Mass separation of $^{225}$Ac from $^{227}$Ac and from irradiated Th targets to support Targeted Alpha Therapy
\(^{225}\text{Ac}\) for medical application

- Direct use as an α emitter
  - 4 α particles in close succession
  - \(T_{1/2} \sim 10\) days

- As a generator for \(^{213}\text{Bi}\)
  - 100% α emission
  - \(T_{1/2} \sim 45\) min

- Can be combined with \(^{68}\text{Ga}\) for theranostics applications

Sources of $^{225}\text{Ac}$

**Existing supply**
- In the decay chain of $^{229}\text{Th}$
- Extracted from $^{233}\text{U}$ bread during the XX$^\text{th}$ century weapon research
- 3 main suppliers: ORNL, ITU, IPPE
- Global annual production of 63 GBq
- Supporting some clinical trials worldwide but insufficient for future use & not sustainable

**Considered alternative routes**
- $^{226}\text{Ra}(\gamma,n)^{225}\text{Ra} \rightarrow ^{225}\text{Ac}$
- $^{226}\text{Ra}(p,2n)^{225}\text{Ac} @ 16.8$ MeV
  - Best on paper
  - Difficulties associated with $^{226}\text{Ra}$
- $^{232}\text{Th}(p,x)^{225}\text{Ac} @ >70$ MeV
  - Co-production of $^{227}\text{Ac}$
- ISOL
  - TRIUMF ISAC
  - CERN ISOLDE / MEDICIS
# Sources of $^{225}\text{Ac}$

<table>
<thead>
<tr>
<th>Production Method</th>
<th>Facility</th>
<th>Capabilities</th>
<th>Monthly $^{225}\text{Ac}$ Production [GBq (Ci)]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Current Sources</strong></td>
<td><strong>$^{229}\text{Th}$ generator</strong></td>
<td>ORNL</td>
<td>0.704 g (150 mCi) of $^{229}\text{Th}$</td>
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<td></td>
<td></td>
<td>ITU</td>
<td>0.215 g (46 mCi) of $^{229}\text{Th}$</td>
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<td></td>
<td></td>
<td>IPPE</td>
<td>0.704 g (150 mCi) of $^{229}\text{Th}$</td>
</tr>
<tr>
<td><strong>Potential</strong></td>
<td><strong>$^{232}\text{Th}(p, x)^{225}\text{Ac}$</strong></td>
<td>TRIUMF</td>
<td>500 MeV, 120 $\mu$A</td>
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<tr>
<td></td>
<td></td>
<td>BNL</td>
<td>200 MeV, 173 $\mu$A</td>
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<td></td>
<td></td>
<td>INR Arronax</td>
<td>160 MeV, 120 $\mu$A</td>
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<td></td>
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<td></td>
<td>70 MeV, 2×375 $\mu$A</td>
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<td></td>
<td></td>
<td>LANL</td>
<td>100 MeV, 250 $\mu$A</td>
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<td></td>
<td>iThemba LABS</td>
<td>66 MeV, 250 $\mu$A</td>
</tr>
<tr>
<td><strong>Future</strong></td>
<td><strong>$^{226}\text{Ra}(p, 2n)^{225}\text{Ac}$</strong></td>
<td>20 MeV, 500 $\mu$A cyclotron</td>
<td>3983.1 (107.65)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>15 MeV, 500 $\mu$A cyclotron</td>
<td>1157.4 (31.28)</td>
</tr>
<tr>
<td><strong>Sources</strong></td>
<td><strong>ISOL</strong></td>
<td>TRIUMF (existing)</td>
<td>0.37 (0.01)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TRIUMF (potential upgrades)</td>
<td>190.6 (5.15)</td>
</tr>
<tr>
<td></td>
<td><strong>$^{226}\text{Ra}(\gamma, n)^{225}\text{Ra}$</strong></td>
<td>medical linac</td>
<td>18 MeV, 26 $\mu$A</td>
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<td></td>
<td></td>
<td>ALTO</td>
<td>50 MeV, 10 $\mu$A</td>
</tr>
<tr>
<td></td>
<td><strong>$^{238}\text{Ra}(n, 2n)^{225}\text{Ra}$</strong></td>
<td>fast breeder reactor</td>
<td>~37 (1)</td>
</tr>
</tbody>
</table>
Handling Ac with the ISOL method

- High-energy spallation of $^{232}\text{Th}$ or $^{238}\text{U}$ yields to the co-production of Ra / Ac with $A=220-230$
- Radiochemistry yields a mix $^{225}\text{Ac} / ^{227}\text{Ac}$ (2%), deteriorating in time
  - Waste management problem
- Mass separation yields a mix $^{225}\text{Ac} / ^{225}\text{Ra}$
  - Acceptable as a co-generator
  - Efficiency?

![Diagram of ISOL method]

Radioactive isotopes are produced in a target, and a magnetic field bends ions according to $A/q$. Light mass ions are separated from heavy mass ions, and selected mass ions are extracted. Production beam leads to the target, and the separator collects the desired ions.
Handling Ac with the ISOL method

- Surface ionization of Ra has a long history at ISOLDE & laser ionization is now available as well
- Laser ionization of Ac has been demonstrated at Mainz / TRIUMF / LISOL / ISOLDE
- Release of Fr/Ra/Ac from UCₓ has been studied at ISOLDE under IS637 yielding ~ few % efficiency
MED024: $^{225}$Ac at MEDICIS

- Production route 1: mass separation of chemically-separated actinium, namely $^{225}$Ac / $^{227}$Ac (2%). This sample may be engineered from separate supplies of either isotope as well to reproduce the conditions.

- Production route 2: direct extraction and separation of $^{225}$Ac from an irradiated $^{232}$Th sample (metallic foil, ThO$_x$, ThC$_x$?). Considering irradiation at TRIUMF while CERN undergoes LS2.

- Characterization
  - Pre-separation & post-separation (full post-analysis of the sample at SCK•CEN)
  - Total activity and specific activities of $^{225}$Ac & $^{227}$Ac
  - Determining the process efficiency and enrichment factor
MED024: aims & request

• Characterize the separation of $^{225}$Ac / $^{227}$Ac in a quantitative way
• Start from chemically-separated Ac, as well as from various forms of irradiated Th
• Provide $^{225}$Ac for the future operation of MEDICIS and offer a long-term solution for the purification of $^{225}$Ac.
Irradiation at TRIUMF

- Irradiations planned at Beam Line 1A
- Radiochemistry to be performed on site prior to shipping