IMPORTANCE AND ROLE OF ISOTOPES TO THE RADIOPHARMACEUTICAL AND INDUSTRIAL COMMUNITIES

Workshop on the Nation's Needs for Isotopes: Present and Future
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Background on CORAR

- CORAR is the North American Trade Association for the manufacturers and distributors of radionuclides & radiopharmaceuticals
- All of the major manufacturers are members of CORAR
- Members utilize radionuclides to produce radiopharmaceuticals and calibration sources for medical diagnosis and therapy, radionuclides for life science research, and industrial sources
- CORAR wants to assure a reliable supply of radioisotopes for Industrial, Medical, and Research applications

CORAR Membership

- Bracco Diagnostics, Inc.
- Cell Therapeutics, Inc.
- Cardinal Health
- Cellectar, LLC
- Covidien (formerly Tyco Healthcare/Mallinckrodt, Inc.)
- DRAXIMAGE, A division of DRAXIS Specialty Pharmaceuticals Inc.
- Eckert & Ziegler Isotope Products
- EUSA Pharma (formerly Cytogen Corporation)
- GE Healthcare
- GlaxoSmithKline
- International Isotopes Inc.
- Lantheus Medical Imaging (formerly Bristol Myers Squibb)
- MDS Nordion
- Molecular Insight Pharmaceuticals, Inc.
- PerkinElmer Life and Analytical Sciences, Inc.
- PETNET Solutions, Inc./Siemens
- QSA Global, Inc.
- Radiopharmacy of Indianapolis

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Isotopes Marketed by CORAR Companies

Actinium-227
Aluminum-26
Americium-241
Americium-243
Antimony-124
Antimony-125
Barium-133
Berylium-107
Bismuth-207
Cadmium-109
Calcium-45
Californium-252
Carbon-11
Carbon-14
Cerium-139
Cerium-141
Cerium-144
Cesium-134
Cesium-137
Chlorine-36
Chromium-51
Cobalt-56
Cobalt-57
Cobalt-58
Cobalt-60
Copper-64
Curium-244
Europium-152
Europium-154
Flourine-18
Gadolinium-148
Gadolinium-153
Gallium-67
Germanium-68
Gold-195
Gold-198
Holmium-166m
Indium-111
Iodine-123
Iodine-125
Iodine-129
Iodine-131
Iridium-192
Iron-55
Iron-59
Krypton-85
Lead-210
Lutetium-177
Manganese-54
Mercury-203
Molybdenum-99
Neptunium-237
Nickel-59
Nickel-63
Niobium-93m
Niobium-95
Palladium-103
Phosphorus-32
Phosphorus-33
Plutonium-236
Plutonium-238
Plutonium-240
Plutonium-241
Plutonium-242
Polonium-208
Polonium-209
Promethium-147
Radium-224
Radium-226
Radium-228
Rubidium-86
Ruthenium-103
Ruthenium-106
Samarium-151
Scandium-46
Selenium-75
Silicon-32
Silver-108m
Silver-110
Sodium-22
Sodium-24
Strontium-82
Strontium-85
Strontium-89
Strontium-90
Sulfur-35
Tantalum-182
Technetium-95
Technetium-99
Thallium-201
Tellurium-123m
Thorium-228
Thorium-230
Thorium-232
Thullium-170
Tin-113
Titanium-44
Tritium-3
Tungstun-188
Uranium-232
Uranium-233
Uranium-234
Uranium-235
Uranium-236
Vanadium-49
Xenon-133
Ytterbium-169
Yttrium-88
Yttrium-90
Zinc-65
Zirconium-95

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Background on Nuclear Medicine

- Nuclear medicine relies on the use of specialized drugs called radiopharmaceuticals, which are radioactive compounds or radioactive isotopes. These drugs are administered under the supervision of a physician typically intravenously, but sometimes also through inhalation or orally.
- The majority of nuclear medicine procedures are diagnostic, but there are also a number of therapeutic nuclear medicine treatments including for bone pain palliation related to Prostate Cancer, Non-Hodgkin's Lymphoma, Liver Cancer and Thyroid Cancer.

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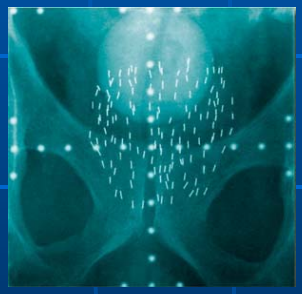
Background on Radiopharmaceuticals - Cont'd

- Nuclear medicine procedures are primarily performed in a hospital or independent imaging facility. Only physicians trained in nuclear medicine and licensed to handle radioactive materials can perform these procedures.
- The radiopharmaceutical concentrates in the area of the body to be examined where special cameras capture the nuclear particles or photons emitted by the radiopharmaceutical producing a visual image of the body system, organ or tissue providing physicians with physiological and physical information.
- Other modalities cannot provide this important functional information to physicians.

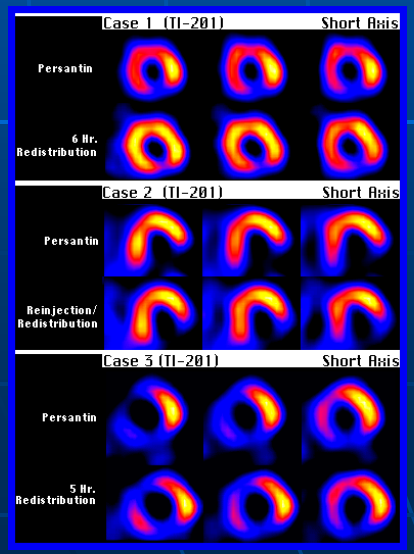
Important Radionuclides in Nuclear Medicine

- Radiopharmaceuticals are used more than 100,000 times each day worldwide
- More than 100 diagnostics tests and therapeutic procedures:
  - Detection and staging of cancer
  - Detection of heart and thyroid diseases
  - Bone pain palliation from cancer, treatment of neuroendocrine tumors and liver cancer
  - Imaging of stress fractures
  - Treatment of prostate cancer with I-125 and Pd-103 seeds
- Many radionuclides are produced by radiopharmaceutical manufacturers (Tl-201, I-123, Ga-67, In-111)
- Many radionuclides are produced by non-power reactors (Mo-99, I-125, I-131, Xe-133, P-32)

Tc-99m Whole Body Scan



Implanted I-125 Brachytherapy Seeds



Cardiac Perfusion Study w/ Tl-201

Cardiac Imaging w/ Rb-82

Microspheres labeled w/ Y-90

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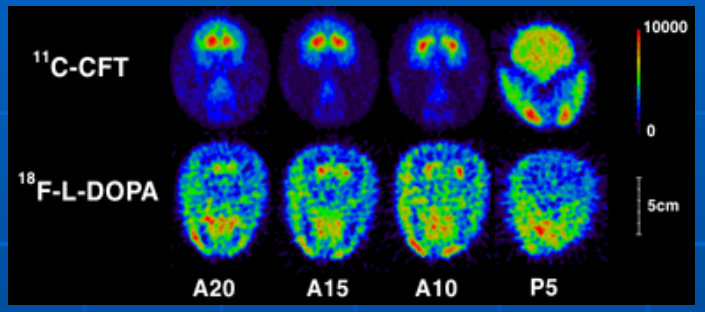
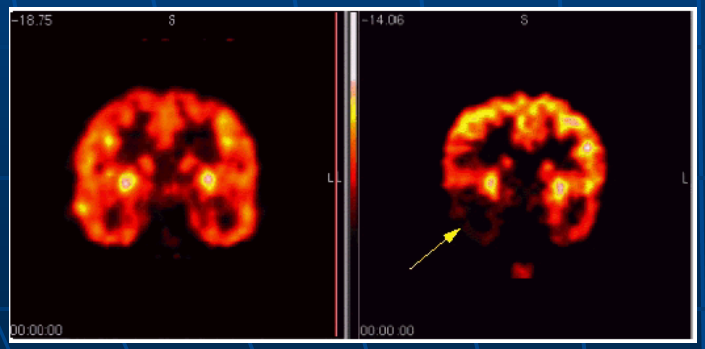
Positron Emission Tomography (PET) in Nuclear Medicine

- PET Imaging is the fastest growing segment of Nuclear Medicine
- Uses of PET
  - Detection & staging of cancer
  - Detection of heart disease
  - Detection of thyroid disease
  - Study of brain function
- PET radionuclides are produced in small cyclotrons at nuclear pharmacy or hospital (F-18, N-13, O-15) w/ stable isotopes



Imaging of Parkinson's patent with C-11 & F-18



Imaging of Epilepsy patient with F-18 FDA

F-18 FDG Research sponsored by BER at UCLA

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Background on Commercial Sources

- **Process Control:**
  - **Level/fill/density gauges – Cs-137, Co-60, Am-241, Am/Be, Cf-252, Kr-85, Pm-147, Sr-90, Tl-204, Ba-133, C-14**

Industrial level & density gauges

Level/density measurement

Process control of thickness

Paper thickness gauging

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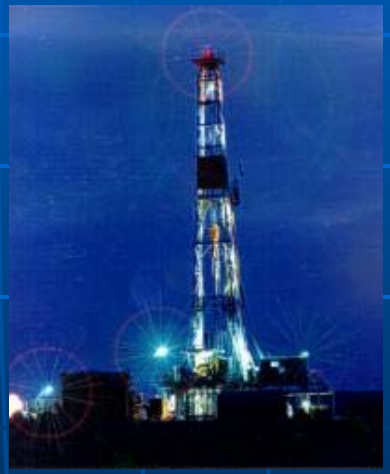
Background on Commercial Sources – Cont'd

- **Analytical Uses – Am-241, Co-57, Fe-55, Cd-109, Cm-244, Ni-63, H-3, Co-60, Cf-252, Am/Be, Cs-137**

Weld quality assurance



Oil well logging

Bulk material analysis

Metals detection using x-ray diffraction

Road bed analysis

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Background on Commercial Sources – Cont'd

- **Other Uses (non-destructive testing, geology, safety & quality, health physics, gamma sterilization) –**

  Ir-192, Co-60, Se-75, Yb-169, Tm-170, Cs-137, Am/Be, Cf-252, Po-210, Co-57, Ge-68, Gd-153

Ge-68 check sources

Homeland security

Chemical agent detection

Ge-68 phantom

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Stable Isotopes Needed for Isotope Production

- **Key enriched stable isotopes are needed for the production of medical & commercial isotopes**

Stable Isotope	Used to produce	Product Used for:
Tl-203	Tl-201	Myocardial perfusion imaging
Cd-108	Cd-109	Calibration Sources
Cd-112	In-111	White blood cell labeling/infection localization
N-15	O-15	PET production of oxygen compounds
O-18	F-18 FDG	Cardiac/brain metabolic studies
Pd-104	Pd-103	Brachytherapy seeds
Te-123/124	I-123	Thyroid Imaging
Zn-68	Ga-67	Tumor & infection localization
Yb-168	Yb-169	Industrial radiography
Se-74	Se-75	Industrial radiography
Ni-60	Co-57	Gamma Camera Calibration sources

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Mo-99 Supply

- Mo-99/Tc-99m is the most used radionuclide in diagnostic nuclear medicine
- Patient needs for Tc-99m must be reliably met
- CORAR is supportive of conversion to LEU fuel and targets for isotope production
- CORAR members are embracing new technology and each company is evaluating new opportunities themselves
- Conversion to LEU will take significant time to resolve new processing and clear regulatory hurdles

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DOE's Rich History of Technology Development & Routine Production

- Initial development work on Tc-99m generator done at Brookhaven
- Tc-99m MAG3 developed by Brookhaven
- IPF at Los Alamos provides important Ge-68, Sr-82, As-73
- Oak Ridge has been a major source of Cf-252 used by the nuclear power industry, U.S. Navy and for commercial uses
- DOE BER has funded productive nuclear medicine research last several years

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Missed & Future Opportunities

- DOE was not able to start Mo-99 production in 1990's
- Shutdown of the calutrons have required U.S. industry to turn to Russian suppliers of stable isotopes
- Shutdown of Cf-252 production would leave industry without an alternative supply
- Shutdown of Am-241 production has caused problems for U.S. industry
- CORAR looks forward to working with the Office of Science on creating improvements in Isotope Production & Distribution at DOE

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What Industry Needs From DOE

- DOE has unique resources that cannot be easily duplicated
  - HFR at ORNL, ATR at INEL, LANSCE/IPF at LANL
  - Calutrons at ORNL, U-233 stockpile at ORNL
- These resources should be used to provide industry with isotopes that are not otherwise available to the U.S.
- Many key isotopes can only be acquired from DOE or imported from a very limited number of countries
- Industry representatives should be included in any DOE advisory committee to determine which isotopes will be produced and policies affecting isotope production
- Advisory committee should include industry reps, not just R&D reps

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Summary

- Industry is willing to work with DOE and pay fair prices for its radionuclides
- Industry is supportive of conversion to LEU, but it will take time
- Industry deserves a role in DOE advisory committees on isotope production, bringing their expertise on which isotopes will be needed
- Industry needs DOE's help for key stable and radioactive isotope production

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