Fluorine-18 Production using Petawatt Laser Technology

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A theoretical analysis of a new method of producing Fluorine-18 for medical purposes is performed. The results of various experiments, and previous theoretical work are used to estimate the amount of F-18 that can be generated through the $^{18}O(p,n)^{18}F$ reaction if protons accelerated using a Petawatt laser are used instead of the conventional cyclotron method. We show that the yield of such a device would be far too low for practical use, and discuss how laser technology would need to change in order to make the device technically feasible.

I. INTRODUCTION

Fluorine-18 is a radioactive isotope of Fluorine that is used in Positron Emission Tomography (PET) scans. During these scans, 200 MBq to 400 MBq of F-18 are administered via a saline drip. Fluorine-18 has a relatively short half-life of 110 minutes[5] which means that it cant be stored effectively and must be produced immediately prior to its use.

The current method of F-18 production makes use of the proton capture reaction $^{18}O(p,n)^{18}F$, meaning that an Oxygen-18 nucleus absorbs a proton and ejects a neutron, leaving behind a Fluorine-18 nucleus. The protons must first be accelerated to high energies in order to overcome the coulomb repulsion of the O-18 nucleus. This is currently accomplished using cyclotrons that accelerate protons up to energies between 13.5 and 19 MeV, which are then directed into a target of water enriched with O-18 ($H_2^{18}O$)[8].

Recent experimental results from Snavely et al[3], as well as theoretical results from the Institute of Plasma Physics and Laser Microfusion[2], have shown that Petawatt lasers are able to create intense, short, pulses of protons with energy high enough to initiate nuclear reactions when they are shot at hydrocarbon targets. Using these results, as well as available cross section data for the $^{18}O(p,n)^{18}F$ reaction, a simple analysis on the technical feasibility of using these laser accelerated protons for medical isotope production will be performed. Microfusion[2], have shown that Petawatt lasers are able to create intense, short, pulses of protons with energy high enough to initiate nuclear reactions when they are shot at hydrocarbon targets. Using these results, as well as available cross section data for the $^{18}O(p,n)^{18}F$ reaction, a basic feasibility study on the use of these laser accelerated protons for medical isotope production will be performed.

II. MATHEMATICAL ANALYSIS

A. Deriving the differential equations describing isotope production

When an Oxygen-18 target is irradiated by a proton flux, the number of O-18 atoms per cubic centimeter decreases at a rate that is proportional to the proton flux, and the current number of O-18 atoms. This is a standard assumption in nuclear physics.

$$\frac{dO^{18}}{dt} \propto -O^{18}\phi \quad (1)$$

This proportionality is made into an equality by inserting a constant known as the cross section. This value is a material property that is dependent on the energy of the incident protons, determined experimentally. After adding the cross section, we obtain the equation describing the O-18 concentration.

$$\frac{dO^{18}}{dt} = -O^{18}\phi\sigma \quad (2)$$

The reaction we are interested in for Fluorine-18 production is $^{18}O(p,n)^{18}F$. This means that the term which represents a loss in the O-18 equation can be represented as a source of Fluorine-18.

$$\frac{dF^{18}}{dt} \approx O^{18}\phi\sigma \quad (3)$$

However, since the Fluorine has a relatively short half-life, we must include a loss term which is proportional to the current concentration of Fluorine.

$$\frac{dF^{18}}{dt} = O^{18}\phi\sigma - \lambda F^{18} \quad (4)$$

The constant λ is called the decay constant, and is related to the half-life of Fluorine-18 through $\lambda = \frac{ln2}{t_{1/2}}$. This concludes the derivation of differential equations needed to describe the production of Fluorine-18, shown again below.

$$\frac{dO^{18}}{dt} = -O^{18}\phi\sigma \quad (2)$$

$$\frac{dF^{18}}{dt} = O^{18}\phi\sigma - \lambda F^{18} \quad (4)$$

B. Solving the differential equations

Equation (2), which describes the Oxygen concentration is a simple separable equation. Bringing the terms in O-18 to one side of the equation and the terms in t to the other results in equation (5), shown below.

$$\frac{dO^{18}}{O^{18}} = -\phi\sigma dt \quad \text{(5)}$$

We now integrate both sides, giving us equation (6), describing the O^{18} concentration over time.

$$\ln O^{18} = -\phi\sigma t + C \text{ (6)}$$

By isolating for O^{18} in equation (6) we can obtain O^{18} as a function of time.

$$O^{18}(t) = Ae^{-\phi\sigma t} \quad \text{(7)}$$

This expression can be substituted into equation (4), in order to yield an inhomogenous, first-order, differential equation.

$$\frac{dF^{18}}{dt} = Ae^{-\phi\sigma t}\phi\sigma - \lambda F^{18} \text{ (8)}$$

Multiplying equation (8) by the integrating factor $e^{\lambda t}$ then reorganizing yields another separable differential equation.

$$\frac{d(e^{\lambda t}F^{18})}{dt} = A\phi\sigma e^{\lambda - \phi\sigma t} \quad \text{(9)}$$

Integrating this equation and isolating for the F-18 concentration leaves us with the general expression for the Fluorine concentration over time.

$$F^{18}(t) = \frac{A\phi\sigma}{\lambda - \phi\sigma}e^{-\phi\sigma\ t} + Be^{-\lambda t} \text{ (10)}$$

C. Applying Initial Conditions

The concentration of Oxygen-18 at t=0 is equal to the atom density of O-18 in enriched water. Call this value O_0^{18} , and solve equation (7) for when t = 0.

$$O_0^{18} = Ae^0 = A \quad \text{(11)}$$

This result allows us to eliminate the first constant in equation (10), giving us a new expression for the F^{18} concentration.

$$F^{18}(t) = \frac{O_0^{18}\phi\sigma}{\lambda - \phi\sigma}e^{-\phi\sigma t} + Be^{-\lambda t} \text{ (12)}$$

We also know that the initial amount of Fluorine is zero, as none has been produced yet. This allows us to solve for the other constant B in equation (12).

$$B = -\frac{O_0^{18}\phi\sigma}{\lambda - \phi\sigma} \quad \text{(13)}$$

Substituting equation (13) into equation (12) yields the final expression for the F^{18} concentration over time:

$$F^{18}(t) = \frac{O_0^{18}\phi\sigma}{\lambda - \phi\sigma}(e^{-\phi\sigma\ t} - e^{-\lambda t}) \text{ (14)}$$

III. RESULTS

The values of the flux obtained in *Badziak et al.*[2] are given in *Table 1*. It must be noted that the only estimate directly quoted in their text is an order of magnitude estimate, so these results will only be correct to one order of magnitude. Cross section data is obtained from E. Hess[1]. In the data presentation section of their paper, the intensity is approximately constant over the energy ranges with the highest flux, so for this analysis, three energies were assumed, each containing one third of the measured intensity.

Table 1: Flux Values and Cross-sections

Energy (MeV)	$\sigma(mb)$	$\phi(\frac{W}{cm^2})$	$\phi(\text{cm}^{-2}s^{-1})$
7.6	249.2	0.33×10^{21}	2.71×10^{32}
8.1	192.1	0.33×10^{21}	2.54×10^{32}
8.19	232.7	0.33×10^{21}	2.52×10^{32}

The value for the decay constant of Fluorine-18 was obtained from an International Atomic Energy Agency database[5]. The atomic concentration of O^{18} in enriched water was obtained on the website of the chemical supplier *Sigma-Aldrich*[7], and the pulse length of the proton beam was found in the work of *Badziak et al.*[2]. These values are all shown below in *Table 2*.

Table 2: Physical Constants

Parameter	Value
λ	$1.050 \times 10^{-4}s^{-1}$
O_0^{18}	$3.339 \times 10^{22}cm^{-3}$
t	1 ps

We now use the values for each energy group, along with equation (14), gives us the F-18 atom production for each energy group at the boundary of the H_2O^{18} target. These values are shown in *Table 3*.

Energy (MeV)	Production (cm^{-3})
7.6	2.25×10^{18}
8.1	1.63×10^{18}
8.19	1.96×10^{18}

The fluorine production will not remain constant throughout the entire depth of water, since the protons will be scattered away, absorbed, etc. This causes the flux to exponentially decay, with the total macroscopic proton scattering cross-section representing the length scale of the decay. Note that since the F-18 production is proportional to the flux, we can say that the production decays at the same rate. In the MeV energy range, the total macroscopic proton cross-section for H_2O^{18} is $\Sigma_t = 500\mu m^{-1}$.[4] The production function is therefore given by equation (15). P_s is the production at the surface for whatever energy group we're looking at.

$$P_s e^{-\Sigma_t x} \quad \text{(15)}$$

Finally, to get the total yield, we will integrate over the volume that the production is happening in. We will assume that the protons will only undergo one interaction in the water, so that either it is scattered off of its original trajectory, or it produces a Fluorine-18 atom. Because the initial proton beam is travelling perpendicular to the surface of the water, and is in the shape of a circle, we will integrate over the semi infinite cylinder with diameter equal to that of the proton beam. This means that the total number of atoms produced is given by equation(16), where A is the area of the spot.

$$P_s A \int_0^\infty e^{-\Sigma_t x} dx \quad \textbf{(16)}$$

Simplifying equation (16) leaves us with equation (17), which gives the net number of F-18 atoms produced.

$$Total Atoms = \frac{AP_s}{\Sigma_t} \textbf{ (17)}$$

In *Badziak*[1], it is stated that the area of the proton beam resulting from the interaction of the laser and its target, will be approximately the same diameter as the laser beam. The laser beam has a diameter of $20 \mu m$, so the spot will have an area of 3.142×10^{-6}[1]. Substituting these values into equation (17), and summing over all three energy groups, gives a final yield of:

$$F^{18} = 3.67 \times 10^6 atoms$$

The activity of this many atoms is found by multiplying by the decay constant λ, which can be found in *Table 1*. The activity of F-18 generated by a single pulse is:

$$Activity = 385 \text{ Bq}$$

This activity is well below the activity required for a single course of treatment of F-18; around 200 MBq to 400 MBq. It would be possible to increase this yield by sending multiple pulses in a short period of time, but since most Petawatt lasers require an hour between pulses[6], that is not feasible, as 30% of the generated fluorine would decay in this time.

IV. CONCLUSIONS

In conclusion, with our current Petawatt laser technology, we cannot construct a device to produce enough Fluorine-18 for medical treatments. In the future this might be possible, if the cool down time for laser pulses is decreased drastically, or the proton yield from the laser target is increased. It must be stated that this was a very elementary analysis of this phenomenon. Only 3 energy groups were considered, and no scattering between groups or thermalization of the protons was taken into account. If one wishes to expand on this work the most straight forward way to do so would be to get accurate numerical values for the proton flux, instead of the order of magnitude estimates used in this work, and use multiple energy groups in the analysis. As of right now, and into the near future, hospitals should continue to use cyclotrons as theyre more cost effective and better at production than lasers.

References

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