At-211 User Forum

5 – 6 pm

June 23rd, 2019

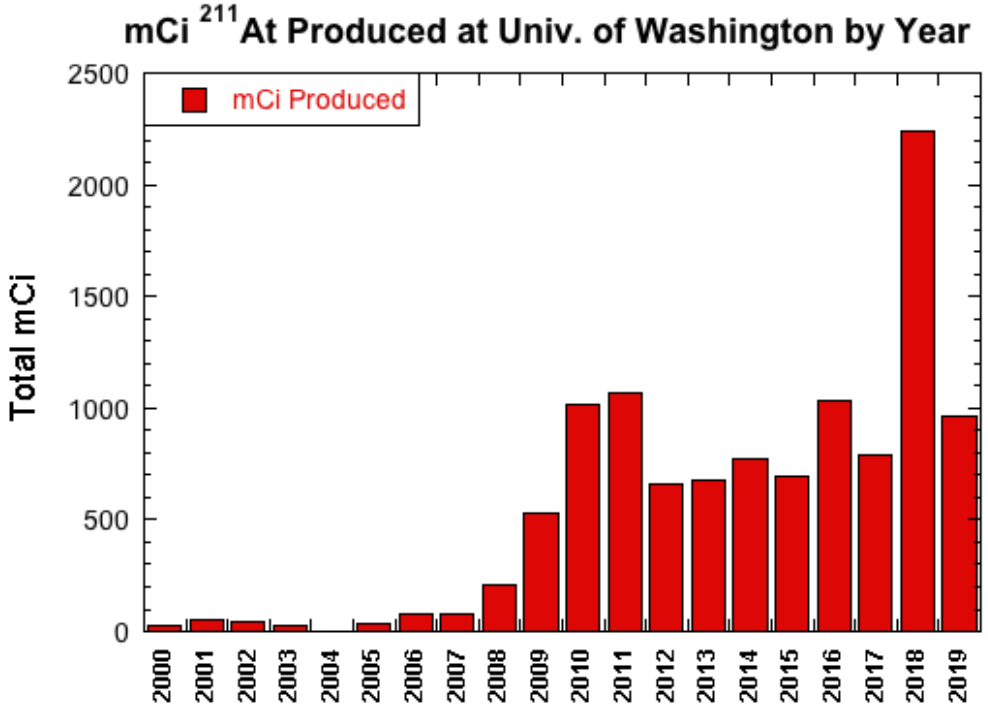
Platinum Ballroom, Salon 3

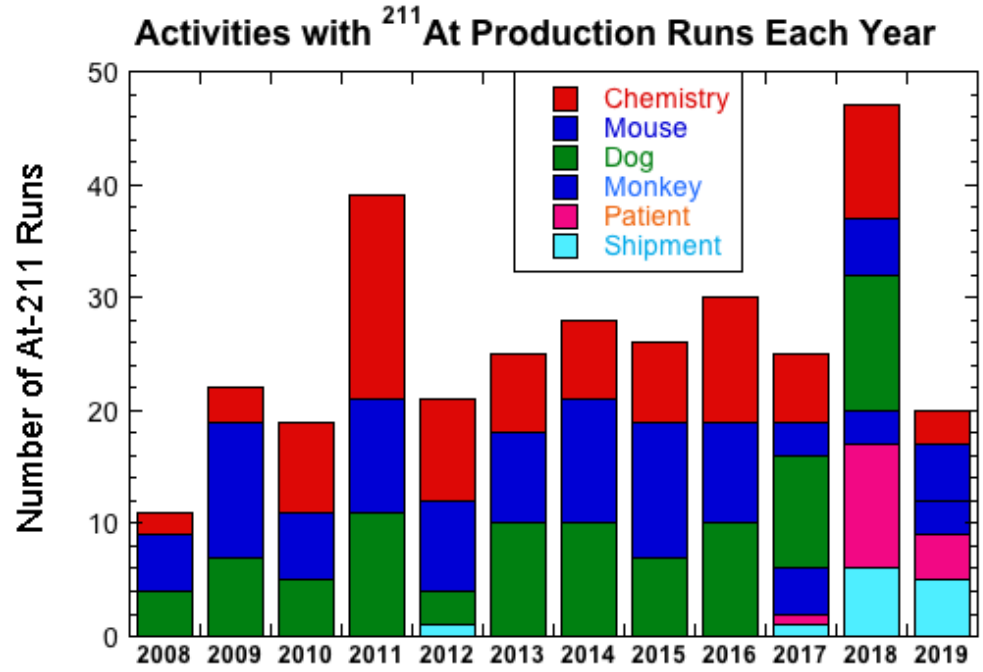
Anaheim Marriott

A forum on Issues Related to At-211 Availability and Use for Researchers

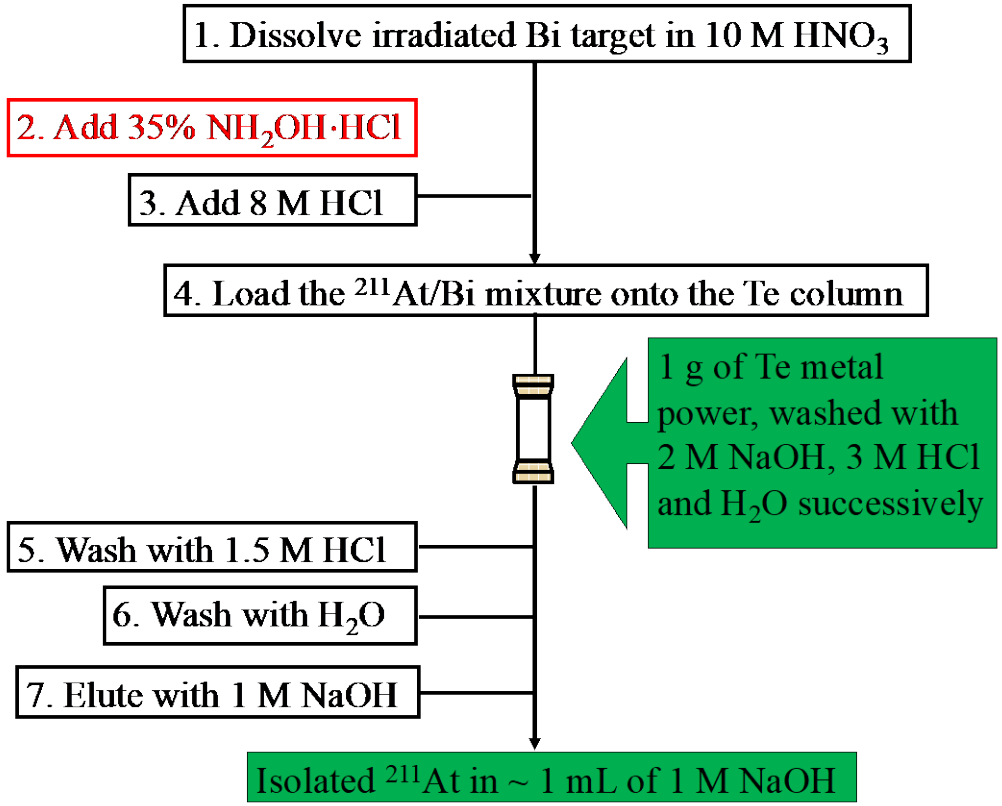
- Introduction around room (please sign in)
- DOE Funding of At-211 production and research – Ethan Balkin
- Open forum – any discussion points
- Comments from current/future production sites –Mehran Makvandi, Scott Wilbur, others?
- Comments on automation of isolation process – Matt O'Hara, Stosh Kozimor, Scott Wilbur
- Comments on clinical trials & regulatory issues – Scott Wilbur, Others?
- Panel - Topics for discussion
  - Cyclotron upgrades
  - Targets and target stations
  - Radiation Safety Issues
  - Transportation Issues
  - Labeling methods
  - Alternate Production routes – $^{211}Rn/^{211}At$

At-211 Production and Use at UW





At-211 Isolation Using Te-Packed Column (Dr. Yawen Li)

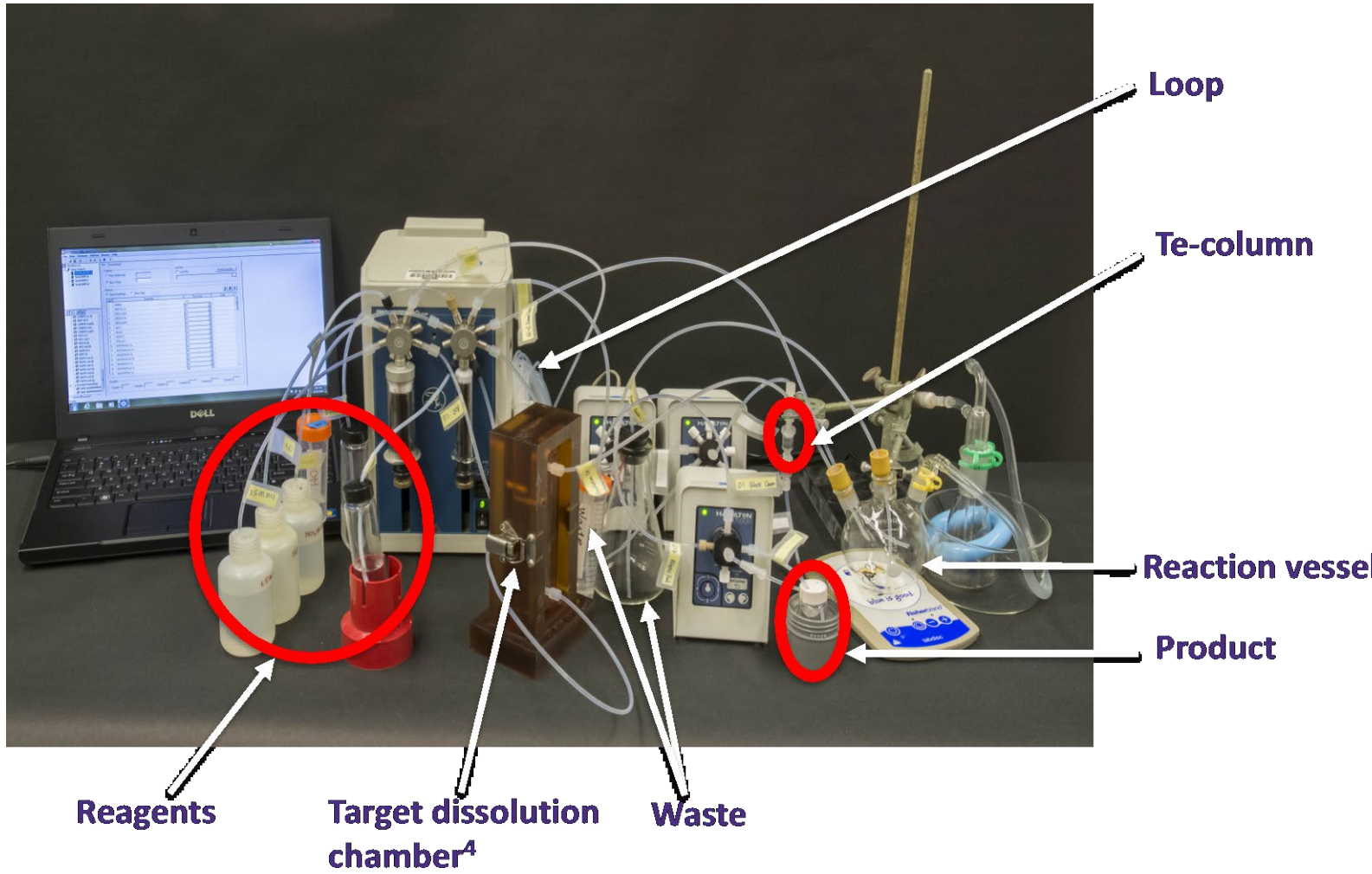


Run #	% Captured	% Eluted	% labeled
1	99	80	23
2	99+	77	10
3	99+	83	17
4	99+	82	12
5	99+	78	26
6	99	82	21
7	99	67	73
8	99+	80	83
9	98	80	70
10	99	79	77

Bochvarova, M. et al., Radiokhimiya, 1972, 858-865
(separation of At-211 from irradiated thorium targets)

*Isolation process for full run takes ~100 min

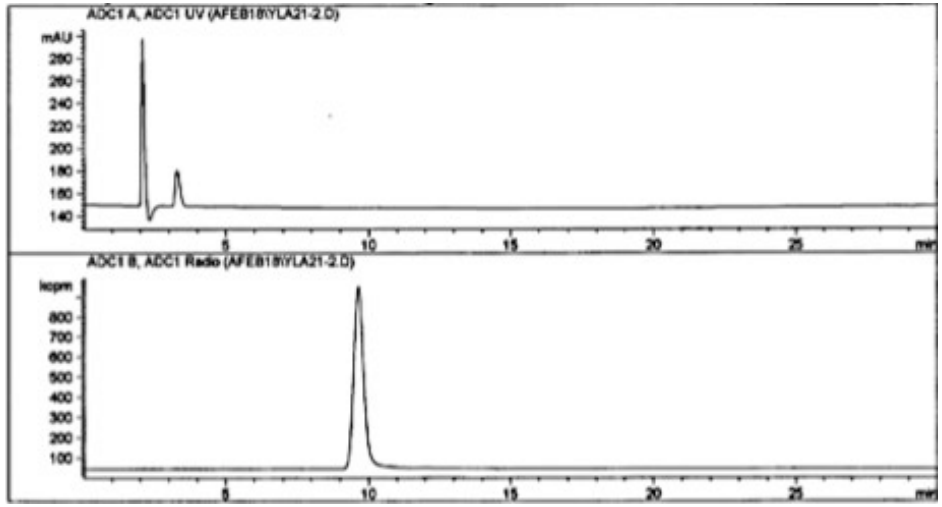
Automated At-211 Isolation Setup



[4]O'Hara, M. J. et al., Appl. Radiat. and Isot. 122, 202-210, 2017

Radiochemical and Chemical Purity

- Ion Exchange RadioHPLC analysis



Radio-HPLC conditions:

- Column: Dionex IonPac AS 20 (4 × 250 mm)
- Eluent: 50 mM NaOH
- Flow rate: 1.3 mL/min, isocratic

- ICP-MS

Equipment and software

- Agilent 7900 ICP-MS
- MassHunter Workstation

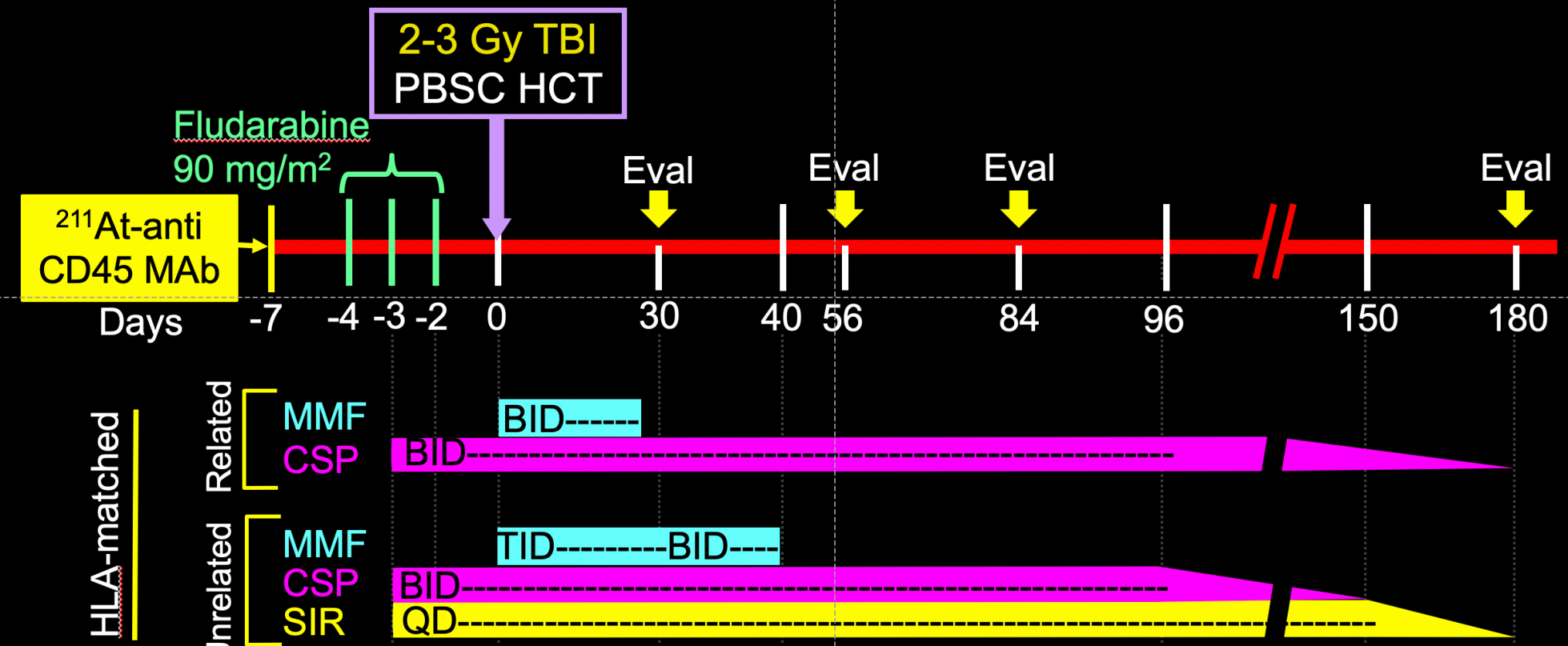
Material Tested	Concentration (ppm)	
	Te	Bi
[^{211}At]NaAt	46 ± 19	1.0 ± 0.6
^{211}At-MAb-B10	0.04 ± 0.01	0.05 ± 0.04

Open Phase I/II Clinical Trial with At-211

(ClinicalTrials.gov identifier: NCT03128034)

- P.I.: Dr. Brenda Sandmaier, Fred Hutch, Seattle, WA
- Study Title: ^{211}At-BC8-B10 Before Donor Stem Cell Transplant in Treating Patients with High-Risk AML, ALL or MDS
- Conditions treated:
  - Acute lymphoblastic leukemia in remission
  - Acute myeloid leukemia arising from previous myelodystplastic syndrome
  - Acute myeloid leukemia in remission
  - High risk myelodysplastic syndrome
  - Chronic myelomonocytic leukemia
  - Myelodysplastic syndrome with excess blasts
  - Recurrent adult acute myeloid leukemia
  - Refractory adult acute lymphoblastic leukemia
  - Recurrent adult acute lymphoblastic leukemia

Protocol 9595: AML, ALL, MDS



Protocol 9595: Dose escalation/De-escalation

Dose level	^{211}At-BC8-B10 Amount of ^{211}At (uCi/kg) based on ideal body weight of patient or actual body weight for patients below ideal body weight
1	25
2	50
3	75
4	100 (starting dose level)
5	150
6	200
7	250
8	300
9	350
10	400
11	450
12	500
13	550

Outcome Measures

- Primary
  - Maximum tolerated dose defined as dose of ^{211}At-BC8-B10 used in combination with reduced intensity HCT that is associated with grade III/IV regimen-related toxicity or true toxicity rate of 25% (up to 100 days following transplant)
- Secondary
  - Achievement of remission (up to 2 years)
  - Disease-free survival (up to 100 days)
  - Duration of remission (up to 2 years)
  - Non-relapse mortality (up to 2 years)
  - Overall survival (up to 100 days)
  - Rates of acute graft vs. host disease (up to 180 days)
  - Rates of chimerism (up to 84 days)
  - Rates of engraftment (up to 100 days)