Sr-82 PRODUCTION WITH HIGH-ENERGY CYCLOTRONS

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Strontium-82

- Strontium-82 (Sr-82) decays through electron capture to Rubidium-82 (Rb-82)
- $T_{1/2} = 25.55$ days
- Employed in the fabrication of the transportable $^{82}$Sr/$^{82}$Rb generator
Rubidium-82
\(^{82}\text{RbCl}\)

- Rubidium-82 (Rb-82) is produced by decay of Strontium-82 (Sr-82)
- \(T_{\frac{1}{2}} = 75\) seconds
- Kinetics:
  - Potassium analog
  - High extraction fraction at high flow rates
- Defects visualized 2-7 minutes after injection
Rubidium-82 Cardiac Imaging
# Production of Strontium-82

<table>
<thead>
<tr>
<th>Nuclear Reaction</th>
<th>Target</th>
<th>Projectile Energy (MeV)</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{89}$Y(p, spallation)</td>
<td>Yttrium oxide</td>
<td>60-240</td>
<td>Low radiopurity &amp; yield</td>
</tr>
<tr>
<td>natMo(p, spallation)</td>
<td>Mo metal</td>
<td>500-700</td>
<td>Low radiopurity, high cost</td>
</tr>
<tr>
<td>natRb(p,xn)</td>
<td>RbCl or Rb metal</td>
<td>40-90</td>
<td>Preferred</td>
</tr>
<tr>
<td>natKr(α,pxn)</td>
<td>Kr gas</td>
<td>20-120</td>
<td>Low radiopurity, low yield, little availability</td>
</tr>
<tr>
<td>natKr($^3$He,xn)</td>
<td>Kr gas</td>
<td>20-90</td>
<td>Low radiopurity, low yield, very little availability</td>
</tr>
</tbody>
</table>
$^{85}\text{Rb}(p,4n)^{82}\text{Sr}$
Excitation function for the $^{85}\text{Rb}(p, 4n)^{82}\text{Sr}$ reaction.
Sr-82 Yield @ EOB vs Proton Energy

Yield (mCi/μA × h)

Proton Incident Energy (MeV)
The \textsuperscript{nat}RbCl (or metallic \textsuperscript{nat}Rb) target is irradiated with a 200-\(\mu\)A proton beam, at 70 MeV, for 5 days to yield the radioisotope Sr-82.

Rb-83/84/86 and P-32 are co-produced, but chemically separated. Sr-83 (\(t_{1/2} = 1.35\) days) and Sr-85 (\(t_{1/2} = 64.8\) days).

After irradiation and transfer, the target shuttle remains stored for 6 days inside the hot cell (to allow for the decay of Sr-83) waiting for subsequent chemical processing.

After 6-day storage, the encapsulated target is disassembled and the chemical processing started. This includes simple separations by column chromatography to yield a final solution of purified Sr-82.
An FDA approved commercial generator (trade name CardioGen-82) is available from Bracco Diagnostics Inc.

This generator is composed of a small plastic column (~4 cm (height) x 0.5 cm (diameter) loaded with hydrous tin oxide. The distribution coefficient for Sr ions is about 21,000 and less than 3 for Rb ions when eluted with normal saline solution.

The generator is typically loaded with 100 mCi (3.7 GBq) of $^{82}$Sr, and infusions are microprocessor controlled.
CardioGen-82®
(Rubidium Rb-82 Generator)
To Date Rb-82 Clinical Use Was Mainly Supply Driven
Current Sr-82 Production

- Irradiation is performed at six sites
- **Five** of the six sites are not dedicated to radionuclide production but each is instead a unique, expensive to build, maintain and run, relatively old high-energy physics machine.
- As such their schedules are determined to a major extent by their physicist/engineer ‘owners’.
- This results in an uneven supply chain.
## The “Virtual” Isotope Center

<table>
<thead>
<tr>
<th>Laboratory</th>
<th>Target type</th>
<th>Irradiation conditions</th>
<th>Typical batch yield at EOB (GBq)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BLIP @ Brookhaven National Lab (BNL), NY USA</td>
<td>RbCl pressed pellet in inconel</td>
<td>2 targets, 93-70 &amp; 64-41 MeV</td>
<td>220-300 (5.9-8.1Ci)</td>
</tr>
<tr>
<td>IPF @ Los Alamos National Lab (LANL), NM USA</td>
<td>RbCl cast puck in inconel</td>
<td>2 targets, 97-71 &amp; 65-45 MeV</td>
<td>300-450</td>
</tr>
<tr>
<td>Institute for Nuclear Research (INR), Troitsk Russia</td>
<td>Rb metal in stainless steel</td>
<td>100-40 MeV</td>
<td>120-220</td>
</tr>
<tr>
<td>iThemba Labs, Faure S. Africa</td>
<td>Rb metal in stainless steel</td>
<td>66-44 MeV</td>
<td>100</td>
</tr>
<tr>
<td>Arronax, Nantes France</td>
<td>RbCl pressed pellet in stainless steel</td>
<td>8 thin targets, 69-44 MeV</td>
<td>80-90</td>
</tr>
<tr>
<td>Nordion/TRIUMF, Vancouver Canada</td>
<td>Rb metal in stainless steel</td>
<td>60-48 MeV</td>
<td>60-100</td>
</tr>
</tbody>
</table>
LANL = Los Alamos National Labs
BNL = Brookhaven National Labs
TRIUMF = University British Columbia
ITHEMBA = Laboratory for Accelerator Sciences
TROITSK = Institute for Nuclear Research
ARRONAX = Nantes University
6 irradiation sites and 3 Active Pharmaceutical Ingredients (API) production sites.

Overall procedure involves the following steps: (1) Irradiation (three weeks), (2) Cool down and shipping targets (two weeks), (3) Chemistry (one week), (4) Generator production (one week).

If there is a failure anywhere in the process it is almost unrecoverable.

Reliability
Jubilant Life Sciences arm gets US FDA nod for coronary drug

Jubilant Life Sciences today said its wholly-owned subsidiary has received approval from the US health regulator for RUBY-FILL - Rubidium 82 generator and elution system - used in diagnosis of coronary artery disease in the US market.

ETHealthworld.com Oct, 03, 2016
New Producers Are Entering the Market
Zevacor Molecular Installs Only Commercial 70 MeV Cyclotron Dedicated to Medical Use in the United States

*Cyclone 70 to stabilize U.S. supply of Strontium 82, produce next generation of radiopharmaceutical products*

Noblesville, Indiana (September, 10, 2016)
Installation of the 70 MeV cyclotron

Study of neutron-rich nuclei for astrophysics

Production of radionuclides for medicine

Production of high-intensity neutron sources
The 70 MeV cyclotron installed at Legnaro National Laboratories
Acknowledgement

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Thank You!