High Energy Accelerator Production of Actinium-225 at BNL

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Role of the Department of Energy

- The development of most, if not all, isotopes used in medicine was fostered by DOE or its predecessor agencies; e.g.:
  - C-14 (Oak Ridge National Lab)
  - Mo-99/Tc-99m (Brookhaven National Lab)
  - I-131 (Lawrence Berkeley National Lab)
  - Sr-90/Y-90 (ORNL)
  - F-18 FDG (BNL)
  - Pb-212/Bi-212 (Argonne National Lab)
  - Sr-82 (Los Alamos National Lab)
  - Ac-225/Bi-213 (ORNL)

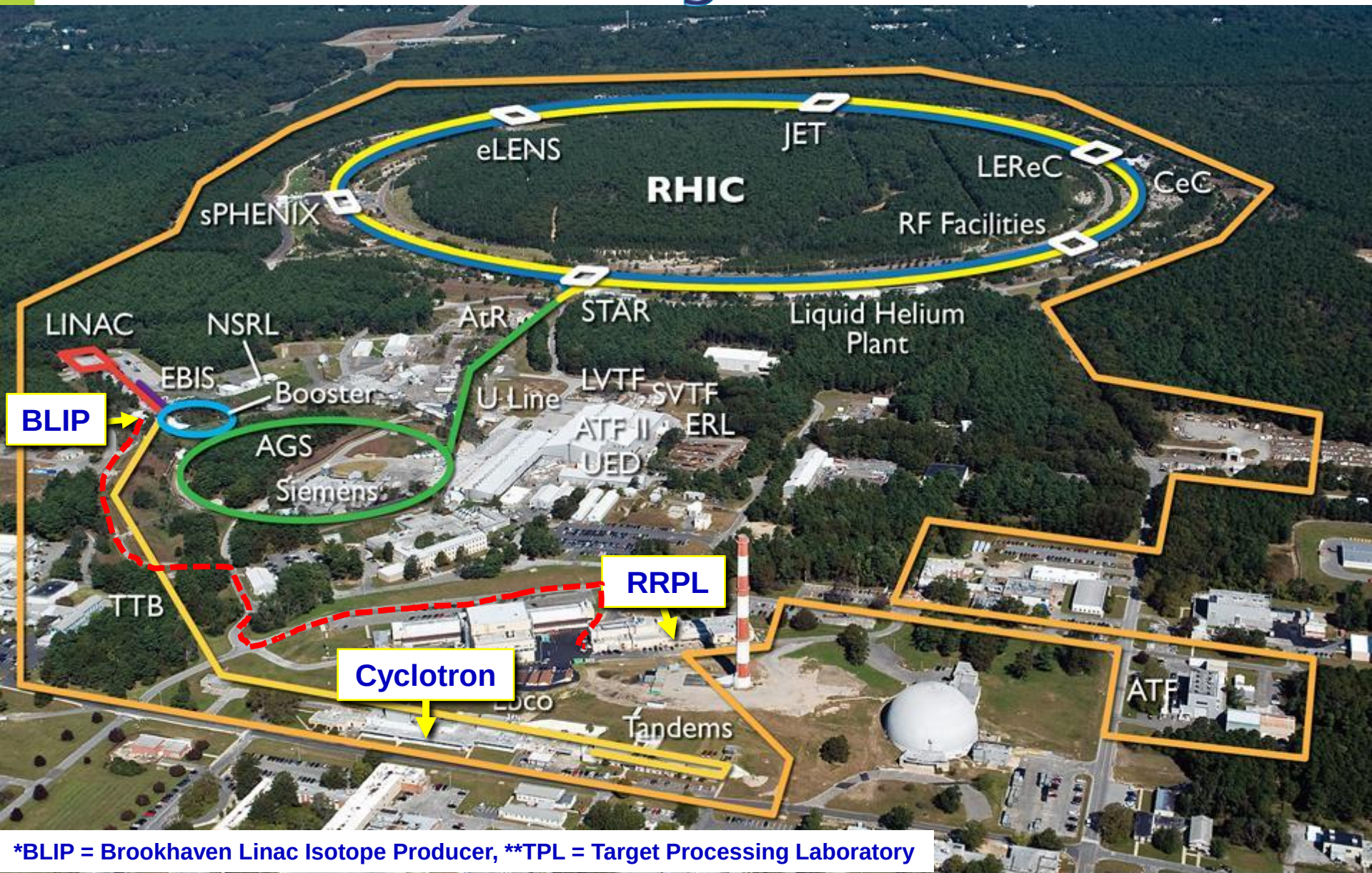
Isotope Program Missions

- Produce and/or distribute stable and radioactive isotopes that are in short supply, including valuable by-products, surplus materials and related isotope services
- Maintain the infrastructure required to produce and supply isotope products and related services
- Conduct R&D on new and improved isotope production and processing techniques which can make available new isotopes for research and applications

Attributes:

- Core R&D where there are programmatically stewarded activities
- Competitive R&D
- SBIR/STTR, Early Career Award Program
- Nuclear and Radiochemistry Summer School, Workforce Development

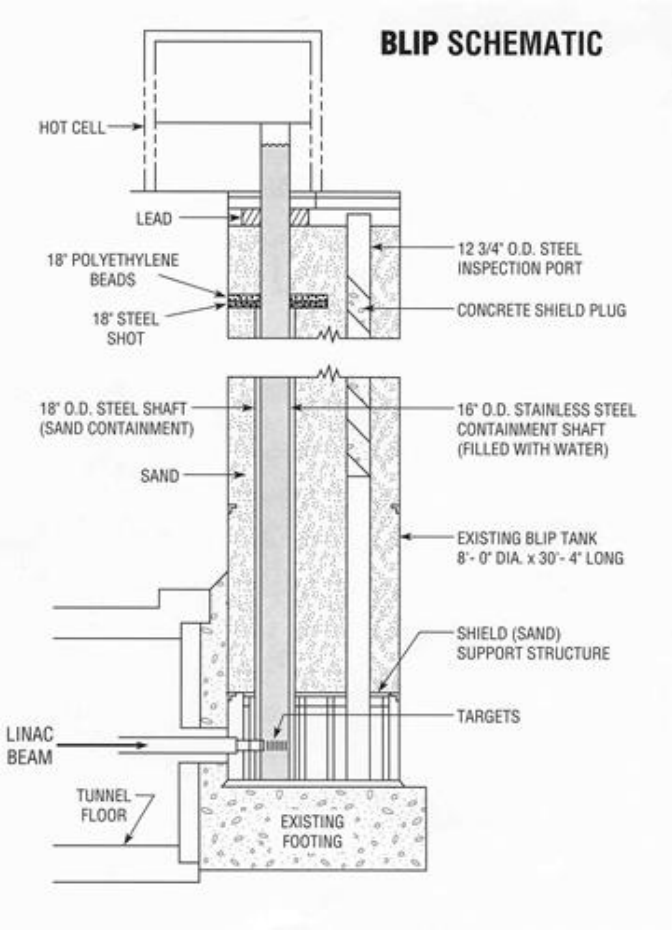
BNL Isotope Program – Aerial View of Integrated Facilities



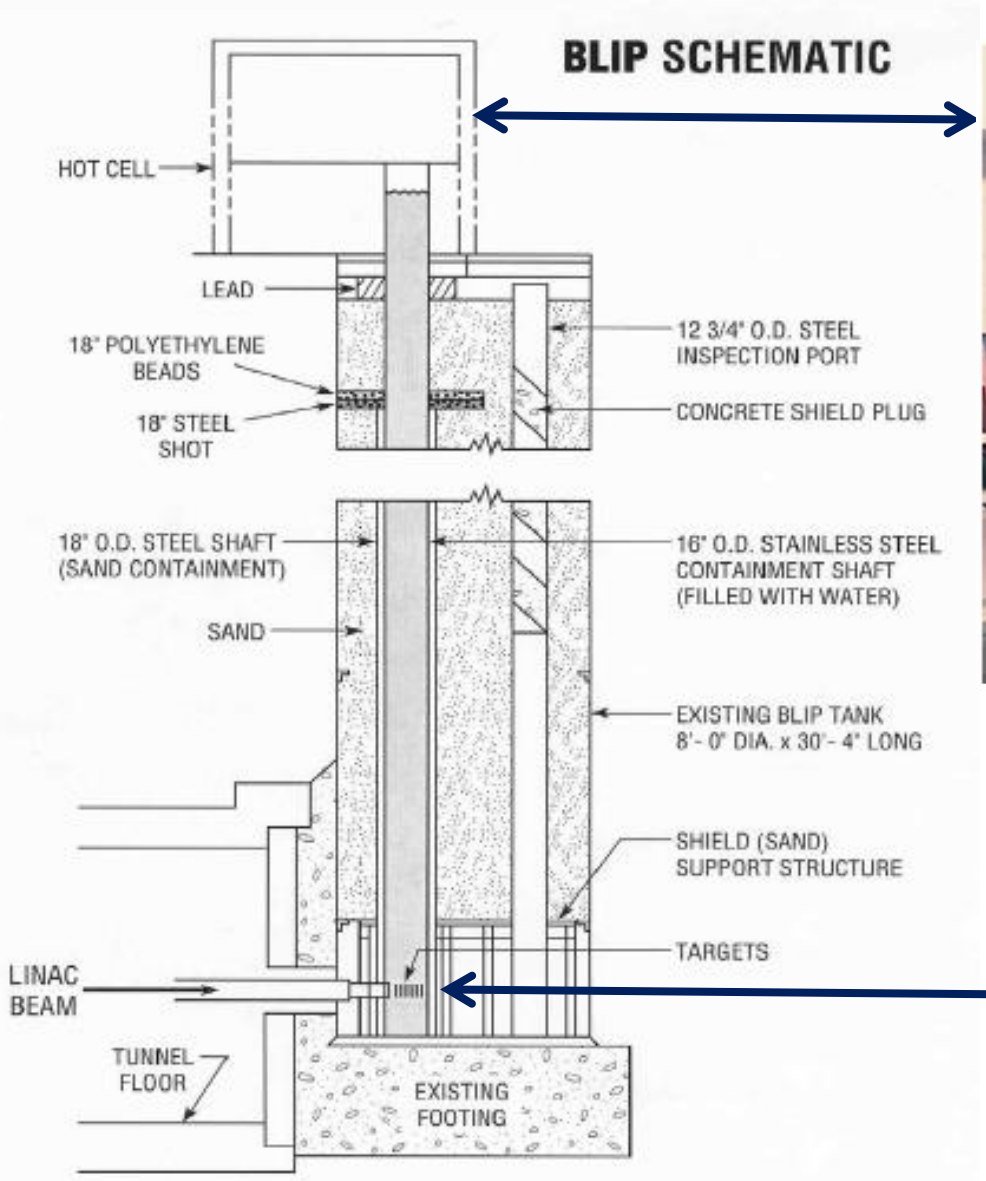
*BLIP = Brookhaven Linac Isotope Producer, **TPL = Target Processing Laboratory

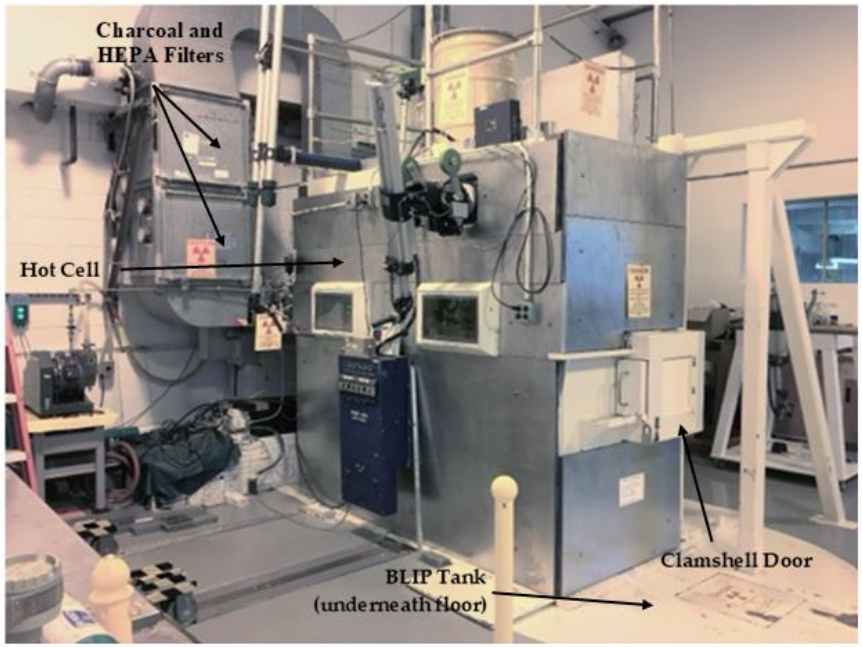
Brookhaven Linac Isotope Producer (BLIP)

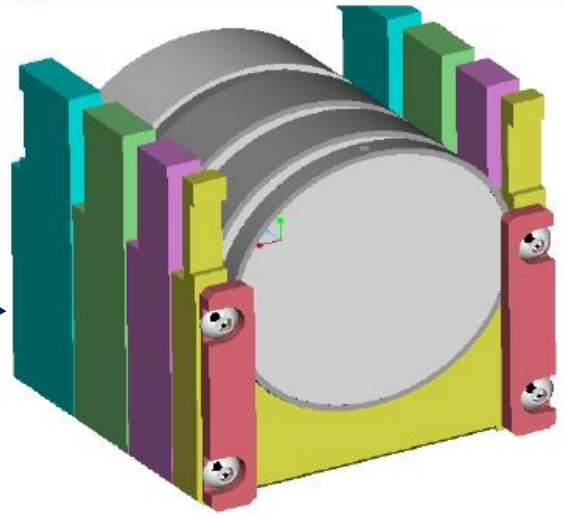
- First to use a high energy proton accelerator to produce isotopes (1972)
- BLIP utilizes the beam from the 200-MeV Linac that injects the Booster, which leads to AGS and RHIC accelerators (nuclear physics)
- Excess Booster pulses (~90%) are diverted to BLIP. Energy is incrementally variable from 66-202 MeV
- The BLIP beam line is synergistic operation with nuclear physics programs for more cost effective isotope production



Brookhaven Linear Isotope Producer







Building 801(Houses the RRPL)

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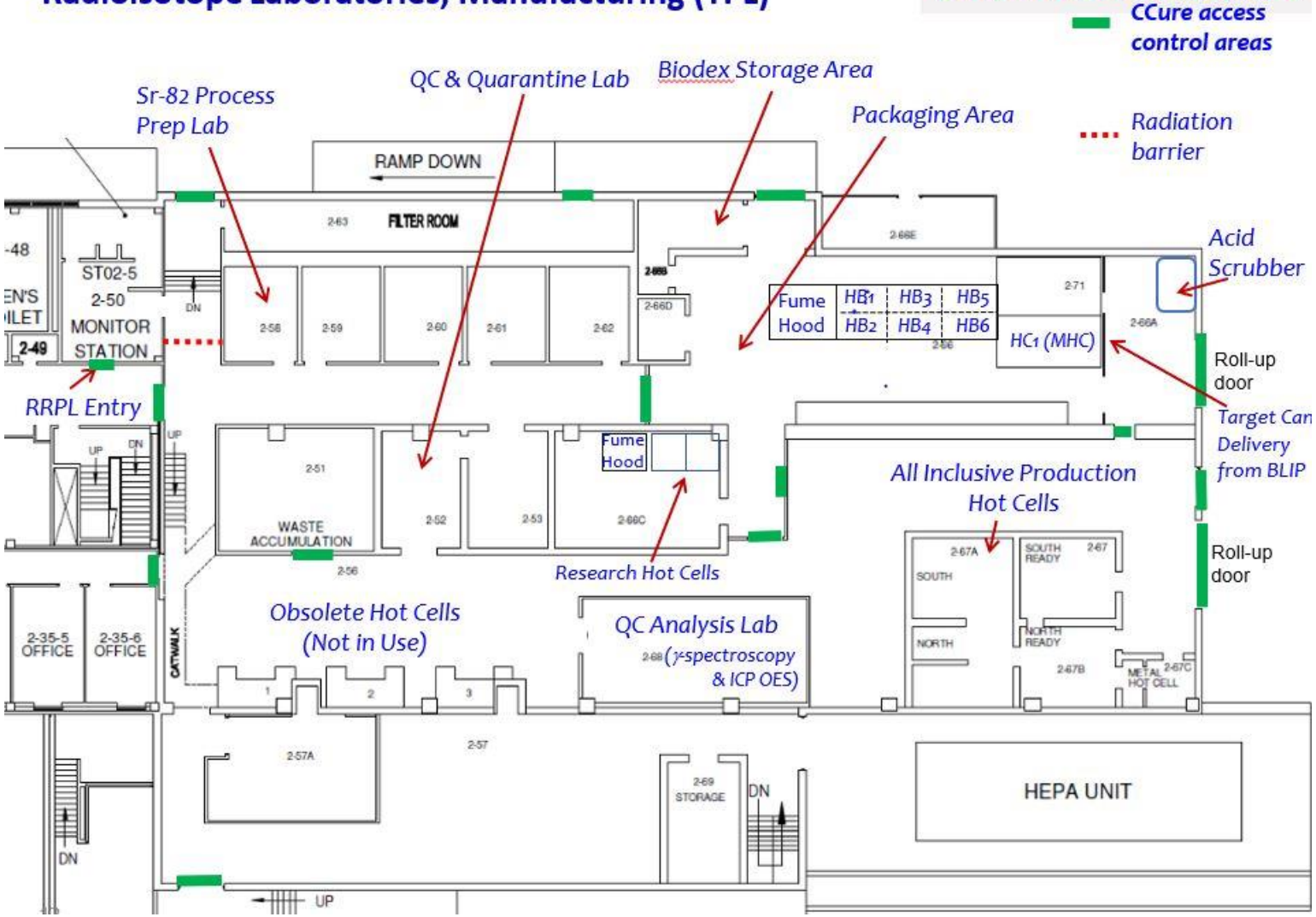
Radioisotope Laboratories, Manufacturing (TPL)

Business Sensitive



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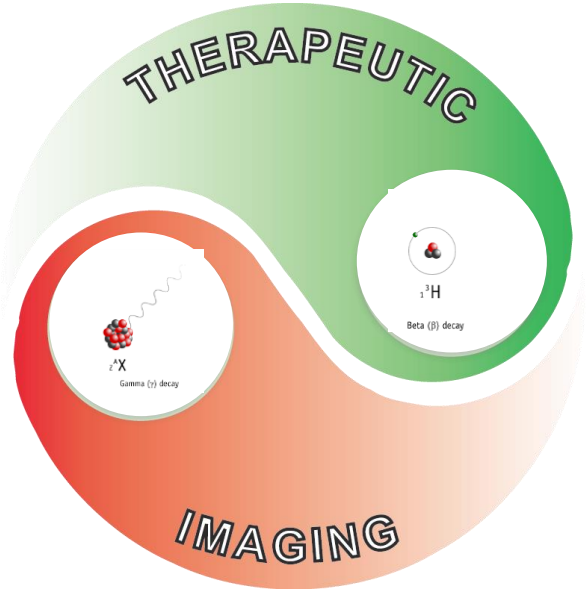
Theragnostics

- The combination of a Diagnostic tool that helps to define the right Therapeutic tool for a specific disease
- An old concept in nuclear medicine, easy to apply and to understand, because of an easy switch of radionuclide on the same vector
- Theranostics match well with the concept of Personalized Medicine: The right treatment for the right patient at the right time and at the right dose



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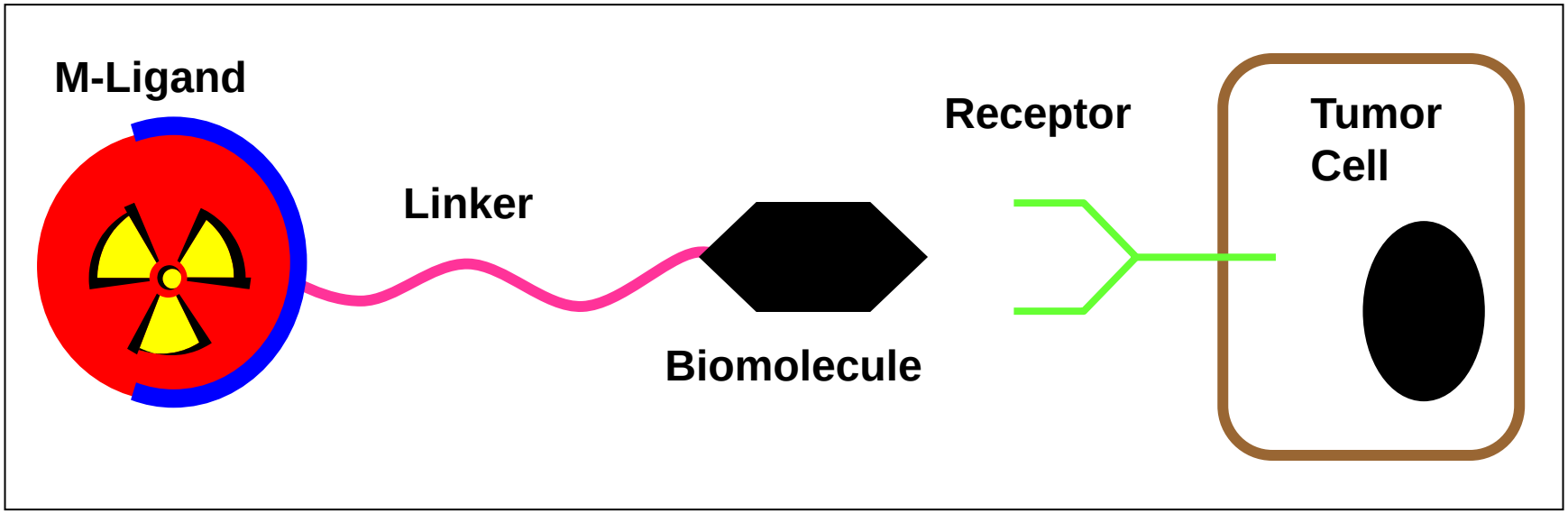
Targeted Approaches

- Bifunctional Chelating Agent
- Requires high specific activity



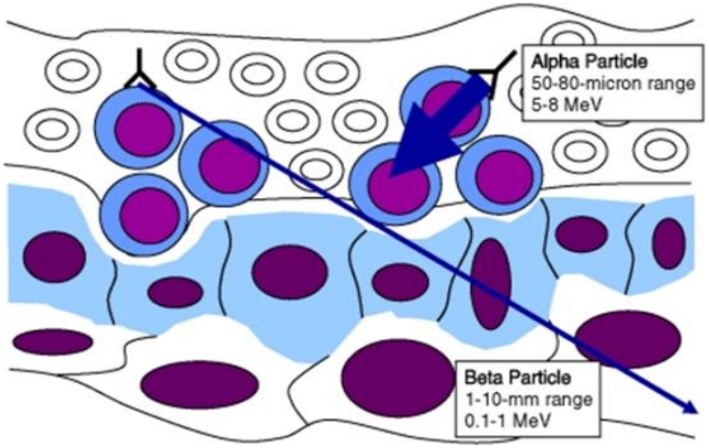
Physicochemical characteristics of β-emitters and α-emitters

β-emitters

- Intermediate LET radiation (0.50–2.30 MeV) ; long range in tissues (1–12 mm of tissue penetration).
- ß-particles range: target clusters of cells (from 10 to 1,000 cells)

α-emitters

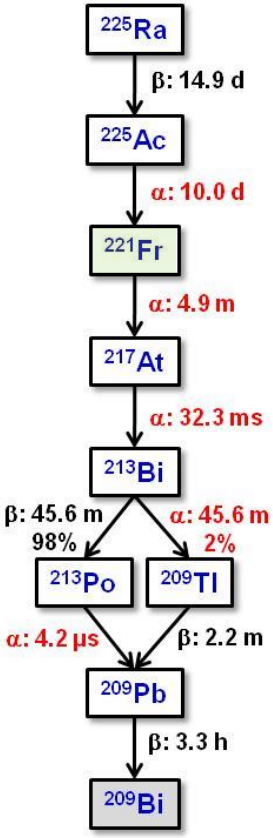
- High-LET radiation (60–230 keV/μm)
- Short to intermediate path length (^{212}Pb: 50–80 μm) in tissues
- Path length: target several cells (2–10 cells)
- High LET causes Irreversible damage of double stranded DNA



Nuclide	$T_{1/2}$	Emission	Mean path length
I-125	60.0d	auger	10nm
At-211	7.2h	alpha	65nm
Pb-212	10.6h	alpha	50-80 um (0.05-0.08mm)
Lu-177	6.7d	beta/gamma	0.7mm
Cu-67	2.58d	beta/gamma	0.7mm
I-131	8.04d	beta/gamma	0.9mm
Sm-153	1.95d	beta/gamma	1.2mm
Re-186	3.8d	beta/gamma	1.8mm
P-32	14.3d	beta	2.9mm
Re-188	17h	beta/gamma	3.5mm
In-114m	50d	beta/gamma	3.6mm
Y-90	2.67d	beta	3.9mm

Slide courtesy of Dr. M. McDevitt, Memorial Sloan Kettering

Accelerator-produced Ac-225 For Targeted Therapy



Clinical data suggests both alpha-emitting Actinium-225 (half-life 10 days) and its daughter, Bismuth-213 (half-life 45.6 min.) will be powerful isotopes for targeted alpha therapy for cancer

- Current worldwide, annual supply is 1.7 Curies per year
  - 50+ Curies/yr. required to support expanded clinical trials and drug development
- We're developing a novel accelerator-production method to address this demand
  - Tri-lab partnership (BNL, ORNL, LANL)
  - Working with clinical sites to evaluate material

ORNL Final Ac-225 Product

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OAK RIDGE National Laboratory

Los Alamos NATIONAL LABORATORY EST. 1943

Basis of the Tri-Lab Effort: Leveraging Unique DOE Isotope Program Facilities, Capabilities and Expertise to Address 225Ac Supply

LANL Isotope Production Facility (IPF) at LANSCE; 100 MeV incident energy up to 250 μA for routine production

ORNL - Approximately 20 years of experience in the isolation of ^{225}Ac from fissile ^{233}U via ^{229}Th

BNL Linac at the Brookhaven Linac Isotope Producer (BLIP) 160 μA intensity to targets at incident energies ranging from 66-202 MeV

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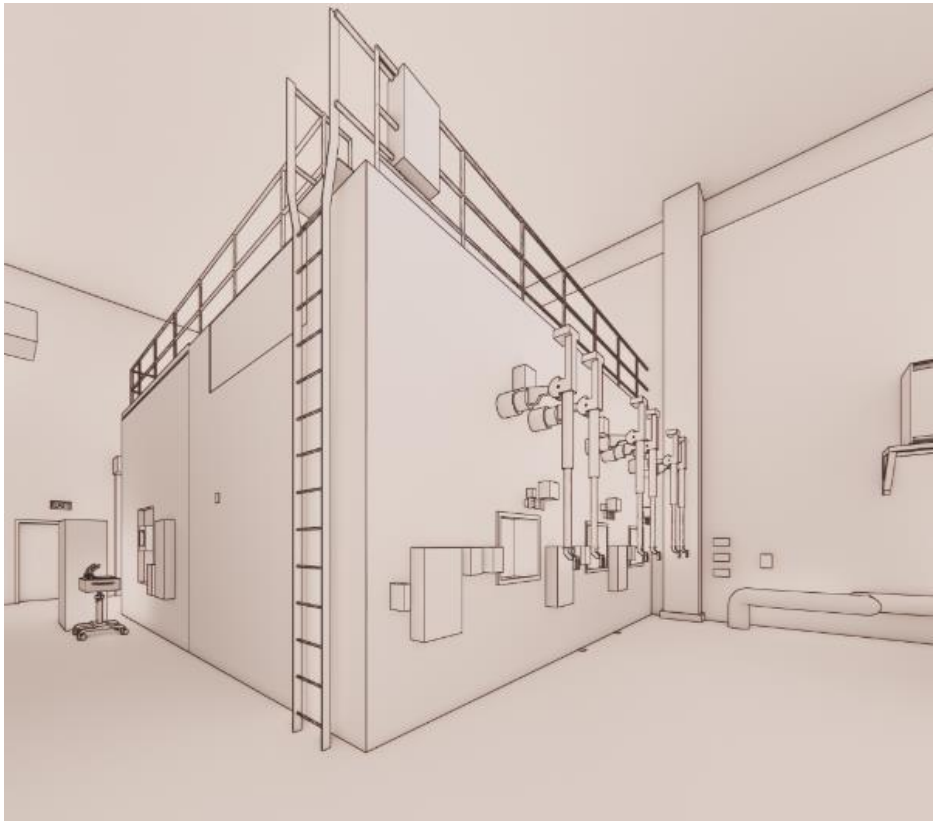
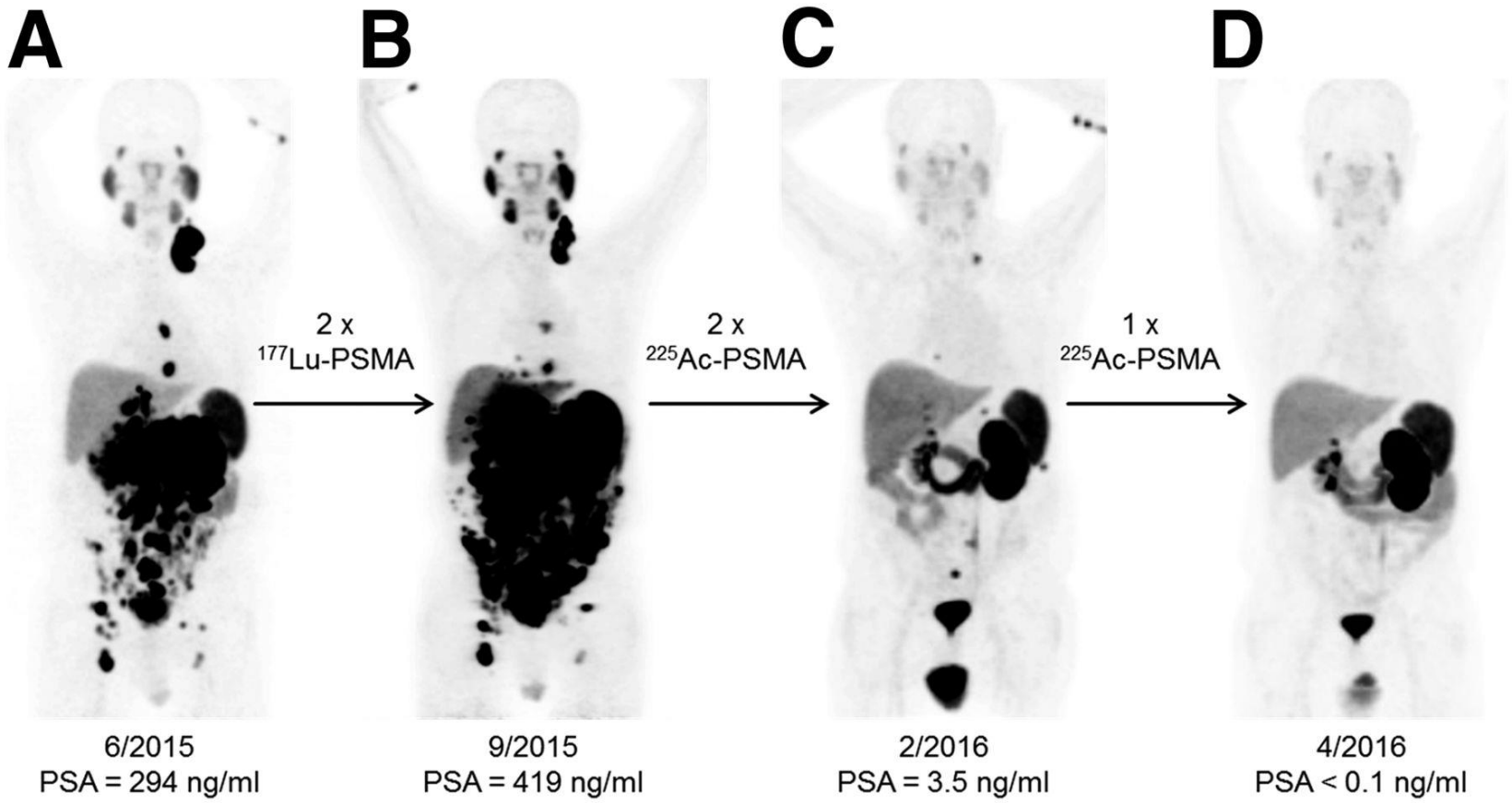
Front Face of the AP Hot Cells



Prostate Cancer Therapy



68Ga-PSMA-11 PET/CT scans of patient B. In comparison to initial tumor spread (A), restaging after 2 cycles of β-emitting 177Lu-PSMA-617 presented progression (B). Clemens Kratochwil et al. J Nucl Med 2016;57:1941-1944

JNM The Journal of NUCLEAR MEDICINE

Questions?