Radioisotope Research and Production at Brookhaven Linac Isotope Producer

Suzanne V Smith

Production Manager

Medical Isotope Research and Production Program (MIRP)

Collider Accelerator Department

Brookhaven National Laboratory, USA

suzanne@bnl.gov

NNDCA 27 May 2015

BROOKHAVEN NATIONAL LABORATORY

a passion for discovery

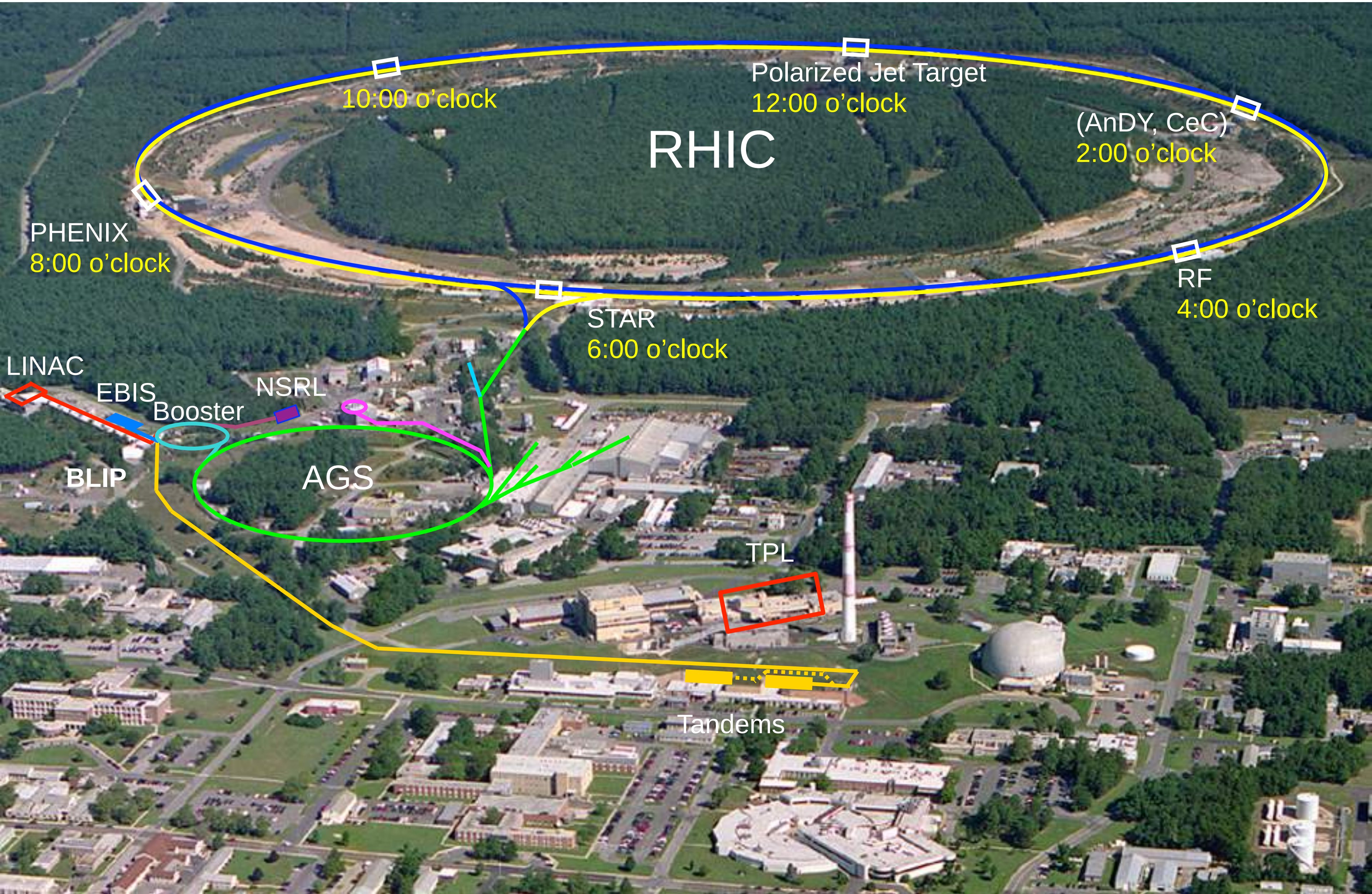
U.S. DEPARTMENT OF ENERGY | Office of Science

- MIRP Program Goals and Brookhaven Linac Isotope Producer (BLIP)
- Next Generation of Radioisotopes.
- Nuclear Data needs

Goals For MIRP Program

1. **Supply ^{82}Sr active pharmaceutical ingredient (API) compliant with current Good Manufacturing Practices (cGMP).**
2. Supply **selected radioisotopes** (such as ^{55}Fe and ^{83}Rb etc) of **national interest** based on guidance from DOE Isotope Program and the National Isotope Development Center (NIDC).
3. Support R & D national effort for **large-scale production of ^{225}Ac**.
4. **R & D into new radioisotopes for theranositc and radiotherapeutic applications**.
5. Provide **irradiation services for radiation damage studies** in support of Long Baseline Neutrino Beam project at Fermilab, the Facility for Rare Isotope Beams (FRIB) at Michigan State University and the CERN Large Hadron Collider (LHC) in Europe (LARP program).
6. Maintain and upgrade the accelerator, hot cell and laboratory infrastructure to meet the demands for goals 1 – 5.

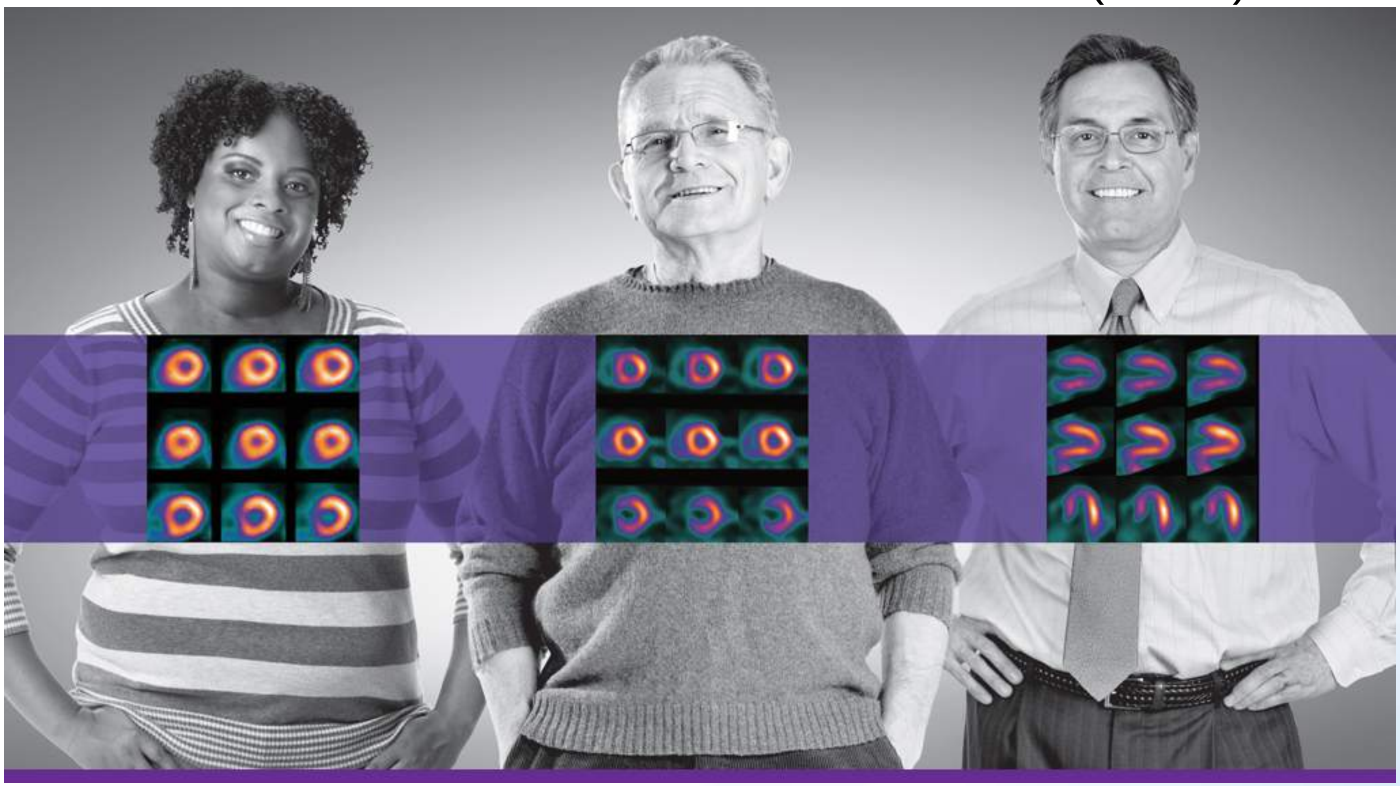
High energy accelerator – Relativistic Heavy Ion Collider (RHIC)



Strontium-82 for $^{82}Sr/^{82}Rb$ generators

$$^{82}Sr \xrightarrow{25.5\ \text{days}} {}^{82}Rb \xrightarrow{75\ \text{sec}} {}^{82}K_{(\text{stable})}$$

Cardiac PET Imaging



Patient Dose 30-60 mCi - $^{82}RbCl$

Radiocontaminates ^{82}Sr, ^{85}Sr, ^{83}Sr,or ^{83}Rb quantification important

Brookhaven Linac Isotope Producer (BLIP)

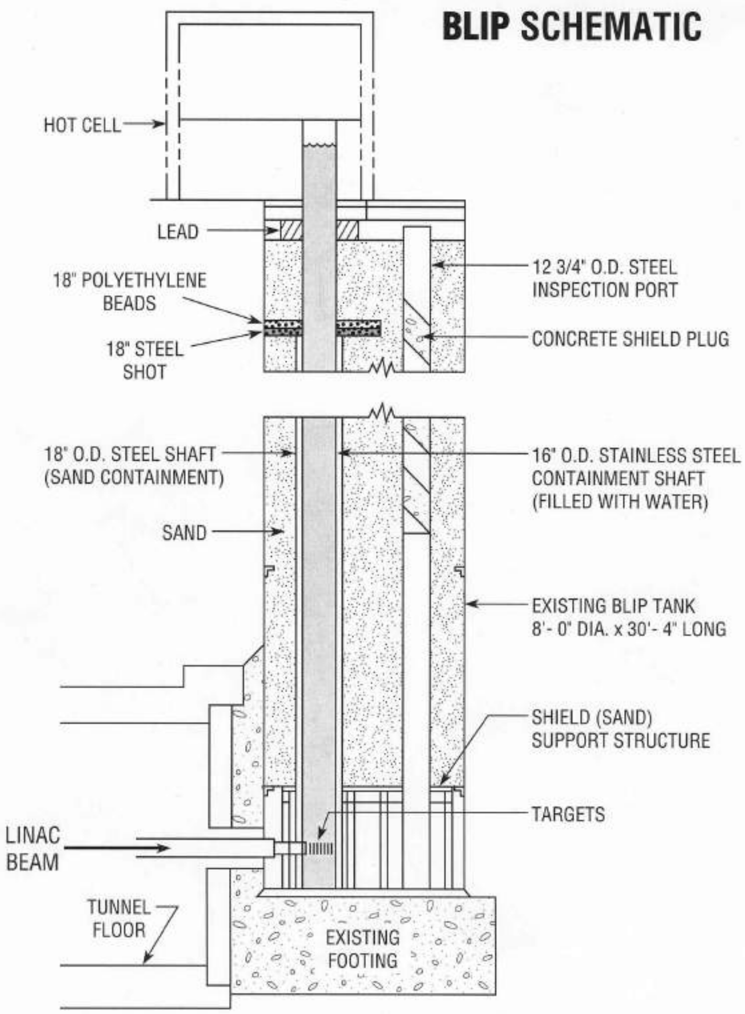
The Brookhaven Linac Isotope Producer (BLIP) was the world's first facility to seriously exploit the isotope production capabilities of a high energy proton (up to 200 MeV) accelerator. (1972)

Two upgrades last in 1994.

BLIP gets 90% of beam

RHIC – 10% of beam – BLIP runs at significant cost reduction

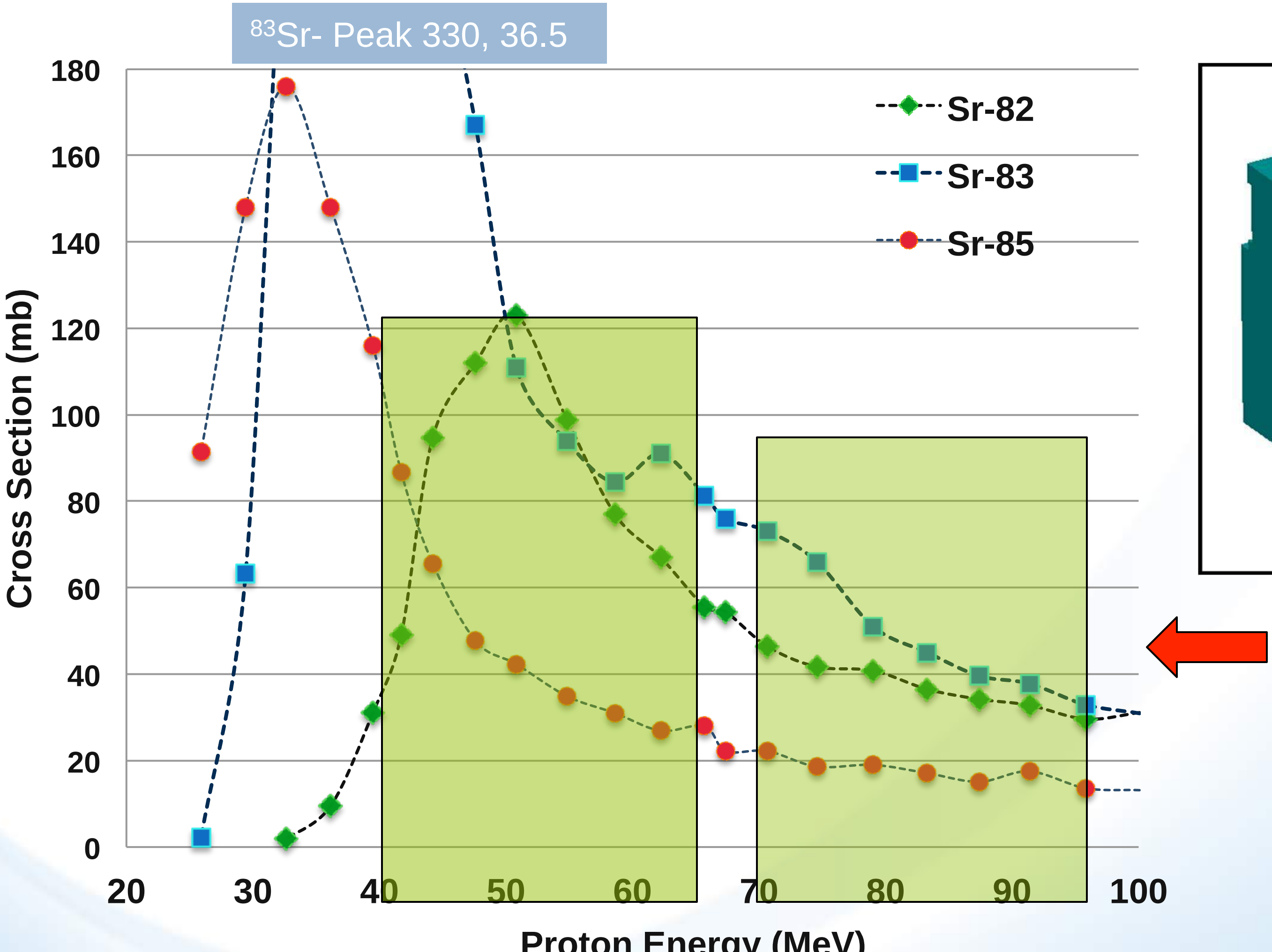
BLIP target station



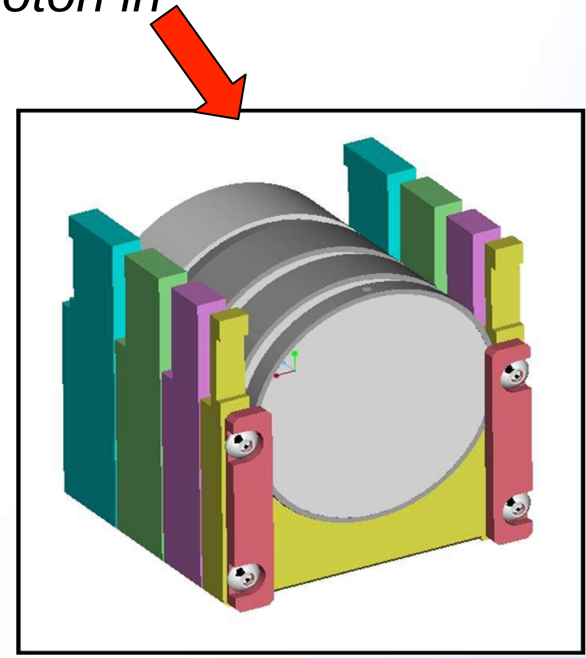
- Target position 30 feet under ground in 500 litre tank of water.
- Proton energies are fixed at 66, 90, 118, 140, 162, 184 or 200 MeV.
- The protons are accelerated in bunches at very high current (up to 45 mA) for short periods of time (400 µsecs).
- Average current – 115 µA – recently 140uA
- Tunable beam to fit target 1.0 to 2.75 inch diameter.

Manufacture of Sr-82 – Nuclear Reaction – Target RbCl

Note: rapid increase in Sr-83 production after 41 MeV



Proton in



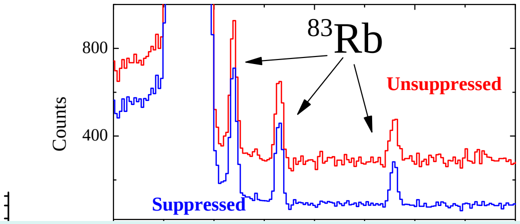
$^{nat}Rb(p,xn)^{82}Sr, ^{83}Sr, ^{85}Sr$

Compton-suppressed gamma spectrometry

Collaboration with NNDC and Uni Mass Lowell

Argonne Nat Lab – Gammasphere

^{82}Sr:^{83}Rb 100:1

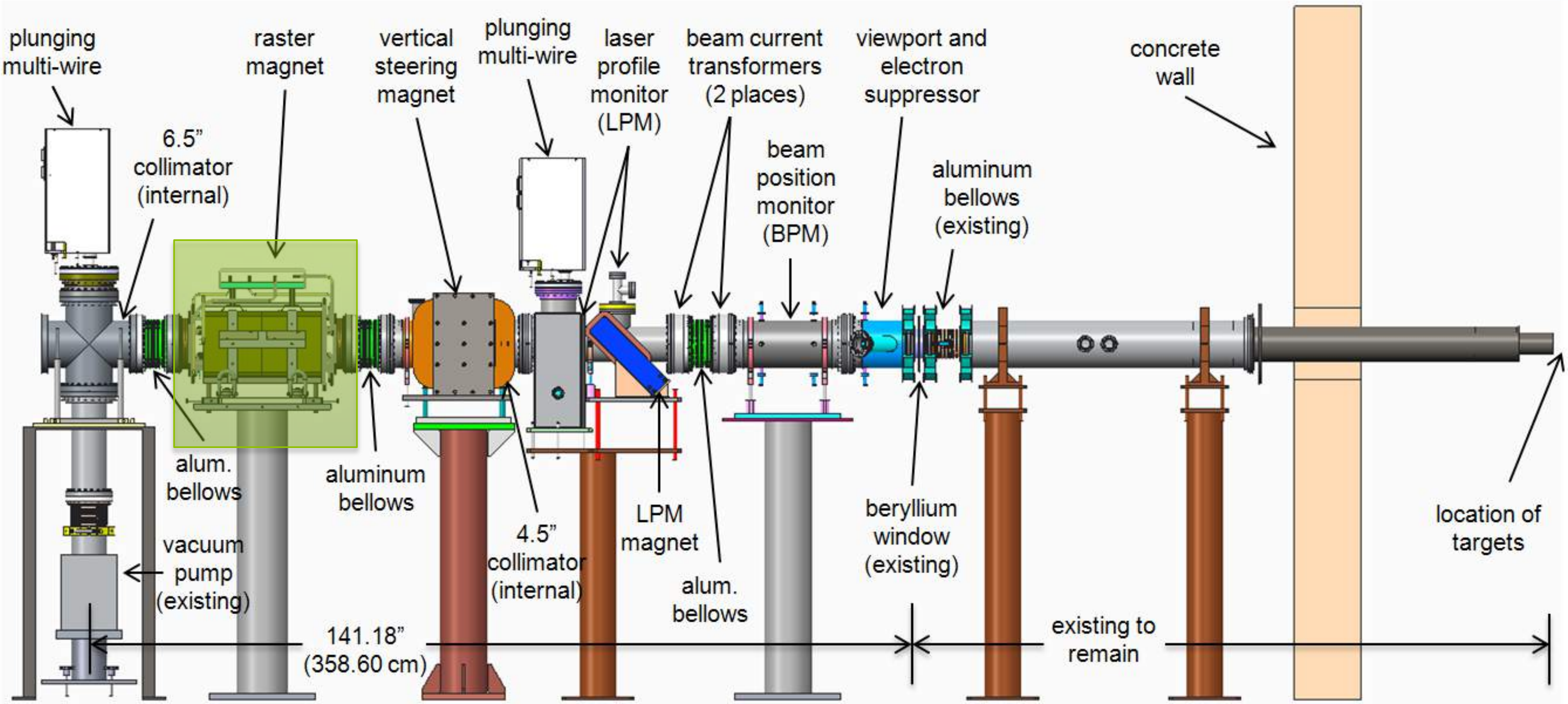


^{82}Sr:^{83}Rb 1000:1

- *Compton-suppression reduced uncertainty up to 3 fold.*
- *Commercial software over estimates Rb-83 contaminates.*
- *Compton-suppressed provided confidence in setting new thresholds, nuclide peak assignments and quantification.*
- *Reset QC performance criteria and expiry of final products*

New Raster beam-line

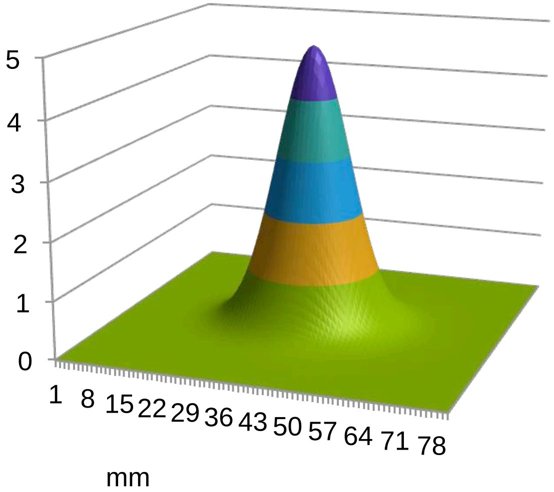
All components except raster magnet were installed Dec. 2014

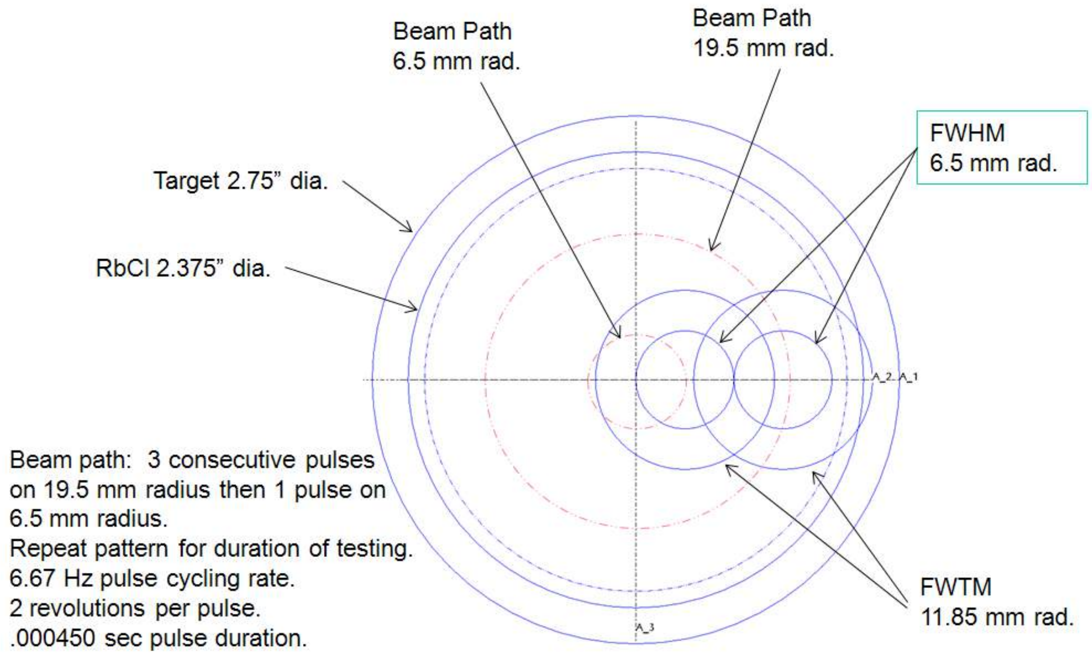


Project cost: $4.5M - completion May 2016

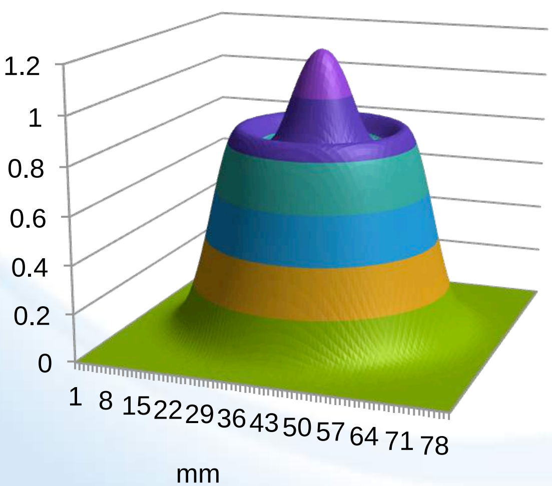
Raster motion and distribution on target

Beam distribution without raster





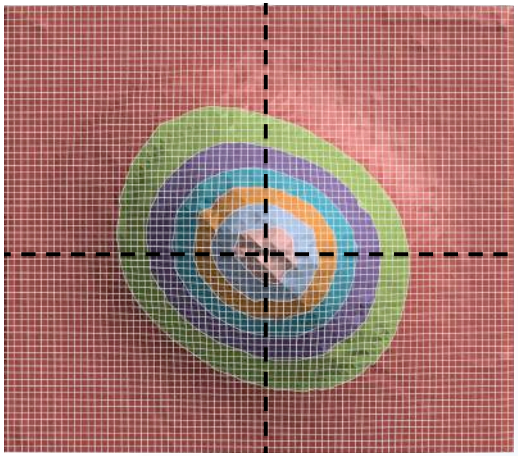
Beam distribution with raster



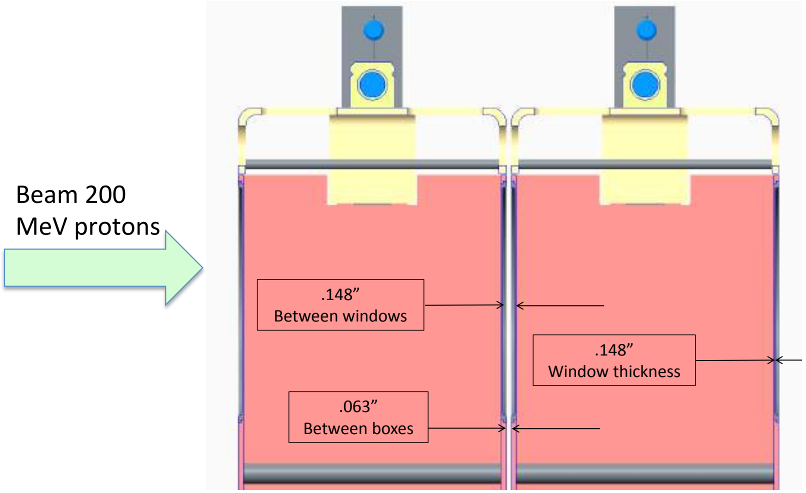
- *Beam spread over larger target area*
- *Rotation of beam spot allows for higher beam current - therefore higher yields*

Gaussian Proton Beam

NO vertical or horizontal beam monitor 2015



Vertical and horizontal beam monitors fitted allows better tuning of beam- 2015



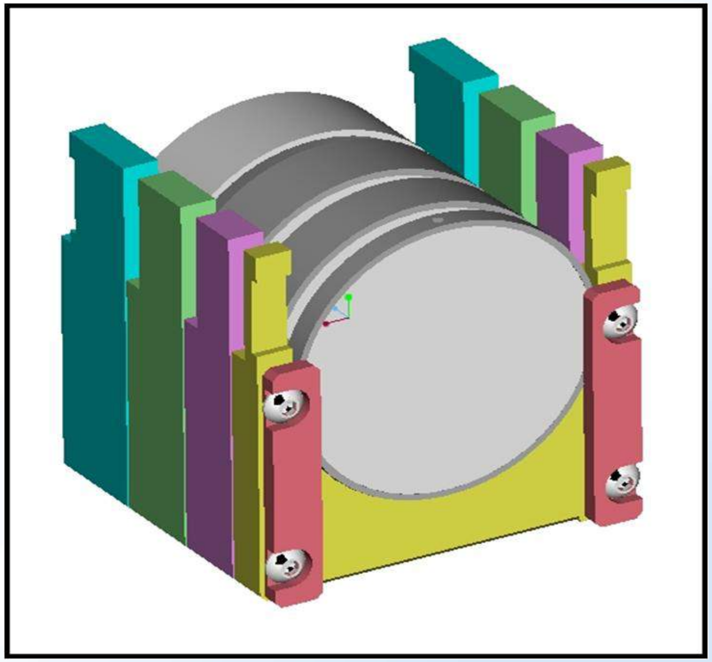
Use thin foils in clam shell holder – 5 secs irradiation to verify beam shape and current.

Research Targets – Low Impact to Sr-82

Multiple Target Array Options

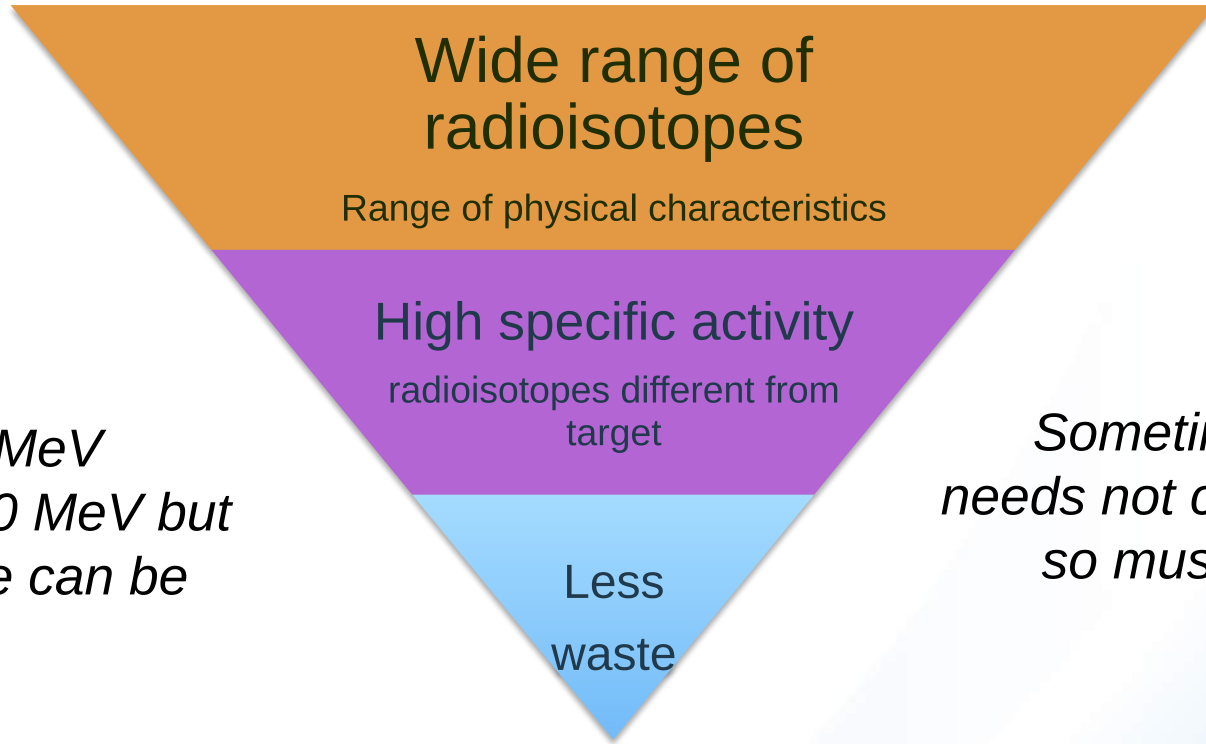
Established an Independent Safety Analysis Protocol for oversight of operations and facility modifications.

Sr-82 only		Scenario one
Sr-82 only	Research Target	Scenario Two
Research Target	Sr-82 only	*Scenario Three*
Research and Sr-82	Research Target	*Scenario Four- 2015*
Research Target	Sr-82 and Research	*Scenario Five – 2015* *Up to eight targets*



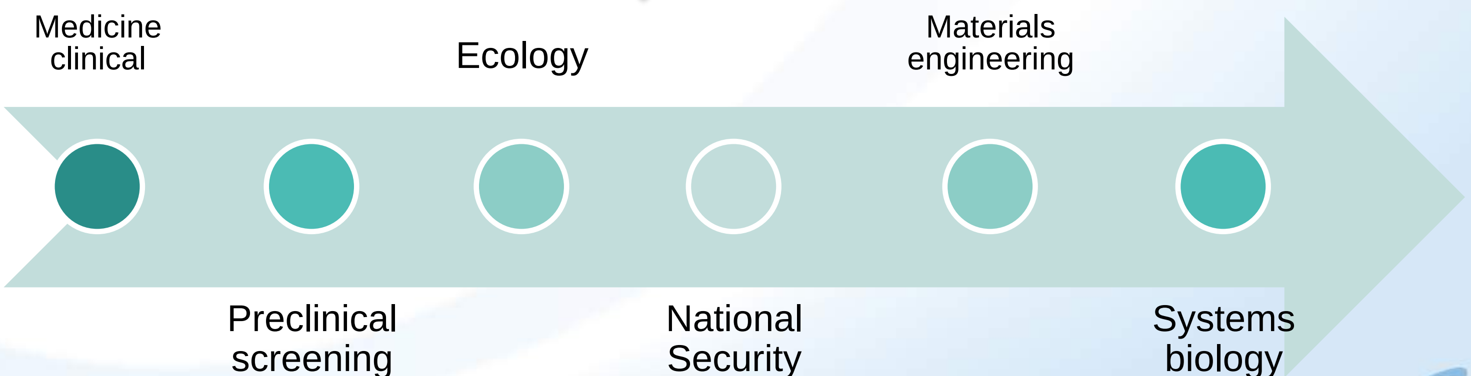
- MIRP Program Goals and Brookhaven Linac Isotope Producer (BLIP)
- **Next Generation of Radioisotopes.**
- Nuclear Data needs

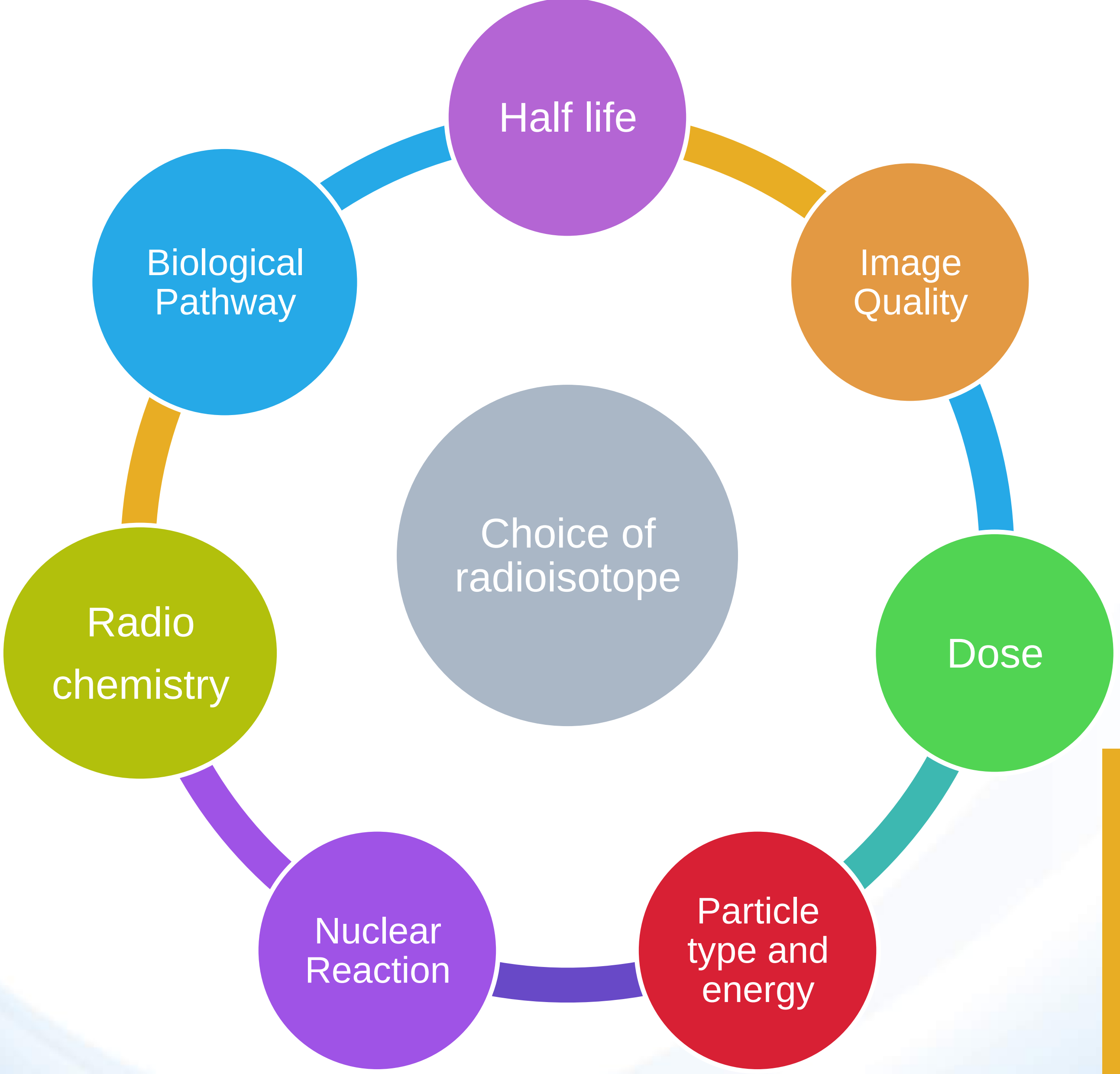
Accelerator Produced Radioisotopes



200 MeV – 66 MeV
Can do low <20 MeV but energy straggle can be challenging.

Sometimes customer needs not clearly defined so must be driven by technical data





Unique to BLIP – Thick targets and new separation methods provide for use of low cross section nuclear reactions.

Research Radioisotopes

Theranostic and Radiotherapeutic Applications (TRA)

- ***DOE Isotope Program***

  Ac-225 – alpha therapy – identified in NSAC report 2007

- ***NSAC 2014 –*** *aligns with initial feedback TRA* ✔

  Pt-191, Pt-195m and Pt-188 – drug risk assessment, personalized medicine (core R and D)

- **DOE Isotope Program – SCGCR Fellowship** ✔

  Re-186 – radiotherapy – carrier free

  Funded DOE office of Science Graduate Student Research Fellowship (SCGSR) Matt Gott - first Isotope Program

- **FOA DOE Isotope Program** – *collaboration Missouri Uni*
  - **Cu-67** – SPECT and beta radiotherapy (FOA DOE Isotope Program funded – Dennis Phillips) ✔
  - **Se-72** – Generator option for **As-72** positron emitter.

Platinum Radioisotopes

- Over 25% cancer patients received platinum chemotherapeutic agents in combination other agents or radiation (first and second line treatment.
- New knowledge on intrinsic and acquired drug resistance – drug development applications
- Many platinum isotopes with range of half lives and emissions.

Radionuclides	Half-life	Imageable Eγ (Iγ %)	Radiotherapy
^{188}Pt	10.2 d	187.59 (19.4); 195.05 (18.6); 381.43 (7.5); 423.5 (4.36)	
^{191}Pt	2.802 d	96.52(3.3);129.4(3.2);172.19(3.7);351.17 (3.4); 359.88 (6.0);409.44 (8.0); 538.87 (13.7)	
^{193m}Pt	4.33 d		Beta
^{195m}Pt	4.02 d	98.9 (11.40);129.79 (2.83)	Auger
^{197}Pt	0.83 d	77.58 (17.0); 191.44 (3.7)	Beta

Platinum Radioisotopes

NNDC

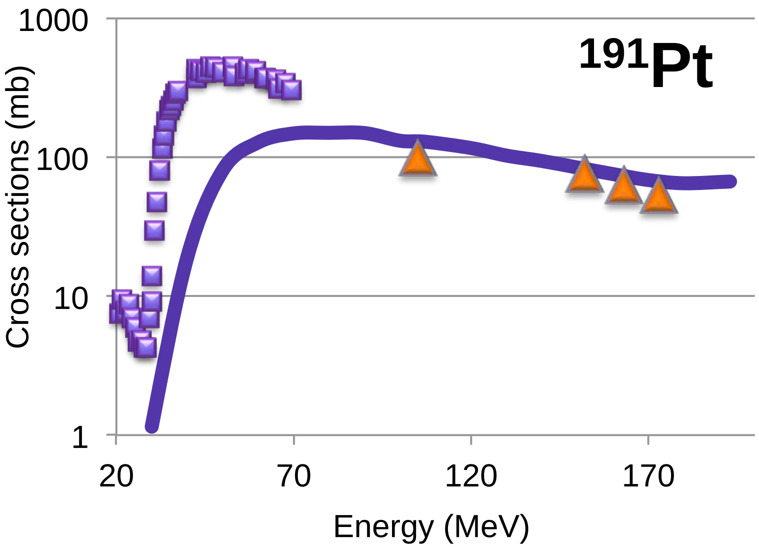
Irradiated platinum foils varying proton energies 193 – 105 MeV. Digest in aqua regia and HCl.

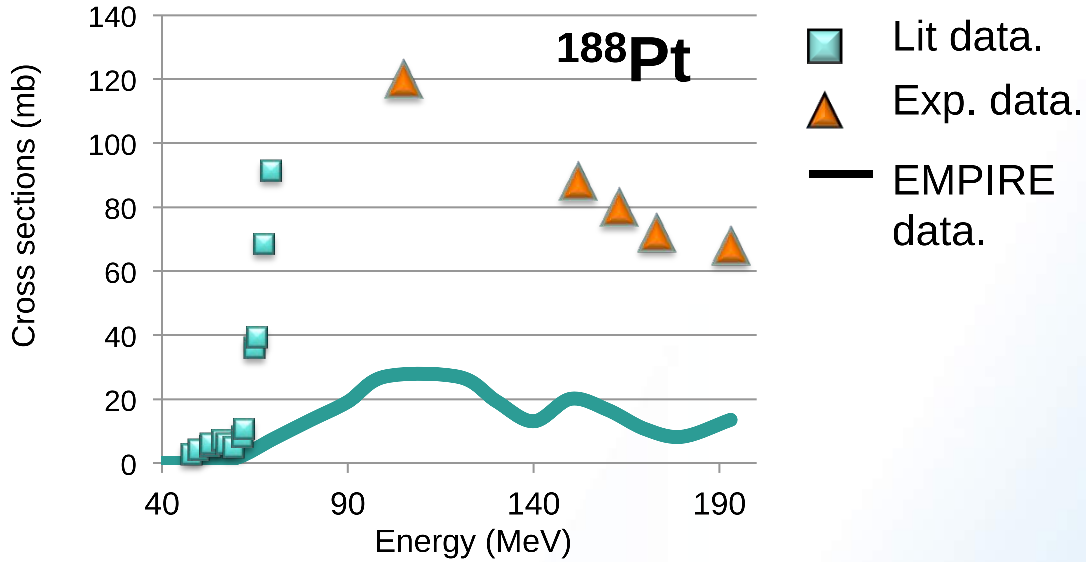
Unsuppressed and Compton-suppressed gamma-ray spectroscopy were used to assign radionuclides present.

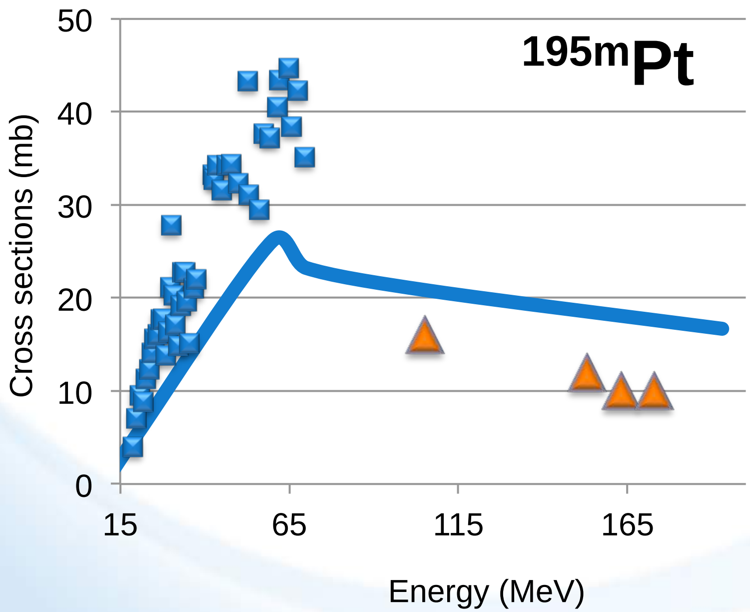
Samples were analyzed for a wide range of radioisotopes (i.e. ^{188,189,191,195}**Pt;** ^{191,192,193,194,195,196m,g,196m2,198g}**Au;** ^{186,188,189,190,192,194m}**Ir**). (over 22 isotopes and 100 gamma emissions)

The use of **Compton-suppressed gamma-ray spectroscopy** provided significant reduction of the overall background leading to **improved quantification of the gamma-ray emissions and higher sensitivity to weak production channels.**

Comparison of theoretical and experimental data from BLIP







- Overall theoretical data compared well with literature[A] and experimental data obtained at BLIP.
- Pt-188 compares well with literature cross sections at low energies
- Data shows Platinum radioisotopes can be produced over a range of energies up to 200 MeV

A. F. Tarkanyi et al. Nucl. Instr. and Meth. in Phys. Res. B 226 (2004) 473–489

Separation of Platinum Isotopes

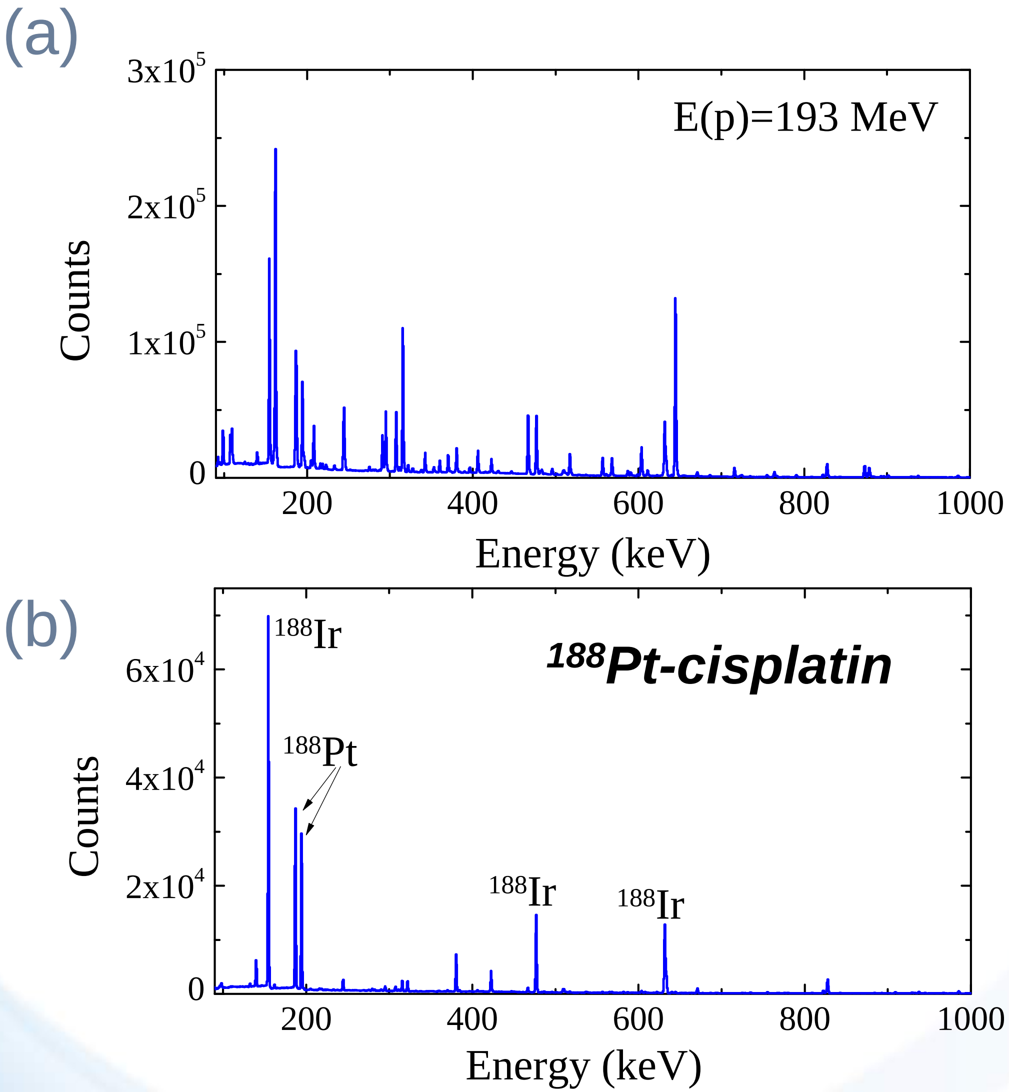


Fig. 1 Typical Compton-suppressed gamma spectra of irradiated crude (a) and purified (b) platinum foil at irradiated at 193 MeV.

- Separation of nobel metals at carrier free levels is challenging.
- Preliminary data show separation of Pt radioisotopes from large quantities of Ir and Au is feasible.
- Gammasphere and compton-suppressed gamma spectrometry for peak assignment.
- Enriched Pt foils to identify preferred reaction routes.

Rhenium-186 – *Proof of Concept*

- **Favorable β_{max}^{-} energy (1.07 MeV)** *[Lower than Re-188 β_{max}^{-} 2.1 MeV]*
- Emits a low abundance **γ-ray** (137.2 keV, 9.42%)
- Favorable **half-life** ($t_{1/2}$ = 3.718 days)
- Perrhenate (ReO_4^-) chemically analogous to pertechnetate (TcO_4^-)
- **Carrier Free Production** (60 fold higher for Accelerator vs Reactor).

DOE office of Science Graduate Student Research Fellowship (SCGSR) funded fellowship with Matt Gott from Uni Missouri- first for DOE Isotope Program

Rhenium-186 - *empirical approach*

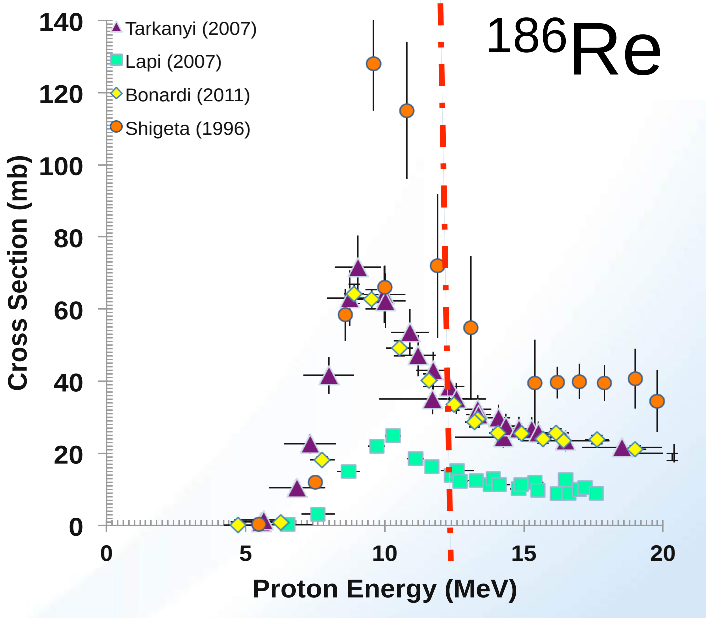


Fig. 1 Cross section for ^{186}Re production using proton on tungsten

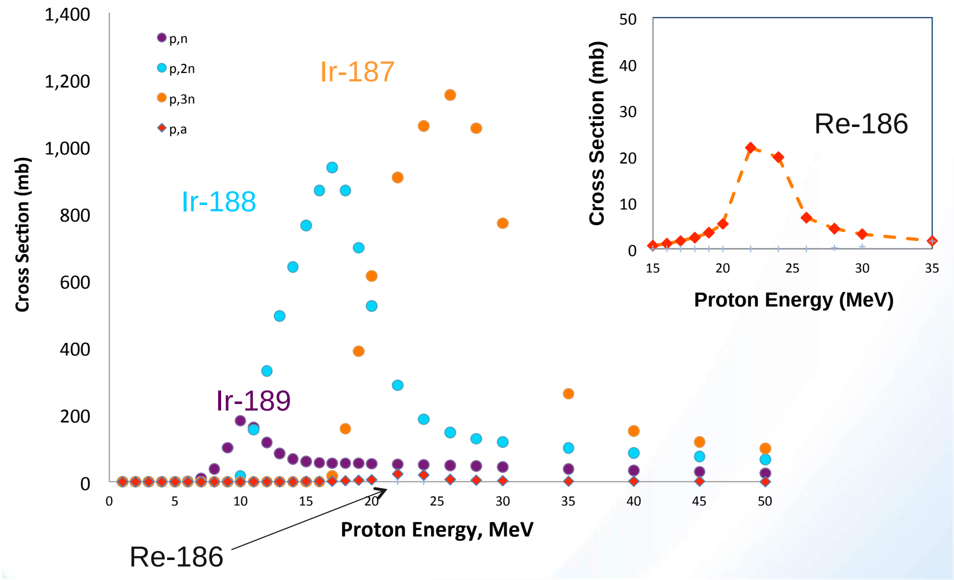


Fig.2 Theoretical Nuclear Reaction on enriched Osmium-189 from TENDL database

- Maxima for cross sections in literature are in agreement but large variation absolute values (Fig 1).
- Only TENDL data available for osmium target (Fig 2).
- Optimizing beam energy, target thickness and chemical separation is possible for favourable Re-186 production.

Se-72 and As-72 at BLIP

As-72

- half life is 26 hour.
- E_{β}^{+} = 2.5 MeV (88%)
- behaves like C and N – covalently attached to target molecules

Se-72

- parent of As-72
- half life 8.4 days
- supply as Se-72/As-72 generator.

Natural As (As-75 - 100% abund.).

Developed a new target material and target canning system for irradiation at 50 MeV

Nuclear Data Needs for R and D into New Isotopes

Key Goals

- *To capitalize on total 200 MeV beam at BLIP without compromising production –Sr-82.*
- *Enhance transfer of R & D to production.*
- *To prepare for next generation accelerators/cyclotrons*

Developed an ability to conduct feasibility studies and short irradiations

Demonstrated Compton-suppressed gamma spectrometry is essential for rapid, accurate and precise radioanalysis of radioactive samples in initial and latter stages of product development.

Gamma gamma coincidence spectra was invaluable for full characterization of irradiated material at high proton energies.

Excellent training ground for budding nuclear/radiochemistry scientists

Nuclear Data Needs for R and D of New Isotopes

Need Nuclear Data above 70 MeV for a range of materials for new isotope development.

- *Energy calibration monitors for high proton energies*
- *Chemistry - process target materials prior to gamma spectrometry*
- *Target material need to be representative of target application – engagement of material science*
- *Used for input for improving modelling codes EMPIRE.*

Dedicated 200 MeV low current beamline

Provide a training ground for budding nuclear scientists

Rapid turnaround for development of new products.