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A theoretical model for the production of Ac-225 for cancer therapy by photon-induced transmutation of Ra-226

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Abstract

Radium needles that were once implanted into tumours as a cancer treatment are now obsolete and constitute a radioactive waste problem, as their half-life is 1600 years. We are investigating the reduction of radium by transmutation on a small scale by bombarding Ra-226 with high-energy photons from a medical linear accelerator (linac) to produce Ra-225, which subsequently decays to Ac-225, which can be used as a generator to produce Bi-213 for use in 'targeted alpha therapy' for cancer.

This paper examines the possibility of producing Ac-225 with a linac using an accurate theoretical model in which the bremsstrahlung photon spectrum at 18 MV linac electron energy is convoluted with the corresponding photonuclear cross sections of Ra-226. The total integrated yield can then be obtained and is compared with a computer simulation.

This study shows that at 18 MV, the photonuclear reaction on Ra-226 can produce low activities of Ac-225 with a linac. However, a high power linac with high current, pulse length and frequency is needed to produce practical amounts of Ac-225 and a useful reduction of Ra-226.

Keywords: Medical linear accelerator (linac); Actinium-225; Radium-226; Radium-225; Bismuth-213; Targeted alpha therapy; Cancer therapy

1. Introduction

1.1. Actinium-225

Ac-225 is an alpha emitting radiosiotope with a 10-day half-life that decays to produce Bi-213. Either Ac-225 or Bi-213 can be used as an agent for radio-immunotherapy.

Alpha particle emitters are the most potent sources for lethal irradiation of single cancer cells and micrometastases because of their densely ionising radiation. Alpha particles are of considerable interest for radio-immunotherapy applications since their short range in soft tissue is limited to only a few cell diameters.

Alpha particles have high linear energy transfer (LET) in tissues. High LET radiation induces far more biological damage over a shorter range than low LET beta radiation, and is therefore much more cytotoxic. The delivery of such a high energy in so small a volume makes alpha particles especially well suited for targeting micrometastatic disease and single cancer cells such as leukaemia and other blood-borne disease.

The Bi-213 radioisotope is of special interest because of its unique nuclear properties, which include a short 46-min half-life and high-energy (8.4 MeV) alpha-particle emission. Its availability from the Ac-225/Bi-213 (Actinium Pharmaceuticals, 2005) generator system makes this radioisotope particularly well suited for medical use.

Cancer trials are being conducted at the Cancer Care Centre, St. George Hospital in Sydney, where the Targeted Alpha Therapy (TAT) (Allen et al., 2004) programme using Bi-213 offers the potential to inhibit the growth of micrometastases by selectively killing isolated and pre-angiogenic clusters of cancer cells. In TAT, the radioisotope is bound to a monoclonal antibody or protein and their molecular subunits attach to the receptors on cancer

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cells, allowing radiation to attack the cancer while minimising the potentially negative impact to surrounding tissue.

1.2. Uranium-233 decay chain

The Bi-213 isotope that is holding promise for cancer treatment is produced through a complex process that starts with U-233 (Fig. 1). The key intermediates in this process are Th-229 and Ac-225. Ac-225 is currently derived from purified Th-229 extracted from U-233 at ORNL (Boll et al., 2005).

There are a number of ways to produce Ac-225. The most practical way at present is to derive these isotopes from the decay of Th-229, which is produced by the decay of U-233. Ac-225 is the product being shipped to medical facilities. Bi-213 is separated from the Ac-225 at the hospital and combined with the targeting agent.

1.3. Production method

Ac-225 could be produced using accelerators or reactors or by separation techniques. Methods include producing Th-229 directly as opposed to obtaining it by the decay of U-233; producing Ra-225, which decays into Ac-225; and producing Ac-225 directly. While each of these methods eventually results in a supply of Ac-225 for use in a Bi-213 generator, they all require additional chemical processing and/or separation steps that are yet to be determined and will likely increase production costs.

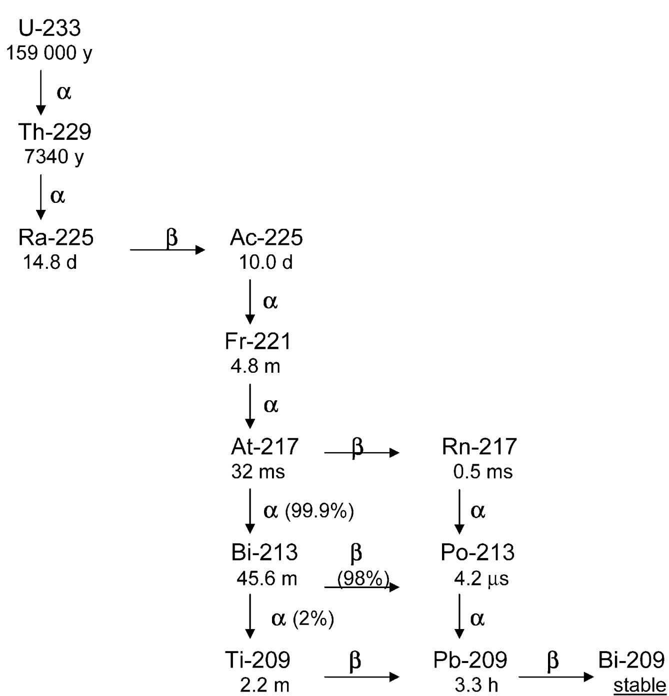

Fig. 1. U-233 decay chain (Korea Atomic Energy Research Institute, 2005).

Possible ways of producing Ac-225 (Koch et al., 1999) are:

- ^{232}Th (n; γ, 2β) ^{233}U: This method involves bombarding Th-232 with thermal neutrons to produce U- 233, which will then follow the U-233 decay chain leading to Ac-225 as shown in Fig. 1.
- ^{226}Ra ($3n$; 2β) ^{229}Th: This method involves bombarding radium with thermal neutrons to produce Th-229 after 3 neutron capture events, which decays to Ac-225.
- ^{226}Ra (p; $2n$) ^{225}Ac: In this method protons from a cyclotron produce Ac-225 directly with the peak cross section being about 540 mb at 16 MeV proton energy. (Private communication: G Dracoulis, Australian National University) using the standard fusion-evaporation code.) The ^{226}Ra (p; $3n$)^{224}Ac reaction rapidly takes over at higher energies.
- ^{226}Ra (n; $2n$, β) ^{225}Ac: Neutrons bombard radium to produce Ac-225.
- ^{226}Ra (γ; n) ^{225}Ra: This reaction produces Ra-225, which subsequently decays to Ac-225 through beta decays.

A number of the above reactions involve neutron bombardment at thermal energies. For industrial applications that require neutrons, users have three primary sources from which to choose: nuclear reactors, radioisotopes, and accelerator-based high-energy neutron sources. Nuclear reactors are the largest and most prolific sources of neutrons.

This paper investigates the photonuclear reaction route as medical linacs are routinely used for radiotherapy in hospitals.

1.4. Photonuclear production

Linacs are the mainstay of radiotherapy treatment. They deliver megavoltage electron beams accelerated by klystron or magnetron generated radio-frequency fields through copper waveguides (Dowsett et al., 2001). The beam of electrons from the gridded electron gun is focused by a solenoid to a beam of less than 2 mm in diameter to strike a 0.76 mm thick tantalum or tungsten target and produce bremsstrahlung radiation.

Although the theoretical model in this paper is based on a 2100C MV Clinac from Varian, it would be very similar to any linac once the energy range was adjusted. The spectrum of bremsstrahlung photons produced by the linac extends from zero energy up to the maximum energy of the electrons hitting the target, which is 18 MeV in this case. Measuring or calculating the bremsstrahlung spectrum is very difficult. The most common approach today is to use Monte Carlo methods (Ahnesjo, 1989) for calculating the spectra.

The photonuclear reaction is

$$^{226}_{88}\mathrm{Ra} + Y \rightarrow {}^{225}_{88}\mathrm{Ra} + {}^{1}_{0}n. \tag{1}$$

Reaction (1) involves exciting the radium nucleus with bremsstrahlung photons so that a neutron is ejected. The reaction threshold of 6.4 MeV is easily achievable with a linac. The reaction is electromagnetic in nature and would be virtually instantaneous. This means after irradiation, Ra-225 will be at a maximum yield and will decay slowly over time, the half-life being 14.9 days, producing Ac-225 by beta emission, by the following decay:

$$^{225}_{88}\mathrm{Ra} \rightarrow {}^{225}_{89}\mathrm{Ac} + {}^{0}_{-1}e. \quad (2)$$

2. Theory

2.1. Bremsstrahlung production

An electrically heated filament (cathode) within the linac generates electrons that are accelerated by waveguide from the filament to the tungsten target by the application of high-voltage pulses applied between drift tubes. Once inside the drift tube, they are shielded from the field and drift through at a constant velocity. When they arrive at the next gap, the radiofrequency field accelerates them again until they reach the next drift tube. This continues, with the particles picking up more and more energy in each gap, until they exit onto the target. The drift tubes are necessary because an alternating field is used and without them, the field would alternately accelerate and decelerate the particles. The drift tubes shield the particles for the length of time that the field would be decelerating.

Linac photons or bremsstrahlung radiation (Bueche, 1969) arise when high-energy electrons penetrate the anode material passing close to its atomic nuclei. The electrons are deflected from their initial path by the nuclear coulomb field of the tungsten atoms causing changes in velocity. Energy is lost in the form of electromagnetic radiation, which is called ‘braking radiation’ or bremsstrahlung.

Energy transformations that yield the photon radiation vary since the bombarding electrons approach the nuclei at different impact radii. There is consequently a spread of bremsstrahlung energies from a maximum (where the entire kinetic energy is transformed into photon radiation) to the lowest energy photon emission when the electron is only slightly deflected by the nuclear field.

A polar diagram (Nordell et al., 1984) showing the variation of the intensity of bremsstrahlung rays with angle produced by the electron bombardment of various targets is shown in Fig. 2. Curve A, shows 34 keV electrons bombarding a thin aluminium foil and curves B and C, 10 and 20 MeV electrons bombarding a thin 0.05 cm tungsten target. Curve D is a typical intensity distribution for a diagnostic X-ray tube with a 16° thick tungsten target, with the beam taken at right angles to the electron beam and excited at 90 kV$_p$. As the energy of the bombarding electrons is increased, the two lobes of curve A, tip forward to yield, at very high energies, a distribution with all the radiation in the forward direction.

Mohan et al. (1985) found that the angular distribution of 15 MeV photons from a Clinac-20 was very narrow with more than 99.9% of all the photons contained within 2 degrees of the central axis of the target. A 2100C Clinac will have a similar photon angle distribution. This means at 100 cm (SSD) the vast majority of the photon beam will be contained in an area with a cross section of less than 7 cm. This, of course, assumes there is no interference with the photons on their journey. In reality, however, photon spread due to the linac collimator and flattening filter would need to be considered.

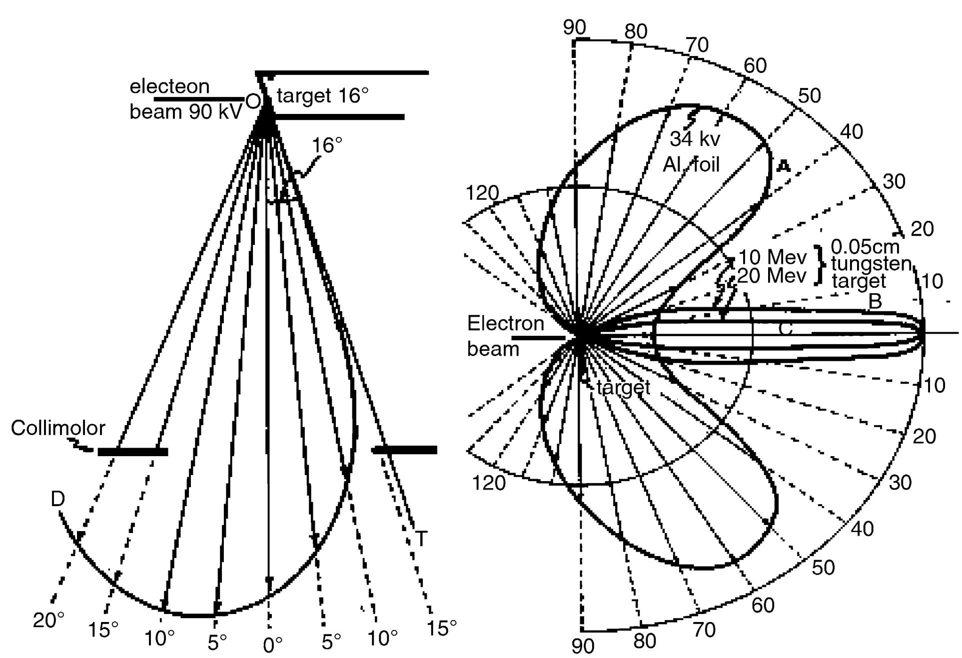

Fig. 2. Bremsstrahlung emission from an accelerated charge.

This study is based on an 18 MV 2100C Clinac. As such the range in photon energies (bremsstrahlung) is a positively skewed Gaussian curve with an average energy of about 6 MeV and peak flux at 1.25 MeV. The photon intensity is high at low energies but quickly tapers off at higher energies. More will be said about this later.

The most accurate way to calculate the yield (Y) of Ra-225 produced by the photonuclear reaction (1) is by summing up the individual yields $Y(E)$ over all bremsstrahlung energies:

$$Y = \int_{E_1}^{E_2} Y(E)\,\mathrm{d}E, \tag{3}$$

where E_1 is the reaction threshold at 6.4 MeV (Centre for Photonuclear Experiments Data (CDFE), 2005) and E_2 is the maximum electron energy of the linac, i.e. 18 MeV.

To perform this integration, the number of bremsstrahlung photons and photon reaction cross section as a function of energy must first be calculated over the bremsstrahlung energy range.

2.2. Reaction cross section

The reaction cross section (Wehr and Richards, 1974) is defined by

$$\sigma = \frac{N_R}{N_1}, \tag{4}$$

where σ is the cross section (barns), the N_I the number of incident particles per unit time (s) per unit area (cm^2), and N_R the number of reactions per unit time (s) per nucleus.

The cross section is a function of energy and can be evaluated at various energies using the cross section for the photonuclear reaction given by the expression below, Eq. (5), which is an application of the Breit–Wigner formula (Allyn and Bacon, 1966). This formula describes the cross section for the formation of a particle resonance, intermediate between two other particle states:

$$\sigma(E) = \frac{(\Gamma/2)^2}{(E-E_r)^2 + (\Gamma/2)^2}\left(\frac{E}{E_r}\right)\sqrt[\sigma_r]{\frac{E-E_t}{E_r-E_t}}, \tag{5}$$

where is the $E_r = 13.45$ MeV (giant dipole resonance (GDR) energy) (Berman, 1976), E_t the 6.4 MeV (reaction threshold energy) (CDFE, 2005), Γ the 3.97 MeV (FWHM at resonance) (Berman, 1976), and σ the 521 mb $= 52.1 \times 10^{-26}$ cm^2 (peak resonance cross section) (Berman, 1976):

- The resonance energy (E_r) and peak resonance cross section (σ) values are unknown for Ra-226 but are assumed to be similar to other nuclides with similar mass number. The values used here are for Bi-209, which is one of the closest radionuclides with known values, which are comparable to Th-232.
- The reaction threshold energy (E_t) has been calculated using the mass formula (CDFE, 2005).
- The full-width at half-maximum (FWHM) at resonance (Γ) is unknown for Ra-226 but is assumed to be similar to nuclides with similar mass number. The value used here is for Bi-209.
- The square root expression in the above cross section equation is the normalisation factor. It will be equal to one at resonance, less than one below resonance and greater than one above resonance.
- The above equation is only accurate up to 18 MeV where single neutron reactions greatly dominate (valid for linac energies). At higher energies (CDFE, 2005) two neutrons are produced. Because of the weak high-energy tail of the photon spectrum (see later) these should not affect the model calculation to any significant degree.

2.3. Convolution

The total yield (Y) of Ra-225 is calculated using Eq. (6):

$$Y = \int_{6.4\,\mathrm{MeV}}^{18\,\mathrm{MeV}} Y(E)\,\mathrm{d}E = \int_{6.4\,\mathrm{MeV}}^{18\,\mathrm{MeV}} N\,\phi(E)\,\sigma(E)\,t\,\mathrm{d}E, \tag{6}$$

where Y is the yield in Ra-225 atoms/s, N the number of atoms of Ra-226/cm^3, ϕ the photon flux/s, σ the cross section (mb), and t the thickness of the Ra-226 target (cm):

$$Y(\mathrm{atoms/s}) = \int_{6.4\,\mathrm{MeV}}^{18\,\mathrm{MeV}} (N\ \mathrm{atoms/cm^3} \times \phi\ \mathrm{photons/s} \times t\ \mathrm{cm})\,\mathrm{d}E. \tag{7}$$

2.4. Transient equilibrium

Once Ra-225 has been produced it will decay to Ac-225, as shown previously in Fig. 1. The ideal theoretical case is shown in Fig. 3, where the half-life of the daughter radionuclide is shorter than the parent radionuclide, resulting in transient equilibrium. This passing matching

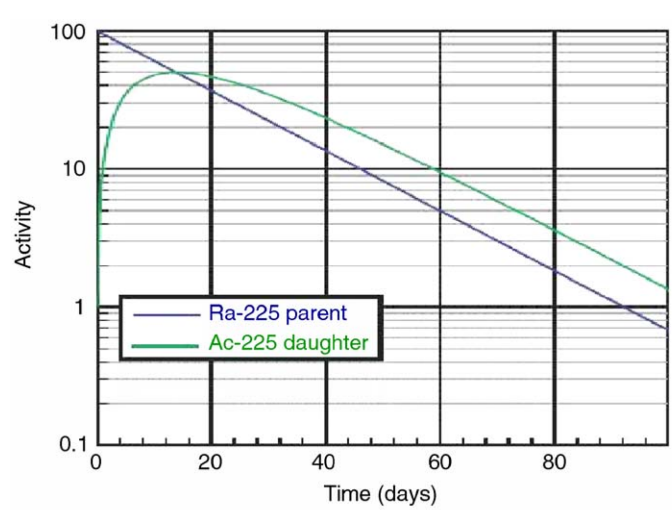

Fig. 3. Theoretical transient equilibrium resulting from the buildup of the shorter-lived Ac-225 activity beginning with a pure sample of the longer-lived parent Ra-225 nucleus.

of activity occurs after about 13 days and the activity of the daughter at this point is about half that of the original parent activity. However, in our situation, the curve only approximates the theoretical since the Ac-225 (daughter) half-life (10 days) is not much shorter than the Ra-225 (parent) half-life (14.8 days).

3. Calculations

3.1. Linac parameters

The relevant specifications of the 18 MV linac (provided by Varian Australia) are listed below (Table 1).

Linacs do not produce continuous current because pulsed electron beams are accelerated by klystron or magnetron generated radio-frequency fields through copper waveguides. This means the actual current-on time is between 3.5 and 4 μS, 180 times/s. Thus, the maximum pulse current of 36 mA is equivalent to an average beam current of 26 μA, using a pulse length of 4μS.

As 1 amp = 1 Coulomb/s = 6.25×10^{18} electrons/s, then 26 μA = 1.625×10^{14} electrons/s.

3.2. Bremsstrahlung production efficiency

The probability, p, for bremsstrahlung photons is about 1–5%/electron (Dowsett et al., 2001) at low energies but increases with both atomic number Z of the anode material (target) and the electron beam energy E_β. Most of the electron energy (99%) is lost as heat. Above a certain energy, called the critical energy (E_c), bremsstrahlung efficiency must be considered. This critical energy can be calculated (Frauenfelder and Henley, 1991):

$E_c \approx 600/Z$ MeV = 8.1 MeV, which is well below the 18 MV energy in this study.

The efficiency η of bremsstrahlung production at electron energy (E_β, eV) at low energies (Dimitar, 1998) can be calculated from

$$\eta = k\, E_\beta\, Z, \tag{8}$$

where k is a constant, which depends on the material, and equals 1.1×10^{-9} for the tungsten target ($Z = 74$) (Dowsett et al., 2001).

The bremsstrahlung yield at low energies increases linearly as the energy of the incident electrons increases (Frauenfelder and Henley, 1991), but is generally less than 5% at low electron energies (125 kV~1%). At 1 MeV the yield can be as high as 8% (Dowsett et al., 2001).

No expression will give the bremsstrahlung efficiency exactly over the entire energy range. At medium energies the general approximation formula (Emilio, 1975):

$$\eta \approx \frac{E_\beta Z}{750} \quad \text{where } E_\beta \text{ is the electron energy in MeV.} \tag{9}$$

This is similar to Eq. (8) but increases to over 100% at energies around 12 MeV. To find the bremsstrahlung electron efficiency at 18 MeV three methods have been examined:

- Use of a higher-energy approximation formula (Meyerhof, 1967):

  $$\eta \approx \frac{6 \times 10^{-4} Z E_\beta}{1 + 6 \times 10^{-4} Z E_\beta} \quad \text{where } E_\beta \text{ is in MeV.} \tag{10}$$

  This formula ensures the efficiency stays below 100% and gives 44.4% efficiency at 18 MeV.
- Use of measured bremsstrahlung efficiencies in water (line of best fit) Fig. 4 (Emilio, 1975).
  The efficiency of bremsstrahlung in elements of different atomic number Z varies nearly as Z^2 (Meyerhof, 1967). Thus, the efficiency for tungsten is about 49% at 18 MeV.
- Table 2 (Spring, 1960) below, gives a small number of measured and theoretical values for tungsten. It shows that roughly a doubling in energy results in an almost doubling in efficiency. This gives an extrapolated efficiency at 18 MeV of about 52%.

The higher-energy approximation formula (1st method) is the most accurate in determining bremsstrahlung efficiency as the other two methods, which rely on comparison with water and Z^2 related bremsstrahlung increases, and are not accurate across the wide energy range.

This model uses a conservative 40% bremsstrahlung efficiency to normalise the photon spectrum in Fig. 5. This means the total number of photons produced by the linac from 0 to 18 MeV is equal to 6.5×10^{13}.

3.3. Linac photon spectrum

A photon spectrum can now be constructed knowing the total number of photons and their intensities. The spectrum in Fig. 5 gives the number of photons as a function of photon energy up to 18 MeV using photon intensity data from Varian Corporation, and allows the calculation of the Ra-225 yield at each of these energies using the reaction cross section at these energies.

With the photoneutron Eq. (1) having a threshold energy of 6.4 MeV, the total number of photons that could produce Ra-225 is 1.61×10^{13}.

Table 1
Parameters of the 18 MV Varian Clinac 2100C

Electron energy (max) = 18 MeV (+3%)
Peak pulse current ~36 mA
Frequency = 180 Hz
Pulse length = 3.5 μ↔4 μS
Mean current = 26 μA

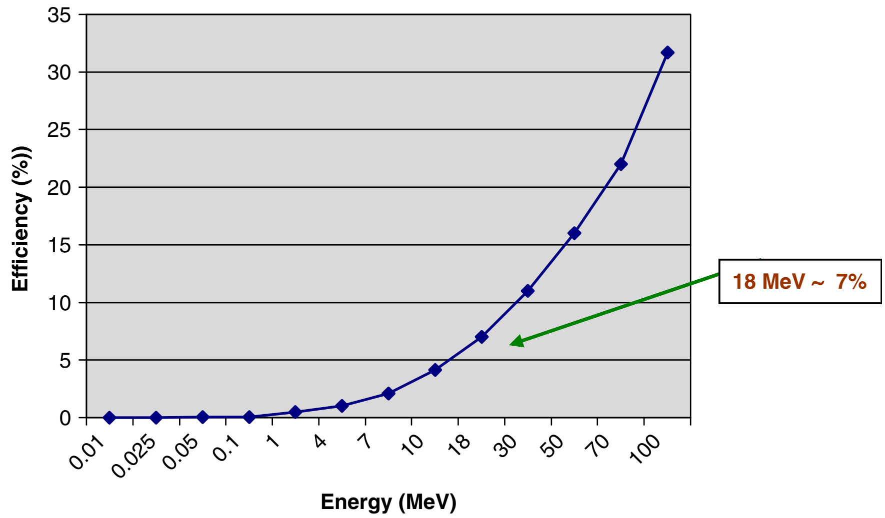

Fig. 4. Electron bremsstrahlung efficiencies in water.

Table 2
Theoretical and measured bremsstrahlung efficiencies for tungsten

Energy (MeV)	Efficiency (%)	
	Experimental	Theoretical
0.90	3.4	3.4
1.63	5.8	5.6
2.35	10.4	8.3

3.4. Calculated reaction cross section

The photoneutron reaction (Eq. (1)) cross section over the range of linac energies can be calculated using expression (5) and is shown in Fig. 6 below.

This graph shows a zero cross section at threshold reaction-energy of 6.4 MeV followed by a steady increase up to a maximum cross section of 532 mb at an energy of 13.75 MeV. The cross section is truncated at 18 MeV, which is the highest electron and photon energy of the linac in this model.

3.5. Yield of Ra-225

The total yield (Y) of Ra-225 can now be calculated using Eq. (7) and the data that was used to construct both Figs. 5 and 6. The result of this calculation is shown in Fig. 7, which is the yield in atoms of Ra-225/s over the complete energy range that the reaction can occur, i.e. from 6.4 to 18 MeV. Maximum yield occurs at 13.5 MeV.

A 1 cm^3 volume of Ra-226 contains 1.33×10^{22} atoms, since 226 g of Ra-226 contains 6.023×10^{23} atoms and Ra-226 has a density of 5 g/cm^3. Using Eq. (7), the total yield $(Y) = 2.8 \times 10^{10}$ atoms/s of Ra-225. Thus, an 18 MV linac bombarding a 1 cm^3 target of Ra-226 (with activity 5 Ci) with bremsstrahlung photons in the energy range from 6.4 to 18 MeV, will produce 2.8×10^{10} atoms of Ra-225/s or about 10^{14} atoms/h of irradiation. This is based on a 40% bremsstrahlung efficiency, which is by far the main source of uncertainty in this simulation. This will be discussed later.

The activity of Ra-225 is given by $A_{225} = \lambda \times N_{225}$ (no of atoms of Ra-225). The decay constant ($\lambda = 0.693/t_{1/2}$) of Ra-225 (half-life: 14.9 days) is $\lambda = 5.38 \times 10^{-7}\,s^{-1}$ and 1 Ci $= 3.7 \times 10^{10}$ dis/s. Thus,

$$\begin{aligned} A_{225} &= 5.38 \times 10^{-7} \times 10^{14} \\ &= 5.38 \times 10^{7}\ \mathrm{Bq\ (dis/s)/h\ irradiation} \\ &= 1.45\ \mathrm{mCi/h\ irradiation.} \end{aligned}$$

3.6. Optimum linac energy

Computer simulation programs using C++ and MATLAB were also used to calculate the theoretical yield of Ra-225 using known Th-232 cross section data (Berman, 1976) and combining it with bremsstrahlung photon spectra. The programme was designed so that it could be used for different energies and currents. MATLAB was particularly useful for plotting the graphs. The results are shown in Fig. 8 and Table 3. One mole of Ra-226 was irradiated in this simulation.

Calculations showed that the linac does not require the highest possible energy, as the yield plateaus with increasing energy. Therefore, the optimal energy for Ac-225 is around 16 MeV. 18 MeV (Siemens) actually provides 15.25 MeV, which is the nearest energy to 16 MeV. On the other hand, 10 MeV (Varian) is not much greater than the threshold energy of photoneutron reaction. 25 MeV (Elekta) provides the highest energy, however, the yield is much less than 15 MeV (Varian) because of lower bremsstrahlung output. The reason for this is that, although linac power is the product of current and voltage,

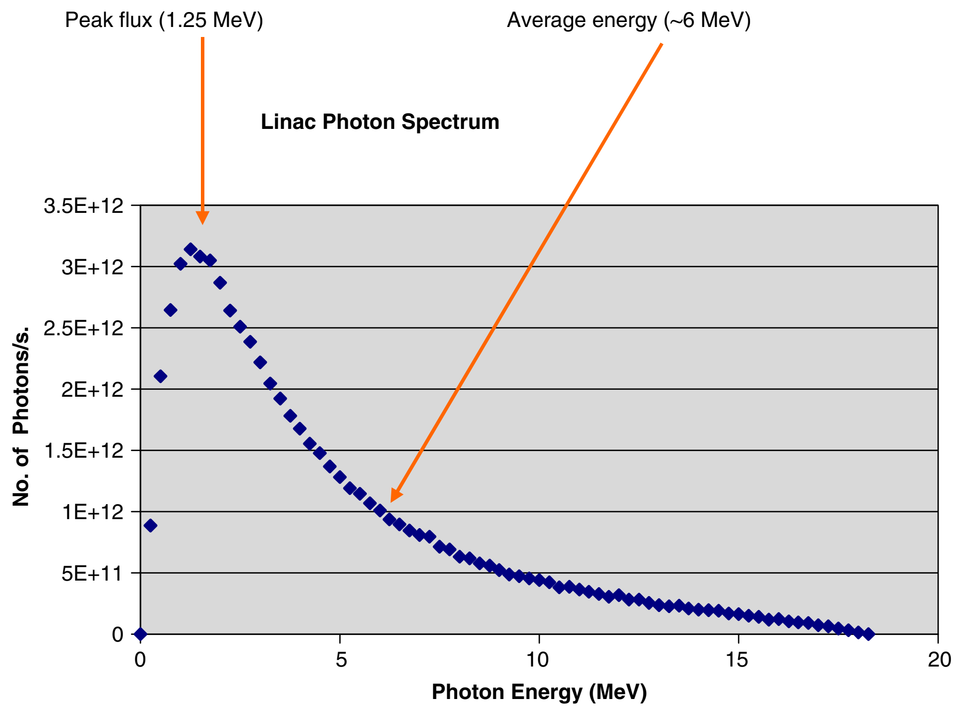

Fig. 5. Photon number/s vs. photon energy (MeV).

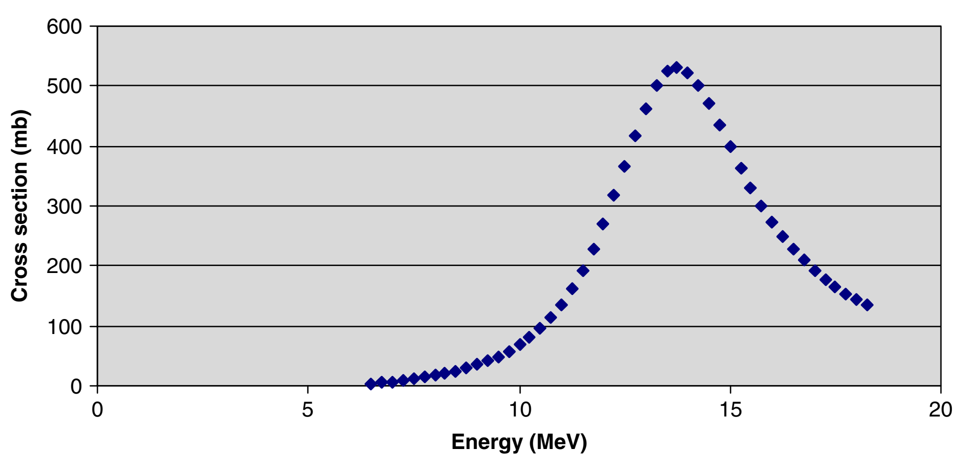

Fig. 6. Photonuclear cross section (mb) vs. photon energy (MeV).

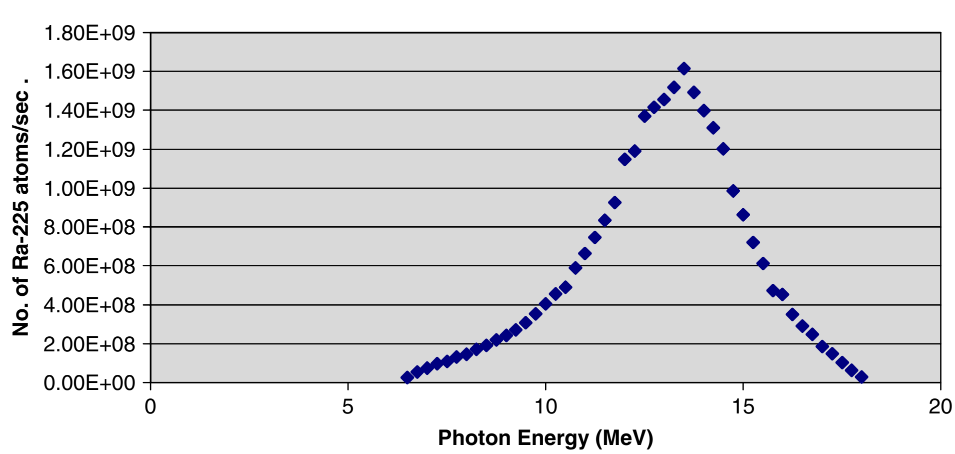

Fig. 7. Yield (Ra-225) in atoms per second vs. Photon energy (MeV).

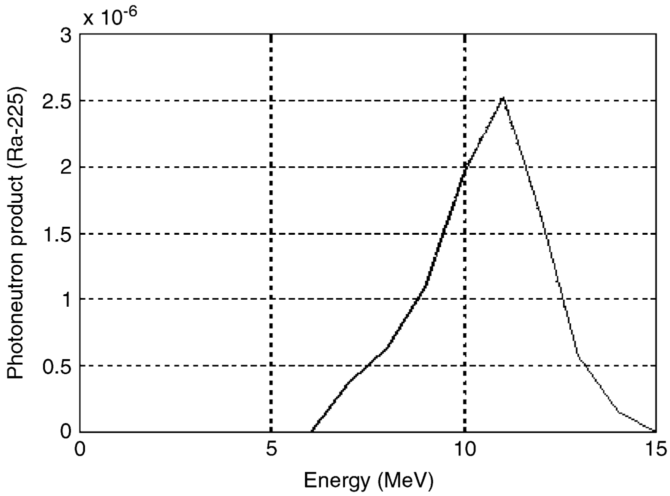

Fig. 8. Yield of Ra-225 using a 15 MeV Varian linac. The peak occurs at about 11.5 MeV.

Table 3
Maximum Ac-225 yields obtained at different linac energies by irradiating 1 mol (6.02×10^{23} atoms) of Ra-226 for 1 h using the simulation programs C++ and MATLAB

Energy (MeV)	Maximum energy (MeV)	C++ maximum Ac-225 (mCi)	MATLAB maximum Ac-225 (mCi)
10 (Varian)	—	4.0	5.1
15 (Varian)	15	24.3	32.6
18 (Varian)	16	25.0	26.4
18 (Siemens)	15	29.1	34.1
25 (Eleka)	16	17.9	17.9

and the voltage determines the electron energy, the electron energy and current is inversely proportional so both cannot increase together at a given power.

4. Discussion

The total yield has been calculated by summing the individual yields over the energy range 6.4 MeV $\leftrightarrow$ 18 MeV, so the calculation is quite precise since average values have not been used. This model has been based on the linac operating at maximum current with a pulse length of 4 μs. In reality, the linac will pulse at between 3.5 and 4 μs, which could further reduce the yield by up to 12.5%.

The important assumption here is that the Ra-226 interacts with all the photons in the beam. Thus, the positioning of the radium source is very important.

A calculation of photon flux can now be done in terms of photons/cm^2/s interacting with Ra atoms/cm^2 as seen in Fig. 9.

This calculation assumes:

- The radium needles are placed at a distance of 49.2 cm from the tungsten target.

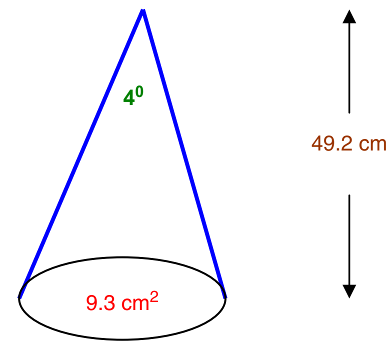

Fig. 9. Angular distribution of bremsstrahlung photons from a linac.

- Angular distribution of photons is 4° in total (see Mohan et al. (1985)).
- Photon flux is evenly distributed within the beam width.

A total photon count of 6.5×10^{13} in an area of 9.3 cm^2 through a distance of 49.2 cm gives a photon flux of 7×10^{12} photons/cm^2/s. However, considering the number of photons above the threshold energy that can actually cause the desired photonuclear reaction, the above photon flux reduces to 1.7×10^{12} photons/cm^2/s.

The low yield results from the low current combined with the low pulse width and frequency. In order to increase the yield so that worthwhile amounts of Ra-225 and daughter radionuclides could be produced, a number of factors need to be considered.

These are:

- increase the maximum current,
- increase the pulse length,
- increase the pulse frequency,
- increase irradiation time,
- irradiate larger amounts of radium.

A high-energy linac is needed to reach the GDR to maximise yield. Irradiation time can be increased by a factor of 10 (1–10 h) or more without too much strain on the linac. Packing as much Ra-226 as possible into the target area is very important especially considering that 1 cm^3 of Ra-226 is 5 g. Other factors such as using an efficient method of separating the Ra-225/Ac-225 from Ra-226 are important when considering the small yield.

One way of obtaining reasonable amounts of Ra-226 is to use radium needles, which were once used to treat cancer. The treatment process involved encapsulating radium in stainless steel needles, which were then imbedded into a tumour. The use of radium for cancer therapy was phased out with the development of cobalt and caesium sources, and with linacs being introduced for radiotherapy. It is estimated there are between 50,000 and 100,000 radium sources (Vicente and Sordi, 2004) worldwide that still need to be processed. The Environmental Protection Agency (EPA) in Australia is known to possess a considerable store of old discarded radium needles. There is also a store of radium needles at some hospitals. These needles are cylindrical in shape and are approximately 1.5 cm long and have a diameter of about 0.25 cm. They contain about 20 mg (20 mCi) of very pure Ra-226.

Irradiating one of these needles for an hour using the model in this paper will produce about 6 μCi of Ra-225 because of the small mass of the radium in each needle (20 mg).

The cross section of the Ra-226 target for the photo-nuclear reaction determined by its GDR. This type of resonance is due to the mode of nuclear vibration in which at any instant the protons and neutrons collectively oscillate in opposite directions, with the centre of gravity remaining constant. The resonance decays by the emission of one or more nucleons of which at least one is normally a neutron in the region of interest. The GDR leads to a broad peak (energy vs. cross section) and occurs in nuclei throughout the periodic table (Williams, 1991).

Linacs have a flattening filter between the tungsten target and the irradiated source; its purpose is to give a more uniform radial field. As expected, the filter absorbs some lower energy photons and thus leads to higher average beam energy. Since the threshold reaction to produce Ra-225 is 6.4 MeV, it makes little difference practically whether the filter is removed or not.

The activity of the Ac-225 depends on the photon flux, irradiation time, the activity of Ra-225, and half-life. The Ac-225 production rate:

$$A_2 = NHA_1(T_1/(T_1 - T_2))(1 - e^{-0.693(T_1-T_2)t/T_1T_2}),$$

where N is the number of atoms H the irradiation time, and t the time. Here, A_1, A_2 are the activities and T_1, T_2 are the half-lives of the Ra-225 and the Ac-225, respectively. A_1 is the product of photon flux and cross section of Ra-226.

The dependence of the two radionuclides is seen in Fig. 10. The C++ computer simulation produced this graph for a 15 MeV Varian (maximum energy: 15 MeV) where a small amount of Ra-226 was irradiated in the simulation. It shows that transient equilibrium occurs after 18 days and compares favourably with the ideal theoretical result (assumes ideal situation where parent radionuclide half-life was a lot longer than daughter radionuclide half-life) in Fig. 3 where transient equilibrium was reached in about 13 days.

The C++ computer simulation programme predicts that using an 18 MeV Varian to irradiate 1 cm^3 of Ra-226 (5 g) for 1 h will give a yield of Ra-225 of 1.25 mCi assuming a consistent 40% bremsstrahlung efficiency, with the maximum yield of Ac-225 being 0.554 mCi and occurs after 430 h or 18 days.

These C++ yield results are very consistent with the other results in this theoretical paper where 1.45 mCi/h of Ra-225 was produced (p. 13) under the same conditions. As mentioned previously, the C++ results were constructed using Th-232 cross section data and differ by only 16% from that where Bi-209 data was used. By far the greatest source of error in these simulations would be in the actual bremsstrahlung efficiency. Although Ra-226 and Th-232 are deformed nuclei, using spherical cross section data from Bi-209 has not significantly (less than 20%) altered the result at linac energies.

5. Conclusion

On the basis of this theoretical approach, very low activities (μCi) of Ra-225 can be produced by a common high-energy linac. The two different simulations gave consistent results when using cross sections data from two different nuclei. An 18 MV linac irradiating 5 g of Ra-226 for one hour will produce between 1 and 2 mCi of Ra-225. The simulation also shows that simply increasing linac energy beyond a certain level does not increase the yield

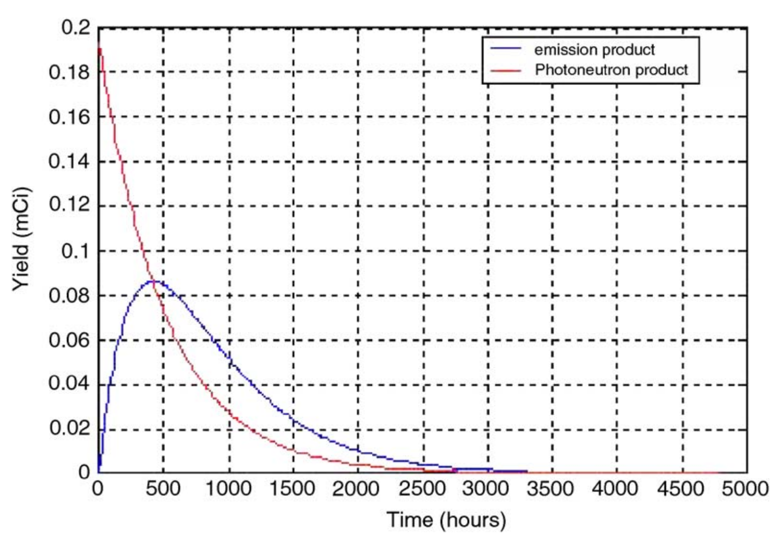

Fig. 10. The photoneutron product (Ra-225) is at a maximum after irradiation using a Varian (15 MeV) and slowly decays while the decay product (Ac-225) builds to a maximum in 430 h before it slowly decays.

unless there is an increase in overall linac power. Although the photonuclear reaction is inefficient, the yield can be greatly increased by using a longer irradiation time, placing the radium target in a prime position and having a high mass Ra-226 target. Stacking together a large number of radium needles may do this.

Furthermore, considering that after the valuable Ac-225 is extracted from the target the residual Ra-226 can again be irradiated in a continuing process (Ra/Ac generator), the project could also slowly reduce obsolete radioactive material as well as produce Ac-225.

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