International Journal of Applied Science and Mathematics
Volume 3, Issue 4, ISSN (Online): 2394-2894

A Theoretical Study for the Estimation of Yield of Technetium-99m Production Using Newton's Forward Difference Formula

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***Abstract* – A theoretical estimation of production yield of Technetium-99m (^{99m}Tc) in a cyclotron using Newton's Forward Difference (N.F.D) formula has been carried out. The aim was to use an alternative numerical method (N.F.D formula) to estimate the production yield of ^{99m}Tc in a cyclotron instead of the Simpsons Numerical Integration method which relies solely on nuclear reaction simulation codes (TALYS code, EMPIRE Code etcetera). The advantage of the N.F.D formula is that, it is simple, easy and does not require sophisticated software coding. Eventually, the two methods were used for the same proton energy ranges and the corresponding ^{99m}Tc radionuclide saturated yields calculated. Through minimization and curve fitting from the results, it has been found out that there exists a factor of 1.59 MBq/µAh in terms of saturated yield of ^{99m}Tc between the two methods within the same proton energy ranges. This implies that in the absence of any nuclear reaction model code, Newton's forward difference formula can be used to estimate a radionuclide production saturated yield within any proton energy range in a cyclotron.**

***Keywords* – Cyclotron, Curve Fitting, Saturated Yield, Technetium-99m.**

I. Introduction

Radioisotopes which are fundamental components of radiopharmaceuticals in nuclear medicines are routinely used in many health centers for the non-invasive diagnosis and treatment of various diseases. The discovery and introduction of radioisotopes for treating and imaging diseases led to the tremendous growth of nuclear medicine [1]. These radioisotopes in trace amounts are capable of pinpointing the underlying causes of many diseases, examining the flow of blood to many organs in the body including the detection of lymphatic pathways of tumours and monitoring the after-effects of surgery and treatment in the body. Thus, stupendous contribution of radioisotopes in nuclear medicine is unquestionably vital.

One of such highly-regarded and unparalleled radioisotopes with almost ideal radiopharmaceutical properties for most nuclear medicine procedures is Technetium-99m (^{99m}Tc). ^{99m}Tc is used in about 70% of all nuclear medicine procedures worldwide principally because of its unique high beta energy emission but low radiation dose to patients [2]. Due to the relatively low dosimetric burden, higher count rates and reasonably short half-life of about six hours of improved image signal can be achieved using ^{99m}Tc [3]. Most importantly, the chemistry of technetium is so versatile that it can form tracers by being incorporated into a range of biologically-active substances to ensure that it concentrates in the tissue or organ of interest [4].

Consequently, coupled with these advantages, the production of ^{99m}Tc using theoretical models with sufficient yield with a cyclotron has proven to be viable. Several models have been developed in predicting the yield of radioisotopes [5-6]. The most common of these methods include using Simpsons Numerical Integration method which relies solely on nuclear reaction simulation codes (TALYS code, EMPIRE Code etcetera). The aim of this study was to estimate the yield of ^{99m}Tc using N.F.D formula within a given energy range and compare the yield obtained with the saturated yields estimated from (3) which employs Simpson's Numerical Integration (S.N.I) method with the aid of Taly's code for the generation of nuclear reaction cross sections. The advantage of the N.F.D formula is that, it is easy, simple and does not depend on nuclear reaction simulation codes.

The yield (Y) of a nuclear reaction is the quotient of the number of the nuclei formed in a nuclear reaction to the number of bombarding particles on the target [7].

A saturated thick target radionuclide yield is the highest yield a target can produce. In radionuclide production two types of target yield are considered: the first type is the one hour per micro amperes (1h/1µA yield): This is the yield after an hour of irradiation time that is produced by a beam current of 1µA;

$$Y = (\Phi N_L / A)(1 - e^{-In/T_{1/2}}) \int_{Eout}^{E_{in}} \frac{\sigma(E)}{S(E)} \,\mathrm{dE} \qquad (1)$$

The second type is the end of saturation bombardment yield (Y_{EOSB}): Activity produced by beam current of 1µA if the irradiation time t is much greater than the half-life ($t >> T_{1/2}$).

$$Y_{EOSB} = (\Phi N_L / A) \int_{Eout}^{E_{in}} \frac{\sigma(E)}{S(E)} \,\mathrm{dE} \qquad (2)$$

where Φ=beam flux; t = irradiation time; N_L= Avogadro constant; A = atomic weight; $T_{1/2}$ = half life of the product nucleus; $\sigma(E)$ = reaction cross section (mb); $S(E)$ = stopping power of targets (MeV.cm^{-2}.g) [8].

The saturated thick target radionuclide production yield (Y) equation [9] is given as:

$$Y = 6.24 * 10^{12} * \frac{N_A}{M} * \int_{E_{ot}}^{E_{in}} \frac{\sigma(E)}{S(E)} dE \qquad (3)$$

II. Materials and Methods

TALYS code is a nuclear reaction code for the simulation of nuclear reactions that involve neutrons, photons, protons, deuterons, tritons, and alpha-particles in

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the energy range of 1 keV - 200 MeV and for target nuclides of mass heavier than carbon. A computer software package called SRIM calculates many features of the transport of ions in matter [10]. The TALYS code is used to generate the nuclear reaction cross sections and the SRIM package is used to process the appropriate stopping power values and ranges.

2.1 *Generation of Nuclear Reaction Cross Sections*

The nuclear reaction equation given in (4) leads to the direct production of ^{99m}Tc.

$$^{100}\text{Mo (p, 2n)}\ ^{99m}\text{Tc} \quad (4)$$

where ^{100}Mo is molybdenum-100 isotope which serves as the target; p is the proton (hydrogen particle) which is accelerated to bombard the target material; 2n represents two neutrons which are emitted during the bombardment process and ^{99m}Tc is the radionuclide of interest.

In estimation of optimum energy range for production of ^{99m}Tc, cross sections of the reaction ^{100}Mo(p, 2n) ^{99m}Tc which are functions of particle energies were generated using the TALYS code

2.2 *Determination of Stopping Power*

The average energy loss of the particle per unit path length, measured for example in MeV/cm is the stopping power [11]. Stopping power values of the molybdenum-100 target for each proton energy were obtained for use by the SRIM software package.

2.3 *Numerical Method for Saturated Thick Target Radionuclide Production Estimation (Simpson Numerical Integration)*

The cross section values were generated by TALYS code for ^{100}Mo (p, 2n)^{99m}Tc reaction channel for each particle energy range (Table 1). The stopping power values for the corresponding energies were obtained by the SRIM package (Table 2). Using saturated thick target radionuclide production yield (3) and applying Simpson's numerical integration method, the various radionuclide production yields were calculated. A graph of proton energy versus radionuclide production yield was plotted for analysis (Fig. 1).

2.4 *Numerical Estimation of Yield using Newton Forward Difference (N.F.D) Formula*

The cross section [σ(E)] and stopping power [S(E)] are given respectively by (5) and (6) respectively

$$\sigma(E) = \frac{2.678*10^{-10}*N_i A}{\rho t I x} \quad (5)$$

and

$$S(E) = \frac{144 Z z^2}{AE} ln\left(\frac{2195E}{I_p}\right) \quad (6)$$

Where: N_i = number of nuclei present in target during irradiation; A = atomic mass of target in (amu); ρ = density of target (Mo) in (amu); X = thickness of target in (μm); t = irradiation time in hours; Z = atomic number of target in (amu); z = atomic number of charged particle in (amu); I = beam current in (μA); I_p = ionization potential. Putting (5) and (6) in (3) gives

$$Y = 6.24 * 10^{12} \frac{N_A}{M} \int_a^b \frac{2.67*10^{-10} A N_i/\rho t x I}{\frac{14Zz^2}{AE} * ln\left(\frac{2195E}{I_p}\right)} dE \quad (7)$$

For molybdenum-100, the constants in Table 1 applies and Substitution into (7) gives

Table 1. Some constants in the radionuclide production of Tc-99m.

Name of Constant	Numerical Value
Avogadro's Number, Na (particles)	6.02E23
Atomic mass Mo-100 amu	100
Number of nuclei present during irradiation, Ni	6.27E21
Atomic weight Mo, amu	9.60E1
Density Mo, ρ (g/cm3)	10.28
Beam current, I (microamps)	200
Atomic no of Mo, Z	42
Atomic no of H, z	1
Target thickness, X (μm)	223.49
Irradiation time , t (hrs)	6

$$Y = \frac{L_3}{tx} * \int_{Eout}^{E_{in}} \frac{E}{ln(313.17)} dE \quad (8a)$$

and

$$L_3 = \frac{11.54*N_a A^2 N_i}{m\rho I Z z^2} = 3.93*10^{13} \quad (8b)$$

Let

$$f(E) = \frac{E}{ln(313.17E)} = K_1 + K_2E + K_3E^2 + K_4E^3 + K_5E^4 \quad (9)$$

Then

$$F(E) = \int f(E)dE = \int_{E_{in}}^{E_{ot}} \frac{E}{ln(313.17E)} dE = \left[K_1E + \frac{K_2E^2}{2} + \frac{K_3E^3}{3} + \frac{K_4E^4}{4} + \frac{K_5E^5}{5}\right]_{E_{in}}^{E_{ot}} \quad (10)$$

with $C_1 = K_1, C_2 = \frac{K_2}{2}, C_3 = \frac{K_3}{3}, C_4 = \frac{K_4}{4}$ and $C_5 = \frac{K_5}{5}$ gives $Y = \frac{3.93*10^{13}}{t*x} * \left[C_1E + C_2E^2 + C_3E^3 + C_4E^4 + C_5E^5\right]_{E_{ot}}^{E_{in}}$ (11)

The Microsoft excel program was used to determine the numerical value of the coefficients of E and arranged in Table 2.

Table 2. Values of some variables and constants

E_0=8 MeV	E_1=10 MeV	E_2=12 MeV	E_3=14 MeV	E_4=16 MeV
K_1=7.5419E-2	K_2=0.1305	K_3=-1.72E-3	K_4=5.3467E-5	K_5=-7.7135E-7
C_1=K_1=7.5419E-2	C_2= K_2/2=6.5248E-2	C_3=K_2/3=-5.7E-4	C_4=K_4/4=1.3367E-5	C_5=K_5/5=-1.5427E-7

Note: the energy step interval is 2MeV.

The final radioisotope production yield equation becomes

$$Y = \frac{393*10^{13}}{t*x} *[0.075E + 0.065E^2 \ -5.7*10^{04}E^3 1337*10^{05}E^4 - 154*10^{07}E^5]_{E_{out}}^{E_{in}} \quad (12)$$

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III. Results and Discussion

3.1 *Variation of Saturated Thick Target Yield with Proton Energy*

Results of various particle energies in MeV and values of saturated thick target radionuclide production yields obtained using (3) and Simpson Numerical Integration method is provided in Table 3 It can be seen that thick target yields for radionuclide production increases with an increase in proton energies.

Table 3. Particle Energies and Corresponding saturated thick target Radionuclide Production Yields at different times of irradiation (Simpson's Rule)

E_{in}/MeV	E_{out}/MeV	Saturated Yield/(MBq/μAh)
8	0	0.5
11	8	90.67
15	8	309.17
18	8	505.17
20	8	620.00
22	8	691.67

To analyze the effect of particle energy on radionuclide production yield, a graph of thick target radionuclide production yield versus proton (projectile) energy is plotted in Fig 1. It was realized that, radionuclide production yields in saturated thick targets increases exponentially with proton energies.

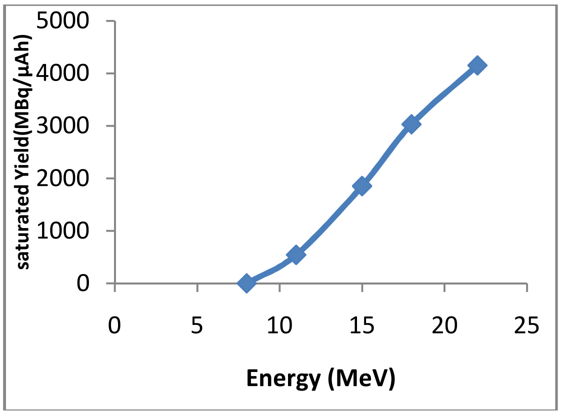

Fig.1. Saturated thick target radionuclide production yield versus particle energy.

An alternative method to estimate the radionuclide production thick target yield was to numerically solve the radionuclide production yield (3) using Newton's Forward Difference Formula. Table 4 contains the apportioned energy ranges and the corresponding saturated thick target radionuclide production yields calculated from the numerically solved formula from (12).

Table 4. Particle Energy Ranges and Corresponding Radionuclide Production Yields (Newton's Formula).

E_{in}/MeV	E_{out}/MeV	Saturated Yield/(MBq/μAh)
11	8	127
15	8	245
18	8	316
20	8	358
22	8	395
24	8	432

To aid in the analysis a plot of saturated yield against the projectile energy (Figure 2) shows that a thick target yield of radionuclide production increases almost proportionally with projectile energy.

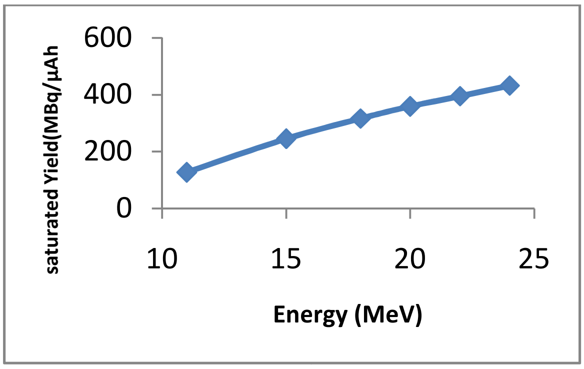

Fig. 2. Saturated thick target Radionuclide Production Yield versus particle Energy

3.2 *Comparison of saturated yields obtained by Newton's Forward Difference (N.F.D) formula and Simpson Numerical Integration (S.N.I) method*

To establish a relationship betweein the saturated yield obtained by N.F.D method and S.N.I method, values of the saturated yield within the same particle energy ranges for the production of Tc-99m are tabulated in Table 5. Although, saturated yield values in both methods increases with particle energy, the quantum of increase within the same energy range is not the same. Through the process of curve fitting and a trend line equation for the curve of best fit was obtained for each method. Subsequently, respective particle energies were substituted into these trend line equations (Fig. 3) and the corresponding new $S.N.I_2$ and $N.F.D_2$values obtained.

Table 5. Particle energy ranges and saturated yield values for N.F.D and S.N.I

Energy (MeV)		Saturated Yield(MBq/μA)				
E_{in}	E_{out}	N.F.D 1	S.N.I 1	N.F.D 2	S.N.I 2	$S.N.I_2$/ $N.F.D_2$
11	8	127	91	92.28	146.73	1.59007
15	8	245	309	215.20	342.30	1.59061
18	8	316	505	309.39	488.98	1.59073
20	8	358	620	368.85	586.76	1.59078
22	8	395	692	430.31	684.44	1.59082

Note: SNI_1 = cross section values obtained using equation (3) and employing Simpson's numerical integration method. NFD_1 = cross section values obtained using equation (12) which employed Newton's forward difference formula. SNI_2 = cross section values obtained by using the trend line equation(y = 48.892x - 391.08) after curve fitting and minimisation. NFD_2 = cross section values obtained by using the trend line equation(y = 30.73x - 245.75) after curve fitting and minimisation. (y = saturated yield in MBq/μAh and x = energy in MeV).

A factor of 1.59 has been established as the ratio of $S.N.I_2$ to $N.F.D_2$ values for each of the energy range considered in Table 5. In Figure 3, N.F.D method

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underestimates the saturated yield values as compared to S.N.I method. In the absence of appropriate nuclear reaction code and the SRIM software package to generate cross section values and stopping power values respectively. One can employ the N.F.D. method and then to correct it by multiplying by 1.59 to obtain the values for the S.N.I method.

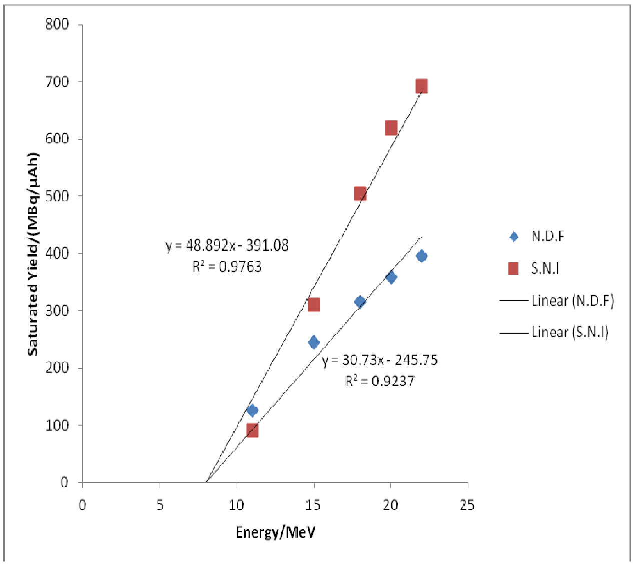

Fig. 3. Graph of particle energy against saturated yields for N.F.D and S.N.I

IV. Conclusion

Saturated yield values increses with projectile energy. A trend line fitting to the curve established that Simpsons Numerical Integration and Newtons Forward Difference methods values of saturated yield differ by a factor of 1.59. In the absence of appropriate nuclear reaction code and the SRIM software package to generate cross section values and stopping power values respectively, one can employ the N.F.D. method and then to correct it by multiplying by 1.59 to obtain the values for the S.N.I method.

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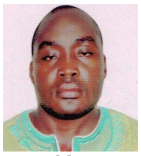

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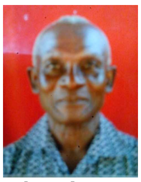

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