Medical Isotope Production and Use

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Pacific Northwest NATIONAL LABORATORY

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Our isotope world

- All matter consists of elements in many chemical forms (atoms and molecules)
- 112 (or more?) elements
- Each element comprises several isotopes
- About 1600 isotopes have been characterized
- Either stable or unstable (radioactive)

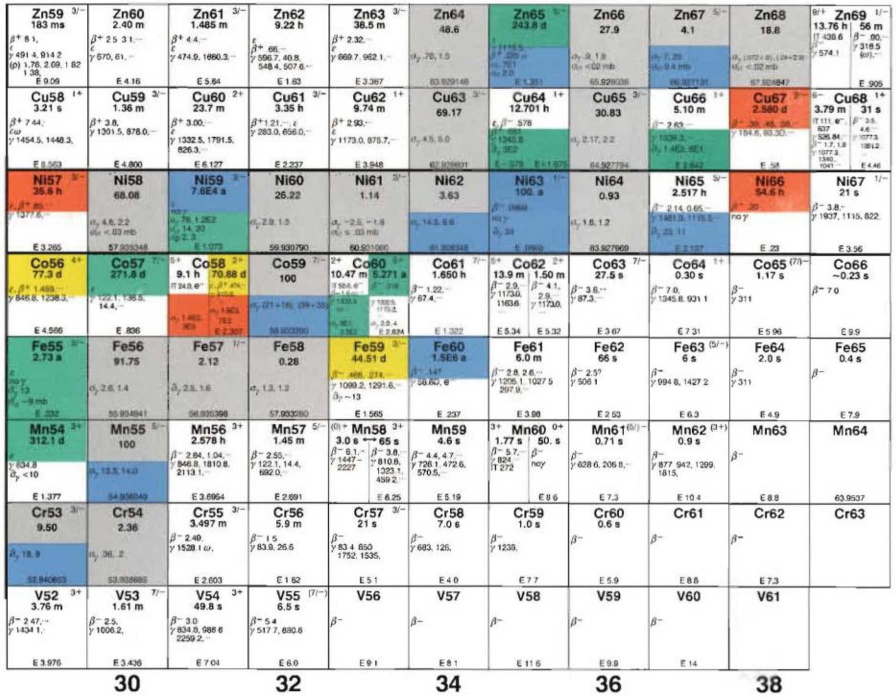
Hydrogen: H-1 (99.985%, stable), H-2 (0.015%, stable), H-3 (trace, radioactive)

Carbon: C-8, C-9, C-10, C-11, C-12 (98.9%, stable), C-13 (1.1%, stable), C-14, C-15, C-16, C-17, C-18, C-19, C-20

$T_{1/2}$ C-14 = 5715 years Emits a beta(-) particle	$T_{1/2}$ C-11 = 20.3 minutes Emits a beta(+) particle, gammas

Chart of the nuclides

- Organizes all elements and isotopes according to:
  - number of protons in the nucleus
  - number of neutrons in the nucleus
  - percent natural abundance of stable isotopes (266)
  - half-lives of radioactive isotopes
  - major emissions and energies (alpha, beta, positron, gamma)
  - cross-sections for nuclear reactions
  - other interesting data



Natural or “man-made”?

- Nuclear reactions result in isotope production

  $^{14}N + {}^{4}He \rightarrow {}^{17}O + {}^{1}H$ (accelerated helium ion)

  $^{235}U + n \rightarrow {}^{236}U \rightarrow {}^{92}Kr + {}^{141}Ba + 3n$ (nuclear fission)

- Isotopes are created as the result of radioactive decay of something else

  $^{24}Na \rightarrow \beta^- + {}^{24}Mg$ (radioactive decay)

- Isotopes may be naturally-occurring or man-made

  $^{39}K + n \rightarrow {}^{40}K$ (cosmic ray reaction)

- Some isotopes have valuable applications in science, medicine, defense, space, homeland security

- Most have no practical value

The natural decay series

- Uranium-238 (4.5E9 yr) $\rightarrow$ ^{234}U $\rightarrow$ ^{234}Pa $\rightarrow$ ^{234}U $\rightarrow$ ^{230}Th $\rightarrow$ ^{226}Ra $\rightarrow$ ^{222}Rn $\rightarrow$ ^{218}Po $\rightarrow$ ^{214}Pb $\rightarrow$ ^{214}Bi $\rightarrow$ ^{214}Po $\rightarrow$ ^{214}Pb $\rightarrow$ ^{210}Pb $\rightarrow$ ^{210}Bi $\rightarrow$ ^{210}Po $\rightarrow$ ^{206}Pb(stable)
- Thorium-232 (1.39E10 yr) $\rightarrow$ ... $\rightarrow$ ^{208}Pb(stable)
- Uranium-235 (7.13E8 yr) $\rightarrow$ ... $\rightarrow$ ^{207}Pb(stable)
- Neptunium-237 (2.2E6 yr) $\rightarrow$ ... $\rightarrow$ ^{209}Bi(stable)
- Branching decays characteristic of each decay chain

$$
\begin{array}{ccc}
^{218}\text{Po} & \rightarrow & ^{214}\text{Pb} \\
\downarrow & & \downarrow \\
^{218}\text{At} & \rightarrow & ^{214}\text{Bi} \rightarrow
\end{array}
$$

Some of these are important medical isotopes!

Medical isotope production methods

- Nuclear reactors
- Charged-particle accelerators
  - Proton cyclotrons, linear accelerators
  - Alpha-particle accelerators
  - Electron beam (x-ray) interactions
- Chemical separation from longer-lived parent isotopes
  - $^{90}Sr \rightarrow \beta^- + {}^{90}Y \rightarrow \beta^- + {}^{90}Zr$ (stable)
  - $^{224}Ra \rightarrow ... \rightarrow {}^{212}Pb \rightarrow \beta^- + {}^{212}Bi$ (alpha emitter)

Medical isotope shortages

Officials Scramble for Solutions to Global Isotope Shortages

As global demand continues to grow for the medical isotope necessary for imaging procedures, most of the reactors used to produce technetium-99m (Tc-99m) will be permanently decommissioned within six years.

A task force set up last year in the EU to consider solutions to isotope shortages released its first report this month to the European Commission. The report suggests convening stake-holders to discuss alternative diagnostic and therapeutic procedures.

Reactor shutdown causes another isotope shortage

Updated Fri. Dec. 12 2008 7:08 PM ET

CTV.ca News Staff

A temporary shutdown at the Chalk River, Ont. nuclear reactor is causing a shortage of medical isotopes, forcing Canadian doctors to scramble to cancel and rearrange appointments with their patients.

The isotope shortage is expected to last until the middle of next week, CTV News has learned.

The shortage is expected to affect Ontario, Quebec, parts of the Maritimes, the northern United States and perhaps even Mexico.

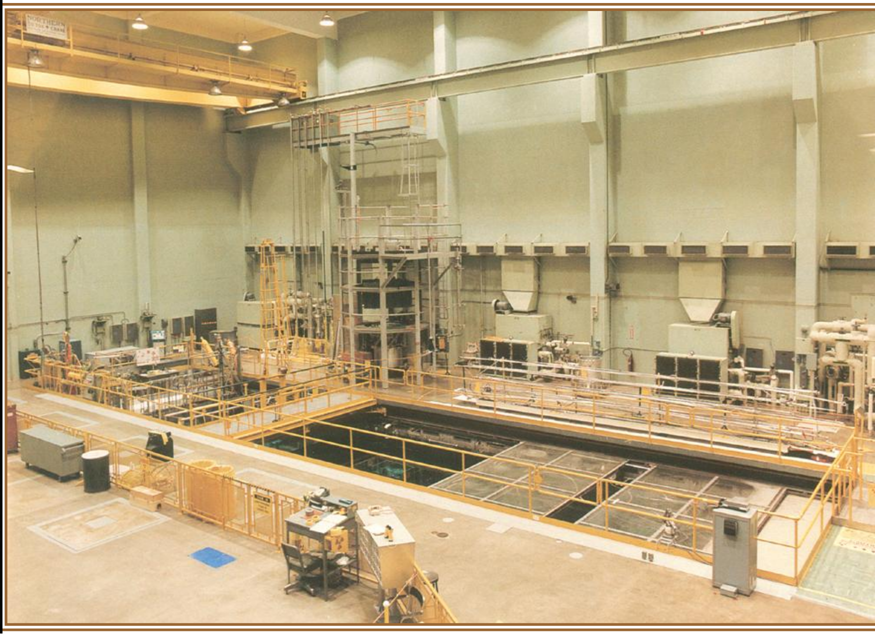
Atomic Energy of Canada Ltd., responsible for the Chalk River nuclear facility, told CTV News that the shutdown was "normal" on Thursday night, but on Friday said the shutdown was "longer than expected."

Nuclear reactors

- National Research Universal (Chalk River, Ontario)
  - Operated by Chalk River Laboratories, AECL
  - 135 MW, low-enriched uranium fuel, high-enriched targets
  - Produces Mo-99, I-131, I-125, Xe-133, Ir-192
  - The major isotope-production facility in the world
  - Isotopes separated from targets and sold by MDS Nordion, Kanata, Ontario
  - Serves the isotope needs of 20 million patients per year

Nuclear reactors

- High-Flux Isotope Reactor (HFIR, Oak Ridge, TN)
  - Operated by Oak Ridge National Laboratory for DOE
  - Uses highly-enriched uranium fuel elements
  - 85 MW, 4E15 neutrons/cm^2-s^2, 26-day irradiation cycles
  - Produces Se-75, Cf-252, W-188/Re-188, Ni-63



Nuclear reactors

- Advanced Test Reactor (ATR, near Idaho Falls, ID)
  - Operated by Idaho National Laboratory for DOE
  - 85 MW, 4E14 n/cm^2-s^2, large core volume, 57-d irradiation cycles
  - Hydraulic tube for short-term target irradiations
  - Produces mainly cobalt-60

Co-60 is produced for medical "gamma knife" irradiators for high-precision treatment by external radiation of brain tumors

Particle accelerators

- Brookhaven Linac Isotope Producer (BLIP) on Long Island, NY
  - Operated by Brookhaven National Laboratory
  - 200 MeV/150 µA proton beam drawn from the Alternating Gradient Synchrotron
  - System for target insertion/retrieval
  - Main isotopes produced:

    Ge-68/Ga-68, and Sr-82/Rb-82, also Zn-65, Mg-28, Fe-52, Rb-83
  - Considerable down-times

Particle accelerators

- Isotope Production Facility (IPF) at Los Alamos, NM
  - 100 MeV/250 μA proton beam from the LANSCE 0.5 mile linear accelerator at TA-53
  - Targets processed at TA-48
  - Available 30-40 weeks per year
  - Main isotopes: Ge-68/Ga-68 and Sr-82/Rb-82, and also smaller amounts of Al-26, Si-32

Particle accelerators

- Commercial cyclotrons
  - Accelerates charged hydrogen atoms (protons, deuterons)
  - Energies 13-40 MeV and up to 100 MeV, current up to 2 mA
  - Efficient, reliable, expensive to operate
  - For production of proton-rich isotopes, including: **^{18}F, ^{82}Sr, ^{64}Cu,^{15}O, ^{11}C, ^{77}Br, ^{77}Br, ^{124}I, ^{86}Y, ^{66}Ga, ^{60}Cu, ^{61}Cu, ^{89}Zr**
  - Several manufacturers:
    Ion Beam Applications (IBA, Belgium)
    Ebco Technologies (Canada)
    Sumitomo Heavy Industries, Ltd. (Japan)
    General Electric (United States)
    Siemens (Germany)

Left: 17 MeV GE PETtrace cyclotron

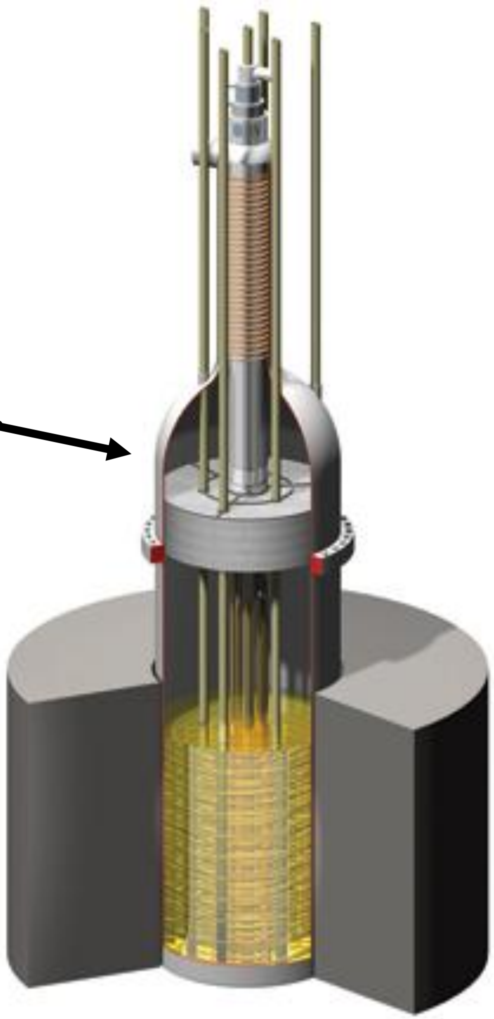
Right: Compact French 65 MeV cyclotron for proton and neutron therapy.

How will the U.S. address isotope shortages?

- A number of important isotopes are needed in the U.S. that are not currently available in sufficient amounts and quality for special applications in medical research, applied clinical nuclear medicine, science, oil exploration, construction, homeland security, national security, defense.....including:
  - Americium-241
  - Californium-252
  - Molybdenum-99
  - Actinium-225
  - Uranium-232
  - Gadolinium-153
  - Promethium-147
  - Copper-67
  - Astatine-211
  - Zirconium-89
  - Tin 117m

Plans for U.S. production of Mo-99

- Upgrade of the University of Missouri Research Reactor (MURR)
  - Low enriched U-235 targets
  - Low-enriched U-235 fuel
  - New target processing facility
- Babcock & Wilcox partnership with Covidien on an Aqueous Homogenous Reactor (solution reactor) fueled by low-enriched U-235 in an acid bath
  - Propose several 100-200 kW reactors
- Advanced Medical Isotope Corporation and the University of Missouri on a proprietary (gamma,n) system



Compact systems

"For decades, particle colliders have used microwave cavities to propel particle beams to nearly the speed of light. That approach, exemplified by the 8.6-km diameter Large Hadron Collider at CERN, is reaching its technological and economic limits.

"A new technique, in which electrons or positrons gain energy by surfing on a wave in an ionized gas, or plasma, promises to slash the size and expense of these high energy accelerators used by physicists to study questions such as the origins of mass in the universe.

"The plasma machines will enable construction of tabletop accelerators for a wide range of lower-energy applications, including materials science, structural biology, nuclear medicine, and food sterilization." (Chandrashekhar Joshi, *Scientific American*, February 2006)

What are "compact systems"?

- Bench-scale electronic devices for achieving various high-energy nuclear reactions and isotope enrichment processes
- "Next-generation" approach to isotope production where nuclear reactors and cyclotrons are not available, too complex, or too expensive to acquire and operate

  - Proton accelerators
  - Alpha accelerators
  - Neutron generators
  - Electron beam x-ray systems
  - Stable isotope plasma separation systems

Compact systems

Compact systems will be dedicated, 24-hour machines, “right-sized” to produce the most-needed isotopes, highly flexible, and much lower cost than reactors and large accelerators

- Bring new isotope production capabilities to the Tri-Cities
- Partner with small business and other national laboratories
- Develop new capabilities that will attract research and development investments
- Develop and test next-generation isotope-producing systems for various applications
- Address critical national needs for research isotopes
- Develop new intellectual property

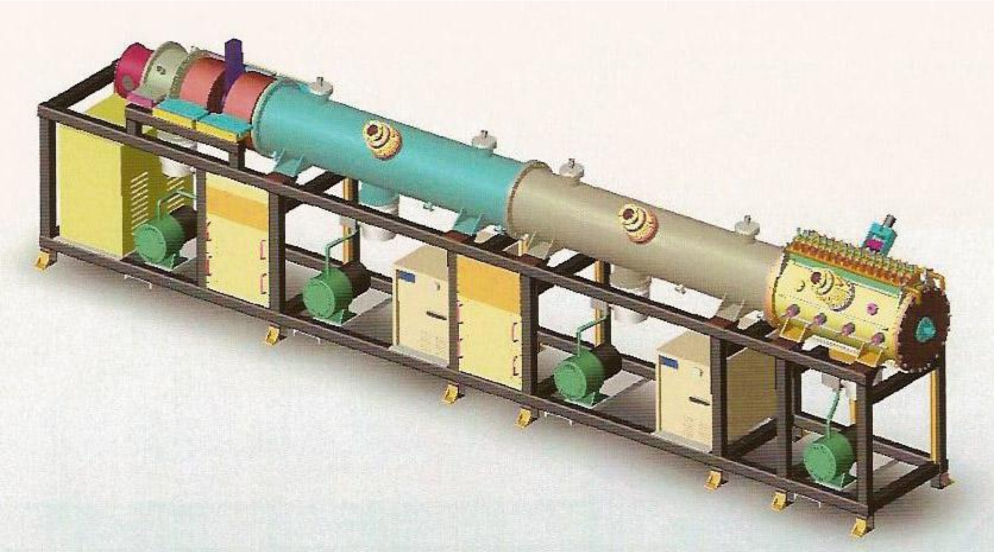
Compact systems: proton accelerator

- First U.S. 7 MeV proton linear accelerator for medical isotope production
- Up and running, producing ^{18}F for regional hospitals

- For production of ^{18}F, ^{111}In, ^{123}I, ^{11}C, ^{13}N, ^{15}O
- In partnership with Advanced Medical Isotope Corporation, PNNL will perform research and development on target preparation and processing
- May be upgraded to 10.5 MeV

Compact systems: alpha linac

- Helium or deuterium accelerator up to 40 MeV at 1.5 mA m
- Radiofrequency quadrupole-driven confinement and acceleration
- Electron cyclotron resonant plasma source for helium ions
- For production of isotope such as: ^{117m}Sn, ^{225}Ac, ^{73}As, ^{55}Fe, ^{211}At, ^{109}Cd, ^{88}Y, ^{75}Se, ^{210}Po, etc.
- In partnership with the private sector, PNNL will perform research and development on target preparation and irradiated target separations
- Under construction

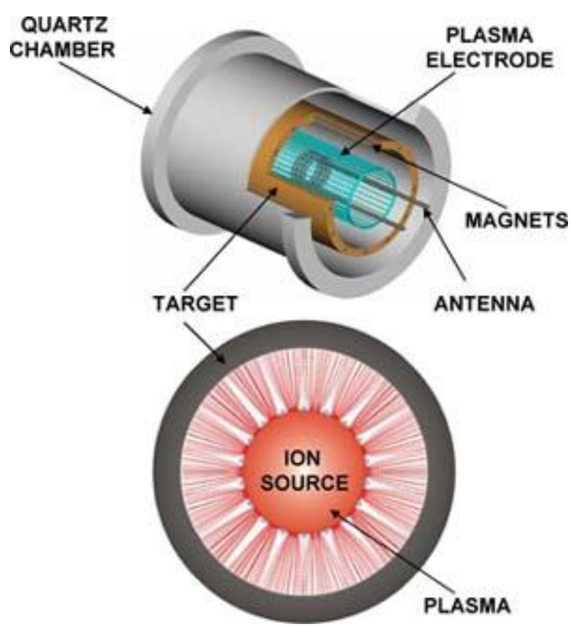


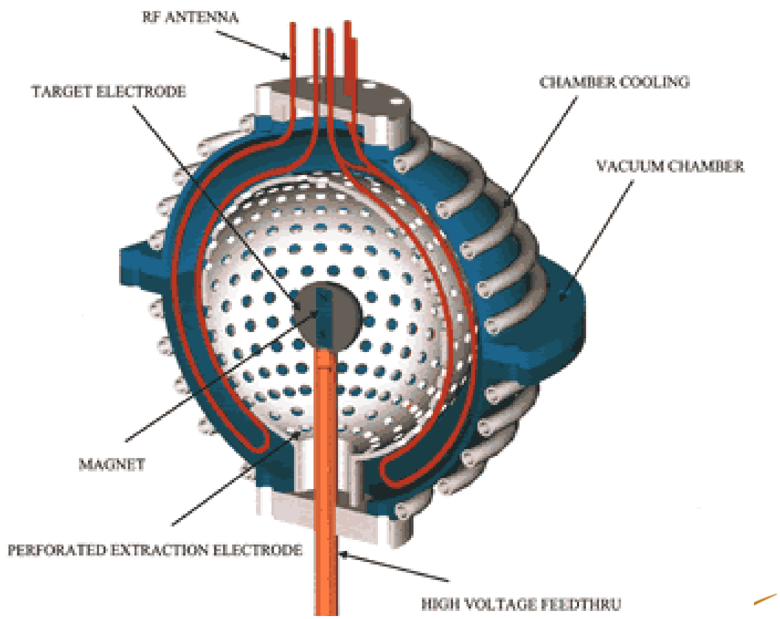
Compact systems: neutron generators

1. Berkeley coaxial D-T radiofrequency-driven plasma ion source, cylindrical neutron generator
2. Deuteron accelerator (Ukraine)

   ^{2}H on $^{9}Be \rightarrow {}^{10}B + n$ (10^{13} n/cm^{2}-s)

In partnership with Advanced Medical Isotope Corporation

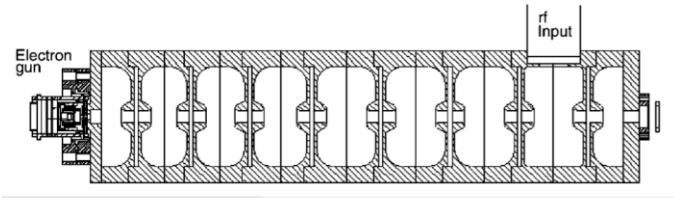




Spherical D-T neutron generator with multi-hole extraction electrode surrounding a spherical target electrode

Compact systems: electron-beam accelerator

- Bremsstrahlung from 10-25 MeV electrons proposed for isotope production through:
  - Photo-fission of heavy elements
  - (γ,n) reactions
  - Photo-neutron activation and (n,2n) reactions
- $^{226}Ra(\gamma,n)^{225}Ra \Rightarrow {}^{225}Ac$ for ^{213}Bi production
  - Target design, heat dissipation, target recycling are critical research problems
- 3 MeV photo-neutrons for radioisotope production
  - ^{99}Mo production using low-enriched uranium (proposed)
  - ^{67}Cu production via (n,p) on enriched ^{67}Zn with high fluxes
- Homeland security research



What is a good medical isotope?

- For applications in medicine, nature and “man-made” physics approaches provide many different radionuclides to choose from.
- The choice of radionuclide is critical for achieving successful diagnostic imaging and cancer treatment outcomes.
- Objectives:

1) Diagnostic nuclear medicine: high quality images of activity in the patient, with low patient radiation dose

2) Therapeutic nuclear medicine: high amount of energy imparted to the target tissue (to destroy cancer cells) relative to critical normal organs and tissues (to prevent radiation damage and side-effects)

Broad categories

Radiopharmaceuticals

- Positron Emitters
- Beta/gamma Emitters
- Alpha Emitters

Medical Devices

- Sealed Sources
- Microsphere Applications
- Nanosphere Applications

FDA product categories

Drugs

^{89}Sr-chloride

^{131}I-sodium iodide

^{99m}Tc sestamibi

Biologics

^{90}Y-peptide

^{131}I-antibody

Radiopharmaceuticals in nuclear medicine

Devices

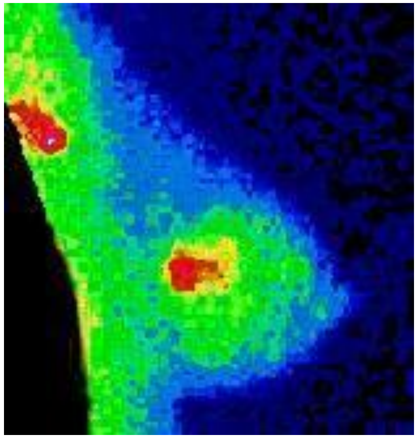
^{90}Y-microspheres

^{125}I-seeds

^{137}Cs-intracavitary brachytherapy

Standard photon-emitter clinical imaging agents

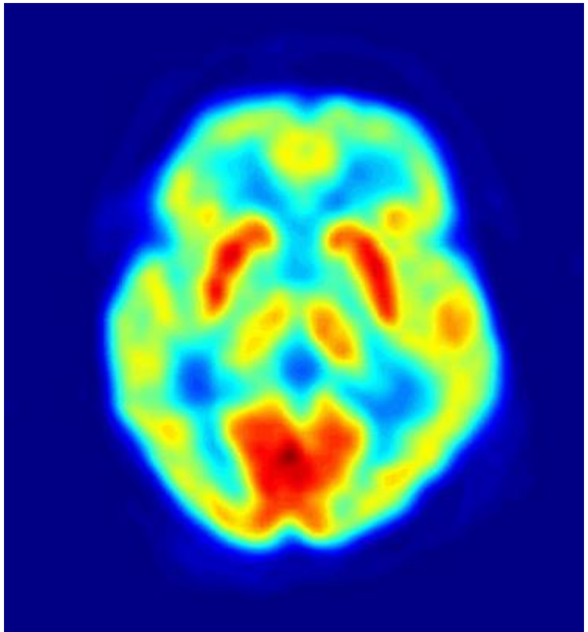
- Tc-99m (about 35 common diagnostic radiopharmaceuticals)
- I-131 sodium iodide
- In-111, I-123, Tl-201, Ga-67, Xe-133



Tc-99m-sestamibi scan shows breast tumor

Positron emitters

- Cancer Metabolism and Functional Imaging
  - F-18-fluorodeoxyglucose (FDG) glucose analog, measures hexokinase activity (glucose metabolism), phosphorylated by hexokinase to F-18-FDG-6-PO_4, elevated in tumor cells, chemically trapped in cells
  - F-18-amino acids (phenylalanine, tyrosine) image metastatic lesions
  - F-18-fluorothymidine measures thymidine kinase activity (DNA synthesis)
  - F-18-flouromisonidazol (FMISO) images tumor hypoxia
  - F-18-estradiol breast tumor detection



PET radiopharmaceuticals other than fluorine-18

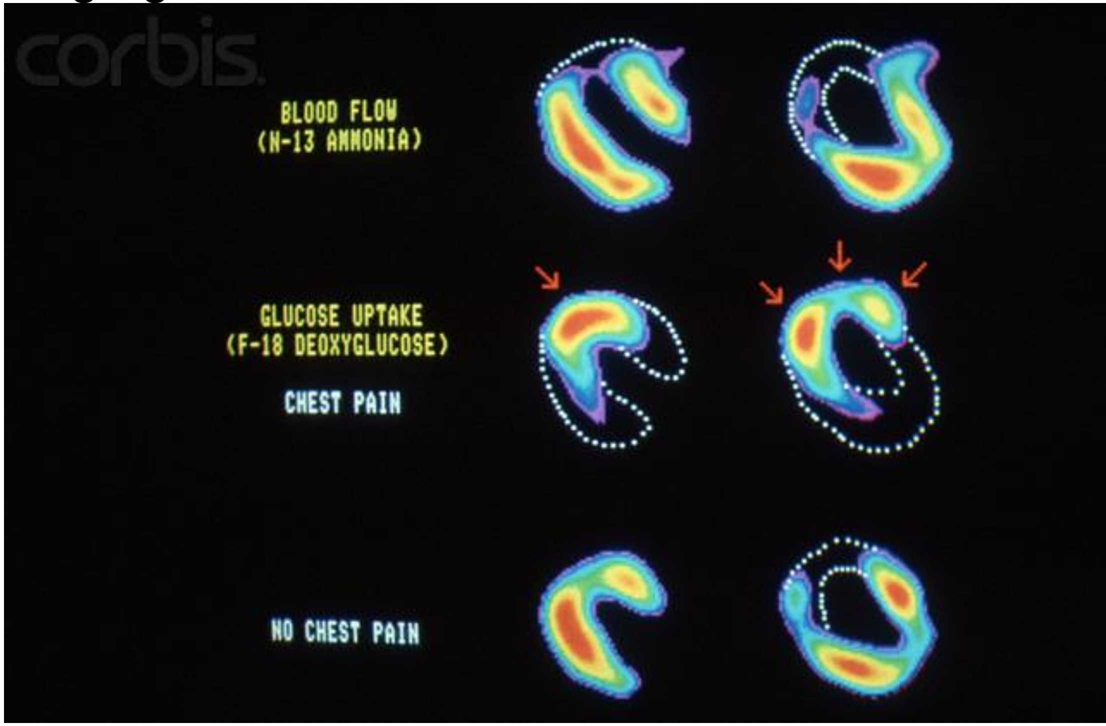
- C-11-thymidine incorporates in DNA, indicates rapid metabolism
- C-11-choline incorporates in cell membrane phospholipids
- C-11-carbon monoxide indicates blood flow
- C-11-methionine amino acid uptake and protein metabolism
- C-11-acetate measures oxidative activity
- Ga-68-DOTATOC/DOTATATE imaging of somatostatin receptors in neuroendocrine tumors
- Cu-64-labeled antibody cancer receptor imaging
- Other positron-emitter antibody labels: Br-76, Br-77, As-72, Zr-89, I-124

PET brain imaging

- Neuroimaging
  - F-18-FDG glucose metabolism, brain activity
  - F-18-PIB binds amyloid placque in Alzheimer's disease
  - F-18-fallypride targets dopamine receptors in neuropsychiatric disease and addiction
  - C-11-raclopride dopamine receptors in addiction, alcoholism
  - [C-11-]-3-amino-4-(2-dimethylaminomethyl-phenylsulfanyl)-benzonitrile (DASB) binds to serotonin transporter for imaging depression
  - O-15 oxygen gas metabolism

PET heart imaging

- Cardiac Imaging
  - F-18-FDG myocardial viability
  - Ru-82-chloride (Sr-82) myocardial perfusion studies
  - N-13-amonnia for assessing myocardial blood perfusion in the evaluation of coronary artery disease
  - O-15-water myocardial imaging
  - C-11-palmitate and 11-acetate for myocardial metabolism

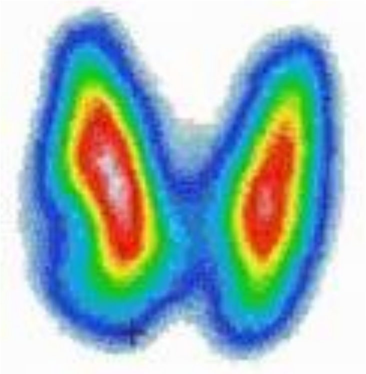


FDA-approved therapeutics

- I-131 sodium iodide for thyroid cancer, hyperthyroidism
- P-32 orthophosphate for polycythemia vera
- P-32 chromic phosphate (Phosphocol™): intercavitary malignancies, and peritoneal and pleural effusions from metastatic disease
- Sr-89 chloride (Metastron®) for painful bone metastases
- Sm-153 EDTMP (Quadramet® Lexidronam) for painful bone metastases
- I-131-B1-anti-CD-20 monoclonal antibody, tositumomab, Bexxar™) for non-Hodgkin's lymphoma
- Y-90-Y2B8-anti-CD-20 monoclonal antibody, ibritumomab, Zevalin®) for non-Hodgkin's lymphoma

Therapy agents

- Thyroid disease (benign and malignant)
  - Iodine-131 sodium iodide, oral
  - Targets thyroid (hormone-secreting) tissues, salivary glands, cancer metastases



I-131 scan of normal thyroid

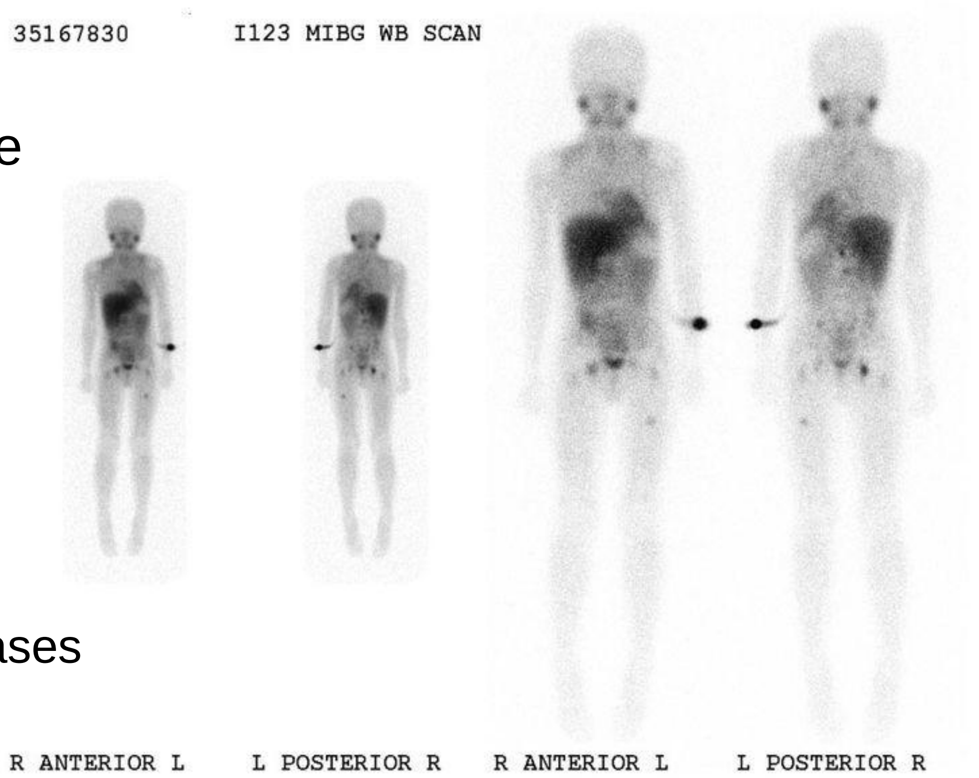
Therapy agents

- Myeloproliferative diseases (bone marrow)
  - P-32 sodium phosphate (targets trabecular bone surfaces)
  - P-32 orthophosphate for polycythemia vera
  - Ho-166-DOTMP plus melphalan for multiple myeloma

- Malignant ascites (intraperitoneal cavity)
  - P-32 chromic phosphate colloid
  - Y-90 silicate, colloidal suspensions
  - Y-90-labeled anti-ovarian-cell antibodies
    - Targets cell-surface antigens
    - Problem achieving sufficiently high, uniform radiation doses

Therapy agents

- Neuroendocrine tumors
  - I-131-meta-iodobenzylguanidine (mIBG)
  - Targets the neurosecretory granules of catecholamine-producing cells in neuroblastoma
  - Bladder cancer
  - Experimental only in the US, in combination with high-dose chemotherapy



Neuroblastoma metastases

Therapy agents

- Neuroendocrine tumors (continued)
  - Radiolabeled somatostatin analog peptides (peptide receptor radionuclide therapy, PRRT)
  - Target somatostatin receptors overexpressed on hormone-secreting tumors, internalizing
  - Somatostatin, gastrin, bombesin, calcitonin, VIP, PACAP, GRP, oxytocin, α-MSH, GLP-1
  - Conjugated with In-111, Y-90, Lu-177
  - Y-90-DOTA-Tyr^3-Octreotides, octreotates
  - Problem with high kidney uptake, renal failure

Therapy agents

- Liver cancer
  - P-32 albumin colloids (1970s)
  - I-131- or Re-188-HDD-lipiodol fatty acid ester for treating nonresectable hepatocellular carcinoma by endocytosis (not effective for metastases, diffuse disease)
  - Y-90 silicate microspheres (Theraspheres, SIR-spheres) administered intra-arterially with lung shunt

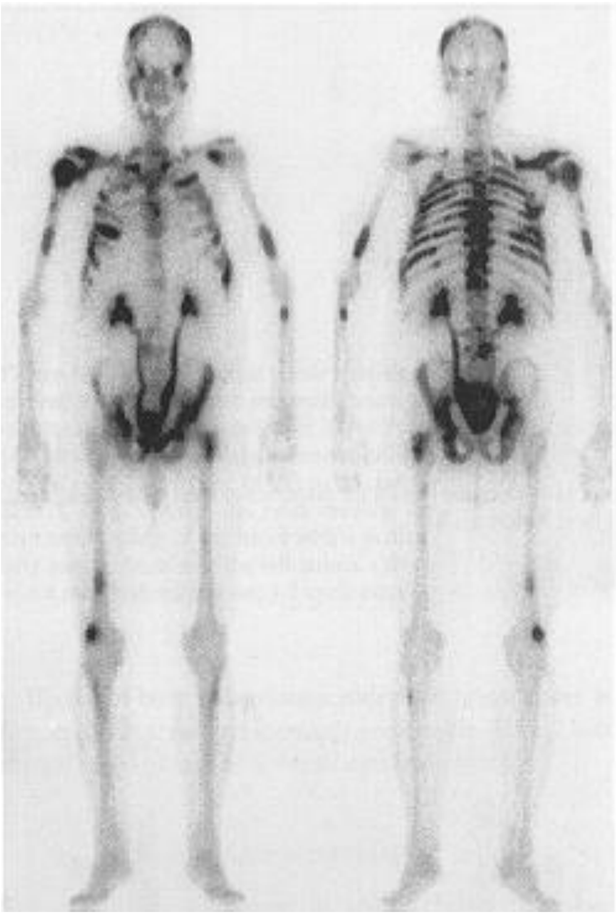
    (classified as devices)

Therapy of benign diseases

rheumatoid arthritis	Y-90 silicates, colloids
	P-32-colloid
	Dy-165-FHMA, Ho-166-FHMA*
	Sm-153-hydroxyapatite
synovitis	Au-198-colloid
	P-32-chromic phosphate
ankylosing spondylitis	Ra-224 chloride
hyperthyroidism	I-131-sodium iodide

*Ferric hydroxide macroaggregate

Bone pain agents



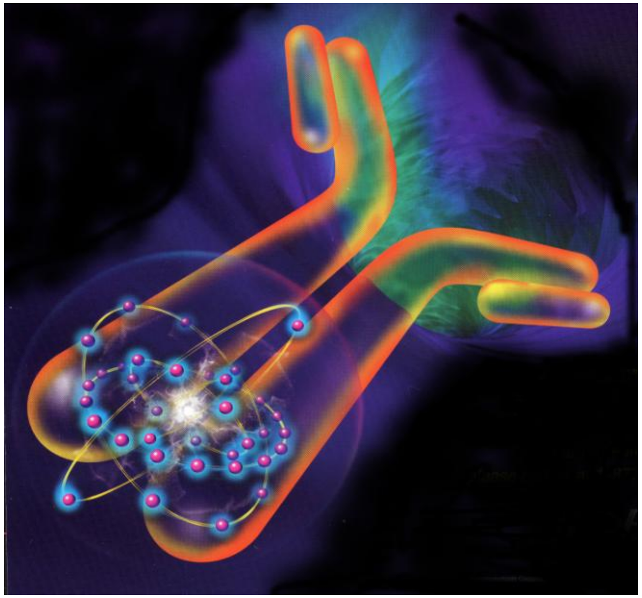
P-32-orthophosphate
Sr-89 chloride (Metastron)
Sm-153-EDTMP phosphonate (Quadramet)
Ho-166-EDTMP phosphonate
Sn-117m(stannic 4+)-DTPA
Lu-177 DOTMP/EDTMP
Re-188-hydroxyethylidene diphosphonate (HEDP)
Re-186, -188-HEDP hydroxyethylidene diphosphonate
Re-188 dimercaptosuccinic acid
I-131-α-amino(4-hydroxybenzylidene)-disphosphonate
Y-90-chloride
Ra-223-chloride (AlphaRadin)

Recent advances in radionuclide therapy

- Very-high-dose radioimmunotherapy
  - University of Washington, Johns Hopkins Univ., others
- Pretargeting strategies to achieve higher tumor uptakes
- Radiogels for direct intra-tumoral injection
- Advanced brachytherapy seeds
- Nanoparticles

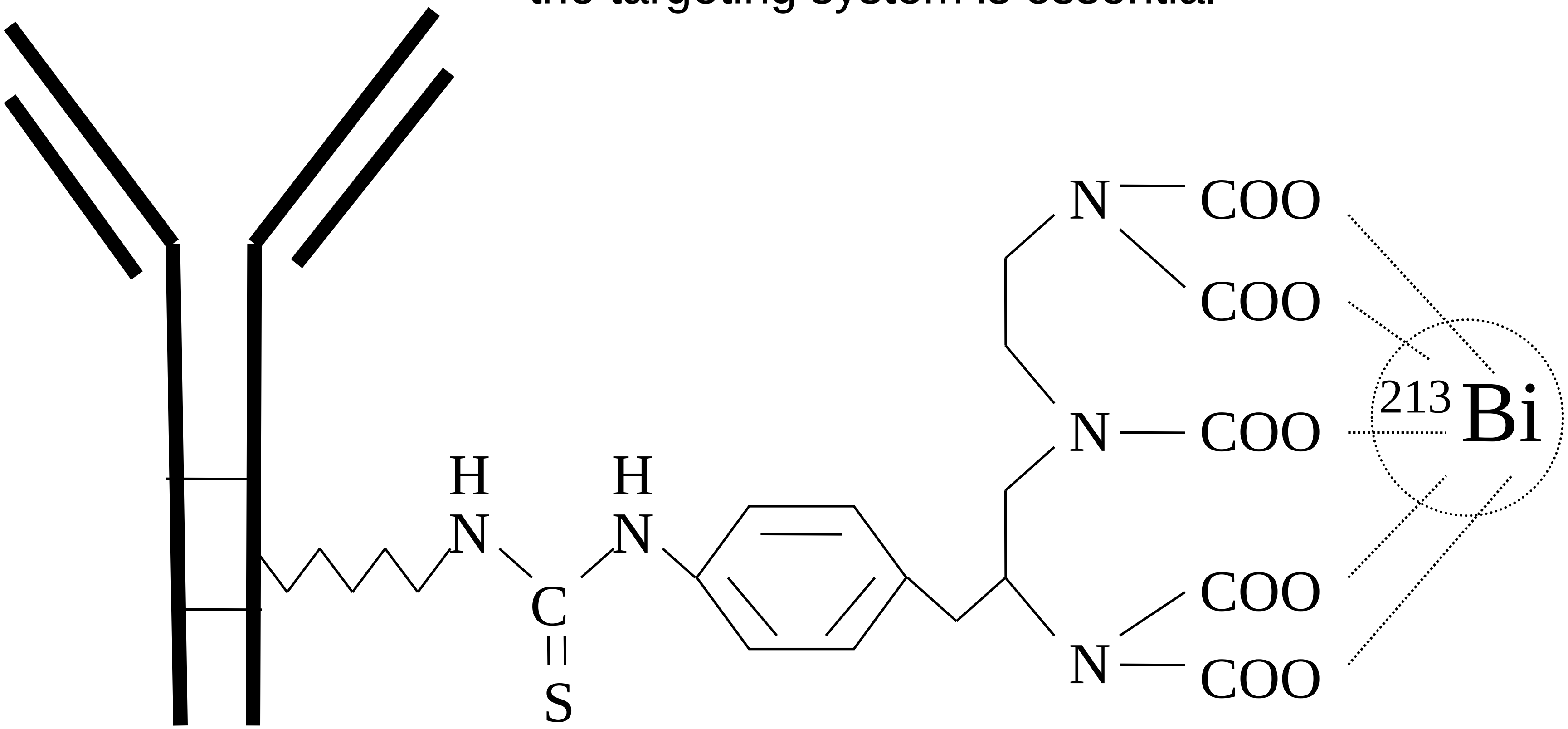
Radiolabeled antibodies, antibody constructs, engineered antibodies, diabodies, hormones, peptides

Hodgkin's disease	Y-90-antiferritin, Y-90 mAb
Acute leukemia	I-131-mAb, Bi-213 mAb
Colorectal cancer	Y-90-mAb, I-131-mAb
Brain glioma, astrocytoma	At-211-anti-tenascin Ab
Melanoma	Pb-212/Bi-212 peptide
Many others	(Cu-67, Lu-177, Bi-213, Ac-225, At-211, Bi-212)



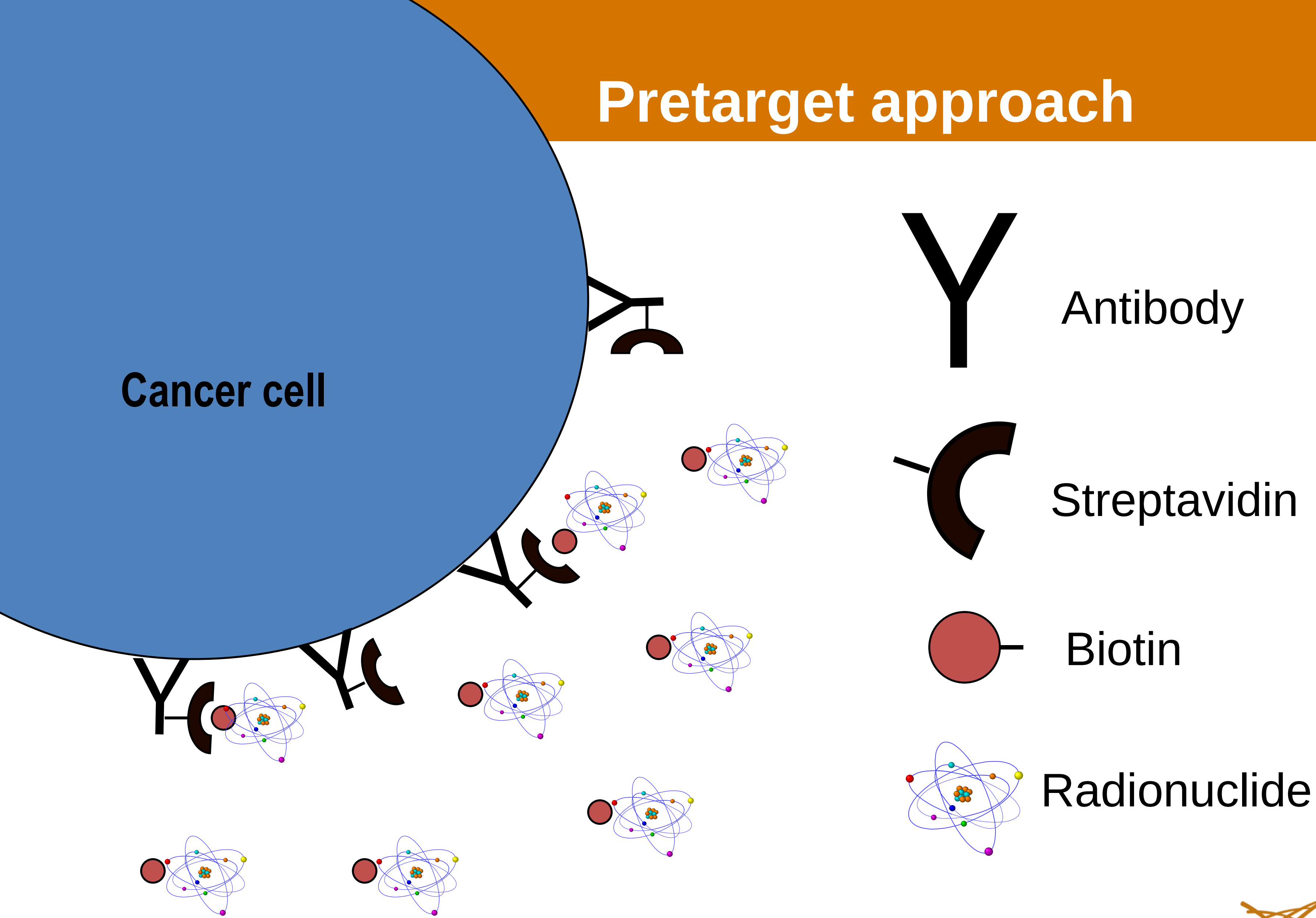
Radionuclide conjugation

- Ability to effectively label an isotope to the targeting system is essential



antibody + isothiocyanatobenzyl-DTPA-Bi-213

Pretarget approach



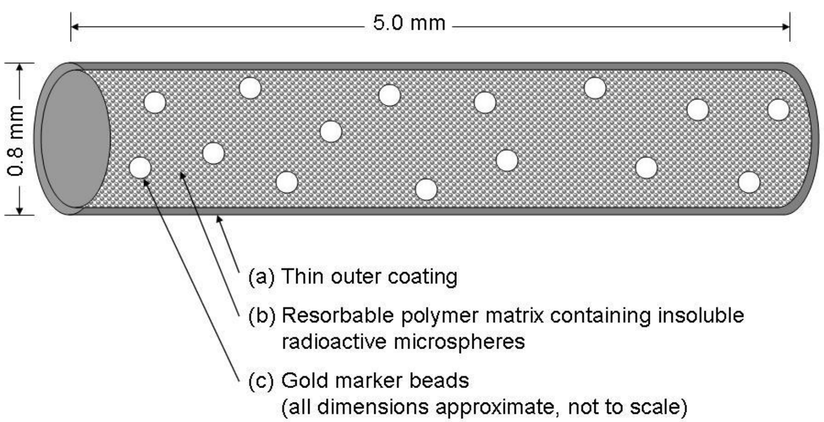
Radiogel polymer composites

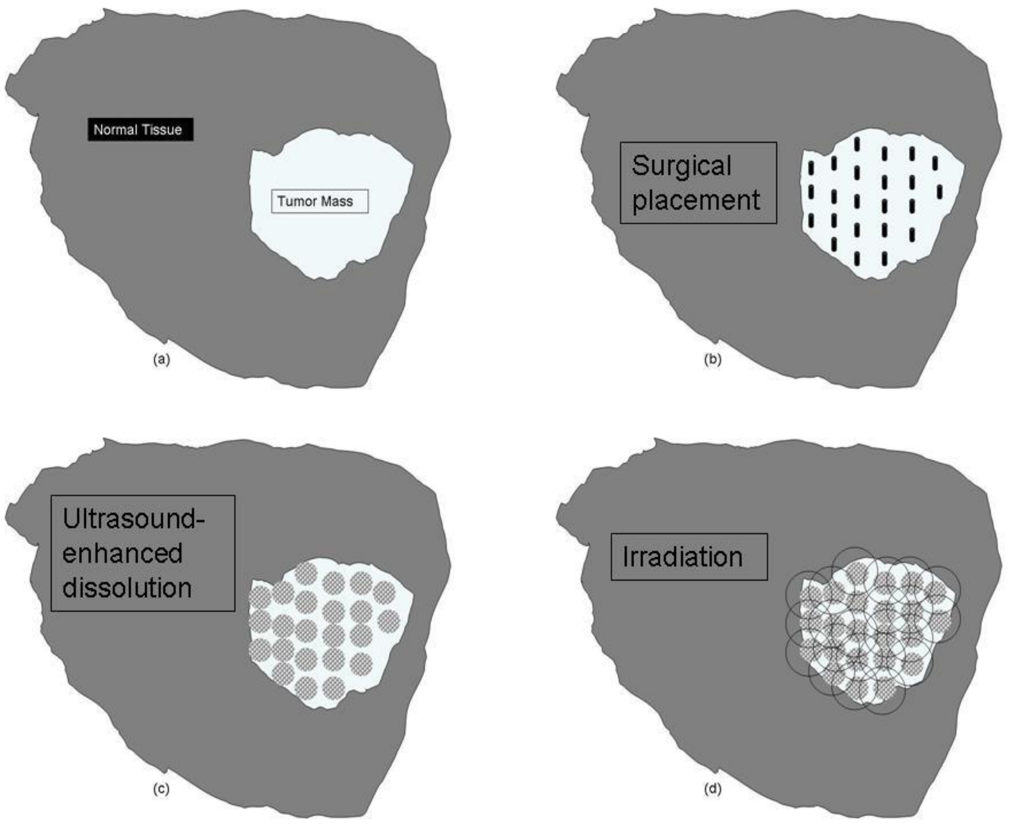
- Direct injection/perfusion of non-resectable solid tumors
- Temperature-sensitive gelation
- Very high absorbed radiation doses achievable with sparing of adjacent normal tissues
- Improved localized distribution of radiation dose
- Applications in therapy of cancers of the prostate, brain, liver, pancreas, colon, kidney
- May be combined with imaging agents for ultrasound, MRI, gamma-camera, and PET

Sealed-source medical devices

- Intra-uterine, cervical brachytherapy
  - Ir-192, Cs-137 sealed sources
- Seed implants
  - I-125, Pd-103, Cs-131, Au-198
- Y-90 microspheres (liver tumors)
- Y-90 eye plaques
- Y-90 intraocular therapy sources (wet age-related macular degeneration)

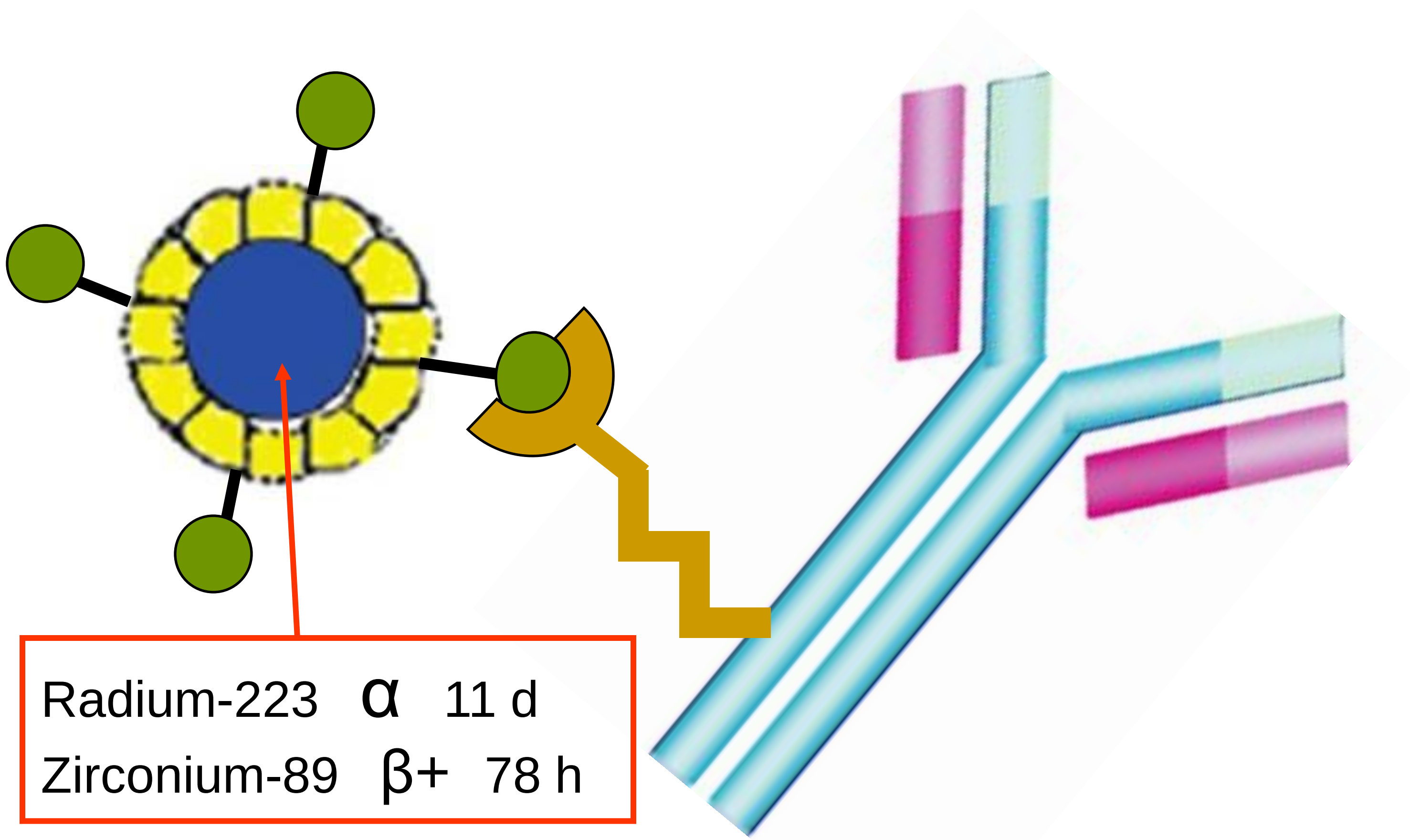
Next-generation Y-90 microsphere brachytherapy seed (prostate, brain, liver)





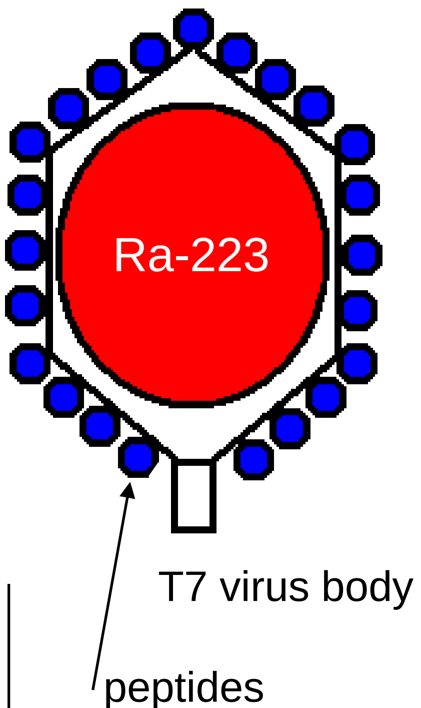
Advantage: controlled delivery of Y-90 microspheres

Novel immunoconjugate constructs



Apoferitin nanoparticle-biotin-streptavidin-antibody

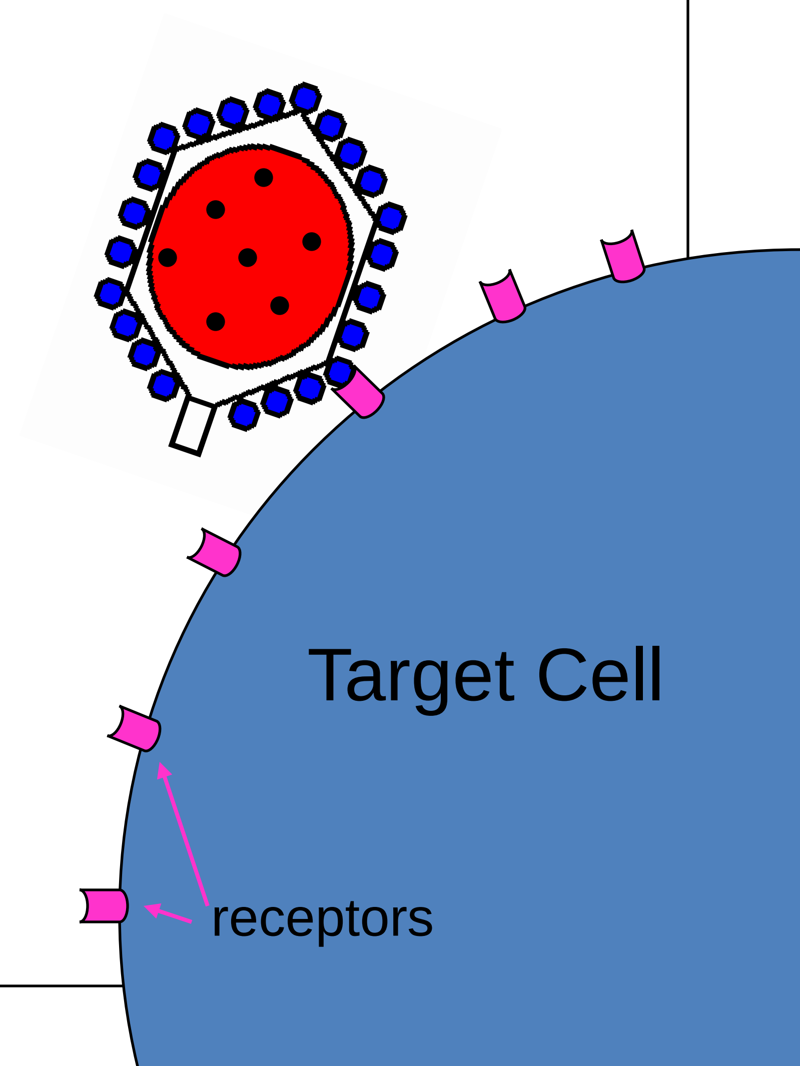
Nanoparticle virus phage capsid



1. Fuse an affinity reagent by phage display or protein expression

2. Remove DNA

3. Replace with an insoluble radioisotope core



Radioisotopes used in diagnostic applications

Beta/gamma Emitters

Technetium-99m	Iodine-131	Indium-111	Thallium-201

Positron Emitters

Fluorine-18	Carbon-11	Oxygen-15	Nitrogen-13
Rubidium-82	Germanium-68	Copper-64	Copper-60
Copper-61	Bromine-76	Bromine-77	Iodine-124
Technetium-94m	Yttrium-86	Zirconium-89	Gallium-66

Auger-electron Emitters

Indium-111	Iodine-123	Iodine-125

Radioisotopes used in cancer treatment

Beta Emitters

Iodine-131	Strontium-89	Samarium-153	Holmium-166
Yttrium-90	Lutetium-177	Promethium-149	Gold-199
Copper-64	Rhenium-186	Rhenium-188	Others?
Copper-67	Tin-117m	Phosphorus-32	

Alpha Emitters

Astatine-211	Radium-223	Actinium-225	Terbium-149
Radium-224	Bismuth-212	Bismuth-213	Thorium-227

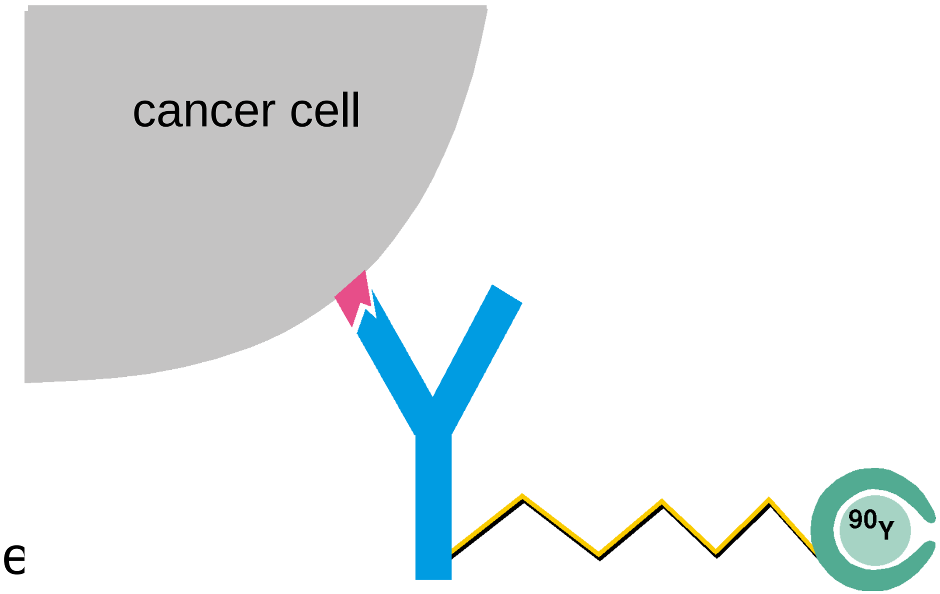
Auger-electron Emitters

Bromine-77	Indium-111	Iodine-123	Iodine-125

Medical isotope selection criteria

- ✓ Appropriately short physical half-life
- ✓ Radiation emissions (alpha, beta, gamma, Auger) and energy for therapeutic efficacy;
- ✓ Photons for imaging and dosimetry
- ✓ Optimum energies for imaging, therapy
- ✓ Reasonable cost
- ✓ Ready availability (current and future)
- ✓ Desired specific activity, purity, labeling yield
- ✓ Regulatory acceptance and approval
- ✓ Therapeutic index

Desirable carrier properties



- Highly specific targeting
- Non-specificity for normal tissues
- Rapid uptake in the target
- High uptake concentration in the target
- Long-term retention in the targe
- Non-immunogenic
- Non-toxic, biodegradable
- Chemically stable linkers and chelates
- Radionuclide binding stability

PNNL Isotope Sciences Capabilities

Support R&D in production and use of radioisotopes

- Ultra-pure separations
- Target design
- Miniature radioisotope power sources
- Medical isotope generators
- Legacy materials disposition and beneficial re-use
- Radiopharmaceutical and medical device design

Radiopharmaceutical and medical device design

- Radionuclide polymer composites for direct intra-tumoral injection
- Next-generation radioactive seeds
  - IsoRay Proxcelan™ ^{131}Cs (R&D 100, Federal Laboratory Consortium awards)
  - New resorbable seed design for controlled delivery of ^{90}Y microspheres (in partnership with Advanced Medical Isotope Corporation)
  - Resorbable radioisotope composites & radiogels for direct intra-tumoral therapy
- Novel radioimmunoconjugate constructs

Medical isotope generators

Developed at PNNL

- ^{225}Ac / ^{213}Bi generator
- ^{227}Ac / ^{223}Ra generator
- ^{90}Sr / ^{90}Y generator
- ^{224}Ra / ^{212}Pb / ^{212}Bi generator
- Automated generator systems

- In partnership with AlphaMed, Actinium Pharmaceuticals, MedActinium, Perkin-Elmer, and Lynntech Inc.

Legacy materials disposition and beneficial re-use

Management of radioactive source material with potential value for useful applications

- Recovery of orphan radioactive sources
  ^{227}Ac, ^{137}Cs, ^{226}Ra, ^{90}Sr
- Matching excess radioactive sources with end-users in need of those materials
- Chemical reprocessing and remanufacturing of radioisotope sources for special applications

Recovery and Recycle — enhances national security and protects the environment

Questions?