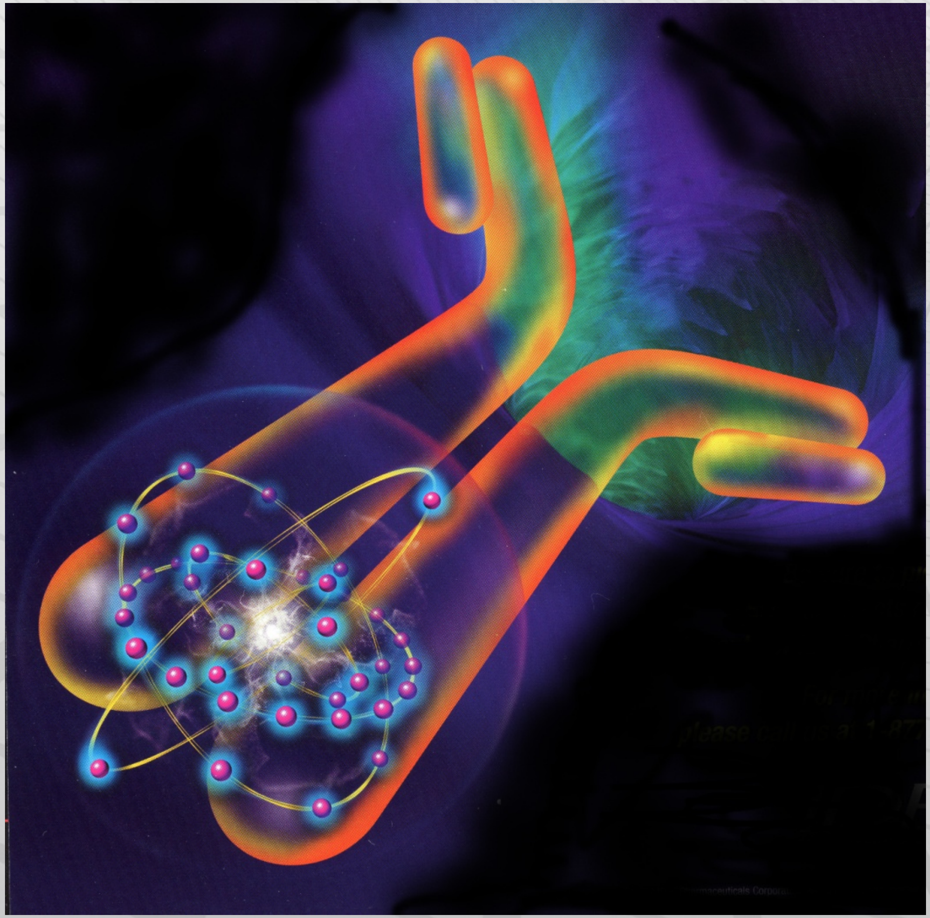
The Future of Medical Isotope Production and Use



Darrell R. Fisher, Ph.D.
Isotope Sciences Program

March 18, 2011
PNNL-SA-78497

Our objective: Improve the supply of radioisotopes and develop exciting, new medical and industrial applications

Our isotope world

- All matter consists of elements (atoms and molecules)
- 112 (or more?) elements
- Each element comprises several isotopes
- About 1600 isotopes
- Either stable or unstable (radioactive)

Hydrogen: ^{1}H (99.985%, stable), ^{2}H (0.015%, stable), ^{3}H (trace, radioactive)

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

$T_{1/2}$ ^{14}C = 5715 years

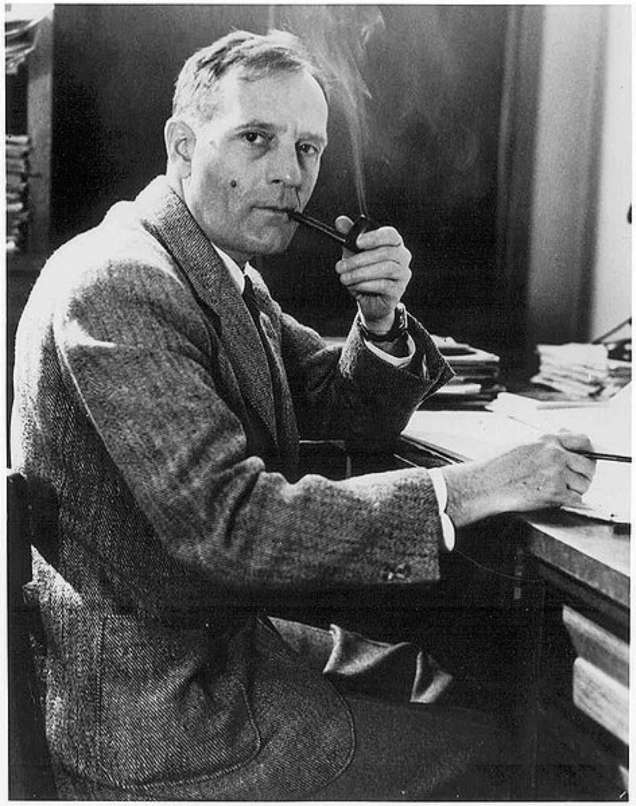
Emits a beta(-) particle

$T_{1/2}$ ^{11}C = 20.3 minutes

Emits a beta(+) particle, gammas

"Equipped with his five senses, man explores the universe around him and calls the adventure *science.*"

-- Edwin Powell Hubble, *The Nature of Science*, 1954



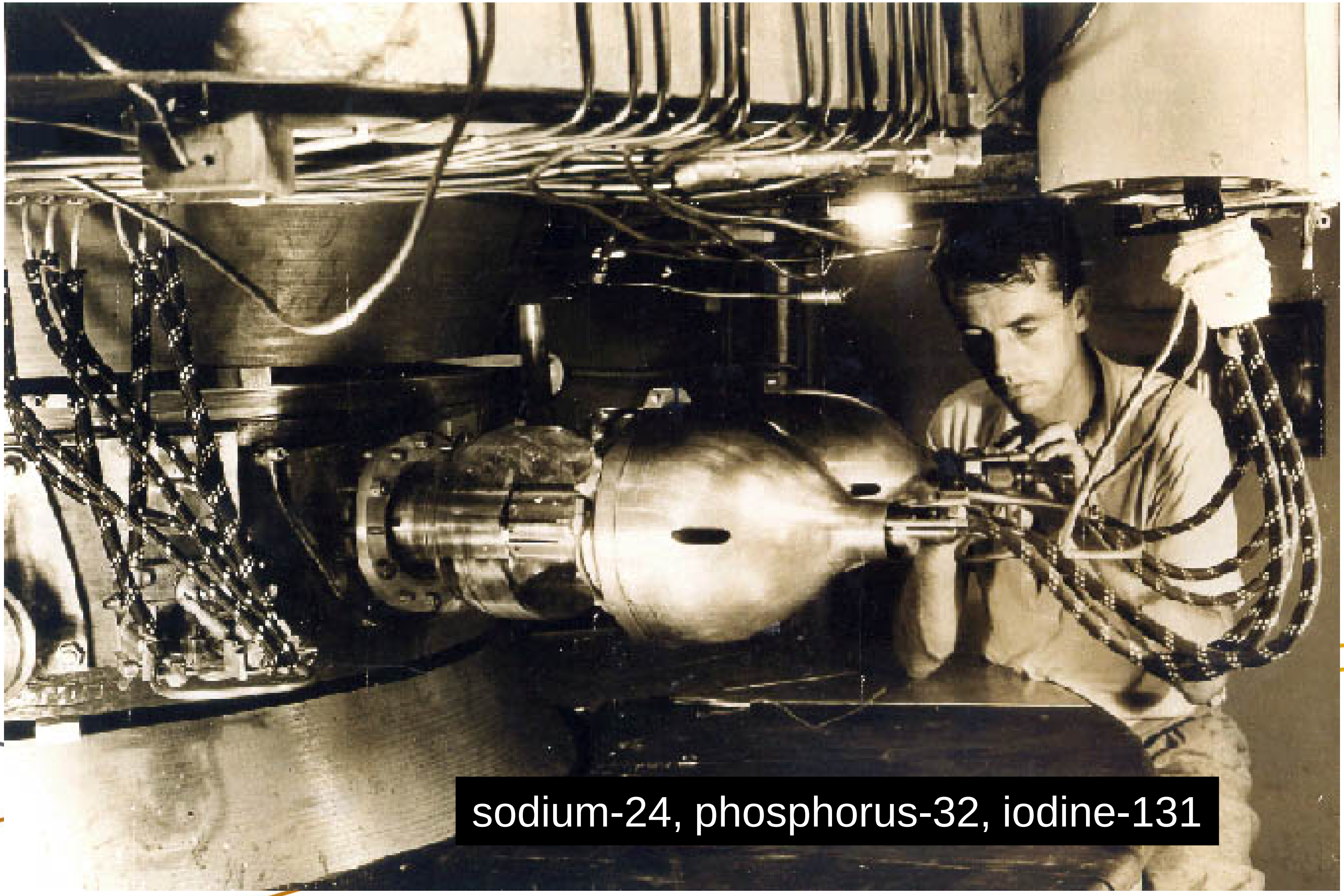
George Charles de Hevesy (1885 – 1966), Hungarian radiochemist; Nobel laureate (1943) for development and use of radiotracers in the study of chemical processes and metabolism

Of Sunday dinner and recycled pot roast, Manchester, (1911)

Ernest O. Lawrence (1901-1958), Nobel laureate in physics (1939) for work on the cyclotron and isotope production

University of California Radiation Laboratory, circa 1936

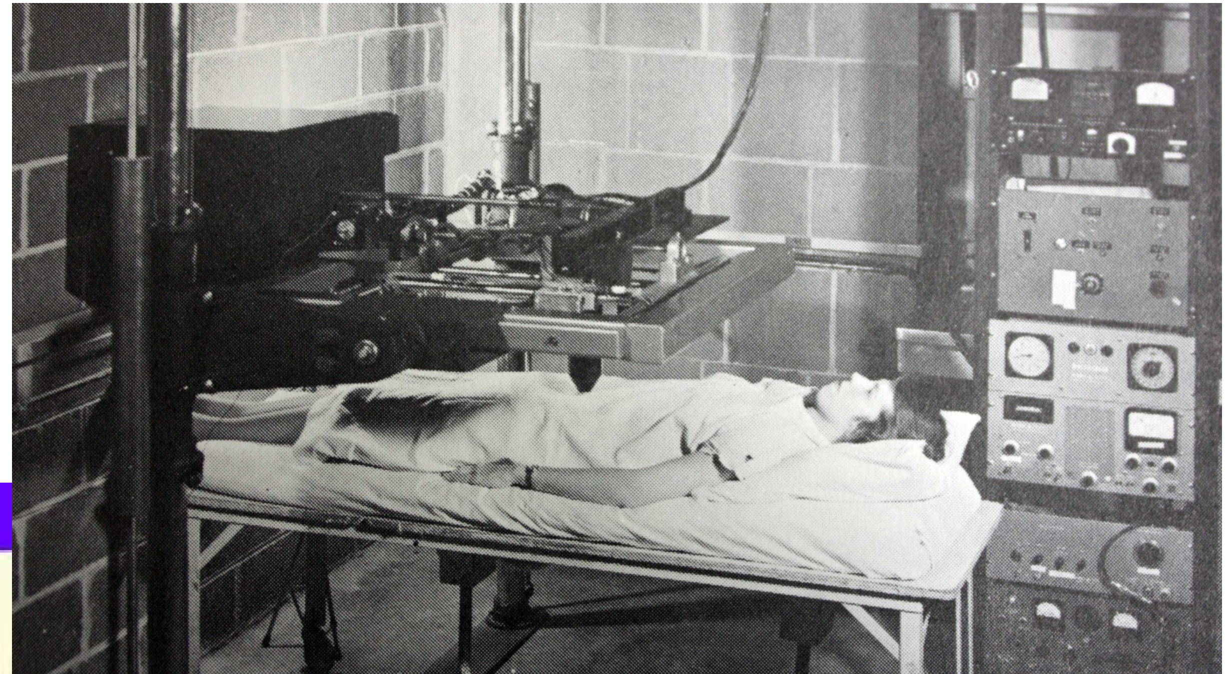
Building the 60-inch Berkeley cyclotron in 1937 with its 220-ton magnet

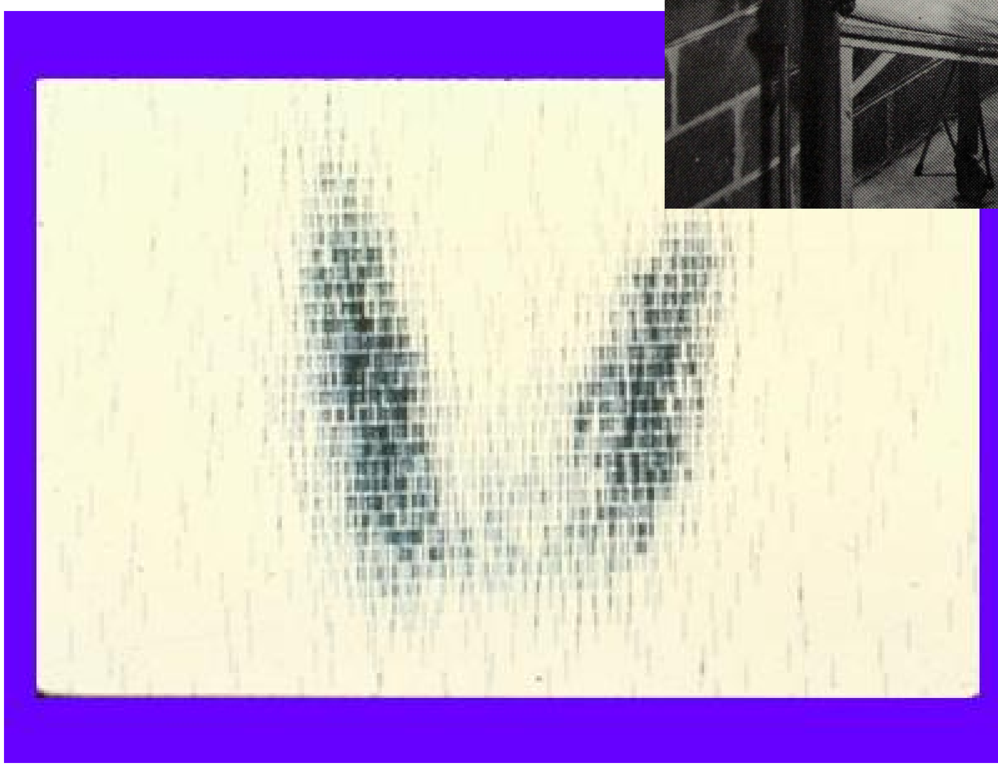


Dr. Joseph Hamilton (1907–1957), University of California at San Francisco

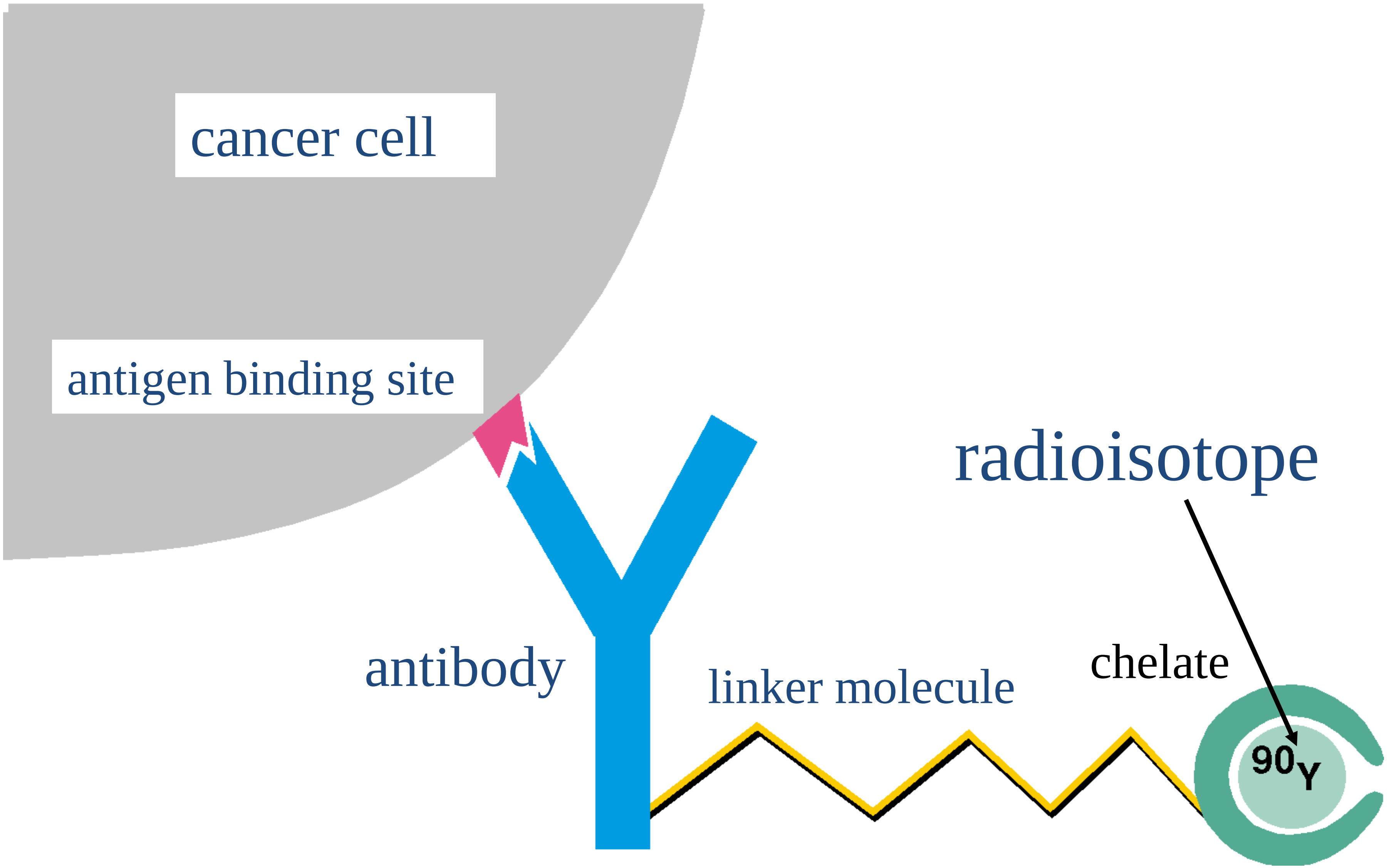
- worked closely with John and Ernest Lawrence and Glenn Seaborg on medical applications of newly discovered isotopes.
- helped transform the isotope sciences into a new field: nuclear medicine

Early thyroid rectilinear scan using iodine-131 (1954)

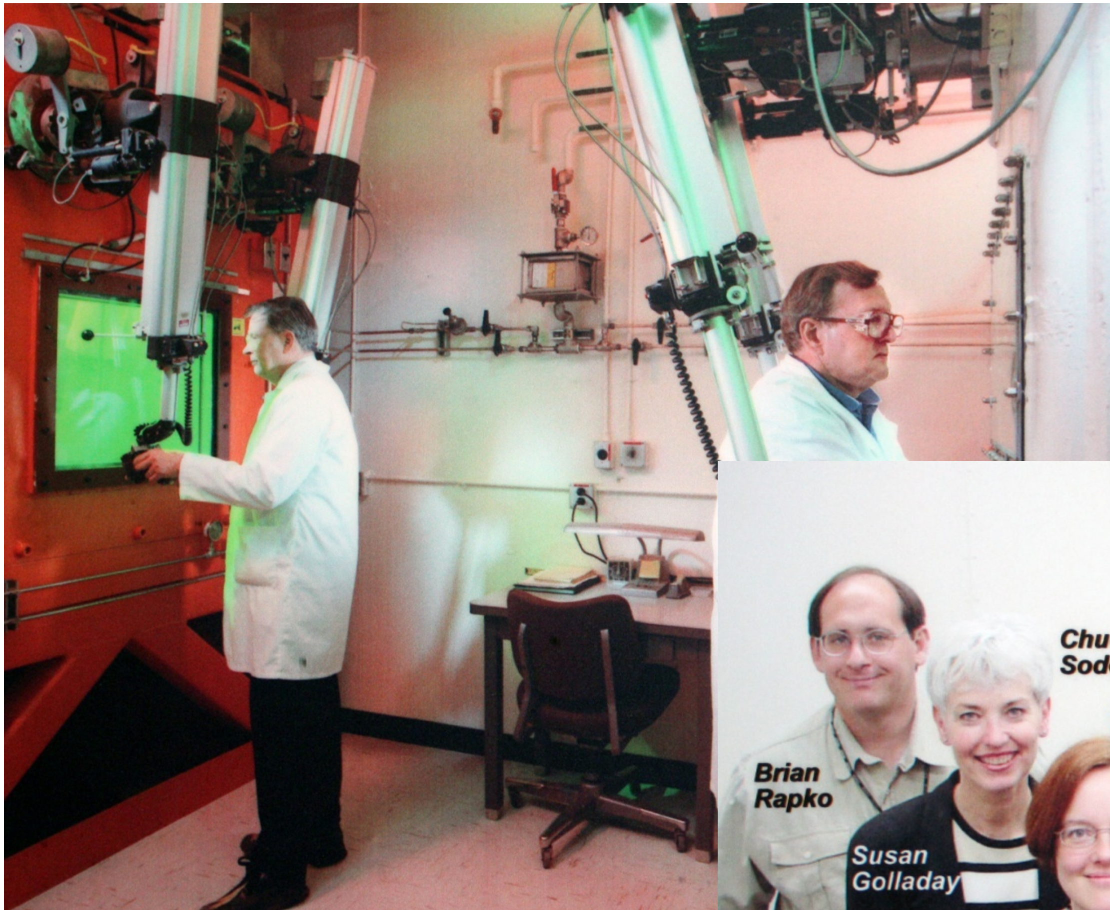


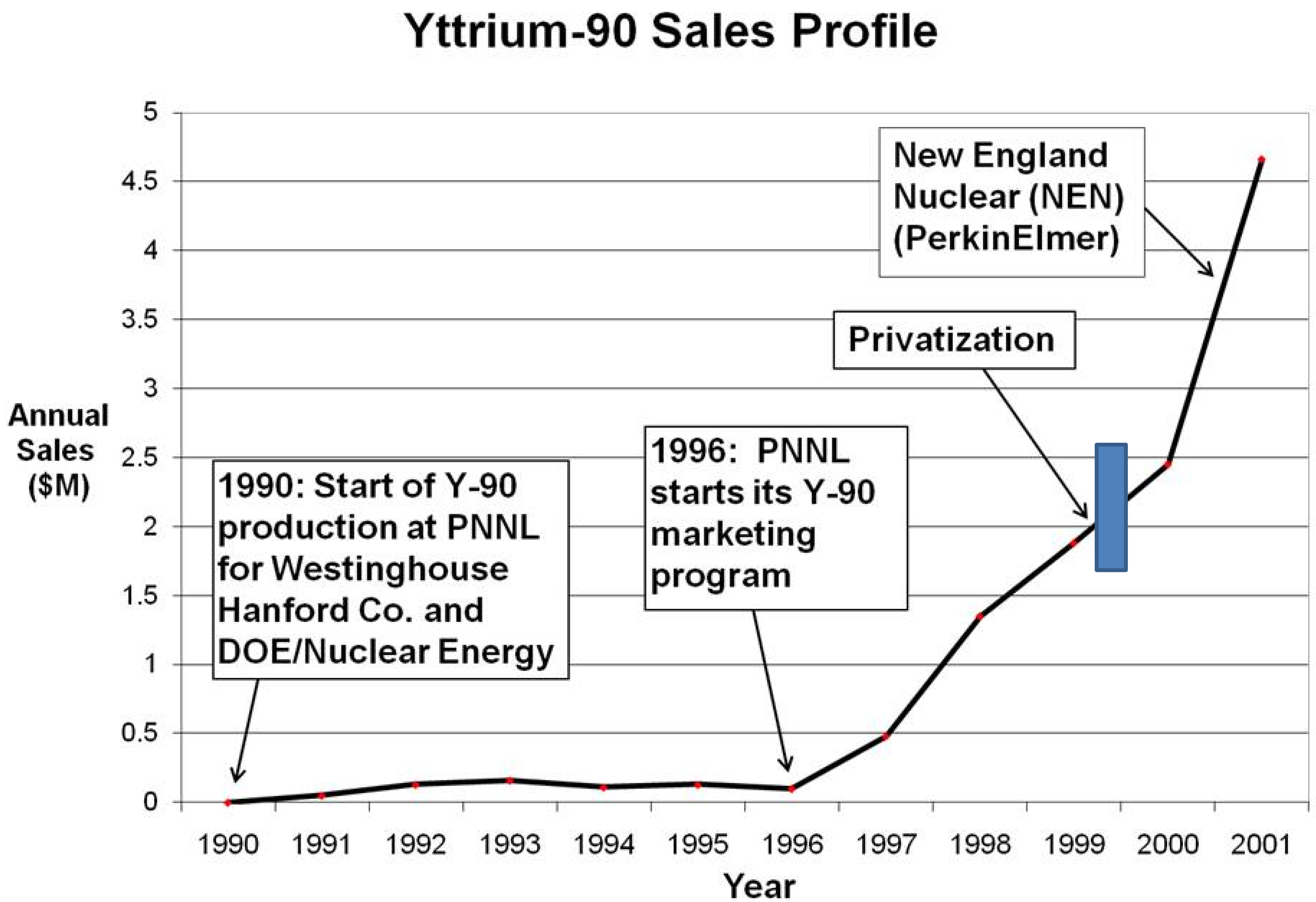


Radiolabeled antibodies: created new interest in yttrium-90



Yttrium-90 production at PNNL (1990-1999)




Yttrium-90 Sales Profile
Annual Sales ($M)
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
1990
1991
1992
1993
1994
1995
1996
1997
1998
1999
2000
2001
Year
1990: Start of Y-90 production at PNNL for Westinghouse Hanford Co. and DOE/Nuclear Energy
1996: PNNL starts its Y-90 marketing program
Privatization
New England Nuclear (NEN) (PerkinElmer)

The dark ages (1999-2003)

- Total loss of funding and mission responsibility
- Loss of key staff
- Struggle to keep the Fast Flux Test Facility viable as a production source for medical isotopes

The Renaissance (2003-2009)

- New program strategy focused on technical support to the private sector
  - → IsoRay Medical, cesium-131 seeds
  - → AlphaMed, Inc.
  - → Advanced Medical Isotope Corporation
- New program support from the Department of Energy in isotope production
- New purpose and mission
- Collaboration with other national laboratories
- New staff

Today: Enabling science, medicine, and industry

The Isotope Sciences Program at PNNL:

- *represents a national technology resource*

Our signature capability:

- ✓ high-purity radiochemical separations

Nicole Green

Reid Peterson

Pacific Northwest
NATIONAL LABORATORY

Proudly Operated by Battelle *Since 1965*

Our greatest asset: people


Garrett Brown

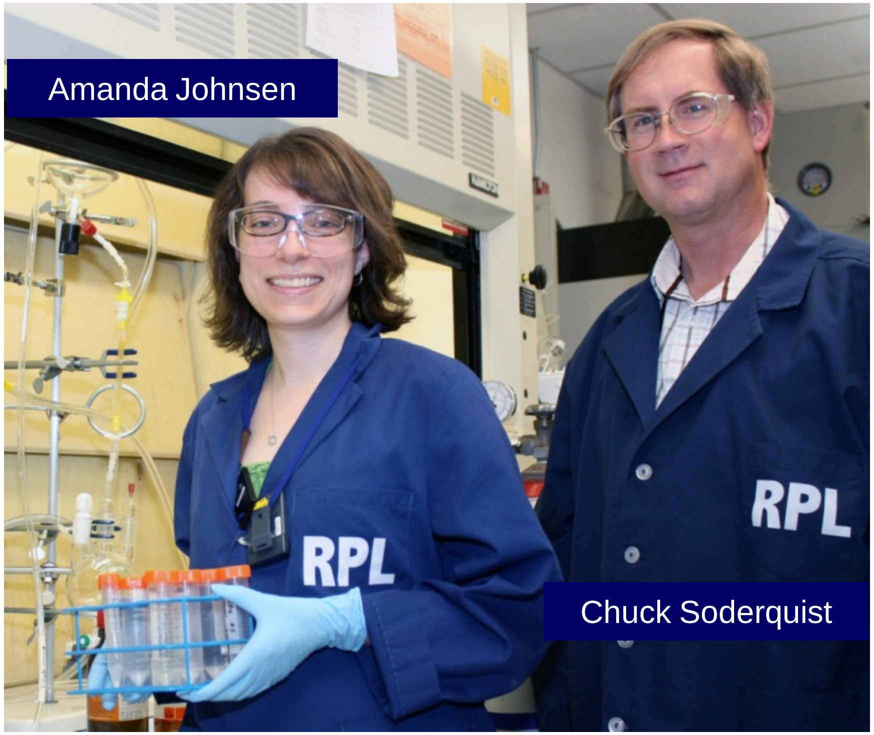

Brian Rapko


Larry Greenwood


Clark Carlson


David Blanchard


Gregg Lumetta




Mike Urie


Jim Toth


Matt O'Hara

Pacific Northwest
NATIONAL LABORATORY

Proudly Operated by Battelle *Since 1965*

Facilities: Radiochemical Processing Lab

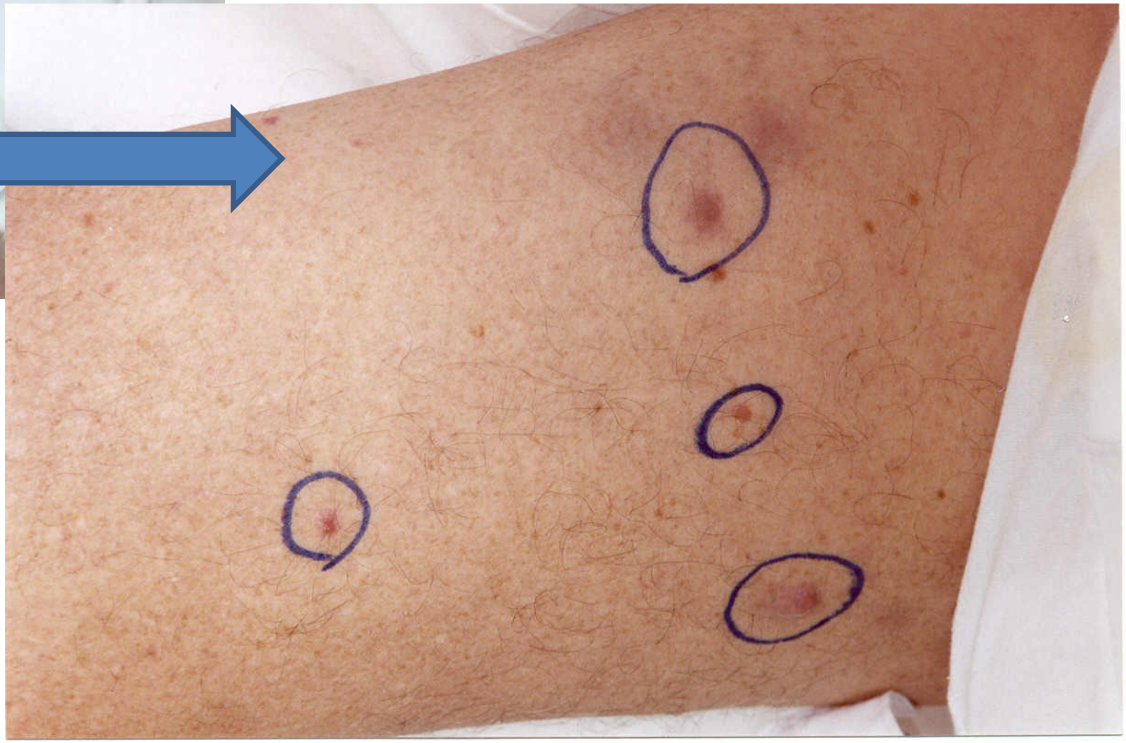
- DOE hazard category 2 facility for work with micrograms to kilograms of fissionable and non-fissionable radioactive materials
- 144,092 ft^2 building with 40,000 ft^2 of laboratory and more than 8,500 ft^2 of hot cell space
- Extensive wet laboratories, shielded glove boxes, wet radiochemistry fume hoods, and a modern analytical laboratory
- 16 hot cells (4 new)

Isotope production and distribution

- Strontium-90 production as source for yttrium-90
- Radium-224 generators for $^{212}Pb/^{212}Bi$
- Gadolinium-153 in collaboration with Idaho National Laboratory
- Radium-223 and thorium-227 production from legacy actinium-227 (neutron sources)
- Radium-226 beneficial re-use for producing short-lived alpha emitters ($^{225}Ac/^{213}Bi$)
- Neptunium-237 distribution
- Cesium-137 recycle for beneficial re-use

Focus on alpha-emitting radionuclides

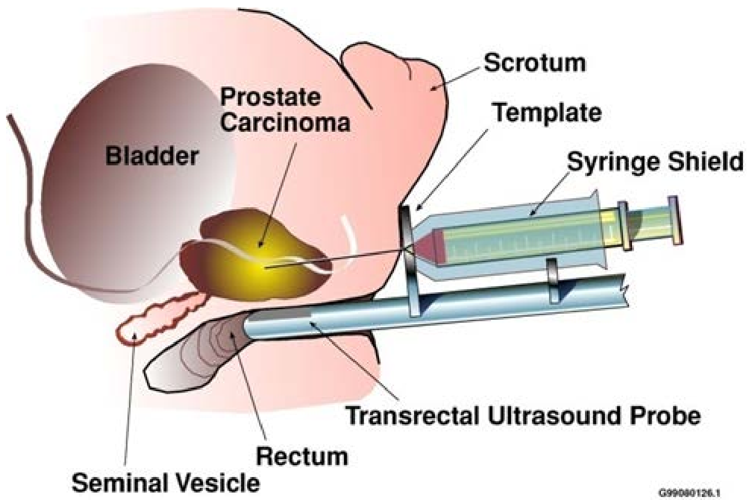
- Greatest cell-kill efficiency
- Normal-tissue sparing
- Ideal for treating metastatic cancer



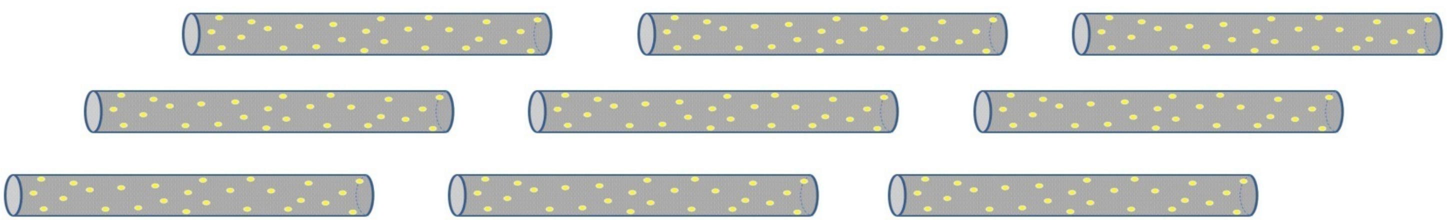
Melanoma to complete remission using targeted alpha therapy

Radiopharmaceutical and medical device design

- Radionuclide polymer composites for direct intra-tumoral injection

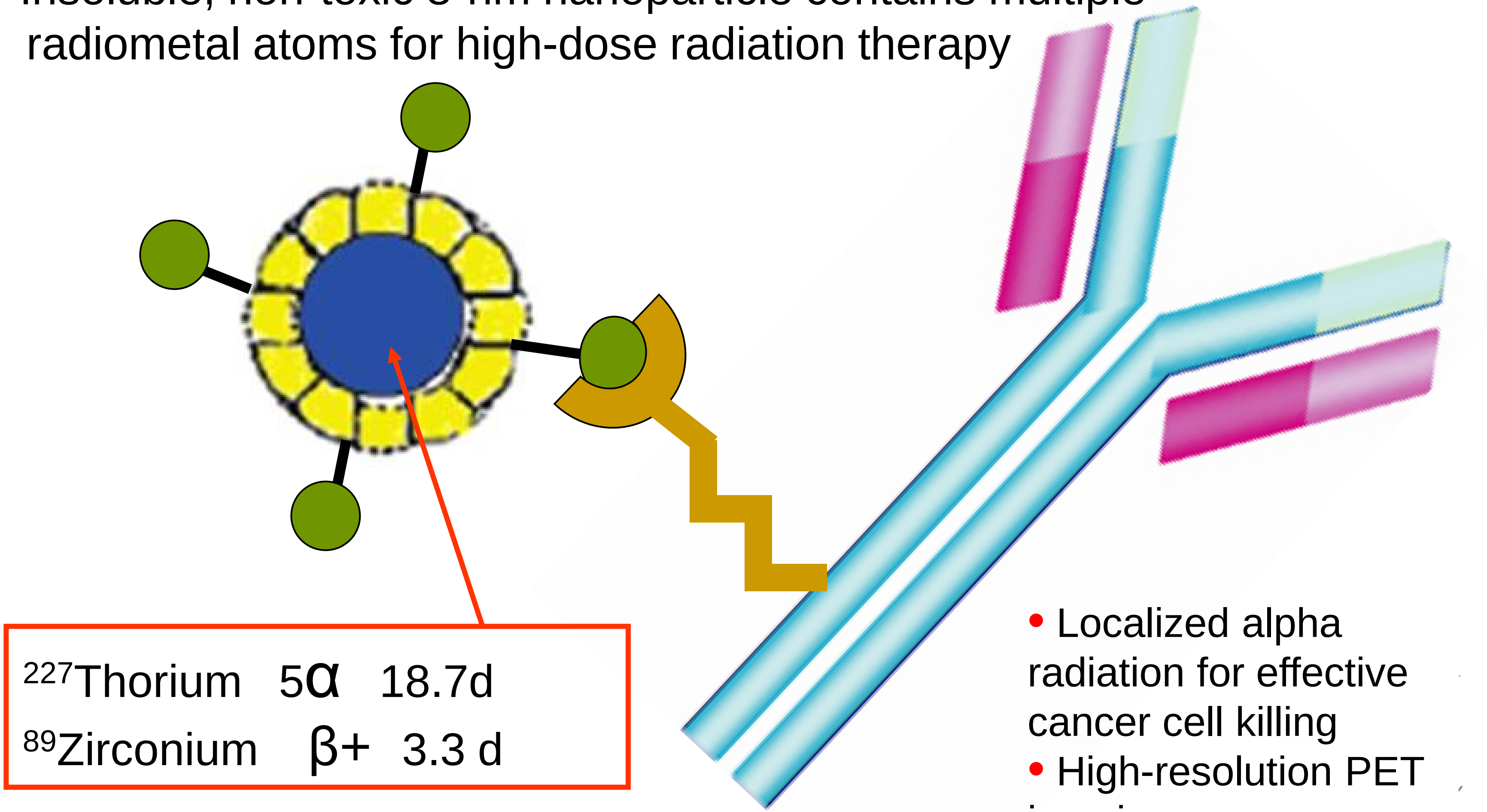


- New, fast-resorbable seed design for controlled delivery of yttrium-90 microspheres



Apoferritin nanoparticle-biotin-streptavidin-antibody

- ✓ Non-toxic, biodegradable construct
- ✓ Secure binding of radiometals and decay products
- ✓ Insoluble, non-toxic 8-nm nanoparticle contains multiple radiometal atoms for high-dose radiation therapy



- Localized alpha radiation for effective cancer cell killing
- High-resolution PET imaging

Where’s the nuclear reactor?

Although we do not have an operating nuclear reactor or a charged-particle accelerator as on-site isotope-production tools, we nonetheless:

- partner with other facilities and organizations with nuclear reactors and charged-particle accelerators
- prepare and ship radioisotopes extracted from long-lived (legacy) radioactive materials

Pacific Northwest
NATIONAL LABORATORY

Proudly Operated by Battelle *Since 1965*

Compact systems

- "Next-generation" approach to isotope production where full-scale nuclear reactors and cyclotrons are too expensive or too complex to acquire and operate
- Fully dedicated, right-sized, "on/off" systems
  - Proton accelerators
  - Alpha accelerators
  - Neutron generators
  - Electron beam x-ray irradiation systems
  - Stable-isotope plasma-separation systems

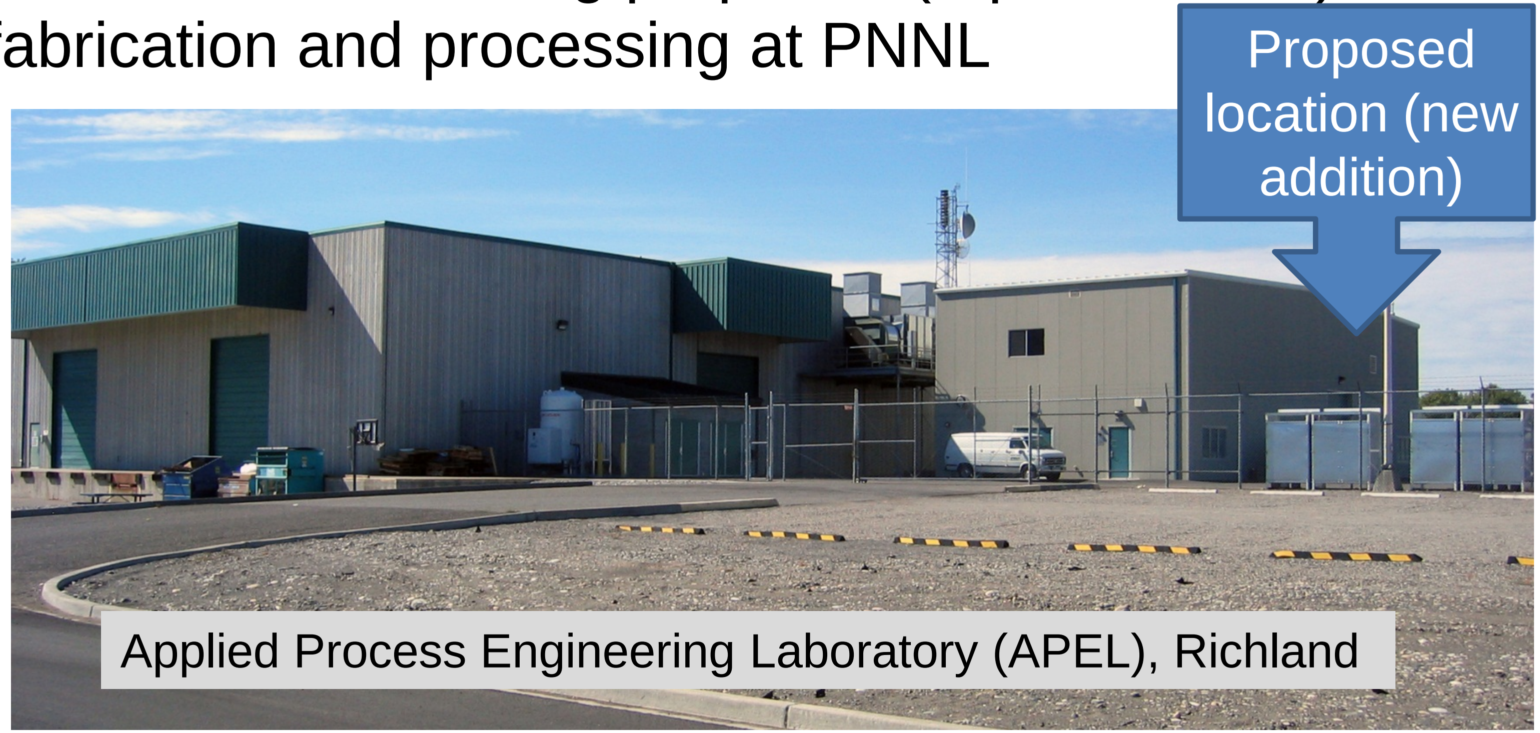
Compact systems: proton accelerator

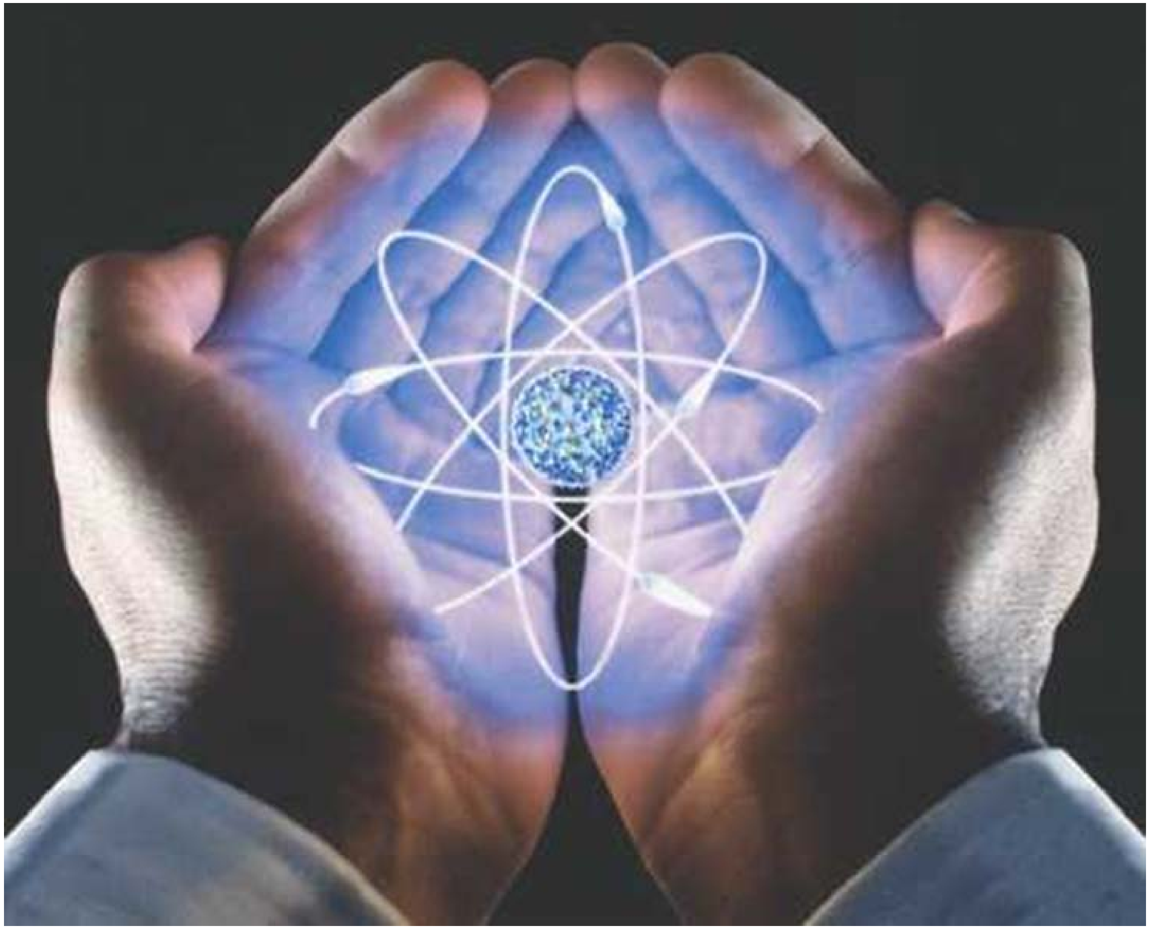
Advanced Medical Isotope Corporation, Kennewick

- First U.S. "compact" 7-MeV proton linear accelerator for medical isotope production (2008)
- Up and running, producing ^{18}F for local hospitals

Next: compact alpha-particle linear accelerator

- Advanced 30 MeV, 1.5 mA, high-efficiency, pulsed or continuous, plasma radiofrequency quadrupole drift tube
- Also accelerates protons, deuterons, ^{3}He,^{12}C
- Lowest cost, highest output of key isotopes identified as critical need: ^{82}Sr, ^{67}Cu, ^{211}At, ^{117m}Sn, ^{210}Po, ^{123}I, ^{125}I
- $12M Private/federal funding proposed (Alpha Source)
- Target fabrication and processing at PNNL





Dream lofty dreams,
and as you dream,
so you shall become.
Your vision is the promise of what
you shall one day be.
-- James Allen