Astatine-211 Production Activities at the University of Washington

2023 DOE IP VIRTUAL SEMINAR SERIES - ASTATINE-211

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UW SCHOOL OF MEDICINE
DEPARTMENT OF RADIATION ONCOLOGY

Isotope Program
U.S. Department of Energy

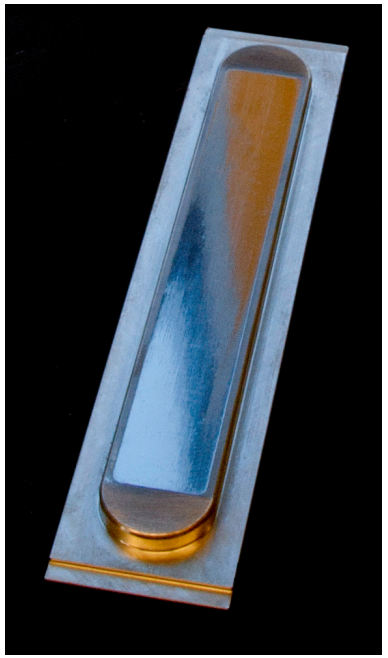
TOPICS COVERED

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

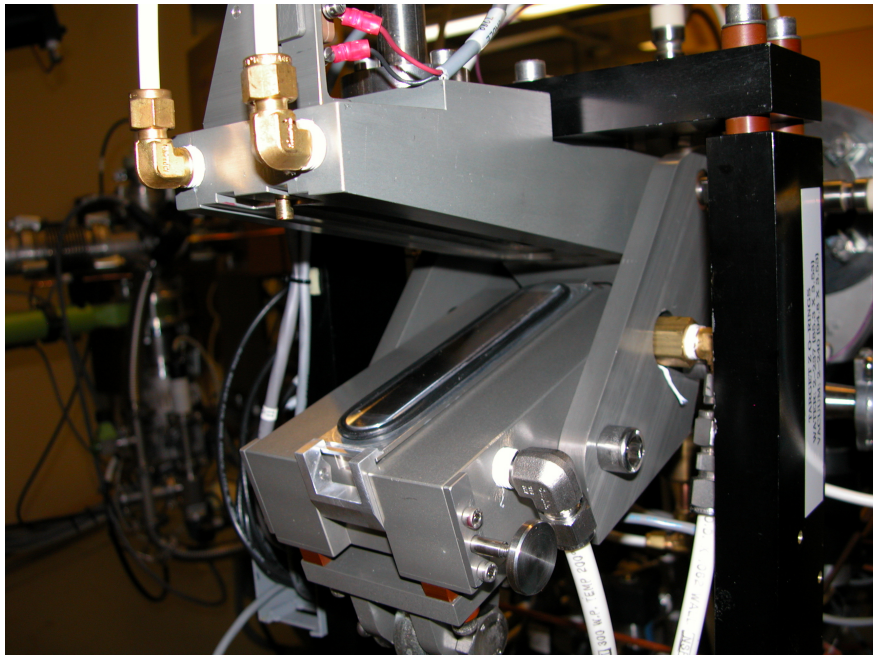
ASTATINE-211 FOR TAT

- **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

10-DEGREE TARGET AND TARGET STATION



Bi target



^{211}At 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

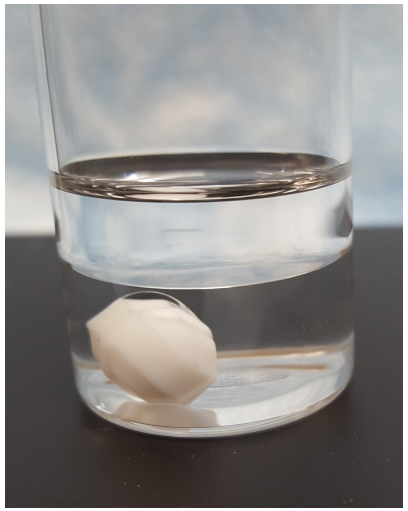
K. Gagnon, et al., *J. Label Compd. Radiopharm*, 2012, 55 436-440

“WET CHEMISTRY” ISOLATION METHOD

1. Bi/^{211}At is dissolved in conc. HNO_3

2. HNO_3 is distilled away, leaving Bi salts containing ^{211}At

3. Bi/^{211}At salts are dissolved in 8 M HCl



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

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

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

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

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

Run time: 2.5 hours

Non-decay corrected yield: ~60%

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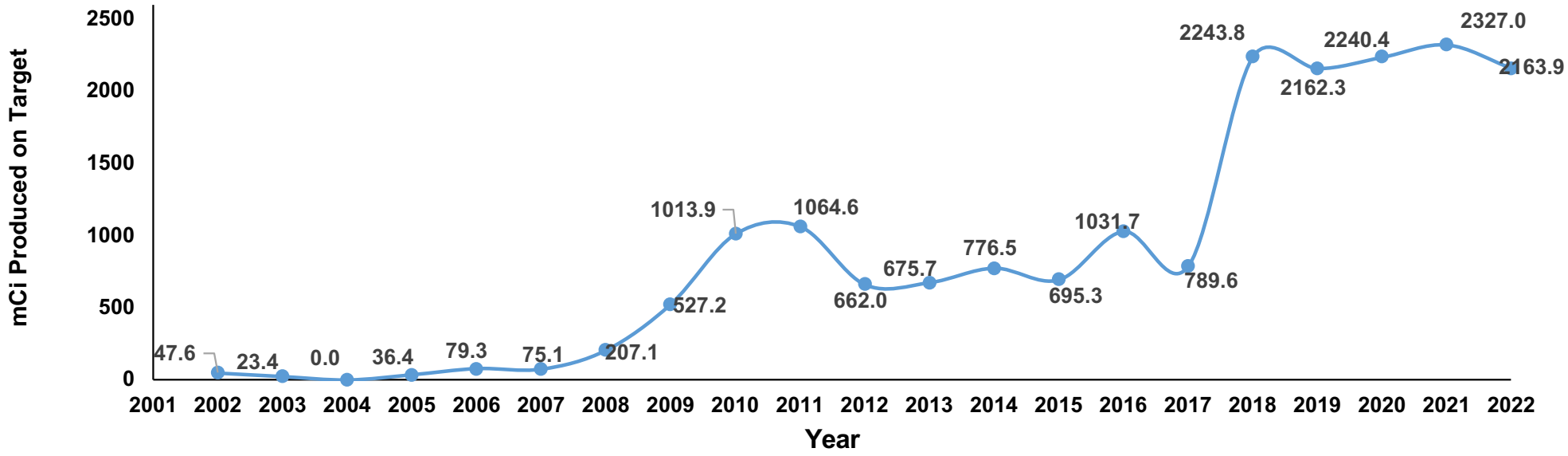
E.R. Balkin et al., *Applied Sciences, 3, 636-655.*

QA/QC

Characteristic	Test Method	Acceptance Criteria
Identity	Radio-TLC	Conforms to reference TLC scan
Chromatographic Purity Using Gamma-Detection	Radio-TLC	≥85% (area %) Na[^{211}At]At Other ^{211}At species may be present (e.g. [^{211}At]astatate)
Radionuclide Purity (test for other nuclides present)*	HPGe purity validation of 4 separate At-211 runs	>99+%; Evaluated quarterly (no At-210 or other radionuclide detectable)

*Test is run quarterly as results do not change during shorter testing periods

YEARLY ASTATINE-211 PRODUCTION

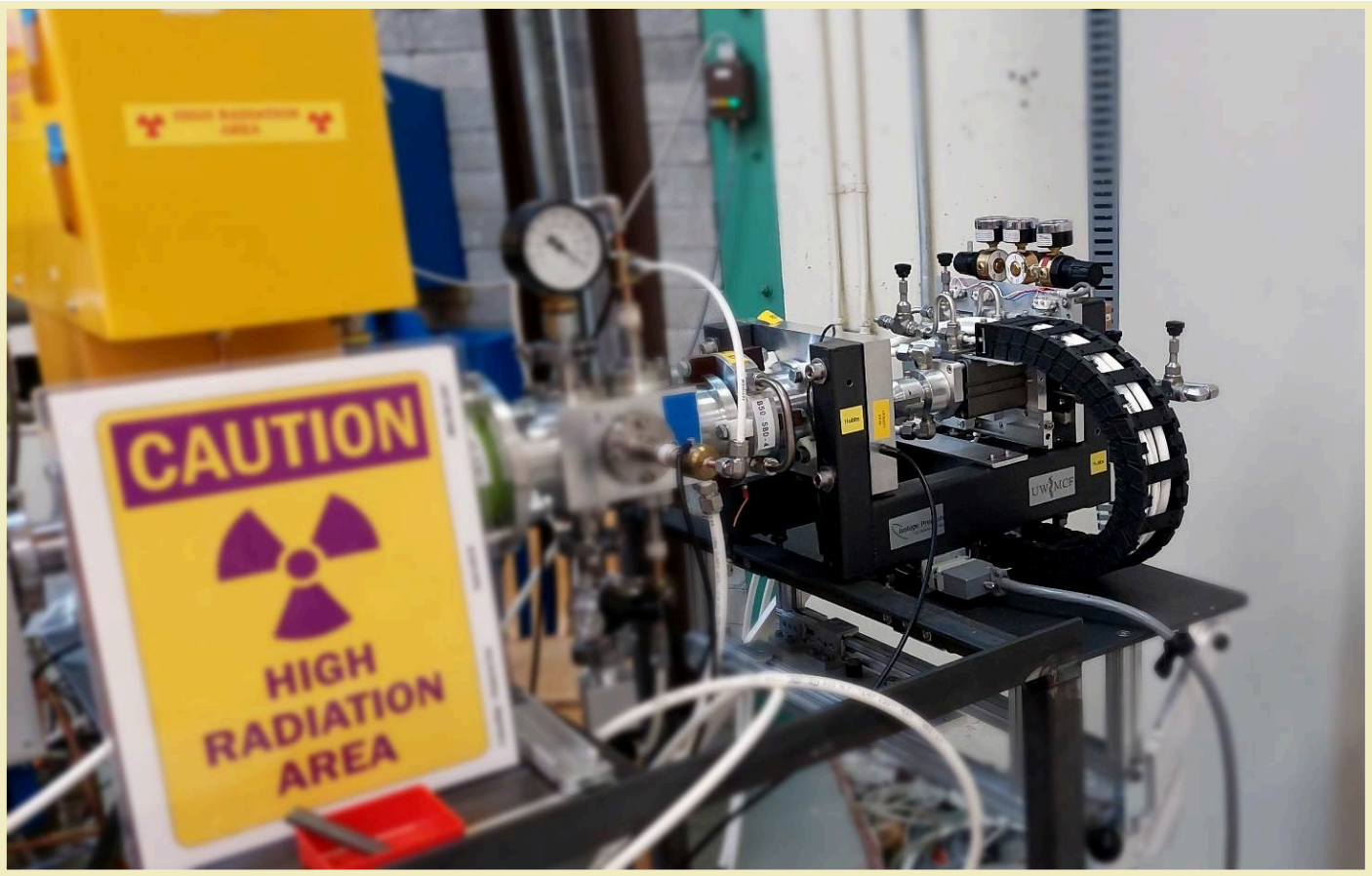


- More than 2 Ci of ^{211}At produced in each year over the last five years.
- The total activity of 2023 is expected to be lower due to a pause in multiple clinical trials due to FDA review of the current results.

PRODUCT INFORMATION

- **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

90-DEGREE ASTATINE-211 TARGET STATION



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

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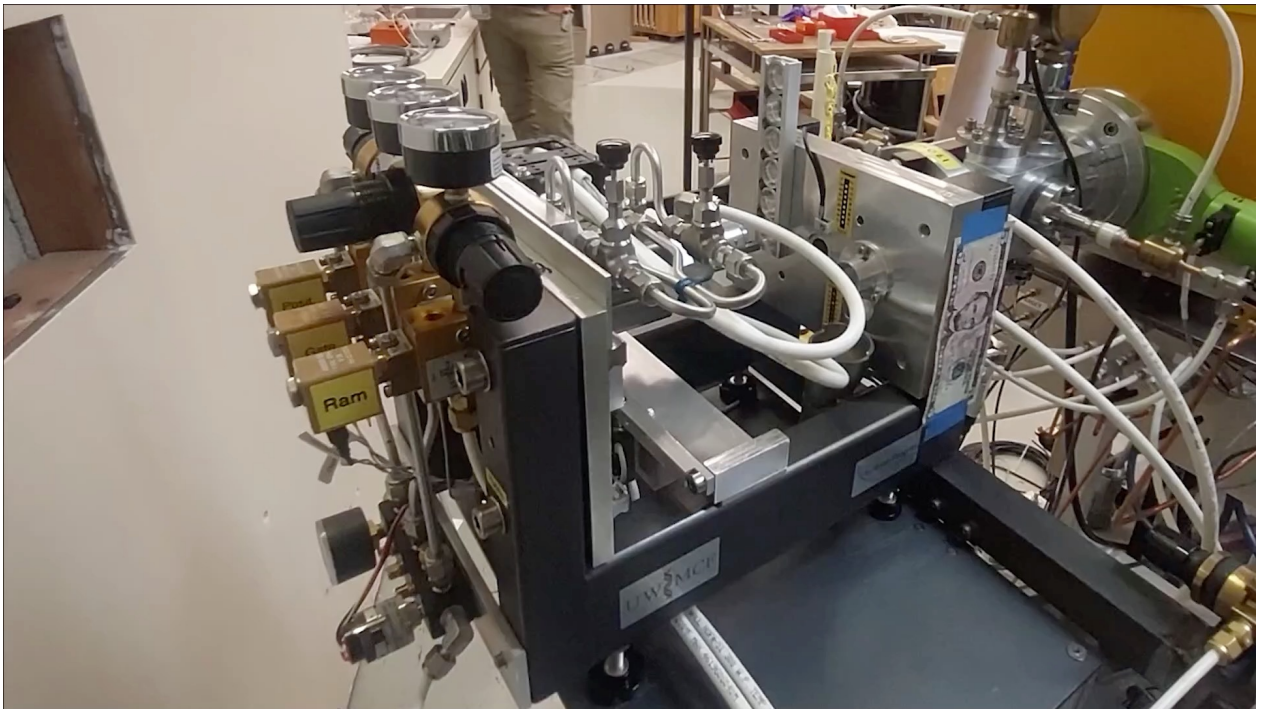
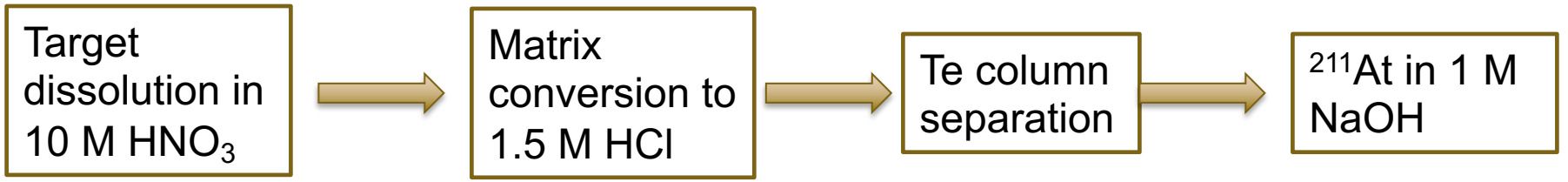
AUTOMATED TARGET LOADING AND UNLOADING



TELLURIUM-PACKED COLUMN METHOD

- Eliminated the nitric acid distillation step
- Hydroxylamine hydrochloride is used to destroy the nitrate
- Final product contains tellurium impurity (i.e. Na_2TeO_3) ~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%



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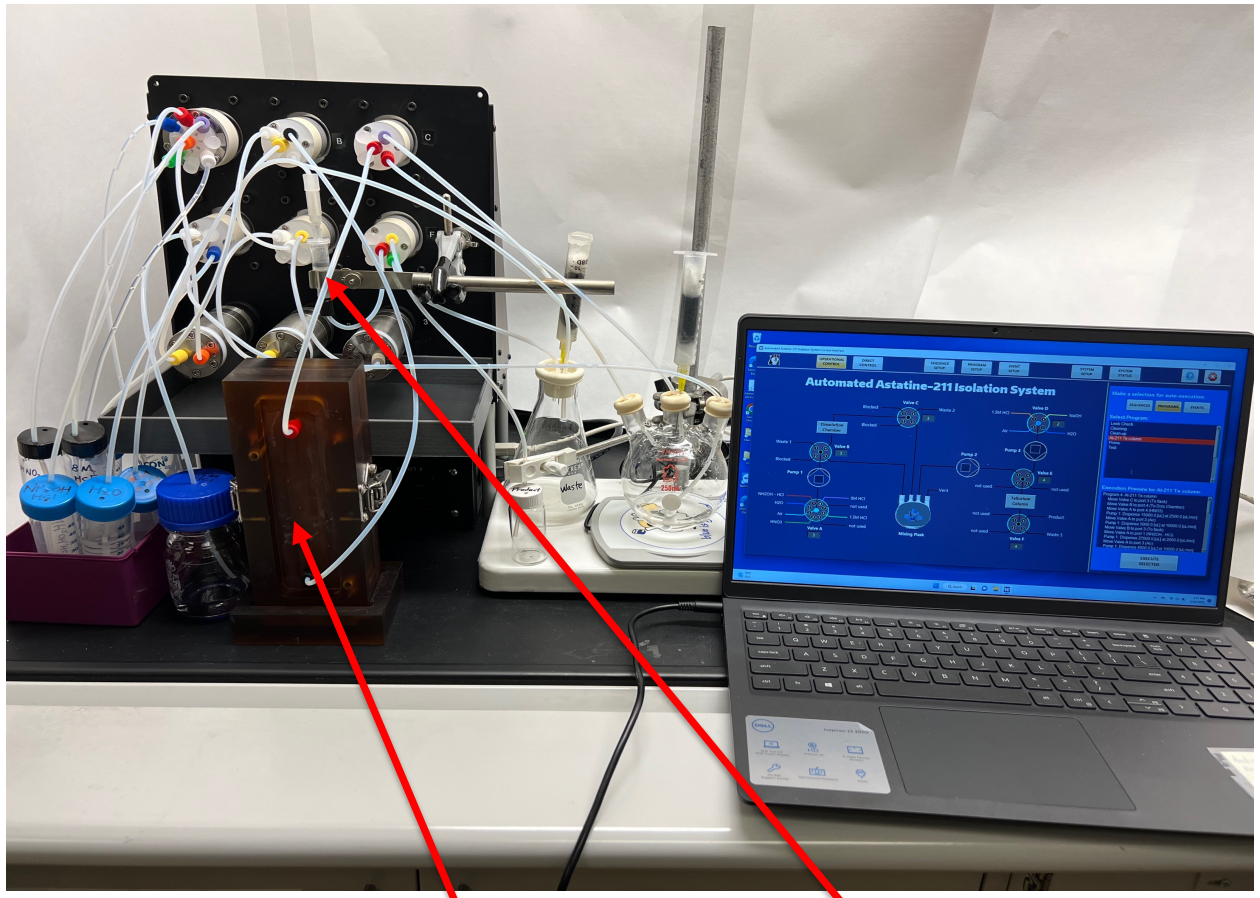
Li, Y., Hamlin, D.K., Chyan, M. *et al*. *Sci Rep* **9**, 16960(2019).

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

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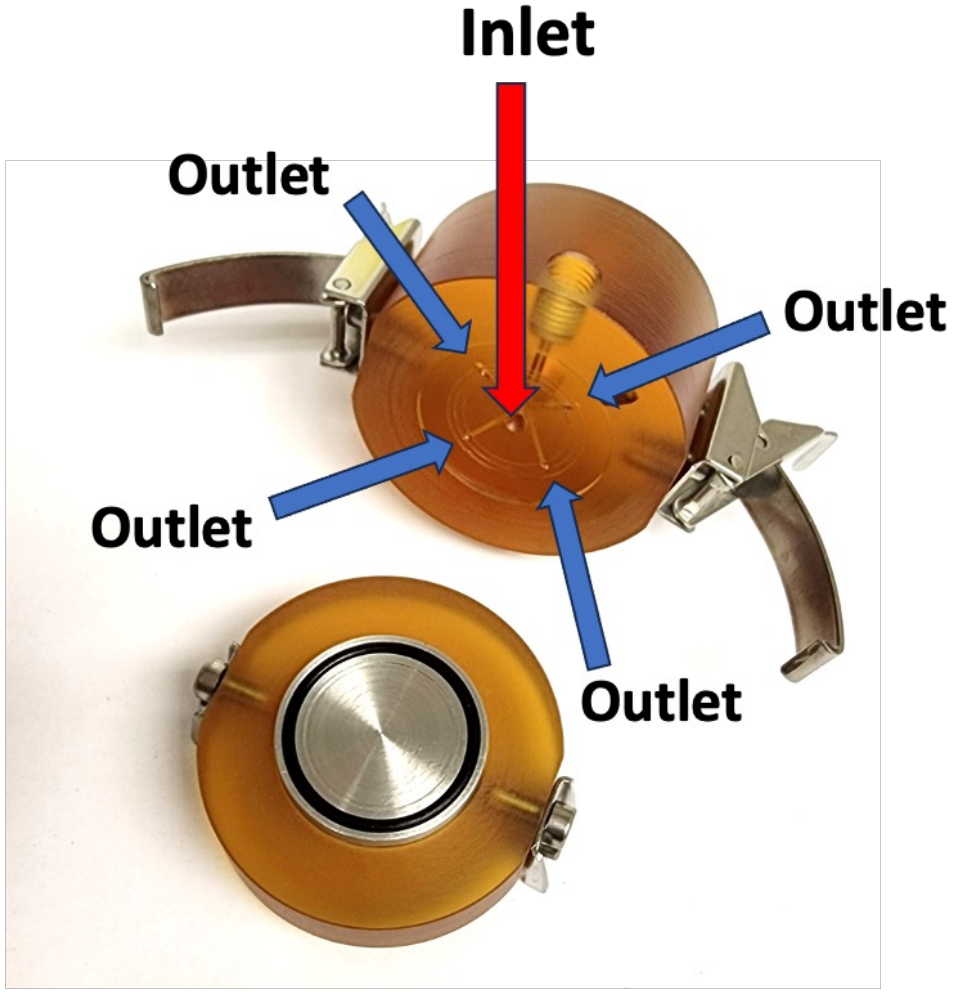
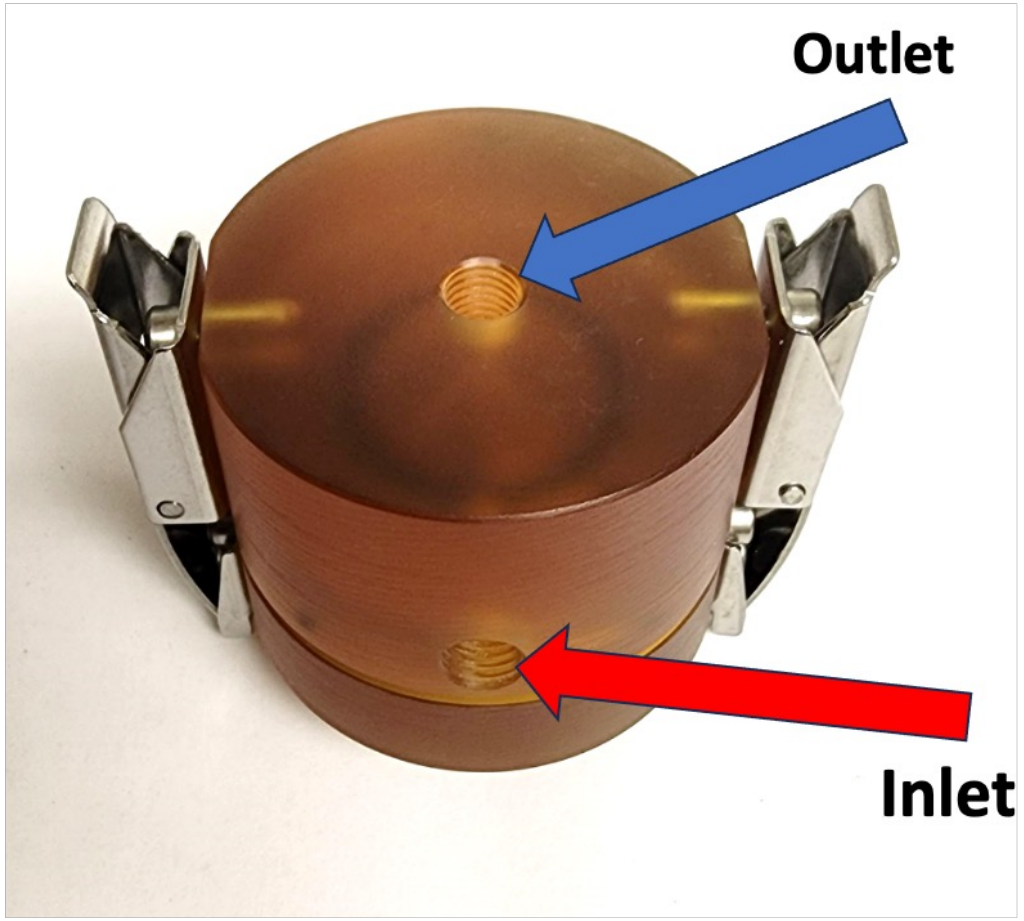
COIN-SHAPED BISMUTH TARGET

- 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

SUMMARY

- Routinely produce up to 2 Ci of ^{211}At per year
- Evaluating new target system for production
- Optimizing a new automated process for isolation

THANK YOU !

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