MODELLING PET RADIONUCLIDES PRODUCTION IN TISSUE AND EXTERNAL TARGETS USING GEANT4

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Abstract

The Proton Therapy Facility in TRIUMF provides 74 MeV protons extracted from a 500 MeV H^- cyclotron for ocular melanoma treatments. During treatment, positron emitting radionuclides such as ^{11}C, ^{15}O and ^{13}N are produced in patient tissue. Using PET scanners, the isotopic activity distribution can be measured for in-vivo range verification. A second cyclotron, the TR13, provides 13 MeV protons onto liquid targets for the production of PET radionuclides such as ^{18}F, ^{13}N or ^{68}Ga, for medical applications. The aim of this work was to validate Geant4 against FLUKA and experimental measurements for production of the above-mentioned isotopes using the two cyclotrons. The results show variable degrees of agreement. For proton therapy, the proton-range agreement was within 2 mm for ^{11}C activity, whereas ^{13}N disagreed. For liquid targets at the TR13 the average absolute deviation ratio between FLUKA and experiment was 1.9±2.7, whereas the average absolute deviation ratio between Geant4 and experiment was 0.6±0.4. This is due to the uncertainties present in experimentally determined reaction cross sections.

INTRODUCTION

This paper presents Positron-Emission Tomography (PET) isotope production at TRIUMF from two different medical applications at different energy regimes: proton therapy (PT) at 74 MeV and medical isotope production at 13 MeV. The Monte Carlo (MC) code FLUKA and Geant4 toolkit have long been essential tools in accelerator design and shielding studies; their application at lower energies for medical application is gaining in popularity, and it is therefore important to explore their limitations in this energy regime. The accuracy, relies on the quality of reaction cross section data used by the MC codes.

Compared to traditional X-ray therapy, in proton therapy (PT) the therapeutic protons stop within a defined target, sparing healthy tissue or organs of the cancer patient. Due the rapid dose fall off in proton therapy, patient alignment is extremely critical for the success of the treatment. Unfortunately, the range of protons inside the patient is not always well known, thus treatment plans rely on large error margins. To verify the dose to the patient, secondary particles such as prompt-gammas or positron emitters (e.g. ^{11}C, ^{15}O and ^{13}N) can be measured. Using MC simulations such as MCNP(X), FLUKA or Geant4, the secondaries can be used to trace back the dose deposited. In this work, PET isotope production was simulated in a Poly(methyl methacrylate) (PMMA) phantom with a raw Bragg peak (RBP) and a spread-out Bragg peak (SOBP).

Radioisotopes are an essential component in the diagnosis and treatment of cancer. In the near future, several isotope producing research reactors are scheduled to shut down. This has shifted the attention of the isotope community to accelerator based isotope production. MC codes can be used to simulate the production yields of various isotopes from different targets. This allows the optimization of the target design to maximize the isotope to contaminant ratio [1]. Details of all isotopes investigated in this paper are listed in Table 1.

MATERIALS AND METHODS

Experiments

Experiments were carried out at the TRIUMF PT Facility and the TR13, a 13 MeV medical cyclotron. At the PT facility, isotope production via a 74 MeV proton beam (raw-Bragg Peak - RBP) as well as a 23 mm spread-out proton beam of a maximum energy of 74 MeV (spread-out Bragg peak - SOBP) was measured in a PMMA phantom at the University of British Columbia PET centre. For more details, see [2].

TR13 is a 13 MeV self-shielded cyclotron and accelerates negative hydrogen ions. The H^- ions have their electrons stripped off and are extracted to the target through collimators. The beam enters through an aluminium foil that separates the cooling helium from the vacuum conditions of the cyclotron, and then a HAVAR foil which isolates the target liquid from the cooling helium inside the target assembly. The target body is composed of niobium. Liquids targets of enriched ^{18}O water, of natural water, and of zinc nitrate in water were irradiated, and the resulting isotopes, ^{18}F, ^{13}N and ^{68}Ga respectively, were measured via an ionization chamber and gamma spectroscopy. For more details see [1, 3].

Table 1: Details of PET Isotopes Investigated [4]

Isotope	Half Life [mins]	$E_{\beta+}$ [keV]	Positron yield
$^{12}C(p,pn)^{11}C$ $^{16}O(p,3(pn))^{11}C$	20	386	100%
$^{16}O(p,2(pn))^{13}N$	10	492	100%
$^{18}O(p,n)^{18}F$	110	250	97%
$^{68}Zn(p,n)^{68}Ga$	68	836	88%

Monte Carlo Simulations

Geant4 is a MC code implemented in C++ for simulating interactions between particles and matter. In this work Geant4 version 10.1 was used [5]. At TRIUMF's PT facil-

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ity a PMMA cylindrical phantom of length 55 mm and diameter 22 mm was irradiated with a dose of 50 Gy. The density of the target was 1.2 g/cm^3. The elemental compositions of the TR13 targets are listed in Table 2. The table details enriched ^{18}O and natural water along with the isotopic composition of natural Zn in Zn nitrate hexahydrate salt $^{nat}Zn(NO_3)_2.6H_2O$. The Zn solution was prepared by dissolving 0.743, 0.225 and 0.032 weight fractions of zinc salt, water and nitric acid respectively. The Zn solution had a density of 1.56 g/cm^3, whereas the remaining two solutions were of density 1 g/cm^3.

Table 2: Composition of Targets at the TR13 (The desired target isotopes are highlighted in bold.)

^{18}O Water		Nat. O		Nat. Zinc	
^{16}O	4%	**^{16}O**	**99.757%**	^{64}Zn	48.63%
^{18}O	**96%**	^{17}O	0.038%	^{66}Zn	27.9%
		^{18}O	0.205%	^{67}Zn	4.1%
				^{68}Zn	**18.75%**
				^{70}Zn	0.62%

In Geant4, the saturation yield Y_v of isotope v at the End Of Bombardment (EOB), normalized to beam current in units of Bq/µA was calculated by:

$$Y_v = \frac{N_{iso}}{N_p e} \tag{1}$$

where N_{iso} is the number of isotopes produced, N_p is the number of incident protons per second, and e is the proton electric charge.

In this work, QGSP-BIC-ALLHP was used from the several physics models available in Geant4 to describe hadronic interactions. It is a high precision model that uses TALYS-based Evaluated Nuclear Data Library (TENDL) for isotope production. For electromagnetic interactions, electromagnetic option 1 was used. Isotopic yields have been normalized to incident beam current by simulating 10^9 primaries with 0.01 mm spatial resolution in liquid targets and 0.1 mm in PMMA.

The FLUKA MC package version 2011.2b.6 was used for the isotope production at the medical cyclotron. For more details, see [1, 6]. For the PT simulation, FLUKA version 2011.2c-4 was used, see [7] for more details. Isotope production in FLUKA is always handled internally and the tabulated cross sections used are not accessible to the user for comparison.

RESULTS

The MC results for the PT facility are shown in Fig 1 and 2. Table 3 lists TR13 experimental saturation yields (Y_{Exp}) and compares them to MC saturation yields of FLUKA and Geant4 (Y_F, Y_G) as ratios. Saturation yield decay corrected to EOB has been normalized for a beam current of 1 µA incident on the liquid target for a 1 hr irradiation. The simulated TENDL cross section (X_T) and an experimental EXFOR cross section (X_{EXFOR}) is also compared. It must be noted that the cross section ratio is limited to only the most significant contributing proton reactions, whereas in simulations incident protons and all secondaries are taken into account.

PT: ^{11}C and ^{13}N Production

For the irradiation with a RBP and a SOBP, the production of ^{11}C inside the PMMA phantom from FLUKA and Geant4 are in good agreement, as illustrated in Fig 1. The 50% fall off for the RBP irradiation from FLUKA and Geant4 is 23 mm and 25 mm respectively; for the SOBP irradiation, the fall offs are 17 mm and 18 mm.

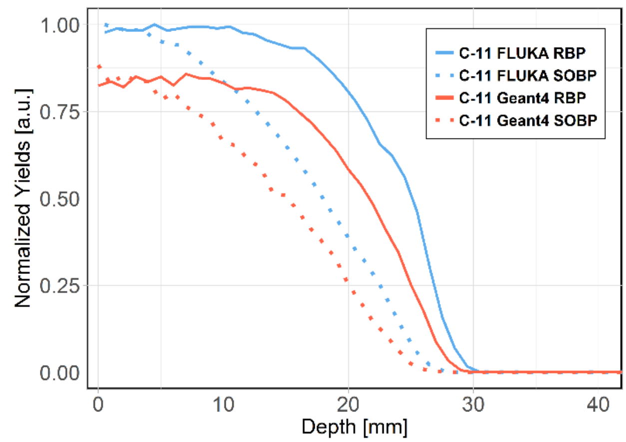

Figure 1: Yields of ^{11}C from a 74 MeV RBP and SOBP from Geant4 and FLUKA.

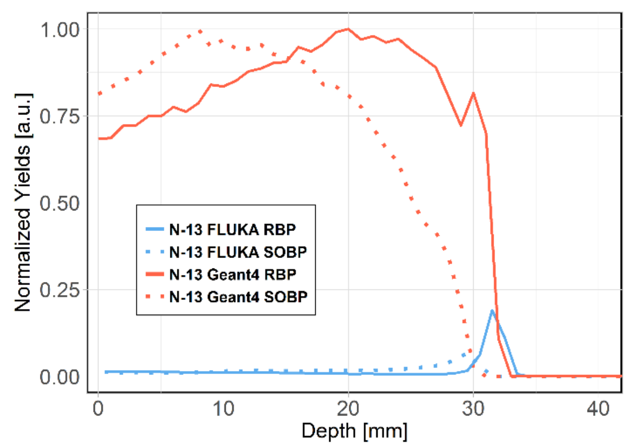

Figure 2: Yields of ^{13}N from a 74 MeV RBP and SOBP from Geant4 and FLUKA.

In Fig. 2 the ^{13}N yield is significantly larger in Geant4 using TENDL cross sections. For PT, the beam energy inside the PMMA target is 70 to 0 MeV denoted by the blue and red regions in Fig 3. Compared to EXFOR cross sections, TENDL grossly overestimates the ^{13}N yield to be even greater than for the ^{11}C production. This overestimation propagates through to the proton range inside the target. At 70 MeV beam energy FLUKA is therefore better able to calculate the ^{13}N yield than Geant4. The 50% fall off from overall PET activity measurements for RBP was 27.9±1.7 mm (Geant4: 30.6 mm, FLUKA: 25.5 mm) and for SOBP was 21.9±1.7 mm (Geant4: 22.9 mm, FLUKA: 18.4 mm) [2]. Consequently, FLUKA better agrees with measurements when comparing the total yield of all isotopes for RBP whereas for a SOBP Geant4 performs better.

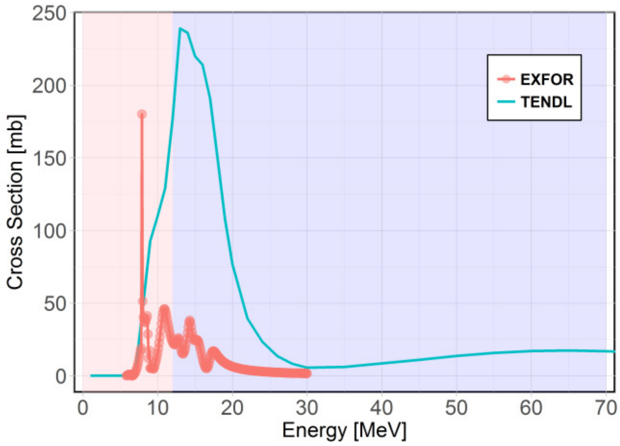

Figure 3: Comparison between IAEA and TENDL cross section for $^{16}O(p,2(pn)))^{13}N$ reaction [8, 9]. The relevant energy range for the TRIUMF PT facility is from 0 MeV to 70 MeV (red and blue), while for the TR13 cyclotron only from 0 MeV to 12 MeV (red).

TR13: ^{18}F, ^{13}N, and ^{68}Ga Production

For the production of ^{18}F, Geant4 underestimates the yield by 53% whereas FLUKA overestimates the yield by 66%, see Table 3. To investigate the cross section data used in Geant4, we compared with experimental cross sections from EXFOR. Even though numerous resonances are present in the EXFOR cross section library, but not taken into account in TENDL, the ratio of cross sections is approximately 1 in this case. At this point, no explanation has been found as to why such a large difference exists between the yields and cross sections ratio. However, at 16.5 MeV, the saturation yield of ^{18}F calculated using FLUKA was in perfect agreement with the recommended IAEA saturation yield. For more details, see [10].

For the ^{13}N production at the TR13, the liquid target is exposed to significantly lower proton energies (13 MeV versus 74 MeV for PT). This greatly reduces the discrepancy between the experimental and TENDL cross section for the $^{16}O(p,2(pn))^{13}N$ reaction. In Fig. 3 the red region illustrates a fairly acceptable level of agreement, with TENDL and EXFOR having the same threshold energy. The yield ratios from FLUKA and Geant4 are 5.92±0.01 and 2.07±0.01 respectively. Geant4 yield ratio compares well with the cross section ratio of 2.38. Therefore, at energies closer to the production threshold, Geant4 provides a better approximation for ^{13}N yield than FLUKA.

Table 3: Saturation Yield and Cross Section Comparison

Isotope	Y_{Exp} [MBq/μA]	Y_F/Y_{Exp}	Y_G/Y_{Exp}	X_T/X_{EXFOR}
^{18}F	4920±60	1.66±0.01	0.47±0.01	0.98
^{13}N	259±3	5.92±0.01	2.07±0.01	2.38
^{8}Ga	138±2	1.03±0.01	0.69±0.02	0.73

For ^{68}Ga the yield ratio for FLUKA is much more accurate than Geant4. The underestimation in Geant4 can be attributed to the relatively lower TENDL cross sections for the reaction compared to EXFOR. The yield ratio of 0.69±0.02 in Geant4 agrees well with the cross section ratio of 0.73. While both codes calculated ^{68}Ga yield accurately, FLUKA was slightly better with a ratio of 1.03±0.01.

CONCLUSIONS

The PET isotopes in the medical applications of proton therapy and PET isotope production using a 13 MeV medical cyclotron at TRIUMF have been simulated in Geant4 and FLUKA. For PT, the production of ^{11}C had good agreement between MC codes, whereas ^{13}N calculated using TENDL cross sections showed large discrepancies. This was traced back to deviating experimental cross section from EXFOR and TENDL cross sections used in Geant4. It can be concluded that TENDL cross sections are not suitable for calculating ^{13}N at an energy range of 10 to 70 MeV.

For saturation yields of ^{18}F, ^{13}N, and ^{68}Ga produced at the TR13 medical cyclotron results are mixed. While FLUKA calculated the saturation yield for ^{68}Ga better than Geant4, the situation is reversed for ^{13}N. Overall FLUKA had a mean absolute deviation of 1.9±2.7, whereas Geant4 had a deviation of 0.6±0.4 for the three isotopes here being investigated. This may indicate that saturation yields calculations from Geant4 are slightly closer to measured yields than from FLUKA, despite the MC models not taking into account any thermal effects or density changes in the liquid target or loss in the transfer system. A wider range of isotopes needs to be examined for a better assessment.

By comparing TENDL and EXFOR cross sections, it can be seen that the availability of accurate cross sections greatly affects the isotopic yield calculations. Therefore, in order to improve the accuracy of calculations, the cross sections available should be well known and widely accepted by the community.

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