Radiation Protection at Nuclear Pharmacies

US NRC & ORISE

Course Instructors, Schedule & Facility Information

- Instructors
  - Roger Moroney, CHP – ORISE (roger@moroney.org)
  - Bryan Parker, NRC (Bryan.Parker@nrc.gov)
  - Lizette Roldan, NRC (Lizette.Roldan@nrc.gov)
- Schedule
  - Day 1: Health Physics Aspects of Nuclear Pharmacy
  - Day 2: Licensing & Inspection activities at a Nuclear Pharmacy
  - Day 3: Tour Nuclear Pharmacy (schedule & transportation to be announced)
- Facility
  - Emergencies
  - Restrooms

Outline & Objectives for Day 1

- **Overview of Nuclear Pharmacy Products, Operations, & Radiation Protection Issues**
  - **Typical radionuclides, radiopharmaceuticals & their applications for both Single Photon Emission Computed Tomography (SPECT) & Positron Emission Tomography (PET)**
  - **Staffing at SPECT and PET pharmacies**
  - **Facility Design, Layout, Equipment, and Process Flow**
  - **Radiation Protection Issues for SPECT & PET**

Outline & Objectives for Day 1

- Accelerators & PET Topics
  - Basic accelerator overview
  - Types, shielding, hazards (electrical & radiological)
  - Manufacturing vs. compounding

History of Medical Applications of Radionuclides

- **See handout**

What is Nuclear Medicine?

- In nuclear medicine procedures, radionuclides are combined with other chemical compounds or pharmaceuticals to form radiopharmaceuticals. These radiopharmaceuticals, once administered to the patient, can localize to specific organs or cellular receptors. This property of radiopharmaceuticals allows nuclear medicine the ability to image the extent of a disease-process in the body, based on the cellular function and physiology, rather than relying on physical changes in the tissue anatomy. In some diseases nuclear medicine studies can identify medical problems at an earlier stage than other diagnostic tests.

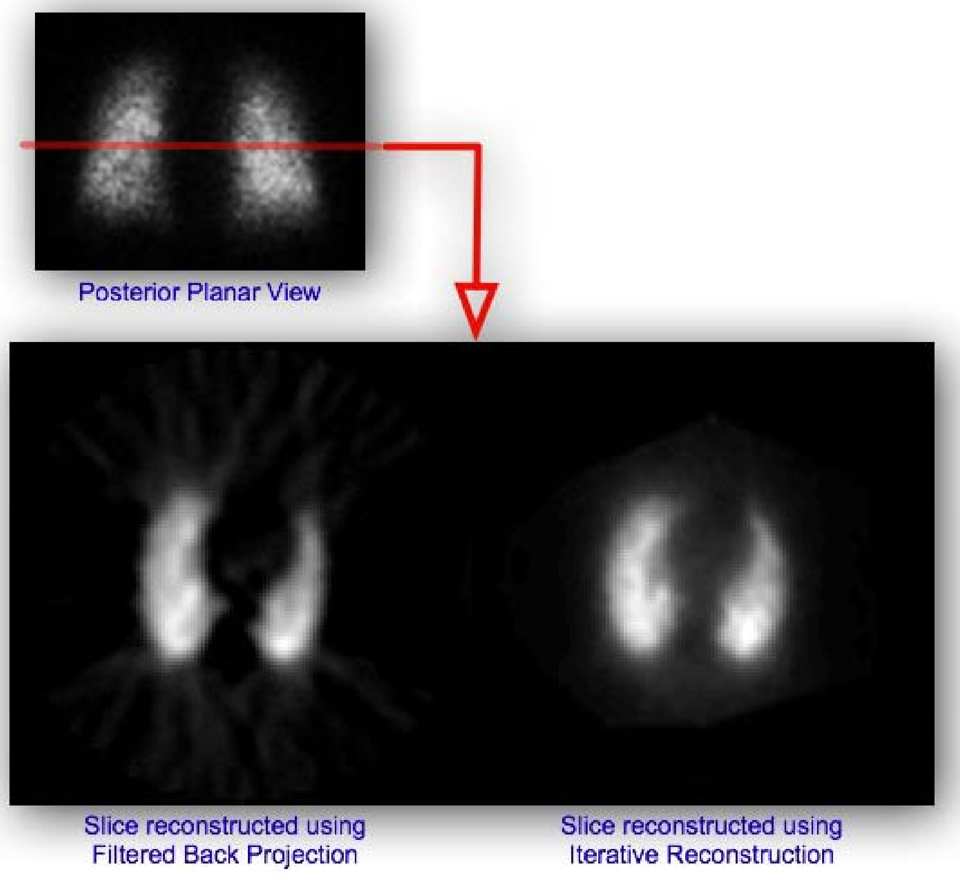
What is SPECT?

- Single Photon Emission Tomography
- Conventional imaging in nuclear medicine uses a gamma camera, also known as an Anger camera after its inventor, Hal Anger
- Planar images render a three-dimensional object in two dimensions
- SPECT uses a series of images taken at different angles around the patient, with the resulting images fed into a computer algorithm that reconstructs slices, giving images at different depths

What is SPECT?

- SPECT uses the same radiopharmaceuticals as conventional planar imaging
- Use of two or three cameras will decrease scan time, thereby increasing patient throughput
- Gated acquisition techniques, using signals from an EKG, are used with cardiac imaging to isolate different aspects of cardiac function

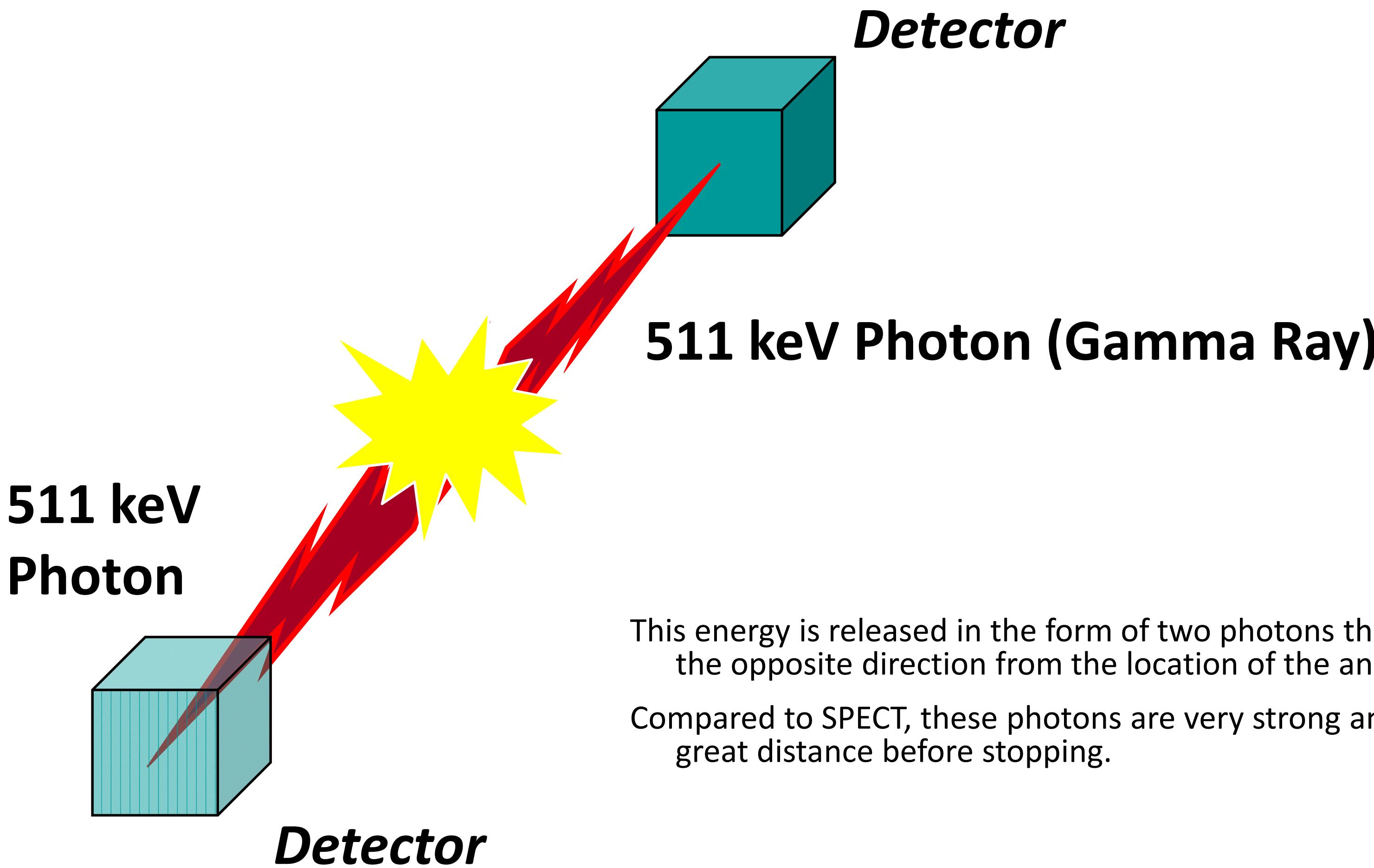
Planar and SPECT Images



What is PET?

- Positron Emission Tomography
- Uses radiopharmaceuticals which emit positrons
- Coincident capture of the two annihilation photons (511 keV) gives spatial information when combined with multiple images taken at various angles around the patient and processed by computer algorithms

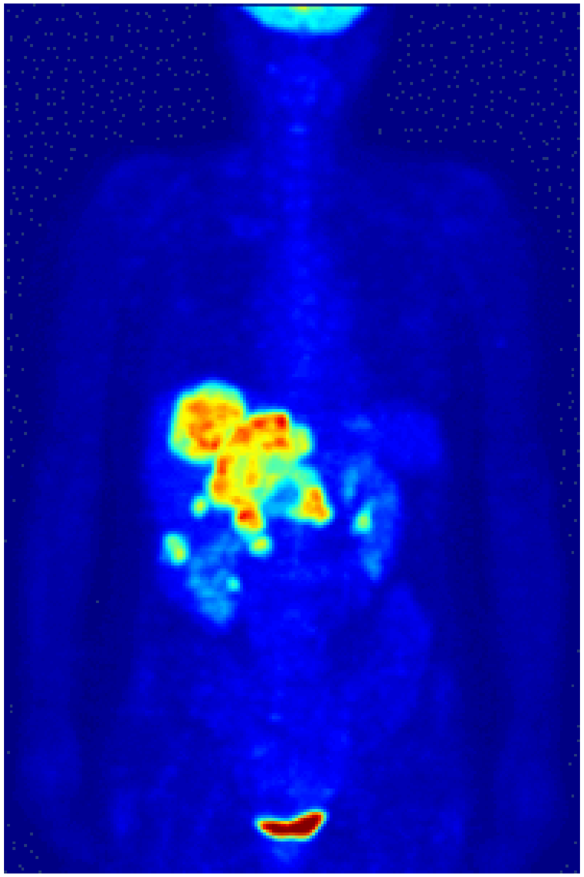
PET Physics



This energy is released in the form of two photons that are emitted in the opposite direction from the location of the annihilation event

Compared to SPECT, these photons are very strong and can travel a great distance before stopping.

What is PET?



- F-18 FDG whole-body PET acquisition, abnormal uptake in the region of the stomach. Normal uptake is seen in the brain, renal & bladder

NUCLEAR PHARMACY

What is Nuclear Pharmacy?

- The Practice of Nuclear Pharmacy is recognized as a specialty within Pharmacy Practice. The American Pharmaceutical Association defines it as follows:
  - The "Practice of Nuclear Pharmacy" means a patient-oriented service that embodies the scientific knowledge and professional judgment required to improve and promote health through the assurance of the safe and efficacious use of radiopharmaceuticals and other drugs.

Nuclear Pharmacy Networks & Independents

- "Traditional" or "SPECT" nuclear pharmacies
  - Part of a network or independent
  - Cardinal Health (formerly Syncor) ~150
  - Covidien (formerly Mallinckrodt and now Triad) ~37
  - Triad Isotopes ~26
    - Triad has acquired the Covidien network
  - GE Healthcare (formerly Amersham) ~30
  - IBA Molecular (acquired Eastern Isotopes) ~10
  - Pharmalogic ~10
  - UPPI (actually a buying group) ~70 members excluding Triad & Pharmalogic
  - Other independents
  - Hospital and University based nuclear pharmacies
    - May or may not distribute commercially

Nuclear Pharmacy Networks & Independents

- "PET" nuclear pharmacies
  - Part of a network or independent
  - PETNET Solutions (Siemens) ~50
  - Cardinal Health (formerly Syncor) ~32 locations with a cyclotron
    - Cardinal operates their cyclotron sites as manufacturing only and ships bulk FDG to a nearby nuclear pharmacy for dispensing & distribution under the practice of pharmacy
  - Triad Isotopes ~10 locations with cyclotrons
  - IBA Molecular (acquired former Eastern Isotopes + Pharmalogic's PET sites) ~10
  - Independents ~20 (some belonging to UPPI also)
  - Hospital and University based
    - May or may not distribute commercially
    - Consortium requirements for PET

Nuclear Pharmacy Networks & Independents

- Operations
  - Large networks typically have a single program developed centrally and implemented at each location by site RSOs with a corporate RSO having global responsibilities
  - Cardinal holds a license similar to a Master Materials License that allows designation of ANP's, and other limited functions based on a standardized Training & Experience requirement
- Services
  - Nuclear Pharmacies often provide not only unit doses of radiopharmaceuticals, but also assistance with many aspects of clinical practice for their customers
    - Licensing, reimbursement, radiation safety, back office support, etc.

Nuclear Pharmacy Networks & Independents

- Regulatory Landscape
  - NRC and Agreement States for possession & distribution of Radiochemicals/Radiopharmaceuticals
  - States administer programs associated with radiation-producing machines (accelerators)
  - State Boards of Pharmacy (BoP) regulate compounding and licensure of Nuclear Pharmacists & Pharmacies
  - Federal and/or State drug manufacturing requirements (FDA) i.e. current Good Manufacturing Practices (cGMP)
  - DOT for transport of hazardous materials
  - EPA or State equivalent for regulation of hazardous waste – usually classified as a conditionally exempt small quantity generator
  - Federal OSHA or State equivalent for worker safety

Suppliers of Radiopharmaceuticals

- Covidien (St Louis & Petten, Netherlands)
  - ^{99}Mo/^{99m}Tc generators
  - ^{131}I (diagnostic & therapeutic) , ^{125}I, ^{123}I
  - ^{201}Tl, ^{67}Ga, ^{111}In,
  - ^{32}P, ^{51}Cr, ^{57}Co, ^{133}Xe
  - Cold kits (Sestamibi, Octreoscan, MAG3)
  - Accessories (shields, Xe dispenser)

Suppliers of Radiopharmaceuticals

- Lantheus (Billerica, MA)
  - ^{99}Mo/^{99m}Tc generators
  - ^{201}Tl, ^{67}Ga, ^{133}Xe
  - Cold kits (Neurolite®, Cardiolite®)
- Draximage
  - ^{131}I (diagnostic & therapeutic)
  - Cold kits (Sestamibi, MDP, MAA)
- EUSAPharma
  - ProstaScint® (^{111}In product)
  - QUADRAMET® (^{153}Sm product)

Suppliers of Radiopharmaceuticals

- GE Healthcare
  - ^{123}I mIBG, ^{111}In, ^{201}Tl, ^{123}I, ^{89}Sr
  - Cold kits
- Bracco Diagnostics
  - ^{82}Sr/^{82}Rb generators, ^{51}Cr
  - Cold kits
  - http://usa.braccoimaging.com/nuclear-medicine/nuclear-medicine.html
  - http://www.cardiogen.com/
- GSK
  - Bexxar
- Spectrum Pharmaceuticals
  - Zevelin (^{111}In & ^{90}Y)

CardioGen-82®
(Rubidium Rb 82 Generator)

- Generator replaced every 28 days
- Rb-82 dose is provided within 10 minutes
- Generator must be utilized with the calibrated CardioGen-82® Infusion System
- Infusion System is automated for the infusion and patient dose
- Permits accurate dosing with minimal operator interface, thus decreasing radiation exposure
- Contains shielding vault for CardioGen-82® Generator and waste container

TYPICAL NUCLEAR PHARMACY RADIONUCLIDES

Typical Nuclear Pharmacy Radionuclides

- Diagnostic Products
  - Most common
    - $^{99}Mo/^{99m}Tc$, ^{131}I, ^{123}I, ^{201}Tl, ^{67}Ga, ^{111}In, ^{133}Xe
  - Less common
    - ^{51}Cr, ^{57}Co, $^{81}Rb/^{81m}Kr$, ^{125}I
- Therapy Products
  - ^{131}I, ^{153}Sm, ^{90}Y, ^{89}Sr, ^{32}P
- ^{131}I – many nuclear pharmacies compound diagnostic and therapy products locally from bulk ^{131}I acquired from a radiopharmaceutical supplier

DIAGNOSTIC RADIONUCLIDES

Overview of Typical Nuclides – Diagnostic

Molybdenum-99/Technetium-99m (^{99}Mo/^{99m}Tc)

- “Moly Generators” are the mainstay of Nuclear Pharmacies
  - Produced in the US by Covidien and Lantheus using “fission Mo”
  - Primary production reactors are located in Canada, Netherlands, Belgium, Australia, and South Africa
  - Controversy over the use of high enriched uranium (HEU) targets and/or fuel due to proliferation concerns
    - Use of LEU tends to create more waste volume
  - Covidien has lead, tungsten and depleted uranium shields
  - Lantheus uses lead shields
- Contains ^{99}Mo on an ion exchange resin (alumina)
  - Sterile Saline solution is added to one side
  - Evacuated sterile vial on the other side
  - Vacuum pulls saline through column and ^{99m}Tc, as sodium pertechnetate, is eluted

Overview of Typical Nuclides – Diagnostic

^{99}Mo

- Reactor produced, HEU
- 66.7 hour $t_{1/2}$
- β^- decay (E_{max} = 1.23 MeV)
- γ Tc x-rays
- γ 41 keV (2%)
- γ 181 keV (7%)
- γ 372 keV (1%)
- γ 740 keV (12%)
- γ 780 keV (4%)
- Γ = 1.25 R/hr per Ci @ 30 cm

Overview of Typical Nuclides – Diagnostic

^{99m}Tc

- Decay product of ^{99}Mo
- Decays to ^{99}Tc (2.15E5 yrs)
- 6.04 hour $t_{1/2}$
- IT decay
- γ Tc x-rays
- γ 140 keV (90%)*
- HVL = 0.17 mm Pb
- Γ = 0.78 R/hr per mCi @ 1cm

*Primary photon for imaging

Overview of Typical Nuclides – Diagnostic

Gallium-67 (^{67}Ga)

- 77.9 hour $t_{1/2}$
- EC decay (no betas)
- γ Zn x-rays
- γ 93 keV (40%)
- γ 184 keV (24%)
- γ 296 keV (22%)
- γ 388 keV (7%)
- HVL = 2.5 cm Pb
- Γ = 0.8 R/hr per mCi @ 1 cm

Overview of Typical Nuclides – Diagnostic

Indium-111 (^{111}In)

- 2.8 day $t_{1/2}$
- EC decay (no betas)
- γ Cd x-rays
- γ 173 keV (89%)*
- γ 247 keV (94%)
- HVL = 0.023 cm Pb
- Γ = 3.21 R/hr per mCi @ 1 cm

Overview of Typical Nuclides – Diagnostic

Iodine-123 (^{123}I)

- 13.2 hours $t_{1/2}$
- EC decay (no betas)
- γ Te x-rays
- γ 159 keV (83%)*
- HVL = 0.05 mm Pb
- Γ = 1.6 R/hr per mCi @ 1 cm

Overview of Typical Nuclides – Diagnostic

Iodine-125 (^{125}I)

- 60 day $t_{1/2}$
- EC decay (no betas)
- γ Te x-rays
- γ 35 keV (7%)
- HVL = 0.02 mm Pb
- Γ = 1.5 R/hr per mCi @ 1 cm

Overview of Typical Nuclides – Diagnostic

Iodine-131 (^{131}I)

- 8.02 day $t_{1/2}$
- β^- decay (E_{max} = 806 keV 0.6%)
- β^- decay (E_{max} = 606 keV, E_{avg} = 190 keV)
- γ Xe x-rays
- γ 80 keV (2.6%)
- γ 364 keV (82%)
- γ 637 keV (6.8%)
- γ 723 keV (1.6%)
- Γ = 2.27 R/hr per mCi @ 1 cm
- HVL = 0.24 cm Pb

Overview of Typical Nuclides – Diagnostic

Xenon-133 (^{133}Xe)

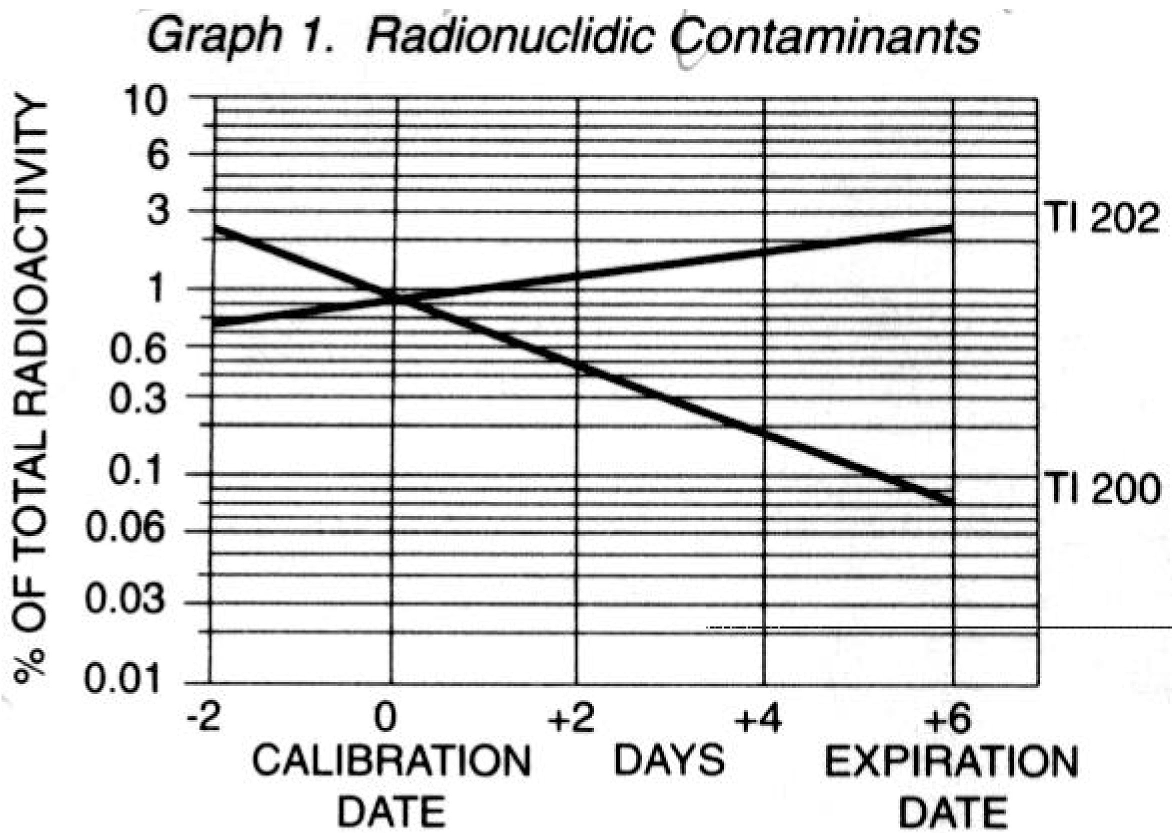
- 5.24 day $t_{1/2}$
- β^- decay (E_{max} = 346 MeV, E_{avg} = 190 keV)
- γ Cs x-rays
- γ 81 keV (37%)
- Γ = 0.51 R/hr per mCi @ 1 cm
- HVL = 0.035 mm Pb

Overview of Typical Nuclides – Diagnostic

Thallium-201 (^{201}Tl)

- 73.1 hour $t_{1/2}$
- EC decay (no betas)
- γ Hg x-rays
- γ 135 keV (2%)
- γ 167 keV (8%)
- HVL = 0.006 mm Pb
- Γ = 4.7 R/hr per mCi @ 1 cm

Overview of Typical Nuclides – Diagnostic



Overview of Other Nuclides – Diagnostic

Chromium-51 (^{51}Cr)

- 27.7 day $t_{1/2}$
- EC decay (no betas)
- γ V x-rays
- γ 320 keV (9%)*
- HVL = 0.17 mm Pb
- Γ = 0.18 R/hr per mCi @ 1 cm

*Primary photon for imaging

Overview of Other Nuclides – Diagnostic

Rubidium-82 (^{82}Rb)

- 75 second $t_{1/2}$
- β^{+} decay (E_{max} = 3.15 MeV)
- γ Kr x-rays
- γ 511 keV (192%)*
- γ 777 keV (9%)
- HVL = 0.7 cm Pb
- Γ = 6.1 R/hr per mCi @ 1 cm
- from Strontium-82 (^{82}Sr) generator 25 day $t_{1/2}$

THERAPEUTIC RADIONUCLIDES

Overview of Typical Nuclides – Therapeutic

Phosphorus (^{32}P)

- **14.3 day $t_{1/2}$**
- **β^- decay (E_{max} = 1.71 Mev, E_{avg} = 690 keV)**
- **No γ (*bremsstrahlung*)**
- **Range ~ 1 cm tissue, 30 feet in air**

Overview of Typical Nuclides – Therapeutic

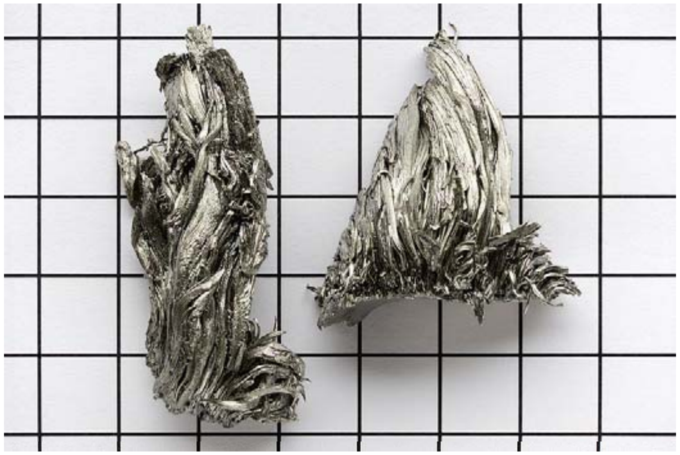
Strontium-89 (^{89}Sr)

- 52.7 day $t_{1/2}$
- β^- decay (E_{max} = 1.46 Mev)
- γ 91 keV (<1%)
- Range ~ 1 cm tissue

Overview of Typical Nuclides – Therapeutic

Yttrium-90 (^{90}Y)

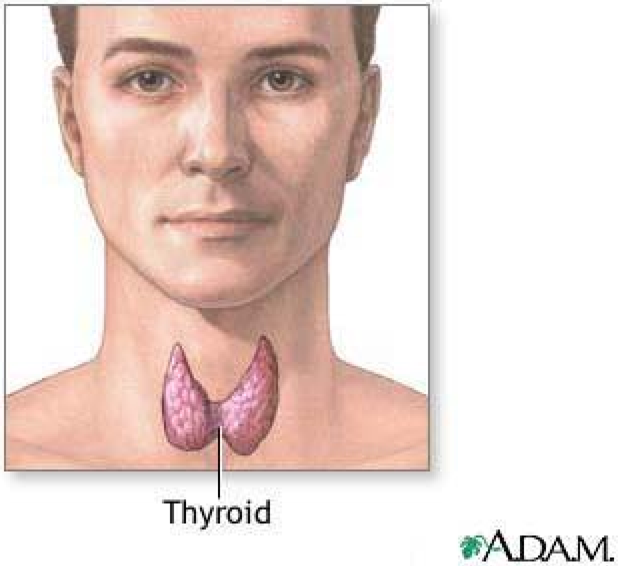
- 2.67 day $t_{1/2}$
- β^- decay (E_{max} = 2.27 MeV, E_{avg} ~900 keV)
- No γ (*bremsstrahlung*)
- Range ~ 1.5 cm tissue



Overview of Typical Nuclides – Therapeutic

Iodine-131 (^{131}I)

- 8.02 day $t_{1/2}$
- β^- decay (E_{max} = 806 keV 0.6%)
- β^- decay (E_{max} = 606 keV, E_{avg} = 190 keV)
- γ Xe x-rays
- γ 80 keV (2.6%)
- γ 364 keV (82%)
- γ 637 keV (6.8%)
- γ 723 keV (1.6%)
- e- 46 and 330 keV
- Γ = 2.27 R/hr per mCi @ 1 cm
- HVL = 0.24 cm Pb



Overview of Typical Nuclides – Therapeutic

Samarium-153 (^{153}Sm)

- 46.3 hour $t_{1/2}$
- β^- decay (E_{max} = 635 keV 32%)
- β^- decay (E_{max} = 705 keV 49%)
- β^- decay (E_{max} = 808 keV 18%)
- γ 70 keV (5.4%)
- γ 103 keV (30%)
- γ 388 keV (7%)
- Γ = 0.9 R/hr per Ci @ 1 cm
- HVL = 0.1 mm Pb

SPECT PHARMACY PRODUCTS

NUCLEAR PHARMACY COLD KITS & APPLICATIONS

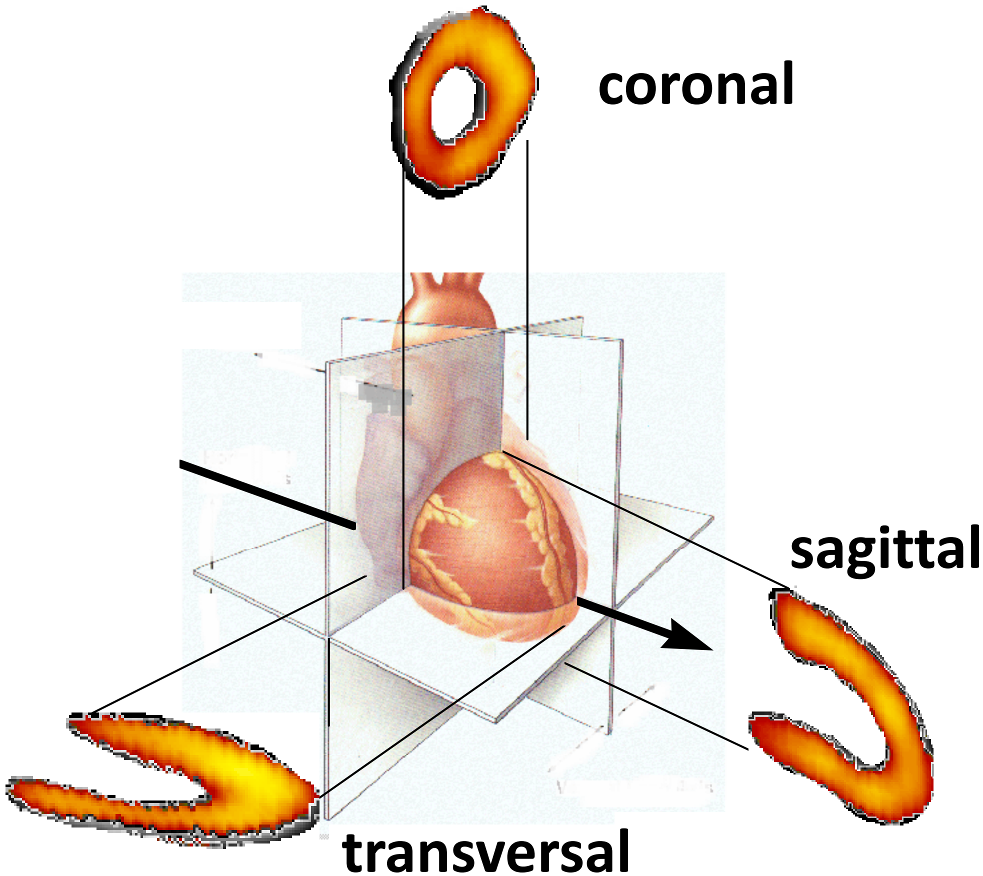
Overview of cold kits

- ^{99m}Tc , in its various chemical forms, accounts for 80% of all nuclear medicine procedures.
- There are over 25 different cold-kits with which various physiological processes can be imaged
- Most common are cardiac, bone, neuro, and GI

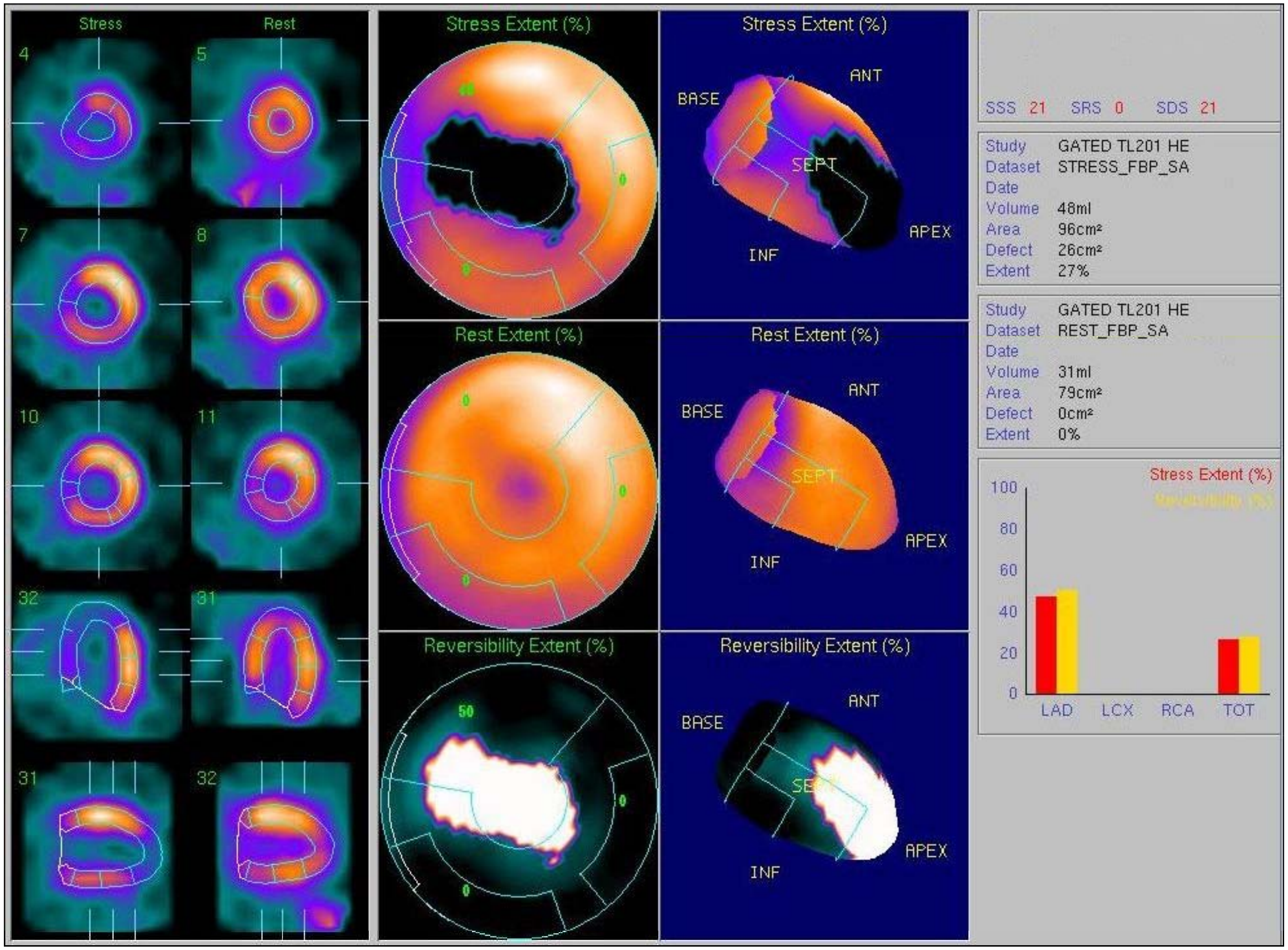
Cardiovascular applications

- Quantify myocardial perfusion
  - Identifies stenosis in coronary arteries during stress
  - ^{201}Tl was the preferred radionuclide
  - ^{99m}Tc sestamibi (Cariodlite) and tetrofosmin (Myoview)
  - Can use higher activity of ^{99m}Tc to gain improved image quality
  - Sometimes both Tl and Tc will be used, one for the rest phase and the other for the stress phase

TOMOGRAPHIC SLICES



Cardiovascular applications



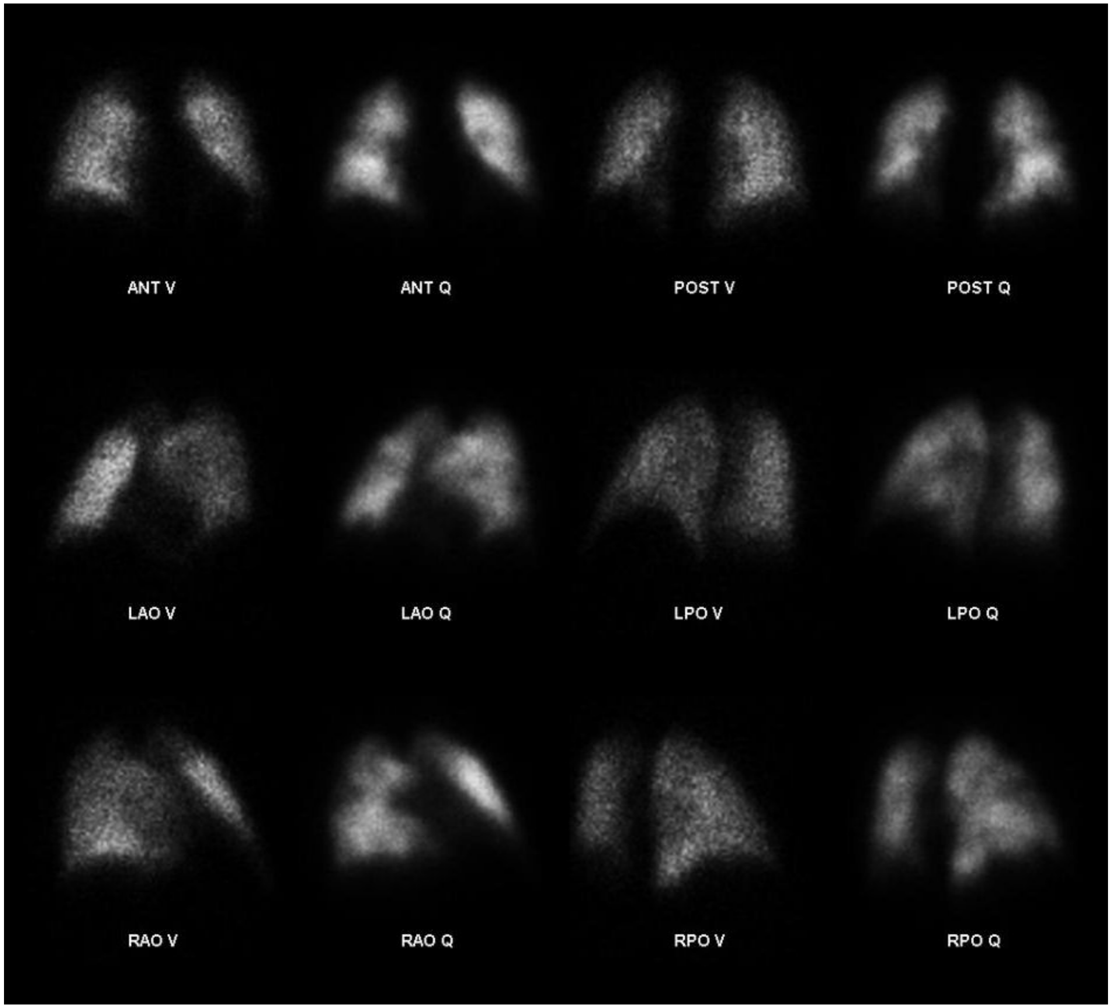
Cardiovascular applications

- Left ventricular ejection fraction (MUGA)
  - In vitro: Blood is withdrawn from pt and sent to the pharmacy, labeled with 10 – 20 mCi ^{99m}Tc, and returned. Best image
  - In vivo: inject chelating agent followed a few minutes later with ^{99m}Tc – poorer image

Pulmonary applications

- Ventilation/perfusion lung scans
  - Diagnosis of pulmonary embolisms
  - ^{99m}Tc macroaggregated albumin (MAA) 2 – 5 mCi
  - ^{99m}Tc DTPA aerosol (~1 mCi) or ^{133}Xe gas (5 – 20 mCi)

Pulmonary applications



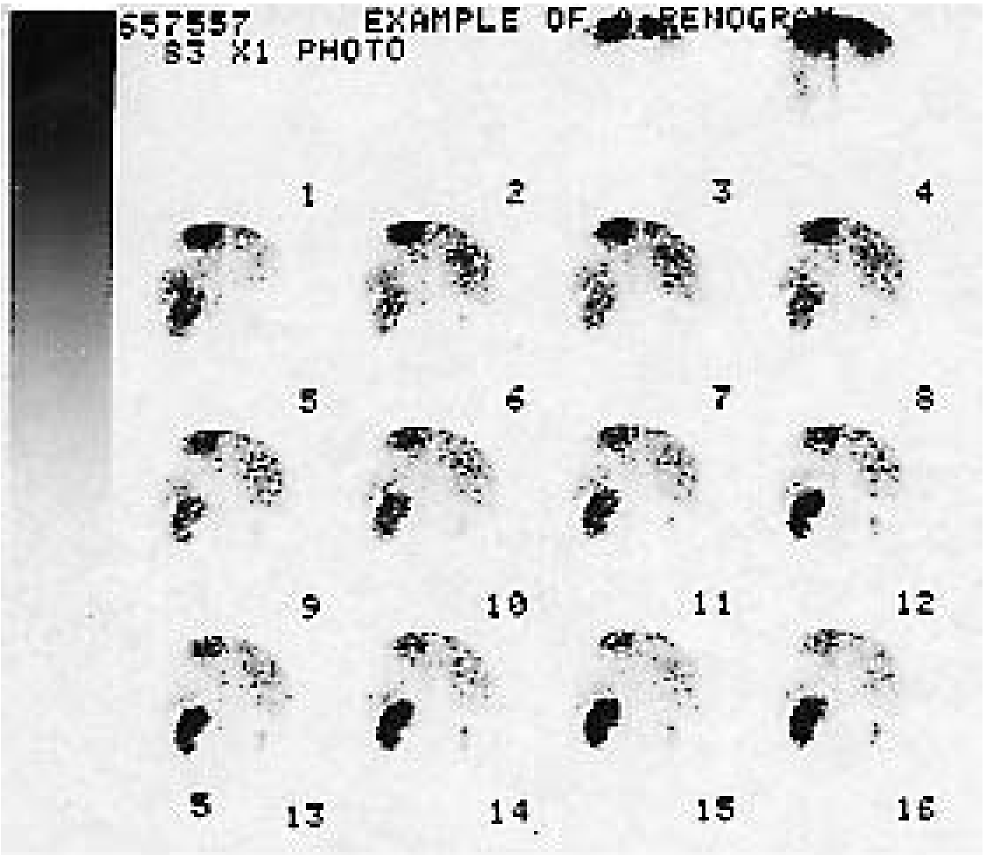
Renal applications

- Renogram
  - Series of images as tracer is removed from the blood, enters the lidneys, and then to the bladder
  - Provides a measurement of renal function
  - ^{99m}Tc (MAG3) most common for renal (1 – 10 mCi)
  - ^{99m}Tc DTPA less common but cheaper (1 – 10 mCi)
  - ^{131}I (OIH) rare, can lead to higher kidney dose if obstructed or impaired renal function

Renal applications

- ACE-inhibitor
  - Assess renovascular hypertension
  - Provides a measurement of renal function
  - ^{99m}Tc (MAG3) or (DTPA) (1 – 10 mCi)
- Renal transplant scintigraphy
  - Detects rejection post-tranplant
  - ^{99m}Tc (MAG3) or (DTPA) (1 – 10 mCi)
- Cystography
- Diagnosis reflux and/or infection
  - ^{99m}Tc (DTPA), pertechnetate, or sulfur colloid

Renal applications



Spleen & Hepatobiliary applications

- IDA scan
  - Evaluates biliary system
  - ^{99m}Tc (Choletec) or (Hepatolite) (1.5 – 5 mCi)
    - Visualization of bilirubin pathway
- Hemangioma scan
  - Uses pt's red blood cells that are tagged with ^{99m}Tc (20 – 25 mCi)
  - differentiates between tumor and hemangioma masses in liver to guide biopsy
  - Correlation with a CT scan can assist
- Radiocolloid scans
  - Mostly replaced with CT, ultrasound or MRI

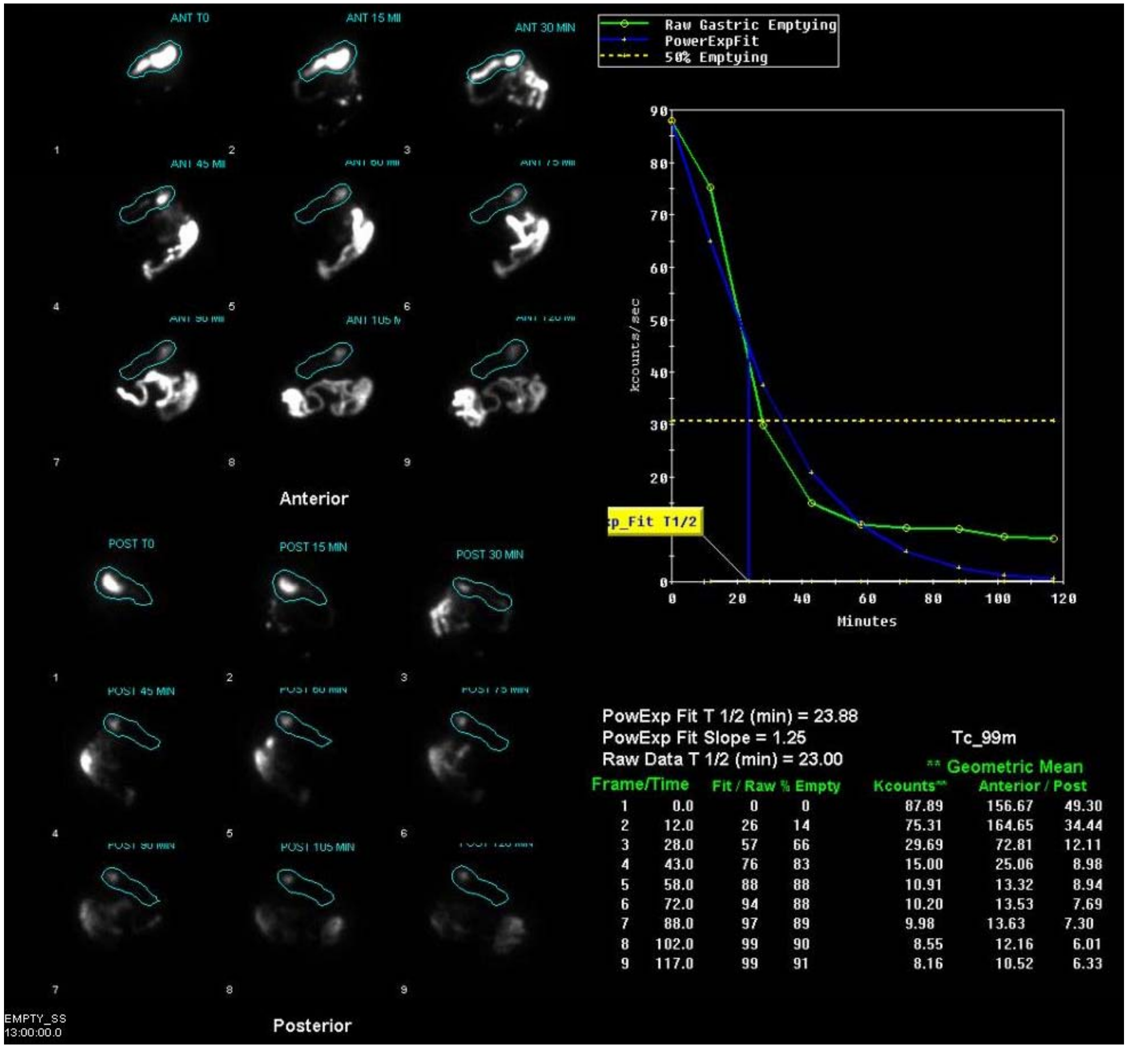
GI system applications

- GI bleeding
  - Localization of bleeding
  - ^{99m}Tc labeled RBC (20 – 30 mCi) or sulfer colloid (10 mCi)
- GI motility studies
  - ^{99m}Tc sulfer colloid (0.2 – 1 mCi) complexed to eggs as they are cooked
  - ^{111}In or ^{99m}Tc DTPA is also used for liquids

GI system applications

- Schilling Test
  - Identifying B_{12} malabsorption
  - ^{57}Co labeled B_{12} (0.5 µCi) capsule followed by non-radiolabeled B_{12}
  - Urine collected for 24 hours and the excretion fraction determined
- H Pylori Breath Test
  - ^{14}C urea (1 µCi), which is exhaled as $^{14}CO_2$ if H Pylori is present (generally licensed)

GI system applications



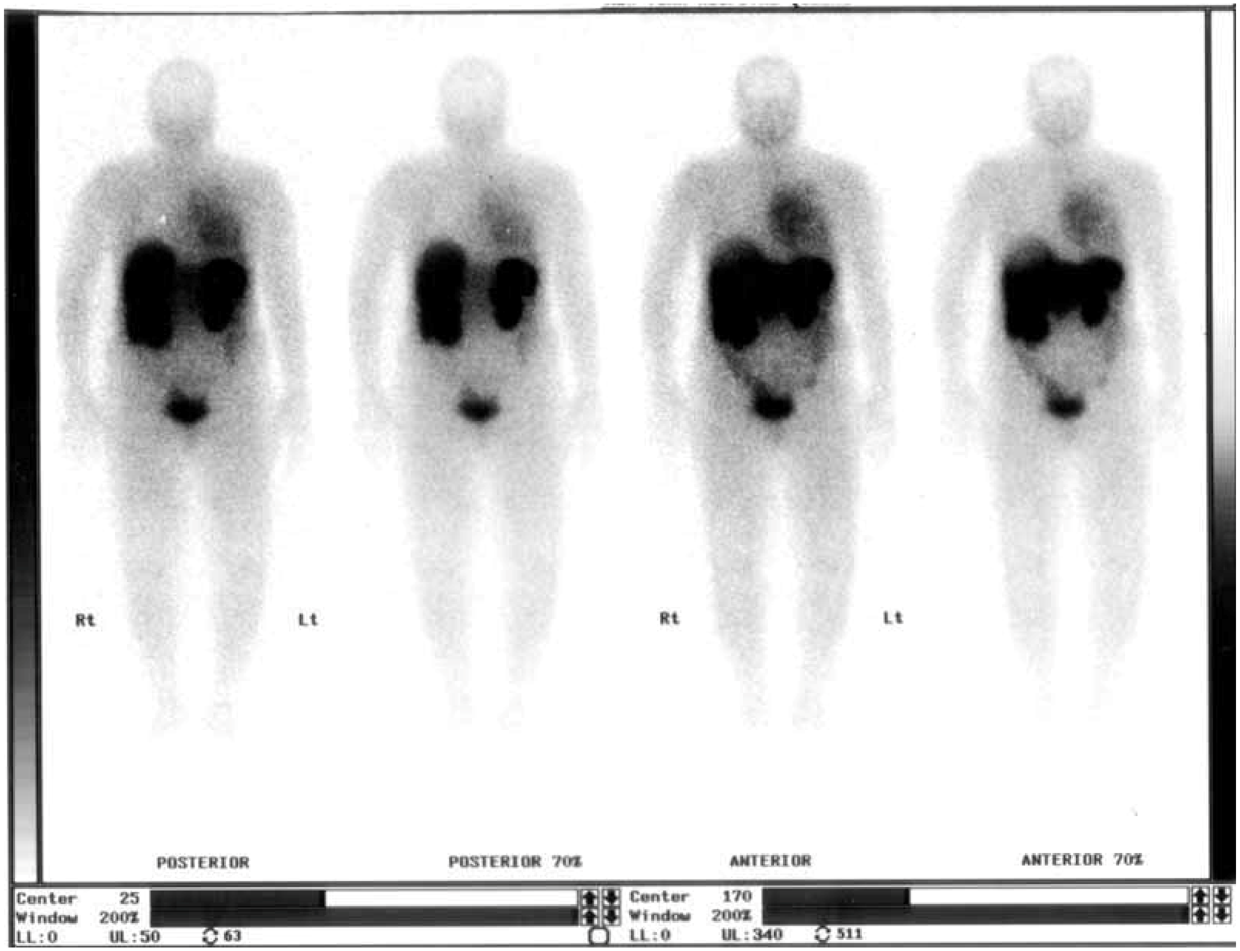
Infection Imaging

- Soft tissue infection, inflammation etc
  - ^{111}In (0.5 mCi) or ^{99m}Tc HMPAO (5 – 15 mCi) labeled leukocytes
    - Requires separation of the leukocytes from blood sample for labeling
    - Imaging performed 18 – 24 h later for In, 1 – 4 h later for Tc
  - ^{67}Ga – citrate (4 – 6 mCi) acts as iron analogue
    - Binds to circulating transferrin which then localizes at infection sites
    - widely used for assessing infection in acquired immune deficiency pts

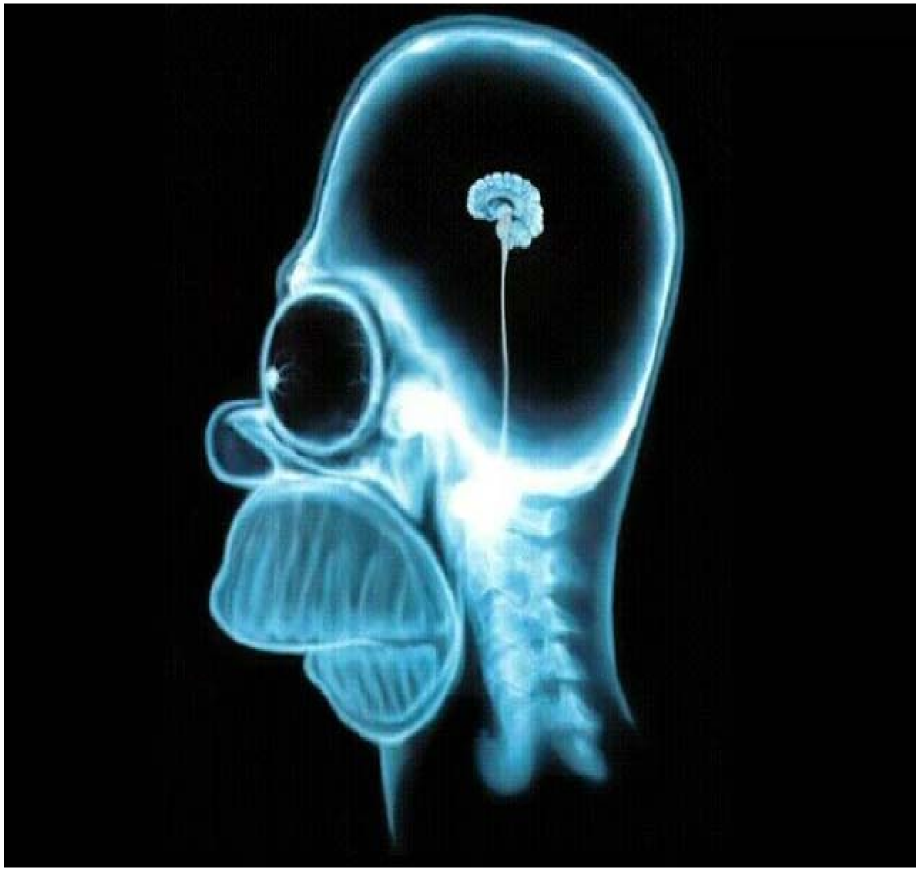
Infection Imaging

- Osteomyelitis
  - Three-phase bone scan
  - ^{99m}Tc MDP (20 – 25 mCi)
    - Images every 2 – 3 sec for 30 – 60 sec
    - Static blood pool image
    - 2-3 h static image
- Leukoscan (monoclonal antibody)
  - Not available in the US, eliminates need to extract & label pt's leukocytes

Infection Imaging



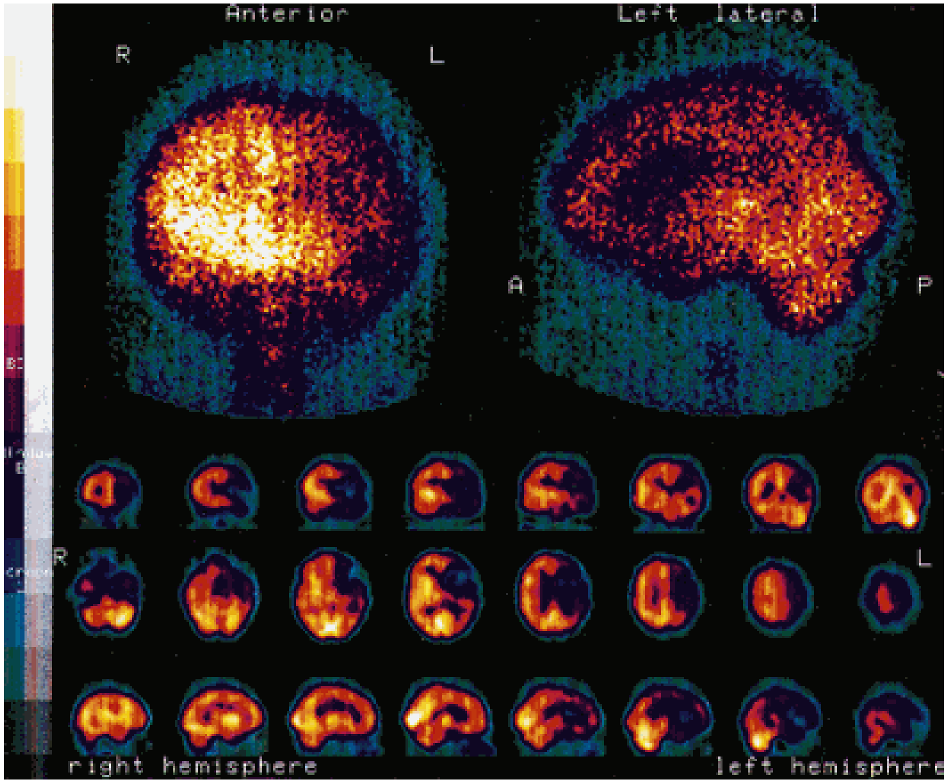
Neuro Imaging



Neuro Imaging

- Brain Perfusion SPECT Imaging
  - ^{99m}Tc Ceretec (HMPAO) distributes in the brain proportional to blood flow
  - ^{99m}Tc Neurolite is also used for brain perfusion with slight advantage in brain to background ratio
  - Administered adult dose is 15 to 30 mCi and requires ~15 min quiet time before and after injection plus a further 15 to 90 min delay prior to scanning

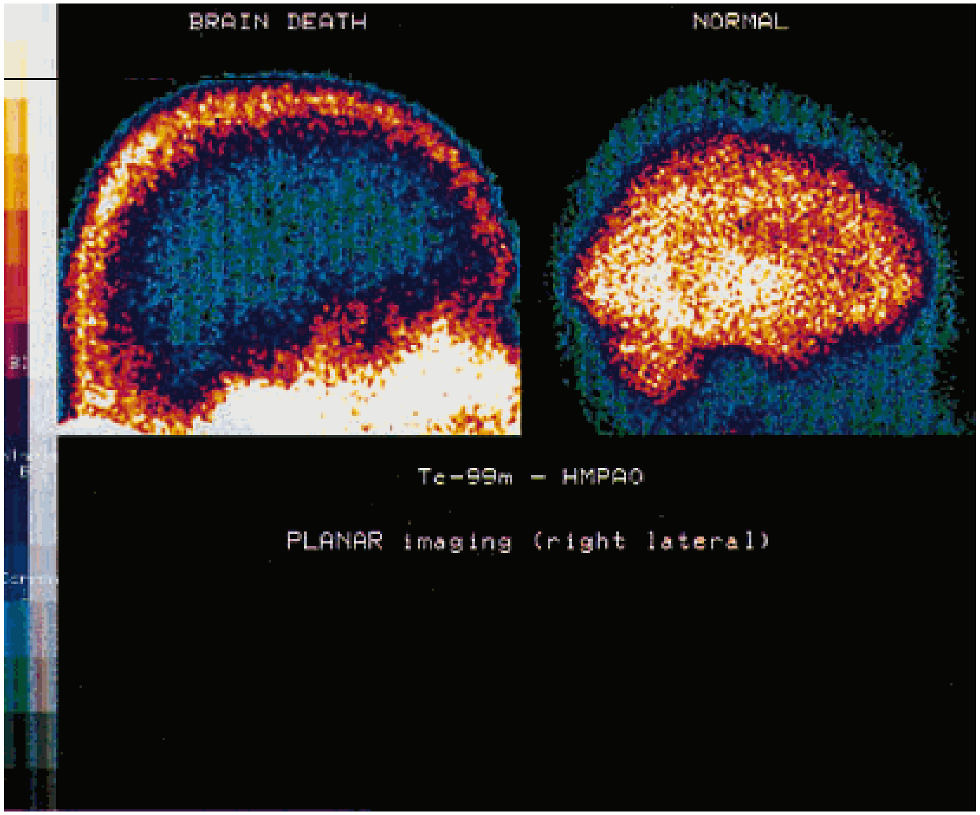
Neuro Imaging



Neuro Imaging

- Brain Death Imaging
  - ^{99m}Tc Ceretec (HMPAO) or Neurolite used to identify normal cerebral perfusion is present
  - Administered adult dose is 15 to 30 mCi
  - Other clinical criteria should be met prior to performing the procedure

Neuro Imaging



Neuro Imaging

- CSF Flow Scan
  - ^{111}In DTPA
  - Administered adult dose is 250 – 500 µCi via lumbar puncture
  - Multiple images acquired up to 72 hours post-injection
- CSF Leak
  - Similar as above with cotton pledgets placed into nasal cavity or ears, and counted afterwards for activity
  - Corrected pledget to plasma count ratio > 1.5 indicates CSF leakage

Thyroid Imaging

- ^{123}I scan to evaluate functional uptake, questionable nodules, goiter, and Graves disease. Also used to determine activity of ^{131}I to be administered for therapy
  - 200 – 400 µCi capsule and imaged 4 to 24 hours later
- ^{131}I Diagnostic uptake test for thyroid function (100 µCi)

Thyroid Imaging

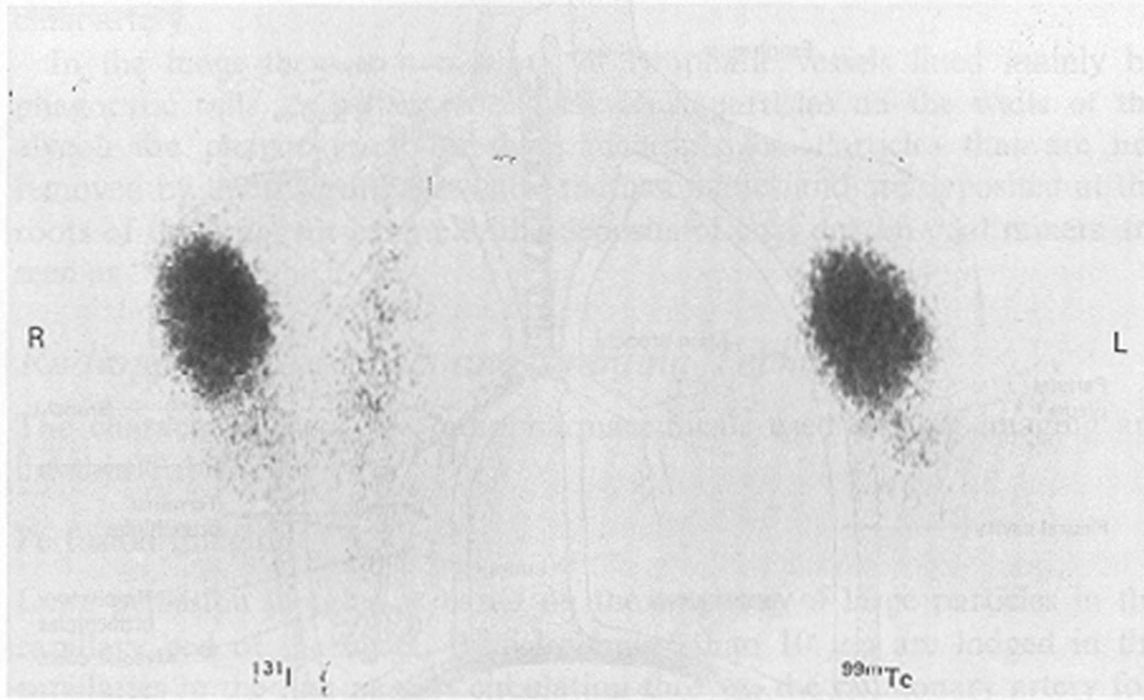


FIGURE 13.9. Thyroid scintiphotographs obtained with ^{131}I (24 hr after oral administration) and ^{99m}Tc (1 hr after injection) and showing a "hot" nodule in the upper right lobe. Both images are similar in the distribution of radioactivity except that there is slightly more uptake of ^{131}I in the left lobe.

Thyroid Therapy

- ^{131}I Therapy is very successful >80% with a single dose
- Beta particle deposits energy within the thyroid
- Typical dose for Graves disease is 8 to 20 mCi
- Concerns with release of patients and exposure to family & friends

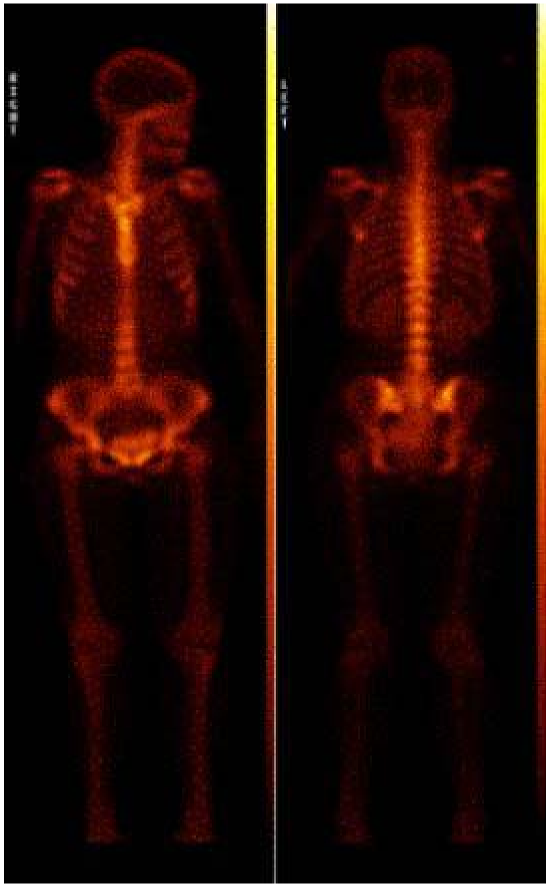
Skeletal Imaging

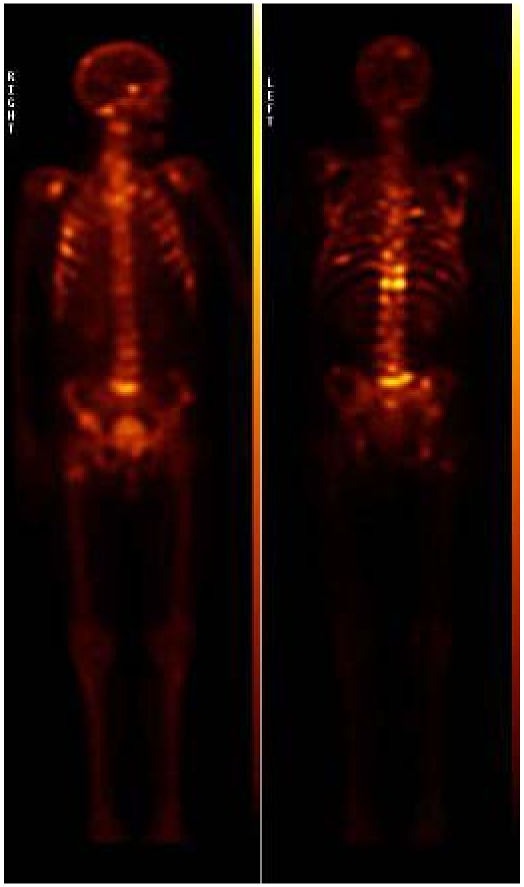
- The bone scan is the cornerstone of skeletal imaging and provides valuable physiological information beyond the information available on a standard x-ray image
- ^{99m}Tc diphosphonates (MDP) are used and once the unbound Tc clears in 2-3 hours a clear image of the entire skeletal system can be obtained
- Areas with higher blood flow or metabolic activity will be evident

Skeletal Imaging

- Two types of bone scan are common, both using 20 – 30 mCi
  - Standard
  - Three-phase

Skeletal Imaging





Therapy Products

- Metastron ($^{89}SrCl_2$)
  - –Relief of bone pain in patients with skeletal metastases
- Sodium Phosphate ^{32}P
  - –Treatment of polycythemia vera and chronic myelocytic leukemia
- Chromic Phosphate ^{32}P
  - –Intracavitary instillation peritoneal or pleural effusions
- Quadramet (^{153}Sm)
  - –Relief of bone pain in patients with oesteoblastic metastases

Therapy Products

- Therapies for B-cell Non-Hodgkin's Lymphoma
  - Zevalin
    - Two phase imaging and treatment
    - 1st phase is labeled with In-111 to insure uptake at desired sites
    - 2nd phase labeled with Y-90, 7 days later
    - QC is very important. Improper production could lead to DTPA which would take out a liver
  - Bexxar
    - Labeled with I-131 for both imaging and therapy dose
    - Imaging dose followed by higher therapy dose, 7 days later