Isotope Production for Nuclear Medicine

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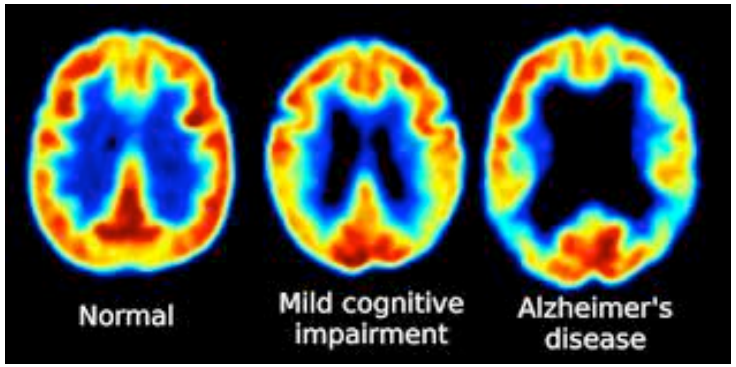
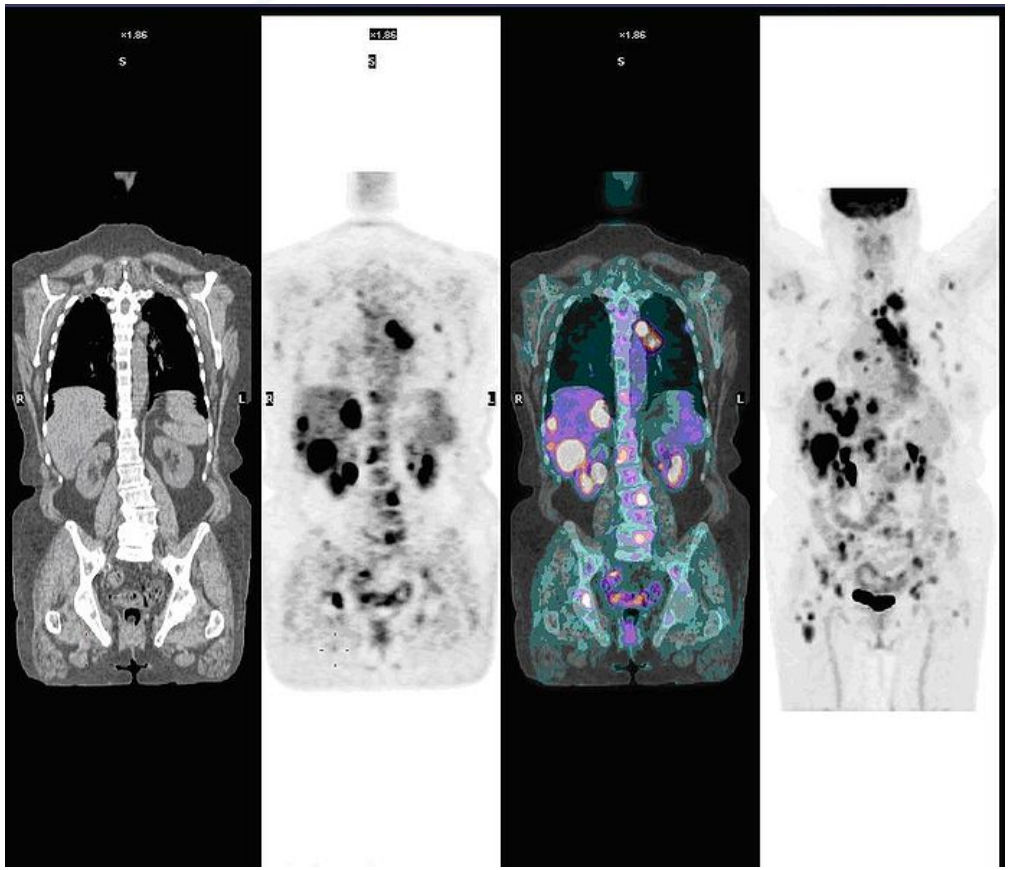
Isotopes for Nuclear Medicine

- More than 20 million nuclear medicine procedures are performed each year in the United States.
- Nuclear medicine is a ~ $2 billion/year industry.
- Diverse applications
  - Diagnostics and Imaging
    - PET – positron emission tomography
    - SPECT – single photon emission computed tomography
  - Therapy
    - Implants
    - Targeted Therapy (Bexxar®, Zevalin®, Xofigo®)



- The health benefits and economic impact are enormous.

Diagnosis – Isotopes allow us to see where cancer has spread in the body



PET (Positron Emission Tomography) is an important tool in the evaluation of cancer and other diseases.

The LANL accelerator is well suited to make isotopes for PET imaging.

Therapy – cancer can be treated with external radiation or via direct application of isotopes

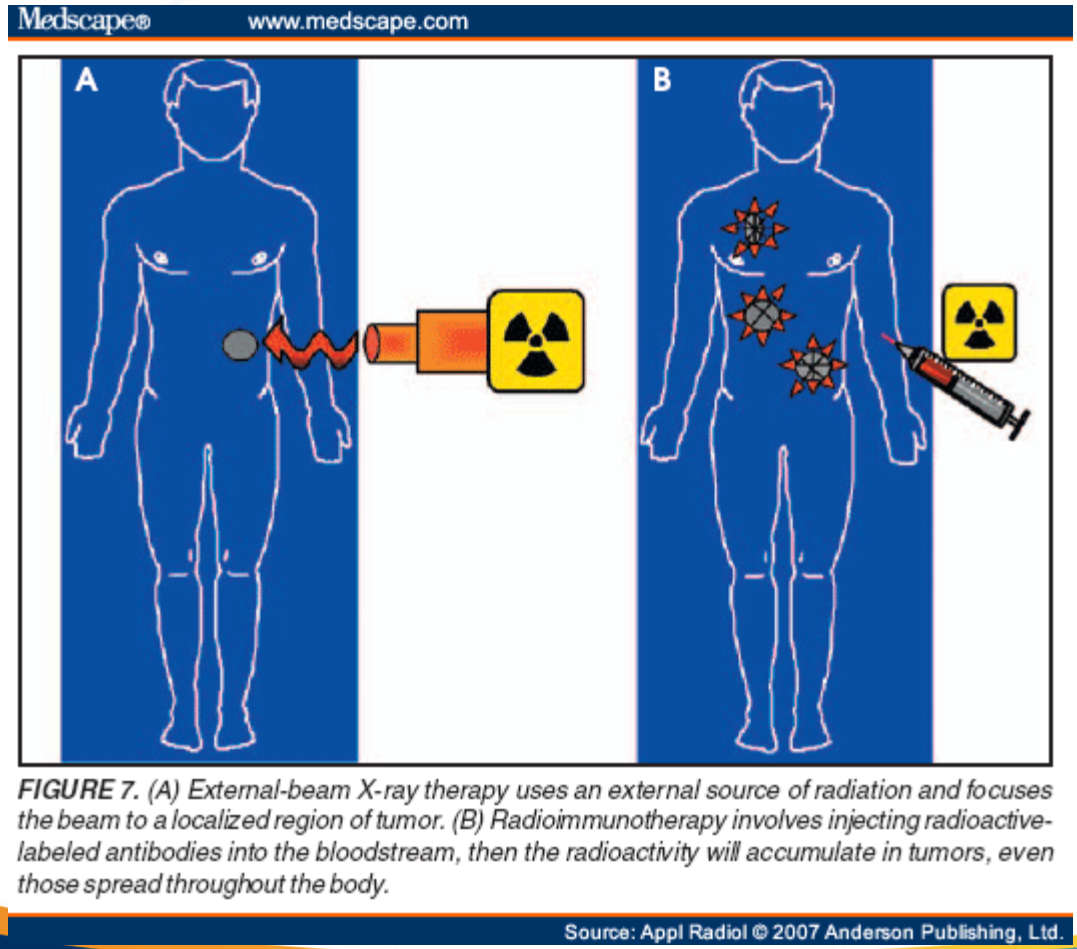


FIGURE 7. (A) External-beam X-ray therapy uses an external source of radiation and focuses the beam to a localized region of tumor. (B) Radioimmunotherapy involves injecting radioactive-labeled antibodies into the bloodstream, then the radioactivity will accumulate in tumors, even those spread throughout the body.

Source: Appl Radiol © 2007 Anderson Publishing, Ltd.

The use of isotopes in therapy reduces the impact to the surrounding tissue while maximizing impact on tumors.

Only a few isotopes are FDA approved for therapeutic use.

Producing Isotopes for the Nation

- Security of Domestic Radioisotope Supply
  - **Medical Use:** Isotopes for diagnostic imaging
  - **Security/ Stockpile Stewardship:** Isotopes for improvement of physics codes
  - **Research & Development:** future applications
- Complement, not compete with industry
- Partner with other national labs for constant supply

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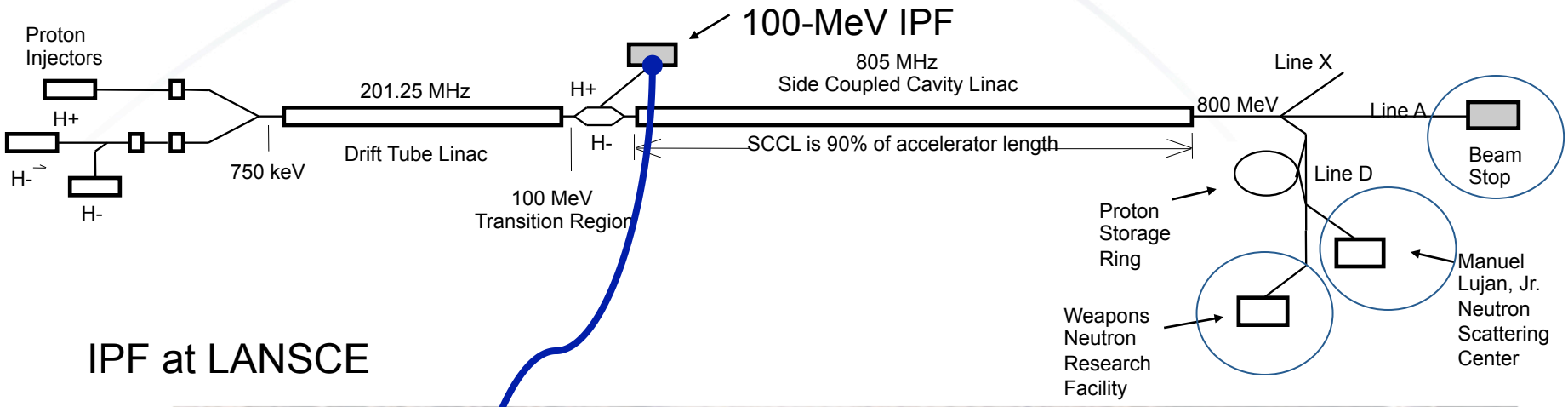
Products From LANL's Isotope Production Facility

Isotope	Half-life	Main Use
^{82}Sr	25.5 d	Parent of ^{82}Rb used in cardiac perfusion studies with PET
^{68}Ge	270 d	Parent of ^{68}Ga being tested for diverse PET applications
^{22}Na	2.6 a	PET isotope used as a tracer and source material
^{32}Si	153 a	Environmental tracer; produced in partnership w/ TRIUMF
^{73}As	80.3 d	Tracer for toxicology studies
^{109}Cd	462.6 d	Source for X-ray fluorescence
^{225}Ac	10 d	Alpha emitter used in cancer therapy clinical trials
^{186g}Re	90.6 h	Bone pain palliation, cancer therapy
^{44}Ti	58.9 a	Generator for PET isotope ^{44}Sc
^{236}Np	1.5 10^5 a	Standard for Np quantification by IDMS
^{119}Sb	38.5 h	Auger emitter for cancer therapy

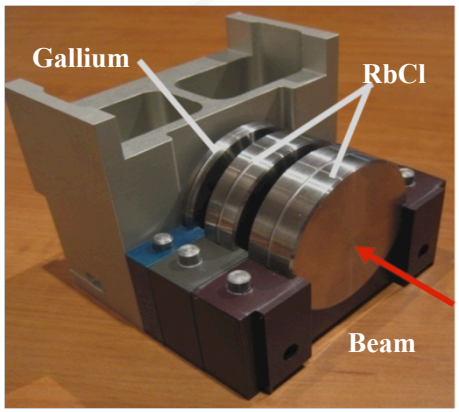
Other available isotopes include ^{207}Bi, ^{148}Gd, ^{26}Al, ^{85}Sr, ^{88}Y, ^{88}Zr

Isotope Production Facility at the Los Alamos Neutron Science Center



IPF at LANSCE

High energy and high current allow us to make large quantities of unique products

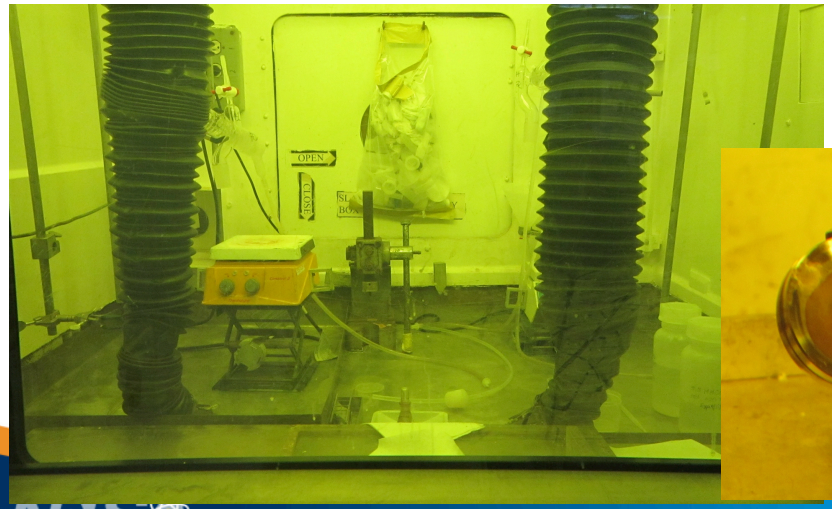


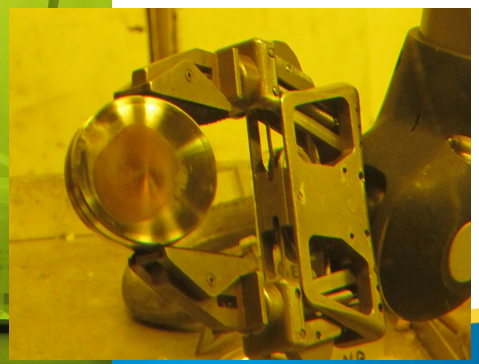
- The Isotope Production Facility accepts proton beam from the LANSCE accelerator at 100 MeV, 250 microAmp (roughly 60% of the speed of light)
- Proton beam strikes the IPF targets, creating new radionuclides

- Small industrial machines near hospitals can make some needed isotopes
- ***Only LANL and BNL can make PET isotopes for FDA approved cardiac imaging***

Radiochemical Processing

- Standard wet chemistry techniques to separate isotopes
- Purified isotopes are incorporated into commercial products or used for R&D
- FDA approved (cGMP) facility



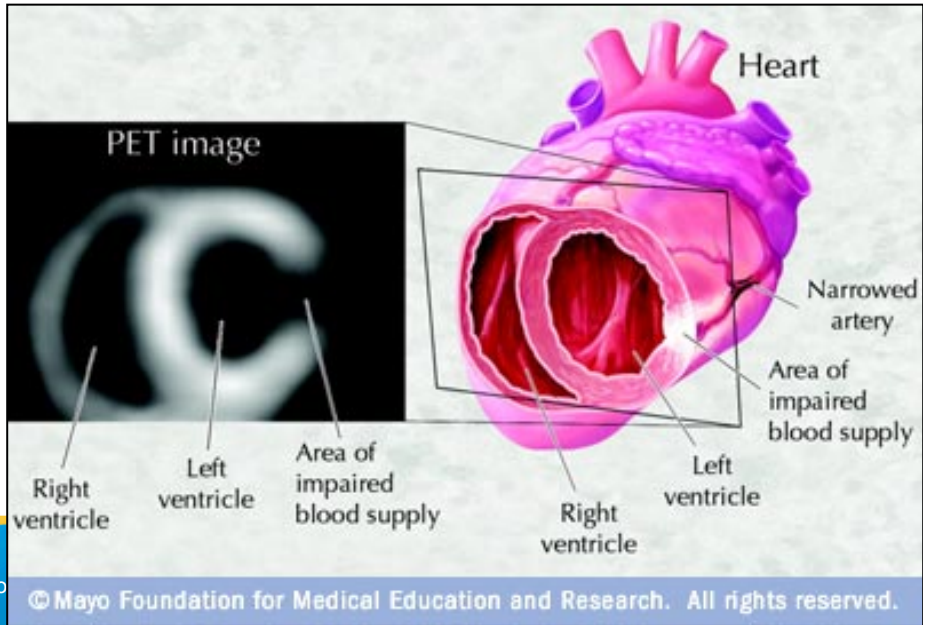


Facility has thirteen hot cells for safe handling of highly radioactive materials

Sr-82 leads to 30,000 patient images/mo

- LANL-supplied strontium-82 manufactured into a medical generator (Cardiogen-82®)
- Generator delivers short lived Rb-82 to patient for diagnosis via positron emission tomography
- Sr-82 results in sharper images than alternative methods for cardiac perfusion imaging

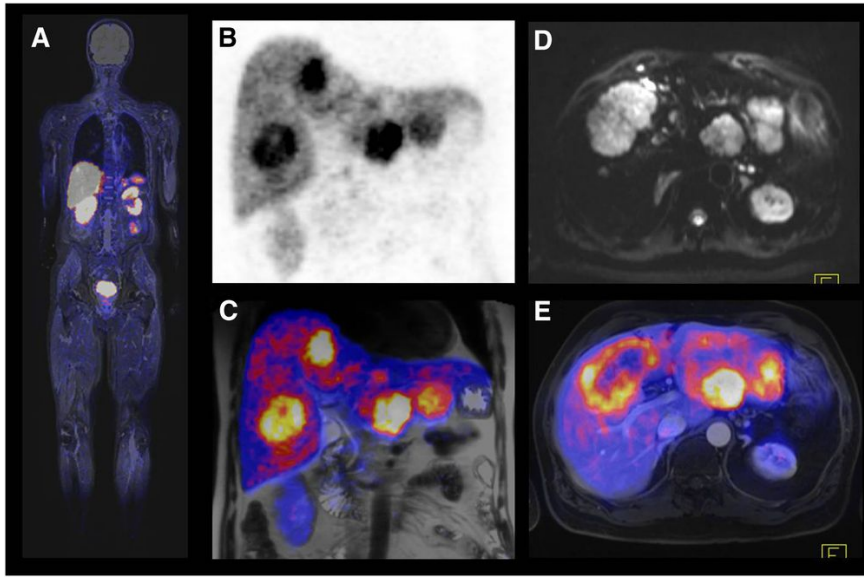
Cardiogen-82®
(Rubidium Rb 82 Generator)



Ge-68 for disease imaging

- LANL-supplied Ge-68 is manufactured into medical generators
- Daughter Ga-68 is complexed into targeted imaging agents for diagnosis of cancer and other disease

Active area of research in the clinical community

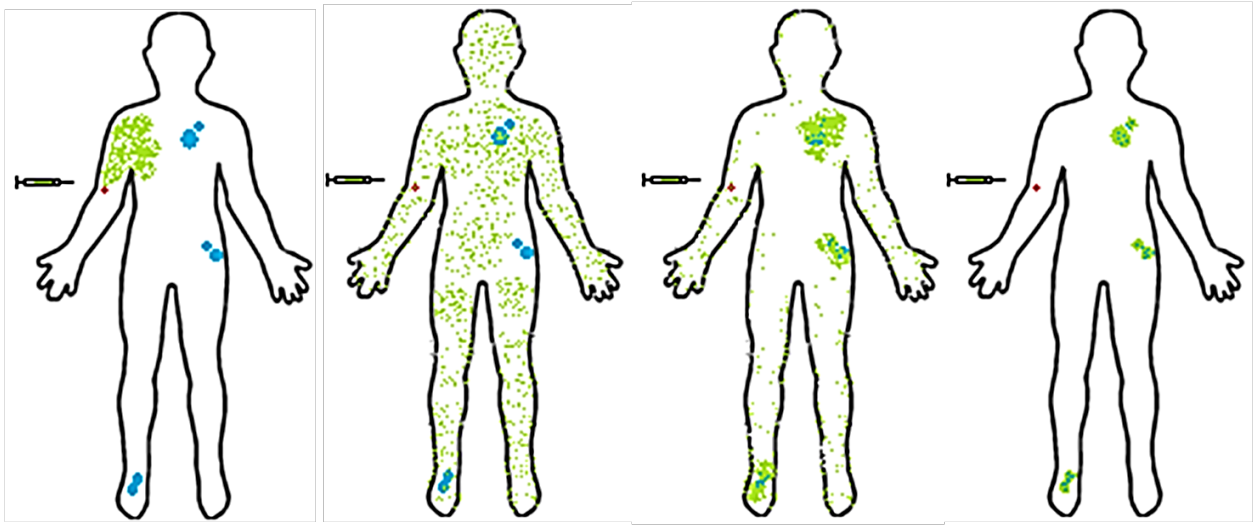


Example of whole body PET/MRI imaging with ^{68}Ga. Martinez-Moller et al 2012 Jnumed.

How can we meet future needs?

- While several different diagnostic isotopes are used clinically, only a few FDA approved, isotope-based drugs are available for ***therapy***

Targeted isotope therapy is a key research area



1.The targeted radioligand is administered systemically to the patient.

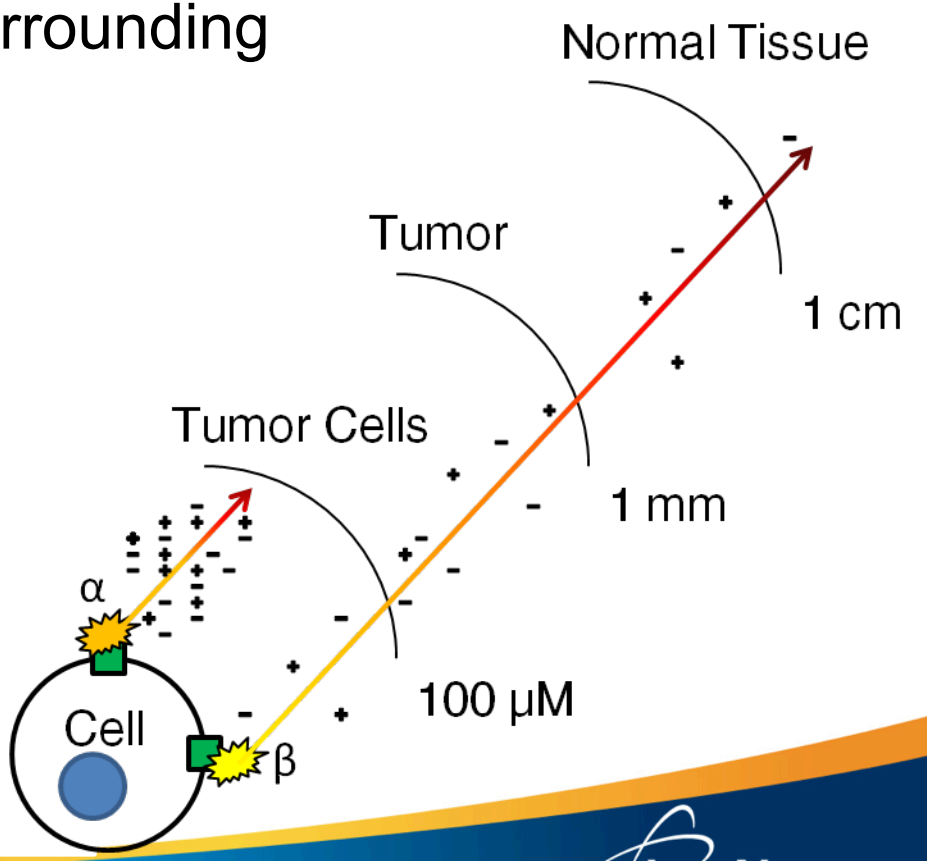
2.The radioligand distributes throughout the patient.

3.The radioligand localizes and concentrates in target tissues (e.g. tumors) reducing radiation dose to non-target normal tissues.

4.The radioligand is retained within the target tissues (tumors) to selectively deliver cytotoxic doses of radiation.

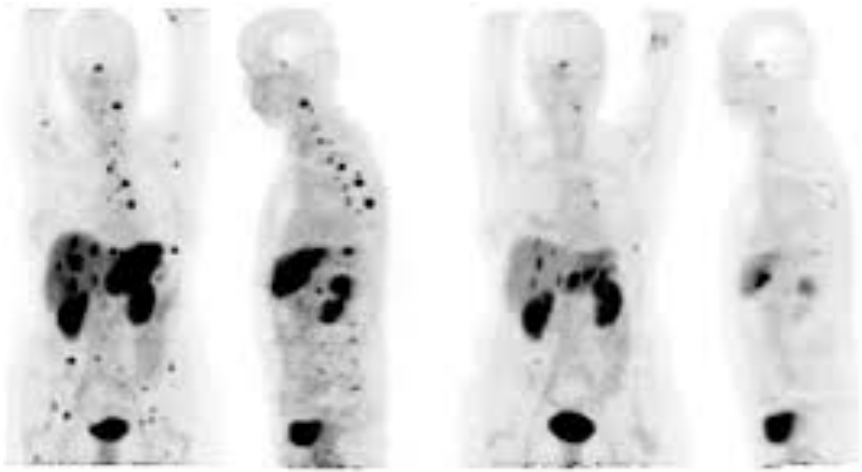
Isotopes to Support Targeted Alpha Therapy (TAT)

- Alpha emitters travel a short distance in the body
- Lethal to tumors but leave surrounding healthy tissue unharmed
- Actinium-225 is extremely promising for TAT
- Ac-225 can only be produced at higher energy machines such as LANSCE



The Promise of Isotope Therapy Being Realized

SNMMI Image of the Year (2012): Treatment Response from Bismuth-213

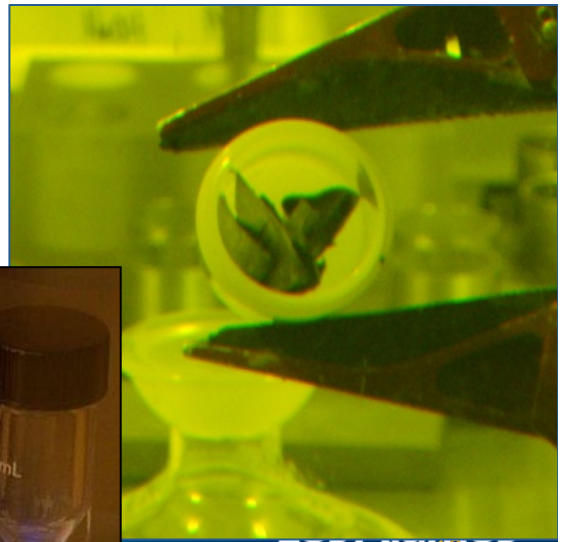


- Remarkable patient response in preliminary testing
- Research and clinical application limited by insufficient supply of Ac-225/Bi-213

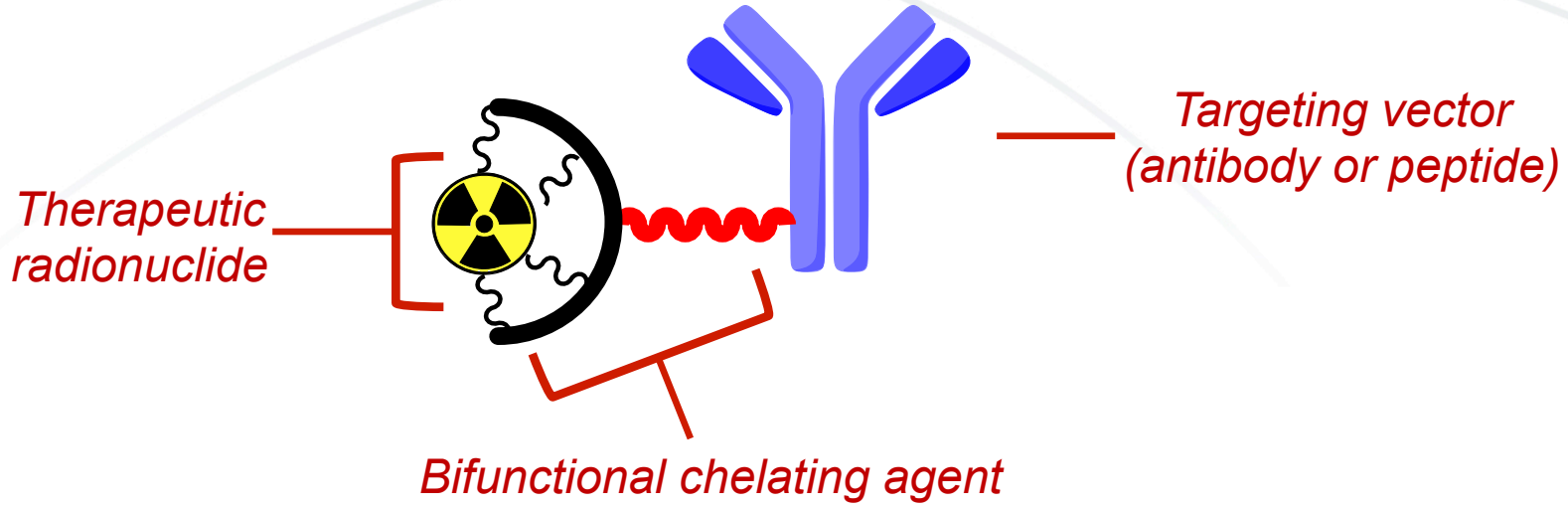
Shrinkages in liver lesions and bone metastases (top) and liver lesions after treatment with Bi-213 DOTATOC. Images from J Nucl Med. 2012;53:23N.

Actinium-225 from R&D to Production

- Current world-wide, annual supply of ^{225}Ac is ~1.7 Ci; 50+ Ci required to support clinical trials and drug development
- Developing accelerator-production method to address demand; possible to match current annual supply with two 10-day irradiations of thorium targets at IPF
- Targetry, radiochemistry, and logistical hurdles to be addressed in the next 3 – 10 years



Moving from Isotope Production to Treatment



In order to utilize new isotopes for treatment, they must be tightly bound into a chelating agent and highly directed by a vector. The knowledge to build these constructs is still in its infancy.

- Developing collaborations with universities to explore the biology of targeted alpha therapy.
- Using new tools to understand actinium as an element and inform the design of future drug candidates.

Isotope Production & Delivery
-- Factors to consider in new applications

- Processing – is the isotope purity sufficient?
- Properties – is the isotope of an appropriate half-life and give off the “right” radiation (dose)?
- Delivery –
  - is it chelated (will it fall out of the vector)?
  - is the isotope properly targeted in the body?
  - Is the biological half-life tolerable?
- Must consider patient risk early in the development process

Isotopes for Medicine

U.S. DEPARTMENT OF ENERGY
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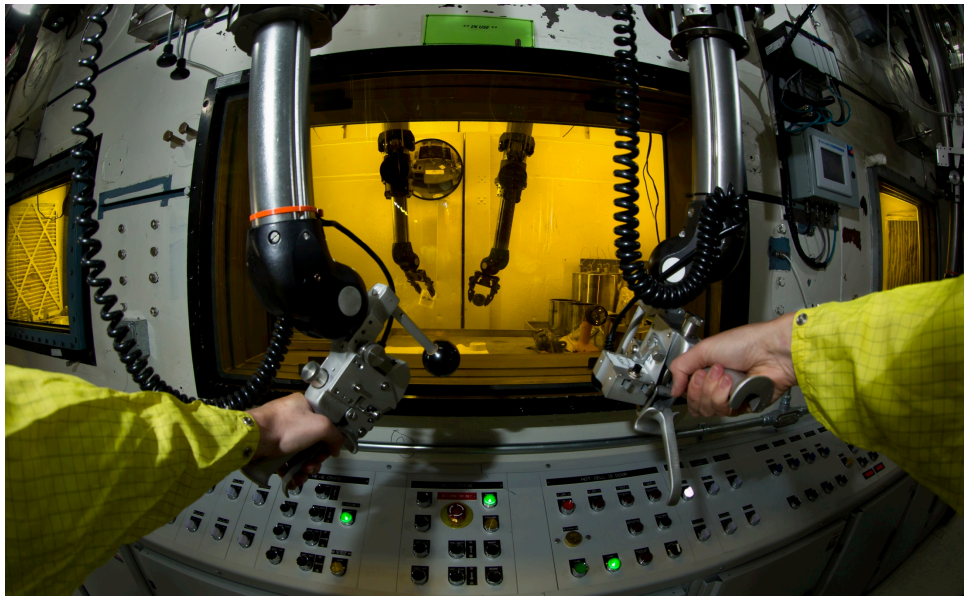
The LANL Isotope Program produces isotopes that are in short supply to meet the need for the Nation. The LANSCE accelerator is uniquely capable to produce critical medical isotopes for cardiac and cancer imaging, with LANL as a leading world supplier for strontium-82 and germanium-68.

- Sr-82 produced at LANL results in ~ 30,000 diagnostic cardiac procedures each month
- LANL is leading an effort to make Ac-225 available in large quantities for clinical therapy
- We are bridging the gap between production and clinical applications through strategic partnerships



Thank you to the many people who make this program a reality!

Questions?

More information at isotopes.lanl.gov