Isotope Production at LERF

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for

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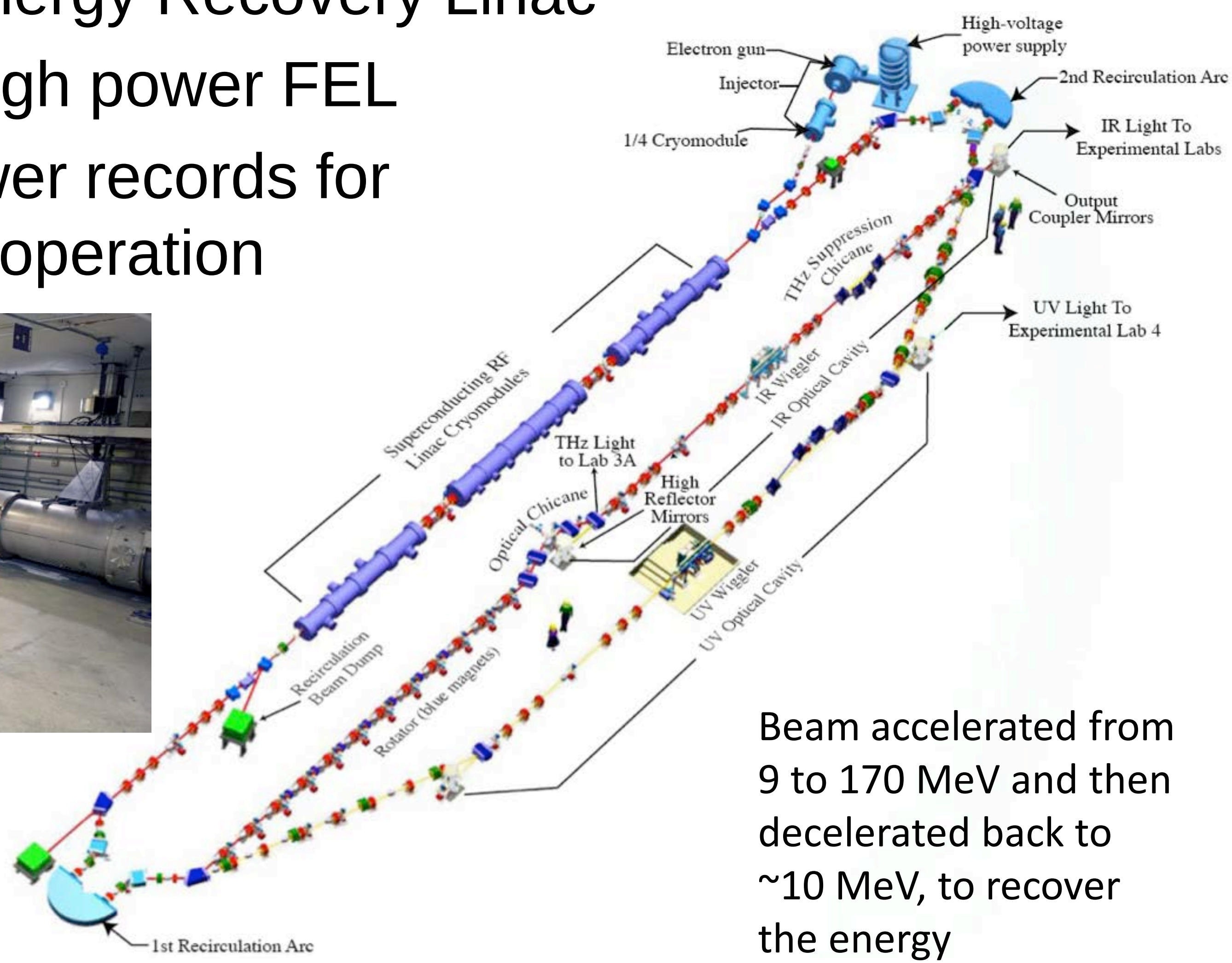
JLAB Low Energy Recirculator Facility (LERF)

- LERF is an Energy Recovery Linac
- World's first high power FEL
- Still holds power records for FEL and ERL operation



Beam accelerated from 9 to 170 MeV and then decelerated back to ~10 MeV, to recover the energy

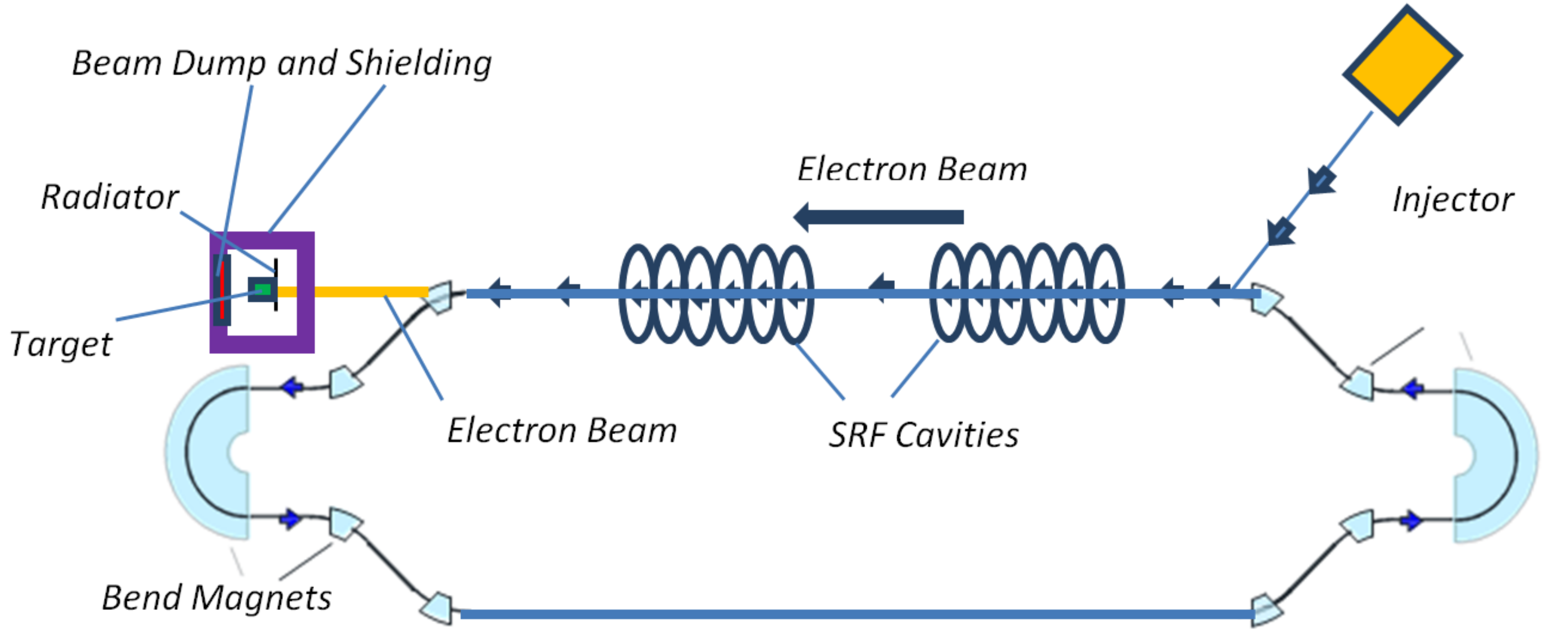
LERF Capabilities

- The ERL in the LERF is available for:
  - Fixed target experiments at medium current
  - Internal target experiments at high current
  - Offline accelerator research and development
  - Diagnostic development
  - FEL studies in the IR and UV
  - THz production

Parameter	Maximum value
Current (ERL)	8 mA
Energy	170 MeV
Charge	150 pC
Frequency	75 (750) MHz
Current (fixed target)	0.5 mA

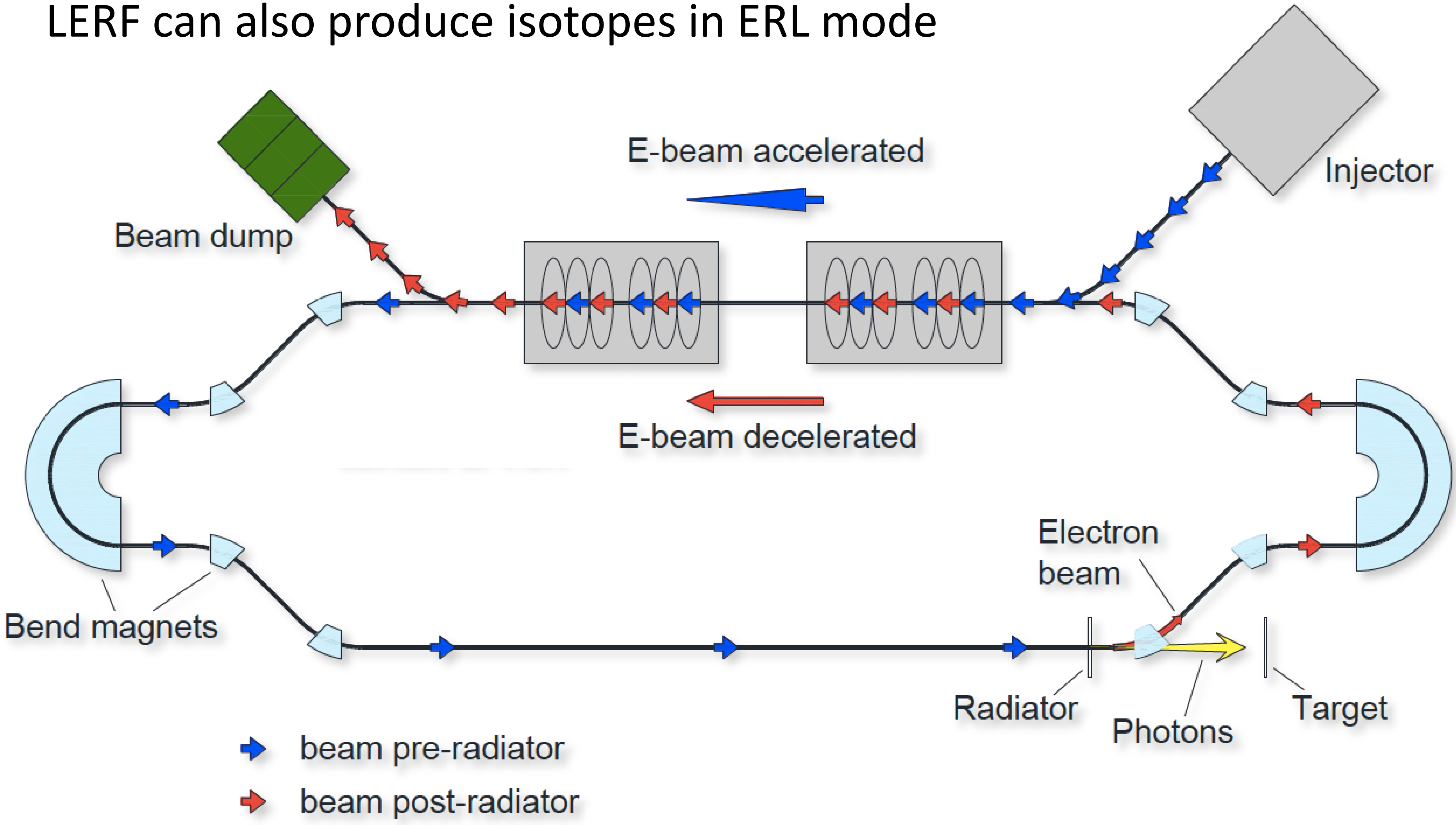
Jefferson Lab for Isotope Production

- Low Energy Recirculator Facility (LERF) is proposed for isotope production in non-ERL mode
  - Up to 150 MeV energy electron beam
  - Up to 100 kW beam power

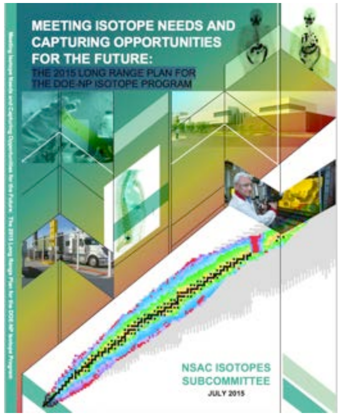


Schematic of ERL-Based Isotope Production

LERF can also produce isotopes in ERL mode



NSAC Isotopes Recommendations on Isotope R&D



- *"Continue support for R&D on the production of **alpha-emitting** radioisotopes"*
- *"Support R&D into the production of **high specific activity theranostic** radioisotopes"*
- *"Continue support for R&D on the **use of electron accelerators** for isotope production"*
- *"Support R&D on the development of **irradiation materials for targets** that will be exposed to **extreme environments** to take full advantage of the current suite of accelerator and reactor irradiation facilities"*

This study addresses all of these

Isotope Production Collaboration

Jefferson Lab:

- Hari Areti, Pavel Degtiarenko, George Kharashvili, Joe Gubeli, Kevin Jordan, George Neil
  - Radiation physics, health physics, Monte-Carlo modeling, radiation metrology, high-power SRF electron accelerators, targetry, beam diagnostics, beam dumps

Virginia Commonwealth University:

- Jamal Zweit, Sundaresan Gobalakrishnan
  - Radiochemistry, radiopharmaceuticals, medical imaging, nanotechnology

New Mexico Tech:

- Doug Wells
  - Photonuclear physics, activation analysis, isotope production

Recent Activities

2012 – Proposal for isotope production using LERF in ERL configuration submitted to DOE Isotope Program

- not funded (DE-FOA-000743)

2015 – Pre-R&D Proposal Funded by DOE Isotope Program

2015 – White paper for photoproduction of ^{67}Cu

2016 – R&D proposal for ^{67}Cu production – DOE Isotope Program

- not funded in 2017, under consideration for 2018 funding (DE-FOA-0001588)

2017 – US patent application: ^{67}Cu Photoproduction in Gallium

2015/2017 – Proof of concept studies

- ^{67}Cu production in gallium and zinc targets at CEBAF injector
- ^{67}Cu separation from gallium at VCU

^{67}Cu for Targeted Radiotherapy

- *Theranostic* radionuclide
  - 141 keV mean energy β^- for therapy (range in tissue is about a cell diameter)
  - 185 keV energy γ for SPECT imaging
  - Can be paired with ^{64}Cu for PET imaging
- Near-ideal half-life of 61.8 hours
  - Convenient for production, transportation, and delivery to patient
  - Same order as biological half-life of copper and zinc (^{67}Cu decays to stable ^{67}Zn)
- Favorable biochemistry – approved for human trials
  - Copper and zinc are essential for structural and functional activities of many proteins, enzymes and transcription factors
  - Not acutely toxic – both copper and zinc are essential trace nutrients

Demand and Availability of ^{67}Cu

- Historical lack of an adequate and reliable supply has impeded the development of ^{67}Cu applications
- Estimate of potential long-term US demand based on treating half of all new Non-Hodgkin Lymphomas gives ~12,000 Ci / year
  Smith, Bowers, Ehst, "The production, separation, and use of ^{67}Cu for radioimmunotherapy: A review", *Applied Radiation and Isotopes* 70 (2012) 2377–2383
- ^{67}Cu is currently produced at:
  - Brookhaven National Laboratory: Proton irradiation of zinc, produced periodically, ~60% of activity upon delivery is composed of ^{64}Cu
  - Argonne National Lab LEAF: Photoproduction reaction producing 100 mCi batches on demand, expandable to 2 Ci batches
  - Idaho Accelerator Center: Photoproduction in zinc up to 10s of mCi / week, not intended for human use
- Higher specific activities and improved radiological purity are desired

Photoproduction of ^{67}Cu in Gallium via $^{71}Ga(\gamma,\alpha)^{67}Cu$ (1)

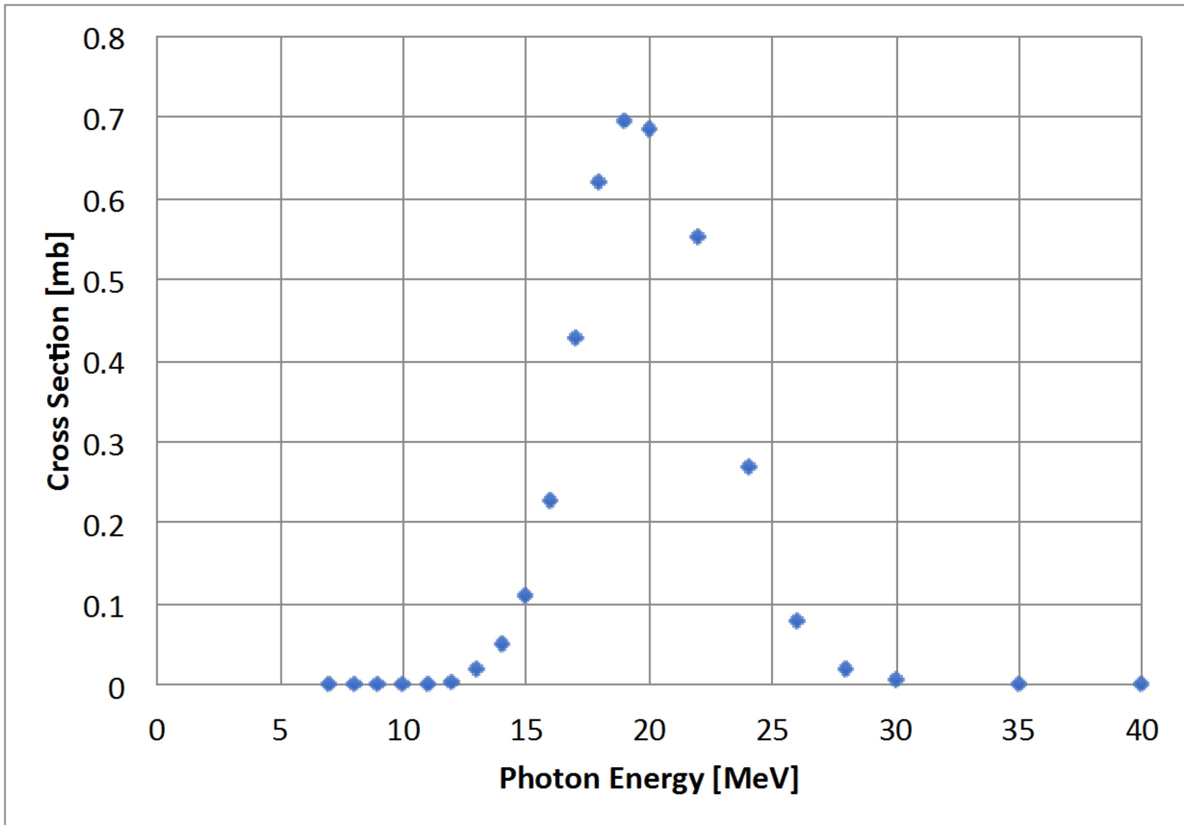
- Gallium has favorable properties for high power targets
  - ✔ Low melting point of 30 °C
  - ✔ High boiling point of 2204 °C
  - ✔ Low vapor pressure
  - ✖ Corrosive to metals except tungsten and tantalum

- 50 kW irradiation of a Gallium target once per week will produce*
  - 100s mCi of ^{67}Cu per week in natural gallium
  - > 1 Ci/week in ^{71}Ga (40% of natural Gallium)
  - Typical medical dose of ^{67}Cu – order of 10 mCi

* Yields are calculated using FLUKA and scaled with data

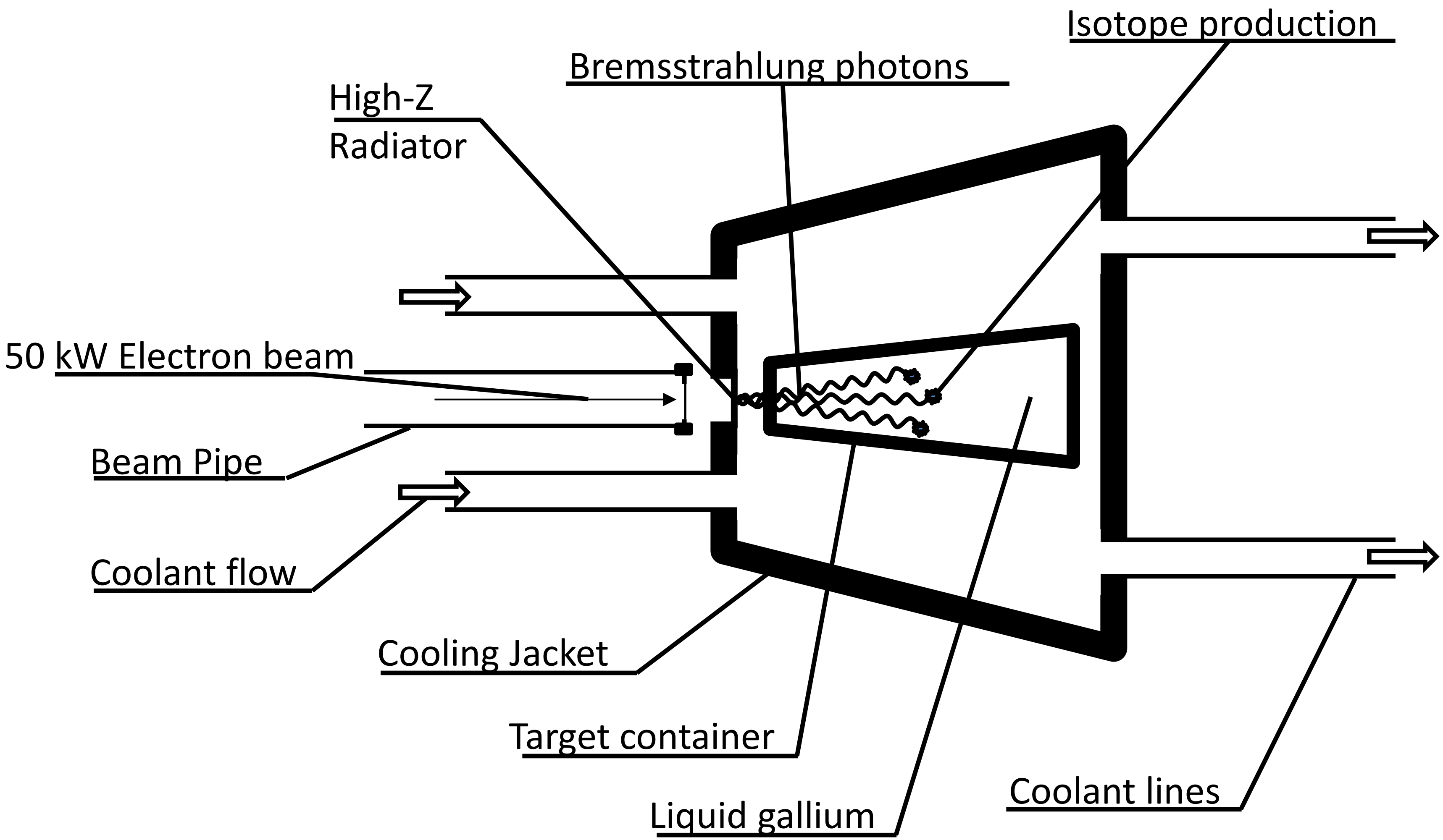
Photoproduction of ^{67}Cu in Gallium via ^{71}Ga(γ,α)^{67}Cu (2)

- Modest cross-section of ^{71}Ga(γ,α)^{67}Cu reaction can be compensated by high beam power and a thick target



Koning *et al.* "TENDL-2015: TALYS-based evaluated nuclear data library" https://tendl.web.psi.ch/tendl_2015/tendl2015.html

Photoproduction of ^{67}Cu in Gallium via ^{71}Ga(γ,α)^{67}Cu (3)



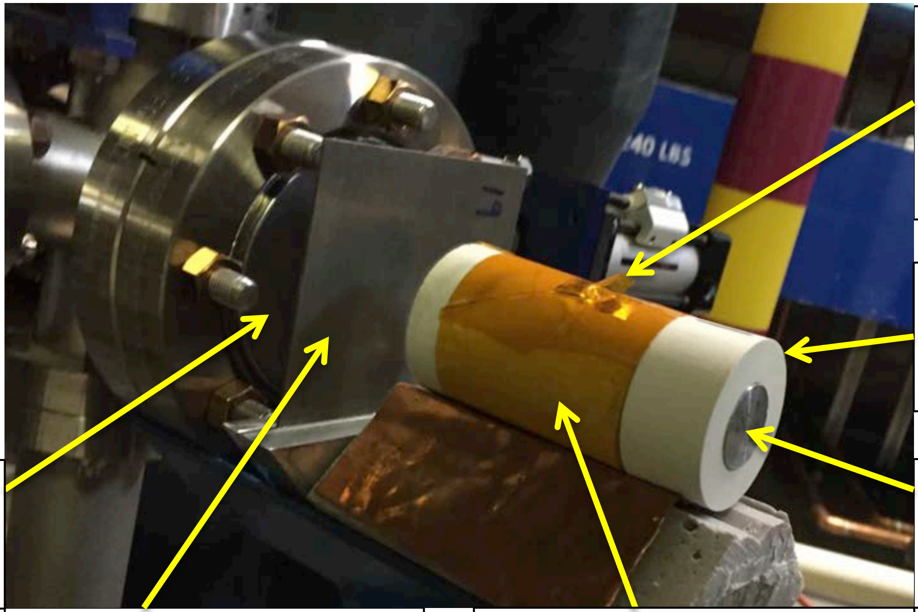
Overall Objectives and First Steps

- The overall objective is to integrate
  - Production
  - Chemical Separation
  - Delivery

- First (opportunistic) steps
  - Confirm ^{67}Cu production in gallium
  - Chemically separate ^{67}Cu from gallium
  - Investigate ^{67}Cu delivery mechanisms

First Opportunistic Irradiation Test

- Irradiation of Gallium and Zinc targets during beam studies in CEBAF injector:
  - 18.5 MeV (to avoid interference from ^{67}Ga), 2.5 µA, 1 h
  - ~ 0.1 µCi ^{67}Cu detected in each target



Natural Gallium target

Boron Nitride crucible

Beryllium window

Natural Zinc target

1mm Tungsten radiator

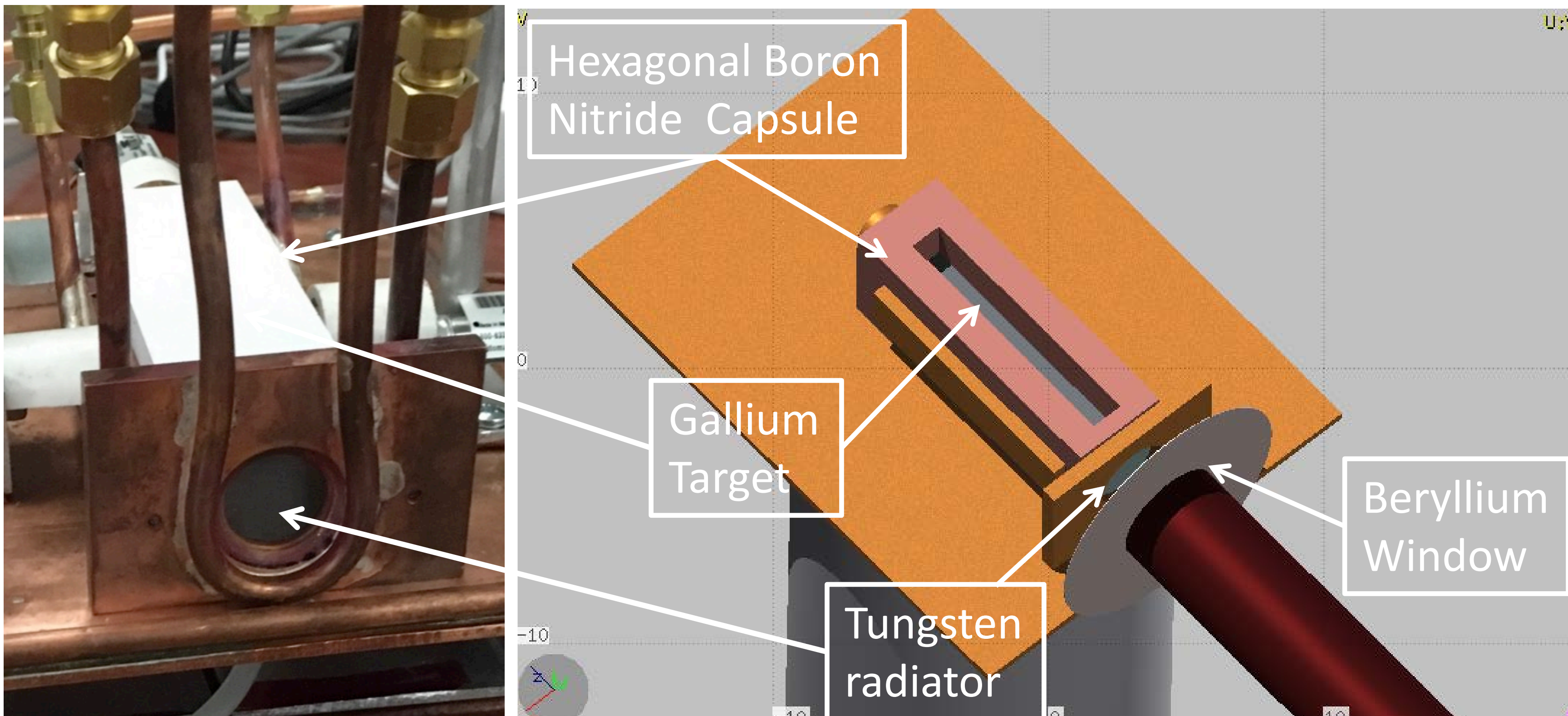
Kapton tape to prevent Gallium spills

Chemical Separation Test

- Chemical separation test at Virginia Commonwealth University (VCU)
  - 1 mCi of 67Cu was obtained from the National Isotope Development Center
    - Shipped from BNL to VCU
  - The sample was dissolved in hydrochloric acid and added to gallium chloride in solution
  - Separation by liquid-liquid extraction and column chromatography recovered ~95% of the radioactive copper after a single pass

Second Opportunistic Irradiation Test (1)

- During 2017 beam studies of 4K operation in CEBAF injector, there was a parasitic opportunity for isotope irradiation
  - 85 g gallium target irradiated for several hours at 18.65 MeV, 50 µA (~1 kW) with the goal of chemically separating ^{67}Cu



Second Opportunistic Irradiation Test (2)

- Due to failure of monitoring instrumentation, run was terminated earlier than anticipated
- ~130 µCi ^{67}Cu was produced, ~70 µCi was available at the time of sample retrieval (aimed to produce ~500 µCi)
- Due to transportation and communication issues did not proceed with chemical separation
- The two, low-energy irradiation tests showed reasonable agreement with the model predictions
  - FLUKA (our primary tool for activation calculations) appears to overestimate ^{67}Cu yields in Gallium by approximately a factor of 2 at 18.5 MeV maximum bremsstrahlung energy

Summary and Proposed Future Work

- ^{67}Cu production via the ^{71}Ga(γ,α)^{67}Cu reaction at LERF: Production of **high specific activity, theranostic** isotope using a **high-power** ***electron accelerator***
  - ✔ Measured photoproduction of ^{67}Cu at low energies (< 20 MeV)
    - No ^{64}Cu content detected
  - ✔ Chemically separated ^{67}Cu from Gallium
    - Obtained from BNL, then dissolved in Gallium
  - Proposed future work
    - Complete smooth integration of photoproduction and chemical separation
    - Produce ^{67}Cu in Gallium target at optimal electron beam energies (> 30 MeV)
    - Develop high power target system
- Investigate photoproduction of ***α-emitters***
  - **^{225}Ac** production in ^{226}Ra, ^{230}Th, ^{232}Th targets