11} Bq/day. This amount would satisfy the requirements of Armenia and neighboring regional countries. Once it is successfully proven, enough radioisotopes could be provided for direct use in Armenia as well as for potential clients (according to list of IAEA).

ION LINACS

PET Radionuclides

The feasibility of using compact ion linacs for medical applications had been studied for both particle radiation therapy [14] and isotope production [15]. Since 2005 Hitachi, Ltd. and AccSys Technology, Inc. (Hitachi's subsidiary company) manufactured a linear accelerator-based system for PET radiopharmaceuticals production. The system has the advantages of lower installation cost and complexity for areas where a large production center may not economically justified [2].

The AccSys PULSAR® – 7 is a radiofrequency linear proton (H^+) accelerator system for PET radionuclide production. It consist of H^+ duoplasmatron ion source (30 keV), radiofrequency quadrupole (RFQ) as first stage accelerator (up to 3.5 MeV), drift tube linac (DTL) as second stage accelerator (up to 7 MeV), shielded PET radionuclide target system, and a PC-based control system. The proton energy of 7 MeV is sufficient to produce PET radionuclide ^{18}F (Fig. 3).

In August of September 2006 Wisconsin Medical Cyclotron (WMC) facility in West Allis, Wisconsin, tested the PULSAR® – 7 in a mobile configuration, mounted in a Medical Coaches 16 m semi-trailer (Fig. 4). The semi-trailer was located on a parking area without additional parking pad or support. On-board equipment included a radiopharmaceutical synthesis module (GE MX_{FDG}) in a shielded mini-cell, a complete quality testing laboratory, and patient dose preparation equipment. For the evaluation tests, [^{18}F] FDG qualification and unit dose preparation were carried out in the WMC facility.

The drift tube linac produces a pulsed beam of 125 μs length at 85 Hz repetition rate at a beam current of 9 mA with a 1% duty cycle. The target system uses a support grid over a titanium target window to aid in cooling and support the pressurized

target (about 315 psi). The transmission of beam through the grid is about 65%. Two thin target bodies, one made of silver and one made of niobium, were evaluated each with an ^{18}O water capacity of 0.35 ml. A one hour bombardment yield 634 mCi ^{18}F and a two hour 1068 mCi. This production was lower than one observed at a similar fixed (not mobile) unit, which has routinely produced over a Ci/hour. This was most likely caused by marginal chiller in the mobile system which restricted power to lower sustained beam current and caused interrupted bombardment. The trailer cooling system was later rebuilt by the manufacturer. The beam alignment might be also slightly offset, resulting in a beam transmission through the grid of less than 65%.

The trial has demonstrated the mobile proton linac unit to achieve a 94% ^{18}F production batch reliability, to perform multiple daily bombardments of several hours, to produce ^{18}F

suitable for [^{18}F] FDG manufacture for small scale distribution, and the product met quality standard.

CONCLUSION

The electron and proton linear accelerators have been proven to have feasibility for medical isotope production, which at present mostly produced commercially by using cyclotrons or nuclear reactors. For the electron accelerators, however, due to lower cross sections and higher energy thresholds, further efforts are still underway to prove that it is commercially feasible. As for the proton linear accelerators, fixed and mobile compact models have been developed and commercially available, providing more choices other than compact or baby cyclotrons, which could be considered for installation.

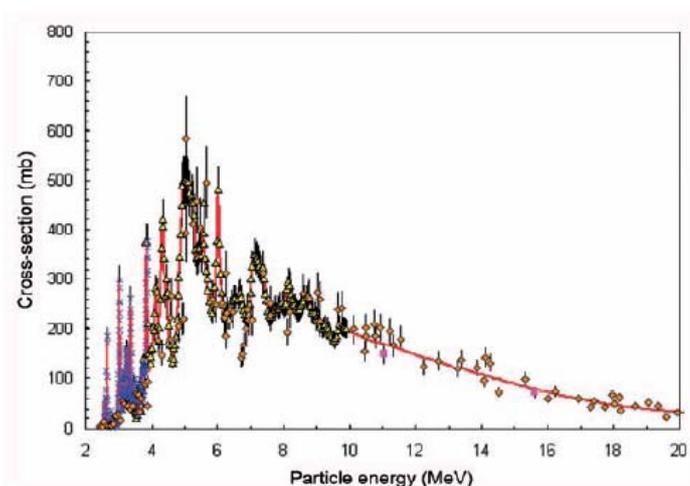


Figure 3. Proton cross sections for $^{18}\text{O}(p,n)^{18}\text{F}$ yielding PET radionuclides ^{18}F . [16]



Figure 4. AccySys PULSAR® - 7 in a mobile configuration, mounted in a Medical Coaches 48 ft semi-trailer [2].

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REFERENCES

1. **A.N. DOVBNYA, A.S. ZADVORNY AND B.I. SHRAMENKO**, Production of Short-Lived Radionuclides on the Electron Linac for PET, in: Problems in Atomic Science and Technology 3 (1999) 105.
2. **ANONYMOUS**, Test Results for Mobile PULSAR® System, Cyclomedical Application Group (2008).
3. **Y.S. KIM, D.H. AN, J.S. CHAI, ET AL.**, New Design of the KIRAMS-13 Cyclotron for Regional Cyclotron Center, Proceedings of APAC 2004, Gyeongju, Korea (2004) 338.
4. **M.H. MCGREGOR**, Nucleonics 15 (1957) 11.
5. **G.J. LUTZ**, ANAL. Chem. 41 (1969) 425.
6. **ANONYMOUS**, Handbook on photonuclear data for applications, Cross sections and spectra, IAEA-TECDOC-Draft 3, March (2000).
7. **H.V. PILTINGSRUD**, Med. Phys. 9 (1982) 514.
8. **V.F. GERASIMOV, ET AL.**, Voprosy Atomnij Nauki i Techniki 4 (1985) 57.
9. **ANONYMOUS**, Charge particle cross-section database for medical radioisotope production: diagnostic radioisotopes and monitor reactions, IAEA-TECDOC 1211, May (2001).
10. **ANONYMOUS**, International Journal of High-Energy Physics, January 27, CERN Courier (2009).
11. **T. RUTH**, Nature 457 (2009) 536.
12. <http://admin.triumf.ca/facility/5yp/comm/isotope-task-force.php> (2009).
13. **ANONYMOUS**, Accelerator in Medical Isotopes Production, International Science and Technology Center, Project #A-1444 (2009).
14. **J.N. BRADBURY, E.A. KNAPP AND D.E. NAGLE**, IEEE Trans. Nucl. Sci. NS-22 (1975) 1755.
15. **R.W. HANN**, Compact Ion Linacs for Radionuclide Production, AccSys Technology Inc. (1989).

TANYA JAWAB

Dewita

1. Dari ketiga jenis linac, manakah yang paling muda?
2. Manakah konsumsi daya terbesar dari ketiga jenis linac tersebut?
3. Pemilihan target untuk ketiga jenis linac?

Pramudita Anggraita

1. Yang paling muda adalah linac proton
2. Konsumsi daya terbesar pada linac elektron karena harus bekerja pada tenaga tinggi (20-30 MeV)
3. Target untuk linac proton dan siklotron harus diperkaya (misal $H_2^{18}O$), sedang untuk target linac elektron dapat isotop alam (^{16}O , ^{14}N , ^{12}C , ^{19}F)

Anhar Riza Antariksawan

1. Bagaimana perbandingan kapasitas produksi (Ci/jam) antara proton linac dan siklotron untuk daya/energi yang sama?
2. Apakah ada aspek teknologi yang *overlapping* antara proton linac dan siklotron?

Pramudita Anggraita

1. Linac proton 7 MeV dapat menghasilkan sekitar 1 Ci/jam sedangkan siklotron dapat menghasilkan sekitar 2 Ci/jam (informasi dari Dr. dr. Kardinah Sp.Rad untuk siklotron Siemen di RS Dharmais)
2. Linac proton dan siklotron mempunyai aspek teknologi yang *overlapping* dalam hal sistem targetnya.

Dr. Abu Khalid Rivai, M.Eng

- Terkait dengan *photoneuclear reaction* yang telah dijelaskan $\gamma + {}^{238}\text{U} \rightarrow {}^{99}\text{Mo} + {}^{135}\text{Sn} + {}^2\text{D} + \dots$ bagaimana probabilitas terjadinya reaksi ini dan berapa energi yang dihasilkan dari reaksi ini?

Pramudita Anggraita

- ✓ Reaksi fotonuklir mempunyaiampang lintang hanya 1/10 hingga 1/100 ampang lintang reaksi nuklir akibat penembakan dengan neutron atau proton.

Drs. Widdi Usada

- Mengapa proton linac lahir belakangan?

Pramudita Anggraita

- ✓ Karena teknologi siklotron lebih dahulu berkembang dan lebih kompak untuk ditempatkan di rumah sakit (siklotron 13 MeV hanya berdiameter sekitar 1 m, sedangkan linac proton 7 MeV panjangnya 16 m).

W. P. Daeng Beta

- Bagaimana aspek keselamatan dan sistem keselamatan dari ketiga jenis teknologi tersebut?

Pramudita Anggraita

- ✓ Karena melibatkan foton dengan tenaga dan daya yang besar, keselamatan pada linac electron harus lebih diperhatikan. Untuk linac

proton yang mobil radiasi foton dan neutron terutama terjadi pada target dan sudah dilengkapi pelindung (shielding) seberat 9 ton sehingga cukup aman meskipun ditempatkan di lapangan parkir. Untuk siklotron diperlukan pelindung radiasi tambahan di sekitar siklotron sehingga dapat ditempatkan di rumah sakit