

# Astatine-211 User Group Meeting 2021

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# Current <sup>211</sup>At Production Sites

### **United States**

- Duke University
- University of Washington
- University of Pennsylvania\*
- National Institute of Health
- Texas A&M University

Europe

- Copenhagen University (Denmark)
- Arronax (France)

### Asia

- Osaka University (Japan)
- QST-Takasaki (Japan)\*
- QST-NIRS (Japan)
- IPCR Riken (Japan)
- Fukushima Medical University (Japan)
- Sichuan University (China)\*

\*Max production capacity < 1 GBq, or < 27 mCi

Yutian Feng, Michael R. Zalutsky, Nucl Med and Biol 100 (2021), in press







# Potential Production Sites in Near Future

### **United States**

- University of California - Davis
- Ionetix, Lansing, MI

Europe

- Nuclear Physics Institute of the CAS (Czech Republic)
- POLATOM (Poland)
- University of Birmingham (UK)
- IFIN-HH, Măgurele (Romania)
- Forschungszentrum Jülich (Germany)

### Asia

- KIRMS (South Korea)
- RIKEN (Japan), Heavy-ion Linac

Yutian Feng, Michael R. Zalutsky, Nucl Med and Biol 100 (2021), in press







# <sup>211</sup>Rn/<sup>211</sup>At Generator

- 42-MeV 6Li ions via 209Bi(6Li, 4n)211Rn, or 60-MeV 7Li ions via 209Bi(7Li, 5n) 211Rn
- $^{211}$ Rn t<sub>1/2</sub> = 14.6 h, daughter  $^{211}$ At reaches its maximum radioactivity at 14.5 h
- Over 80% of the maximum <sup>211</sup>At activity will still be available after 24 h
- Useful method for distribution beyond the production site in the future

Facilities investigating the production of <sup>211</sup>At via a <sup>211</sup>Rn/<sup>211</sup>At generator

- Argonne National Laboratory, USA
- TRIUMP, Canada
- GANIL, France
- JAEA, Japan

Yutian Feng, Michael R. Zalutsky, Nucl Med and Biol 100 (2021), in press







# **Clinical Experience with Astatine-211**

- Duke University (Durham, USA) – Phase I, Completed
  - Recurrent brain tumor
  - <sup>211</sup>At-labeled anti tenascin MAb 81C6
  - Up to 347 MBq, or 9.4 mCi was administered to the resection cavity
  - Treated 18 patients
  - Low-grade neurotoxicity
  - No dose-limiting toxicity

- Gothenburg, Sweden Phase I, Completed
  - Ovarian Cancer
  - <sup>211</sup>At-labeled MX35 (Fab)<sub>2</sub> antibody fragment, targeting NaPi2b
  - Up to 215 MBq/L, or 5.8 mCi/L was administered into the intraperitoneal cavity
  - Treated 12 patients
  - No signs of radiation-related toxicity
  - No decreased tolerance to relapse therapy

- University of Washington and Fred Hutch (Seattle, USA) – two ongoing Phase I/II clinical trials
  - Leukemia
  - Low toxicity HCT conditioning regimen
  - <sup>211</sup>At-labeled anti CD45 MAb BC8-B10
  - Intravenously injected
  - Treated 43 patients
- Two new Phase I trials coming up
  - Multiple Myeloma











### Challenges in Realizing <sup>211</sup>At Targeted Alpha Therapy

- Production at clinical level is still a challenge
- Automated isolation and labeling
- Labeling chemistry
- Distribution of <sup>211</sup>At
- Introducing more <sup>211</sup>At reagents into clinical trials
- etc







Eric Prebys, University of California – Davis Lauren McIntosh, University of Texas A&M Mehran Makvandi, University of Pennsylvania Michael Zalutsky, Duke University Rob Emery, University of Washington Yawen Li, University of Washington







# ASTATINE-211 PRODUCTION UPDATE FOR THE UNIVERSITY OF WASHINGTON

2021 DOE IP ASTATINE-211 USER MEETING

YAWEN LI ROB EMERY

8/10/2021



UW Medicine

OF MEDICINE

DEPARTMENT OF RADIATION ONCOLOGY

# **DOE FUNDING**

UW Medical Cyclotron Facility under DOE Isotope Program Stewardship

- DOE base funding partially supporting cyclotron operations (started 2018)
- Radionuclide production under DOE guidance

Radiochemistry Division is funded through Base & R&D Funding obtained from DOE Isotope Program

- Currently providing At-211 through NIDC; supported by equipment and base funding (started 2015)
- Developing methods for producing other radionuclides through R&D funding
- Will provide other radionuclides when routine productions are achieved, and facilities are adequate for high levels of activity





# **YEARLY ASTATINE-211 PRODUCTION**

52 GBq, or 1.41 Ci produced Jan-Jun



Year





# **ASTATINE-211 PRODUCTION ACTIVITIES**



#### UW Medicine UW SCHOOL OF MEDICINE DEPARTMENT OF RADIATION ONCOLOGY

<sup>a</sup>HIV: human immunodeficiency virus; <sup>b</sup>HCT: hematopoietic cell transplant;

# **PRODUCTION FOR THE NIDC**

- 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
- 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



# PRECLINICAL RESEARCH

- Improving <sup>211</sup>At production through engineering
  - Automation of Isolation  $\bigcirc$
  - New target station design Ο
  - New Bi target design Ο
- Developing new <sup>211</sup>At radioimmunotherapy agents
  - Collaboration with Drs. Sandmaier, Green,  $\bigcirc$ Orozco, and Walter at the Fred Hutchinson Cancer Research Center and Dr. Park at UW
  - Blood cancers, HIV and hepatocellular Ο carcinoma



Green

Brenda Sandmaier Damian Johnnie Orozco





Roland Walter

James Park

UW Medicine UW SCHOOL OF MEDICINE DEPARTMENT OF RADIATION ONCOLOGY

# **ASTATINE-211 PRODUCED FOR CLINICAL TRIALS**

Two <sup>211</sup>At-BC8-B10 Phase I/II clinical trials ongoing

OF MEDICINE

DEPARTMENT OF ADIATION ONCOLOG

NCT03128034, P.I. Dr. Brenda Sandmaier, MD, started Oct, 2017 □ NCT04083183, P.I. Dr. Phuong Vo, MD, started June, 2020



# **NEW ASTATINE-211 CLINICAL TRIALS**

 Two <sup>211</sup>At-OKT10-B10 Phase I clinical trials for the treatment of multiple myeloma

# NCT04579523

- ✓ P.I.: Dr. Sherilyn Tuazon
- ✓ Estimated enrollment: 30 patients
- ✓ Starting August 2021

# NCT04466475

- ✓ P.I.: Dr. Damian Green
- ✓ Estimated enrollment: 25 patients
- ✓ Starting September 2021



# THANK YOU FOR YOUR ATTENTION

Symposium on Advancements in the Chemistry of Targeted Alpha Therapy, Dec 17-18, 2021, Prince Waikiki

December 16 - 21, 2021 | Honolulu, Hawaii, USA & Virtual

# Pacifichem 2021: A Creative Vision for the Future





# **FACILITY OVERVIEW**

50MeV Cyclotron online in 1984 for Conformal Fast Neutron Therapy

- Facility grant specified Deuteron capability to replicate work at UW Nuclear Physics Lab
- PET Isotope Production Station Included as part of separate grant
- Facility Currently Supports:
  - Fast Neutron Therapy
  - Isotope Production <sup>211</sup>At, <sup>117m</sup>Sn, <sup>186</sup>Re, <sup>72</sup>Se/<sup>72</sup>As, <sup>155</sup>Tb, <sup>230</sup>U/<sup>226</sup>Th
  - Radiation Effects Testing Protons/Neutrons SpaceX, Amazon, Blue Origin, NASA
  - Proton Therapy Research FLASH, Mini-Beam, RBE Studies





# **ALPHA BEAM CHALLENGES**







# **ALPHA BEAM CHALLENGES**

### Beam Transport

**Increased Focusing** 





### Wire Loop Scanner

### Fiber Scanner





# **ASTATINE-211 TARGETRY - DEVELOPMENT**

### **Target Station Development**

- Automated ejection to shielded container/remote transport system
- Automated target loading from a magazine
- Works with a variety of target materials Melted, Packed Power, Foil, Electroplated
- Target Development
  - Withstand 100  $\mu A$  of 29 MeV  $\alpha$
  - Compatible with commercial remote retrieval system
  - Low cost, easy to manufacture
  - Target housing materials not to interfere with chemical processing
  - Minimize target housing activity for safe handling





# **ASTATINE-211 TARGETRY DEVELOPMENT- STATUS**

### Completed

- Test runs to a maximum of 16.5 μA on target, 6.75 μA/Hr, 5 mCi <sup>211</sup>At produced
- Successful testing of automated target loading system

To Do

- Perform chemical isolation of <sup>211</sup>At
- Finalize and test target ejection system
- Increase to maximum Alpha current ~ 50 μA
- Modify other isotope targets to fit new target station





# RUN SCHEDULE – CLINICAL TRIAL/130 mCi Astatine-211

1700 -1 – Configure Accelerator for 29 MeV alphas, prepare target station

0030-0115 - Bring Accelerator up, Tune Beam

0115-0700 – Target Bombardment

0700-1000 – <sup>211</sup>At Isolation

1000-1200 – <sup>211</sup>At labeling on BC8-B10

1200-1400 – Quality Control

1500-1700 - Infusion





# **ASTATINE-211 PRODUCTION RUN CHALLENGES**

### 7.2 Hour Half-life

# **Limited Staffing**





### **Eric Dorman**

- Isotope Operations Primary
- Target Design
  Bob Smith
- Target and Target Station Design/Manufacturing

### Marissa Kranz

- Target Design
- CFD Modeling

# **Dave Argento**

Nuclear Modeling

**Rob Emery** 

Support



# THANK YOU FOR YOUR ATTENTION





