Preparation of $^{227}$Ac/$^{223}$Ra by neutron irradiation of $^{226}$Ra

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Abstract Radium-223 is a prospective alpha-emitter for targeted radionuclide therapy. Although $^{223}$Ra is formed naturally by the decay of $^{235}$U, for practical reasons its preparation involves neutron irradiation of $^{226}$Ra. The $\beta^-$ decay of the $^{227}$Ra ($T_{1/2} = 43$ min) produced via $^{226}$Ra(n,γ)$^{227}$Ra reaction leads to $^{227}$Ac, a mother nuclide of $^{227}$Th and subsequently $^{223}$Ra. Radium target material is generally available in multigram quantities from historical stock. The main aim of this study was to experimentally as well as theoretically evaluate and verify the available literature data on production of $^{227}$Ac/$^{223}$Ra. According to the data obtained from the γ-spectra, the approximate yield values were determined and effective cross section value for the $^{227}$Ac production was calculated to $14 \pm 4$ barns.

Keywords Actinium · $^{227}$Ac · Radium · $^{223}$Ra · $^{226}$Ra · Neutron irradiation

Introduction

The development of nuclear medicine involves the use of alpha particle emitting radionuclides like $^{223}$Ra. This nuclide is used for the targeted therapy of bone metastases, because of its similar chemical properties with Calcium. Radium and its most significant decay product $^{211}$Pb have both high affinity to bone tissues. High total released energy (of about 27 MeV), high linear energy transfer (LET) of alpha particles and therefore short range in tissues make $^{223}$Ra and its decay chain very useful in the targeted therapy of small tumors. Alpha particles cause irreversible double-strand breaks of the DNA that lead to the cell death [1].

Several $^{223}$Ra production methods were studied by research groups worldwide. The most convenient method is the use of a $^{227}$Ac/$^{227}$Th/$^{223}$Ra generator. The $^{227}$Ac can be obtained in the $^{226}$Ra(n,γ)$^{227}$Ra → $^{227}$Ac activation/decay sequence [2]. Proton fission of $^{232}$Th as an alternative to the reactor production method appeared quite recently [3, 4]. A natural source of $^{227}$Ac, originating from the decay chain of $^{235}$U, is also available in limited quantities. Thus $^{227}$Ac can be also isolated from $^{231}$Pa sources using extraction chromatography [5]. However, the most feasible method for large scale production of $^{227}$Ac is the neutron irradiation of $^{226}$Ra (see Fig. 1) [2, 6, 7].

The aim of this work was to verify the effective production cross section value and the irradiation yield of $^{227}$Ac. According to the literature the effective cross section of the $^{226}$Ra(n,γ)$^{227}$Ra → $^{227}$Ac reaction sequence lies in the interval from 8 to 23 barns ($10^{-24}$ cm$^2$) [8].

Experimental

Materials and methods

Radium-226 sample (190 kBq of $^{226}$RaCl$_2$ that equals to 5.135 μg of $^{226}$Ra) was prepared by the evaporation of standardized solution of $^{226}$RaCl$_2$ (Czech Metrological Institute, Czech Republic) under infrared lamp. The dry sample was flame-sealed in a quartz ampoule and irradiated in the LVR-15 reactor (Research Centre Rez, Czech Republic) for 11.7 effective days at a neutron flux density of $1.09 \times 10^{14}$ n/cm$^2$s (0–10 keV group). The yield of
223Ra and 227Th together with other activation products was determined several weeks after the end of bombardment (EOB) by the evaluation of γ-spectra recorded on a calibrated γ-spectrometer (Ortec, USA). The activity of 227Ac was determined by back-calculation from activities of its decay products to EOB. Overall uncertainty of the cross section value was estimated according to [10] as the standard combined uncertainty comprising of the type A and type B uncertainty contributions.

Calculations

The theoretical calculations were made with an in-house designed program that includes decay corrections and neutron reactions, based on Eqs. 1–5 (see also Fig. 1). The calculation program was written in Pascal language. The decay constants were based on literature data [9].

\[
\frac{dN_{226Ra}}{dt} = -\lambda_{226Ra} N_{226Ra} - \varphi \sigma_{226Ra} N_{226Ra} N_{226Ra}
\]

\[
\frac{dN_{227Ra}}{dt} = \varphi \sigma_{226Ra} N_{226Ra} N_{226Ra} - \lambda_{227Ra} N_{227Ra} - \varphi \sigma_{227Ra} N_{227Ra} N_{227Ra}
\]

\[
\frac{dN_{227Ac}}{dt} = \lambda_{227Ra} N_{227Ra} - \lambda_{227Ac} N_{227Ac} - \varphi \sigma_{227Ac} N_{227Ac}
\]

\[
\frac{dN_{227Th}}{dt} = \lambda_{227Ac} N_{227Ac} - \lambda_{227Th} N_{227Th}
\]

\[
\frac{dN_{223Ra}}{dt} = \lambda_{227Ra} N_{227Ra} - \lambda_{223Ra} N_{223Ra}
\]

Here \( \lambda \) is the decay constant (s\(^{-1} \)), \( \varphi \) is the neutron flux density (n/cm\(^2\)s\(^{-1} \)), and \( \sigma \) is the corresponding reaction cross section (10\(^{-24} \) cm\(^2\)).

**Results and discussion**

The comparison of experimental and calculated data from the fit is shown in Fig. 2. Irradiation results were obtained from γ-spectrometry measurements (see Table 1 and Fig. 3). Less than one month after EOB peaks with acceptable resolution can be found in the γ-spectra. Peaks of 214Pb and 214Bi, which are the decay products of 226Ra were dominant. Also peaks of 227Ac, 227Th, 223Ra, 211Pb, 228Th and 224Ra can be found in the spectra, but due to the complex matrix, some of them interfered with each other. Moreover, the dominant peaks of 214Pb and 214Bi could cause Compton scattering to interfere with the analysis of the low intensity peaks. Thus precise evaluation of the γ-spectra was problematic. Despite of worse resolution and quality of the spectra, good agreement (within the error bars) between the experimental and the predicted values was observed.

The effective cross section of 227Ac production was determined empirically by the activity measurements of the 227Th and 223Ra daughter nuclei in partial equilibrium with 227Ac using back-calculation to EOB. The activation intermediate 227Ra was neglected in the cross section determination. The effective cross section value of 227Ac production was then estimated to 14 ± 4 b. This value is in good agreement with available literature data (8–23 b). However, the proper \( ^{226}{\text{Ra}}(n,\gamma)^{227}{\text{Ra}} \) reaction cross section is generally confused with the effective cross section of 227Ac production [8]. According to the recent data of Kuznetsov et al. [7] the \( ^{226}{\text{Ra}}(n,\gamma)^{227}{\text{Ra}} \) reaction cross section value is estimated to \( \sigma^{(227)Ra} \approx 1.5 \times 10^3 \) b. The comparison between the recent data on 227Ac production via neutron irradiation of 226Ra is summarized in Table 2. Although very different irradiation conditions were used and relatively high uncertainty was estimated
Fig. 2  Fit of experimental data measured in two intervals after EOB (88 and 136 days). Curves represent calculated, while points, experimental values (\(^{227}\text{Ra dashed line}, \^{227}\text{Ac plain black line}, \^{227}\text{Th dash-dot line}, \^{223}\text{Ra dotted line}). Error bars represent the standard combined uncertainties of the determined activities.

Table 1  Calculated and measured activities of studied nuclides. Detection of \(^{227}\text{Ac}\) by \(\gamma\)-spectrometry was problematic due to high uncertainties at 100 keV peak (abundance of only 0.3 %).

<table>
<thead>
<tr>
<th>Nuclide</th>
<th>Activity (88 days after EOB) (kBq)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(^{226}\text{Ra})</td>
<td>-</td>
</tr>
<tr>
<td>(^{227}\text{Ac})</td>
<td>19</td>
</tr>
<tr>
<td>(^{227}\text{Th})</td>
<td>18</td>
</tr>
<tr>
<td>(^{223}\text{Ra})</td>
<td>17</td>
</tr>
</tbody>
</table>

Table 2  Comparison of recent data on \(^{227}\text{Ac}\) production.

<table>
<thead>
<tr>
<th>Yield (EOB) (Ci/(\text{g} ^{226}\text{Ra}))</th>
<th>Irradiation conditions: (\sigma_{\text{eff}}(b))^b</th>
<th>Calculated</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.10(^a)</td>
<td>1.09 (\times) 10(^{14}) n/cm(^2)/s 11.7 days</td>
<td>14 (\pm) 4</td>
<td>This work</td>
</tr>
<tr>
<td>1.7</td>
<td>1.0 (\times) 10(^{15}) n/cm(^2)/s 24 days</td>
<td>12</td>
<td>[6]</td>
</tr>
<tr>
<td>2.5</td>
<td>1.5 (\times) 10(^{15}) n/cm(^2)/s 25 days</td>
<td>9</td>
<td>[9]</td>
</tr>
</tbody>
</table>

\(^{a}\) Yield was determined by the back-calculation from daughter nuclei activities

\(^{b}\) Calculation based on the experimental data taken from the corresponding reference.

Fig. 3  Gamma-spectrum of irradiated sample of \(^{226}\text{Ra}\) (88 days after EOB)
in the cross section value, the overall results are in good agreement. The slightly lower cross section values reported in previous literature \cite{6, 9} could possibly be explained by the target burn-up and parasitic neutron capture by $^{227}$Ra and $^{227}$Ac.

**Conclusion**

We have verified the yield of the $^{226}$Ra(n,$\gamma$)$^{227}$Ra $\rightarrow$ $^{227}$Ac/$^{227}$Th/$^{223}$Ra production route in this study. The obtained effective cross-section value of the $^{227}$Ac production of $14 \pm 4$ barn is in good agreement with the literature data, although the evaluation of the data measured was complicated and the uncertainty of the determined value is high.

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**References**
