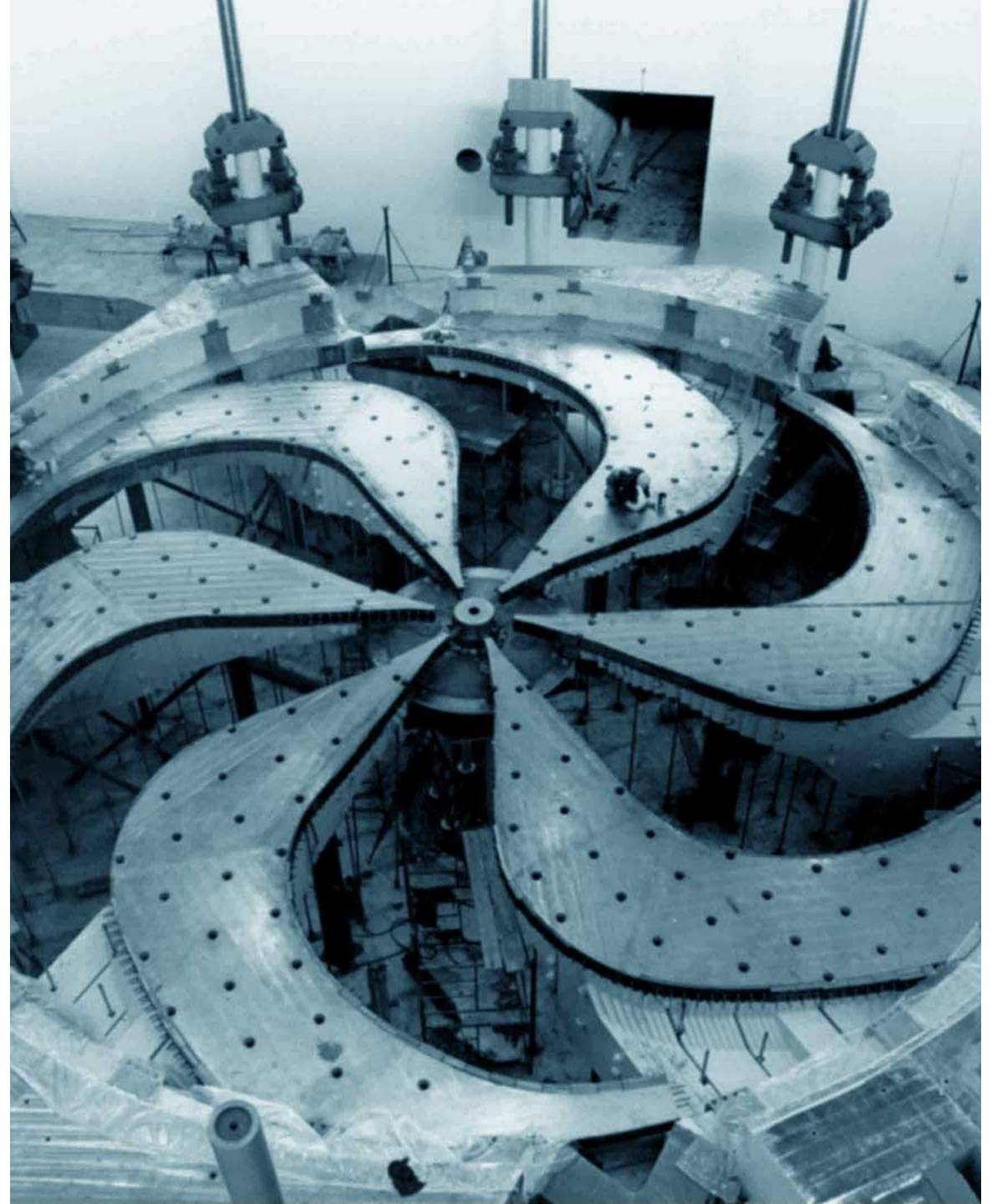


Five year plan within the 20-year vision – Town Hall Life Sciences Division

July 22nd, 2022
Paul Schaffer, PhD
Director, Life Sciences

2022-07-22



Today's presentation:

The Basics: LS Vision, Mission; The Team; Our Pillars

Research Summary

Current Priorities

Future Ambitions, Upcoming Priorities

Life Sciences Vision and Mission Statements

Vision Statement:

The Life Sciences Division will place TRIUMF as a global leader in the **application of accelerator research toward the life sciences** in a manner that derives maximum societal and economic benefit.

Mission Statement:

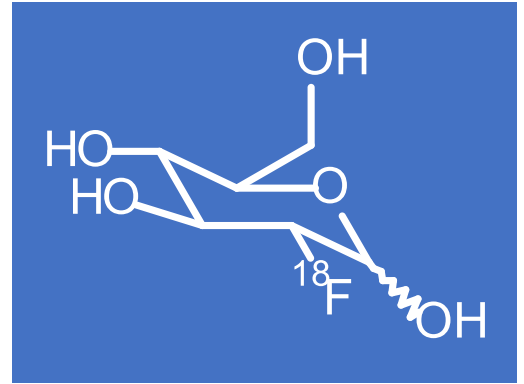
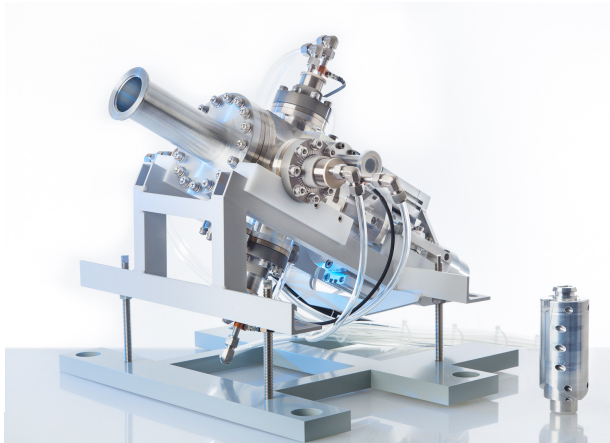
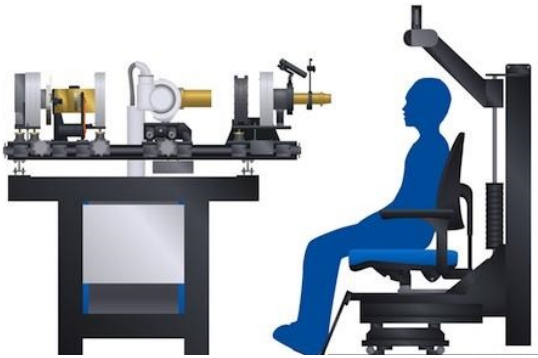
The Life Sciences Division at TRIUMF will innovate **new accelerator technologies, isotopes and radiopharmaceuticals to better health, understand life and better the environment**. The Division will leverage its core expertise to lead in our community as an interdisciplinary centre of excellence that enables ourselves, and our partners, with world-class people and state-of-the-art facilities.

Life Sciences at TRIUMF

Applied Ion Beams

Nuclear Chemistry

Applied Isotopes



TRIUMF Life Sciences focuses on advancing accelerator-based technology for the development of isotopes that can improve life

Life Sciences BAEs at TRIUMF

Applied Ion Beams



Monika
Stachura



Cornelia
Hoehr

Nuclear Chemistry



Valery
Radchenko



Paul
Schaffer

Applied Isotopes



Hua
Yang



Caterina
Ramogida
(joint SFU)

Research within TRIUMF Life Sciences focuses on advancing accelerator-based technology for the development of ion beams and isotopes that can improve life

Current Life Sciences Priorities

- 1) Build IAMI
- 2) Implement GMP capabilities – complete validation master plan
- 3) Grow/Enable Therapeutic Isotope Program
- 4) Deliver on our commitments (to our researchers and our partners)

These priorities are set via internal reviews, coupled with external peer evaluation (LSPEC)

Align with TRIUMF's goals within:

- Science and Technology
 - Make ground-breaking discoveries across our multidisciplinary research portfolio
 - Strengthen our position as a world-leading particle accelerator centre
- People and Skills
 - Become a hub for interdisciplinary education and training
 - Inspire Canadians to discover and innovate
- Innovation and Collaboration
 - Translate science and technology into innovation
 - Drive national and international collaboration in research, technology and innovation

Research Summary

Bio- β NMR at TRIUMF

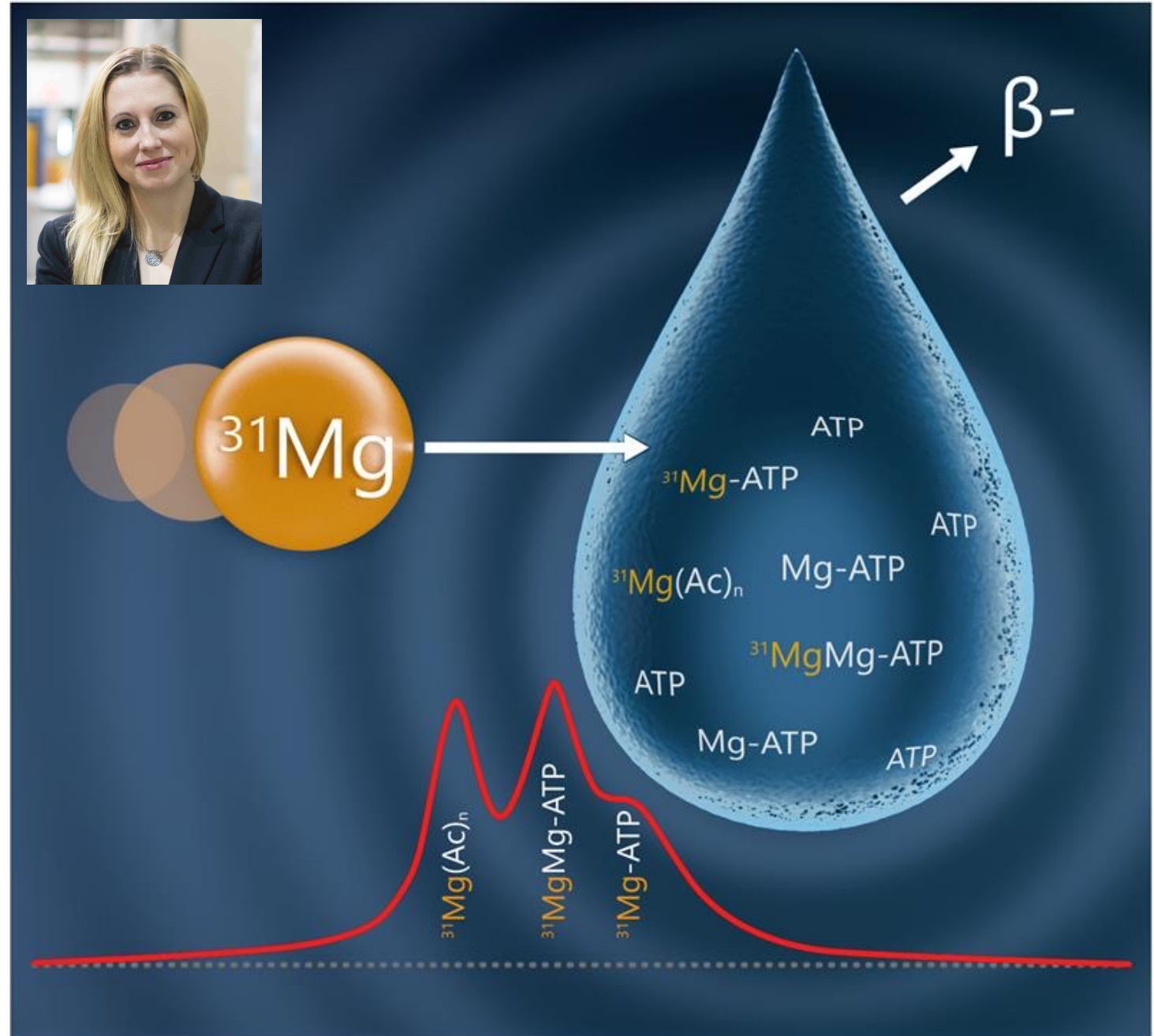


Current interests:

- $^{31}\text{Mg} + ^8\text{Li}$ (routine)
- $^{58/74}\text{Cu}$ (under development)
- $^{226,230}\text{Ac}$ (under development)

Attributes:

- Unique, high-impact science;
- International collaboration;
- Private sector interest;
- Threats: beam availability





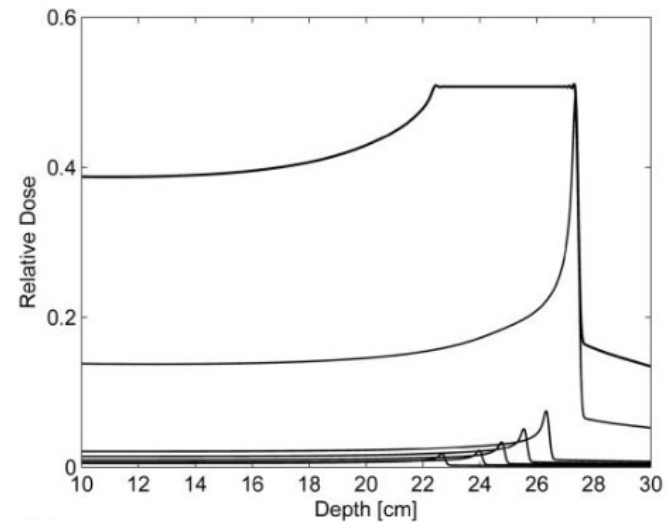
Proton (and photon) FLASH at TRIUMF

Current status:

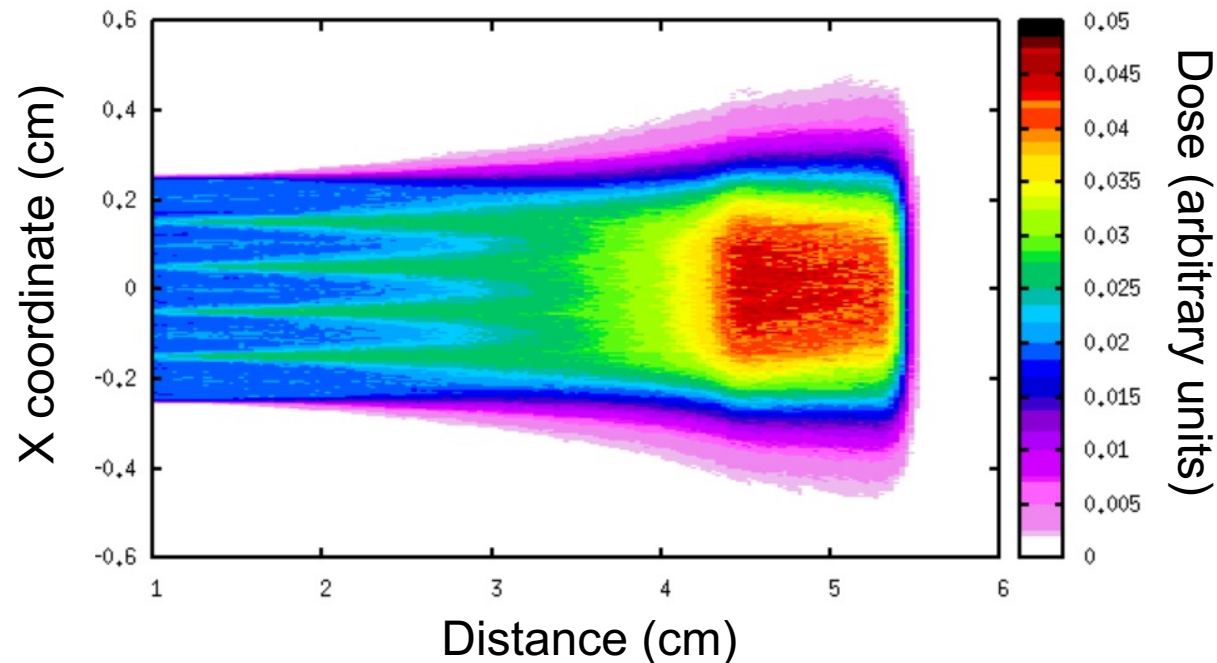
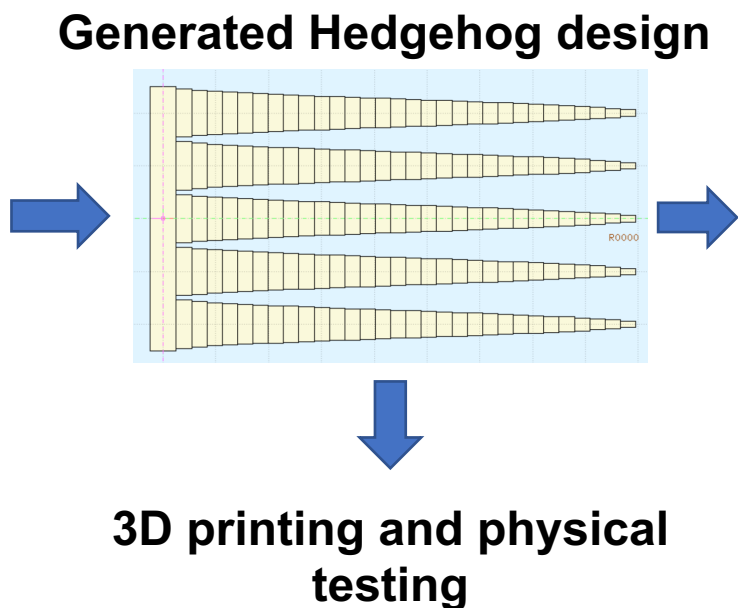
- Grant funding used to install prototype hardware; collect feasibility data

Attributes:

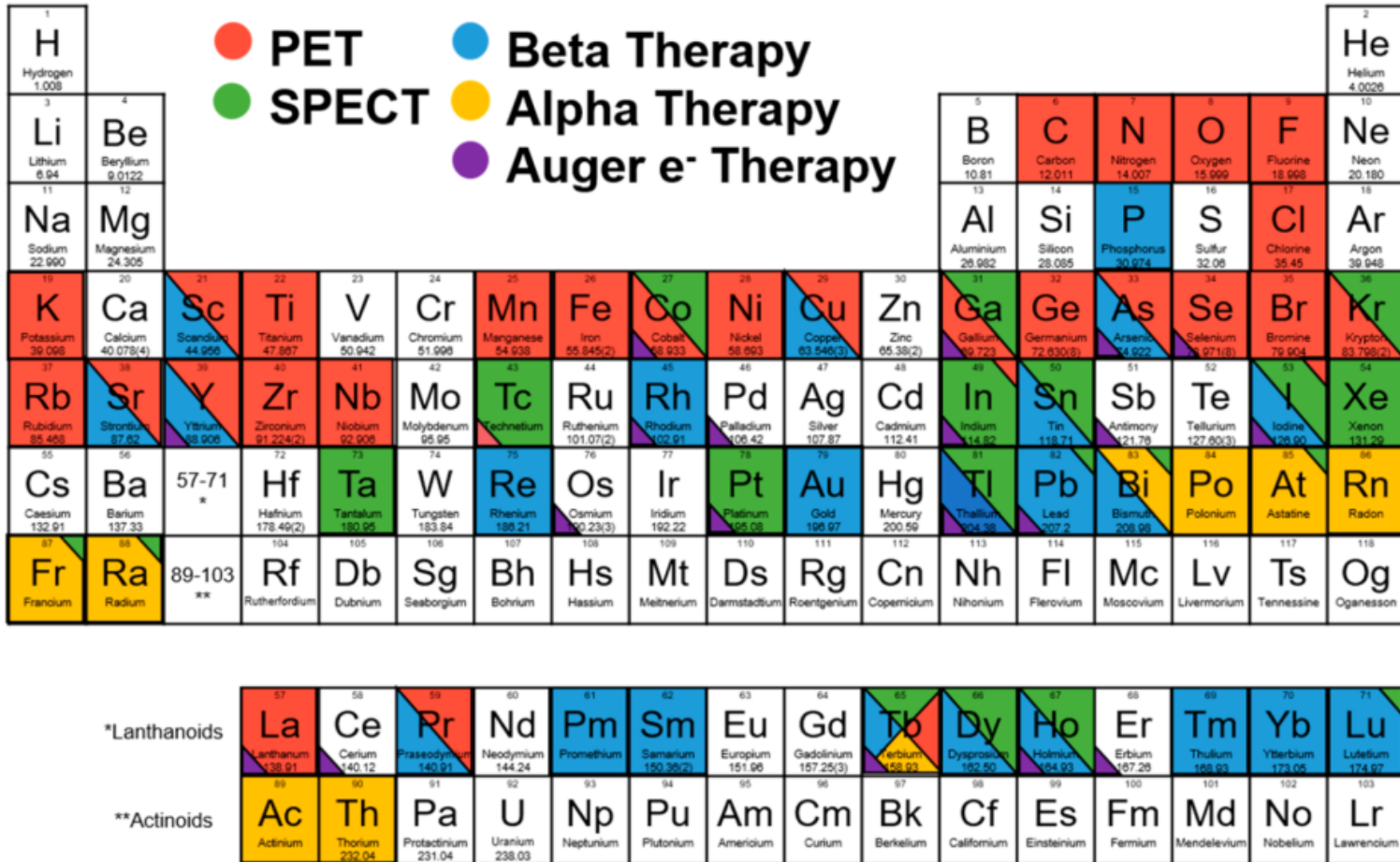
- Builds on decades of PT experience at TRIUMF;
- Threats: need for program/infrastructure investment



Desired
SOBP
parameters



Medical Isotopes: Metals offer many options



TR13 MeV

- Legacy machine operating at ideal energy for many isotopes

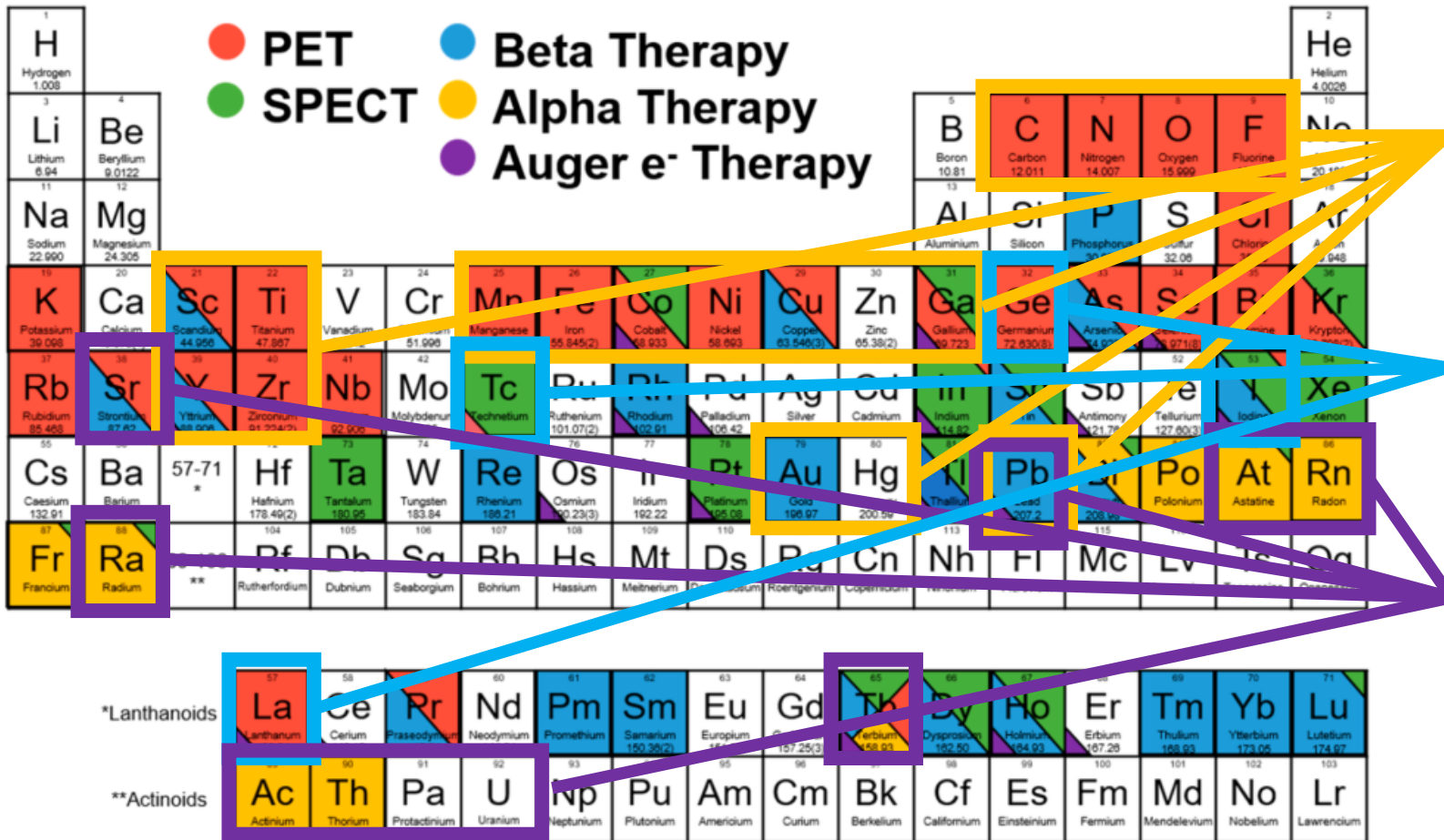
24 MeV

- Modern, high-intensity machine that expands on TRIUMF's isotope repertoire

520 MeV

- Globally unique machine that provides access to equally unique isotopes, applications

Medical Isotopes: Metals offer many options



TR13 MeV

- Legacy machine operating at ideal energy for many isotopes

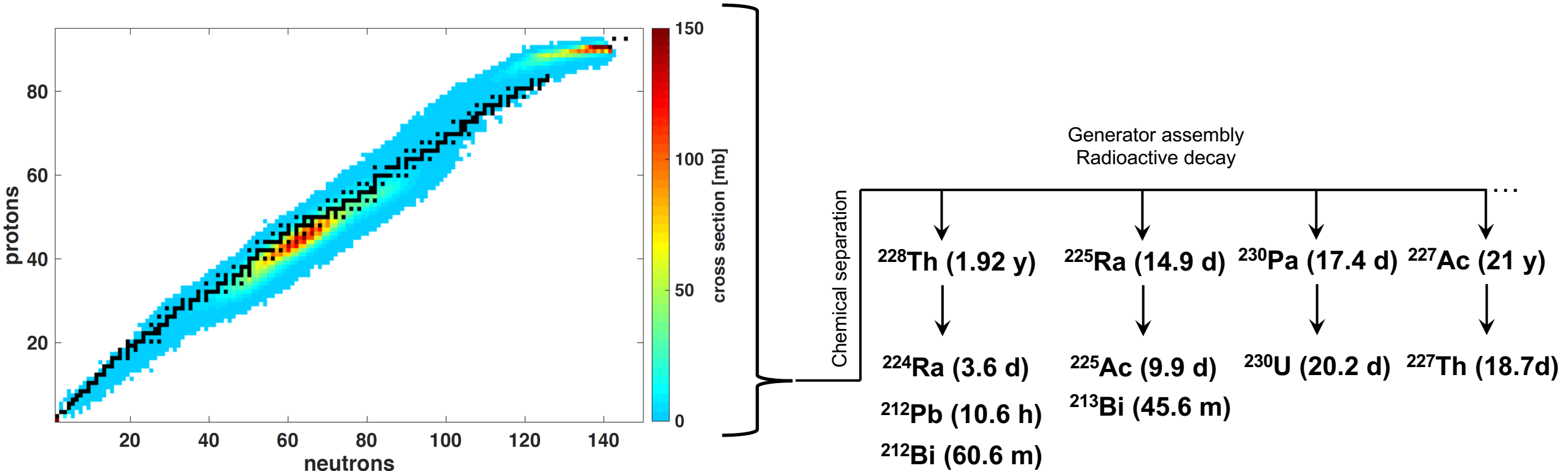
24 MeV

- Modern, high-intensity machine that expands on TRIUMF's isotope repertoire

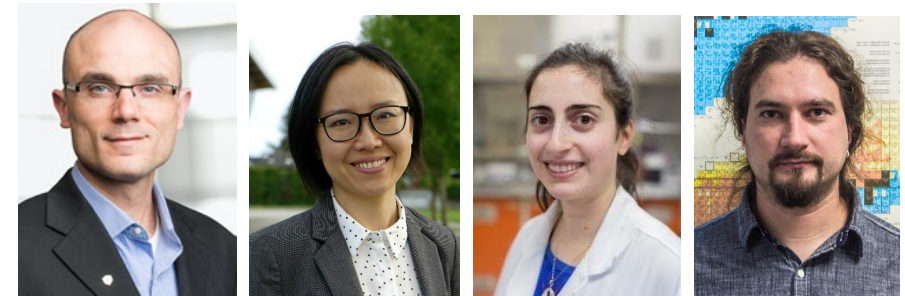
520 MeV

- Globally unique machine that provides access to equally unique isotopes, applications

520 MeV Isotope Production

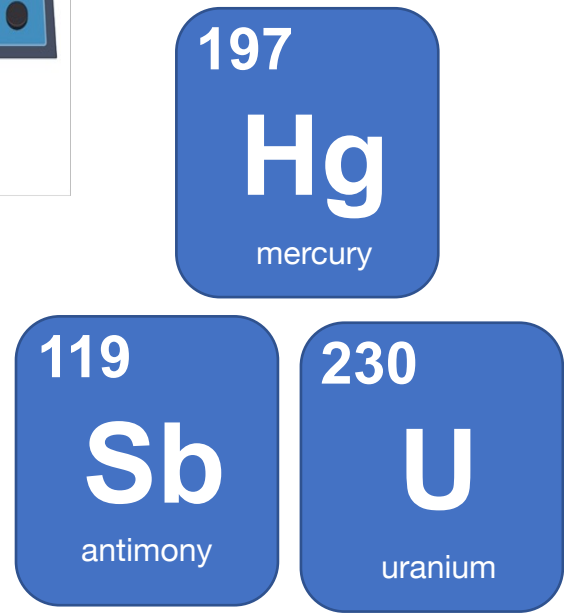
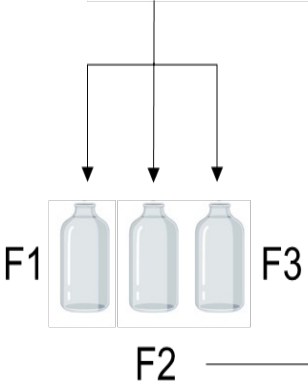
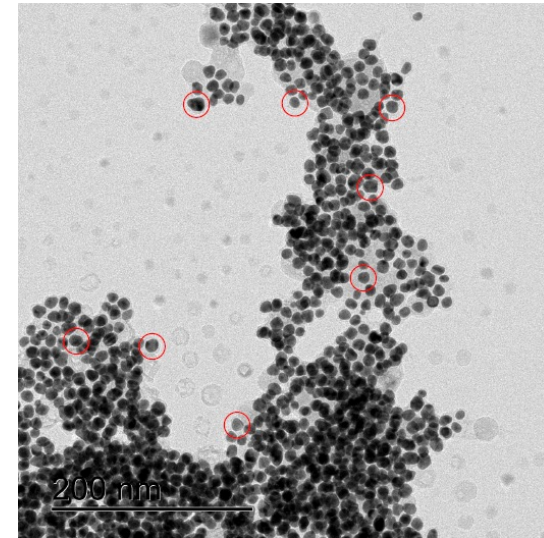
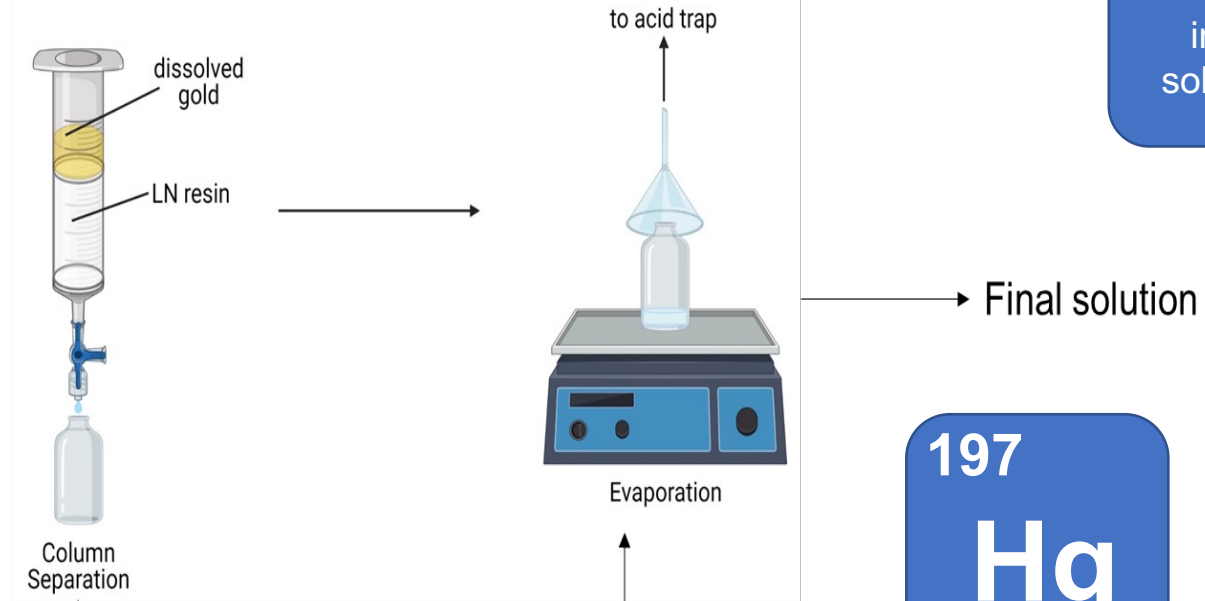
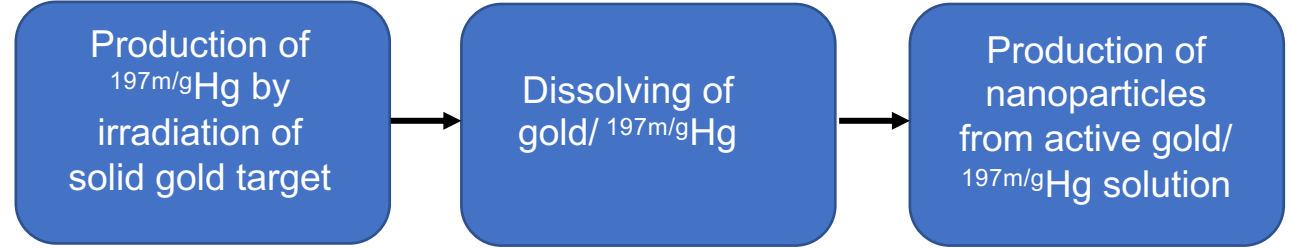


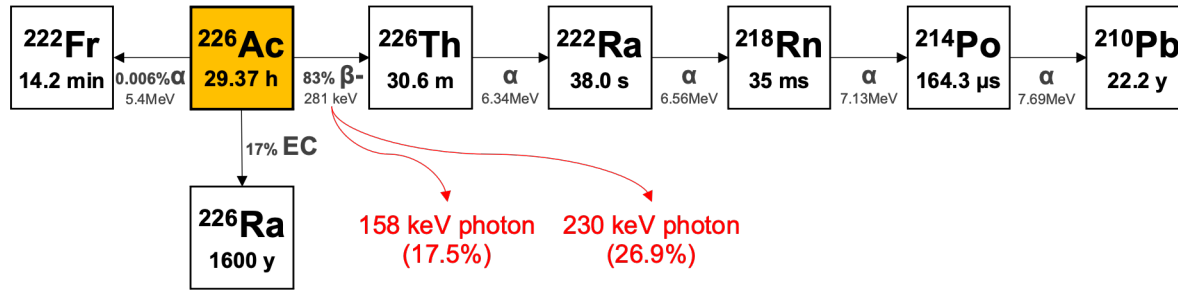
- High-energy proton-induced spallation provides a virtual treasure trove of isotopes
- Many isotopes produced have therapeutic/theragnostic potential
- Threat: significant potential waste burden



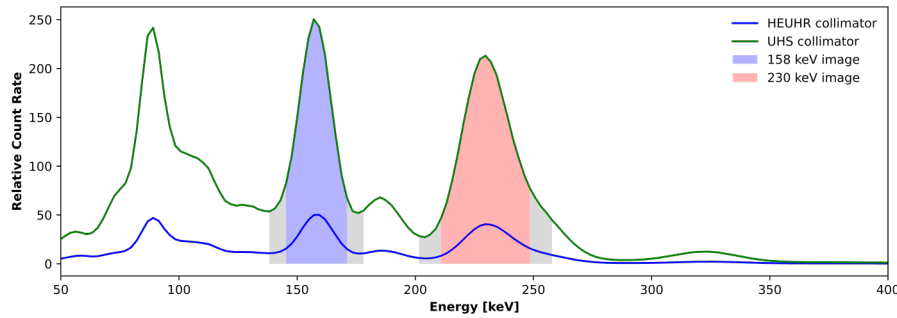
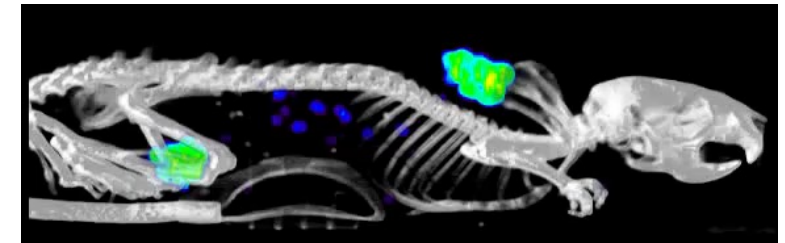


Radionuclide Therapy is not limited to alpha-, beta- emitters

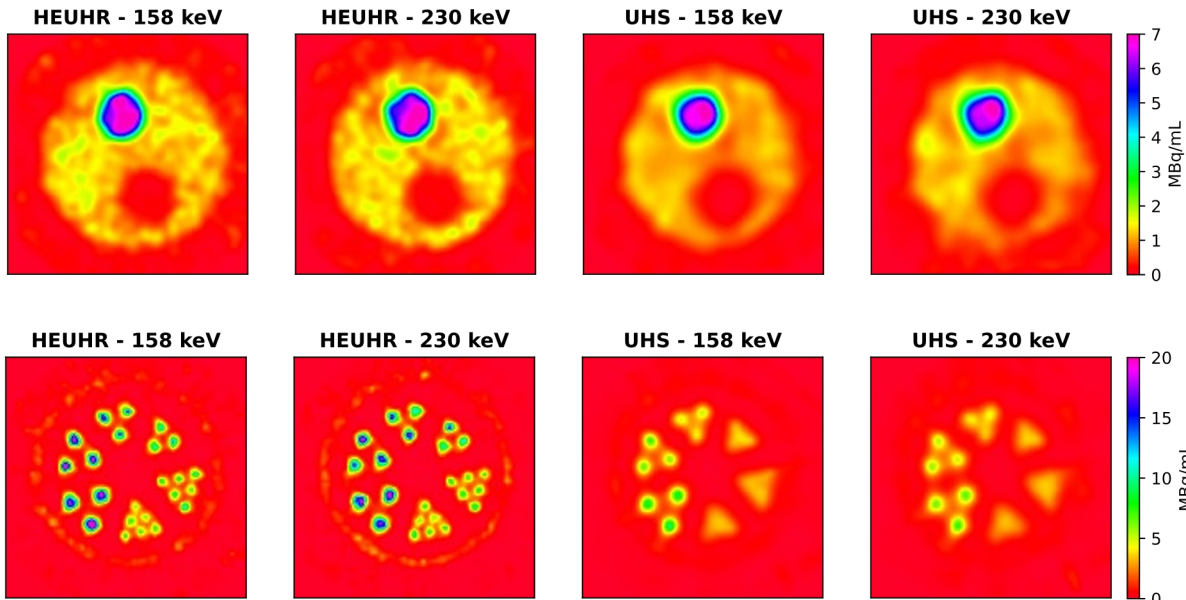
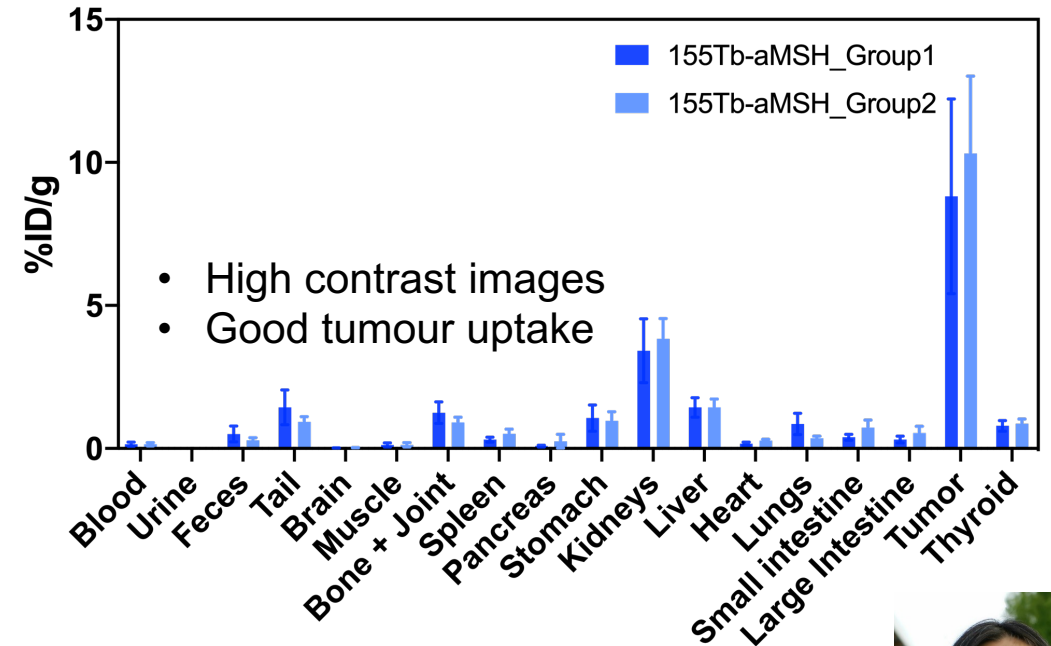




[¹⁵⁵Tb]Tb-crown-αMSH SPECT, 2h p.i.,



[¹⁵⁵Tb]Tb-crown-αMSH Biodistribution 2 h p.i.



UBC; BC Cancer tracer supply (O22, O93)

Status on Tracer deliveries:

- Deliveries of [^{11}C] tracers to UBC resumed in January 2021
- Pandemic continues to challenge demand
- TRIUMF has met production reliability targets that mutually agreed upon between TRIUMF and UBC
- BC Cancer no longer utilizing F-DOPA as a clinical tracer
 - Replaced with [^{68}Ga]DOTATOC

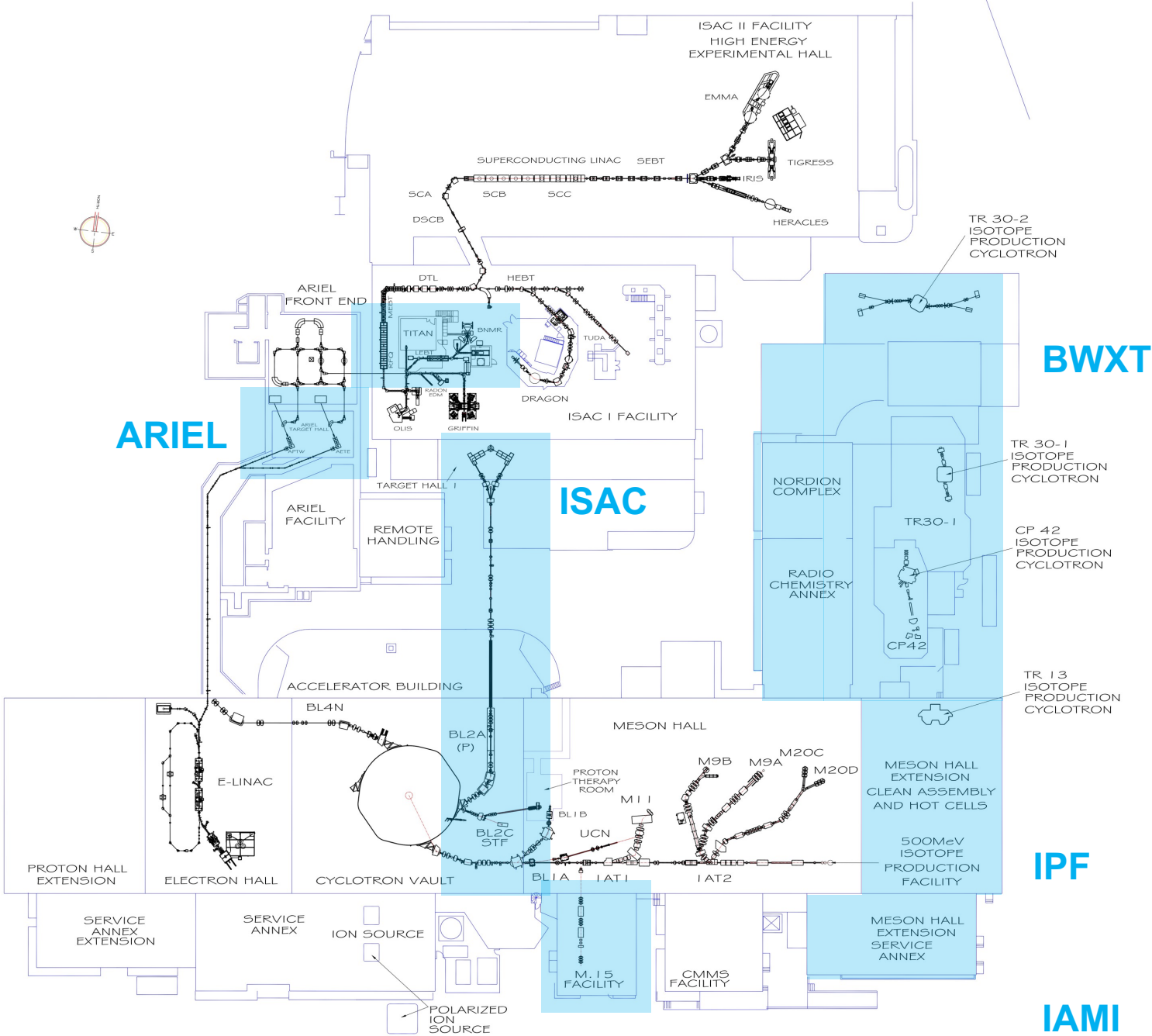


Status on advancing GMP compliance:

- 250 GMP documents released so far (over 60 documents have gone through multiple releases)
- All tracer production is now performed under GMP conditions
- Continuous improvements have been made on the implementation of GMP processes.
 - (61 Change Controls, 43 CAPAs have been filed and put into effect since 2021 Jan)
- New GMP Lab 007 coming online soon



Life Sciences at TRIUMF



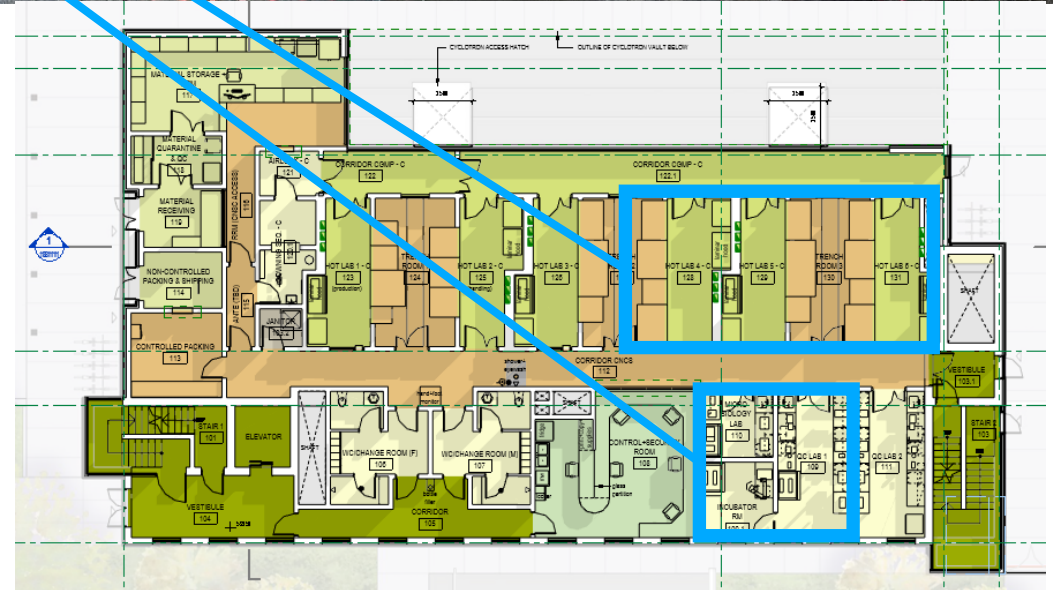
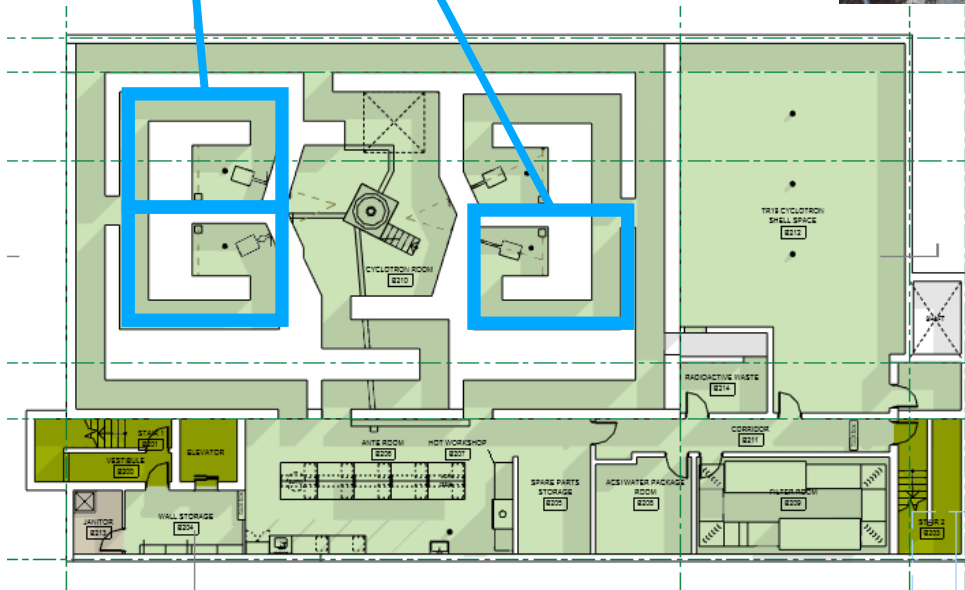
- Many applications derived from beams and isotopes obtained from 13 to 520 MeV machines
 - Isotope production
 - Radiochemistry
 - Proton Therapy
 - Bio-βNMR
- Other drivers: ARIEL, ISAC/ISOL
- Partnerships:
 - UBC: Science, Pharmacy, Medicine, Engineering
 - SFU: Science
 - BC Cancer
 - Fusion, BWXT

Current Priorities

IAMI (P442)



- includes P471, P550, P527
 - Transitioned to TRIUMF
 - Additional funding requests continue in discussion with provincial funding ministries for:
 - Additional lab equipment
 - Additional target capabilities
 - Office space



IAMI: Operations Model

Current proposal (pending full review, ratification by TRIUMF Board, Partners):

Operations and Governance will evolve through phases: Start-up through to Full Ops

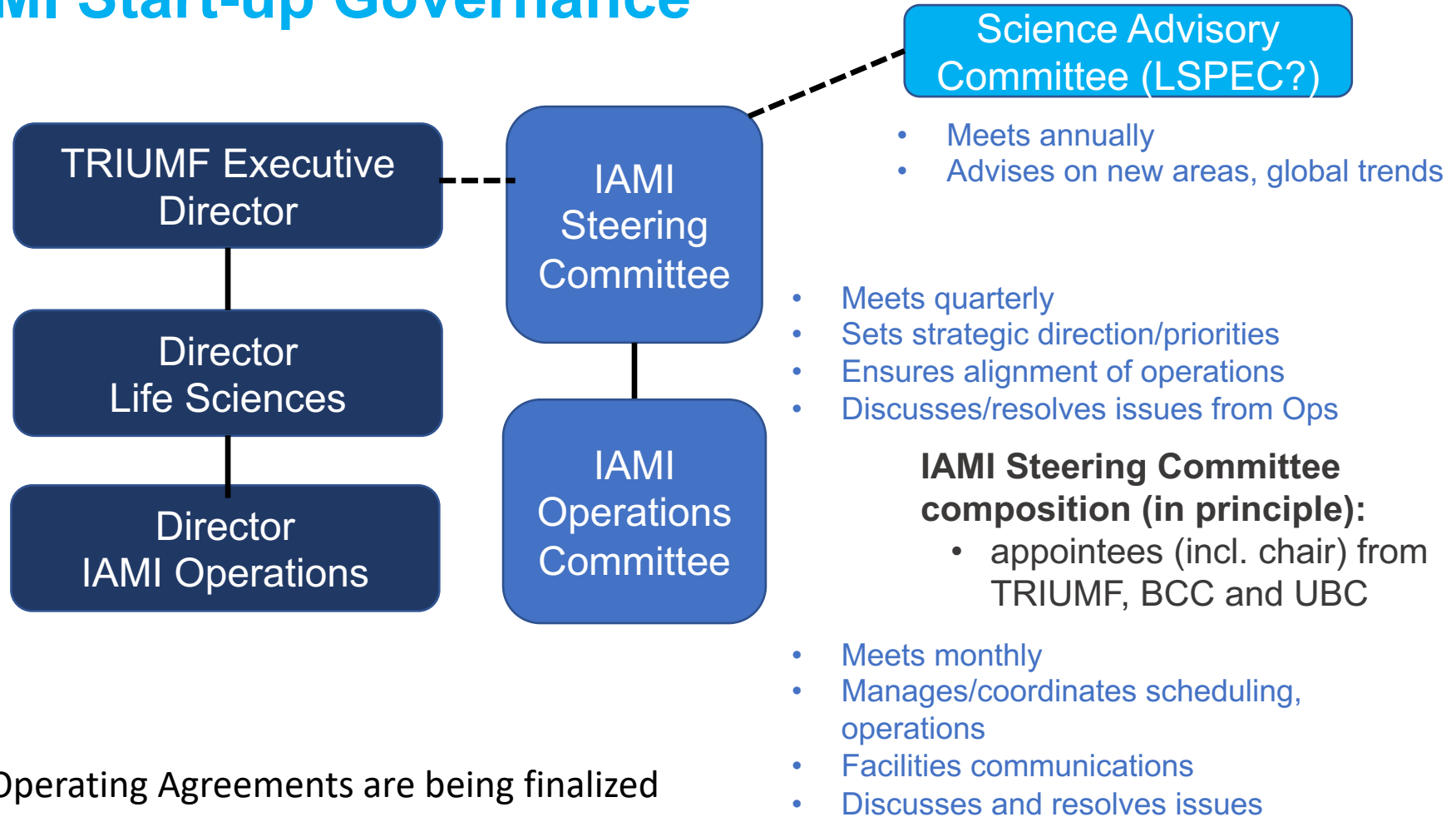
- **Start-up operations** occur in an integrated fashion within an existing, albeit modified Life Sciences organization. Operations supported by TRIUMF and partners;
- **Full operations** are initiated once IAMI crosses a legal, financial or administrative threshold that has yet to be determined

Governance will be achieved through a Steering Committee that will recommend resource allocation to meet IAMI program objectives, including balance between R&D and revenue-generating activities

Next steps:

- Ratification of Operating and Governance Models
- Finalization of Business Plan – collaborate with TRIUMF Innovations

Proposed IAMI Start-up Governance



Status:

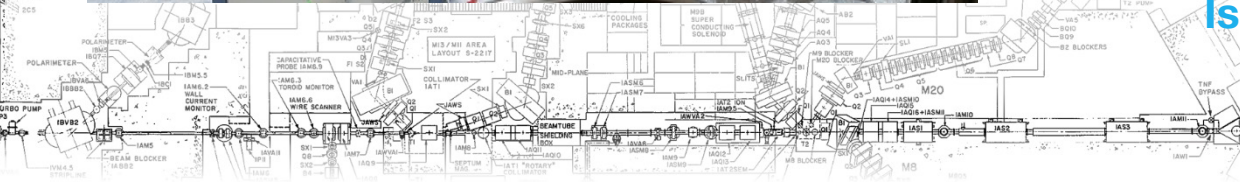
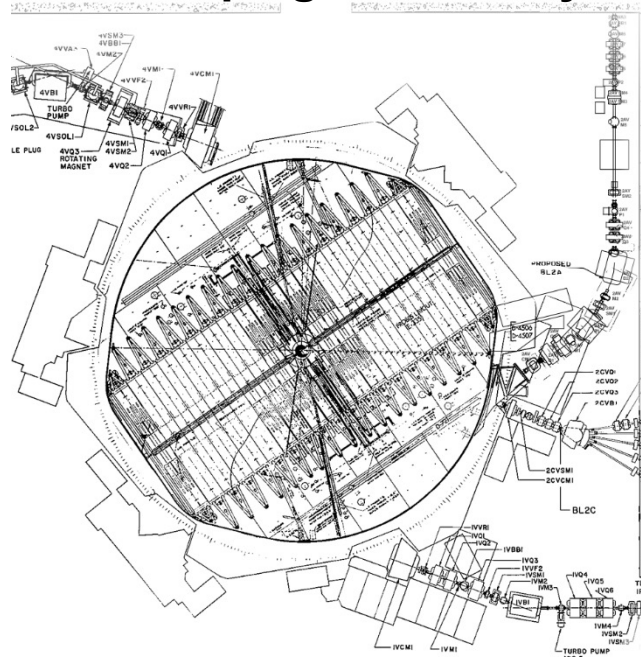
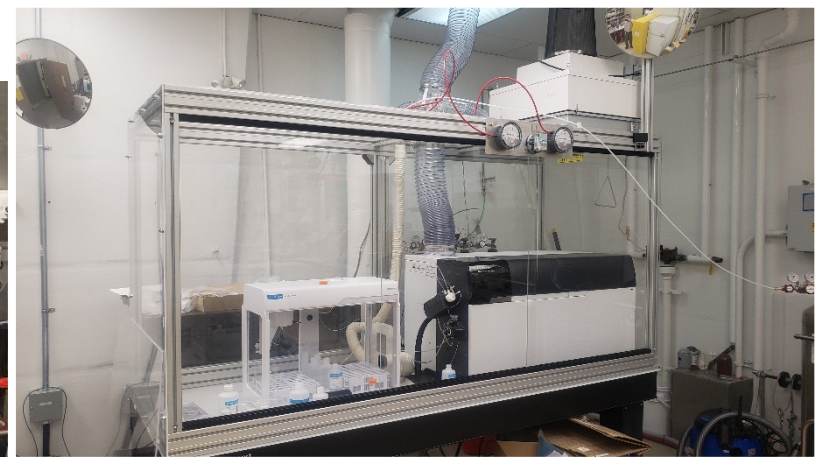
- 1) Phase 1 Lease and Operating Agreements are being finalized
- 2) LOU and LOI for expanded efforts are signed
- 3) Business and operating plans are being updated now that partner activities are becoming more well defined
- 4) Steering and Operating Committee Terms of References are being finalized
- 5) Services Agreement for expanded effort has been drafted and is under review
- 6) Sublease for expanded effort is being drafted

^{225}Ac Production at TRIUMF (P476)

Objective: demonstrate the safe, routine, larger-scale production and quality control of ^{225}Ac via high-energy proton irradiation of ^{232}Th on BL1A

Current Status: 2021 campaign:

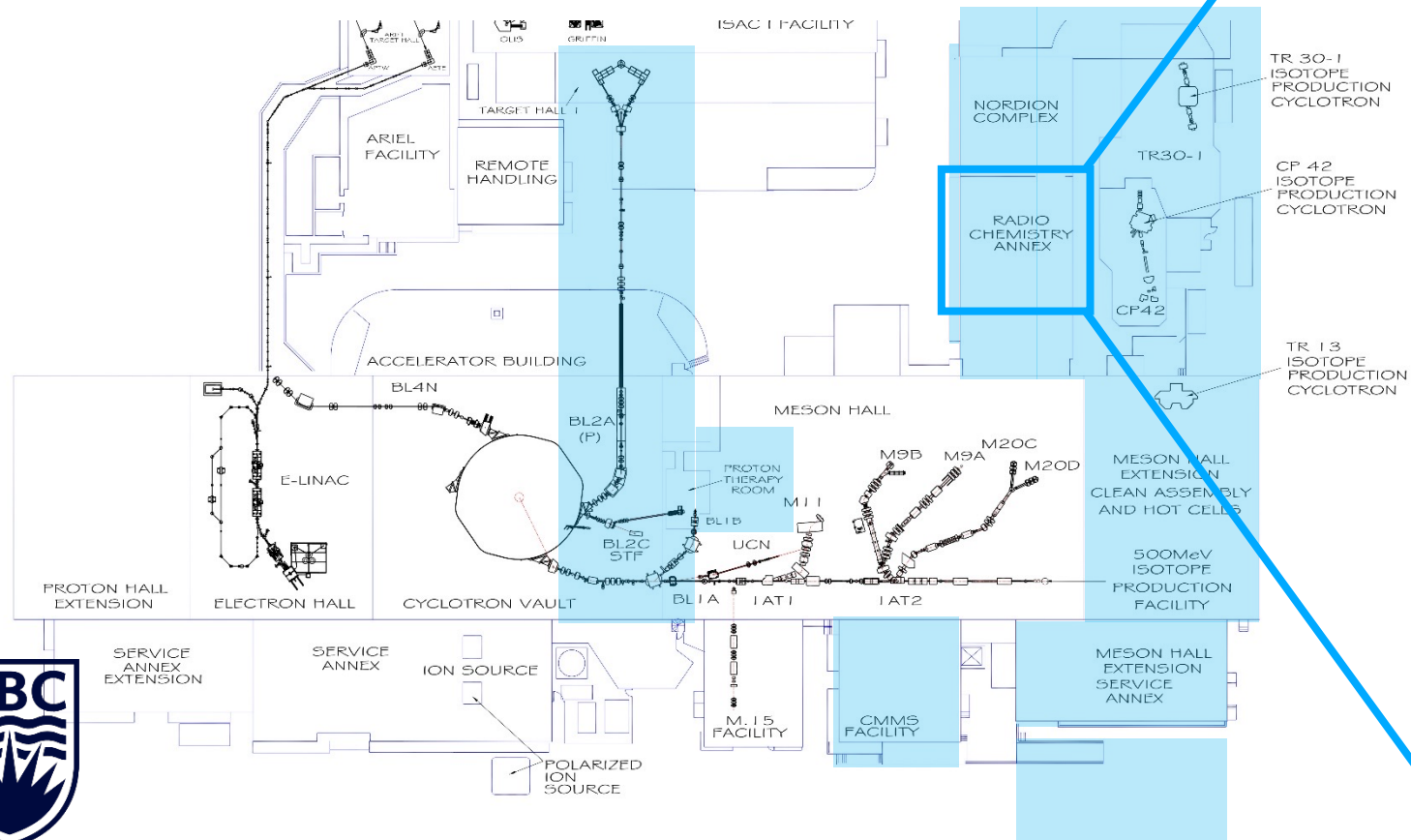
- 5 targets at IPF for a total of 28,900 μAh
- Isolated up to 155 mCi of direct ^{225}Ac (w/ ^{227}Ac ; corrected to EOB)
- Isolated up to 14.7 mCi of ^{225}Ra for generator assembly (corrected to EOB)
- ‘Milked’ $^{225}\text{Ra}/^{225}\text{Ac}$ generators 7 times for a total of 3.6 mCi of high purity ^{225}Ac for distribution to collaborators and TRIUMF researchers
- **2022 campaign underway**



Isotope Production Facility (IPF)

Complete Upgrade of RCA007

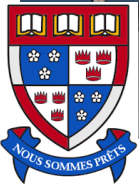
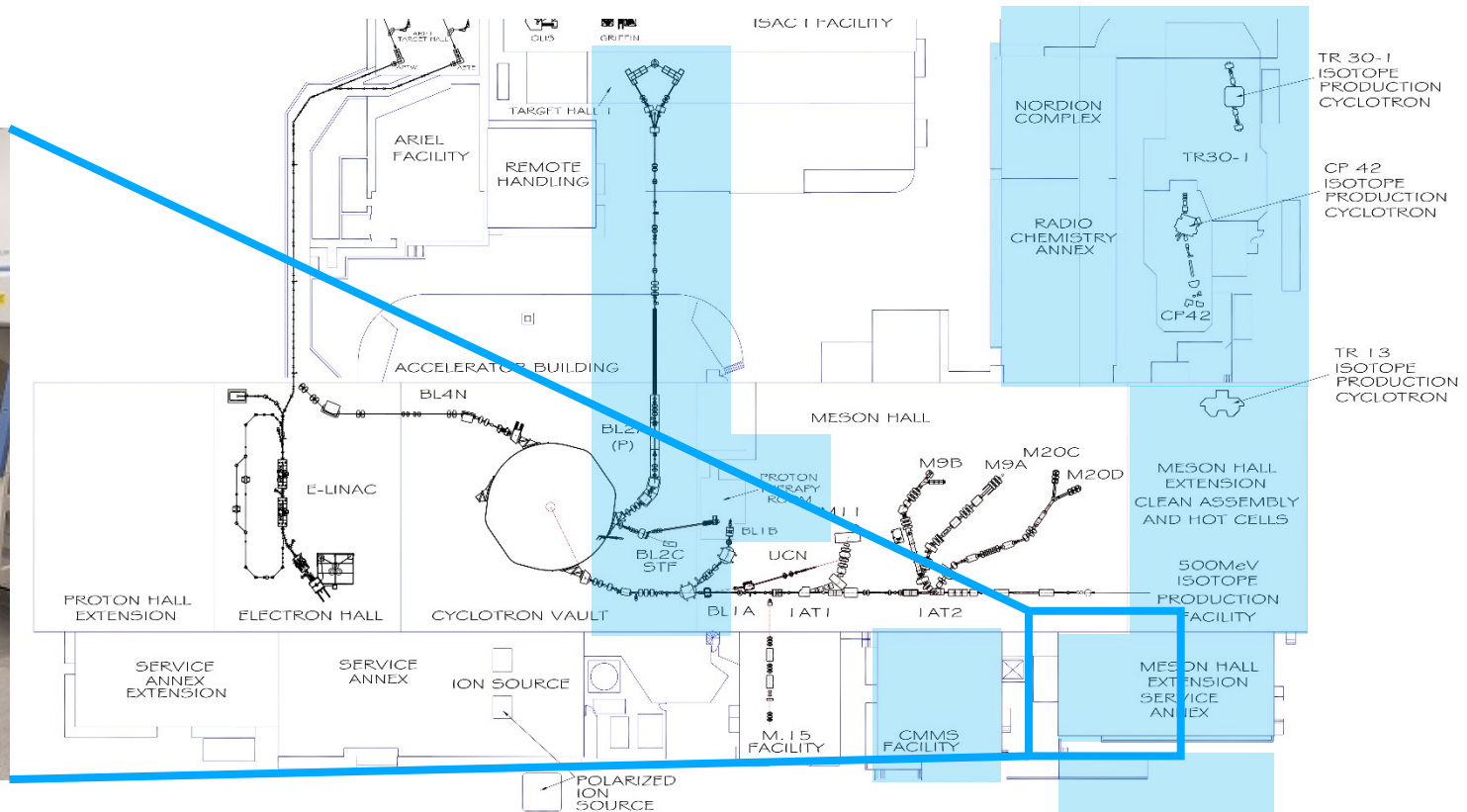
- **Objective:** Expand ^{11}C - GMP neurotracer production capacity
- **Current Status:** New hot cells, automated synthesis units and separate clean room
 - HVAC commissioning for CNSC and GMP completed
- **Next step:** Final lab commissioning (Gate 4A)



Commission TRIUMF Cell Biology Lab (P468)

- **Objective:** Implement a basic cell culture facility in MHESA Lab 01A; leverage CFI JELF (Ramogida)
 - Enable evaluation of radiopharmaceuticals *in vitro*
- **Current Status:** PHAC approval of biohazard safety plan - Oct. 2021
 - Construction complete
- **Next step:** Lab commissioning (Gate 4A)

25



Complete ARIEL (P405 – Symbiotic Isotope Production)

Design efforts underway:

1. Target and transfer system design and prototyping
 - Transfer target prototype built and ready to be tested
 - Thermal target prototype built and ready to be tested
2. ARIEL Hot Cell 2 (HC2) technical specification development
 - Document review complete and sent out for RFI
 - Work underway to re-baseline within cost

Team:

- Efforts underway to build depth in the project team
- Evaluation of project schedule underway to ensure timely delivery



CFI FCI



REQUEST FOR INFORMATION

| | |
|--------------|--|
| Ref Number: | RFI-Hot Cell #2-0122 |
| Description: | ARIEL Hot Cell #2 Budgetary Estimate |
| Date Issued: | January 20, 2022 |
| RFI Closes: | March 8, 2022, 14:00 hours (2:00 PM) Vancouver Time |
| Respond to: | TRIUMF INC. Ms. Kai-Mei Chu, CPPB Procurement Manager 4004 Wesbrook Mall Vancouver, BC, V6T 2A3 Email: kaimei@triumf.ca |

Future Ambitions, Upcoming Priorities

Replace BL1A (P540, P527)

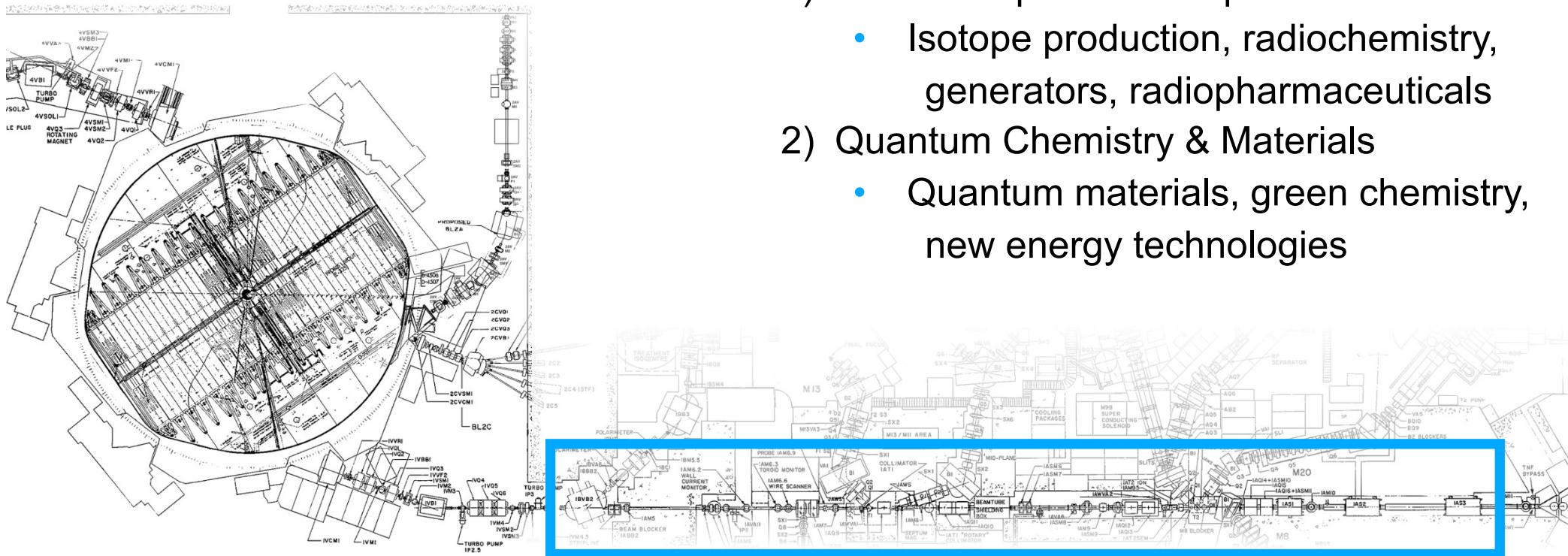
Objective: replace, enhance functionality of BL1A

Next step: 2023 CFI Infrastructure Fund application **submitted!** Provincial applications underway

- Title: TRIUMF High-Energy Accelerator Proton Irradiation Experiments (THErAPIE)
- \$28+M budget (\$9.7M from CFI) involving 9 institutions across 4 provinces

Two Research Programs:

- 1) Radioisotopes & Radiopharmaceuticals
 - Isotope production, radiochemistry, generators, radiopharmaceuticals
- 2) Quantum Chemistry & Materials
 - Quantum materials, green chemistry, new energy technologies



225Ac Production via 226Ra(p,2n) (P526)

Objective: Determine best path forward for production of 225Ac from 226Ra



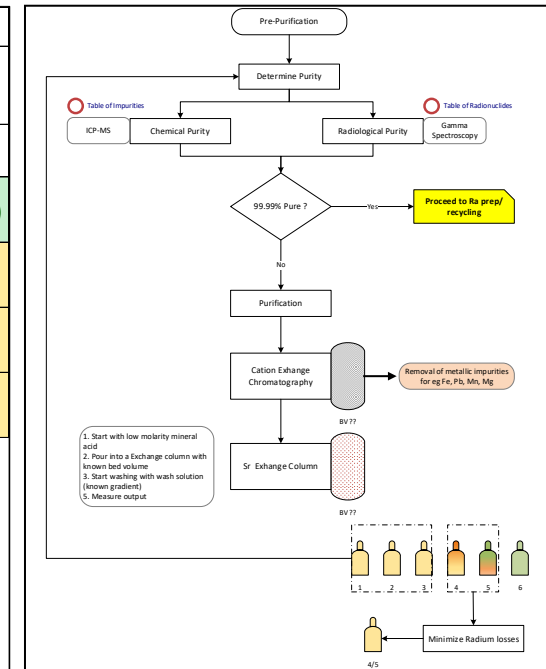
Current Status:

- Efforts underway to initiate radium handling, processing, recycling
- Evaluate path forward for target design

Next Steps:

- Project distillation into WBS structure

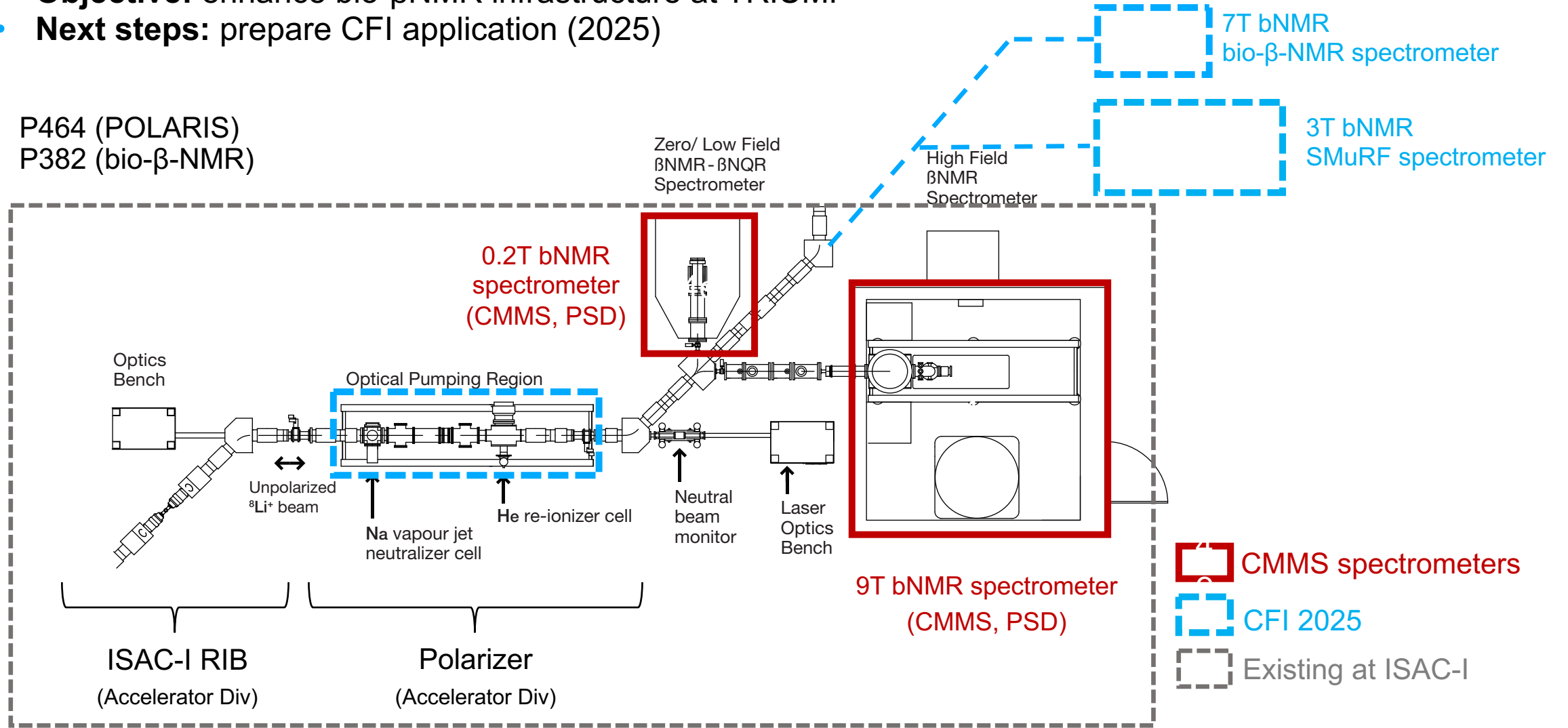
| Type | Solid Target | Liquid Target: Constant flow | Liquid Target: Cartridges |
|-----------------------------|--|---|--|
| Desc | Using a radium salt (nitrate) to a backing plate (glass). Transferring into the proton beam for irradiation. Dissolution of irradiated Ra in Nitric acid and using LN resin for purification and separation of Ac-225 | Using a constant flow system to irradiate and precipitate the Ac-225 required. The aqueous solution of Radium salt in constant circulation in proton beam to cause spallation reactions | Hybrid system utilizing cartridge based system of radium salt |
| Pub | Verified experimentally: Publication & Patents Chigutsu, K., Suzuki, H., Fukuda, M. et al. Cyclotron production of 225Ac from an electroplated 226Ra target. Eur J Nucl Med Mol Imaging 49, 279–289 (2021). https://doi.org/10.1007/s00201-021-05460-7 | | |
| Safety | 1. Elemental Radium is highly reactive with oxygen and Water 2. Radon is a daughter of radioactive decay chain is vented to atmosphere | 1. Radium is always present as a salt in aqueous form so reactivity contained 2. Radon emissions is contained within the liquid phase and can be controlled for venting | 1. Radium is always present as a salt in aqueous form so reactivity contained 2. Radon emissions is contained within the liquid phase and can be controlled for venting |
| Quality | 1. Concentrated source of irradiation 2. High Target to Yield Ratio | 1. Low yield ratios and the concentration of Ac-225 generated might be too low to be commercially viable | 1. Low yield ratios and the concentration of Ac-225 generated might be too low to be commercially viable |
| Prod | 1. Requires management of transferring into subsequent process steps Electroplating-->Irradiation-->Dissolution-->Elution-->Preparation | 1. No manual interaction required in constant flow system. 2. Only manual intervention of "milking" ion exchange stacks required | 1. Requires management of transferring into subsequent process steps Preparation of target-->Irradiation-->Elution-->Preparation |
| Cost | High Capital investment: Requires significant more remote handling interfacing and staffing to run | 1. Medium Capital investment required for constant flow system | High Capital Investment: Requires significant more remote handling interfacing and staffing to run |
| Questions for Consideration | 1. Total yield Ratio may be known from Electroplated targets and studies completed by Nagatsu And team 2. Has the ability to use multiple targets during operation if needed 3. System reliability needs are relatively less, operation can be shut down fairly easily (just dont run) 4. Science is known, experiment is known, need to scale up operation safely 5. Electroplating and dissolution are bottlenecks in process and will require time studies for process set up 6. Thermal modelling to ensure proper heat management is relatively easy 7. Materials research is relatively simple, experiments already established 8. Fail safe containment is easy as target is a solid | 1. Total Yield Ratio is not Known, will need to be experimentally verified 2. Does not have the ability to process multiple target types during operation, if needed, system purge required. 3. Significant system reliability factors to be considered, required constant monitoring 4. High risk involved, but will significantly advance body of knowledge on liquid targets (High publishing potential) 5. No dissolution and electroplating steps required, only time bottleneck is irradiation time 6. Thermal modelling to ensure proper heat management is relatively easy (increase flow rate) 7. Requires materials research to ensure proper containment of material and chemical inertness during irradiation 8. Fail safe containment will be significantly challenging as irradiated targets are constantly flowing. | 1. Total Yield Ratio is not Known, will need to be experimentally verified 2. Has the ability to use multiple targets during operation if needed 3. System reliability needs are relatively less, operation can be shut down fairly easily (just dont run) 4. Medium risk involved, but will advance body of knowledge on liquid targets (High publishing potential) 5. No dissolution and electroplating steps required, only time bottleneck is irradiation time 6. Thermal modelling to ensure proper heat management is critical, phase change will lead to a pressurized vessel. 7. Requires materials research to ensure proper containment of material and chemical inertness during irradiation 8. Fail safe containment will be somewhat challenging as irradiated targets are liquid but contained. |



Expand bio- β -NMR (P382, P464)

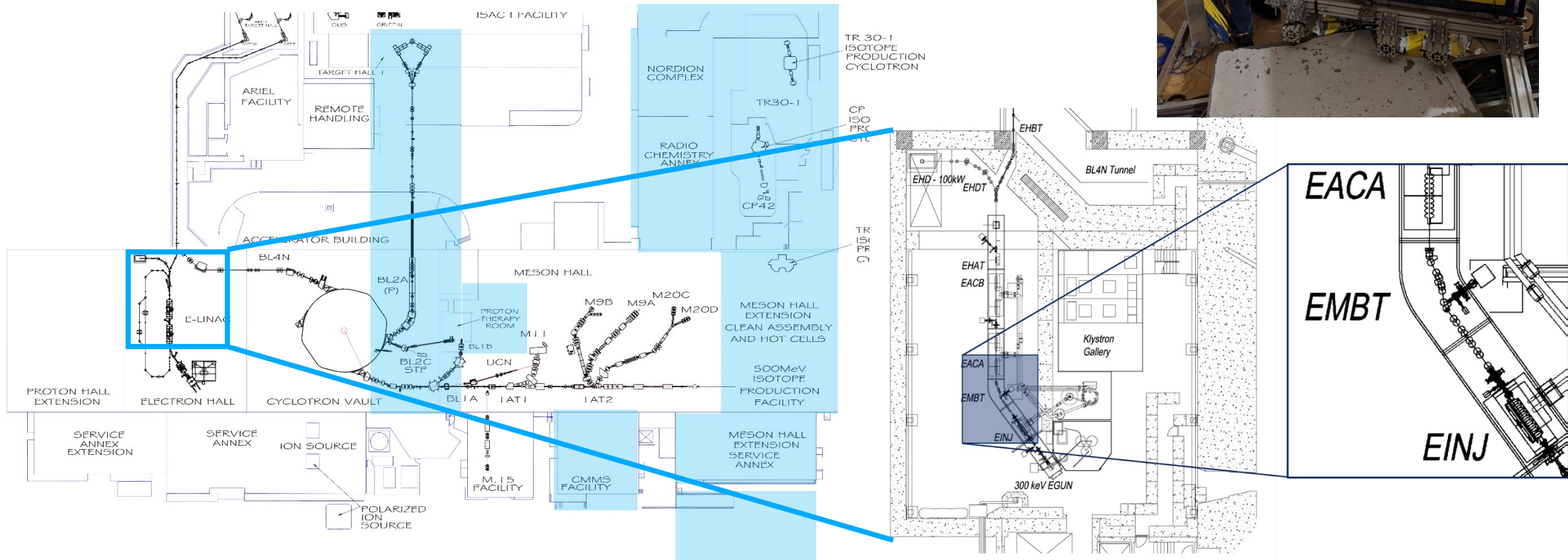
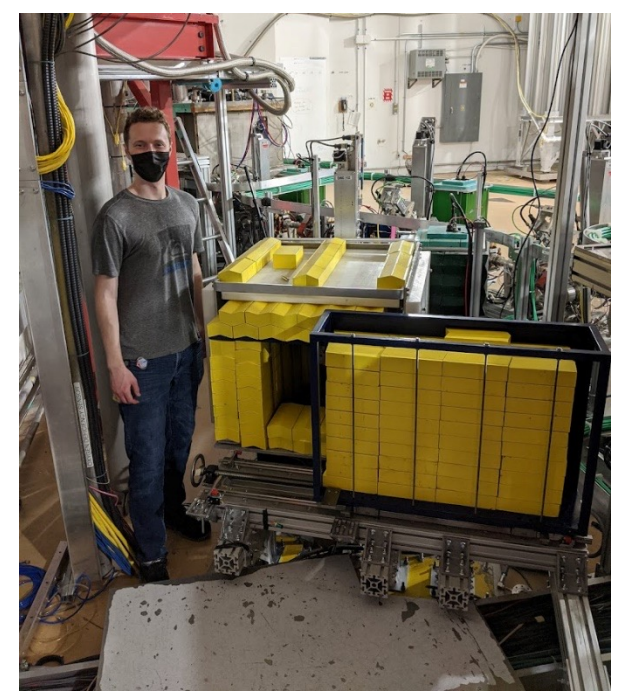
- **Objective:** enhance bio- β NMR infrastructure at TRIUMF
- **Next steps:** prepare CFI application (2025)

P464 (POLARIS)
P382 (bio- β -NMR)



FLASH Proton and X-ray Therapy (P490)

- **Objective:** establish go/no-go for larger-scale infrastructure investment at TRIUMF
- **Current Status:** Feasibility (NFRF-Exploration grant) with animal studies underway
- **Next steps:** prepare CFI application (2025)



Summary

- The Life Sciences Division continues to balance a significant project and operational workload in addition to research efforts
- Current strategic priorities remain as IAMI, ARIEL, Ac-225
- Future initiatives to continue focusing on building LS capabilities and infrastructure; leveraging both to foster strategic partnerships
 - Includes operating IAMI, ARIEL
 - investing in:
 - BL1A
 - bio- β NMR infrastructure
 - Strategic decisions regarding FLASH
 - Expansion of TRIUMF's isotope, radiopharmaceutical portfolio

Our 20 Year Vision for Life Sciences

Think Big

Pursue Creative, Impactful Science

TRIUMF is inherently multidisciplinary and translational, bringing together science, creativity, innovation and novel infrastructure; encouraging and inviting collaborators from around the world to answer some of life's most difficult questions.

Be Different

Apply Physics to Life

TRIUMF Life Sciences will be an engine that applies accelerator science toward the study of life – in order to derive maximum societal benefit.

TRIUMF has globally unique infrastructure, rare talent, and an innovative mindset to better life for all.

Be Bold

Train and Send Forth World-Class Talent

Creative, impactful research will be woven into the cultural fabric of TRIUMF Life Sciences; training a generation of innovative thought and technology leaders to work collaboratively across disciplines to ask tough questions and derive elegant answers.

Thank you

www.triumf.ca

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