

ASTATINE-211 PRODUCTION UPDATE FOR THE UNIVERSITY OF WASHINGTON

2020 DOE IP ASTATINE-211 USER MEETING

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7/28/2020

DOE FUNDING

UW Medical Cyclotron Facility under DOE Isotope Program stewardship

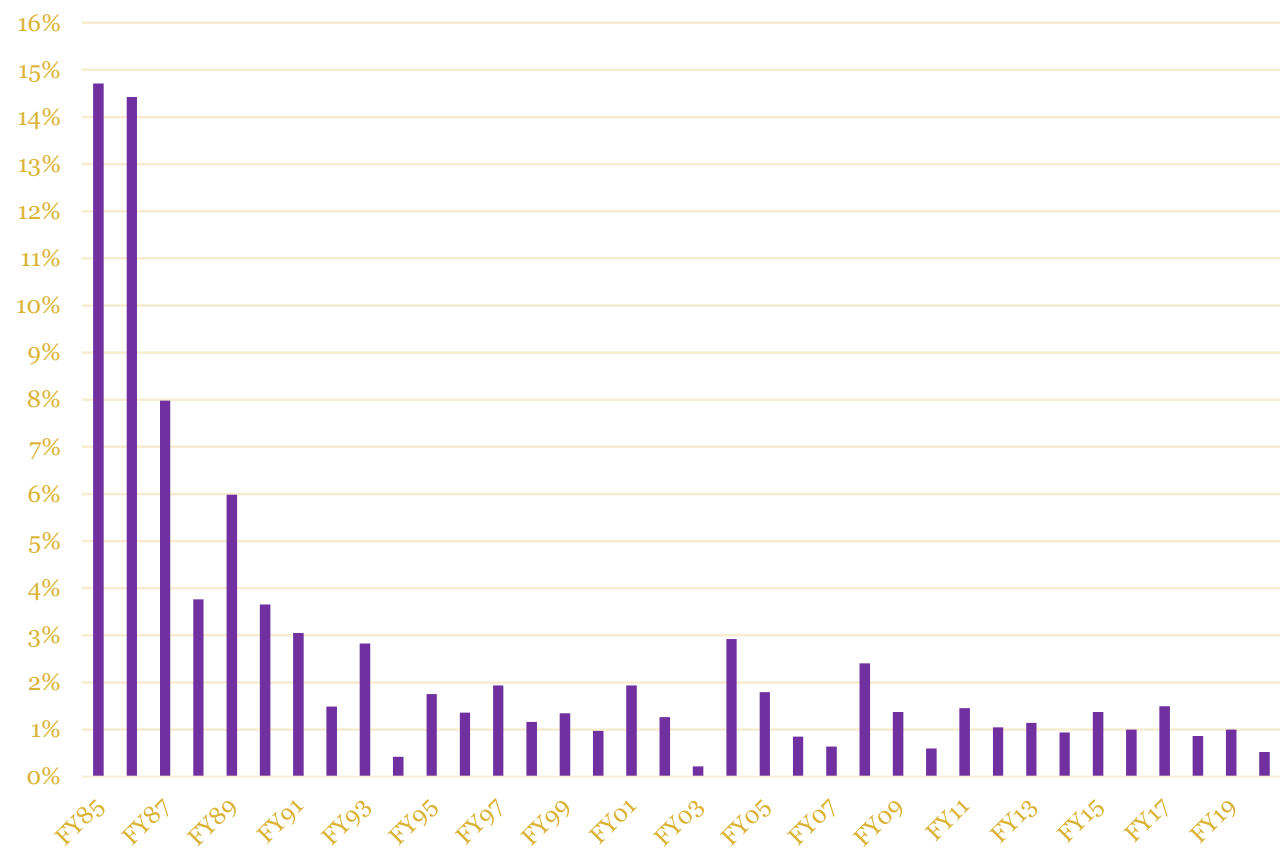
- DOE base funding partially supporting cyclotron operations
- Radionuclide production under DOE guidance

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

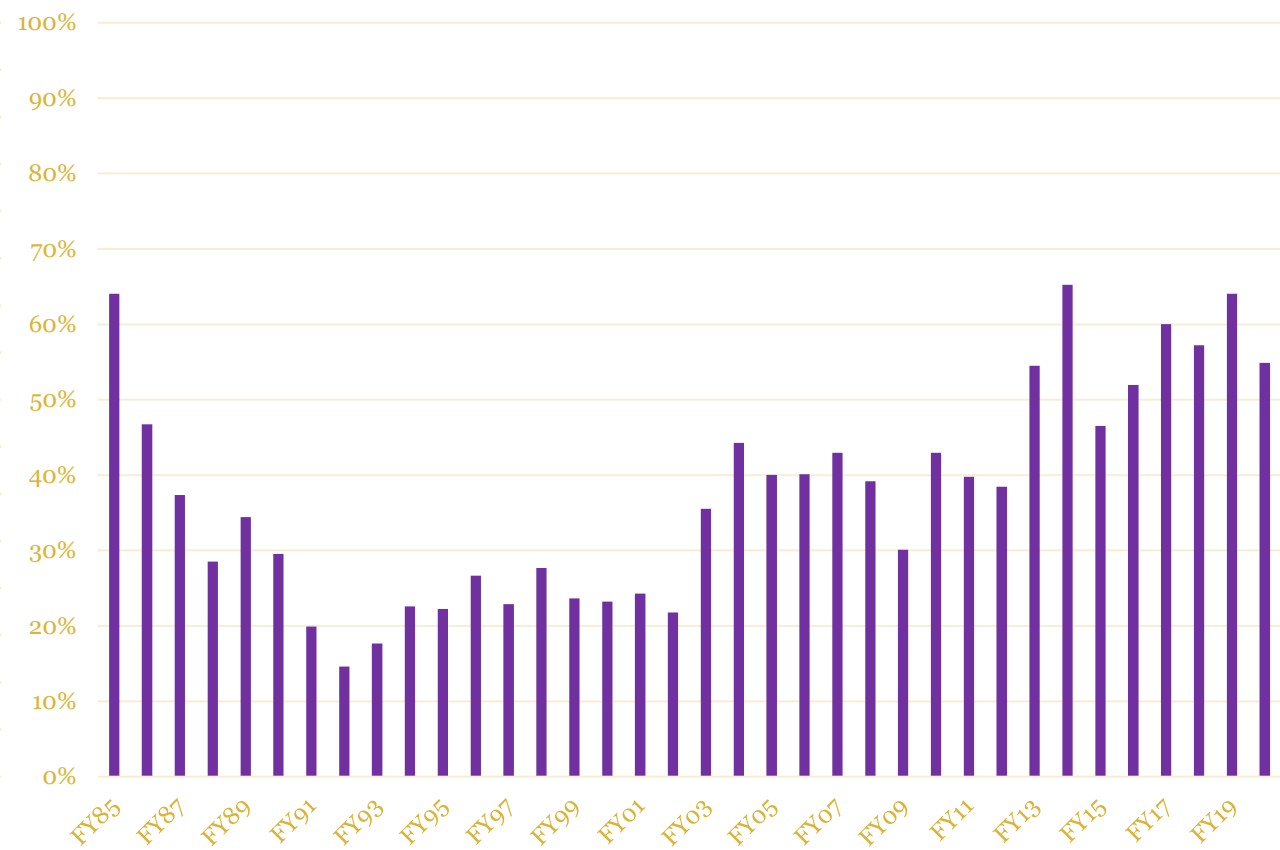
- Currently providing At-211 through NIDC; supported by equipment and base funding (started June 2015)
- Developing other radionuclide production through R&D Funding
- Will provide other radionuclides when production routes are achieved, and facilities are adequate for high levels of activity

UW MEDICAL CYCLOTRON FACILITY - CAPACITY

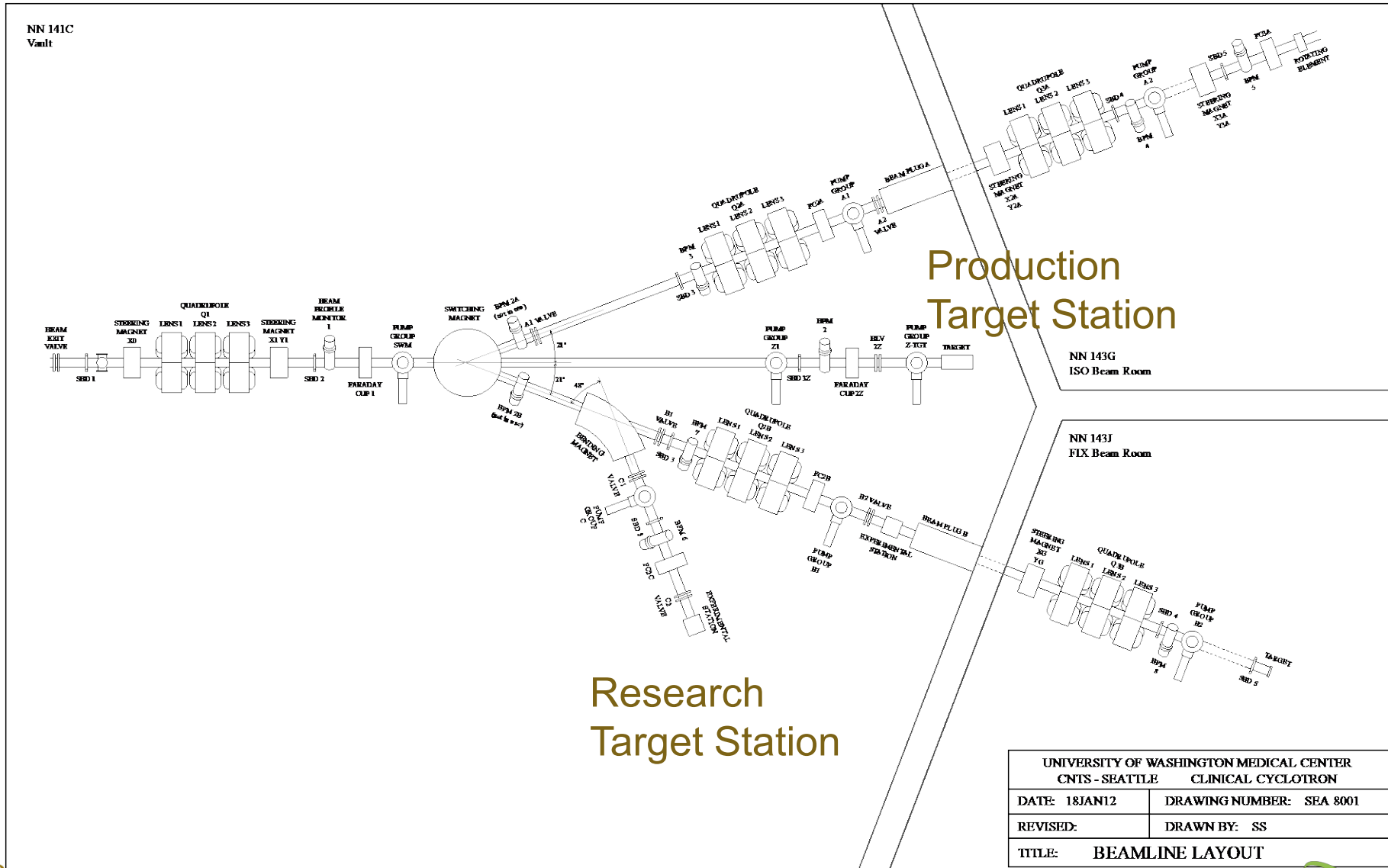
Unscheduled Downtime
(Based on 208 days/yr, 10 hrs/day)



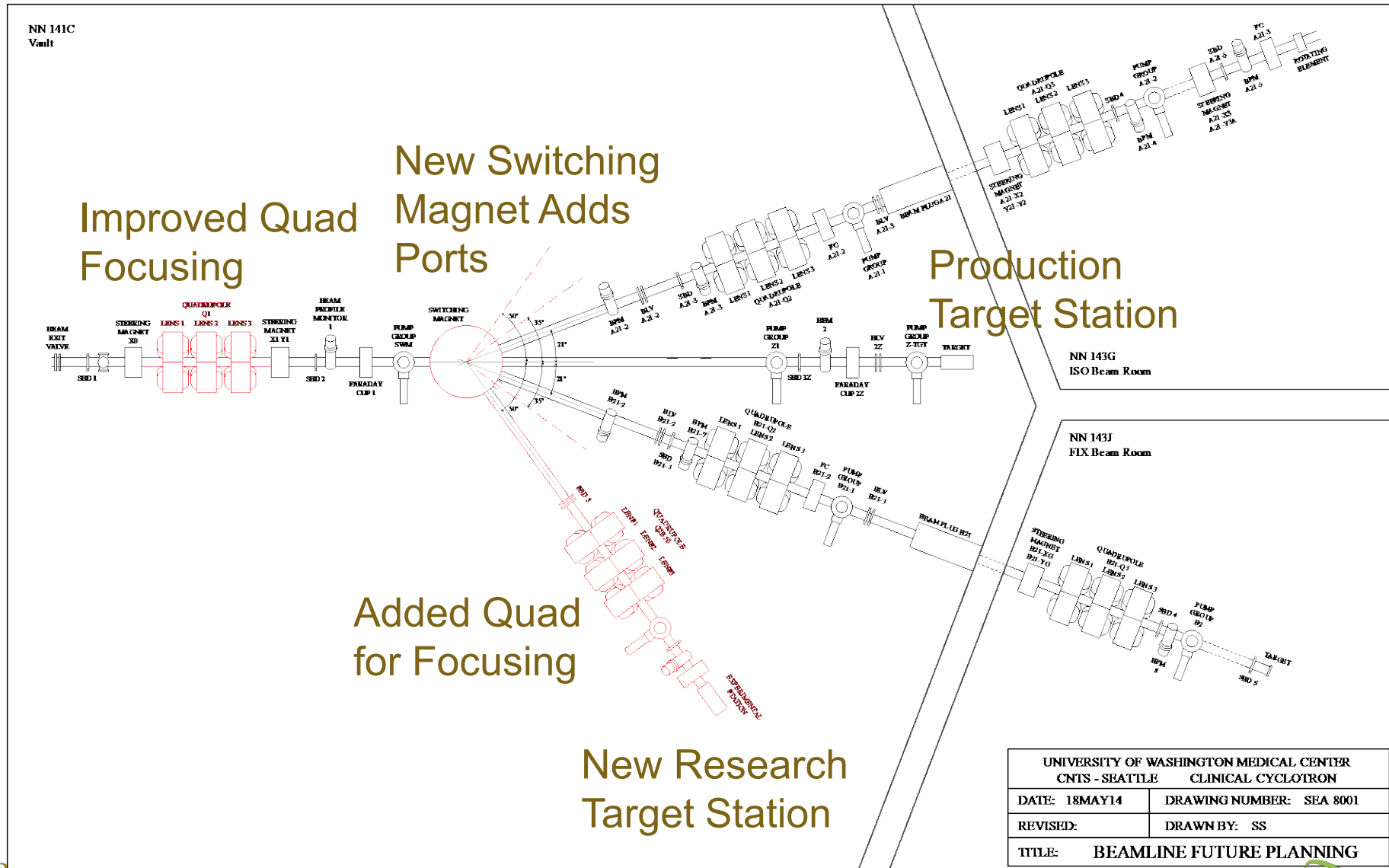
Available Capacity
(Based on 208 days/yr, 10 hrs/day)



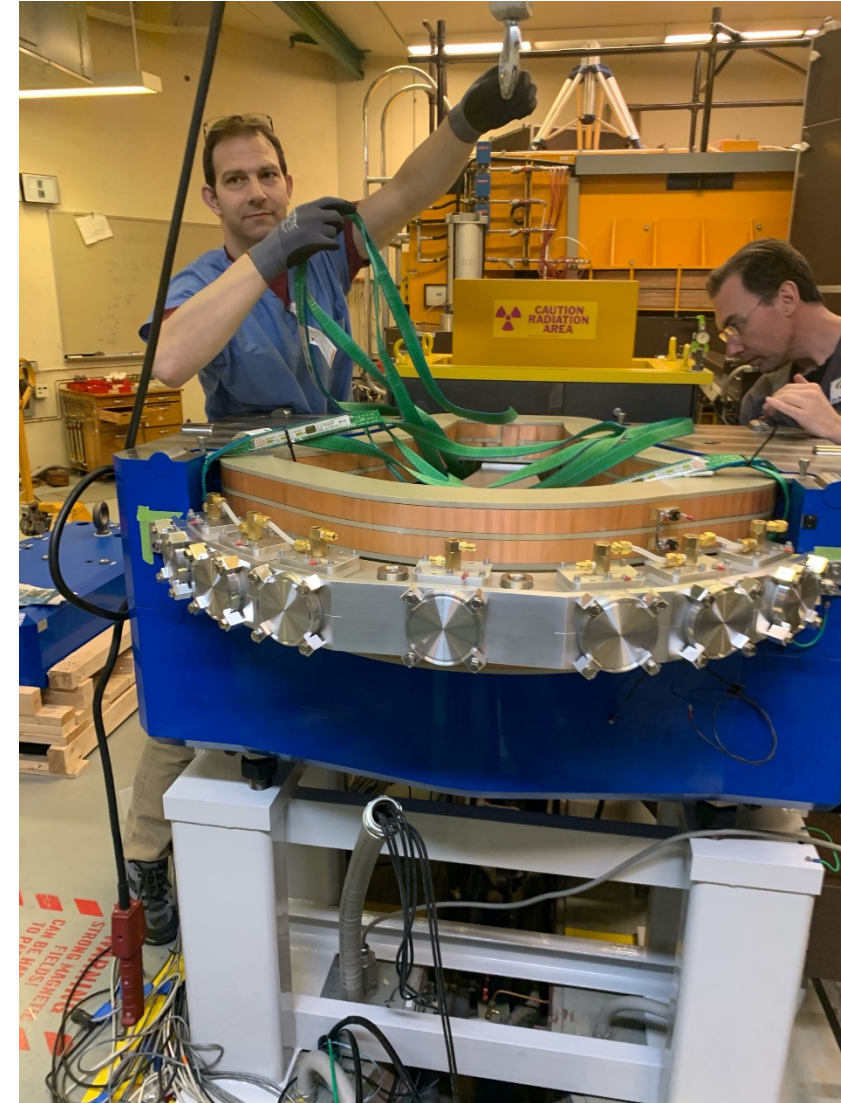
UW MEDICAL CYCLOTRON FACILITY – FACILITY UPGRADE



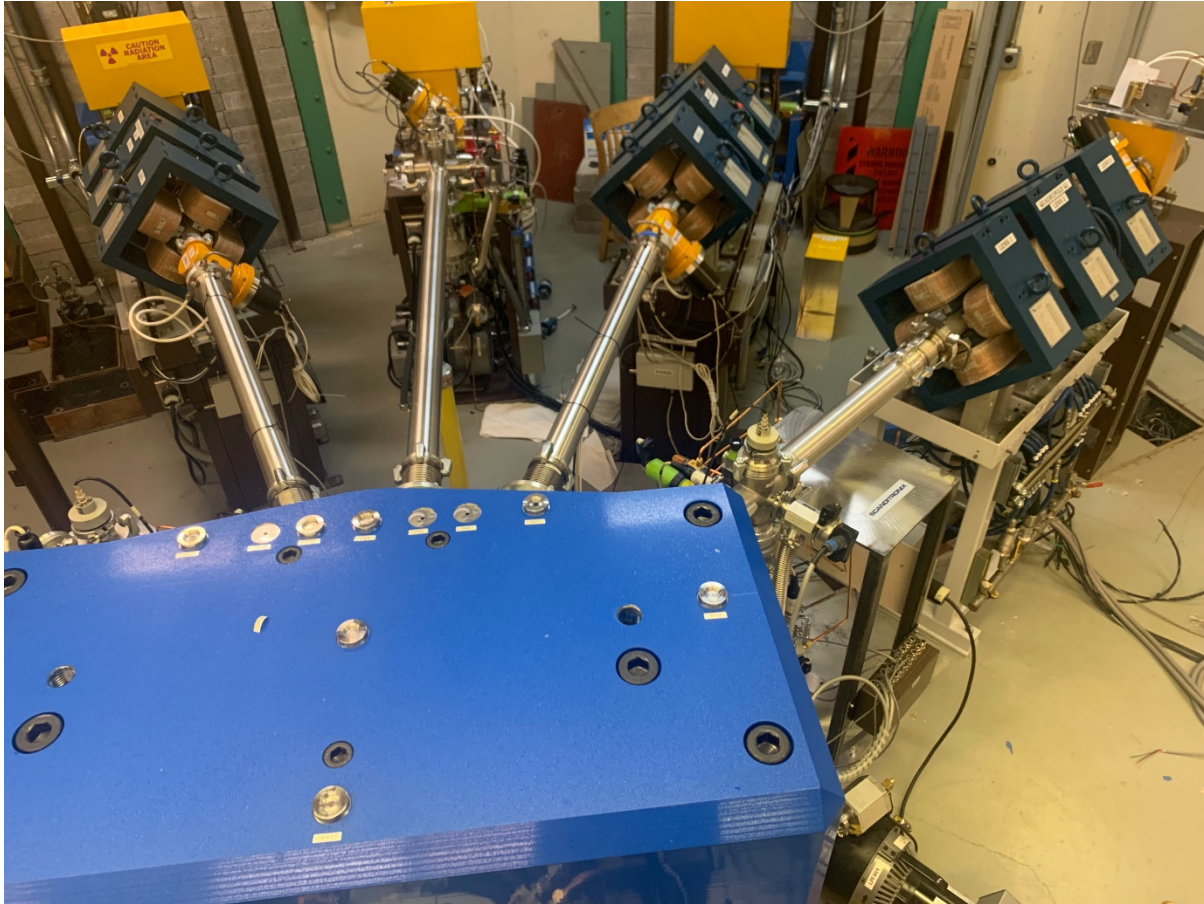
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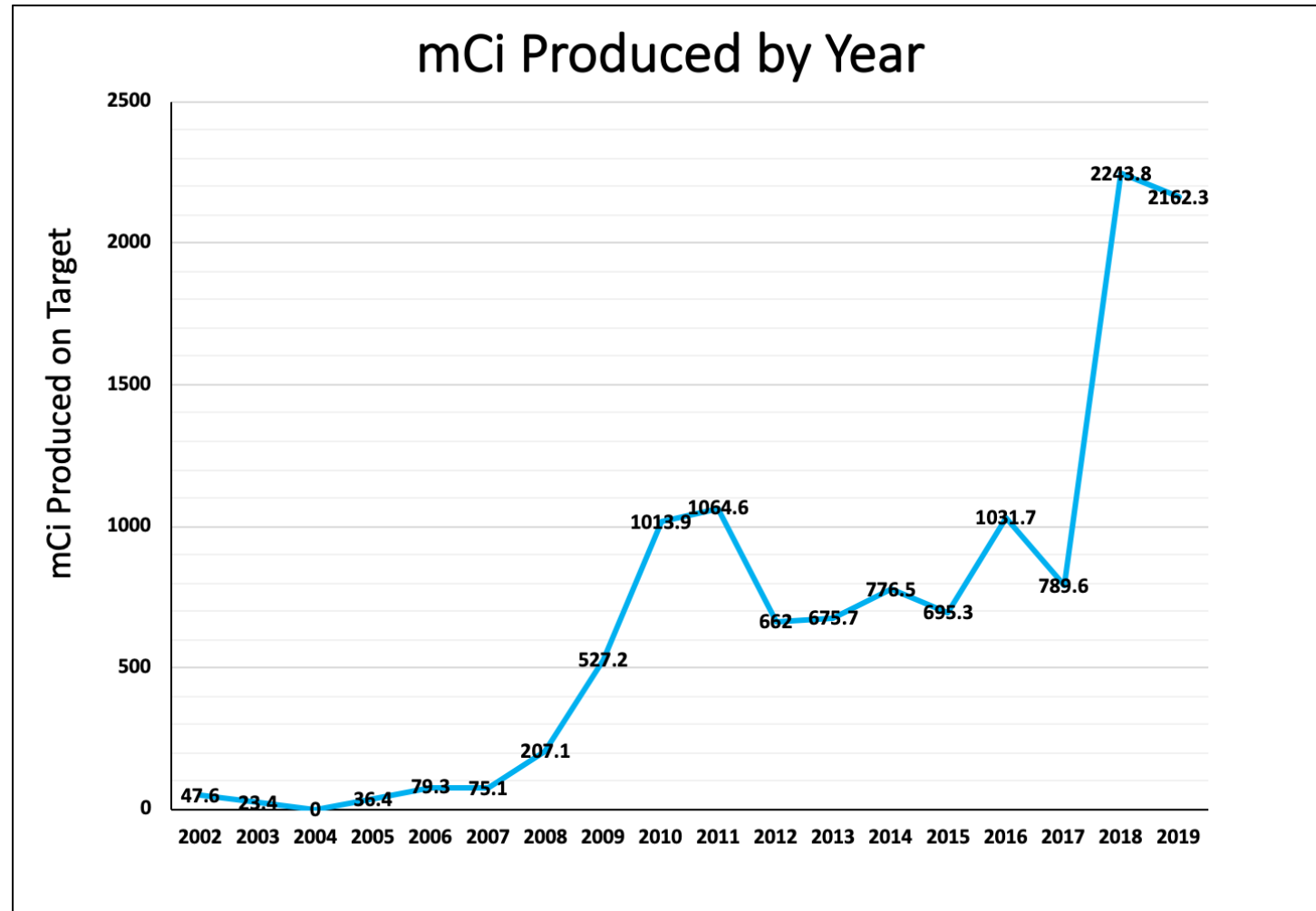
UW MEDICAL CYCLOTRON FACILITY – FACILITY UPGRADE



OVERVIEW OF ASTATINE-211 PRODUCTION AND RESEARCH ACTIVITIES

YEARLY ASTATINE-211 PRODUCTION

- Production for NIDC, preclinical and clinical research
- Automation of isolation
- Blood-borne diseases
- Targeting T-cells harboring latent HIV virus
- Gene therapy with HCT



457.6 mCi produced Jan-Jun, 2020

ASTATINE-211 PRODUCED FOR CLINICAL TRIALS

- Two ^{211}At -BC8-B10 Phase I/II clinical trials on-going
 - NCT03128034, P.I. Dr. Brenda Sandmaier, MD, started Oct, 2017
 - NCT04083183, P.I. Dr. Phuong Vo, MD, started June, 2020
- Have treated a total of 26 patients
- Produced 3.213 Ci for patient treatment
- Applying IND for ^{211}At -labeled anti-CD38 MAb for multiple myeloma treatment

FUNDED PRECLINICAL RESEARCH USING ASTATINE-211

A. Automation of ^{211}At Isolation

1. Dr. Yawen Li (UW), DOE (DE-SC0013618)

Production, Quality Control and Shipment of Radionuclides from the University of Washington

B. Treatment of Blood-Borne Cancers with ^{211}At -labeled MAbs and HCT

2. Dr. Damian Green (Fred Hutch), NIH (R01CA076287)

Pretargeted Radioimmunotherapy of CD20+ Lymphomas

3. Dr. Roland Walter (Fred Hutch), NIH (R37 CA240832)

Novel Approaches to CD33-Directed Radioimmunotherapy

4. Dr. Johnnie Orozco (Fred Hutch), NIH (R37 CA252070)

Combining Targeted RIT and Synergistic Novel Agents to Eradicate AML

5. Dr. Damian Green (Fred Hutch), NIH (R01CA205248)

Anti-CD38 targeted alpha-emitter radioimmunotherapy to eliminate multiple myeloma

6. Dr. Roland Walter (Fred Hutch), ASH (0001002414)

Development of Alpha-Emitting Anti-CD123 Radioimmunotherapy for Cancer (Stem) Cell-Directed Treatment of Acute Leukemias and Other Hematologic Malignancies

FUNDED PRECLINICAL RESEARCH USING ASTATINE-211 (CONT'D)

C. Treatment of HIV Infected Cells

7. Dr. Brenda Sandmaier (Fred Hutch), NIH (R33AI116225)

Alpha Emitter Labeled Anti-T-Cell Antibody: Targeting Latent HIV Infected Cells

8. Dr. Seth Pincus/Dr. Robert Harrington (U. Mont./Fred Hutch/UW), NIH (1R01AI136758)

Cytotoxic immunoconjugates to deplete persistent HIV reservoirs

D. Gene Therapy with HCT

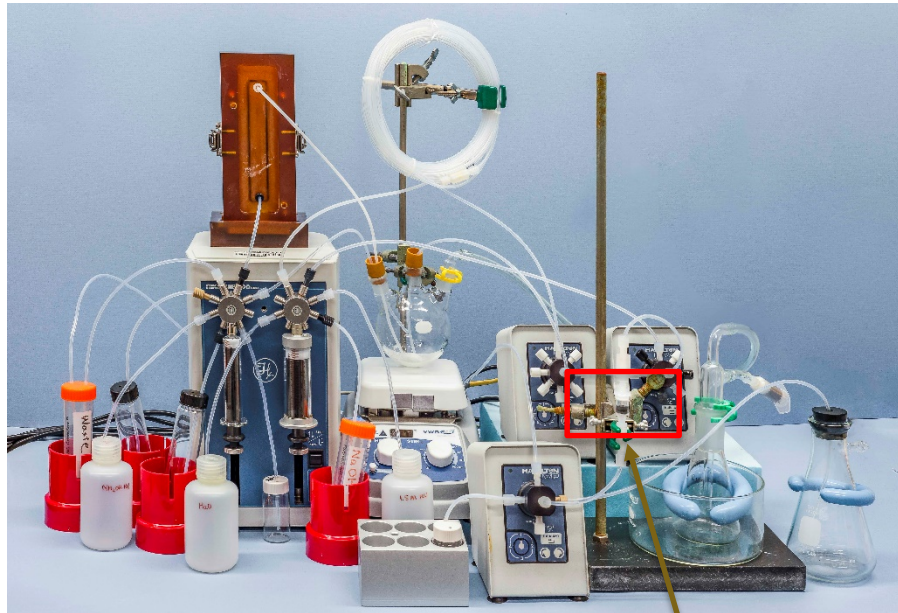
9. Dr. Rainer Storb (Fred Hutch), NIH/NHLB (P01HL122173)

Cell and Gene Therapy for Nonmalignant Blood Disorders

10. Dr. Roland Walter/Dr. Hans-Peter Kiem (Fred Hutch), NIH/NHLB (R01 HL151765)

Development of ²¹¹Astatine-Conjugated Anti-CD45 Antibody-Based Conditioning for Hematopoietic Stem Cell Gene Therapy and Editing

TELLURIUM-PACKED COLUMN METHOD



Te column

- 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
- Process takes ~1.5 h
- Final product in ~1 mL NaOH
- Process still needs to be optimized
- Decay and attenuation corrected isolation yields: >95%
- Non-decay corrected yield: ~90%

QUESTIONS?

