Astatine-211 Production Activities at the University of Washington

2023 DOE IP VIRTUAL SEMINAR SERIES - ASTATINE-211

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TOPICS COVERED

1. Properties that make $^{211}$At attractive for targeted alpha therapy
2. Methods used for routine production
3. QA/QC and product specifications
4. Current development activities
High energy alpha decay: short range in tissue, deliver a high radiation dose to tumor while sparing surrounding healthy tissue

Short half-life: potentially lower toxicity

No alpha-emitting daughter nuclide: less off-target toxicity

Easy production: medium energy alpha beam; low-cost target material

Targeted delivery: established radiolabeling chemistry for incorporating $^{211}$At into various carrier molecules
Bi target

211At production target station

- Developed in collaboration with TRIUMF, Vancouver, Canada
- Irradiated at a 10° slant
- High purity Bi melted onto Al target body, machined to desired thickness
- Large Bi surface: 120 mm x 18 mm
- Fully stopping: ~4.25 g of Bi

1. Bi$^{\text{211}}$At is dissolved in conc. HNO$_3$

2. HNO$_3$ is distilled away, leaving Bi salts containing $^{\text{211}}$At

3. Bi$^{\text{211}}$At salts are dissolved in 8 M HCl

4. $^{\text{211}}$At is extracted into DIPE (top layer)

5. Aqueous layer (bottom - HCl) is removed and discarded

6. Wash the DIPE/$^{\text{211}}$At layer 4 times with 8 M HCl

7. $^{\text{211}}$At is back-extracted into NaOH (~0.5 mL)

8. The NaOH is neutralized (pH 6.5-7.0) and $^{\text{211}}$At is ready to be used for antibody labeling

Run time: 2.5 hours

Non-decay corrected yield: ~60%

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Test Method</th>
<th>Acceptance Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identity</td>
<td>Radio-TLC</td>
<td>Conforms to reference TLC scan</td>
</tr>
<tr>
<td>Chromatographic Purity Using Gamma-Detection</td>
<td>Radio-TLC</td>
<td>≥85% (area %) Na$^{211}\text{At}$ At Other $^{211}\text{At}$ species may be present (e.g. $^{211}\text{At}$astatate)</td>
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<tr>
<td>Radionuclide Purity (test for other nuclides present)*</td>
<td>HPGe purity validation of 4 separate At-211 runs</td>
<td>&gt;99+%; Evaluated quarterly (no At-210 or other radionuclide detectable)</td>
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*Test is run quarterly as results do not change during shorter testing periods
• More than 2 Ci of $^{211}$At produced in each year over the last five years.
• The total activity of 2023 is expected to be lower due to a pause in multiple clinical trials due to FDA review of the current results.
• **Quotes & Orders: isotopes.gov**
• **Batch size:**
  - Activity at shipment - 0.518 GBq or 1.85 GBq (14 mCi or 50 mCi)
  - After overnight shipment, ~10% of shipped quantity at receipt due to half-life
• **Frequency:** once per week with potential for additional runs depending on our schedule
• **Shipped in near neutral solution (~pH 6.5-7.0)**
• **Container:** plastic V-bottom vial
• **Volume:** <1 mL
• **FedEx Overnight Shipping is used**
• **Local courier can be arranged if within driving distance from Seattle, WA**
Design criteria

- $^{211}$At targets to 100 µA of 29 MeV alpha beam
- Automatic target loading and ejection
- Compatible with commercial remote target transport systems
- Adaptable for other isotope production targets
- Cost effective to fabricate and maintain

For questions, please contact Marissa Kranz via kranzm@uwmcf.uw.edu
AUTOMATED TARGET LOADING AND UNLOADING
• Eliminated the nitric acid distillation step
• Hydroxylamine hydrochloride is used to destroy the nitrate
• Final product contains tellurium impurity (i.e. Na₂TeO₃) ~20-50 ppm
• Might have residual hydroxylamine hydrochloride in the final product

• Decay and attenuation corrected isolation yields: >95%
• Non-decay corrected yield: ~90%
• Semi-automated process takes ~1.5 h
• Final product in ~1 mL NaOH
• Radiochemical purity >99%
• Antibody radiolabeling yields: 70-80%

OPTIMIZATION OF AUTOMATED ISOLATION

- Minimize product volume
- Flushing the Te column with air
  - Most of the activity in <0.5 mL
  - Affected radiolabeling yields
- Will evaluate Ar for removing water from column and tubing
- Adapting this method for the 90-degree target
COIN-SHAPED BISMUTH TARGET

- About 90 µm thick – designed to capture 29 – 21 MeV of the excitation function for $^{211}$At
- 18 mm diameter; 230 mg of Bi – 6% of the 10-degree target – potentially simplify the separation chemistry
- 30 $^{211}$At production runs to date
- 15 - 30 mCi for preclinical animal studies
- Ramping up beam current
- Production rate comparable to the 10-degree target
- 30 min wait time after EOB due to short-lived radioisotopes in the Al target backing
TARGET DISSOLUTION CHAMBER

Designed and fabricated by Bob Smith
• Routinely produce up to 2 Ci of $^{211}$At per year
• Evaluating new target system for production
• Optimizing a new automated process for isolation
This research is supported by the U.S. Department of Energy Isotope Program, managed by the Office of Science for Isotope R&D and Production.