Brookhaven National Laboratory

U.S. DEPARTMENT OF ENERGY

Isotope Research and Production Department

Cathy S. Cutler, IP Department Chair

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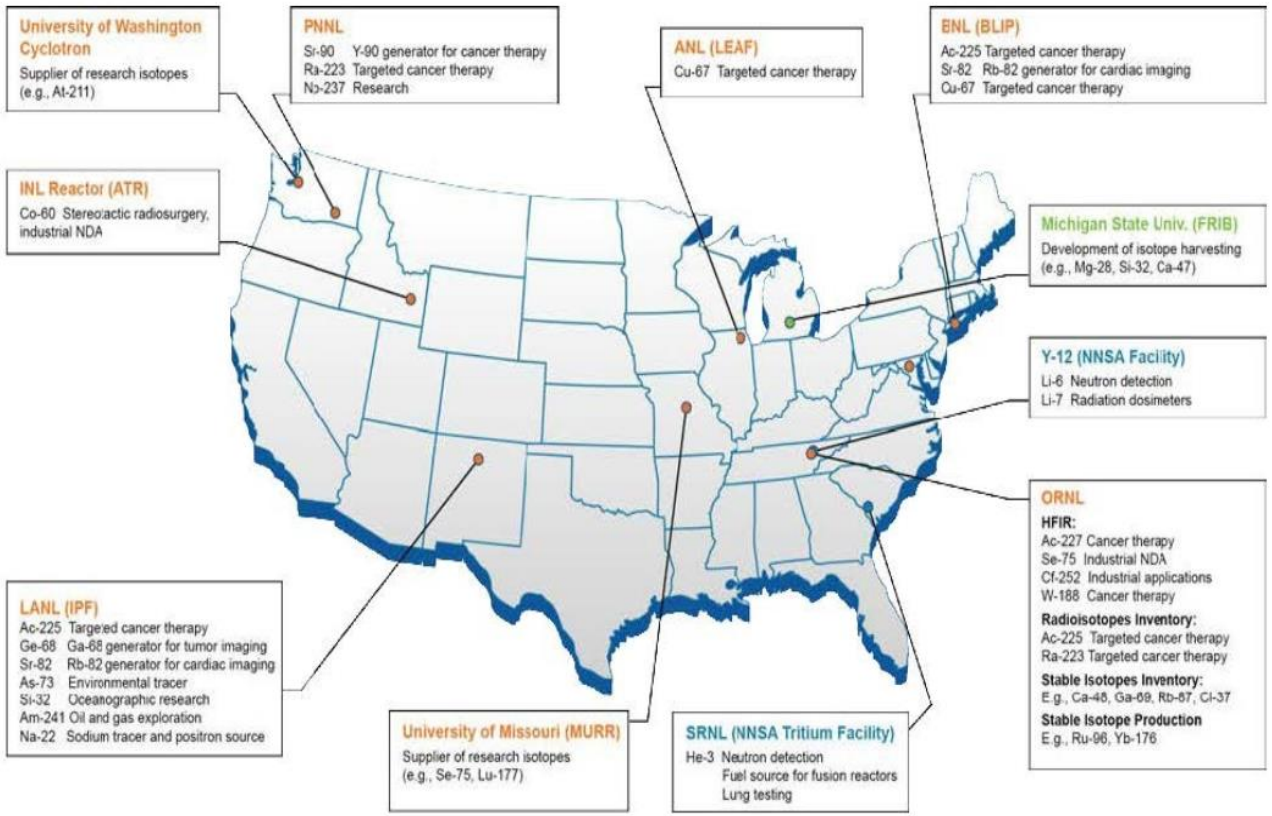
US DOE isotope program



Mission

Produce and/or distribute radioactive and stable isotopes that are in short supply; includes by-products, surplus materials and related isotope services

Maintain the infrastructure required to produce and supply priority isotope products and related service

Conduct R&D on new and improved isotope production and processing techniques which can make available priority isotopes for research and application. Develop workforce.

Reduce U.S. dependency on foreign supply to ensure National Preparedness.

BNL is the Birthplace of Nuclear Medicine

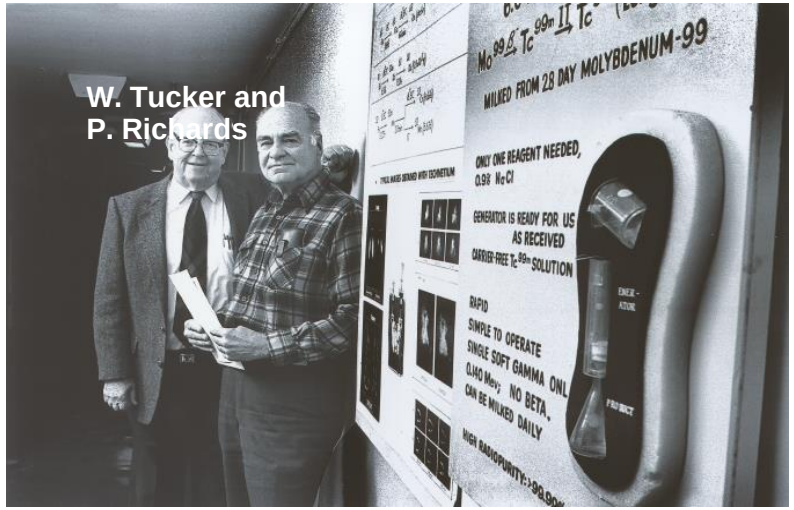
1950s: BNL scientists Walter Tucker and Margaret Greene developed a generator system for producing Tc-99m and Powell Richards suggested its use for medical imaging. Tc-99m is now used in over 10 million patients/year in the U. S. alone

1970s: BNL pioneered the use of high energy proton beams for isotope production (BLIP)

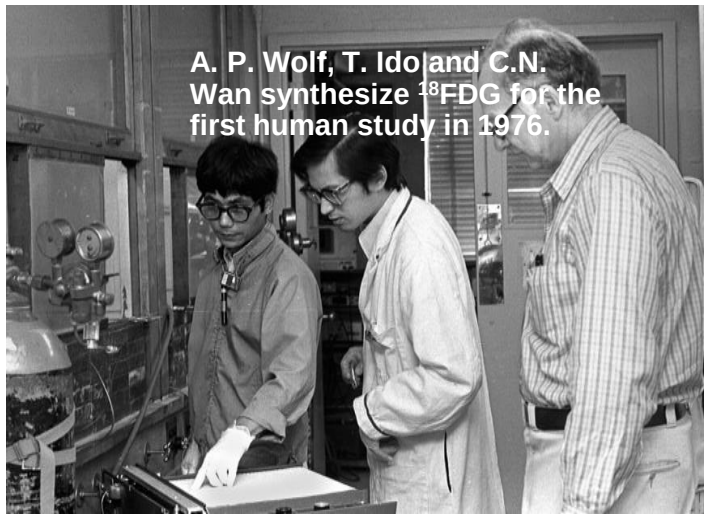
1970s: scientists at BNL, U. Penn and NIH, combined chemistry, neuroscience and instrumentation to develop ^{18}FDG (fluorodeoxyglucose), revolutionizing the study of the human brain

In 1980, BNL scientists first reported high FDG uptake in tumors, leading to FDG/PET for managing the cancer patient

Many radionuclide generator systems developed at BNL: ^{132}Te/^{132}I; ^{90}Sr/^{90}Y; ^{68}Ge/^{68}Ga; ^{52}Fe/^{52m}Mn; ^{81}Rb/^{81m}Kr; ^{82}Sr/^{82}Rb; ^{122}Xe/^{122}I



W. Tucker and P. Richards


A. P. Wolf, T. Ido and C.N. Wan synthesize ^{18}FDG for the first human study in 1976.

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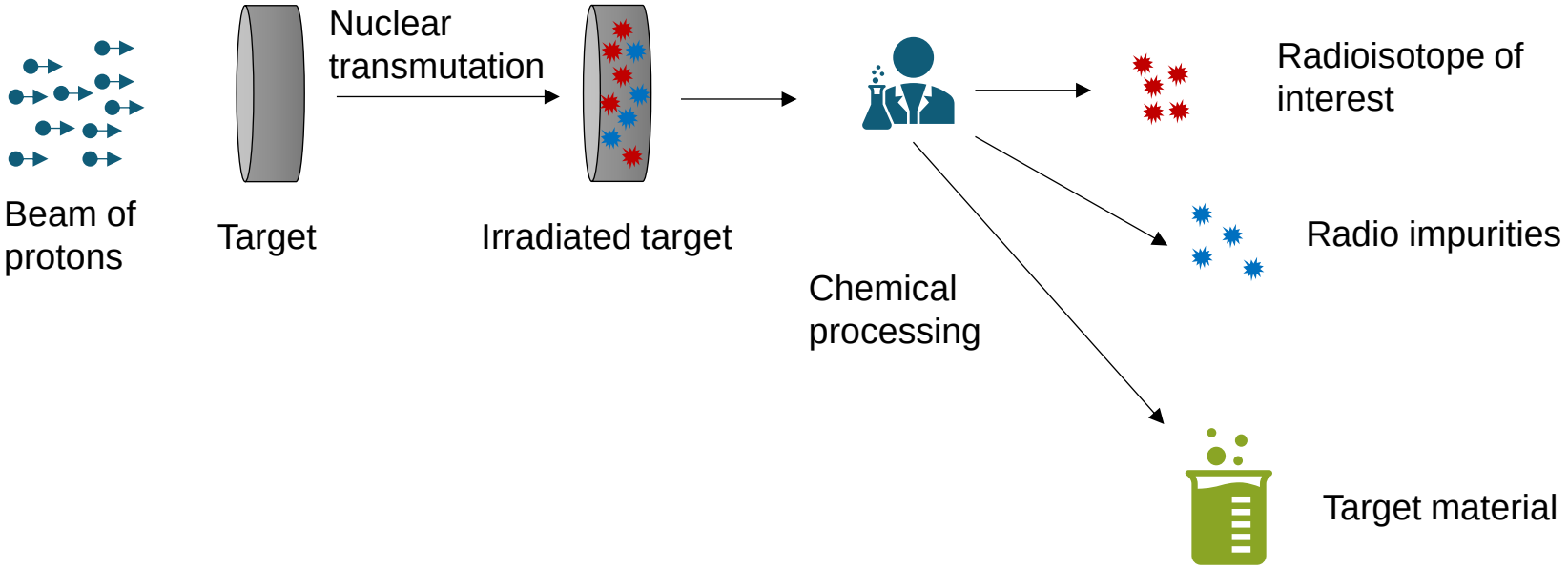
Isotope production with charged particle beam



Targets can be large – up to 100 grams

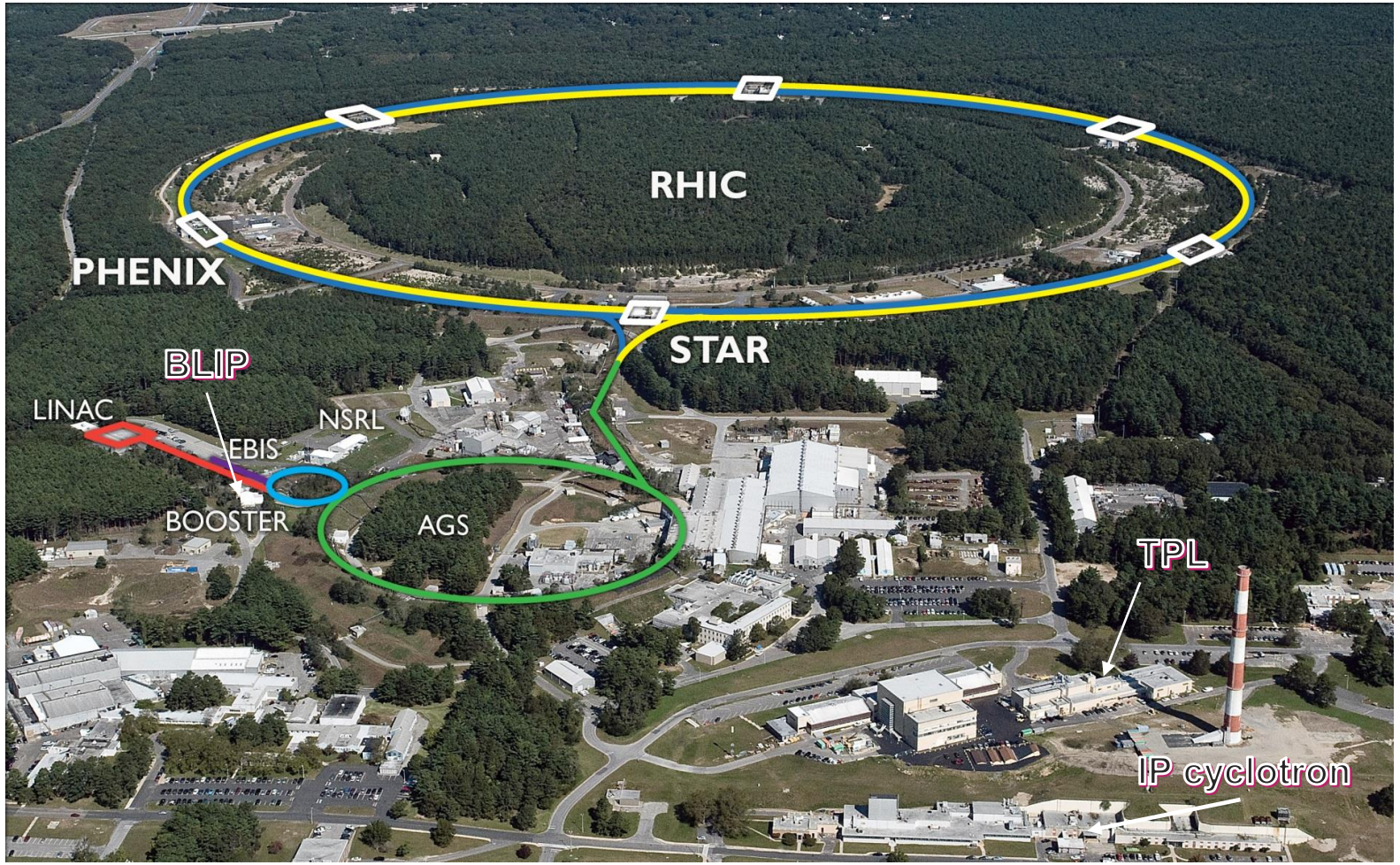
Several targets can be used in stacks, one after another

Complex separations – multistep chemical processes carried out in shielded enclosures

- Ion-exchange resins
- Liquid-Liquid extraction

Large quantities, multiple isotopes, high proton energy (up to 200 MeV)

Brookhaven Lab and its accelerator complex



BLIP – Brookhaven Linac Isotope Producer, TPL – Target Processing Laboratory

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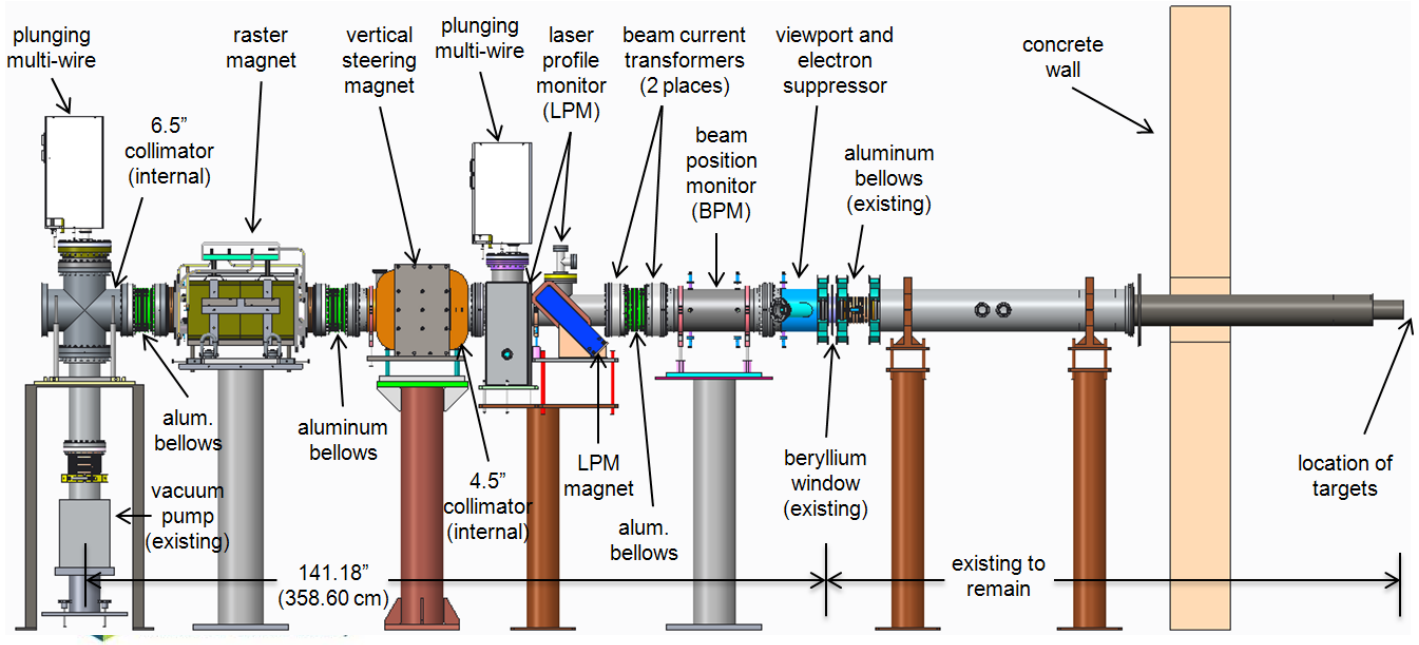
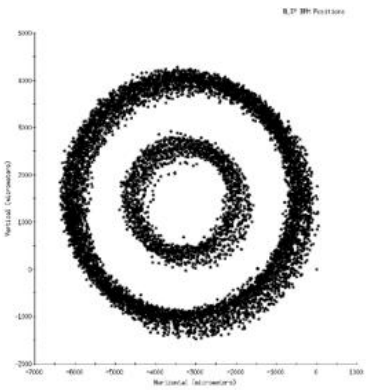
200 MeV LINAC at BNL

- A 459-foot-long LINAC with 9 accelerator RFQ cavities
- Energy is incrementally tunable from 10 to 200 MeV, with 66 MeV the lowest practical energy for isotope production
- Phase 1 complete: Current improved to 165 uA in 2016
- Phase 2 pending: Increase current to 250 uA
- Rastered and focused beam capability

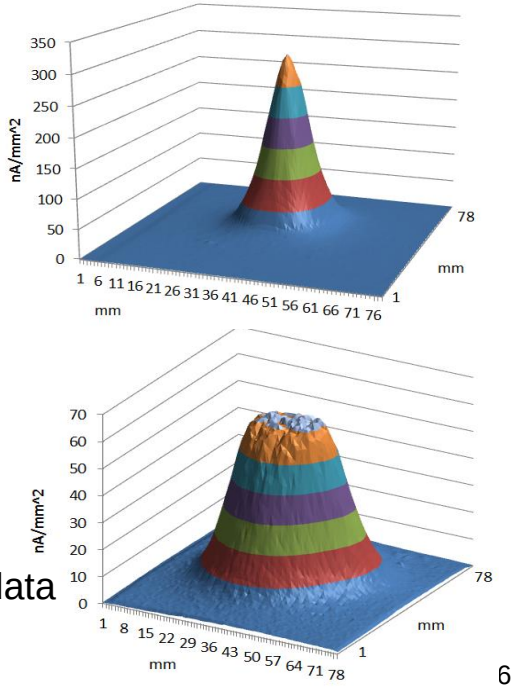
LINAC



BLIP beam-line layout.



Beam position monitor data



Beam profile on target

Brookhaven Linac Isotope Producer (BLIP)

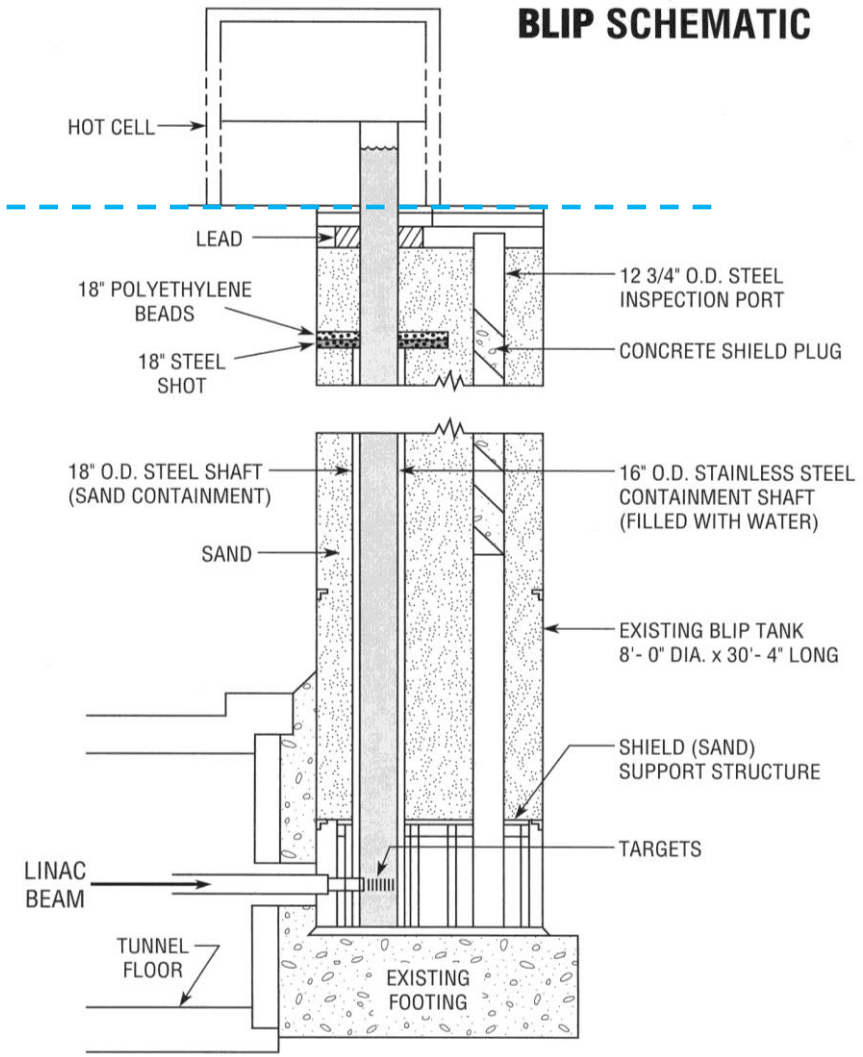
First to use a high energy proton accelerator to produce isotopes (1972)

BLIP utilizes the beam from the 200-MeV Linac that injects the Booster, which leads to AGS and RHIC accelerators (nuclear physics)

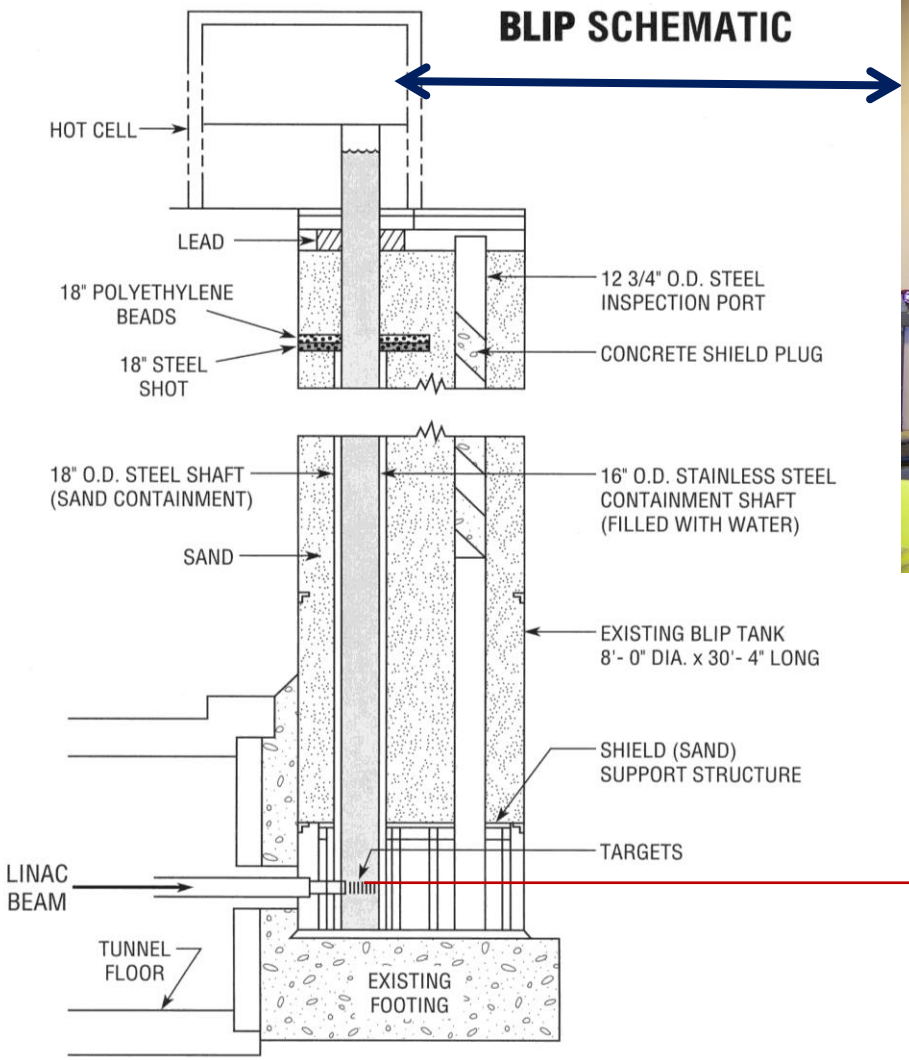
Excess Booster pulses (~90%) are diverted to BLIP. Energy is incrementally variable from 66-200 MeV

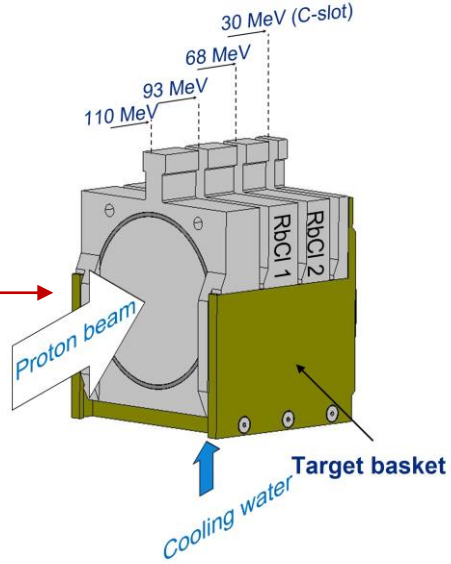
The BLIP beam line is synergistic operation with nuclear physics programs for more cost-effective isotope production

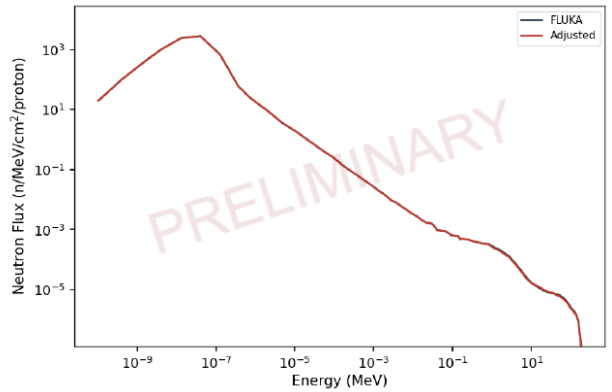
In 2016, implemented beam rastering and increased Linac current to increase isotope production capabilities



Brookhaven Linac Isotope Producer (BLIP)







Secondary neutron spectrum behind 200 MeV target stack

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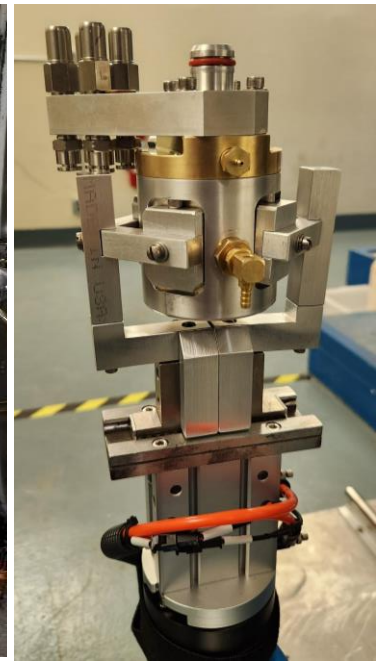
MIRP Cyclotron

- Beam Energy: 13 ~ 19 MeV Beam Current: 200uA
- Commercial Cyclotron has been restored to the original configuration
- Refurbished
  - Ion Source Injection System and all the Lenses
  - RF Tuner and High voltage
  - Chilled water system
  - Vacuum (0.27 x 10-6 Torr) and Cryo systems
  - PLC system, power supplies and controlling PC
  - Target selection station
  - Shielding
  - Interlocks



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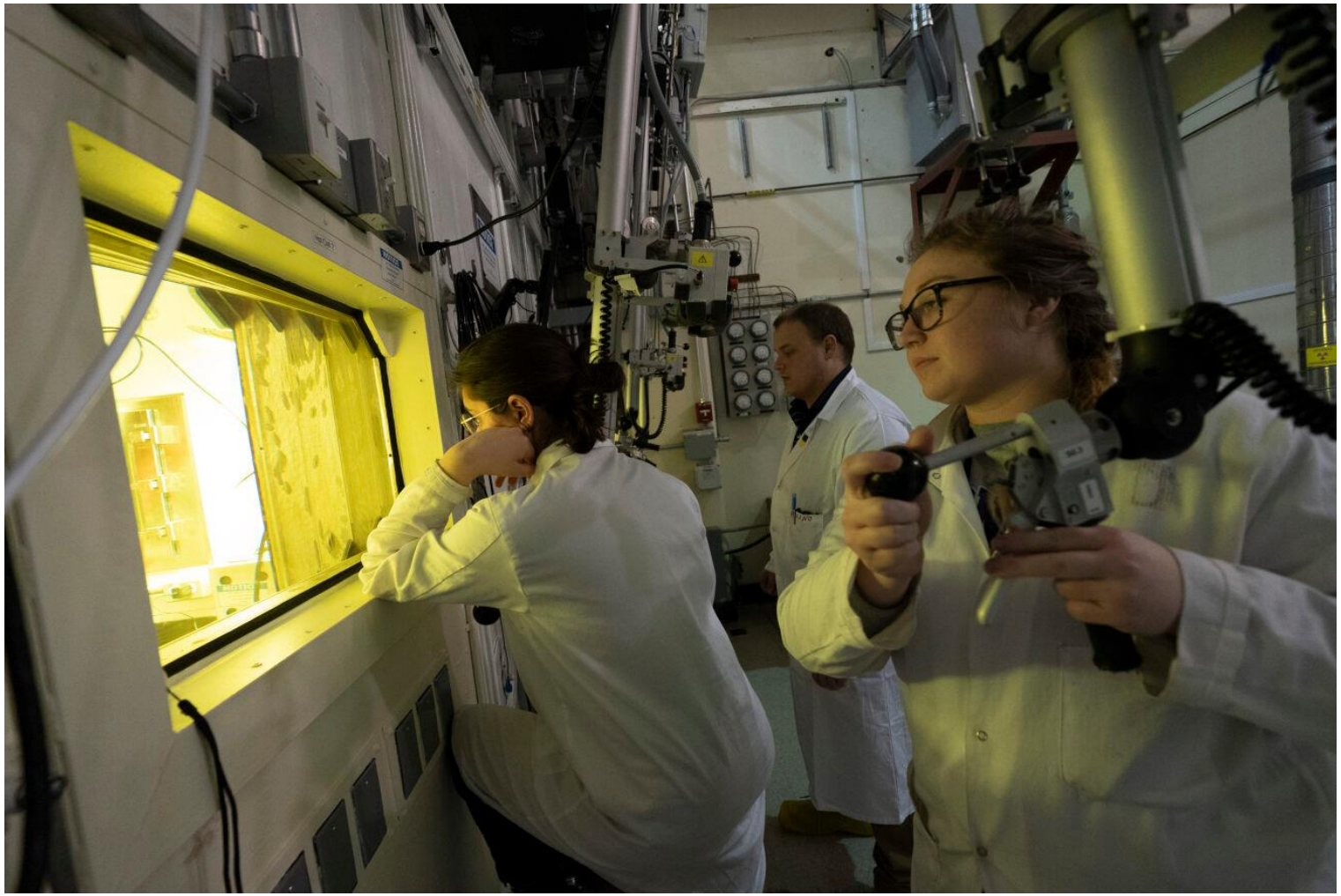
Chemical separations carried out in shielded hot boxes



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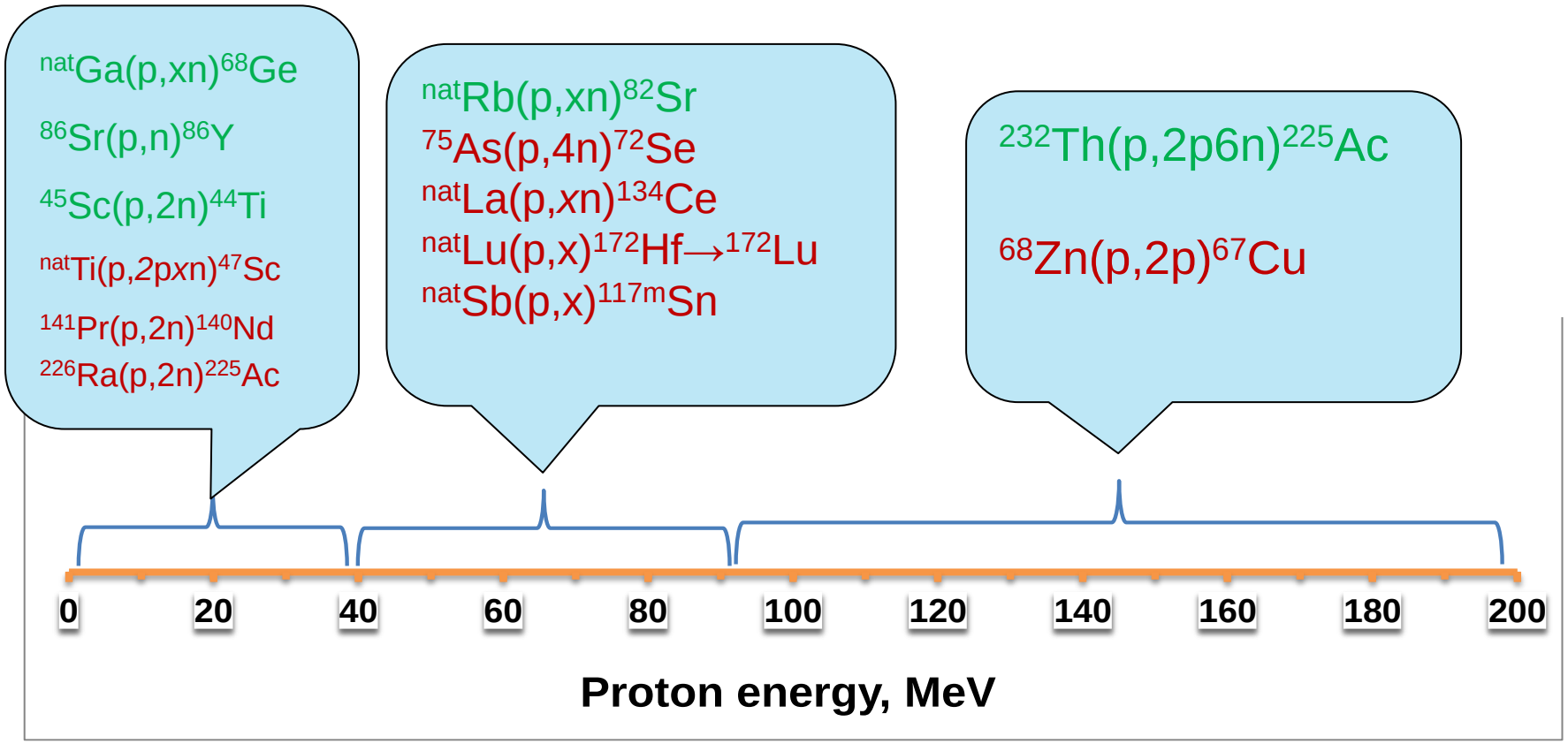
Opportunities for Isotope Production and R&D at IP



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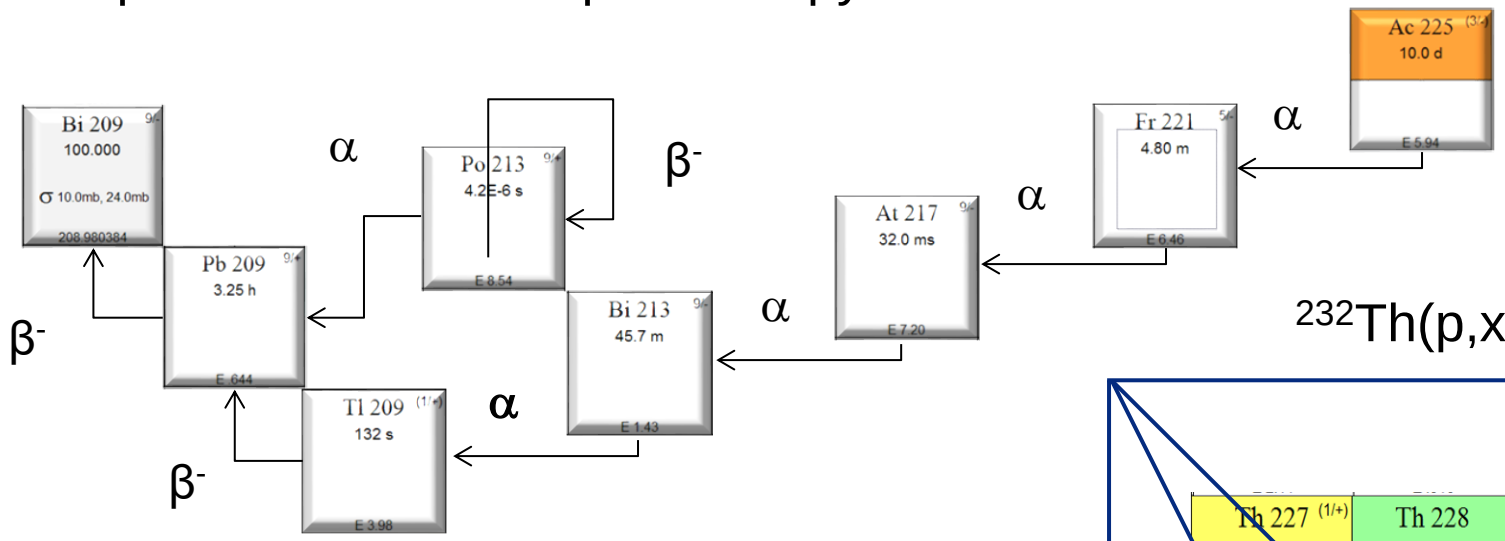
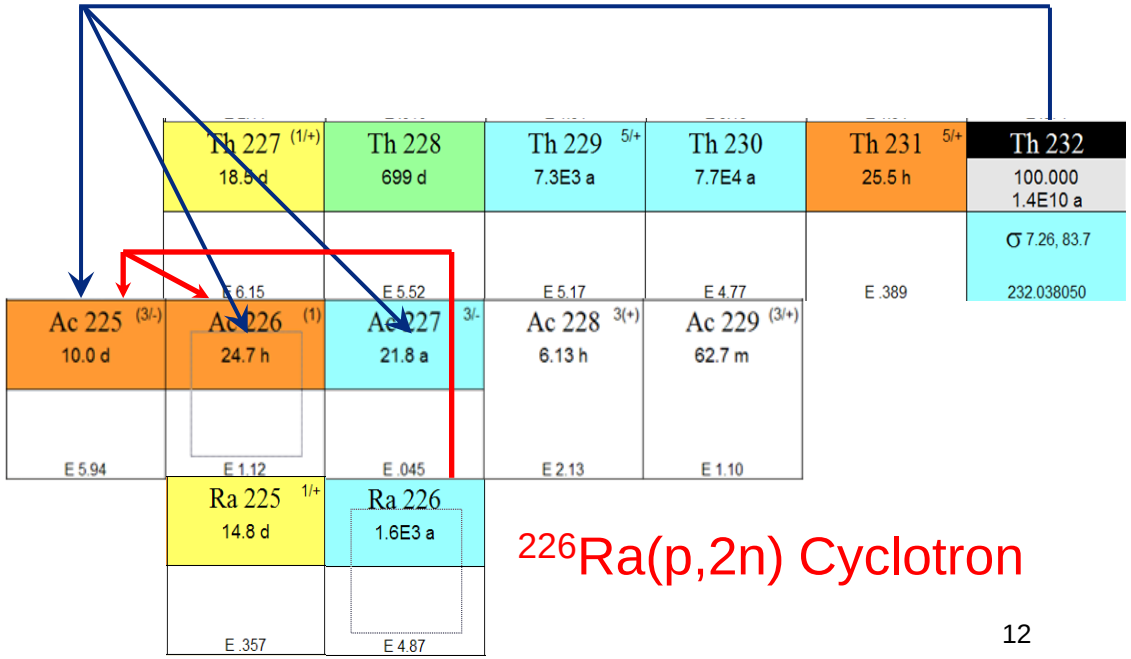
Actinium-225 nuclear data and applications

Ac-225 is an alpha emitter, $T_{1/2}$=10 d, whose decay produces 4 alpha particles – potent nuclide for alpha therapy



Ac-225 is a parent nuclide for Bi-213 ($T_{1/2}$=45.7 min) in an Ac-225/Bi-213 generator pair. Bi-213 radio therapeutic alpha emitter; also emits gamma ray suitable for SPECT imaging Eγ=440 keV, 27.3%

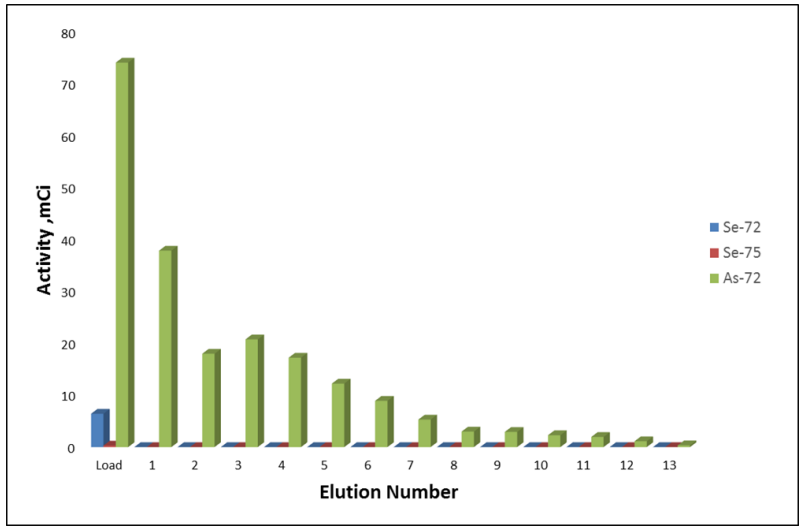
^{232}Th(p,x) BLIP



^{226}Ra(p,2n) Cyclotron

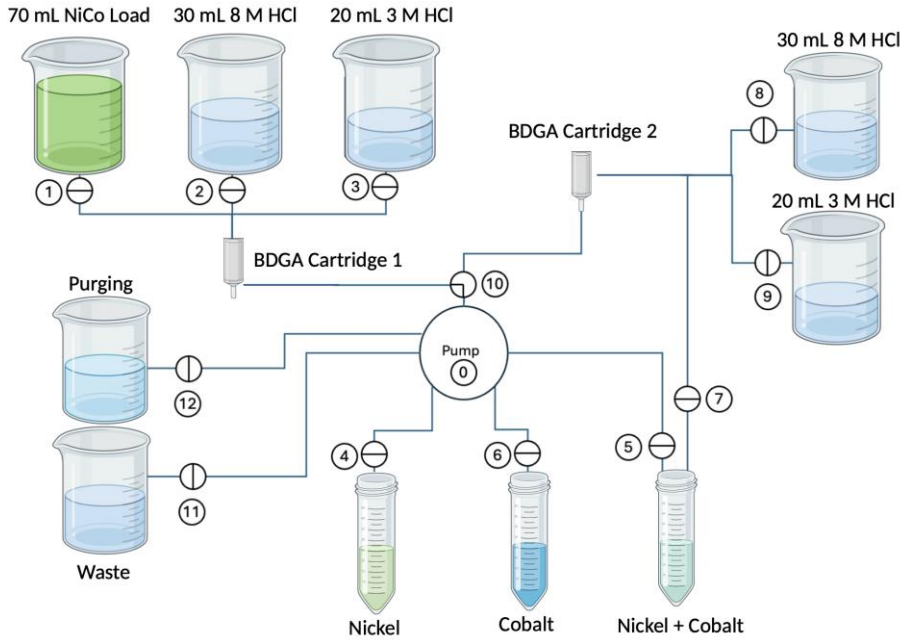
Opportunities within MIRP - Generator Development

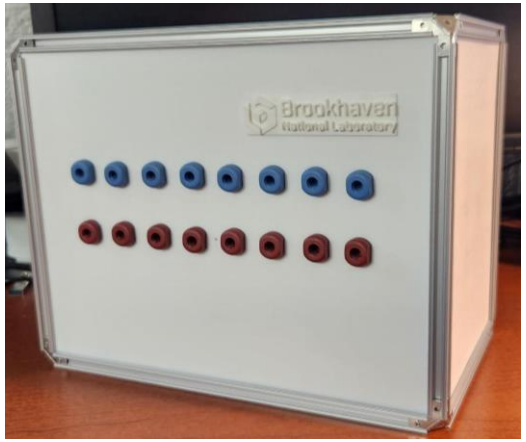
- A device that allows for the production of a short-lived radioisotope (daughter) following the decay of a long-lived radioisotope (parent)
  - Easily transportable
- It allows for the use of shorter-lived radioisotopes without the need for a production facility (i.e. cyclotron) within a close proximity.
- Uses adsorbent material which has strong affinity for the parent nuclide and allows for simple removal of daughter nuclide
  - Ion exchange resin
  - Alumina
  - zirconia



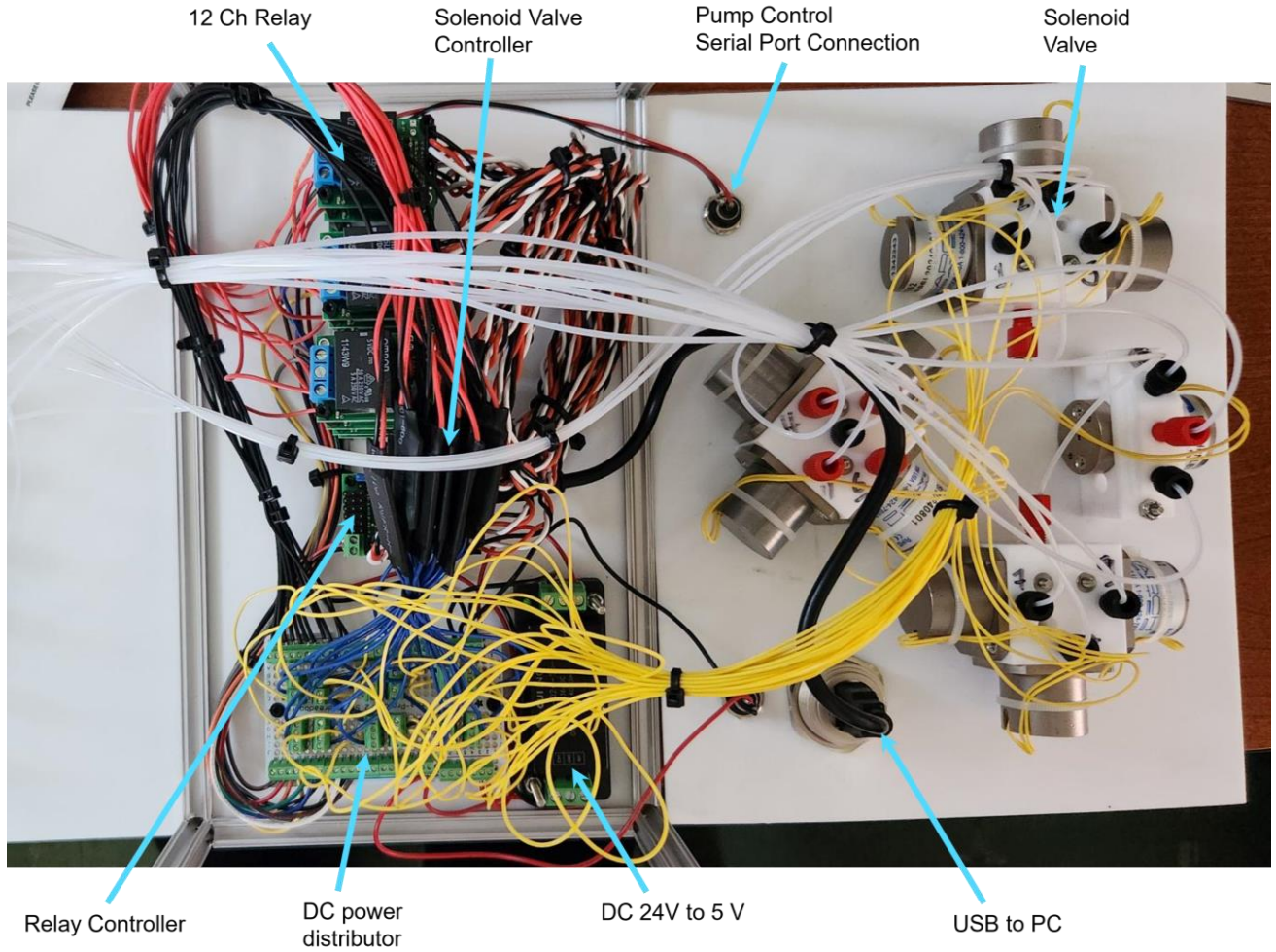
Generator System	Parent Nuclide	Daughter Nuclide		Application
	Half-life	Half-life	Decay Mode	
Ti-44/Sc-44	60 y	3.97 h	β^+	PET
Se-72/As-72	8.4 d h	26.0 h	β^+	PET
Ce-134/La-134	3.2 d	6.5 m	β^+	PET
Rn-211/At-211	14.6 h	7.2 h	α	Therapy
Pb-212/Bi-212	10.6 h	60.6 m	α	Therapy
Ac-225/Bi-213	10.0 d	45.6 m	β^-	Therapy

Co-Ni Separations Automation





In
Out



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AI/ML: Entity Recognition

2. Materials and methods

Optima grade hydrochloric acid (32–35% HCl) comes from Aristar Ultra, VWR (West Chester, PA). Ethanol, 200 proof, and L-Ascorbic acid (TraceSELECT, > 99.9998%) and 28% ammonium hydroxide solution in H_2O (NH_4OH, ≥ 99.99% trace metals) were purchased from Sigma-Aldrich (St. Louis, MO). The chelators NOTA (1,4,7-triazacyclononane-1,4,7-triacetic acid), DOTA (1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid) and TETA (1,4,8,11-tetraazacyclotetradecane-1,4,8,11-tetraacetic acid) were purchased from Macrocyclics (Dallas, TX). The chelator HBED (N,N′-Di(2-hydroxybenzyl)ethylenediamine-N,N′-diacetic acid) comes from Strem Chemicals (Newburyport, MA). Isotopically enriched ^{54}Fe (99.93% ^{54}Fe, 0.06% ^{56}Fe, 0.005% ^{57}Fe, 0.005% ^{58}Fe), ^{57}Fe (95.06% ^{57}Fe, 0.04% ^{54}Fe, 3.06% ^{56}Fe, 1.86% ^{58}Fe) and ^{58}Ni (99.48% ^{58}Ni, 0.505% ^{60}Ni, 0.005% ^{61}Ni, 0.005% ^{62}Ni, 0.005% ^{64}Ni) were purchased from ISOFLEX (San Francisco, CA). Silver disks (1.90 cm diameter × 0.56 mm thickness) were obtained from Artisan Jewelers (Sarasota, FL). Platinum wire (99.997%, 0.25 mm diameter) and ammonium oxalate monohydrate (99.0–101.0%) were purchased from Alfa Aesar (Ward Hill, MA). Radionuclidically pure $^{64}CuCl_2$ in 5 μL 0.1 M HCl (~ 400 MBq at end of bombardment) was obtained from the weekly batch that is distributed nation-wide by the Cyclotron Group of the Medical Physics Department at the University of Wisconsin-Madison. 99% 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid (HEPES) was purchased from Acros Organics. Sodium hydroxide (1 M) solution was prepared from NaOH pellets from Fisher Scientific. Trace metal grade sulfuric acid, ammonium acetate and methanol were also purchased from Fisher Scientific (Pittsburg, PA). TLC silica gel 60 plates and iron test strips were bought from EMD Chemicals (Darmstadt, Germany). Ion exchange resin (AG1-X8) was purchased from Bio-Rad (Hercules, CA). Extraction chromatography resin DGA, branched (50–100 μm) was purchased from Eichrom (Lisle, IL). A 50 ppm multi-element standard for calibration and Agilent's 4200 Microwave Plasma Atomic Emission Spectroscopy (MP-AES) system come from Agilent Technologies (Santa Clara, CA). Deionized water (> 18 MΩ cm^{-1}) was obtained from a Milli-Q filter, Millipore (Billerica, MA). Phosphate buffer saline (PBS) was purchased from Thermo Scientific.

2.1. Cyclotron targetry, irradiations and target yields

The electroplating procedure for iron was an adaptation of the methodology reported by Vosburgh et al. (1948). Briefly, 62.2 ± 10.8 mg of ^{54}Fe (n = 13) or 81.0 ± 7.6 mg of ^{57}Fe (n = 6) metallic powder were dissolved in 5 mL 6 M HCl, the Fe ions were turned to oxidation state 3+ by the addition of 100 μL 30% H_2O_2 and the solution was evaporated to near dryness (< 1 mL). The residue was diluted with 15 mL of saturated ammonium oxalate (concentration ~ 44 mg/mL H_2O) followed by a pH adjustment to between 2 and 3 with either 1 M NaOH or 1 M HCl.

The electroplating procedure for nickel was very similar to the one previously reported for production of ^{64}Cu from ^{64}Ni targets (Avila-Rodriguez et al., 2007; McCarthy et al., 1997; Piel et al., 1992). Briefly, 100.0–196.8 mg of isotopically enriched metallic ^{58}Ni powder (n = 4) was dissolved in 6 M HNO_3, dried down and re-dissolved in 2.3 mL of 2.4 M H_2SO_4 followed by adjustment to pH ~9 with 1.5–1.8 mL of 28%

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Legend
- (Unstable) Isotope
- Element(or Compound)
- Unit
- Other Keyword
- Resin

2. Materials And Methods

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National Nuclear and Radiochemistry Summer School (NCSS)

- An intensive six-week Summer School in Nuclear and Radiochemistry for undergraduates.
- Sponsored by the Division of Nuclear Chemistry and Technology of the American Chemical Society (ACS DNC&T) and funding by the U.S. Department of Energy.
- Provide fundamental training in nuclear and radiochemistry principles, particularly to physical science and engineering students from institutions that do not have such programs.
- 11 students selected for each site primarily from institutions that do not offer nuclear studies
- ~48% of NCSS students continue to graduate studies in nuclear science.