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Production of Ac-225 for cancer therapy by photon-induced transmutation of Ra-226

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Abstract

The increasing application of Ac-225 for cancer therapy indicates the potential need for its increased production and availability. The production of Ac-225 has been achieved using bremsstrahlung photons from an 18 MV medical linear accelerator (linac) to bombard a Ra-226 target. A linac dose of 2800 Gy produced about 64 μCi of Ra-225, which decays to Ac-225. This result, while consistent with the theoretical calculations, is far too low to be of practical use. A more powerful linac is required that runs at a higher current, longer pulse length and higher frequency for practical production. This process could also lead to the reduction of the nuclear waste product Ra-226.

Keywords: Ac-225; Actinium; Linac; Medical linear accelerator; Bi-213; Ra-226; Ra-225; Cancer therapy; Targeted alpha therapy; Alpha emitter; Ac/Bi generator; Linac production

1. Introduction

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 linac to produce Ac-225. The irradiated needles would then be processed to extract the Ac-225, which can then be used for targeted alpha therapy (TAT) of cancer. If successful, this project would slowly reduce obsolete radioactive material, and displace the expensive importation of Ac-225 for cancer therapy.

Linacs are the mainstay of radiotherapy treatment. They deliver megavoltage energy electron beams accelerated by klystron or magnetron generated radio-frequency fields through copper waveguides (Dowsett et al., 2001). The photon beams arise from the bremsstrahlung radiation emitted when the electron beam bombards a tungsten target. Our experiments made use of the high-energy photons produced by an 18 MV medical linac to bombard radium needles for the production of Ra-225, which decays to Ac-225. The Ac/Bi generator can then be used for local production of Bi-213 in the nuclear medicine department of a hospital. Obsolete therapeutic radium needles can contain 20 mCi of high-quality radium. The high activity of these needles, however, poses a challenge in detecting the gamma-rays from small amounts of radionuclides produced among the gamma-rays from the radium background.

There are a number of ways to produce Ac-225 from Ra-226, including proton bombardment (Koch et al., 1997), but the only possible photonuclear reaction at linac energies is:

$$^{226}_{88}\mathrm{Ra} + \gamma \longrightarrow {}^{225}_{88}\mathrm{Ra} + {}^{1}_{0}\mathrm{n} \qquad (1)$$

This reaction is virtually instantaneous, so that after irradiation, Ra-225 will be at a maximum value and will decrease slowly over time (Melville et al., 2006), the

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half-life being 14.9 days. Since, there is no direct step from the irradiation of Ra-226 to the production of Ac-225, the natural decay of Ra-225 is utilised.

This means once produced the Ra-225 subsequently decays to Ac-225 by beta emission, as seen in the decay reaction (2) (Morgenstern, 2005), and then to Bi-213, and ultimately to stable Bi-209 (Morgenstern, 2005).

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

Linac photons or bremsstrahlung radiation (Bueche, 1969) arise when high-energy electrons penetrate the target 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 energy and impact radii. There is consequently a spread of bremsstrahlung energies from a maximum value (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.

2. Method

The first experiment involved irradiating two radium needles each containing 740 MBq (20 mCi) of Ra-226, by an 18 MV 2100 C Clinac (Fig. 1A), at the Illawarra Cancer Centre, for a total time of 175 min at 16 Gy/min, giving a total dose of 2800 Gy. The needles were placed 49.2 cm below the tungsten target in the linac head. The radium needles consisted of only a few millimeter of steel casing used to confine the radium salt.

In the second experiment, a third single radium needle (15 mCi) was placed inside the linac (12.5 cm below the tungsten target) with the flattening filter removed. This filter provides a means to generate a spatial uniformity of the dose rate but on the other hand it would slightly reduce the dose rate. The needle was then irradiated for 90 min.

Performance parameters for the linac (18 MV Varian Clinac 2100 C) used in our experiments were:

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

A high-purity germanium (HPGe) spectrometer was used to measure the gamma-ray spectra (Fig. 1B), because of its superior resolving power and high photon detection efficiency, which is important for this work due to the complexity of the spectrum. Shielding, when necessary, was placed around the detector to reduce interference from the background radiation or in front of the radioactive source to reduce emission intensity, thus lowering the detector's dead time. Some gamma-rays enter the detector after hitting the lead shield and scattering through approximately 180°. They will lose most of their energy in the backscattering event. If they produce a photoelectron in the detector, this electron will have the energy of a backscattered gamma-ray. In such spectra a small 'backscatter peak' will be seen. This was not evident in our experiments, probably because of the intense radium background.

The effective interaction volume of the detector determines its efficiency. The detection limits of an HPGe system are typically 15 times lower than that of low-resolution NaI (Tl) systems. The HPGe detector we used had a diameter of 6.5 cm and a volume of approximately 430 cm^3. Processing pulse height information was by digital signal processor (DSP) instead of an analog-shaping amplifier. The detector preamplifier output, as shown in Fig. 2, was sampled, digitised and filtered with the digitised information being displayed as a histogram.

The Maestro-32 (model A65-B32) software, by ORTEC (2006), was used to analyse the spectra and includes a control program for ORTEC hardware commonly referenced as the UMCBI. The UMCBI provides all the drivers

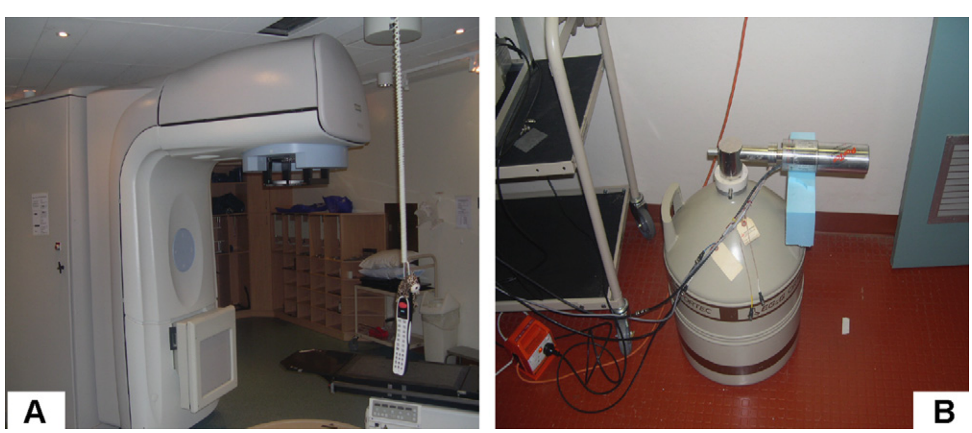

Fig. 1. Photograph (A) shows a medical linac similar to the one used in the experiments. Photograph (B) shows the HPGe detector, which is cooled by liquid nitrogen in a Dewar.