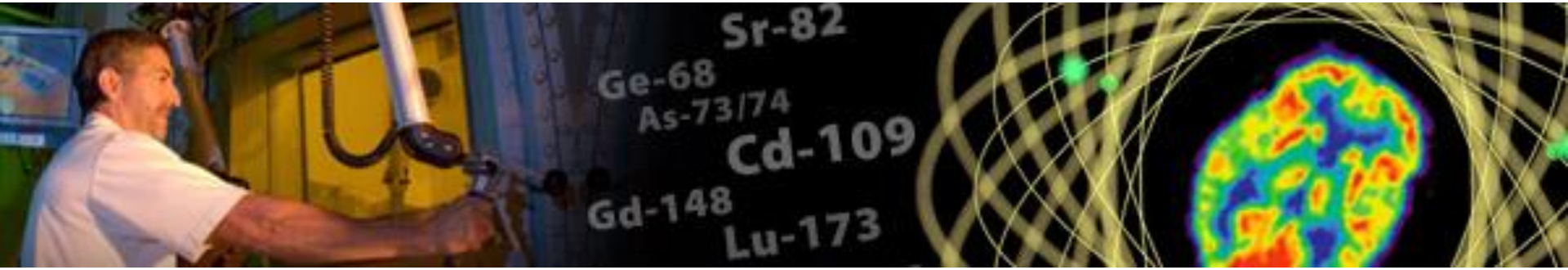
U.S. DEPARTMENT OF ENERGY

OFFICE OF SCIENCE

Recent Novel Isotopes 2019-2020



7th Workshop on Isotope Federal Supply and Demand
January 12, 2021

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Office of Isotope R&D and Production, Office of Science, U.S. Department of Energy

Actinium-225/Bismuth-213

Application: medical, targeted therapy

Agency interest: NIH, FDA, NRC, NIST, DHS, NNSA, …

- Accelerator production of Ac-225 (10 d)
  - $^{232}Th(p,spallation)^{225}Ac$
  - Routine production at BNL/LANL/ORNL
    - First supply of accelerator-produced Ac-225 in the world
    - DMF submitted, cGMP production initiated
    - Ramping up to >1 Ci batches
    - Alleviates shortage of Ac-225, supporting development and ultimately application of targeted alpha therapeutics
  - 4 alpha particles in decay chain
- Parent of Bi-213 (46 m)
  - 1 alpha particle in decay chain
- Additional production in development
  - Cyclotron production at BNL: $^{226}Ra(p,2n)^{225}Ac$
  - Phototransmutation at ANL: $^{226}Ra(\gamma,n)^{225}Ra(\beta)^{225}Ac$
  - Reactor production at ORNL: $^{226}Ra(3n,\gamma)^{229}Th(\alpha)^{225}Ac$

Americium-241

Applications: fundamental research, radioisotope power sources, commercial

Agency interest: DOE BES, DoD, NASA, NRC, NIST, DHS, NNSA, …

- Recovery of legacy Am-241 (433 y)
  - Recovered from plutonium waste solutions
  - Goal is 500 g/year
  - Product now available
- Long-lived radioisotope power sources
- Americium-beryllium neutron sources
  - Oil and gas exploration
  - Neutrons for research

Am-241 glovebox

Astatine-211

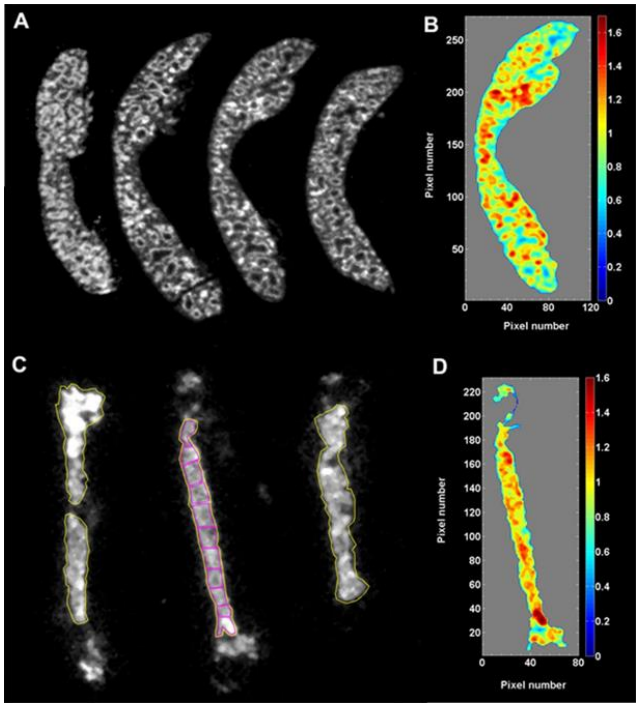
Application: medical, targeted therapy

Agency interest: NIH, FDA, NRC, NIST, DHS, NNSA, …

Provided as At-211 or a Rn-211/At-211 generator (future)

- Cyclotron production of At-211 (7.2 h)
  - $^{209}Bi(\alpha,2n)^{211}At$
  - Production at the University of Washington
    - First university in the DOE IP university network
  - Additional sites being added to the university network
    - Duke, University of Pennsylvania, University of California – Davis, Texas A&M

- Accelerator production of Rn-211 (14.6 h)
  - $^{209}Bi(^{7}Li,5n)^{211}Rn \rightarrow {}^{211}At$
  - DOE investigating production



Targeting blood-borne cancers, images of spleen (top) and femur (bottom)
Blood 2013 121:3759-3767

Barium-133

Applications: research, commercial

Agency interest: DOE, NSF, NIH, FDA, NRC, NIST, DHS, NNSA, …

- Reactor production of Ba-133 (10.6 y)
  - $^{132}Ba(n,\gamma)^{133}Ba$
  - High flux required to achieve high specific activity
    - DOE IP product has highest specific activity available
- Previously only available from Russia
- Gamma radiation standard
- Industrial gamma source

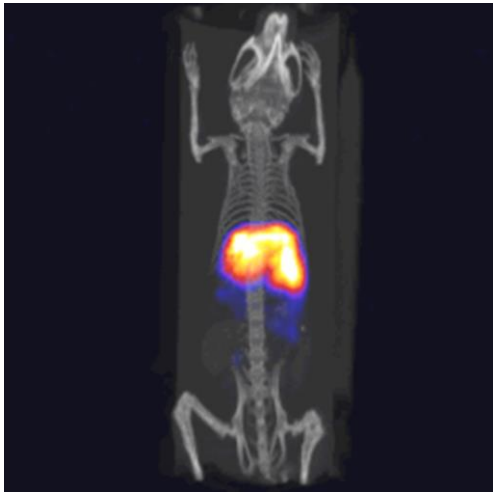
Copper-67

Application: medical, targeted therapy

Agency interest: NIH, FDA, NRC, NIST, DHS, NNSA, …

- Electron linac production of Cu-67 (62 h)
  - $^{68}Zn(\gamma,p)^{67}Cu$
- Theranostic isotope
  - Simultaneous diagnostic imaging and therapy
  - SPECT imaging with Cu-67 gamma ray
  - Combine with Cu-64 (positron emitter) for PET imaging
- Routine production established at Argonne National Laboratory
- Production at Thomas Jefferson National Laboratory in development

Cu-67 ready for shipment



Diagnostic image of Cu-67 in live mouse, courtesy University of Alabama-Birmingham

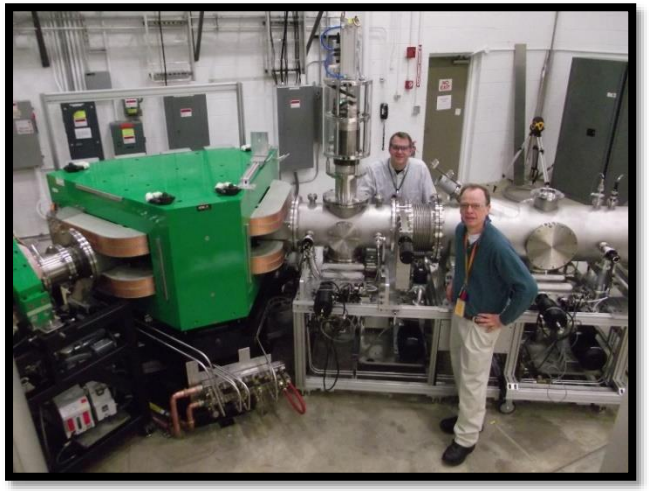
Enriched Stable Isotopes

Applications: fundamental and applied research, tracers, targets, medical, commercial, …

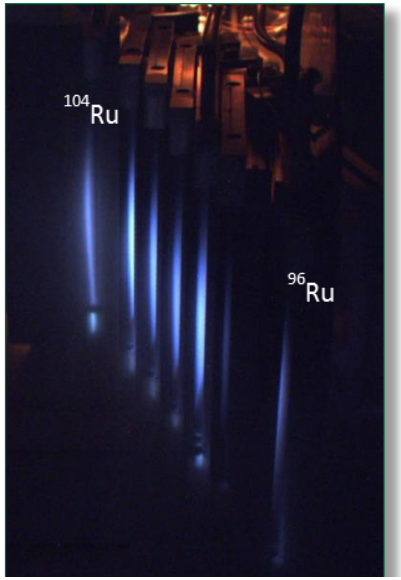
Agency interest: all

- Ruthenium-96
  - First enriched stable isotope produced in the United States since 1998
  - Essential for the performance of a nuclear physics experiment at the Relativistic Heavy Ion Collider

- Additional stable isotope enrichment in progress and planned
  - Will be summarized in the next presentation, Research for Emerging Isotopes



Electromagnetic Isotope Separator (EMIS)



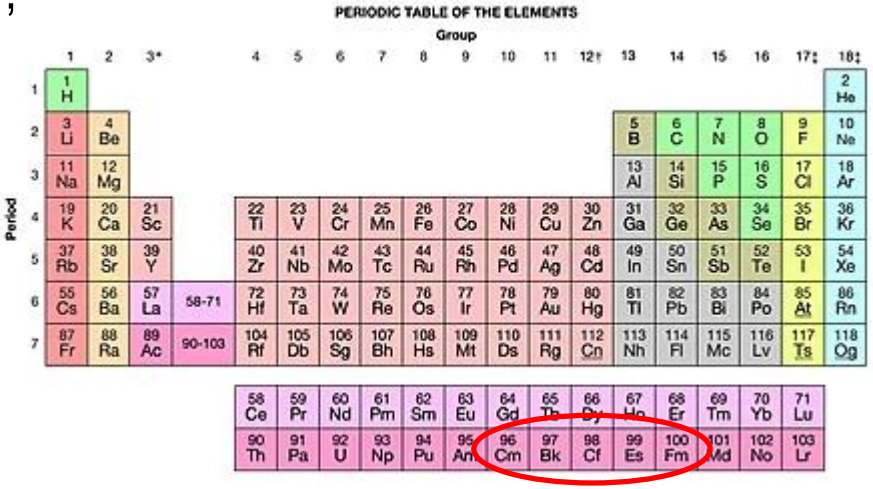
EMIS Ru Beams

Heavy Elements

Application: fundamental research

Agency interest: DOE BES and NP, NSF, NRC, NIST, DHS, NNSA, …

- Berkelium, Einsteinium, and Fermium
  - DOE IP two-year campaigns for production of ^{252}Cf
  - Co-production of:
    - Bk in mg amounts
    - Es in ug amounts
    - Fm in pg amounts
      - 2019 was first production of Fm worldwide in decades
  - R&D in progress to increase yields
- Heavy element chemistry research
- Super heavy element research



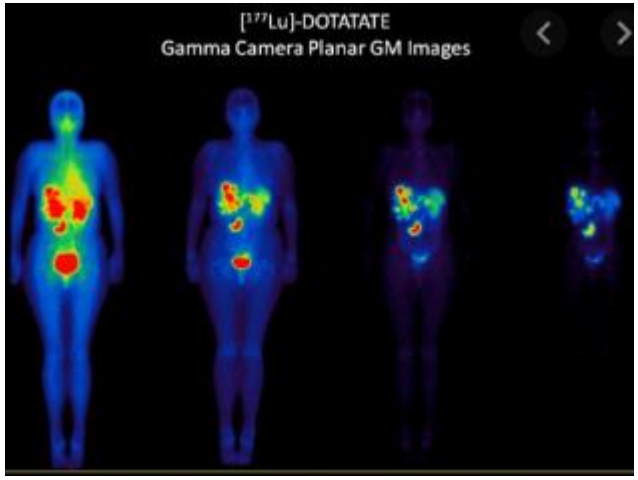
Lutetium-177

Application: medical, targeted therapy

Agency interest: NIH, FDA, NRC, NIST, DHS, NNSA, …

- Reactor production of Lu-177 (6.6 d)
  - $^{176}Lu(n,\gamma)^{177}Lu$
  - Production at the University of Missouri Research Reactor
    - Second university in the DOE IP university network
  - cGMP product for medical application research

- Targeted therapy
  - E.g., the approved drug Lutathera for the treatment of neuroendocrine tumors



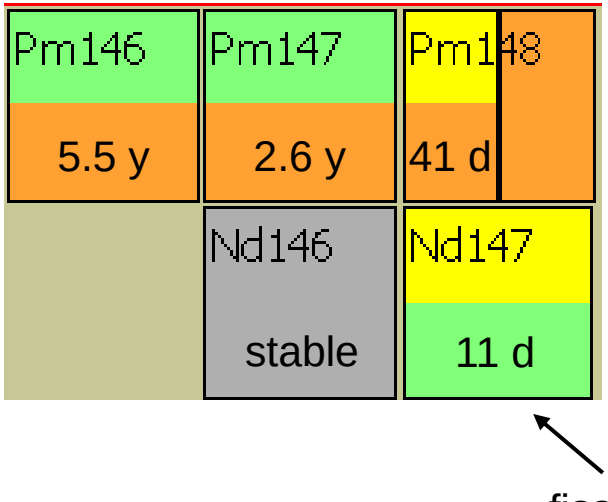
Targeting of neuroendocrine tumors
Asia Oceania Journal of Nuclear Medicine & Biology. 2015 ;3(2):107-115

Promethium-147

Application: radioisotope power sources, industrial processes

Agency interest: NASA, DoD, NRC, NIST, DHS, NNSA, …

- Reactor production of Pm-147 (2.6 y)
  - $^{237}Np(n,fission)^{147}Pm$
    - Now available
  - $^{146}Nd(n,\gamma)^{147}Nd(\beta)^{147}Pm$
    - Production in development
- Previously only available as fission product from Russia
  - Reprocessing of reactor fuel (long irradiation)
- DOE production (both routes) yields a purer product then Russia
  - Less Pm-146 and Pm-148m which have high energy gamma emissions
  - Shorter irradiations (1 or 2 HFIR cycles) than reactor fuel and Nd-147 “delay” reduce production of Pm-146 and Pm-148m



Strontium-89

Application: medical, palliative therapy

Agency interest: NIH, FDA, NRC, NIST, DHS, NNSA, …

- Reactor production of Sr-89 (50.6 d)
  - $^{88}Sr(n,\gamma)^{89}Sr$
  - Production at the High Flux Isotope Reactor
  - High flux required to achieve adequate specific activity

- Palliation (alleviation) of excruciating pain associated with cancers that have metastasized to bone
  - Improved patient quality of life compared to treatment with narcotics and steroids

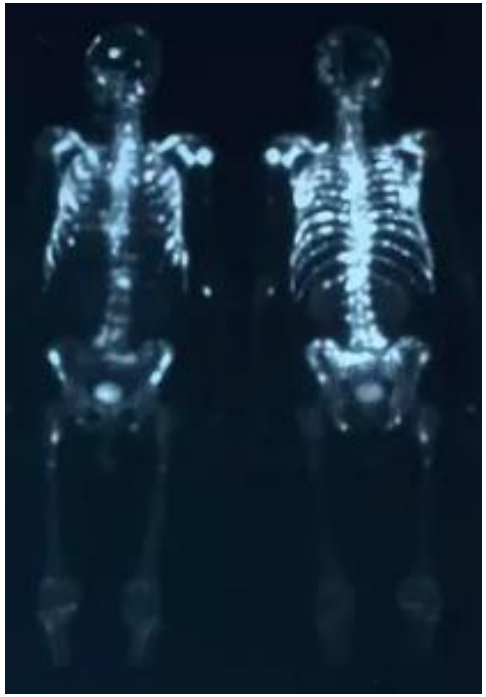


Image of bone metastases

Strontium-90/Yttrium-90

Application: radioisotope power sources, medical

Agency interest: NASA, DoD, NIH, NRC, NIST, DHS, NNSA, …

- Recovery of legacy Sr-90 (29 y)
  - Material generated decades ago from Hanford tank wastes
  - kCi quantities placed in inventory at PNNL

- Moderately long-lived radioisotope power sources

- Parent of Y-90
  - Therapeutic applications
    - Microspheres for liver cancer therapy
    - Targeted therapy

BUP-500 radioisotope power source

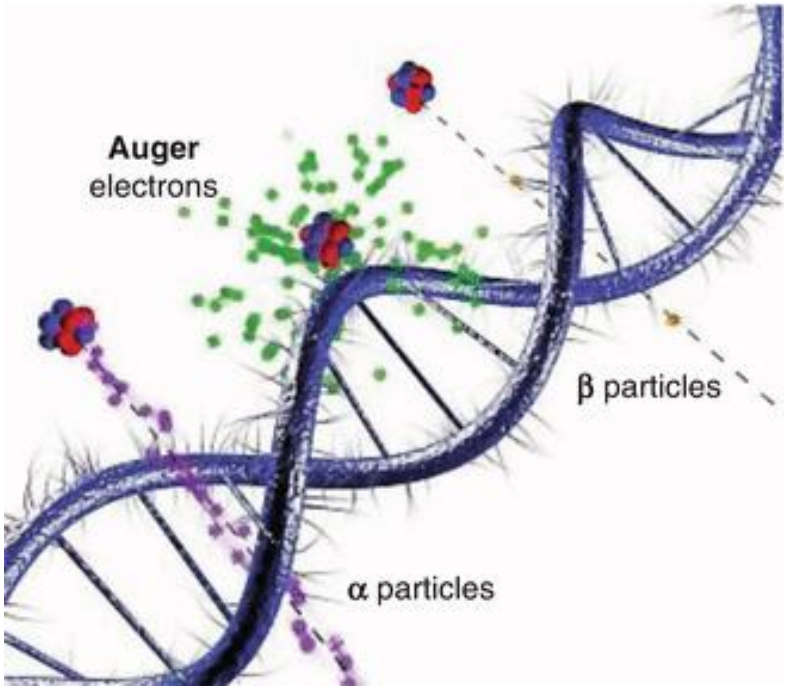
SIR-Spheres Y-90 microspheres are delivered directly to the liver tumor

Tellurium-119m/Antimony-119

Application: medical, targeted therapy

Agency interest: NIH, FDA, NRC, NIST, DHS, NNSA, …

- Accelerator production of Te-119m (4.7 d)
  - $^{121}Sb(p,3n)^{119m}Te/^{123}Sb(p,5n)^{119m}Te$
  - Long-lived parent of Sb-119
  - Te-119m/Sb-119 generator in development
  - Production at BNL and LANL
    - World's supply of Te-119m
    - Product distributed to researchers for evaluation and collaboration on generator development
- Sb-119 (38 h)
  - Therapeutic emission of low energy electron (Auger)



Comparison of range of Auger electrons and α and β particles
DOI: 10.1007/978-81-322-2607-9_4

Thorium-228/Radium-224/ Lead-212/Bismuth-212

Application: medical, targeted therapy and brachytherapy

Agency interest: NIH, FDA, NRC, NIST, DHS, NNSA, …

- Reactor production of Th-228 (1.9 y)
  - $^{226}Ra(2n,\gamma)^{228}Th$
  - Production at the High Flux Isotope Reactor
  - Parent of Ra-224
- Ra-224 (3.6 d) generators produce both
  - Pb-212 (10.6 h)
    - In vivo generator of Bi-212
  - Bi-212 (61 m)
    - 1 alpha particle in decay chain
  - Targeted alpha therapy
- Th-228 also provided
  - Development of clinical-grade Pb-212/Bi-212 generators
  - Development of alpha particle brachytherapy applications

Pb-212/Bi-212 generator

Titanium-44/Scandium-44

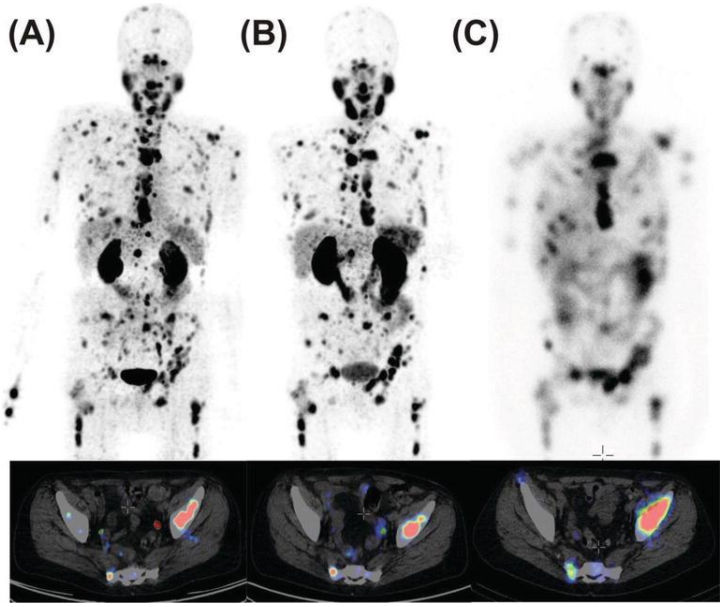
Application: medical, diagnostic imaging

Agency interest: NIH, FDA, NRC, NIST, DHS, NNSA, …

- Accelerator production of Ti-44 (60 y)
  - $^{45}Sc(p,2n)^{44}Ti$
  - Long-lived parent of Sc-44
  - Ti-44/Sc-44 generator in development
  - Production at BNL and LANL
    - World's supply of Ti-44
    - Product distributed to researchers for evaluation and collaboration on generator development

- Sc-44 (4 h)
  - PET diagnostic imaging

Brookhaven Linac Isotope Producer target stack



PSMA-617 labeled with Sc-44 (A), Ga-68 (B), Lu-177 (C)
DOI: 10.5772/intechopen.79157

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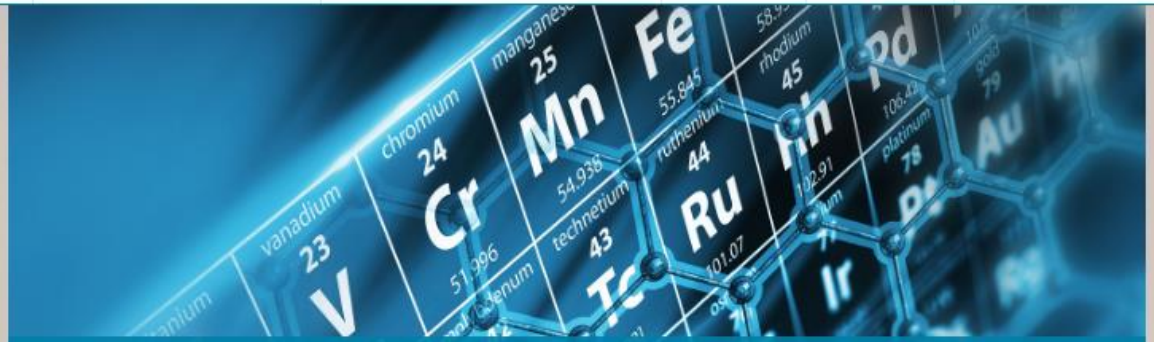

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Thank You!