Title: Application of Nuclear Reaction: Actinium-225

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Abstract:

Actinium-225 (Ac-225) is a synthetic isotope of actinium with significant applications in nuclear medicine, particularly in targeted alpha therapy (TAT) for cancer treatment. Ac-225, with a half-life of 10 days, undergoes a decay sequence that emits highly energetic alpha particles, making it effective for selectively destroying cancer cells while minimizing damage to surrounding healthy tissue. This paper examines the nature, production, and decay pathways of Ac-225, including its role in the 4n+1 neptunium decay series and artificial production through high-energy proton spallation of thorium-232. Furthermore, it explores Ac-225's binding energy, decay characteristics, and the advantages of its daughter isotope, bismuth-213, in therapeutic applications. The use of radionuclide generators for Ac-225 production and its integration into radiopharmaceuticals is also discussed. Given its cytotoxic potential and ability to selectively target tumors, Ac-225 represents a major breakthrough in nuclear medicine, providing an effective alternative to traditional cancer treatments.

Evaluate the nature and production of nuclear decays, radiations and nuclear reactions

Actinium-225(225Ac) is one of the isotopes of actinium (Ac) with atomic mass number (A) of 225 and mass of 225.023229840 u. Ac-225 consists of 89 number of protons (Z) and 136 number of neutrons(N). The ground state of Ac-225 has a spin-parity of $\frac{3}{2}^{-}$.[1] Being an intermediate decay product, Ac-225 is part of the 4n+1 neptunium (Np) series, the decay product of Np-237. Ac-225 is entirely synthetic except for the minuscule amount naturally occur as trace quantities from this decay chain. Actinium-225 was first discovered in 1947 as part of the hitherto unknown neptunium series, which was populated by the synthesis of Uranium-233(U-233).[3] The discovery of Ac-225 and its 10-day half-life was reported F. Hagemann and his team from Agrgonne National Laboratory.[1]

Ac-225 has a half-life of 10 days and undergoes alpha decay process to francium-221 (Fr-221). Aside from Np-237's daughter nuclides U-233 and Thorium-229 (Th-229), it can arise from parent isotopes in the decay chain such as Radium-225(Ra-225) through beta- decay, Protactinium-229 (Pa-229) through alpha decay and Th-225 through electron capture. Its abundance was estimated to be less 1.1×10^{-19} relative to Th-232 and around 9.9×10^{-16} relative to Th-230 in secular equilibrium.[3] The majority of Ac-225 results from the alpha decay of Th-229. Alternatively, Ac-225 can be produced by target irradiating Th-232 with high-energy proton beams in spallation reactions. Fig.1 below show the decay chain of Ac-225. It is the last nuclide in the chain with a half-life over a day until the penultimate product, Bismuth-209 (Bi-209) with half-life of 1.9 x 10^{19} years. Although it still has a final decay product of stable Thallium-205 (Th-205), but here we treat Bi-209 as end-product due to its interminable half-life. Due the 4 highly energized alpha particles emitted from the short decay reactions to stable Bi-209, alpha emitter radionuclide like Ac-225 has become highly attractive in cancer treatment, especially targeted alpha therapy (TAT). For only few alpha-emitting radionuclides are suitable for clinical application in TAT, Ac-225 and its short-lived daughter nuclide Bi-213($T_{1/2}$=45.59 min) will be discussed in this report as they are by far the most clinical experienced and available.[4]

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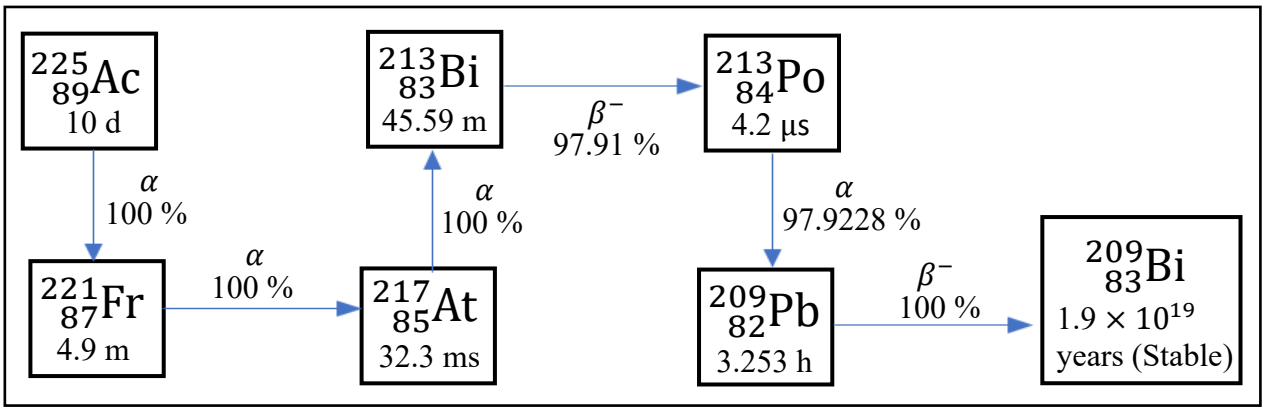

Figure 1. Decay scheme of Ac-225 with total of four alpha-particles emitted until stable isotope Bi-209 is formed. Adapted from [5]

Binding Energy Analysis

Nuclide	Mass (a.m.u)
$^{225}_{89}$Ac	225.023229840
$^{221}_{87}$Fr	221.014254995
$^{217}_{85}$At	217.004719035
$^{213}_{83}$Bi	212.994384864
$^{213}_{84}$Po	212.992856428
$^{209}_{82}$Pb	208.981089197
$^{209}_{83}$Bi	208.980397792

Table 1. Nuclide involved in the decay chain and their respective mass taken from[1] [6]

Binding energy formula $BE = \Delta mc^2 = \left[Zm_p + (A-Z)m_n - m\left(^{A}_{Z}\mathrm{X}\right)\right]c^2$

1) Binding energy of $^{225}_{89}\mathrm{Ac} = [89m(^{1}_{1}\mathrm{H}) + 136m_n - m(^{225}_{89}\mathrm{Ac})]c^2$

$= [89(1.00782503223\ u) - 225.023229840\ u]\left(931.49432\frac{MeV}{u}\right) + 136(939.56542052\ MeV)$

$= 1724.749810475\ MeV$

Binding energy per nucleon, $\frac{BE}{A} = 7.66555471322\ MeV/nucleon$

2) Binding energy of $^{221}_{87}\mathrm{Fr}\ = [87m(^{1}_{1}\mathrm{H}) + 134m_n - m(^{221}_{87}\mathrm{Fr}\ )]c^2$

$= [87(1.00782503223\ u) - 221.014254995\ u]\left(931.49432\frac{MeV}{u}\right) + 134(939.56542052\ MeV)$

$= 1702.389680423\ MeV$

Binding energy per nucleon, $\frac{BE}{A} = 7.70312072590\ MeV/nucleon$

3) Binding energy of $^{217}_{85}\mathrm{At} = [85m(^{1}_{1}\mathrm{H}) + 132m_n - m(^{217}_{85}\mathrm{At})]c^2$

$= [85(1.00782503223\ u) - 217.004719035\ u]\left(931.49432\frac{MeV}{u}\right) + 132(939.56542052\ MeV)$

$= 1680.552225807 MeV$

Binding energy per nucleon, $\frac{BE}{A} = 7.74448030326\ MeV/nucleon$

4) Binding energy of $^{213}_{83}\mathrm{Bi}\ = [83m(^{1}_{1}\mathrm{H}) + 130m_n - m(^{213}_{83}\mathrm{Bi})]c^2$

$= [83(1.00782503223\ u) - 212.994384864\ u]\left(931.49432\frac{MeV}{u}\right) + 130(939.56542052\ MeV)$

$= 1659.458300203\ MeV$

Binding energy per nucleon, $\frac{BE}{A} = 7.79088403851\ MeV/nucleon$

5) Binding energy of $^{213}_{84}\mathrm{Po}\ = [84m(^{1}_{1}\mathrm{H}) + 129m_n - m(^{213}_{84}\mathrm{Po}\ )]c^2$

$= [84(1.00782503223\ u) - 212.992856428\ u]\left(931.49432\frac{MeV}{u}\right) + 129(939.56542052\ MeV)$

$= 1660.099902212\ MeV$

Binding energy per nucleon, $\frac{BE}{A} = 7.79389625451\ MeV/nucleon$

6) Binding energy of $^{209}_{82}\text{Pb}$ $= [82m(^{1}_{1}\text{H}) + 127m_n - m(^{209}_{82}\text{Pb})]c^2$

$= [82(1.00782503223\ u) - 208.981089197\ u]\left(931.49432\frac{MeV}{u}\right) + 127(939.56542052\ MeV)$

$= 1640.340863858$ MeV

Binding energy per nucleon, $\frac{BE}{A} = 7.84852087970\ MeV/nucleon$

7) Binding energy of $^{209}_{83}\text{Bi}$ $= [83m(^{1}_{1}\text{H}) + 126m_n - m(^{209}_{83}\text{Bi})]c^2$

$= [83(1.00782503223\ u) - 208.980397792\ u]\left(931.49432\frac{MeV}{u}\right) + 126(939.56542052\ MeV)$

$= 1640.202776245$ MeV

Binding energy per nucleon, $\frac{BE}{A} = 7.847860173\ MeV/nucleon$

Radioactive reaction analysis

1) Decay process: alpha decay (α-decay); Decay equation: $^{225}_{89}\text{Ac} \rightarrow {}^{221}_{87}\text{Fr} + {}^{4}_{2}\text{He}$

Probability: 100%; Half-life, $T_{\frac{1}{2}} = 10\ days = 864000\ seconds$

Decay energy, $Q = [m(^{225}_{89}\text{Ac}) - m(^{221}_{87}\text{Fr}) - m(^{4}_{2}\text{He})]c^2$

$= [(225.023229840 - 221.014254995 - 4.00260325)u]\left(931.49432\frac{\text{MeV}}{\text{u}}\right)$

$= 5.935104552$ MeV

Decay constant: $\lambda = \frac{ln2}{T_{\frac{1}{2}}} = 0.0693147\ days^{-1} = 8.022536812\ \times 10^{-7}\ s^{-1}$

Lifetime: $T = \frac{1}{\lambda} = 14.42695\ day = \ 1246488.515\ s$

2) Decay process: alpha decay (α-decay); Decay equation: $^{221}_{87}\text{Fr} \rightarrow {}^{217}_{85}\text{At} + {}^{4}_{2}\text{He}$

Probability: 100%; Half-life, $T_{\frac{1}{2}} = 4.9\ minutes = 294\ seconds$

Decay energy, $Q = [m(^{221}_{87}\text{Fr}) - m(^{217}_{85}\text{At}) - m(^{4}_{2}\text{He})]c^2$

$= [(221.014254995 - 217.004719035 - 4.00260325)u]\left(931.49432\frac{\text{MeV}}{\text{u}}\right)$

$= 6.457779987$ MeV

Decay constant: $\lambda = \frac{ln2}{T_{\frac{1}{2}}} = 0.14145861\ min^{-1} = 2.35764347\ \times 10^{-3}\ s^{-1}$

Lifetime: $T = \frac{1}{\lambda} = 7.0692057\ \text{min} = 424.152342\ s$

3) Decay process: alpha decay (α-decay); Decay equation: $^{217}_{85}\text{At} \rightarrow {}^{213}_{83}\text{Bi}\ + {}^{4}_{2}\text{He}$

Probability: 100%; Half-life, $T_{\frac{1}{2}} = 0.0323\ seconds$

Decay energy, $Q = [m(^{217}_{85}\text{At}) - m(^{213}_{83}\text{Bi}) - m(^{4}_{2}\text{He})]c^2$

$= [(217.004719035 - 212.994384864 - 4.00260325)u]\left(931.49432\,\frac{\text{MeV}}{\text{u}}\right)$

$= 7.201309$ MeV

Decay constant: $\lambda = \frac{ln2}{T_{\frac{1}{2}}} = 21.45966503\ s^{-1}$

Lifetime: $T = \frac{1}{\lambda} = 0.046599\ s$

4) Decay process: beta$^-$ decay (β^--decay); Decay equation: $^{213}_{83}\text{Bi} \rightarrow {}^{213}_{84}\text{Po} + {}^{0}_{-1}\text{e} + {}^{0}_{0}\bar{\upsilon}$

Probability: 97.91%; Half-life, $T_{\frac{1}{2}} = 45.59\ minutes = 2735.4\ seconds$

Decay energy, $Q = [m(^{213}_{83}\text{Bi}) - m(^{213}_{84}\text{Po}) - m(^{0}_{-1}\text{e}) - m(^{0}_{0}\bar{\upsilon})]c^2 \approx [m(^{213}_{83}\text{Bi}) - m(^{213}_{84}\text{Po})]c^2$

$= [(212.994384864 - 212.992856428)u]\left(931.49432\,\frac{\text{MeV}}{\text{u}}\right)$

$= 1.423729452$ MeV

Decay constant: $\lambda = \frac{ln2}{T_{\frac{1}{2}}} = 0.01520393\ min^{-1} = 2.533988377 \times 10^{-4}\ s^{-1}$

Lifetime: $T = \frac{1}{\lambda} = 65.77246691\ min = 3946.348\ s$

5) Decay process: alpha decay (α-decay); Decay equation: $^{213}_{84}\text{Po} \rightarrow {}^{209}_{82}\text{Pb} + {}^{4}_{2}\text{He}$

Probability: 97.9228%; Half-life, $T_{\frac{1}{2}} = 4.2 \times 10^{-6} seconds$

Decay energy, $Q = [m(^{213}_{84}\text{Po}) - m(^{209}_{82}\text{Pb}) - m(^{4}_{2}\text{He})]c^2$

$= [(212.992856428 - 208.981089197 - 4.00260325)u]\left(931.49432\,\frac{\text{MeV}}{\text{u}}\right)$

$= 8.536196250$ MeV

Decay constant: $\lambda = \frac{ln2}{T_{\frac{1}{2}}} = 165035.043\ s^{-1}$

Lifetime: $T = \frac{1}{\lambda} = 6.059319172 \times 10^{-6}\ s$

6) Decay process: beta$^-$ decay (β^--decay); Decay equation: $^{209}_{82}\text{Pb} \rightarrow {}^{209}_{83}\text{Bi} + {}^{0}_{-1}\text{e} + {}^{0}_{0}\bar{\upsilon}$

Probability: 100%; Half-life, $T_{\frac{1}{2}} = 3.253\ hours = 11710.8\ seconds$

Decay energy, $Q = [m(^{209}_{82}\text{Pb}) - m(^{209}_{83}\text{Bi}) - m(^{0}_{-1}\text{e}) - m(^{0}_{0}\bar{\upsilon})]c^2 \approx [m(^{209}_{82}\text{Pb}) - m(^{209}_{83}\text{Bi})]c^2$

$= [(208.981089197 - 208.980397792)u]\left(931.49432\,\frac{\text{MeV}}{\text{u}}\right)$

$= 0.644039830$ MeV

Decay constant: $\lambda = \frac{ln2}{T_{\frac{1}{2}}} = 0.2130793669\ hour^{-1} = 5.918871303 \times 10^{-5}\ s^{-1}$

Lifetime: $T = \frac{1}{\lambda} = 4.693086968\ hour = 16895.11308\ s$

Applications

Medical

Ac-225 and Bi-209 are commonly known in therapeutic applications for the field of nuclear medicine. Of these therapeutic applications, targeted alpha therapy (TAT) is one of the most promising and effective new methods of treating various forms of oncologic diseases. It combines new developments in molecular biology and in radionuclides for medical applications. Alpha-emitting radionuclides seem particularly promising to destroy cancer cells.

Targeted alpha therapy (TAT)

Targeted alpha therapy (TAT) is a novel cancer treatment modality, using alpha radiation to selectively destroy tumour cells.[9] The principle of TAT is based on the coupling of alpha-emitting radionuclides to tumour-selective carrier molecules, such as monoclonal antibodies or peptides, allowing the specific targeting of cancer cells. Due to the short path length of alpha particles in human tissue, TAT has the potential of delivering a highly cytotoxic radiation dose to targeted cancer cells, while limiting the damage to surrounding healthy tissue.

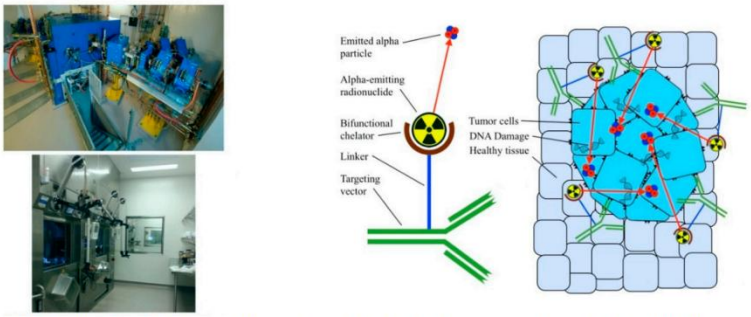

Figure 3. Key aspects of targeted alpha therapy: (a) radionuclide production via cyclotron, nuclear reactor or generator decay, and shielded automated processing; (b) radiolabeling the alpha-emitting radionuclide to a suitable targeting vector to form a bioconjugate; and (c) targeted alpha radiotherapy precisely destroys tumor cells while sparing surrounding healthy tissue [10]

Ac-225 is truly a breakthrough in cancer treatment. As an alpha emitting radionuclide, Ac-225 are favored in cancer treatment because of the short cell diameter range of alpha particles in tissue and their high energy, rendering them highly effective in targeting and killing cancer cells. Specifically, alpha particles are more effective at breaking DNA strands. The 10-day half-life of Ac-225 is long enough to facilitate treatment, but short enough that little remains in the body months after treatment.[3] This contrasts with the similarly investigated Bi-213, whose 46-minute half-life necessitates in situ generation and immediate use. Additionally, Ac-225 has a median lethal dose several orders of magnitude greater than Bi-213 because of its longer half-life and subsequent alpha emissions from its decay products. Each decay of Ac-225 to Bi-209 nets four high-energy alpha particles, greatly increasing its potency.[3][4]

To date more than 500 patients have received Ac-225 and Bi-213 labeled radio conjugates for therapy of leukemia, Non-Hodgkins Lymphoma, malignant melanoma, bladder cancer, glioma, neuroendocrine tumors,

and prostate cancer. The radionuclides obtained from both sites have high radionuclidic and chemical purity, afford high labelling yields and have been found safe for administration to humans by well-trained physicians following established protocols for radiolabeling and quality control.

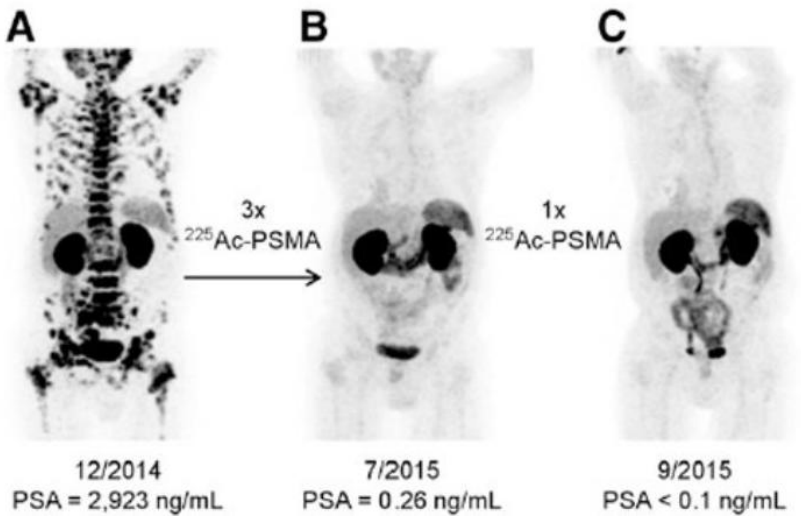

Figure 2. The images of a patient with end-stage prostate cancer before and after treatment with Ac-225[8]

Alpha Source

Radiopharmaceuticals based on alpha emission are generally easier to handle for hospitals and patients because they require less shielding of patient environment compared to beta emitting isotopes due to the short range of alphas. Alpha particles emitted by Ac-225 have high-energy with 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.

Radionuclide generator

According to JRC Karlsruhe, high activity up to 4 GBq Ac-225 or Bi-213 radionuclide generators based on AG MP-50 cation exchange resin have been developed and well established in the medical field. A radionuclide generator is a device which provides a local supply of a short-lived radioactive substance from the decay of a longer-lived parent radionuclide. They are commonly used in nuclear medicine to supply a radiopharmacy. [7] A key feature of this generator is the homogeneous distribution of Ac-225 activity over approximately two-thirds of the generator resin in order to minimize radiolytic degradation of the organic resin and to assure reliable operation over several weeks. The generator has been successfully used for the preparation of therapeutic doses of up to 2.3 GBq Bi-213 P analogue for locoregional treatment of brain tumors.[8]

Because of its scarcity and radioactivity, applications for actinium-225 are minimal. Ac-225 has been mostly investigated for radiation therapy in the treatment of cancers.

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