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### **Laser Production of Medical Radioisotopes**

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#### Abstract

High powered lasers offer an alternative method of producing of medical radioisotopes that are traditionally manufactured by research reactors and accelerators. This paper investigates the current status of laser produced proton and alpha particle beams and their potential for the production of both imaging and therapeutic medical radioisotopes Improvements in laser power, intensity, and efficiency offer the potential for producing heavy ions (e.g., <sup>12</sup>C) for therapy applications. These beams would permit an expanded use of heavy ion therapy utilizing their strong Bragg peak. Photoproduction reactions permit the production of medical isotopes via a currently unused production method. The heavy ion and photoproduction approaches are speculative, and require research and development to be successfully implemented.

**Keywords:** Proton Medical Isotope Production, Alpha Particle Produced Radionuclides, Laser Production of Medical Radionuclides, Heavy Ion Production, Photoproduction, and Imaging and Therapy Applications.

#### Introduction

Medical isotope production is essential for the expansion of imaging and therapy protocols. Currently, there are two primary methods of producing medical radioisotopes. Nuclear reactors (i.e., research reactors) and accelerators (i.e., cyclotrons) are the baseline production approaches. Research reactors utilize neutrons to activate target material to produce the desired radioisotope (e.g.,  $^{90}$ Sr/ $^{90}$ Y and  $^{177}$ Lu). Cyclotrons accelerate protons to strike a target and through an appropriate nuclear reaction yield the desired radionuclide (e.g.,  $^{11}$ C,  $^{13}$ N,  $^{15}$ O, and  $^{18}$ F). Accelerators can also utilize alpha particle beams to produce the desired radionuclide, but this approach is not as commonly utilized as the proton production methods.

Laser generated alpha beams offer an alternative production method for the creation of medical radionuclides. A portion of the medical isotopes have significant therapeutic use due to their short range and associated localized energy deposition. For example, limited quantities of  $^{211}$ At are produced by conventional means, but production could be enhanced through alpha induced nuclear reactions (e.g.,  $^{209}$ Bi +  $^{4}$ He  $\rightarrow$   $^{211}$ At + 2n).

The current medical isotope creation approaches restrict production to organizations having access to a research reactor or cyclotron. Limited isotope production is also occurring via commercial power reactors. In view of the increasing demand, there is an obvious need to develop cost effective and accessible production methodologies that can expand the availability of medical radioisotopes. One possibility is the use of laser systems to produce the desired radionuclides. The technical merit of this approach has been established but the economic viability and production scale capability has yet to be fully demonstrated

[1-3].

The generation of protons from laser irradiation incident on a solid surface has been documented [4, 5]. These effects are different than the physics involved in conventional medical isotope production [6-9]. This laser generation effect occurs through the action of an electrostatic field produced by electron-ion interactions [10].

In Ref. 1, a collimated beam of high-energy photons impinged on a thin solid target and produced protons. The target was irradiated at 1 PW power and peak intensity  $3x10^{20}$  W/cm². Snavely et al. reported that a maximum of 48 J (12%) of the laser energy was transferred to  $2x10^{13}$  protons with energies >10 MeV. The proton energy spectrum had a limit of about 58 MeV on the beam axis. These characteristics are sufficient to offer the potential for medical isotope production [1].

Laser induced proton beams have also been utilized to generate other particles that have the potential for the production of medical isotopes. Bonvalet et al. reported that a high-intensity and high-energy laser system produced alpha particles using a proton-boron reaction driven by laser generated protons. Alpha particles observed in the experiment achieved 10–20 MeV through the energy transfer from 20–30 MeV incident protons. Ref. 2 reports that  $10^8$  – $10^9$  alpha particles per steradian were detected [2].

Batani et al quantified the production of a selected set of medical radioisotopes using laser produced protons that irradiated various targets. Laser parameters included a wavelength of 810 nm, pulse width of 200–250 fs, and energy of about 25 J. [3].

Shots were performed at 2 minute intervals. The targets included boron to generate  $\alpha$ -particles via p + 11B fusion. Ref. 3 created several radioisotopes using laser-generated  $\alpha$ -particles and protons including  $^7\text{Be}$ ,  $^{11}\text{C}$ ,  $^{18}\text{F}$ ,  $^{43}\text{Sc}$ ,  $^{44}\text{Sc}$ , and  $^{48}\text{Sc}$ . Batani et al [3]. Demonstrated the following production values per laser shot:  $\approx 6 \times 10^6$   $^{11}\text{C}$  atoms and  $\approx 5 \times 10^4$   $^{44}\text{Sc}$  systems. Although below desired production levels, these results support the continued development of laser-driven production of radioisotopes for medical applications.

Future advances in laser technology offer the potential for additional methods for the use of lasers in therapy and imaging applications [6-9]. Improvements in laser power, intensity, and efficiency also offer the potential for producing heavy ions (e.g.,  $^{12}\mathrm{C}$ ). These beams would permit an expanded use of heavy ion therapy and their strong Bragg peaks. Photoproduction reactions (e.g.,  $(\gamma, n), (\gamma, 2n), (\gamma, 3n),$  and  $(\gamma, 4n)$ ) permit the production of medical isotopes via currently unused production methods. The heavy ion and photoproduction approaches will require both laser development and experimental research to be successfully implemented.

#### **Overview of Laser Generated Particles**

A laser-driven ion accelerator is capable of producing photons, protons, alpha particles, and heavy ions. The device will include a short-pulse width, high-intensity laser beam that strikes a target such as a thin foil with the components enclosed in a vacuum chamber [10]. The laser radiation interacts with the target to produces plasma consisting of electrons and associated ions. Within the plasma, the electrons are displaced from the ions. An intense electric field is produced in the displacement gap between the layer of electrons and ions. The electric field generates an associated electromagnetic force that accelerates the ions that follow the moving electron layer and create an energy gradient. Energy gradients can reach or exceed tens to hundreds of GeV/cm.

Acceleration of charged particles is produced by the laser radiation incident on a target through the action of electromagnetic (EM) and hydrodynamic forces. The EM forces dominate for high laser beam intensities (i.e.,  $> 10^{15}$  W/cm<sup>2</sup>), and create energy gradients that can accelerate ions to high velocities [10].

The EM field generates a Lorentz force that creates the conditions for accelerating the laser generated ions

$$\vec{F} = q\vec{E} + q\vec{v} \times \vec{B}$$
 (1)

where q is the particle charge, v is the particle velocity, E is the electric field strength, and B is the magnetic field strength that reside within the plasma. This force accelerates both plasma electrons and ions. At laser intensities below 10<sup>24</sup> W/cm², the acceleration of the more massive ions is less significant than the effect of the EM force on the electrons. Given the larger ion mass and inertia, the electron motion is much larger than the ion displacement. Accordingly, the electrons are displaced from the ions, and this separation creates the large electric field between the moving electrons and more stationary ions.

The specification of a mechanism of ion acceleration depends on the laser pulse and the target parameters. Several ion acceleration mechanisms have been identified and include the target normal sheath [11,12], skin-layer ponderomotive [13], radiation pressure [11,12,14], laser break-out afterburner [11,12,15], collisionless electrostatic shock [12,16], ion solitary wave [17] and Coulomb explosion acceleration [18]. In an actual application, two or more acceleration mechanisms can be important in determining the optimum ion production approach [10].

At low laser intensities (e.g., about  $10^{10} - 10^{15}$  W/cm<sup>2</sup>) and long laser pulses (e.g., tens of ps to tens of ns), a significant contribution to the acceleration of plasma ions is attributed to hydrodynamic forces (e.g., hydrodynamic or thermal pressure) induced by the laser pulse [10]. Although the low intensity physics in interesting, this paper is focused on laser-driven ion acceleration at high laser intensities when ions (e.g., protons and alpha particles) are accelerated by EM forces.

## **Production Reactions for Laser Generated Medical Radioisotopes**

Refs. 6-9 provide an overview of medical isotope production that focused on reactor and accelerator based methods. This conventional isotope production approach can be extended by utilizing laser technology. Ref 19- 35. suggested future possibilities for laser produced medical isotopes. Laser methods are a potential element to foster an expansion of the use of medical isotopes in therapy and imaging applications.

Subsequent discussion expands the methods to produce a variety of medical isotopes listed in Refs. and includes various proton and alpha particle production methods. In particular, the focus is on basic activation reactions that facilitate the calculation of the activity of the desired medical radionuclides. Additional discussion addresses the possibility of medical applications of lasers that require significant improvements in power, intensity, and efficiency. These possibilities include heavy ion therapy and photoproduction reactions.

#### Production of Medical Radioisotopes from Candidate Proton and Alpha Induced Activation Reactions

Activation reactions provide a theoretical basis to quantify the amount of a desired radionuclide that can be produced from a given target mass, flux of alpha or proton radiation, and energy dependent cross-section. A general activation reaction can be written as

$$X(a,b)Y (2)$$

where X is the target nucleus, a is the activating particle (p or  $\alpha$  for this section), b is the ejected particle, and Y is the desired medical isotope. The activity of Y produced (A<sub>i</sub>) is given by the standard activation equation [6-9]

$$A_{i} = N \sigma \phi \left(1 - e^{-\lambda_{i}T}\right) e^{-\lambda_{i}t_{d}}$$
(3)

where N is the number of atoms in the target nucleus X,  $\sigma$  is the energy dependent cross-section for the reaction summarized by Eq. 2,  $\phi$  is the activating flux of protons or alpha particles,  $\lambda i$  is the radioactive disintegration constant for the desired medical isotope Y, T is the time the target is irradiated by the flux, and td is the decay time following termination of the activating flux

striking the target.

The target nuclei summarized in Tables 1-5 focus on stable or longer-lived nuclear systems. Some of the proposed reactions may require enrichment of the target nucleus to enhance economic viability. The availability of the desired target nucleus, advances in laser technology, and optimization of the selected beam energy and associated reaction cross-section affect the feasibility of the production of a medical isotope.

Examples of proton and alpha particle activation reactions that are potentially accessible by laser generated particles are summarized in Tables 1 - 3. In each table, the target nucleus, specific production reaction, produced medical isotope, and reaction threshold are presented. Tables 1 and 2 (3) present proton (alpha) induced activation reactions. The threshold energies are determined utilizing mass excess values ( $\Delta$ ) [20]. Following Eq. 2, the threshold energy (E) is

$$E = \Delta(Y) + \Delta(b) - \Delta(X) - \Delta(a)$$
(4)

Additional discussion of possible proton and alpha induced reactions to produce medical radioisotopes is provided in Refs. [21-35]. These production reactions are provided in Tables 1-3. These tables provide alternative production modes for laser generated medical isotopes. Tables 1-5 illustrate possible reactions that should stimulate investigation of medical isotope production modes including heavy ion generation and photoproduction methods.

The following acronyms are utilized in subsequent commentary: alleviation of bone cancer pain (BCP), brachytherapy (BT), targeted alpha therapy (TAT), single-photon emission computed tomography (SPECT), auger electron therapy (AET), and positron emission computed tomography (PET). Therapy applications incorporate the AET, BCP, BT, and TAT approaches, and PET and SPECT are essential imaging techniques. Radionuclides that have general medical applications are listed as imaging and therapy in the tables.

#### **Candidate Proton Activation Reactions**

Tables 1 and 2 provide a selected set of medical radionuclides that could be produced by protons generated by high intensity lasers. These lists are illustrative and could be expanded, but the initial results summarized in Tables 1 and 2 suggest the viability of laser produced protons that could be utilized to generate medical isotopes. Many of the reaction candidates involve (p, n) transfers that can be produced at lower proton energies. As the proton energy increases, additional reaction channels open. Examples of these reactions are summarized in Table 1 (2) for proton energies < (≥) 15 MeV.

The utilization of laser produced medical radionuclides offers the potential to enhance the availability of isotopes that are in limited supply. For example, <sup>67</sup>Cu has the potential for both therapy and imaging applications, but this isotope is not readily produced by existing approaches.

Table 1: Selected Lower Energy Proton (<15 MeV) Induced Activation Reactions to Produce Medical Radioisotopes

Target (X)	Reaction (a, b)	Medical Radioisotope (Y)	Threshold Energy (MeV)	Medical Application <sup>a</sup>
<sup>14</sup> N	(p, α)	<sup>11</sup> C	2.923	PET
<sup>14</sup> N	(p, <sup>2</sup> H)	<sup>13</sup> N	8.329	PET
<sup>20</sup> Ne	(p, 8Be)	<sup>13</sup> N	10.040	PET
<sup>24</sup> Mg	(p, <sup>12</sup> C)	<sup>13</sup> N	11.990	PET
<sup>25</sup> Mg	(p, <sup>13</sup> C)	<sup>13</sup> N	14.374	PET
<sup>16</sup> O	(p, α)	<sup>13</sup> N	5.218	PET
<sup>16</sup> O	(p, d)	15O	13.440	PET
<sup>18</sup> O	(p, n)	<sup>18</sup> F	2.437	PET
<sup>58</sup> Ni	(p, 2p)	<sup>57</sup> Co	8.173	BT
<sup>62</sup> Ni	(p, n)	<sup>62</sup> Cu	4.730	PET
<sup>64</sup> Ni	(p, n)	<sup>64</sup> Cu	2.457	PET
<sup>63</sup> Cu	(p, 2n)	<sup>62</sup> Zn	13.262	PET
<sup>63</sup> Cu	(p, n)	<sup>63</sup> Zn	4.148	PET
<sup>65</sup> Cu	(p, n)	<sup>65</sup> Zn	2.134	PET
<sup>68</sup> Zn	(p, 2p)	<sup>67</sup> Cu	9.977	Imaging/Therapy
<sup>68</sup> Zn	(p, 2n)	<sup>67</sup> Ga	11.980	Imaging
<sup>68</sup> Zn	(p, n)	<sup>68</sup> Ga	3.703	PET

<sup>70</sup> Ge	(p, α)	<sup>67</sup> Ga	1.181	Imaging
<sup>71</sup> Ge	(p, n)	<sup>71</sup> As	2.796	PET
<sup>72</sup> Ge	(p, n)	<sup>72</sup> As	5.138	PET
<sup>73</sup> Ge	(p, n)	<sup>73</sup> As	1.123	Therapy
<sup>74</sup> Ge	(p, n)	$^{74}$ As	3.344	PET
<sup>78</sup> Kr	(p, α)	<sup>75</sup> Br	0.176	PET
<sup>76</sup> Se	(p, n)	<sup>76</sup> Br	5.745	PET
<sup>77</sup> Se	(p, n)	<sup>77</sup> Br	2.147	AET/SPECT
<sup>81</sup> Br	(p, n)	<sup>81m</sup> Kr	8.543	Imaging
89Y	(p, 2n)	<sup>88</sup> Zr	12.935	Imaging
89Y	(p, n)	<sup>89</sup> Zr	3.615	PET
<sup>99</sup> Mo	(p, n)	<sup>99m</sup> Tc	-0.432	SPECT
<sup>103</sup> Rh	(p, n)	<sup>103</sup> Pd	1.325	BT
<sup>105</sup> Pd	(p, <sup>3</sup> H)	<sup>103</sup> Pd	8.595	BT
<sup>111</sup> Cd	(p, n)	<sup>111</sup> In	1.643	Imaging
<sup>112</sup> Cd	(p, <sup>2</sup> n)	<sup>111</sup> In	11.037	Imaging
<sup>123</sup> Te	(p, n)	123 <b>I</b>	2.011	Imaging
<sup>124</sup> Te	(p, n)	<sup>124</sup> I	3.941	PET
<sup>131</sup> Xe	(p, n)	<sup>131</sup> Cs	1.137	BT
<sup>154</sup> Sm	(p, <sup>2</sup> H)	<sup>153</sup> Sm	5.743	ВСР
<sup>159</sup> Tb	(p, <sup>7</sup> Be)	<sup>153</sup> Sm	5.454	ВСР
<sup>182</sup> W	(p, <sup>6</sup> Be)	<sup>177</sup> Lu	6.945	Imaging/Therapy
$^{183}\mathrm{W}$	(p, <sup>7</sup> Be)	<sup>177</sup> Lu	2.459	Imaging/Therapy
<sup>184</sup> W	(p, 8Be)	<sup>177</sup> Lu	-9.029	Imaging/Therapy
<sup>186</sup> W	(p, <sup>10</sup> Be)	<sup>177</sup> Lu	-4.562	Imaging/Therapy
186W	(p, n)	<sup>186</sup> Re	1.361	ВСР
<sup>192</sup> Os	(p, n)	<sup>192</sup> Ir	1.830	BT
<sup>194</sup> Pt	(p, <sup>3</sup> He)	<sup>192</sup> Ir	7.572	BT
<sup>195</sup> Pt	(p, <sup>4</sup> He)	<sup>192</sup> Ir	-6.900	BT
<sup>226</sup> Ra	(p, <sup>2</sup> n)	<sup>225</sup> Ac	6.822	TAT
<sup>a</sup> Current or possi	ible future use.			

Higher energy protons ≥15 MeV also offer alternative production modes for numerous candidate medical radionuclides. Table 2 provides illustrative examples of possible production methods for these higher energy proton induced reactions. The viability of these methods depends on the development of sufficiently powerful lasers, and finding an optimum combination of cross-section and laser flux values to facilitate the economic production of the desired radionuclides.It should be noted

that a number of the reactions summarized in Table 2 require the transfer of multiple nucleons. The efficiency of these production pathways will depend on the capabilities of future laser technology and the magnitude of the relevant nuclear transfer cross-sections. In addition, transfer reactions involving heavy ions are proposed as potential medical isotope production pathways. These transfer reactions offer additional production approaches that have received limited attention.

Table 2: Selected Higher Energy (≥ 15 MeV) Proton Induced Activation Reactions to Produce Medical Radioisotopes

Target (X)	Reaction (a, b)	Medical Radioisotope (Y)	Threshold Energy (MeV)	Medical Application <sup>a</sup>		
<sup>16</sup> O	(p, <sup>6</sup> Li)	<sup>11</sup> C	22.185	PET		
<sup>20</sup> Ne	(p, <sup>10</sup> B)	<sup>11</sup> C	22.454	PET		
<sup>25</sup> Mg	(p, <sup>10</sup> B)	15O	20.811	PET		
$^{26}$ Mg	(p, <sup>14</sup> C)	$^{13}N$	17.291	PET		
<sup>27</sup> Al	(p, <sup>15</sup> O)	<sup>13</sup> C	15.889	PET		
<sup>27</sup> Al	(p, <sup>13</sup> C)	<sup>15</sup> O	15.889	PET		
<sup>27</sup> Al	(p, <sup>10</sup> B)	<sup>18</sup> F	22.833	PET		
<sup>31</sup> <b>P</b>	(p, <sup>14</sup> N)	<sup>18</sup> F	20.889	PET		
<sup>65</sup> Cu	(p, 4n)	<sup>62</sup> Zn	31.089	PET		
<sup>65</sup> Cu	(p, 3n)	<sup>63</sup> Zn	21.975	PET		
<sup>72</sup> Ge	(p, <sup>6</sup> He)	<sup>67</sup> Ga	16.012	Imaging		
<sup>106</sup> Pd	(p, <sup>4</sup> H)	<sup>103</sup> Pd	21.034	BT		
<sup>108</sup> Pd	(p, <sup>6</sup> H)	<sup>103</sup> Pd	36.656	BT		
<sup>113</sup> Cd	(p, 3n)	<sup>111</sup> In	17.577	Imaging		
<sup>114</sup> Cd	(p, 4n)	<sup>111</sup> In	26.620	Imaging		
180 <b>W</b>	(p, 4p)	<sup>177</sup> Lu	19.123	Imaging/Therapy		
<sup>203</sup> T1	(p, 3n)	<sup>201</sup> Pb→ <sup>201</sup> Tl	17.425	SPECT		
<sup>a</sup> Current or po	<sup>a</sup> Current or possible future use.					

#### **Candidate Alpha Induced Activation Reactions**

Table 3 summarizes alpha induced reactions that could produce medical isotopes. The alpha induced reactions provide an additional method for medical isotope production. For example, the availability of  $^{99m}$ Tc could be increased if alpha production is viable. Laser generation of frequently utilized  $99^m$ Tc would offer a diversity of production methods (e.g., through the  $^{96}$ Zr( $\alpha$ , n)  $^{99}$ Mo  $\rightarrow$   $^{99m}$ Tc reaction) without the need for a fission reactor.

Table 3: Selected Alpha Induced Activation Reactions to Produce Medical Radioisotopes

Target (X)	Reaction (a, b)	Medical Radioisotope (Y)	Threshold Energy (MeV)	Medical Application <sup>a</sup>
<sup>40</sup> Ca	(α, p)	<sup>43</sup> Sc	3.522	PET
<sup>42</sup> Ca	(a, np)	<sup>44</sup> Sc	13.666	PET
<sup>66</sup> Zn	(a, 2n)	<sup>68</sup> Ge	15.636	PET
<sup>69</sup> Ga	(a, 2n)	<sup>71</sup> As	15.151	PET
<sup>69</sup> Ga	(a, n)	<sup>72</sup> As	6.744	PET
<sup>70</sup> Ge	( $\alpha$ , $^{7}$ Li)	<sup>67</sup> Ga	16.166	Imaging
<sup>71</sup> Ga	(a, 2n)	$^{73}$ As	12.900	Therapy
<sup>71</sup> Ga	(a, n)	$^{74}$ As	4.926	PET
<sup>72</sup> Ge	(a, <sup>9</sup> Li)	<sup>67</sup> Ga	28.235	Imaging
<sup>75</sup> As	(a, 3n)	<sup>76</sup> Br	24.531	PET
<sup>75</sup> As	(a, 2n)	<sup>77</sup> Br	13.514	AET/SPECT
<sup>75</sup> As	(a, n)	<sup>78</sup> Br	5.226	PET/Therapy
<sup>79</sup> Br	$(\alpha, {}^{2}H)$	<sup>81m</sup> Kr	9.276	Imaging
<sup>81</sup> Br	(α, <sup>4</sup> H)	<sup>81m</sup> Kr	23.947	Imaging
<sup>96</sup> Zr	(a, n)	<sup>99</sup> Mo→ <sup>99m</sup> Tc	5.123	SPECT
<sup>105</sup> Pd	(α, <sup>6</sup> He)	<sup>103</sup> Pd	16.104	BT
<sup>106</sup> Pd	(α, <sup>7</sup> He)	<sup>103</sup> Pd	26.098	BT
<sup>108</sup> Pd	(α, <sup>9</sup> He)	<sup>103</sup> Pd	40.560	BT

<sup>116</sup> Cd	(\alpha, 3n)	<sup>117m</sup> Sn	20.422	ВСР	
<sup>130</sup> Ba	(a, n)	<sup>133</sup> Ce	10.488	PET	
<sup>130</sup> Ba	(α, γ)	<sup>134</sup> Ce	-0.003	Imaging/PET	
<sup>132</sup> Ba	(a, n)	<sup>135</sup> Ce	9.461	PET	
<sup>154</sup> Sm	(α, <sup>5</sup> He)	<sup>153</sup> Sm	8.861	ВСР	
<sup>159</sup> Tb	$(\alpha, {}^{10}{\rm B})$	<sup>153</sup> Sm	6.599	ВСР	
<sup>180</sup> W	$(\alpha, {}^{7}B)$	<sup>177</sup> Lu	22.701	Imaging/Therapy	
<sup>182</sup> W	(α, <sup>9</sup> B)	<sup>177</sup> Lu	5.850	Imaging/Therapy	
<sup>183</sup> W	$(\alpha, {}^{10}{\rm B})$	<sup>177</sup> Lu	3.604	Imaging/Therapy	
<sup>184</sup> W	(α, <sup>11</sup> B)	<sup>177</sup> Lu	-0.439	Imaging/Therapy	
<sup>186</sup> W	$(\alpha, {}^{13}B)$	<sup>177</sup> Lu	4.257	Imaging/Therapy	
<sup>193</sup> Ir	(α, <sup>5</sup> He)	<sup>192</sup> Ir	8.666	BT	
<sup>194</sup> Pt	(α, <sup>6</sup> Li)	<sup>192</sup> Ir	11.592	BT	
<sup>195</sup> Pt	( $\alpha$ , $^7$ Li)	<sup>192</sup> Ir	10.447	BT	
<sup>209</sup> Bi	(a, 2n)	<sup>211</sup> At	20.328	TAT	
<sup>a</sup> Current or possible future use.					

In a similar fashion, the production of <sup>211</sup>At would facilitate another production mode for this TAT radionuclide. An additional <sup>211</sup>At supply would facilitate the expansion of this therapy approach.

The alpha production modes summarized in Table 3 offer additional reaction pathways to produce currently utilized medical isotopes as well as potential new radionuclides. Table 3 does not exhaust the potential modes for the production of useful medical radionuclides.

#### **Production of Heavy Ions for Therapy Applications**

Germany and Japan have successfully treated over 20,000 patients using <sup>12</sup>C beams, but this therapy approach is not universally available. Heavy ions offer the potential for large energy depositions at the location of the Bragg peak, but their utilization has been limited because a specialized accelerator is required to produce the <sup>12</sup>C ions, and experimental nuclear physicists are required for their successful use in therapy applications. These facilities are usually collocated with national accelerators, and are not available in locations without sufficient infrastructure.

Lasers offer a unique opportunity to expand the use of heavy ion therapy, but significant laser energy increases and additional technological advances will be required for successful implementation. Candidate reactions and their threshold energies to produce <sup>12</sup>C and other heavy ions are summarized in Table 4. Both photon, proton and alpha induced reactions are summarized in Table 4. These reactions include less challenging few nucleon reactions and more challenging multiple nucleon transfers. This set of reactions provide a wealth of possibilities to produce heavy ions for therapy applications. Analogous types of reactions would be capable of producing other beams for heavy ion therapy (e.g., <sup>14</sup>N, <sup>16</sup>O and <sup>20</sup>Ne) [6-9]. The viability of the reactions summarized in Table 4 depends on the development of sufficient laser power, proton and alpha beam fluence rates, and determining sufficient reaction cross-sections for economic viability. In addition, the generated 12C could be ionized using conventional accelerator technology, and any subsequent increase in energy would be achieved using EM fields to reach applicable therapy values. Advances is plasma wake field accelerator technology would enhance the efficiency of this approach. These advances in technology require significant research and development.

Direct photoproduction via free electron lasers and powerful conventional systems are alternatives to the use of supplemental EM fields. This option requires a significant increase in laser intensity and power that would directly create heavy ions for therapy applications at the requisite energies [6-9]. Considering the aforementioned options, lasers would be an attractive alternative to the use of specialized accelerators, and would facilitate

Table 4: Selected Photon, Proton, and Alpha Induced Reactions to Produce <sup>12</sup>C and Other Heavy Ions for Therapy Applications.

Target (X)	Reaction (a, b)	Medical Therapy Beam	Threshold Energy (MeV)	Medical Application <sup>a</sup>
<sup>10</sup> B	(α, <sup>2</sup> H)	<sup>12</sup> C	-1.340	HI Therapy
<sup>11</sup> B	(α, <sup>3</sup> H)	<sup>12</sup> C	3.857	HI Therapy
<sup>13</sup> C	(α, <sup>5</sup> He)	<sup>12</sup> C	5.840	HI Therapy
<sup>13</sup> C	(γ, n)	<sup>12</sup> C	4.946	HI Therapy
<sup>13</sup> C	(p, d)	<sup>12</sup> C	2.722	HI Therapy
<sup>14</sup> N	(a, Li)	<sup>12</sup> C	8.799	HI Therapy
<sup>14</sup> N	(p, <sup>3</sup> He)	<sup>12</sup> C	4.779	HI Therapy
<sup>15</sup> N	(p, α)	<sup>12</sup> C	-4.965	HI Therapy
<sup>15</sup> N	(a, <sup>7</sup> Li)	<sup>12</sup> C	12.382	HI Therapy
<sup>15</sup> N	(γ, n)	$^{14}N$	10.833	HI Therapy
<sup>16</sup> O	(α, <sup>8</sup> Be)	<sup>12</sup> C	7.254	HI Therapy
<sup>17</sup> O	(α, <sup>9</sup> Be)	<sup>12</sup> C	9.732	HI Therapy
<sup>17</sup> O	(p, <sup>6</sup> Li)	<sup>12</sup> C	7.607	HI Therapy
<sup>17</sup> O	(γ, n)	<sup>16</sup> O	4.143	HI Therapy
<sup>18</sup> O	(p, <sup>7</sup> Li)	<sup>12</sup> C	8.400	HI Therapy
<sup>18</sup> O	(α, <sup>10</sup> Be)	<sup>12</sup> C	10.963	HI Therapy
<sup>19</sup> F	(p, 8Be)	<sup>12</sup> C	-0.860	HI Therapy
<sup>19</sup> F	(α, <sup>11</sup> B)	<sup>12</sup> C	7.730	HI Therapy
<sup>20</sup> Ne	(p, <sup>9</sup> B)	<sup>12</sup> C	12.169	HI Therapy
<sup>20</sup> Ne	(α, <sup>12</sup> C)	<sup>12</sup> C	4.617	HI Therapy
<sup>21</sup> Ne	(γ, n)	<sup>20</sup> Ne	6.761	HI Therapy
<sup>23</sup> Na	(p, <sup>12</sup> C)	<sup>12</sup> C	2.241	HI Therapy
<sup>23</sup> Na	(α, <sup>15</sup> N)	<sup>12</sup> C	7.206	HI Therapy
<sup>24</sup> Mg	(p, <sup>13</sup> N)	<sup>12</sup> C	11.990	HI Therapy
<sup>24</sup> Mg	(α, <sup>16</sup> O)	<sup>12</sup> C	6.772	HI Therapy
<sup>25</sup> Mg	(p, <sup>14</sup> N)	<sup>12</sup> C	8.767	HI Therapy
<sup>25</sup> Mg	(α, <sup>17</sup> O)	<sup>12</sup> C	9.959	HI Therapy
$^{26}$ Mg	(p, <sup>15</sup> N)	<sup>12</sup> C	9.027	HI Therapy
<sup>26</sup> Mg	(a, 18O)	<sup>12</sup> C	13.009	HI Therapy
<sup>27</sup> A1	(p, <sup>16</sup> O)	<sup>12</sup> C	5.171	HI Therapy
<sup>27</sup> Al	$(\alpha, {}^{19}F)$	<sup>12</sup> C	13.285	HI Therapy

#### **Photoproduction of Medical Radioisotopes**

As laser technology improves, the possibility exists for free electron lasers (FEL) to be extended into the gamma-ray energy range. This advance would open the possibility for the photoproduction of medical radionuclides. Table 5 provides a sample of the radionuclides that could be produced by laser induced photonuclear reactions.

Table 5: Selected Photonuclear Reactions to Produce Medical Radioisotopes

Target (X)	Reaction (a, b)	Medical Radioisotope (Y)	Threshold Energy (MeV)	Medical Application <sup>a</sup>
<sup>12</sup> C	(γ, n)	<sup>11</sup> C	18.721	PET
<sup>14</sup> N	(γ, n)	<sup>13</sup> N	22.546	PET
<sup>16</sup> O	(γ, n)	<sup>15</sup> O	15.664	PET
<sup>19</sup> F	(γ, n)	<sup>18</sup> F	10.432	PET
<sup>33</sup> S	(γ, p)	<sup>32</sup> P	9.570	Therapy
<sup>36</sup> S	(γ, n)	<sup>35</sup> S	9.889	Imaging
<sup>69</sup> Ga	(γ, 2n)	<sup>67</sup> Ga	18.590	Imaging
<sup>71</sup> Ga	(γ, 4n)	<sup>67</sup> Ga	33.544	Imaging
<sup>75</sup> As	(γ, 4n)	<sup>71</sup> As	37.422	PET
<sup>75</sup> As	(γ, 3n)	<sup>72</sup> As	29.015	PET
<sup>75</sup> As	(γ, 2n)	<sup>73</sup> As	18.217	Therapy
<sup>75</sup> As	(γ, n)	<sup>74</sup> As	10.243	PET
<sup>79</sup> Br	(γ, 3n)	$^{76}\mathrm{Br}$	29.992	PET
<sup>79</sup> Br	(γ, 2n)	$^{77}\mathrm{Br}$	18.975	AET/SPECT
<sup>79</sup> Br	(γ, n)	$^{78}\mathrm{Br}$	10.687	PET/Therapy
<sup>82</sup> Kr	(γ, n)	<sup>81m</sup> Kr	11.158	Imaging
<sup>83</sup> Kr	(γ, 2n)	81mKr	18.621	Imaging
<sup>84</sup> Kr	(γ, 3n)	81mKr	29.141	Imaging
89Y	(γ, n)	88Y	11.474	Therapy
<sup>127</sup> I	(γ, 4n)	123 <b>I</b>	33.324	Imaging
$^{127}I$	(γ, 2n)	<sup>125</sup> I	16.289	BT
<sup>193</sup> Ir	(γ, n)	<sup>192</sup> Ir	7.722	BT
<sup>194</sup> Pt	(γ, 2H)	<sup>192</sup> Ir	13.066	BT
<sup>195</sup> Pt	(γ, 3H)	<sup>192</sup> Ir	12.914	BT
<sup>226</sup> Ra	(γ, 3n)	<sup>223</sup> Ra	17.779	ВСР
<sup>a</sup> Current or possi	ble future use.	•	•	-

The results of Table 5 offer an intriguing possibility for the production of medical isotopes that are currently difficult to generate. For example, <sup>223</sup>Ra must be produced in a reactor and the activation products chemically separated. The relevant reaction involves neutron capture followed by beta and alpha decays

$$^{226}_{88}Ra + n \rightarrow ^{227}_{88}Ra \stackrel{\beta^-}{\rightarrow} ^{227}_{89}Ac \stackrel{\beta^-}{\rightarrow} ^{227}_{99}Th \stackrel{\alpha}{\rightarrow} ^{223}_{88}Ra \quad (5)$$

Photoproduction of 223Ra will be considerably simpler (e.g.,  $^{226}$ Ra( $\gamma$ ,  $^{3n}$ ) $^{223}$ Ra) and avoids the use of a reactor and minimizes chemical separations to recover the desired radionuclide. The viability of the photoproduction of medical radionuclides depends on the development of lasers with the appropriate characteristics.

Photoproduction would significantly expand the availability of medical radioisotopes. Although high energy FELs are expensive, national laboratory level projects, technological advances could reduce their cost and size. If these advances are achieved, a new production pathway for medical isotopes would be established.

# **Economic Viability of Laser Produced Medical Isotopes**

The economic viability of the laser production of medical isotopes depends on resolving a number of technological uncertainties. First, lasers must be developed to produce the necessary energies, fluence rates, power levels, pulse repetition rates, and have sufficient reliability to support the desired isotope production reactions. Second, the physics of the reaction process should be established to determine the optimum combination of reaction energy and associated cross-sections. Third, the target radionuclides must be available in sufficient quantities, and that necessity could require enrichment of the desired isotope. Fourth, the need for chemical separation of the final target materials to recover the desired medical radionuclide should be minimized. Finally, the production process must be optimized for efficiency and reliability.

#### **Conclusions**

Efficient, high intensity, and high power lasers offer an alternative method for the production of medical radioisotopes that are traditionally produced by research reactors and accelerators.

These isotopes could be generated using laser induced proton and alpha particle beams. The resulting radionuclides can be utilized in both imaging and therapeutic applications.

Improvements in laser power, intensity, and efficiency also offer the potential for producing heavy ions. These beams would permit an expanded use of heavy ion therapy utilizing their strong Bragg peaks. Photoproduction reactions could facilitate the production of medical isotopes via a currently unused production method. The heavy ion and photoproduction approaches are speculative, and require research and development to be successfully implemented.

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