Chapter 4: Single Photon Emission Computed Tomography (SPECT)

Contents

Emission Tomography (ET) for Nuclear Medicine Applications

- Introduction and basic principle of Emission Tomography
- Early developments
- Generation of radio-nuclides for ET.
- Detector technologies for ET
- System design considerations

Other Related Imaging Applications

- Coded aperture imaging
- Compton Imaging

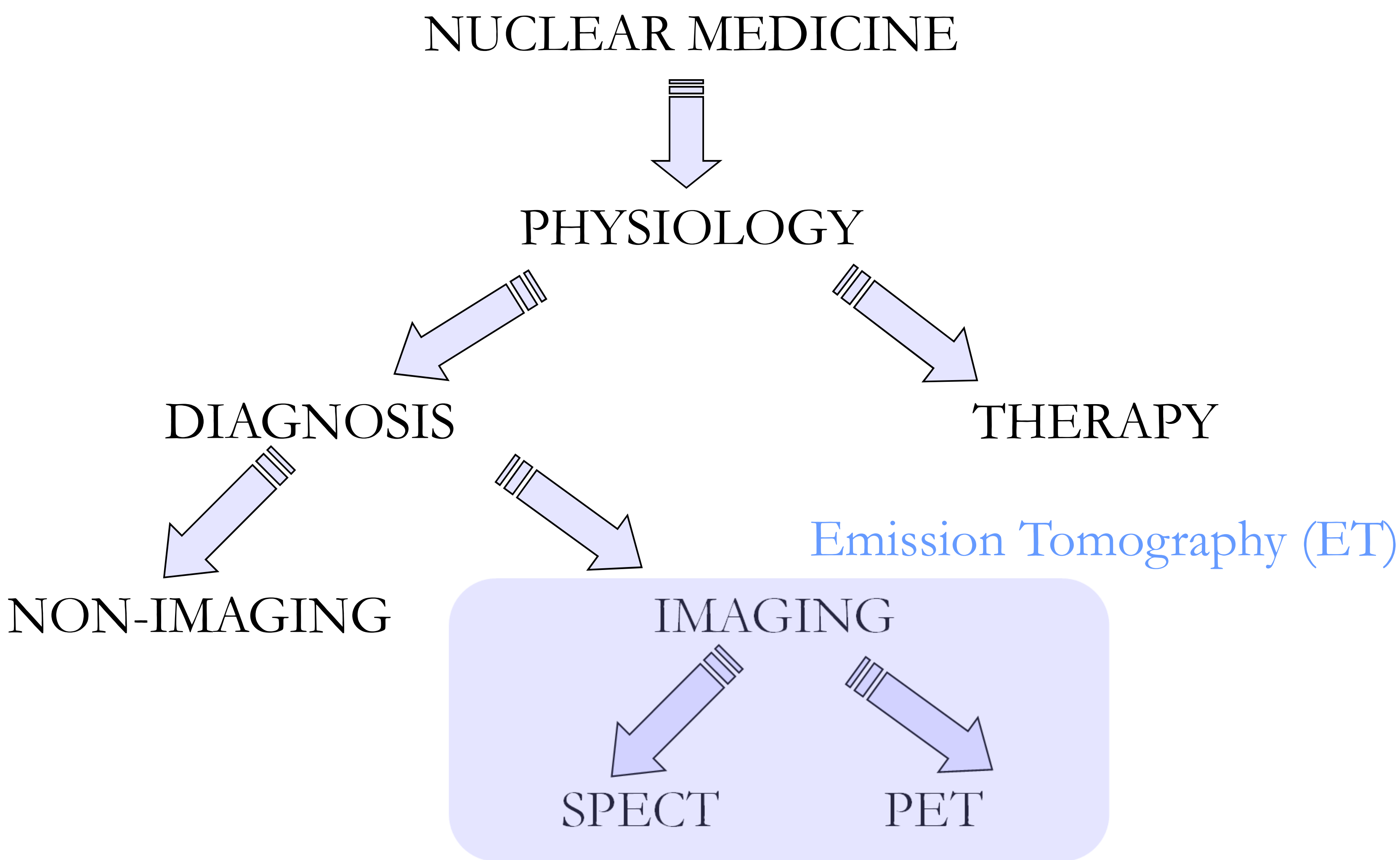
Traditional Definition of Nuclear Medicine

NUCLEAR MEDICINE SHOWS PHYSIOLOGY

Whereas

RADIOLOGY SHOWS ANATOMY

Traditional Definition of Nuclear Medicine



What is Emission Tomography?

- A branch of medical imaging that encompasses two main modalities – single photon emission computed tomography (SPECT) and positron emission tomography (PET)
- It uses radioactive materials to image properties of body's physiology, such as glucose metabolism, blood flow, receptor concentrations.
- ET is categorized as functional imaging techniques to distinguish it from methods such as X-ray CT that principally depict the body architectural structure (anatomy).

The Tracer Principle

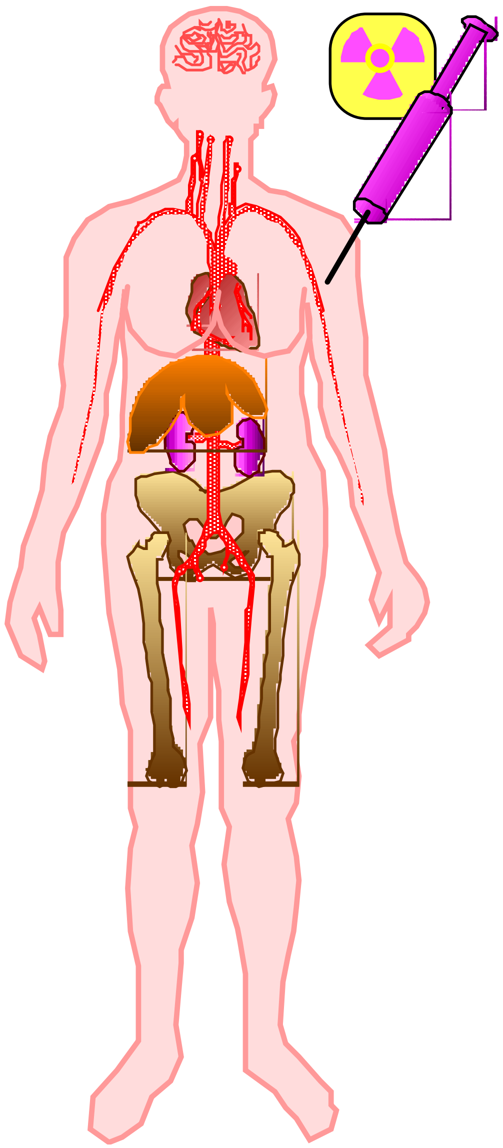
What is the tracer principle?

- Appropriately chosen radioactive compounds participate in an organism ’ s physiological processes in the same way as non-radioactive materials.
- These compounds can be detected through the detecting of their radiation signatures, such as gamma rays.

Two major attributes

- Because one can detect even minute quantities of radioactive material, the tracer principle can be used to measure molecular concentrations with a tremendous sensitivity.
- Tracer measurements are noninvasive – the concentration of tracer is deduced from the number of gamma rays detected.

Emission Tomography

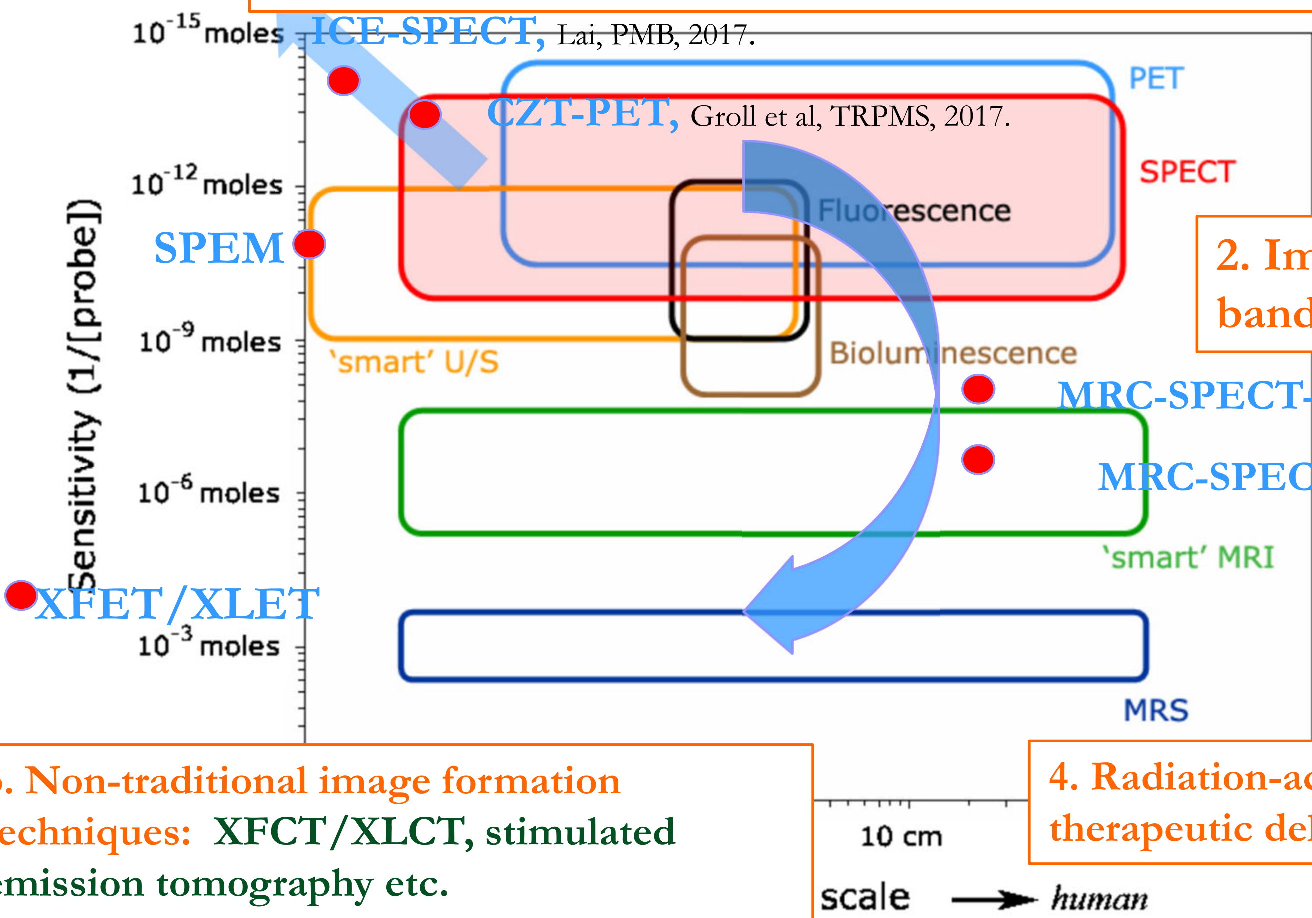


- Drug is labeled with radioisotopes that emit gamma rays.
- Drug localizes in patient according to metabolic properties of that drug.
- Trace (pico-molar) quantities of drug are sufficient.
- Radiation dose fairly small (<1 rem).

Drug Distributes in Body

"Emission tomography and its place in the matrix of molecular imaging technologies"

1. New technological approaches (detectors, system designs etc.) for better balance between spatial resolution and sensitivity



2. Imaging through broad-band EM radiation

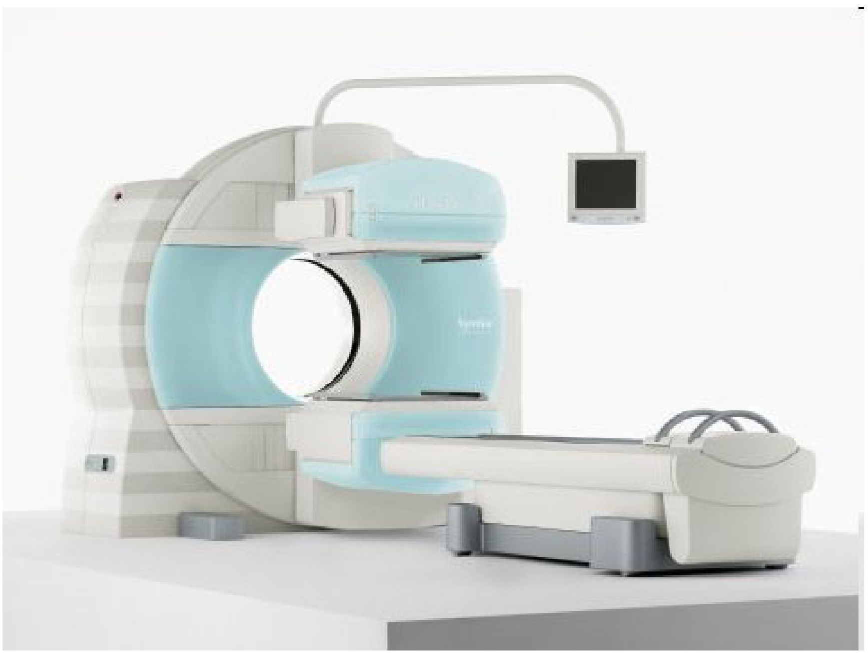
3. Non-traditional image formation techniques: XFCT/XLCT, stimulated emission tomography etc.

Meng, TNS, 2013, G. Fu, Med Phys 2014, Groll, TNS, 2016 …

4. Radiation-activable (nano-) material for therapeutic delivery and imaging

From S. R. Meikle et al, PMB Vol. 50, Topical Review, 2005.

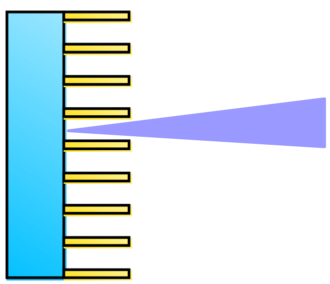
Single Photon Emission Computed Tomography (SPECT)



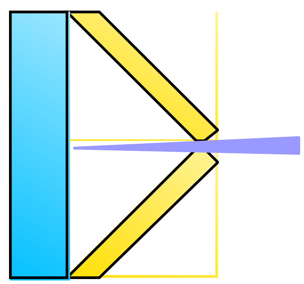
Siemens Symbia SPECT/CT

Philips Precedence SPECT/CT

Single Photon Emission Computed Tomography (SPECT)



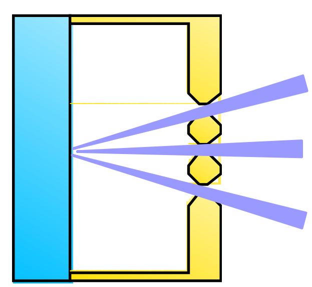
Collimator



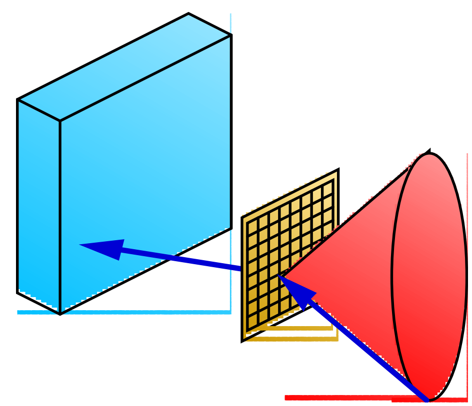
Pinhole

Collimator in front of the detector to select gamma rays from certain directions only …

Rotated around the object for collecting multiple projections …

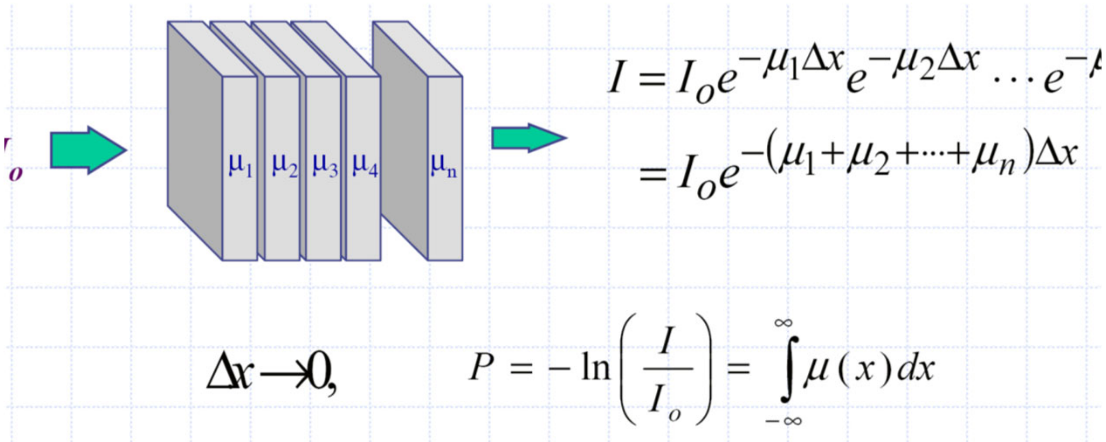


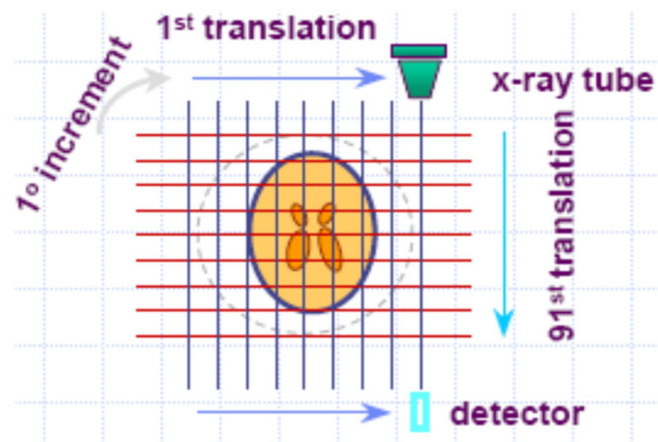
Coded Aperture

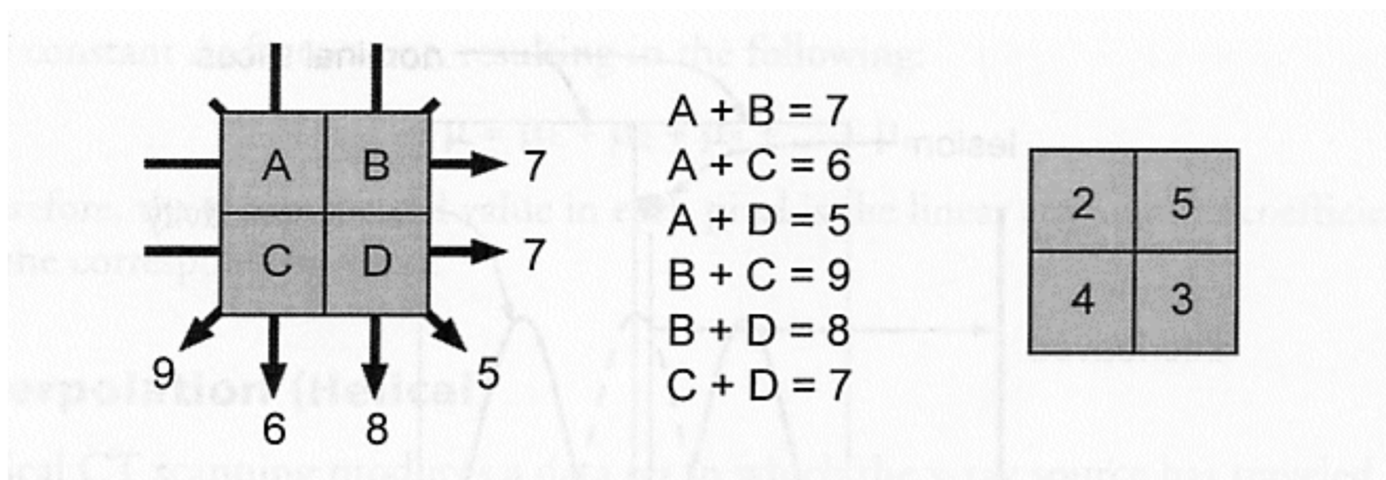


Compton

Single Photon Emission Computed Tomography (SPECT)







What would be an ideal gamma ray emitter for nuclear imaging?

- Reasonably penetrative…
- Half-life comparable to the biological process we are trying to visualize…
- Easy radiochemistry…
- Biologically safe…
- Clean …

Radionuclides are Produced in a Nuclear Reactor or a Cyclotron

Reactor - target bombarded with neutrons

Cyclotron - target bombarded with charged particles

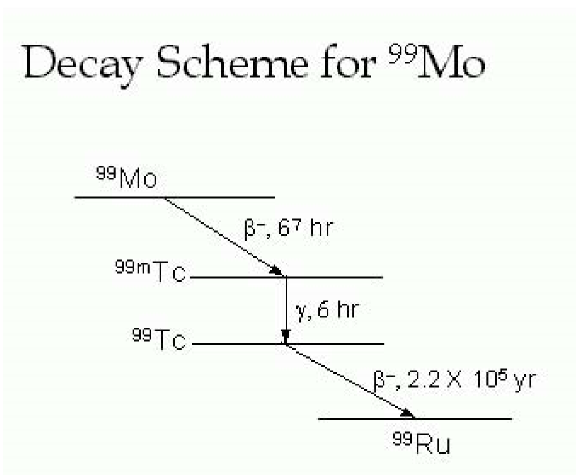
- Diagnosis uses radionuclides from both
- Therapy radionuclides produced in a nuclear reactor
- PET radionuclides produced in a cyclotron

Metastable Nuclear States and Gamma Ray Emission

The lifetimes of nuclear excited states vary, but $\sim 10^{-10}$ s can be regarded as typical. Thus, gamma rays are usually emitted quickly after radioactive decay to an excited daughter state.

In some cases, however, selection rules prevent photon emission for an extended period of time. The excited state of $^{137}_{56}Ba$ following the decay of $^{137}_{55}Cs$ has a half-life of 2.55 min. Such a long-lived nuclear state is termed *metastable* and is designated by the symbol m: $^{137m}_{56}Ba$.

Another example of a metastable nuclide is $^{99m}_{43}Tc$, which results from the beta decay of the molybdenum isotope $^{99}_{42}Mo$.
an isomeric transition (IT) to the ground



Metastable Nuclear States and Gamma Ray Emission

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Tc-99m Generator

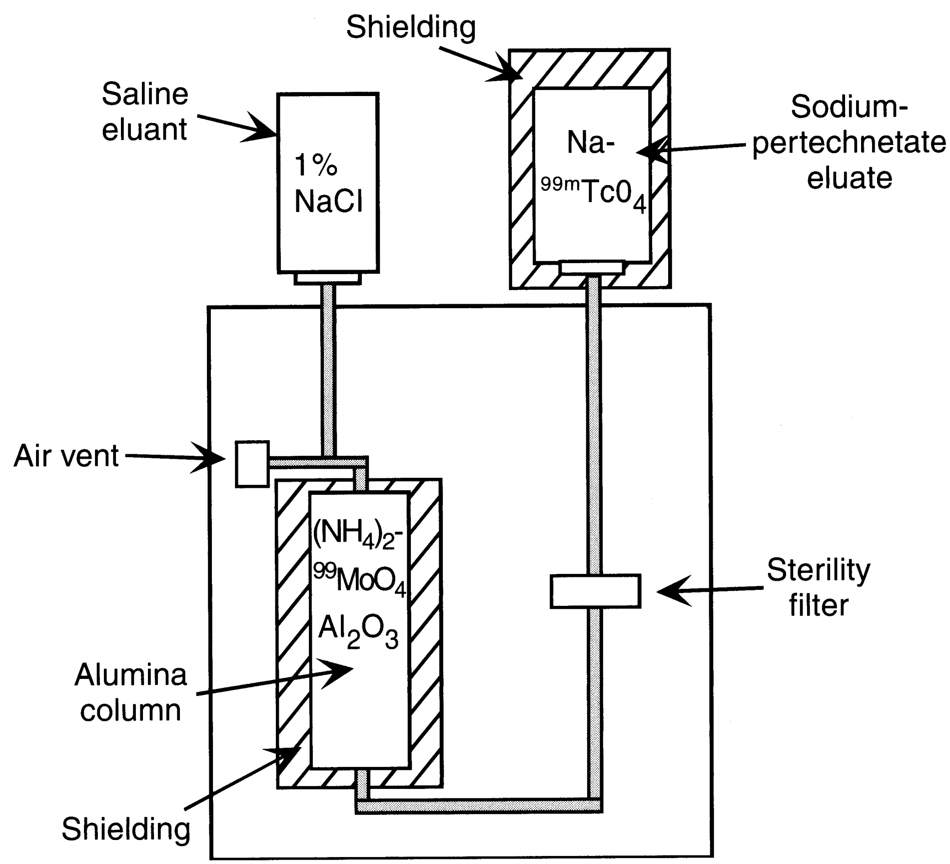


FIGURE 6 Schematic drawing of a ^{99}Mo–^{99m}Tc generator. (Adapted from Rollo, 1977.)

Early Developments

Radionuclides for diagnostic purpose

1935 Hevesy : radiophosphorous for metabolic studies in rats

1949 Cassen : rectilinear scanner consisting of a calcium tungstate crystal coupled to a photomultiplier tube for I-131 uptake in thyroid with ¼" resolution

1957 Anger : stationary area detector.

scintillation camera (Anger or gamma camera) consisting of a large-area sodium iodide crystal coupled to an array of PM tubes

Early Development

Radionuclides for diagnostic purpose – cont.

Early 1960s Kuhl & Edwards : idea of transverse section tomography (cf. X-ray CT), unsatisfactory results because of without the aid of computers & reconstruction algorithms

1977 Keyes & Jaszczak : SPECT (Single-photon emission computed tomography), improved image contrast compared to stationary cameras

1970s : PET (positron emmision tomography), large number of scintillation detectors surrounding the patient, unique capability to study metabolic function in humans.

DISA Applications (1)

BRAIN

- Tc99m/I123: brain dopamine receptor imaging (Parkinson's disease), epilepsy, depression
- Tc99m/Tl201: differentiation in radiation necrosis and recurrent glioma

THYROID/PARATHYROID

- Tc99m/I123 or Tl201: simultaneous thyroid/parathyroid imaging

INFECTION

- Tc99m/In111: Infective endocarditis (111In white blood cells (occult infections) and 99mTc perfusion imaging)
- I123/Tl201: myocardial SPECT with Tl-201 and I-123 MIBG for myocarditis
- Tc99m/In111: osteomyelitis (bone infection),infected pelvic pressure ulcer, infection in the feet of diabetic patients

DISA Applications (2)

MYOCARDIAL VIABILITY (INFARCTION)

- In111/Tl201: dual-isotope SPECT with indium 111-monoclonal antimyosin antibodies and thallium-201 can estimate infarct size and percentage myocardium infarcted

MYOCARDIAL PERFUSION

- Tc99m/Tl201: simultaneous Tc-99m stress and Tl-201 rest

MYOCARDIAL FATTY ACID METABOLISM

- Tc99m/I123: simultaneous perfusion (Tc99m tetrofosmin) and fatty acid metabolism (I123-BMIPP)

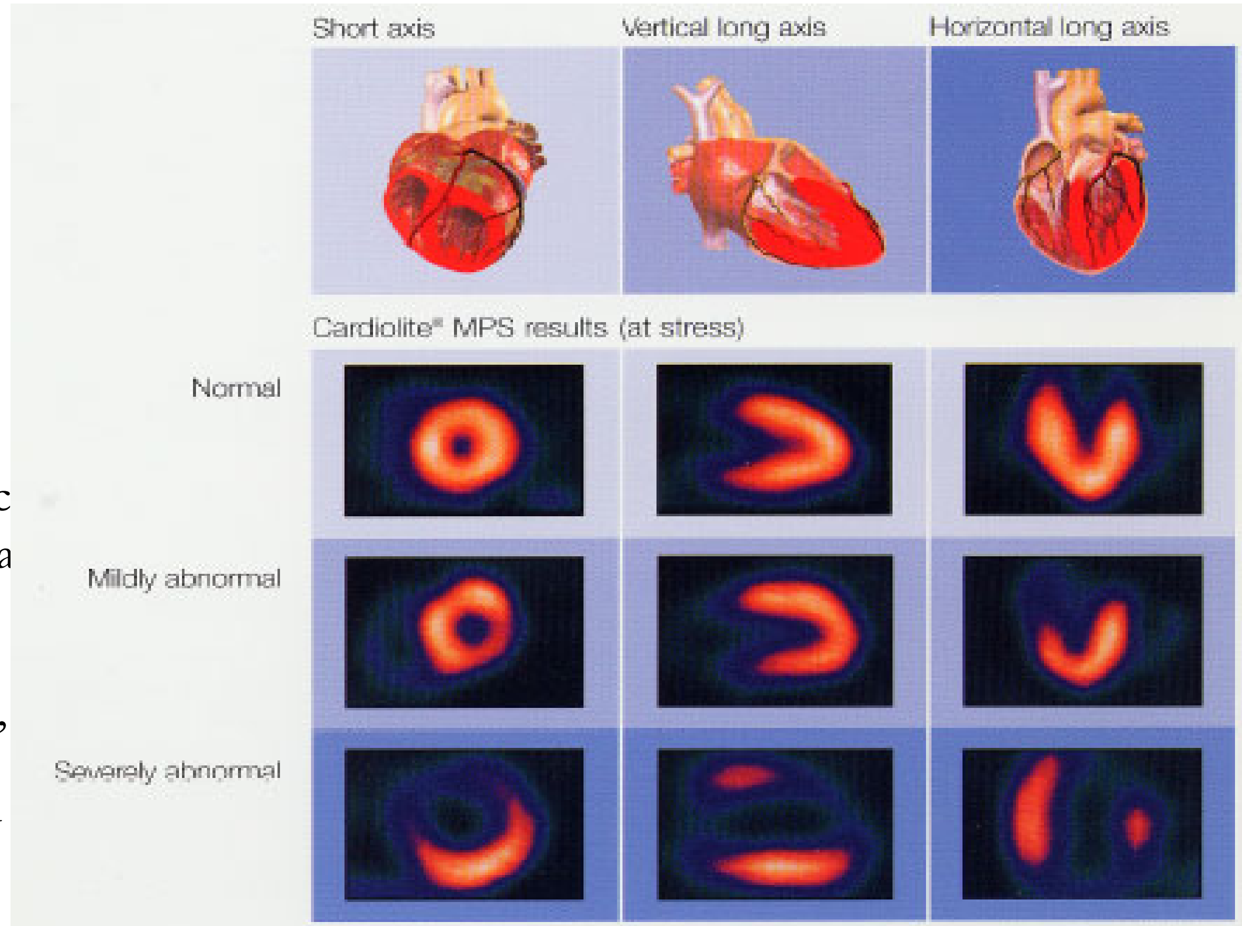
MYOCARDIAL INNERVATION

- Tc99m/I123: simultaneous I-123 mIBG innervation and Tc99m resting perfusion
- Tc99m/I123/Tl201: rest perfusion status with 201Tl, stress perfusion status with a 99mTc labeled agent, innervation status with 123I-MIBG

What do MPI images look like?

In a typical nuclear cardiac imaging exam, the physicia reviews:

- Static “Summed Perfusion Images’
- Dynamic “Gated Images”



Perfusion Images are viewed in three orientations:
SA – Short Axis
VLA – Vertical Long Axis
HLA - Horizontal Long Axis

Example of Dual-Isotope SPECT Imaging

This slide is based on the work by Dr. Eric Frey, at Johns Hopkins University

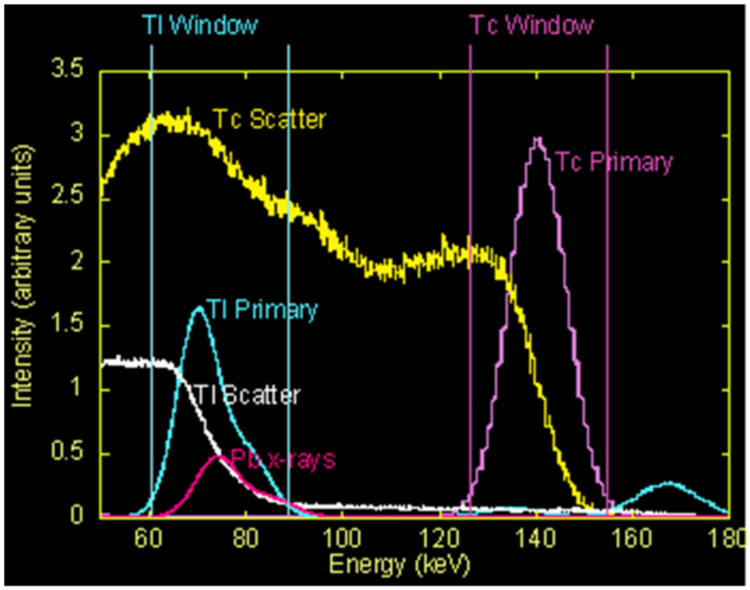


Fig. 1. Sample energy spectra of Tl-201 and Tc-99m.

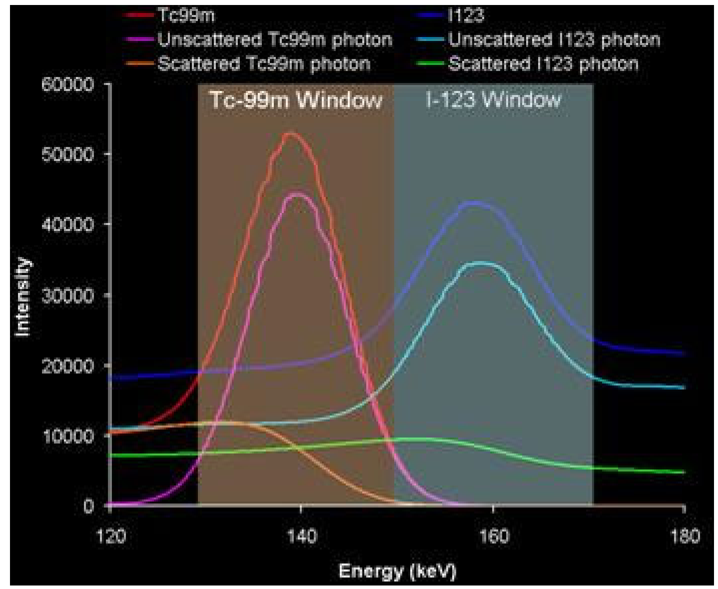
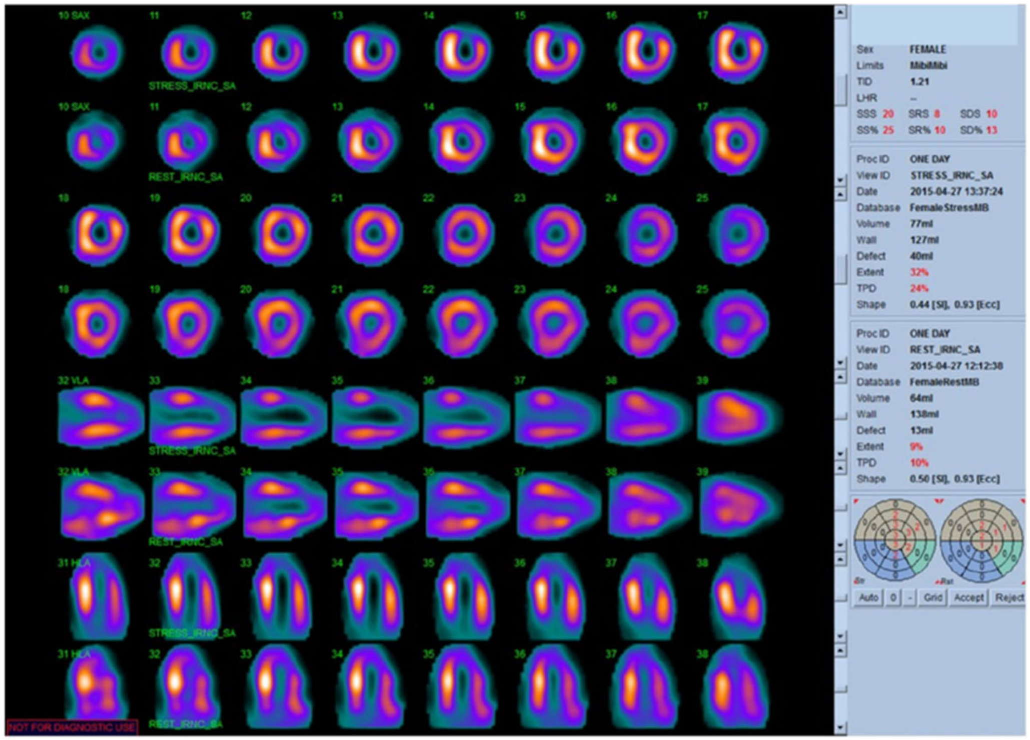
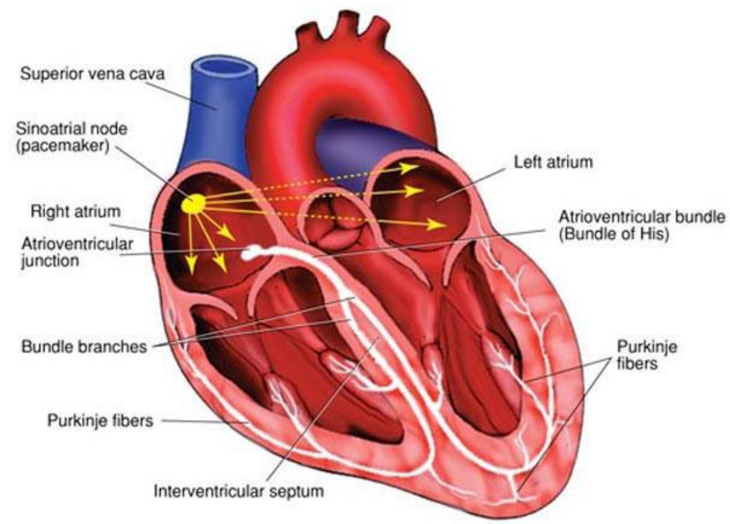


Fig. 2. Sample energy spectra of Tc-99m and I-123.

Typical dual-isotope SPECT imaging: rest/stress myocardial perfusion imaging using Tc-99m and Tl-201 labeled agents and brain imaging using Tc-99m and I-123 labeled isotopes.

Tc-99m Sestamibi Myocardial Perfusion Imaging (MPI)





Exercise stress Tc-99m Sestamibi single day myocardial perfusion SPECT images of the female patient with a significant (80%) distal left main coronary artery disease. Classic features of the high-risk scan are present: severe partially reversible perfusion defect, involvement of the LAD and LCX territory, visual transient ischemic dilation and abnormal TID ratio (1.21). The patient presented with symptoms of stable atypical angina. No significant ECG or hemodynamic changes were noted during the stress portion of the test.

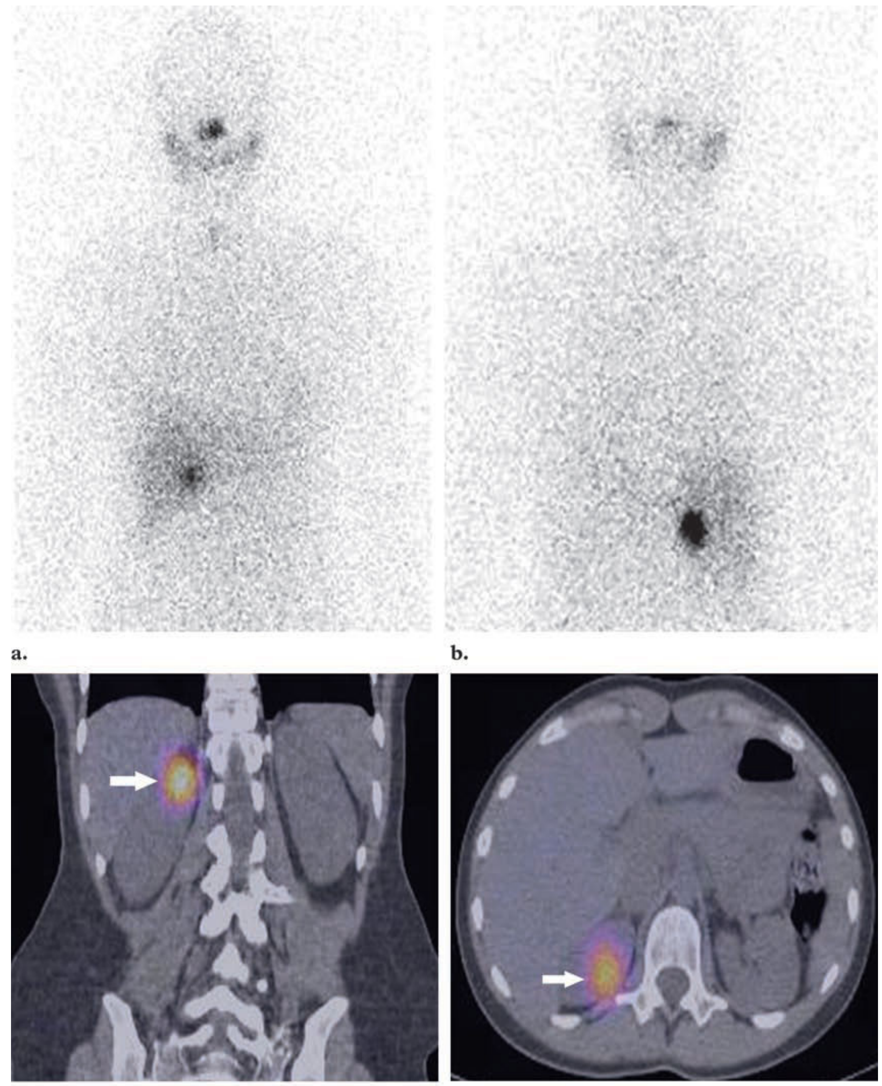
https://www.researchgate.net/figure/Exercise-stress-Tc-99m-Sestamibi-single-day-myocardial-perfusion-SPECT-images-of-the_fig1_283448406

I-131 Whole Body Imaging

Differentiation between malignancy and benign changes with SPECT/CT in a patient with
thyroid cancer who underwent 131I whole-body imaging to assess for residual recurrent disease. Anterior(a) and posterior (b) 131I scans show focal activity in the right suprarenal region.

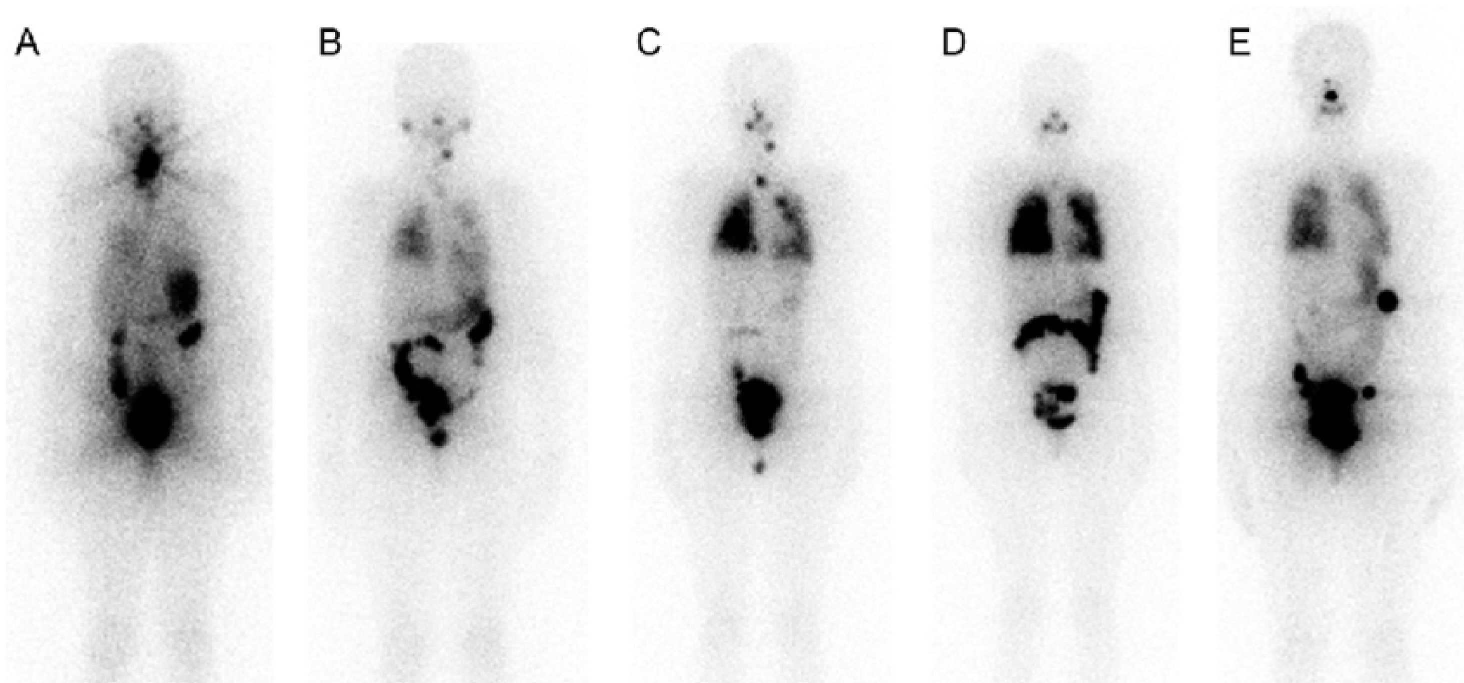
Coronal (c) and axial (d) SPECT/CT images show that the uptake is located in the renal collecting system (arrow),consistent with physiologic urinary activity, and not recurrence of disease.

www.lancastergeneralhealth.org/LGH/ECommerceSite/

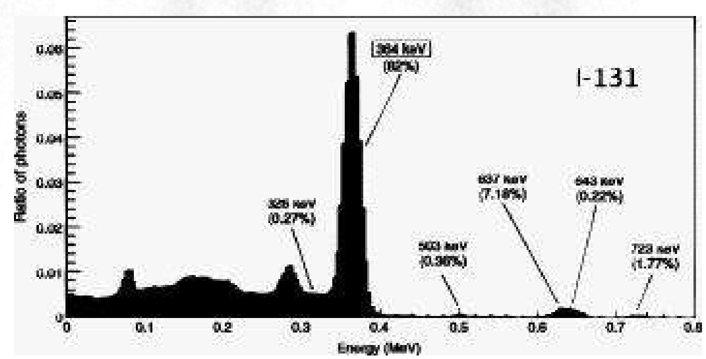


a. b. c. d.

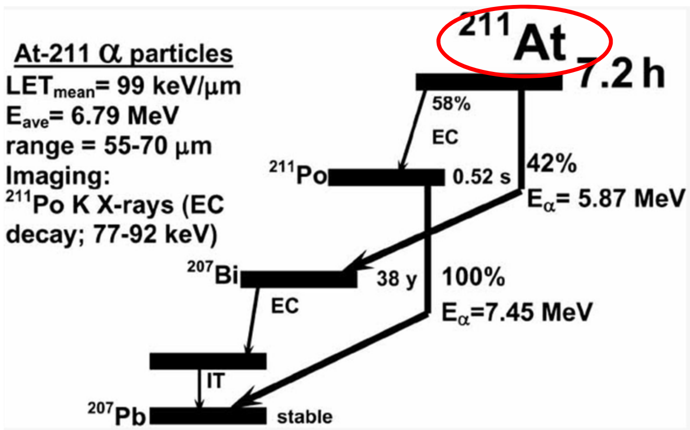
Case Report: “Management of metastatic thyroid cancer in pregnancy: risk and uncertainty”, by Christopher W Rowe et al., Endocrinology, Diabetes and Metabolism, 2016



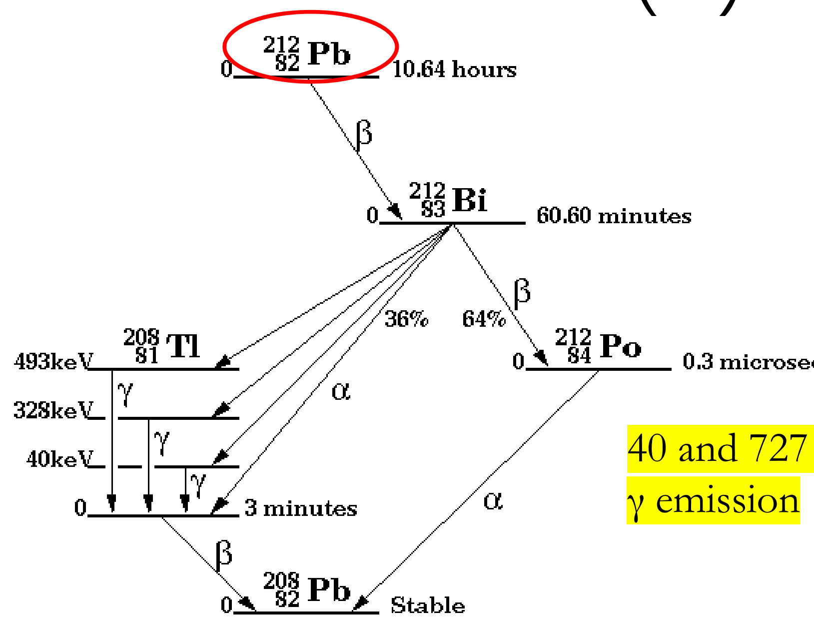
Serial post-I 131 therapy scans (anterior whole body views). (A) Age 10, 3.01 GBq; (B) age 11, 2.95 GBq; (C) age 13, 4.3 GBq; (D) age 14, 5.1 GBq; (E) age 15, 9.9 GBq, 7 months before conception. Neck disease present at age 13 (C) was treated surgically. The final study (E) showed the presence of radioiodine avid bilateral pulmonary metastases (<5 mm maximum diameter on computed tomography) and very small, low-grade lower neck disease. The focal uptake in the left upper abdomen is colonic and is likely physiological in nature.



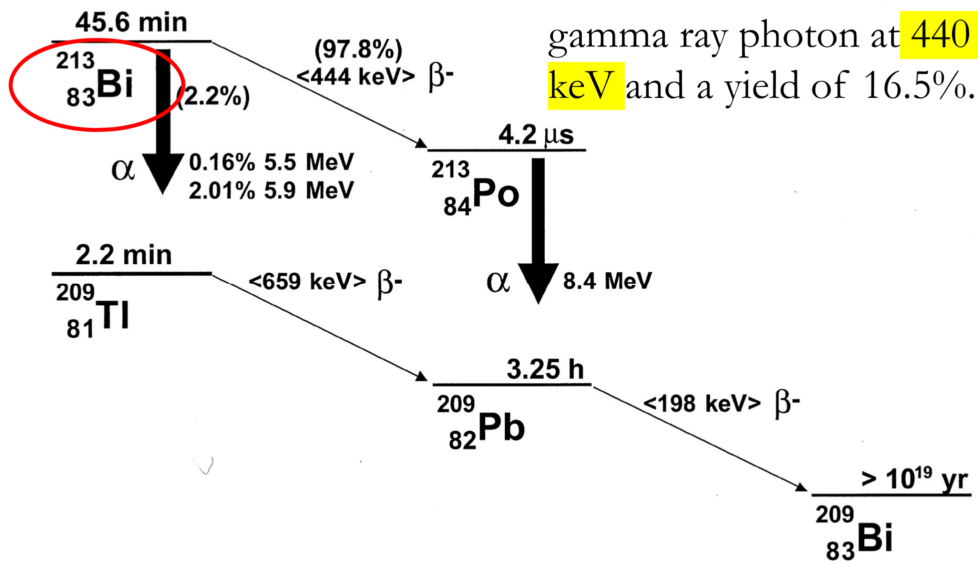
α-emitters of Human Interest (1)



Po K Xrays are emitted that permit external imaging, the two most abundant of these X-rays have energies of 77 and 80 keV, 12 and 20% of all photon emissions, respectively.

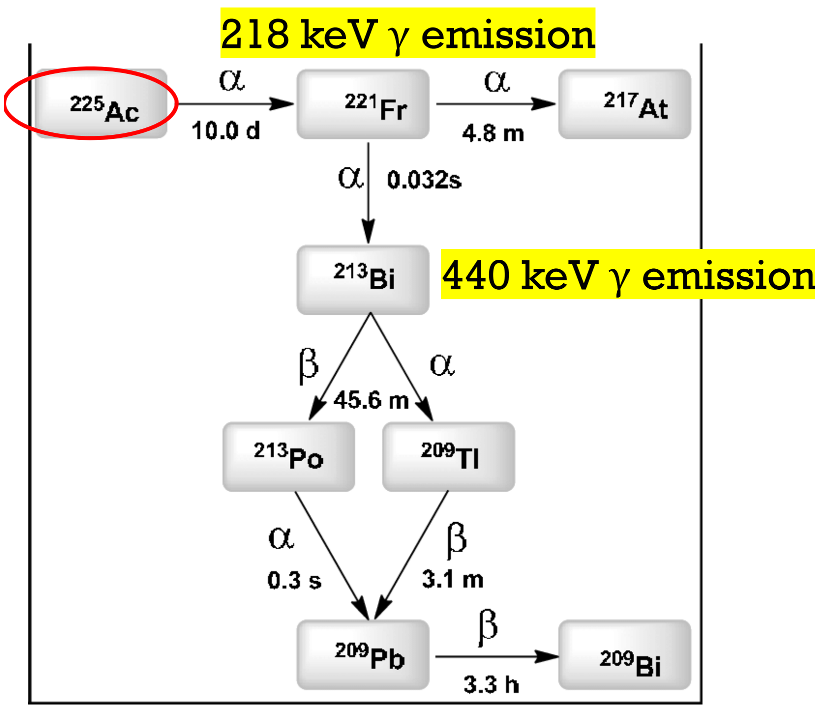


40 and 727 keV γ emission

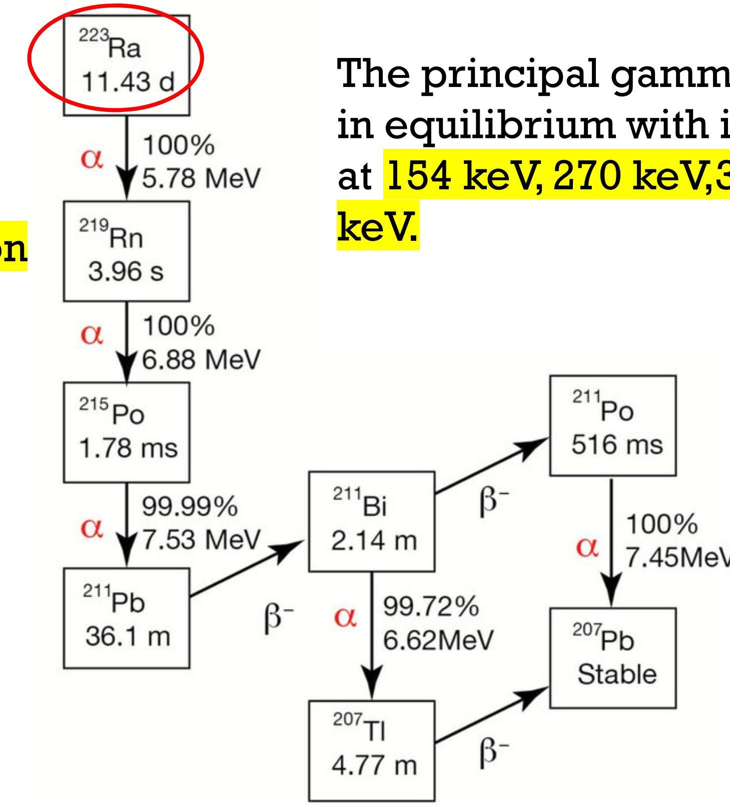


Bismuth-213 emits a gamma ray photon at 440 keV and a yield of 16.5%.

α-emitters of Human Interest (2)



Main problem: reduce the loss of the daughters to non-target tissues and mitigating systemic radiotoxic events.

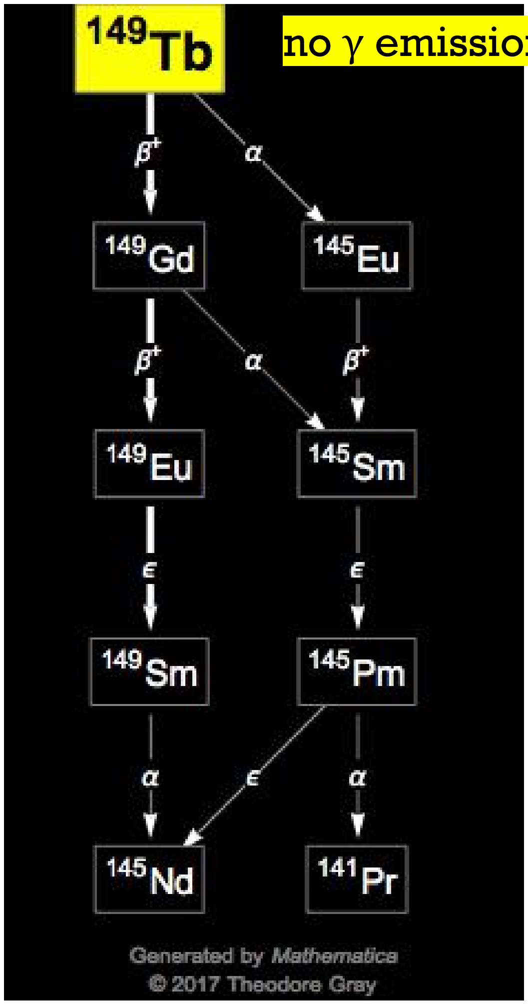


The principal gamma lines for 223Ra in equilibrium with its daughters are at 154 keV, 270 keV,351 keV, and 405 keV.

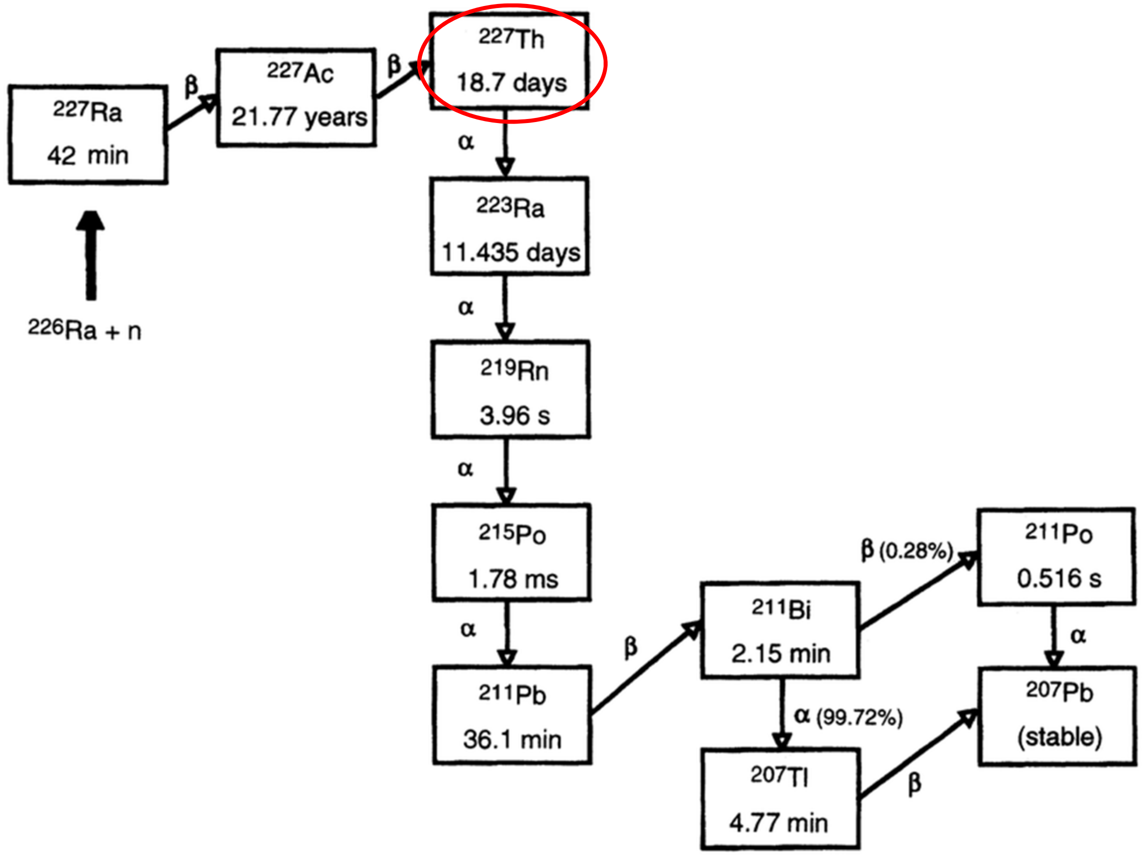
>200 patients have been treated with 223Ra-chloride (Alpharadin, Algeta ASA, Oslo, Norway), in several European countries and has been approved for investigational use in the U.S. The principal characteristics of this radionuclide are high skeletal uptake with long-term retention, minimal uptake in normal organs and other soft tissues, and clearance via the gastro-intestinal tract.

α-emitters of Human Interest (3)

no γ emission



High yield photons occur at 12.3 (17%), 15.2 (21%), and 236 (11%) keV.



Example of Dual-Isotope SPECT Imaging

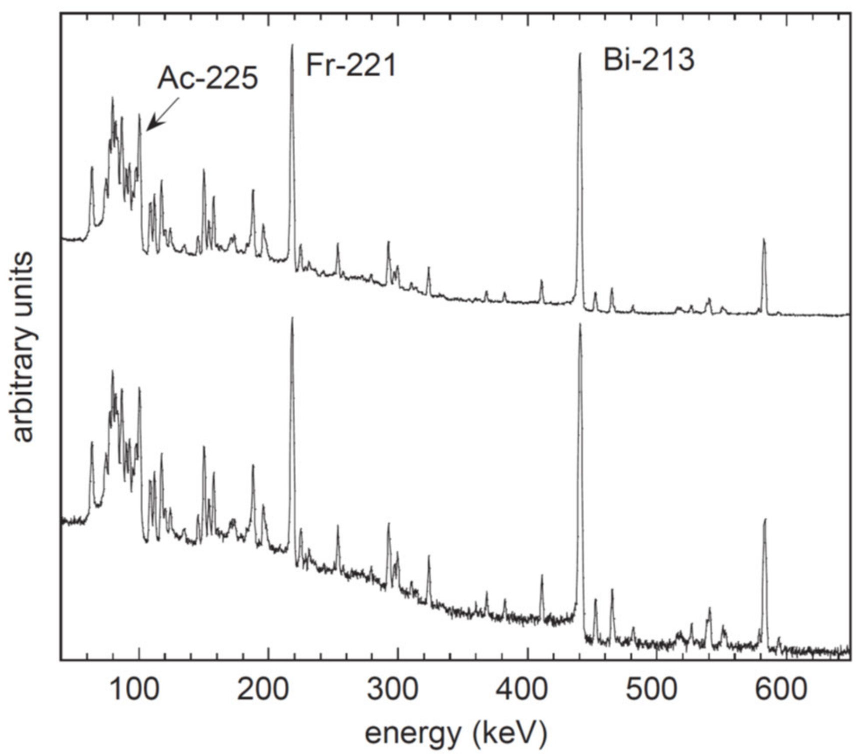
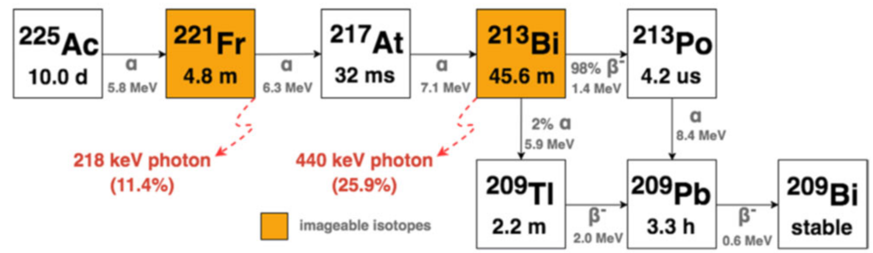
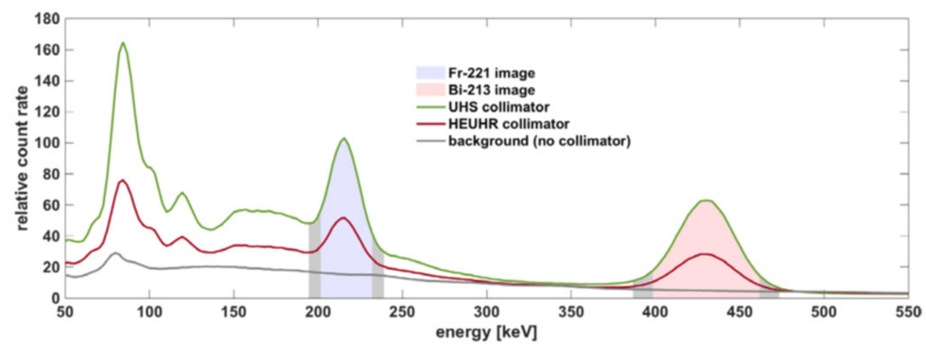


Fig. 4. Gamma spectra of purified Ac-225 produced via cyclotron irradiation (upper spectrum) and Ac-225 extracted from Th-229 (lower spectrum).



The 225Ac decay chain. Photons with a branching ratio >3% relative to 225Ac decay are shown.

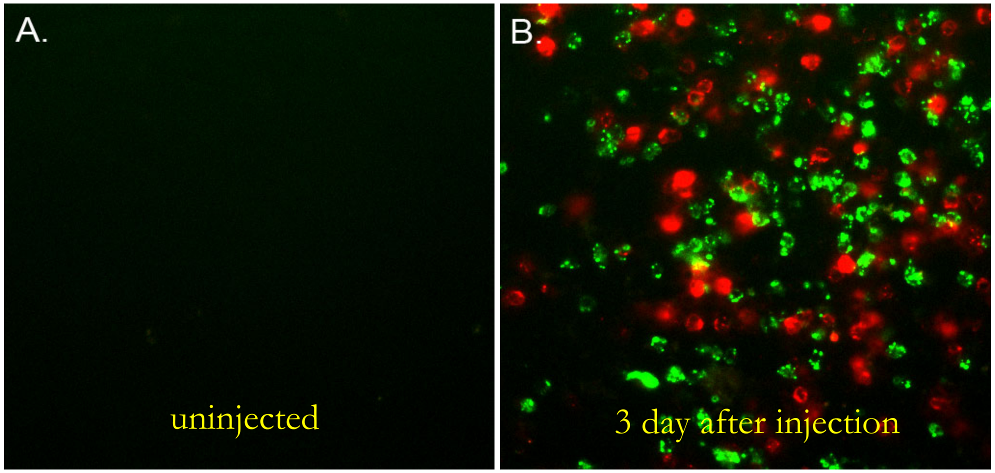


Energy spectra, normalized by acquisition time, acquired by the VECTor scanner for both HEUHR (red) and UHS (green) collimators with a comparison to a background spectrum (grey) acquired with no collimator or activity present. Spectra were acquired using a uniform source containing 1.05 MBq (28.3 μCi) of 225Ac. The energy regions used to reconstruct the 221Fr and 213Bi are shown in blue and red, respectively. The adjacent grey regions indicate the energy windows defined for background and scatter correction.

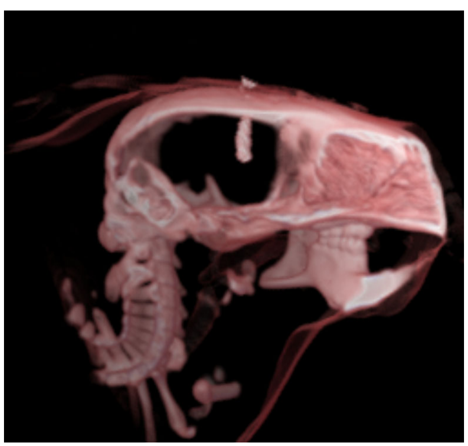
Cyclotron production of Ac-225 for targeted alpha therapy, C.Apostolidis, Applied Radiation and Isotopes, 2005

In Vivo Imaging in T Cells Immunotherapy

A Collaboration with Prof. Ed Roy, Pathology, UIUC



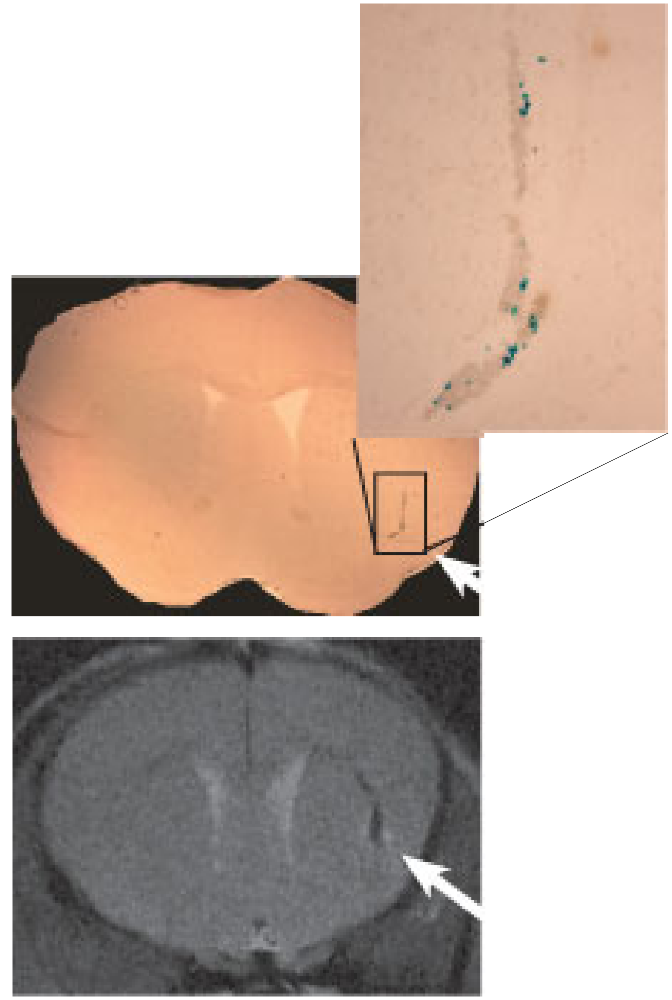
Microscopy of NIR fluorescently labeled T cells. A. Lymph node of uninjected mouse showing the lack of autofluorescence under acquisition conditions used in B. B. Two populations of T cells in the lymph node, labeled with CellVue Burgundy (red) and CellVue NIR815 (green) after intravenous injection. These images were kindly provided by Prof. Ed Roy of Pathology and the Beckman Institute, UI:



Fused SPEM/CT image of a mouse’s brain. Two groups (5μL and 0.3μL) of radiolabeled T cells are visible in the brain.

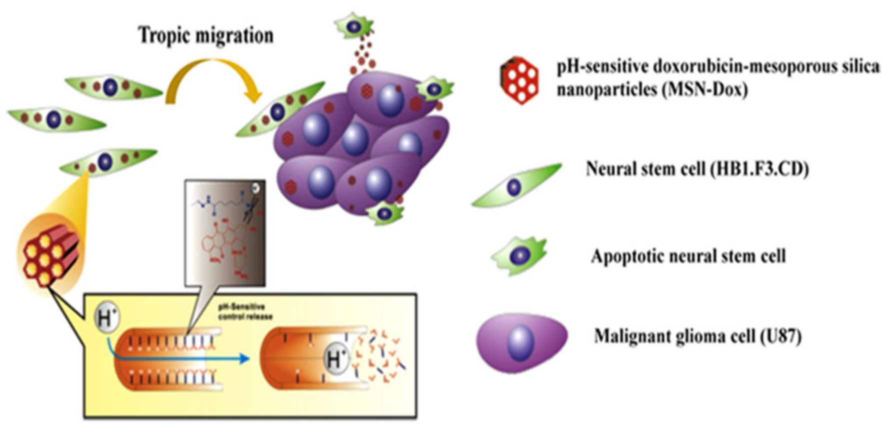
- Spatial reso. ~ 0.1 mm
- a few hundred cells

L. J. Meng et al., NIM 2009



MRI images of Iron oxide labeled T cells in the brain in association with a small brain tumor. Image courtesy Prof. Ed Roy, Univ. of Illinois.

In Vivo Imaging of Neural Stem Cells for Glioblastoma Targeting and Therapy



Scheme 1. Schematic of the pH-senstive MSN-Dox-loaded neural stem cell delivery system.

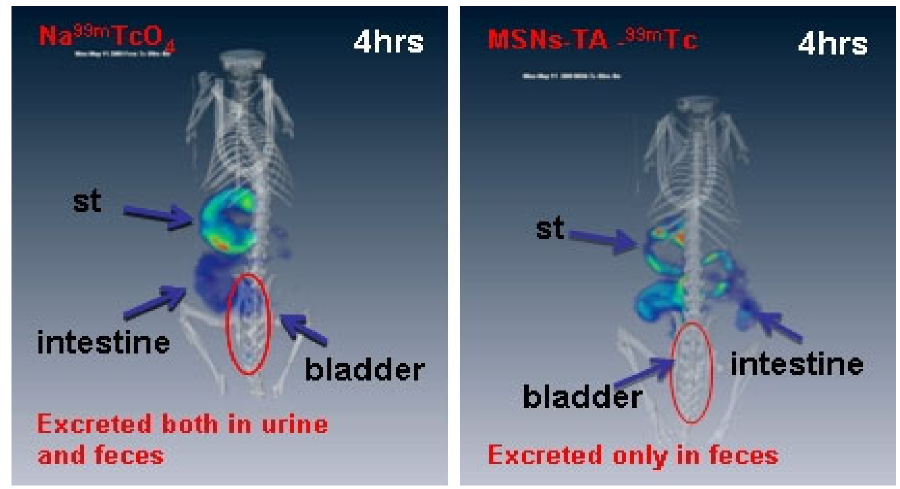


Fig. 1: The SPECT/CT imaging of mice post gavage of MSN-TA-^{99m}Tc and $Na^{99m}TcO_4$.

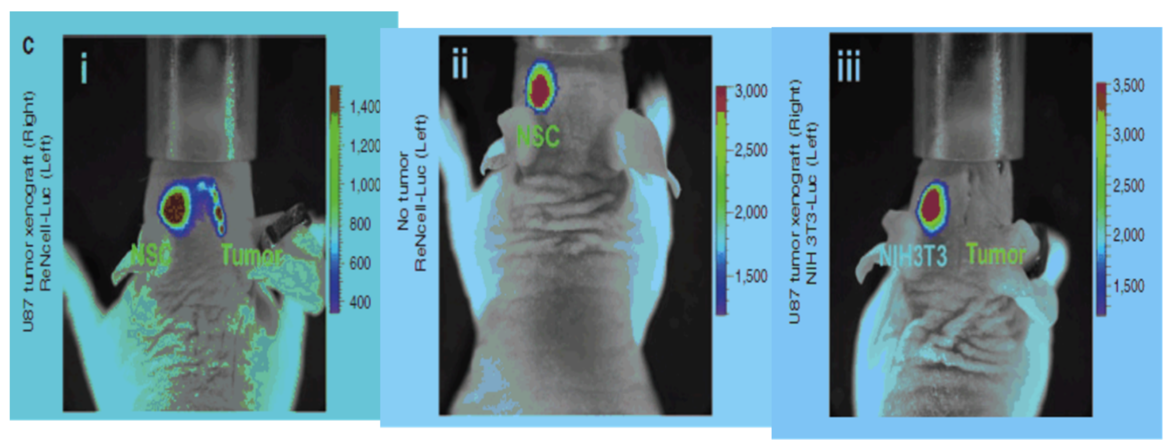


Figure 2. In vivo tumor-tropic migration of ReNcell. Bioluminescent imaging of mice after intracranial injection of ReNcell-Fluc into the left hemisphere of the mice implanted with U87 xenograft tumors on the right side 7 days (i) before or (ii) mice with no tumor. Another group of tumor-bearing mice received control fibroblast NIH-3T3-Rluc cell. Each group had five animals; photographs show a representative animal from each group. Imaging was done 24 hours postimplantation of the NSCs.

Image curtsey, Prof Lesniak University of Chicago.