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Technical note

A possible *in vivo* generator ^{103}Pd/^{103m}Rh—Recoil considerations

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Abstract

The use of Auger emitters as potential radiopharmaceuticals is increasingly investigated. One such radionuclide of interest is ^{103m}Rh. This can be produced from ^{103}Ru or from ^{103}Pd in an *in vivo* generator. A potential problem with this concept is the recoil of the ^{103m}Rh out of the carrier molecule and even out of the target cell. In order to determine whether this would happen in the ^{103}Pd/^{103m}Rh case calculations were done to prove that this does not happen. From theoretical considerations it seems that the ^{103}Pd/^{103m}Rh *in vivo* generator system would be possible.

Keywords: ^{103m}Rh; ^{103}Pd; *In vivo* generators; Recoil

1. Introduction

The well-established use of ^{125}I and ^{111}In Auger emitting radioisotopes has also stimulated the search for other Auger emitters that maybe more practical to use from the perspective of availability, physical half-life and cost. Recently, the potential of ^{103m}Rh ($t_{1/2} = 56.12$ min) as an Auger emitter for internal radiotherapy was mentioned by Nilsson et al. (2006) and brought to attention by the highlights paper of the EANM congress, 2006 (McKillop et al., 2007). Nilsson et al. (2006) proposed that ^{103m}Rh would be available from ^{103}Ru on a generator and used in the S4-chelator (3,11-dihydroxy-1,5,9,13-tertrathiacyclohexadecane) link to octreotate. ^{103}Ru can be extracted from the fission products of Uranium, which implies a large amount of this nuclide is theoretically available. Another isotope which is well known in radiotherapy is ^{103}Pd ($t_{1/2} = 16.96$ d) although it is normally used in brachytherapy where it is highly successful in the treatment of prostate cancer as documented by Sharkey et al. (2002). In this treatment modality the ^{103}Pd is enclosed in a seed and gives a short range of radiation that is effective in treatment of prostate cancer cells. The decay of ^{103}Pd is via ^{103m}Rh.

$$^{103}_{46}\mathrm{Pd} \xrightarrow[\text{branching ratio } 99.974\%]{\text{EC}} {}^{103m}_{45}\mathrm{Rh} \xrightarrow{\gamma\text{-emission}} {}^{103}_{45}\mathrm{Rh}.$$

As both these nuclides are interesting from the cancer treatment point of view, a combination into one radiopharmaceutical is an option to consider. This would be in the form of an *in vivo* generator system. This concept is not new and especially with alpha emitters this is often the case. The decay of ^{225}Ac to ^{209}Bi forms five intermediates and the produces 4 alphas and 2 betas. The release of these decay products from the original carrier molecule and migration out of target cells is well documented (Hassfjell and Brechbiel, 2001). The reason for the release of one viz. ^{221}Fr (1+ ion and mimicking K^{+1}, an alkali metal ion) is (A) that it requires significant different chelation chemistry than actinium and (B) the recoil energy of ^{221}Fr after the alpha particle emission (0.1 MeV) is much larger than the chemical binding energy of an ^{225}Ac conjugate. The change from Pd to Rh is not expected to be so significant as they both are part of the Pt-group metals. However, the recoil is also of concern for the proposed ^{103}Pd/^{103m}Rh *in vivo* generator. As a covalent bond in the chelate-complex molecule such as the S4-diol or DOTA chelates are

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chemical bonds with a strength estimated to be at least 3 eV (NIST, 2007). The likelihood of this taking place was investigated in this article.

^{103}Pd decays by electron capture (EC) which is a beta transition whereby no charged particle is ejected although the accompanying neutrino of such transition is emitted. However, in addition to the neutrino the same event produces a number of Auger electrons, as well as gammas which could contribute to the recoil effect.

Another consideration that requires attention is what happens if the chemical bond would break upon recoil and how far the product would move in the cell nucleus or mitochondria. A typical animal cell has a diameter of at least 30 μm; a typical mitochondrion or cell nucleus has a length of about 10% of the diameter of the cell, i.e. about 3 μm. Under the assumption that the ^{103}Pd is uniformly distributed within the mitochondrion, it can be concluded that the probability of the ^{103}Pd escaping from the mitochondrion, upon recoil from a radioactive transition, will be small if the range of the distance of the recoiling atom in the cell is well below 0.1 μm.

2. Theoretical considerations

From standard expressions for the relativistic relationship between mass, kinetic energy and momentum available in the literature (Beiser, 1969), it follows that the relativistic relationship between momentum p, mass m and kinetic energy T, is

$$p = \frac{\sqrt{2mc^2T + T^2}}{c}. \tag{1}$$

A nucleus with mass M_N will recoil with kinetic energy T_N upon emission of a particle with mass m_p and kinetic energy T_p. The linear moment of the recoiling nucleus and the emitted particle will be numerically equal, according to the law of the conservation of linear momentum, i.e.

$$\sqrt{2M_Nc^2T_N + T_N^2} = \sqrt{2m_pc^2T_p + T_p^2}, \tag{2}$$

and from this it follows that the kinetic energy of the recoiling nucleus, which we shall henceforth simply denote with the symbol E_N, will be

$$E_N = \sqrt{(M_N^2c^4 + E_p^2 + 2m_pc^2E_p)^2} - M_Nc^2. \tag{3}$$

Eq. (3) is a general, fully relativistic expression that holds true for both particles with non-zero mass, and also for zero-mass energy quanta such as photons. The term will $(2m_pE_pc^2)$ be zero for photon emission, because the mass of a photon is zero; the term $(2m_pE_pc^2)$ will be negligibly small for neutrino emission, because the mass of the neutrino is presently estimated as being of the order of 30 millielectron volt (meV), i.e. about 3×10^{-11} amu. For heavy emitted particles such as alpha- and beta-particles, the term $(2m_pE_pc^2)$ will dominate and lead to large recoil energies. Simplifying Eq. (2) according to the above mentioned assumptions the following equations can be created: When a nucleus of mass M_N emits a particle with rest-mass m_p during a radioactive transition, the principles of conservation of energy and linear momentum yields the results that the energy E_p of the emitted particle will be

$$E_p = \left(\frac{M_N}{M_N + m_p}\right)Q, \tag{4}$$

while the recoil energy of the nucleus will be

$$E_N = \left(\frac{m_p}{M_N + m_p}\right)Q, \tag{5}$$

where Q is the transition energy for the radioactive transition process.

From Eqs. (4) and (5) it follows that the following relationship holds between the energy of the emitted particle, E_p, and the recoil energy E_N of the nucleus

$$E_N = \left(\frac{m_p}{M_N}\right)E_p. \tag{6}$$

This result is directly usable, because compilations such as NNDC (National Nuclear Data Center, 2007) give the energies of the emitted particles.

When a nucleus de-excites by the emission of a γ-photon or neutrino, the principle of the conservation of linear momentum dictates that this must also be the momentum M_N of the recoil nucleus. The non-relativistic expression for the energy of the recoil nucleus will hence be,

$$E_N = \frac{1}{2}M_N\left(\frac{E_\gamma}{M_Nc}\right)^2. \tag{7}$$

The above will also be the recoil energy of an atom that emits an X-ray photon.

For ion range calculations for recoil nuclei that break free from chemical bonds, the initial energy E_0 of the ion will be

$$E_0 = E_{recoil} - E_{bind}, \tag{8}$$

where E_{recoil} is the recoil energy and E_{bind} the binding energy of the chemical bond that is broken, i.e. the depth of the potential well from which the recoil process frees the ion to the unbound state.

3. Results and discussion

3.1. Recoil energy of the ^{103}Pd nucleus with auger electron emission

Auger electrons are emitted at five distinct energies (National Nuclear Data Center, 2007) upon the radioactive transition of ^{103}Pd; these electron emissions and consequent recoil energies of the nucleus are summarised in Table 1. The recoil energies of the nucleus were calculated using Eq. (6).

From Table 1 it is clear that all recoil energies are far below 1 eV, so that there is no danger that chemical bonds will be broken as a result of nuclear recoil of ^{103}Pd upon Auger electron emission.