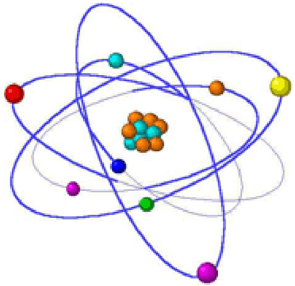
Radioisotope and Radiation Applications (FS2013)



Applications for Medical Diagnosis (Week 3a)

Pavel Frajtag

01.10. 2013

Applications for Medical Diagnosis: Outline

- ❑ Medical Diagnosis
- ❑ Imaging with External Energy Sources
  - Projection radiography
  - Computed tomography (CT)
  - Fluoroscopy
  - Mammography
- ❑ Imaging with Internal Energy Sources (Radioimaging)
  - Gamma camera (Scintigraphy)
  - Radiopharmaceuticals
  - Positron emission tomography (PET)
  - Single photon emission computed tomography (SPECT)
- ❑ Combination of Imaging Techniques

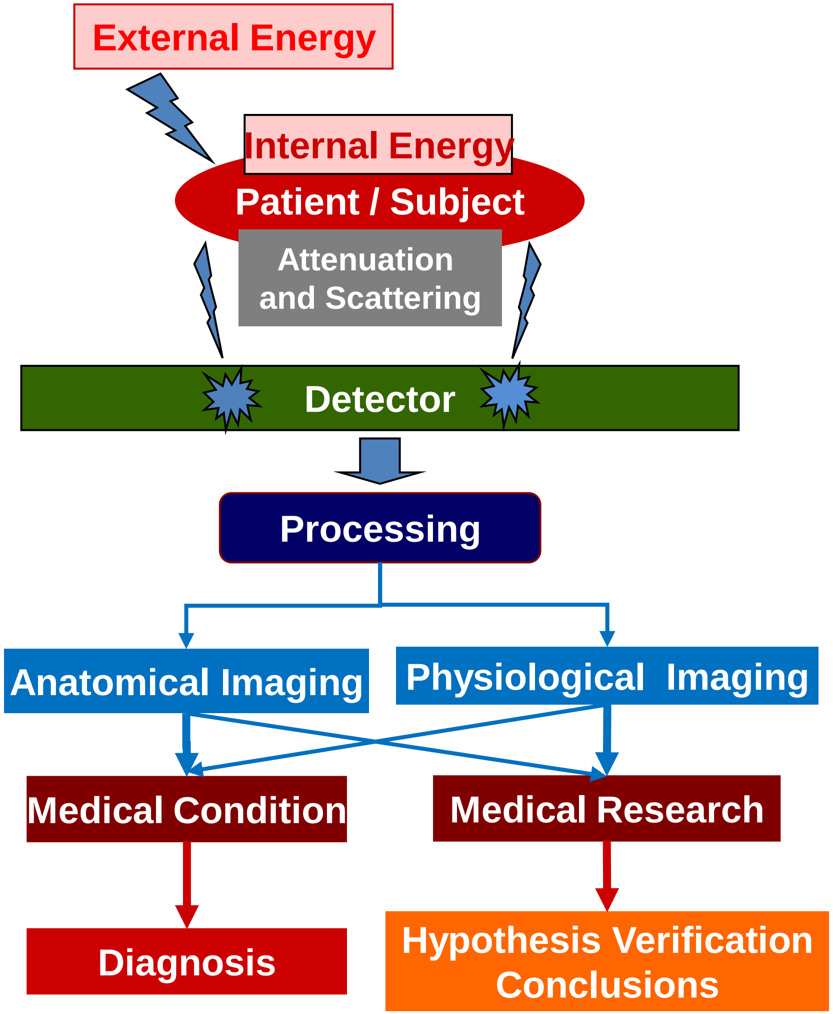
Medical Diagnosis

- **Diagnosis** or **diagnostics** is the process of identifying a medical condition or disease by its signs, symptoms, and from the results of various diagnostic procedures.
- The conclusion reached through this process is called a **diagnosis**.
- **Diagnostic criteria** designates the combination of symptoms which allows the physician to ascertain the diagnosis of a given disease.

Medical Imaging: Basics

- Ensemble of techniques and processes:
  - Used to create **images** of the human body (or parts thereof).
  - For **clinical purposes** (seeking to reveal, diagnose or examine disease) or for **medical science.**
- Medical imaging deals with:
  - Anatomy ("structure") and
  - Physiology ("function").

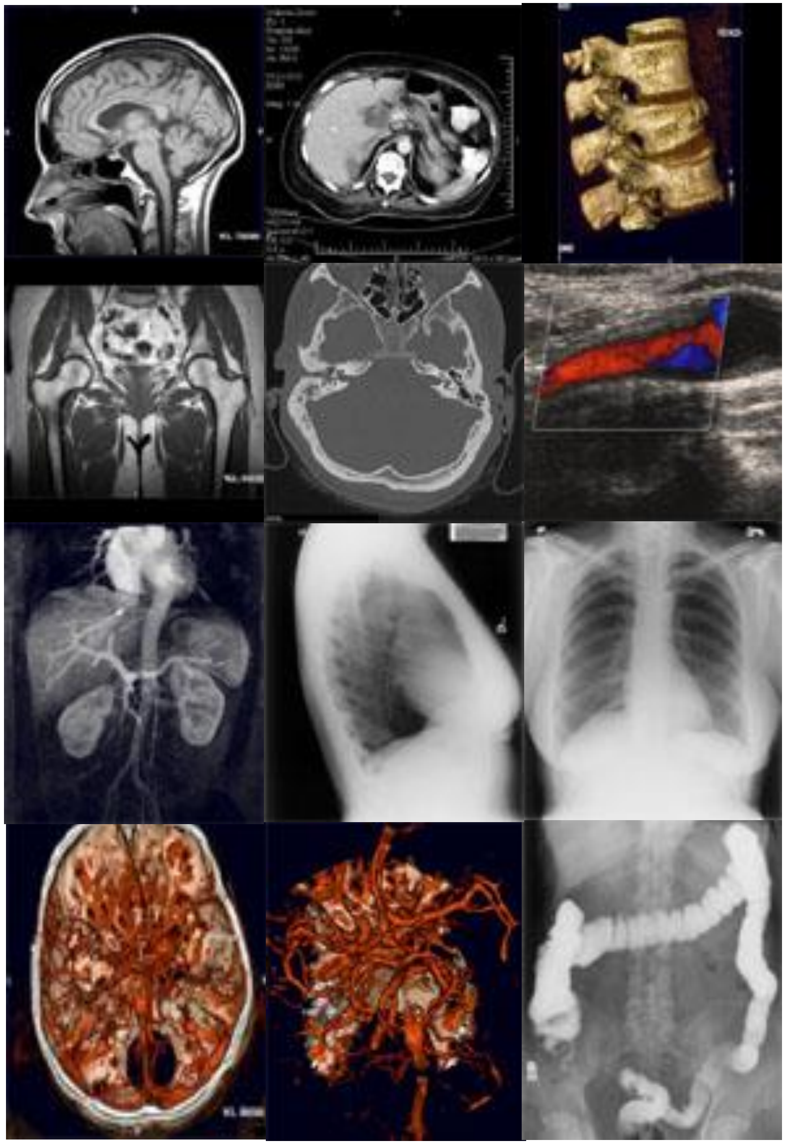
Radiation can be used as a probe to produce medical images useful for diagnosis and research.



Medical Imaging: Technology Overview

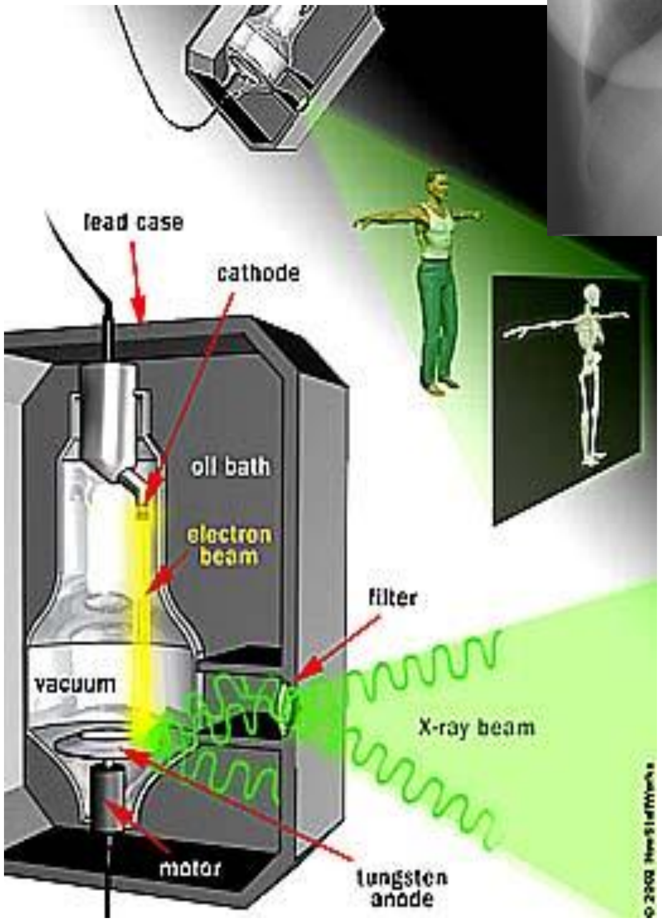
❑ Modern Techniques:

- **Radiography**
- **Computed Tomography**
- **Fluoroscopy**
- **Mammography**.
- Magnetic Resonance
- Ultrasound
- Microwave Imaging
- Electrical Impedance Tomography
- **Radioimaging:**
  - **Scintigraphy**
  - **Positron Emission Tomography (PET)**
  - **Single Photon Emission Computed Tomography (SPECT)**



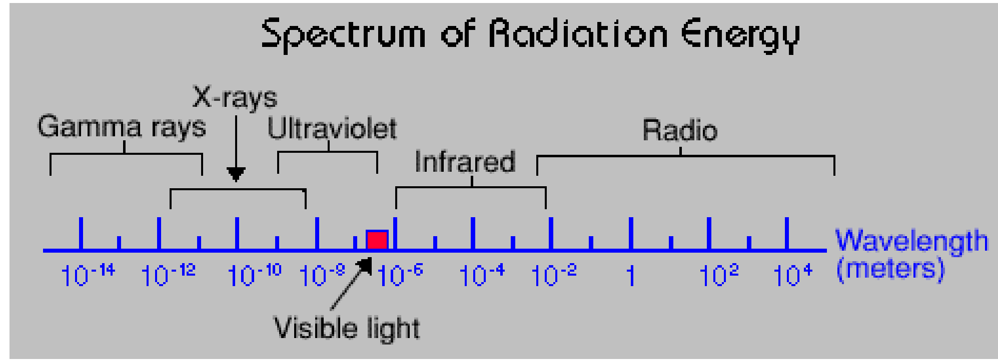
Projection Radiography

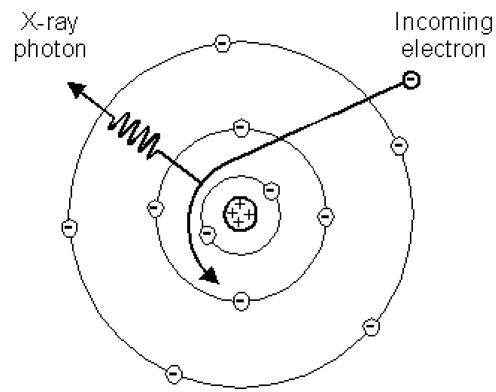
- Radiography is the technique to produce radiographs:
  - photographs made by exposing a photographic film or other image receptor to X-rays.
- X-ray images are based on the **transmission of photons** through the body.
- The image contrast results from the variations of absorption of the X-ray photons by:
  - thickness and
  - material composition.

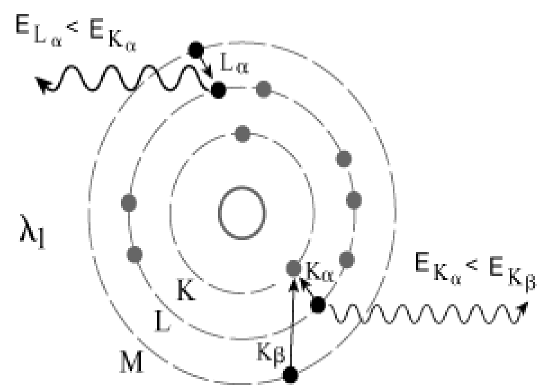


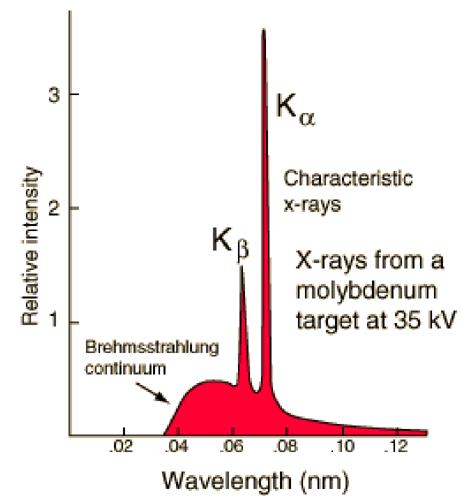
Radiography: Production of X-Rays

- Process based on:
  - Bremsstrahlung radiation.
  - Characteristic X-rays.
- X-ray tubes are the only practical method to produce X-rays for medical applications.
- The X-ray spectrum for the most common tube target material tungsten (W) consists primarily of bremsstrahlung radiation.
  - Continuous spectrum.
  - For high tube potentials the W K-lines contain a small fraction of overall energy.
- The low energy X-rays are filtered:
  - By absorption in the X-ray tube.
  - By adding material for filtration.
  - In order to reduce dose to the patient.
  - As they contribute little to the image.



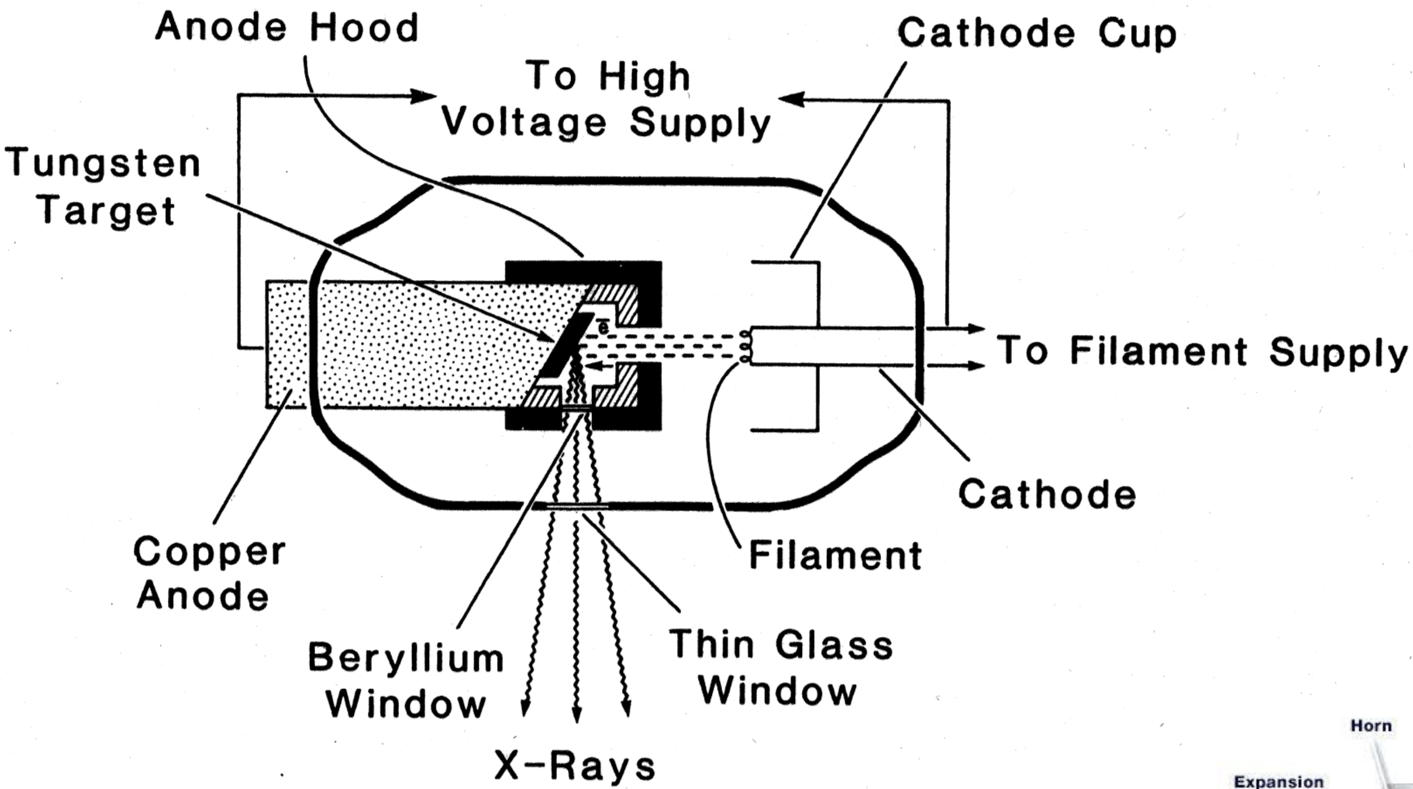






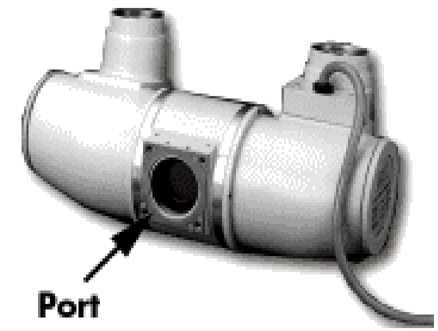
http://hyperphysics.phy-astr.gsu.edu/hbase/quantum/xrayc.html

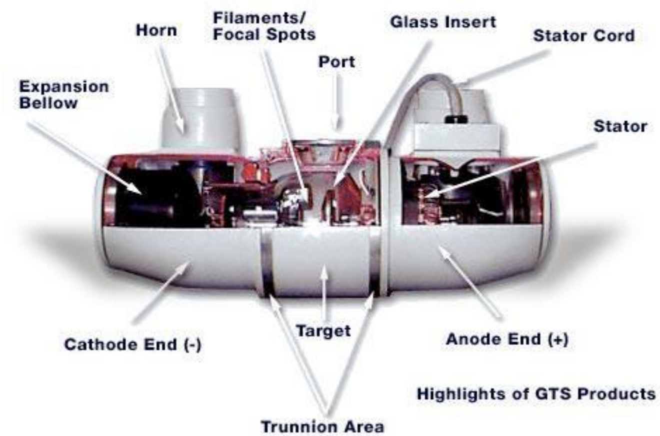
Radiography: X-Ray Tubes



Schematic diagram of a therapy x-ray tube with hooded anode.

Source: Khan (2003)





http://hypertextbook.com/physics/modern/x-ray/

Radiography: Characteristics of X-ray Imaging (1)

Quantum detection efficiency:

- Is the probability of interaction with the detector given by:

$$\eta = 1 - e^{-\mu(E)T}$$

- Can be increased with thicker (T) detectors or with higher Z materials.
- Highest at low energies, decreasing with increasing energy.
- Some materials have an atomic absorption edge ("resonance".)

X-ray Noise:

- Inherent to all radiographies.
- Decreases with increasing exposure (increased dose).

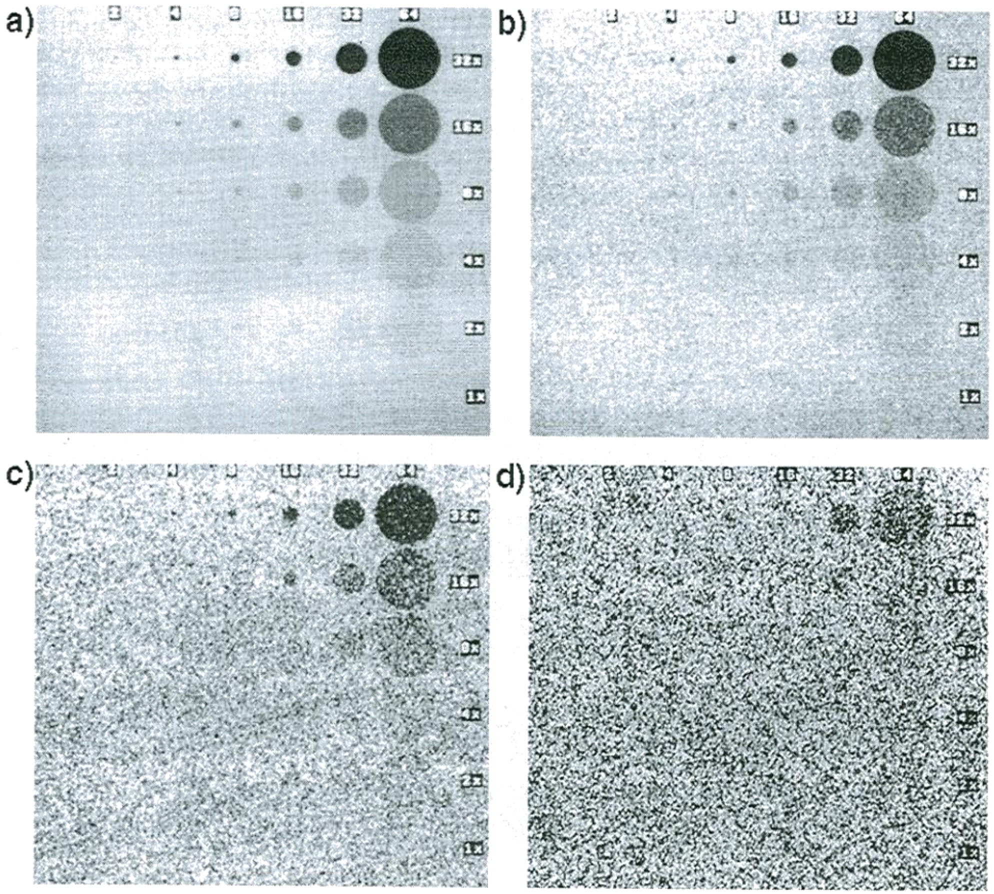
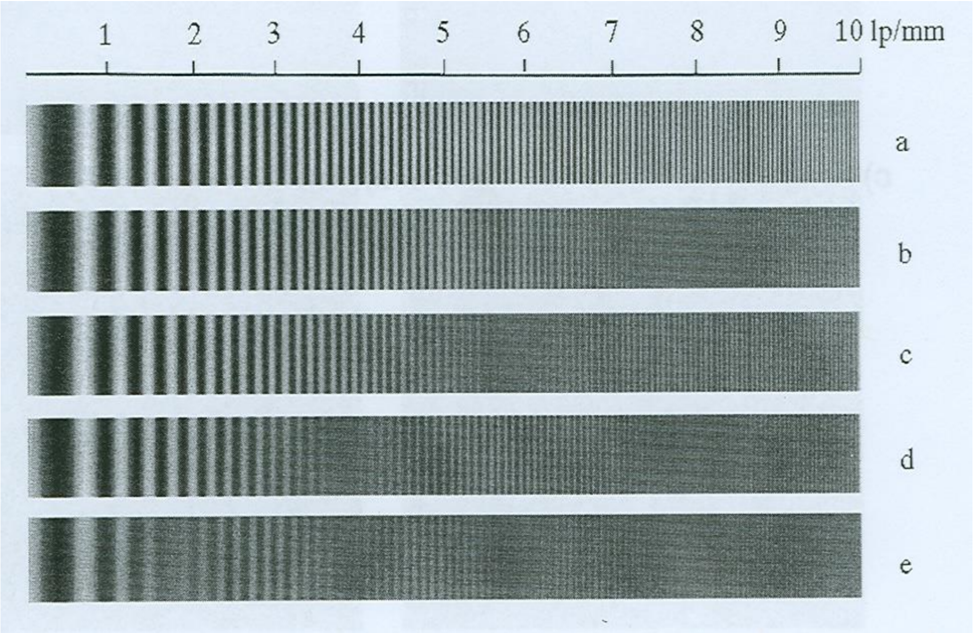
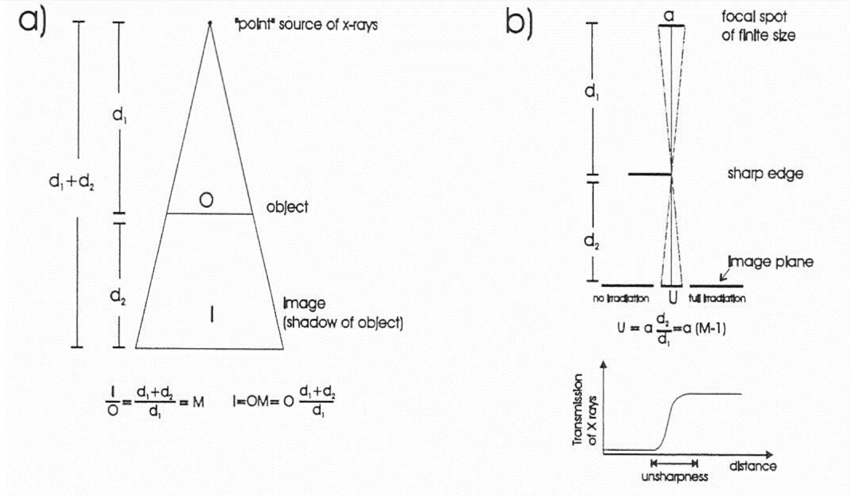


Image obtained with various numbers of X rays per pixel: (a) 1000 X rays/pixel, (b) 100 X rays/pixel, (c) 10 X rays/pixel, and (d) 1 X-ray/pixel. For comparison with X-ray images, fluoroscopic images are taken with ~1μR/frame which corresponds to ~6 photons/pixel/frame and radiographs ~100 μR, which is ~100 photons/frame. (Images courtesy of M.S. Rzeszotarski.)

Radiography: Characteristics of X-ray Imaging (2)

- The **resolution** of an image is the smallest visible interval.
- **Spatial resolution is determined by the characteristics of the detector**:
  - effective aperture size
  - sampling interval
  - lateral signal spreading in detector
- **and by other factors**:
  - effective focal spot size of X-ray source
  - magnification between anatomical structure and plane of detector
  - relative motion between the source, patient and receptor during exposure
- Can, e.g., be measured with a lead bar pattern.





Radiographic magnification: (a) the geometrical increase in object size O, and (b) the focal spot blurring at image plane.

Radiography: Characteristics of X-ray Imaging (3)

Contrast:

- Created by differences in **attenuation** along paths through the body.
- Attenuation due to both **Compton scattering** and **photoelectric effect**.
  - Body tissue has low Z, so Compton is dominant.
  - Mammography uses 10 to 30 keV, and photoelectric effect becomes important.
- Largest contrast materials in human body are bones and air pockets.
- Artificial contrast is generated by ingested or injected materials.
- Contrast can also be varied by changing the X-ray energy, i.e., voltage or filtration.

Tissue attenuation law:

$$N = N_0 \, e^{-\mu(E)x}$$

Image contrast:

$$C = \frac{N_2 - N_1}{N_1}$$

Fluence in adjacent tissue (N_1)

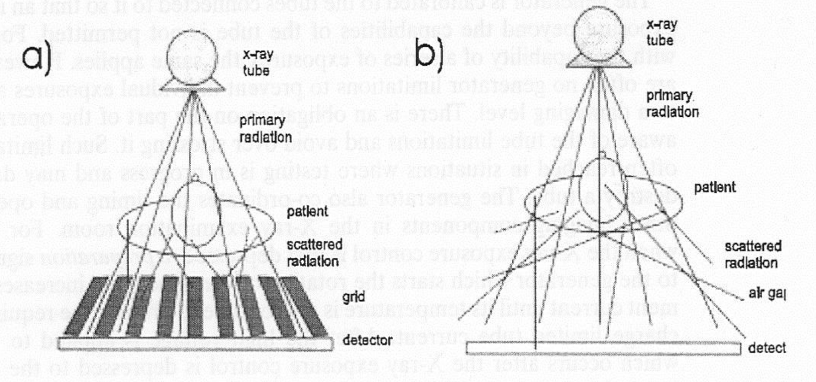
Fluence in tissue of interest (N_2)

Contrast arising from a 1 cm block of tissue compared to a 1 cm block of muscle.

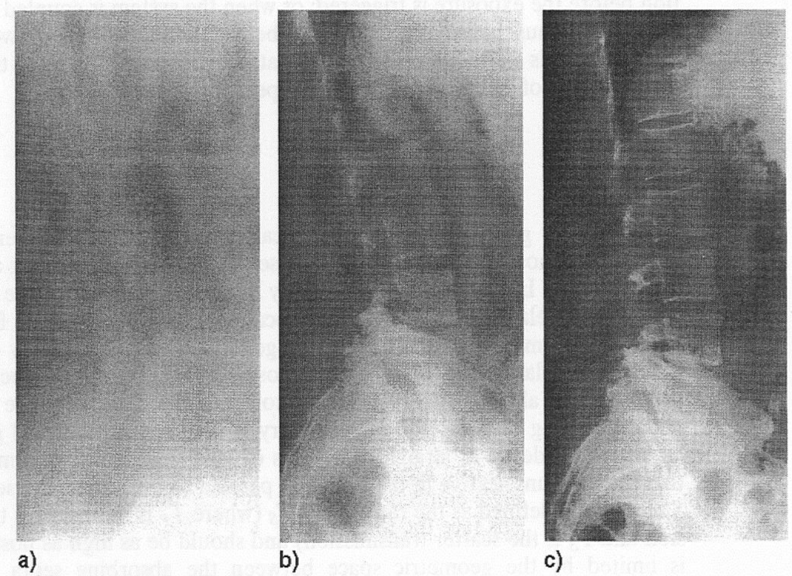
Tissue	μ (cm^{-1})	N/N_0 ($x = 1$ cm)	C wrt muscle (%)
Muscle	0.180	0.835	0
Air	0	1	20
Blood	0.178	0.837	0.2
Bone	0.480	0.619	–26

Radiography: Characteristics of X-ray Imaging (4)

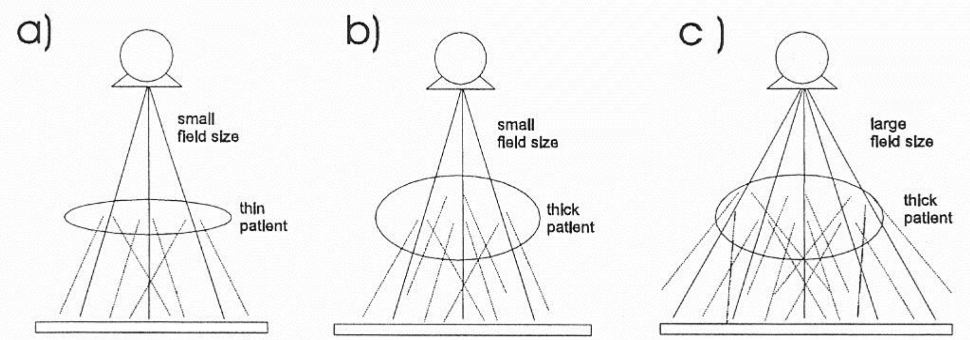
- **Scatter:**
  - The amount of scatter depends on:
    - Thickness of body part,
    - Size of field of vision.
  - Reduction (but not elimination) can be achieved by:
    - Using an anti-scatter grid
    - Reducing the field of view (pencil beam)
    - Increasing the air gap.



Scatter reduction methods: (a) conventional grid, and (b) air gap.



Images of a lateral view of the lower spine obtained by various methods in the presence of scatter and after the removal of scatter: (a) image obtained without any scatter reducing device in place, (b) scatter reduced using a conventional grid, and (c) scatter practically eliminated using an air-spaced scanning grid. (Images courtesy of G.T. Barnes.)

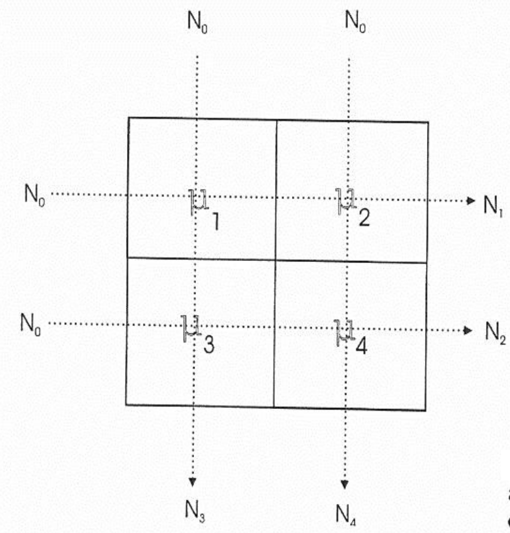


Amount of scatter depending on irradiation conditions: (a) Small field-of-view – small body thickness. Scatter is primarily directed backwards but only the forward scatter is relevant to X-ray imaging. A small body part creates little scatter and a small field-of-view ensures most of that scattered radiation does not reach the detector. (b) Thicker body part with small field-of-view. Scatter radiation still primarily backwards, although forward scatter is increasing. Attenuation combined with attenuation of the primary radiation means the ratio of scatter at the primary is increasing and can be the equivalent of primary or larger. (c) Large field-of-view with a thick body part. There is significant scatter to the primary ratio and it is very difficult to avoid all the scattered radiation impinging on the sensor.

Computed Tomography (CT): Basics (1)

Tomography is based on the measurement of the coefficient of attenuation at every point in the human body rather than a projection.

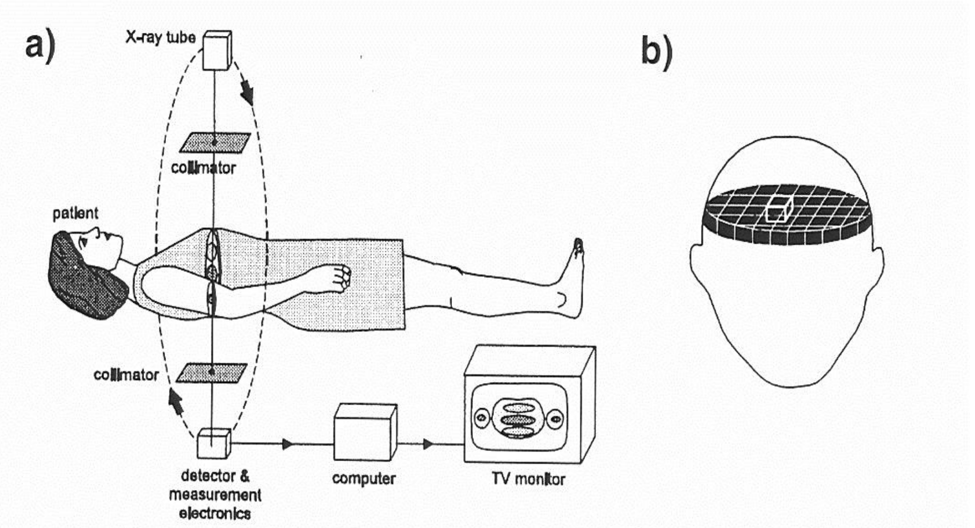
- **CT requires accurate attenuation measurements** along many paths through a slice of the body part to be imaged.
- **Convolution** back-projection methods are used to reconstruct the distribution of attenuation in every pixel (voxel) in which the slice has been divided.



Measure N1, N2, N3 and N4

Solve for μ1, μ2, μ3 and μ4

Measurement and reconstruction attenuation coefficients of a two by two block of tissue.



Concept of tomographic reconstruction. (Reproduced from Reference 12, with permission).

Computed Tomography (CT): Basics (2)

- Pixels obtained by CT scanning are displayed in terms of relative **radiodensity**:
  - The pixel itself is displayed according to the mean attenuation of the tissue(s):
    - On a scale from -1024 to +3071 on the **Hounsfield scale**:

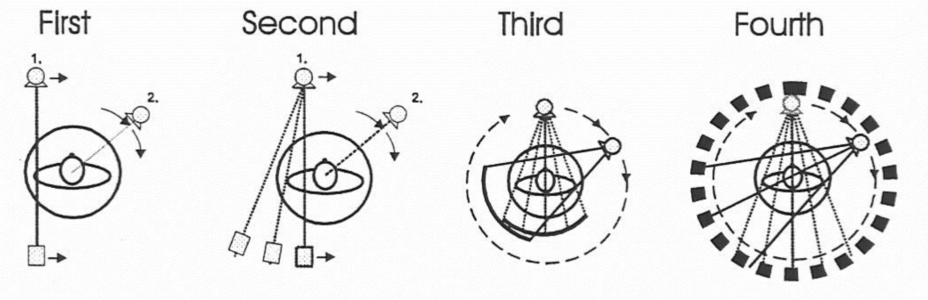
$$\mu_{rel} = 1000 \frac{\mu_{object} - \mu_{water}}{\mu_{water}} \quad \text{in HU}$$

    - Water has an attenuation of 0 Hounsfield units (HU) while air is -1000 HU, cancellous bone is typically +400 HU, cranial bone can reach 2000 HU or more and can cause artifacts.
    - Metallic implants also have very large HU and perturb the reconstruction process.
    - The various radiodensity amplitudes are often mapped to 256 shades of gray.
  - These shades of gray can be distributed over a wide range of HU values to get an overview of structures that attenuate the beam to widely varying degrees.

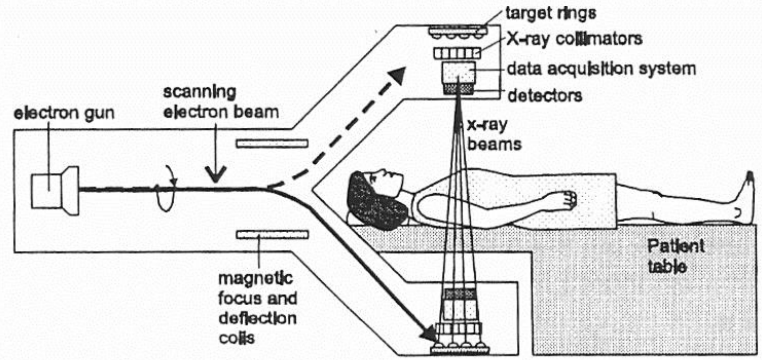
Computed Tomography: Process

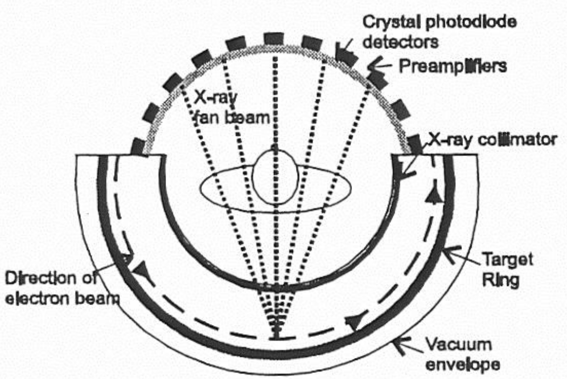
❑ Process:

- X-ray slice data is generated using an X-ray source that rotates around the object.
- X-ray sensors are positioned on the opposite side of the circle from the X-ray source.
- Many data scans are progressively taken as the object is gradually passed through the gantry (rotating beam line).
- They are combined together by the mathematical procedure known as **tomographic reconstruction**.



The CT generation gap.





Cardiac CT scanning concept.

Computed Tomography: Advantages & Applications

Advantages:

- CT completely eliminates the superimposition of images of structures outside the area of interest.
- Due to the inherent high-contrast resolution of CT, differences between tissues that differ in physical density by less than 1% can be distinguished.
- Data from a single CT scan can be viewed as images in the axial, coronal, or sagittal planes.

CT is regarded a moderate to high radiation diagnostic technique.

Applications:

- Although it is still quite expensive, it is the **gold standard** in the diagnosis of a large number of different disease entities.
- Diagnosis of *cerebrovascular accidents* and *intracranial hemorrhage* is the most frequent reason for cranial CT.
- CT is excellent for detecting both acute and chronic changes in the lung parenchyma: pneumonia, cancer, emphysema, fibrosis, pulmonary embolism and aortic dissection.
- CT is a sensitive method for diagnosis of abdominal diseases: Renal/urinary stones, appendicitis, pancreatitis, diverticulitis, abdominal aortic aneurysm, and bowel obstruction.
- CT is often used to image complex fractures, especially ones around joints, because of its ability to reconstruct the area of interest in multiple planes.
- Multi-slice CT (up to 64 slices), high resolution and high speed can be obtained at the same time, allowing excellent imaging of the coronary arteries.

Computed Tomography: Advanced Methods

Basis for 3-dimensional reconstruction:

- Contemporary CT scanners offer isotropic, or near isotropic, resolution.
- Display of images does not need to be restricted to the conventional axial images.
- It is possible for a software program to build a volume by 'stacking' the individual slices.

Multiplanar reconstruction:

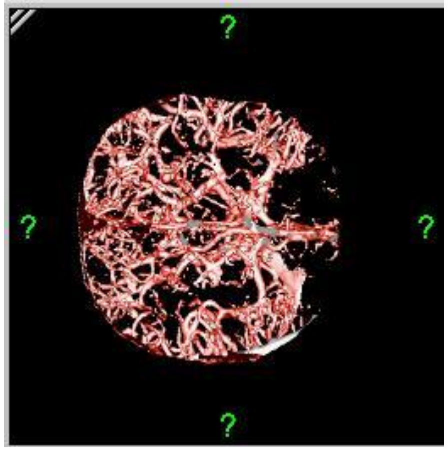
- A volume is built by stacking the axial slices.
- The software then cuts slices through the volume in a different plane (usually orthogonal).

3D rendering techniques:

- *Surface rendering*:
  - A threshold value of radiodensity is chosen by the operator (e.g. a level that corresponds to bone).
  - A threshold level is set, using edge detection image processing algorithms.
- *Volume rendering*:
  - Surface rendering is limited in that it will only display surfaces which meet a threshold density, and only the surface that is closest to the imaginary viewer.
  - In volume rendering transparency and colors are used to allow a better representation of the volume.

Normal CT scan of the head; this slice shows the cerebellum, a small portion of each temporal lobe, the orbits, and the sinuses.

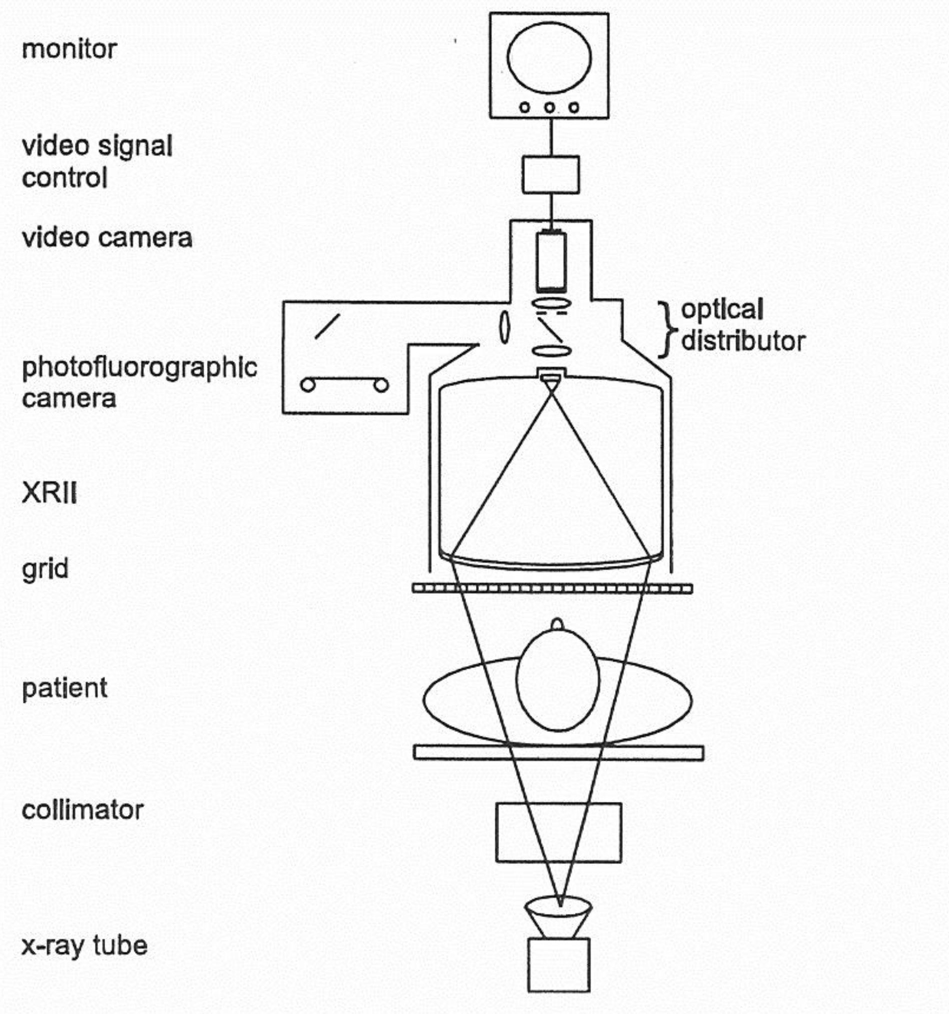
A volume rendering of the skull clearly shows the high density bones.



After using a segmentation tool to remove the bone, the previously concealed vessels can now be demonstrated.

Fluoroscopy (1)

- **Fluoroscopy** provides real-time images of the internal structures of a patient through the use of a fluoroscope.
- A fluoroscope consists of:
  - An X-ray source, and
  - a fluorescent screen between which a patient is placed.
- Modern fluoroscopes couple the screen to:
  - An X-ray image intensifier (**XRII camera**) and
  - A CCD video camera allowing the images to be played and recorded on a monitor.
- Radiation doses to the patient depend greatly on the size of the patient as well as length of the procedure:
  - Typical skin dose rates 20-50 mGy/min.
  - Exposure times vary with procedure being performed (up to 75 minutes).
  - Radiation stochastic effects (cancer risk) and also deterministic effects (burns) are possible.

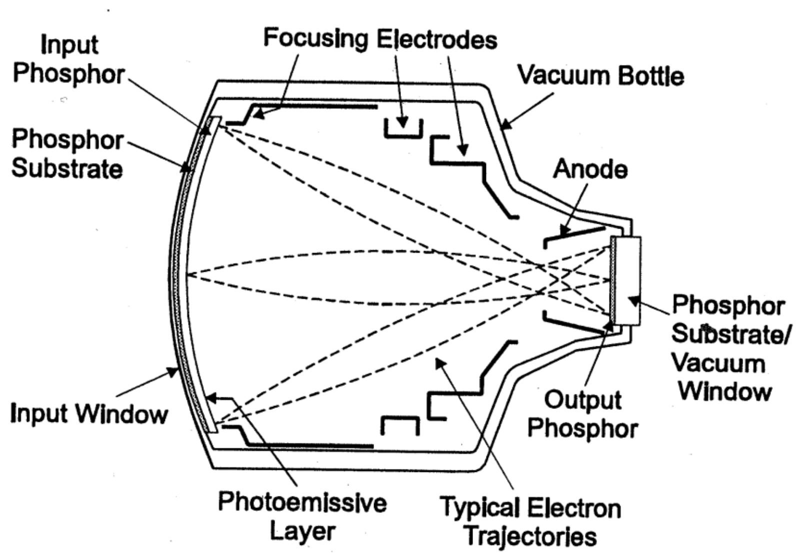


Overview of fluoroscopic/fluorographic clinical imaging chain.

Fluoroscopy (2)

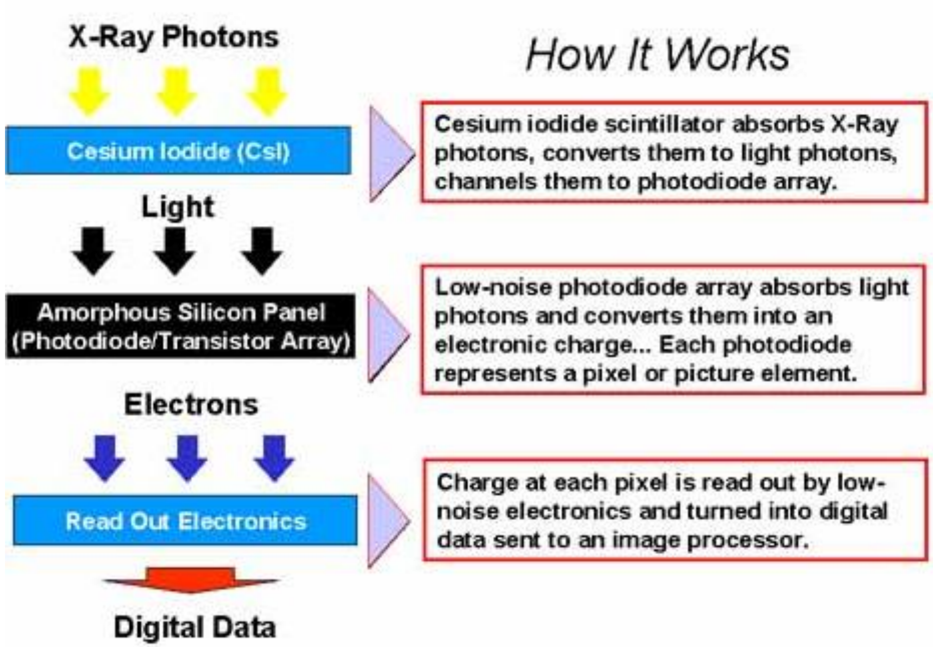
❑ X-ray Image intensifier (XRII):

- Uses CsI phosphor directly on the photocathode of the intensifier tube.
- The output image is approximately 10^5 times brighter than the input image.
- This level of gain is sufficient that quantum noise, due to the limited number of X-ray photons, is a significant factor limiting image quality.



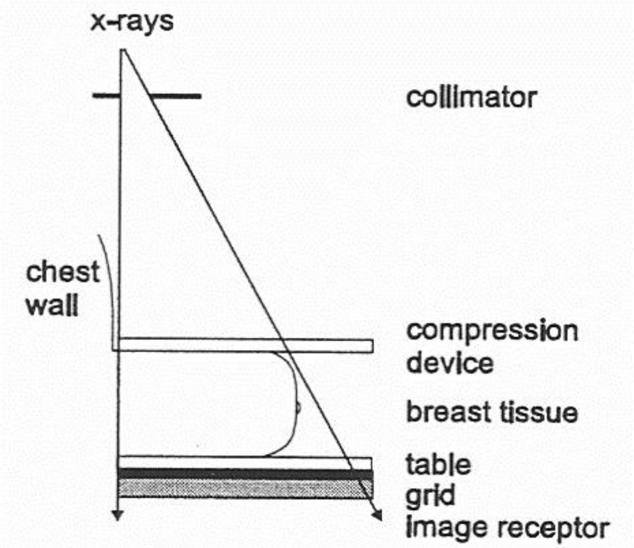
❑ Flat-panel detectors can replace the XRII:

- Consists of a two-dimensional array of amorphous silicon photodiodes and thin-film transistors (TFTs)
- Increased sensitivity to X-rays, potential to reduce patient radiation dose.
- Reduce motion blurring (fast response) and improve contrast ratio.
- Spatial resolution is approximately equal.
- More expensive.



Mammography (1)

- A type of projection X-ray imaging technique to examine the human breast.
- Visualizes soft tissue contrast.
  - Very low energy X-rays (15 keV to 35 keV).
  - Photoelectric effect is used for the contrast.
  - Uses longer wavelength X-rays (typically MoK level rays).
- Geometry uses half of the X-ray field.
  - The central ray grazes the chest wall.
  - This avoids missing breast tissue.
- Low dose procedure: usually around 0.7 mSv.

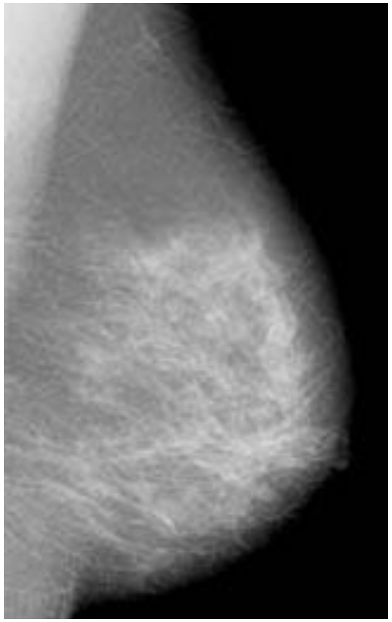


Geometrical arrangement in mammography.

http://www.cancer.gov/cancertopics/pdq/screening/breast/

Mammography (2)

- **Originally non-screen film was used:**
  - excellent images,
  - but high doses: therefore no longer applied.
- **Xeromammography:**
  - Similar to photocopying technique.
  - Substantially reduces the dose.
- **Film screen:**
  - Lower dose, but poor dynamic range.
  - Therefore the breast must be compressed to equalize the X-ray path length to the point that the whole breast can be visualized.
- **Full field digital mammography (FFDM):**
  - Amorphous Selenium detector.
  - Active matrix systems with 50 μm pixels.
  - Excellent resolution and processing of digital images.

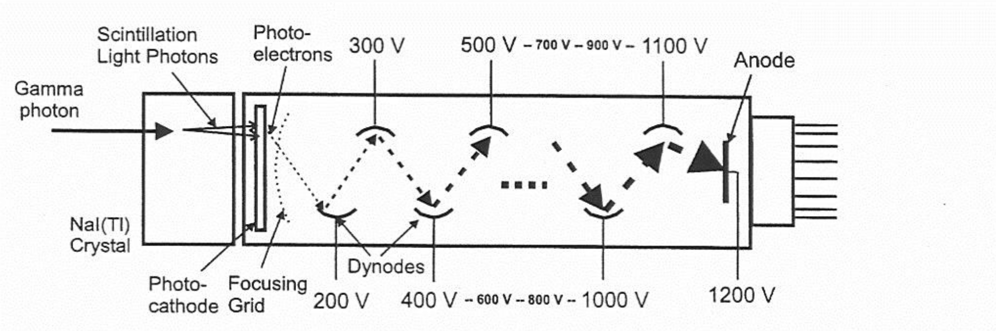


http://www.mayoclinic.org/breastimagingservices-jax/

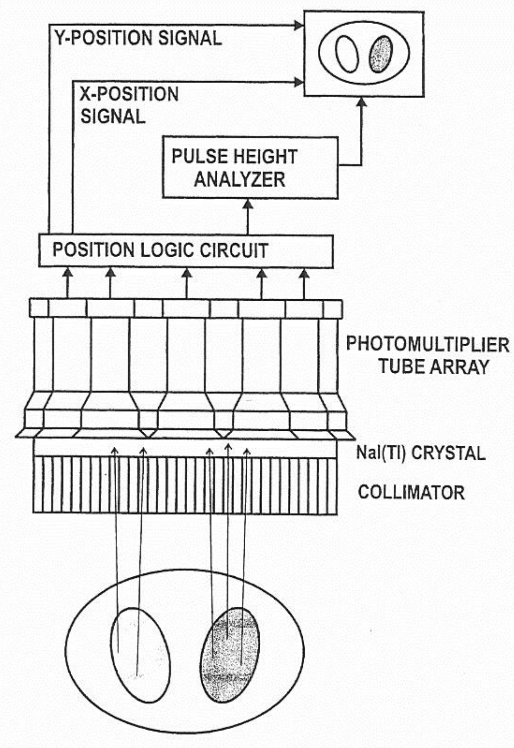
http://www.portermedical.org/

Gamma Camera (Scintigraphy) (1)

- A **gamma camera** produces images of the distribution of γ-ray emitting radionuclides.
- It consists of:
  - One or more detectors mounted on a gantry.
  - Connected to an acquisition system for operating the camera and for storing the images.
- The system accumulates counts of γ-photons:
  - Absorbed by a large flat NaI crystal in the camera,
  - Tl doping and in a light-sealed housing.
- **A photomultiplier increases the gain of a low γ-photon counting.**



Schematic diagram of a typical scintillation detector that consists of a NaI(Tl) scintillator and a photomultiplier tube (PMT).

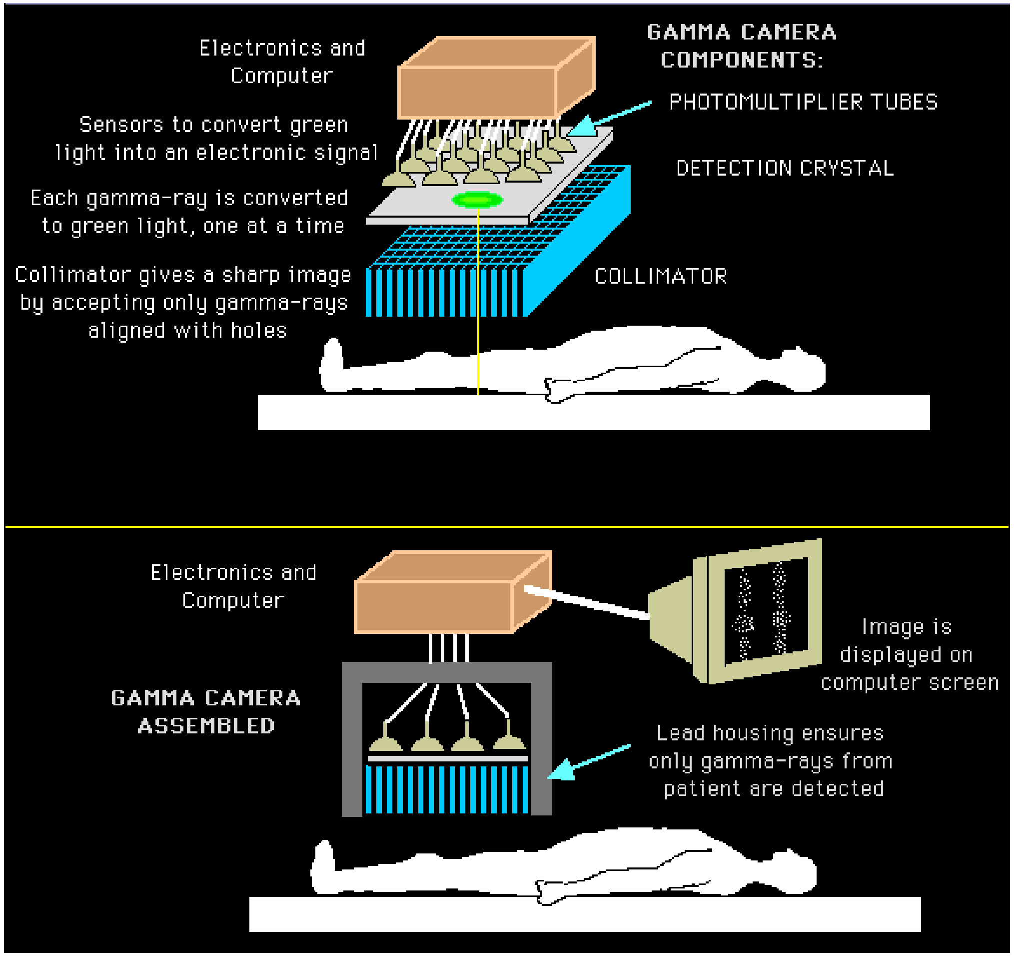


Schematic diagram of the components of a typical conventional scintillation camera system. [From: B.M.W. Tsui, *Physics of SPECT. Radio-Graphics* **16(1)**,173–183 (1996)]

Gamma Camera (Scintigraphy) (2)

- The crystal **scintillates** in response to incident gamma radiation:
  - A gamma photon interacts with an electron from an iodine atom in the crystal (photoelectric effect and Compton effect.)
  - A faint flash of light is produced when the electron finds again a minimal energy state.
  - Photomultiplier tubes (PMT) behind the crystal detect the fluorescent flashes and a computer sums the fluorescent counts.
  - The image then reflects the distribution and relative concentration of radioactive tracer elements present in the organs and tissues imaged.
- The best current camera systems have a resolution of 1.8cm at 5cm away from the camera face.
- SPECT cardiac imaging is performed using gamma cameras, slowly rotated around the patient's torso.

Schematic diagram of the operation of a gamma camera



http://www.med.harvard.edu/JPNM/physics/didactics/basics.html

Radiopharmaceuticals

- What is a Radiopharmaceutical?
  - A radioactive compound used for diagnosis and therapeutic treatment of human diseases.
  - 95% of radiopharmaceuticals are used for diagnostics, the rest for therapeutic treatment.

www.radpharm.com.au

- A radiopharmaceutical is **NOT** a radiochemical.
  - A radiochemical **is not suited** for administration to humans.

Radiolabel	*Ligand*	*Application*
$^{99m}TcO_4 \cdot Na$	Sodium pertechnate	Thyroid function
^{99m}Tc-HAS	Human serum albumine	Blood pool, cardiac function
^{99m}Tc-HAS	Human serum albumine (microspheres)	Regional perfusion, vascular patency
^{99m}Tc-MIBI	2-methoxy-isobutylisonitril	Myocard function
^{99m}Tc-HMPAO	hexamethyl-propylenaminoxim	Cerebral perfusion
^{99m}Tc-HEDP	hydroxyl-ethylene-diphosphonate	Bone metabolism / formation
^{99m}Tc-MDP	methylene-diphosphonate	Bone metabolism / formation
^{99m}Tc-DTPA	diethylene-triamine-tetraacetate	Kidney function, lung function

Radiopharmaceuticals: Characteristics

- Characteristics:
  - Minimal pharmacological effect (used in tracer quantities).
  - Sterile, pyrogen free.
  - Fabrication and application follow quality control measures.

- Types:
  - Radioactive Element ^{133}Xe.
  - Radioactive molecule $H_2{}^{15}O$.
  - Labeled compound ^{131}I-iodinated proteins, ^{99m}Tc-labeled compounds.

Radiopharmaceuticals: Selection

- Components:
  - Radionuclide
  - Pharmaceutical
- The pharmaceutical is selected on the basis of:
  - Preferential localization in a given organ.
  - Participation in the physiological function of the organ.
  - It **must** be non-toxic for humans.
- The radionuclide is selected and tagged to the pharmaceutical.
  - The radioactivity emitted can be easily detected by a radiation detector in the target organ.
  - The radiation dose to the patient should be minimal.

Wish List for the Ideal Radiopharmaceutical

- **Easy availability:**
  - Easily produced.
  - Inexpensive.
  - Readily available in any nuclear medicine facility.

- **Short effective half-life:**
  - The radionuclide decays with a half-life T_p.
  - The radiopharmaceutical is excreted from the organism following an exponential law and with a biological half-life T_b.
  - The effective half-life T_e should be **no longer** than the time necessary to complete the study.

Biological Half-life:

$$T_b = \ln 2 / \lambda_b$$

Physical Half-life:

$$T_p = \ln 2 / \lambda_p$$

Effective Decay Constant:

$$\lambda_e = \lambda_p + \lambda_b$$

Effective Half-life:

$$\frac{1}{T_e} = \frac{1}{T_p} + \frac{1}{T_b} \rightarrow T_e = \frac{T_p T_b}{T_p + T_b}$$

ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE

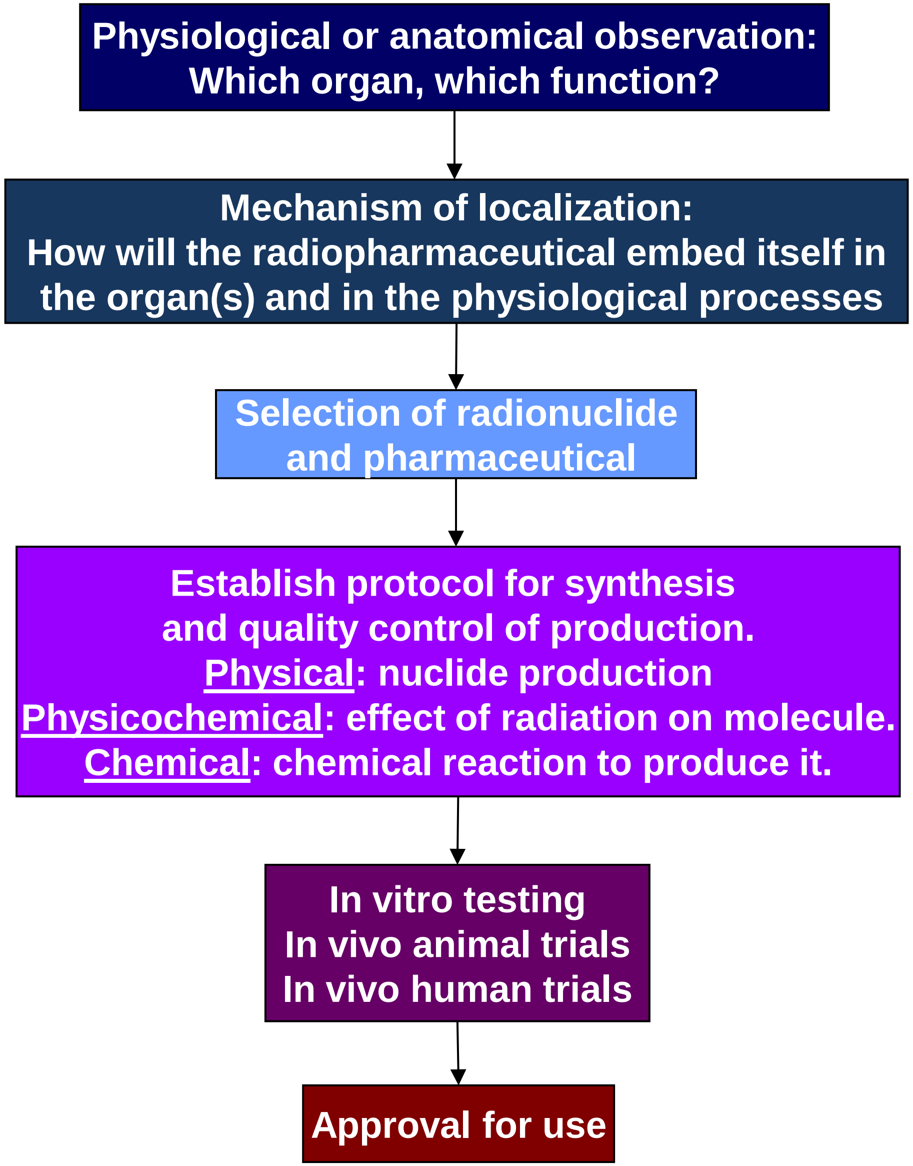
Radiopharmaceuticals: Ideal Characteristics

- **Particle emission:**
  - Alpha-decaying radionuclides should **not** be used for radiodiagnostics. The dose is too large.
  - Beta-decaying radionuclides should not be used, but ^{131}I-iodinated compounds are often used for clinical studies.
  - (Alpha- and beta-emitters are useful for therapy!)
- **Decay by e^--capture or isomeric transition (γ-emitters) without any internal conversion:**
  - γ-photons should be between 30 and 300keV.
    - Below 30 keV, photons are absorbed by tissue.
    - Above 300keV effective collimators are not readily available.
  - Best source: **high flux of monochromatic γ-photons of 150 keV.**
- **High target-to-nontarget activity ratio:**
  - The radiopharmaceutical should be located as much as possible in the target organ.
  - Activities from other locations should be minimum (may obscure picture).
- **The ideal radiopharmaceutical should have all the characteristics presented to provide:**
  - Maximum efficacy in diagnosis.
  - Minimum radiation dose to the patient.

Difficult to fulfill all criteria: choose the best of many compromises!

Design of New Radiopharmaceuticals

- The design of a new radiopharmaceutical must account for the **mechanism of localization** in the structure or organ of interest.
- Based on its physicochemical properties, a protocol must be established for its production and maximum efficacy.
- The clinical efficacy must be evaluated by testing first in animals and then in humans.

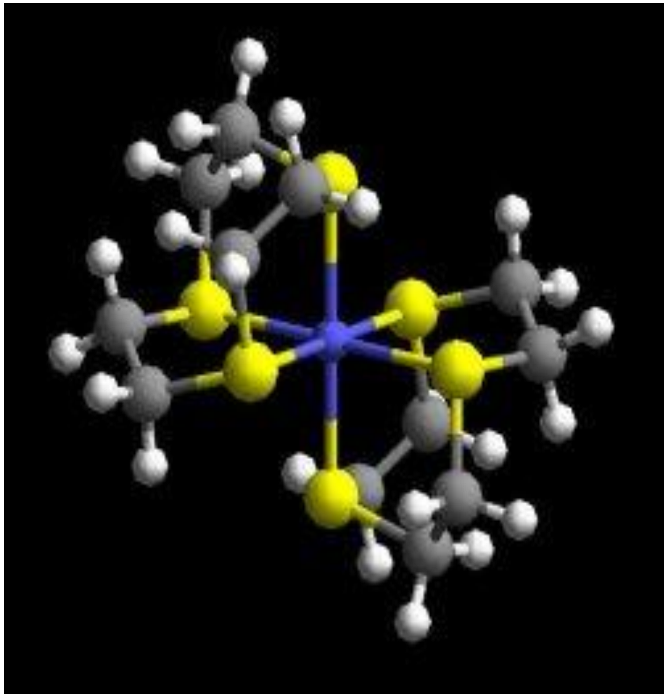


Radiopharmaceuticals: Localization Mechanisms

- **Passive diffusion:** ^{99m}Tc-DTPA in brain imaging, ^{99m}Tc-DTPA in ventilation imaging.
- **Ion exchange:** uptake of ^{99m}Tc-phosphonate complexes in bone.
- **Capillary blockage:** ^{99m}Tc-macroaggregated albumin particles trapped in lung capillaries.
- **Phagocytosis:** removal of ^{99m}Tc-sulfur colloid particles in liver, spleen, bone marrow.
- **Active transport:** ^{131}I uptake in the thyroid, ^{201}Tl uptake in myocardium.
- **Cell sequestration:** sequestration of heat damaged ^{99m}Tc labeled red blood cells by the spleen.
- **Metabolism:** ^{18}F-FDG uptake in myocardial and brain tissues.
- **Receptor binding:** ^{11}C-dopamine binding to the dopamine receptors in the brain.
- **Compartmental localization:** ^{99m}Tc-labeled red blood cells.
- **Antigen-antibody complex formation:** ^{131}I-, ^{111}In- and ^{99m}Tc-labeled antibodies to localize tumors.
- **Chemotaxis:** ^{111}In-labeled leukocytes to localize infections.

Radiopharmaceuticals: Radiolabeling Methods

- Radiolabeling replaces atoms or groups of atoms of a molecule by similar or different radioactive atoms or groups of atoms.
- There are six major methods of labeling:

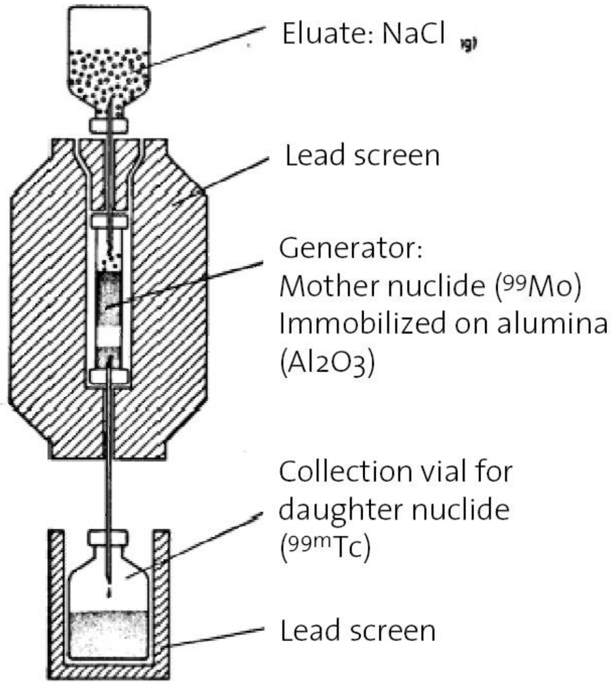


http://lcbcpc21.epfl.ch

Isotope exchange	^{125}I-labeled T3 and T4 ^{14}C, ^{35}S- and ^{3}H-labeled compounds
Introduction of a foreign label	All ^{99m}Tc-radiopharmaceuticals ^{125}I-labeled proteins ^{135}I-labeled hormones ^{111}In-labeled cells ^{18}F-fluorodeoxyglucose
Labeling with bi-functional chelating agent	^{99m}Tc-DTPA-antibody ^{111}In-DTPA-albumin
Biosynthesis	^{75}Se-selenomethionine ^{57}Co-cyanocobalamina ^{14}C-labeled compounds
Recoil labeling	^{3}H-labeled compounds Iodinated compounds
Excitation labeling	^{123}I-labeled compounds (from ^{123}Xe decay) ^{77}Br-labeled compounds (from ^{77}Kr decay)

Radiopharmaceuticals: Production Methods

Example : $^{99}_{42}Mo/^{99m}_{43}Tc$ generator



Radio-Isotopes for Nuclear Imaging

Radioisotope	Energy (keV)	Half-life	Production
^{67}Ga	93, 185. 300	3.3 days	cyclotron
^{99m}Tc	140	6h	generator
^{111}In	173, 247	67h	cyclotron
^{123}I	160	13h	cyclotron
^{133}Xe	81	5.2d	reactor
^{201}Tl	60, 83	73h	cyclotron

Radiopharmaceuticals: Application Examples (1)

- Radiolabeled Leukocytes and Platelets:
  - Separation of Leukocytes (sedimentation) and Platelets (centrifugation).
  - Use of ^{111}In-oxine (lipophilic, can cross cell membrane)
  - Cells damaged by process and radiation from ^{111}In: chromosome aberrations.
- Radiolabeled Monoclonal Antibodies:
  - Antibodies are immunoglobulins (Ig) produced by differentiation of B lymphocytes.
  - Monoclonal antibodies are homogeneous and highly specific for an antigen.
  - Nuclides used: ^{131}I, ^{123}I, ^{125}I, ^{111}In, ^{90}Y, and **^{99m}Tc**.

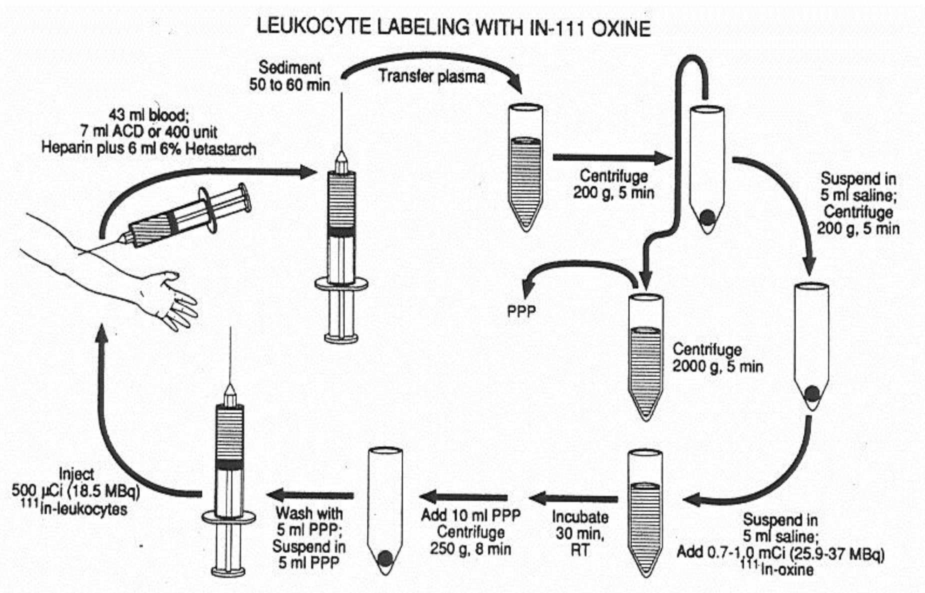


FIGURE 7.4. Method of ^{111}In-labeling of leukocytes (WBCs).

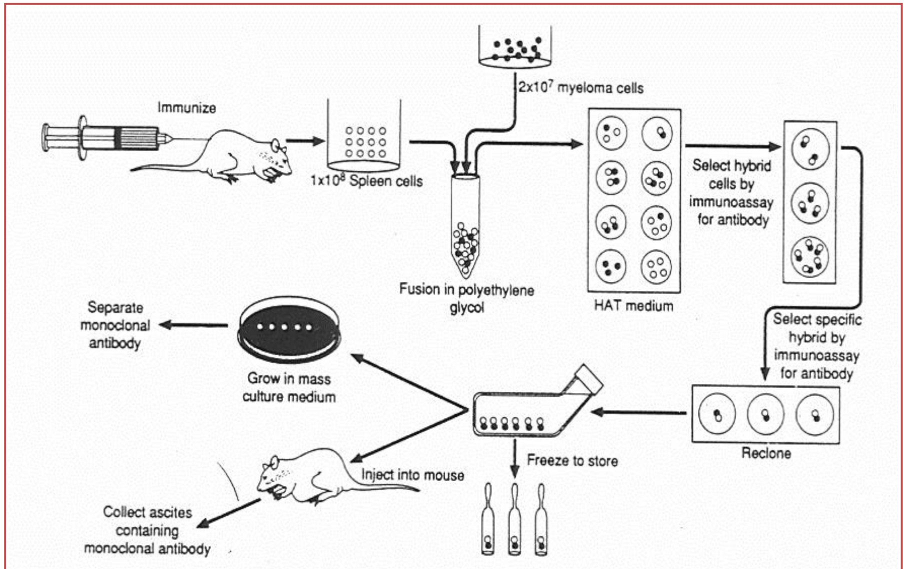
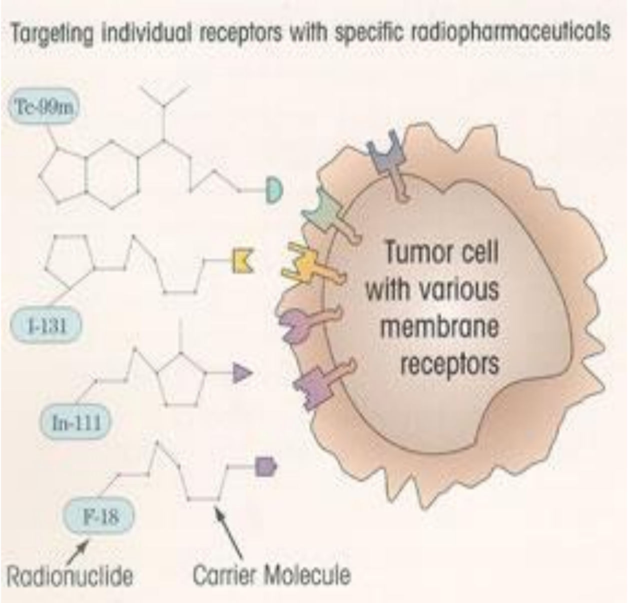


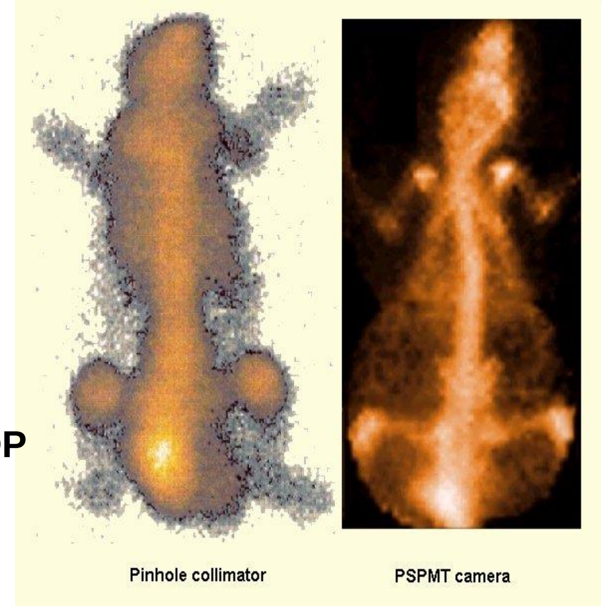
FIGURE 7.7. A basic scheme for the production of hybrid cells that are used to make monoclonal antibodies.

Radiopharmaceuticals: Application Examples (2)

- Radiolabeled Peptides:
  - Smaller molecular size than proteins (antibodies).
  - Better tumor uptake and plasma clearance.
  - ^{111}In labeling preferred. ^{99m}Tc damages small molecules, alters structure and binding sites.
  - Used in detection of:
    - primary and metastatic tumors,
    - acute deep vein thrombosis,
    - inflammation and infection sites.



http://doemedicalsciences.org/pubs/

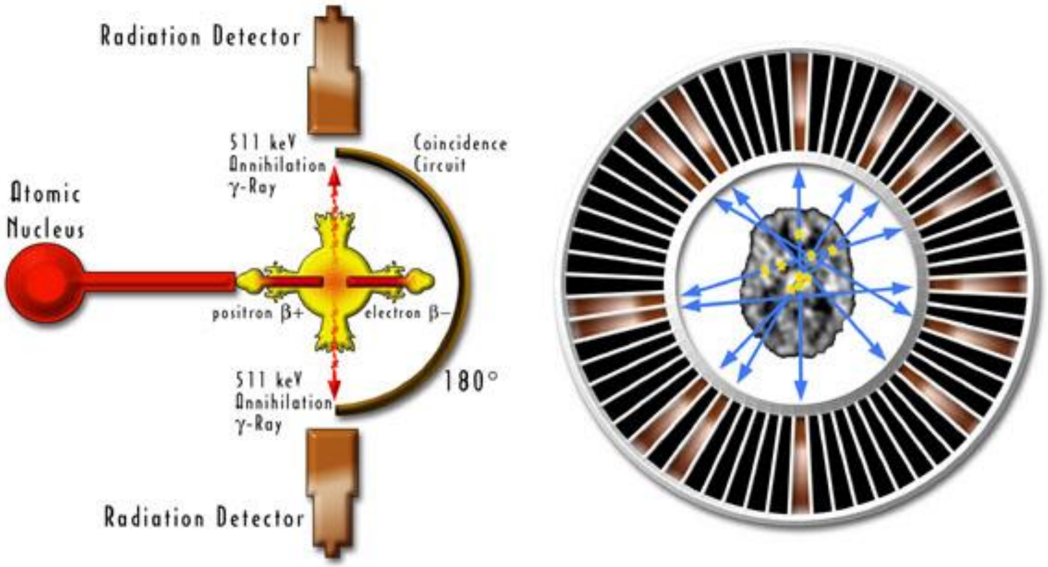


Comparative planar bone images of a normal mouse injected with ^{99m}Tc-MDP

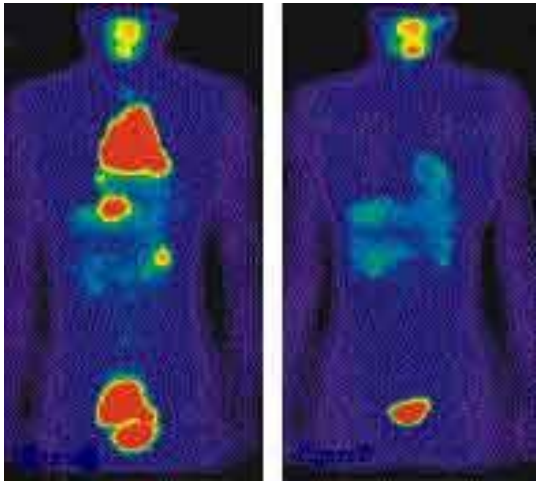
http://www.biosim.ntua.gr/NIMgroup/

Positron Emission Tomography (PET) (1)

- **Positron emission tomography (PET)** produces a 3D-image of **functional processes** in the body.
- PET scan procedure:
  - Injection of a short-lived radiopharmaceutical, most commonly fluorodeoxyglucose (FDG), which decays by emitting a positron (usually into blood circulation).
  - Waiting period while the metabolically active molecule (typically 1h) becomes concentrated in tissues of interest.
  - The subject is placed in the imaging scanner.



http://mni.mcgill.ca/cog/paus/techniques.htm

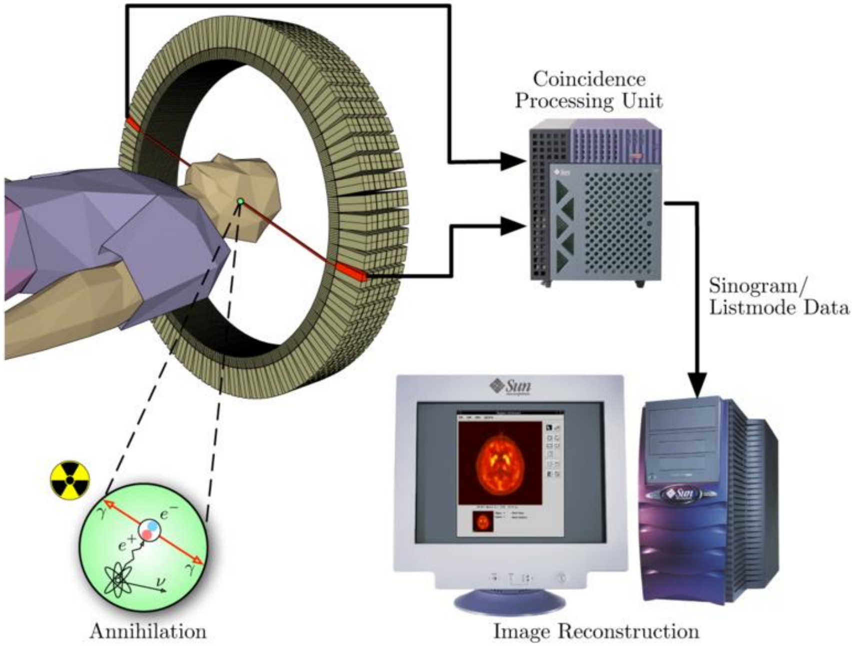


Instead of detecting changes in the physical size or structure of internal organs, as other imaging technologies do, the PET scan assesses and measures changes in cellular function. The figure on the left shows cancer diagnosed by a PET scan while the figure on the right shows successful results of treatment initiated due to the PET scan diagnosis.

http://www.radiologyregional.com/pet.html

Positron Emission Tomography (PET) (2)

- The most significant fraction of electron-positron decays result in two 511 keV gamma photons being emitted at almost 180 degrees to each other.
- It is possible to localize their source along a straight line of coincidence (also called formally the "line of response" or LOR).
- If the recovery time of detectors is in the ps range rather than the 10's of ns range, it is possible to calculate the single point on the LOR at which an annihilation event originated, by measuring the "time of flight" of the two photons.



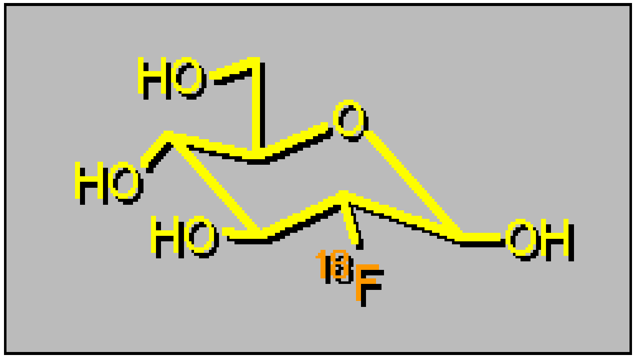
- A technique very like the reconstruction of CT and SPECT data is used.
  - The data set collected in PET is much poorer than CT and reconstruction techniques are more difficult.
  - Use statistics collected from tens-of-thousands of coincidence events.
  - A set of simultaneous equations for the total activity of each parcel of tissue along many LORs can be solved.
  - A map of radioactivities as a function of location for parcels or bits of tissue ("voxels"), may be constructed and plotted.
- The resulting map shows the tissues in which the molecular probe has become concentrated, and can be interpreted by a physician or radiologist in the context of the patient's diagnosis and treatment plan.

Positron Emission Tomography (PET) (3)

- PET is both a medical and a research tool applied in:
  - Clinical oncology (medical imaging of tumors and the search for metastases),
  - Clinical diagnosis of brain diseases such as dementia.
  - An important research tool to map human brain and heart function.
- PET scanners, like SPECT scanners are capable of detecting areas of molecular biology in detail (even prior to anatomic change).
- Radionuclides used in PET scanning:
  - Isotopes with short half-lives such as ^{11}C (~20 min), ^{13}N (~10 min), ^{15}O (~2 min), ^{18}F (~110 min).
  - The radionuclides must be produced in a cyclotron which is not too far away in delivery-time to the PET scanner.
- Cyclotrons have high costs.
  - Few hospitals and universities are capable of maintaining such systems.
  - Most clinical PET is supported by third-party suppliers of radio-tracers which can supply many sites simultaneously. Clinical PET primarily uses radiopharmaceuticals labeled with ^{18}F (cyclotron) or ^{82}Rb (created in a portable generator and used for myocardial perfusion studies).

Some PET Radiopharmaceuticals

FDG structure:



- ^{18}F-Sodium Fluoride:
  - Irradiation of ^{18}O-water with protons in a local cyclotron.
  - Bone scintigraphy.
- ^{18}F-Fluorodeoxyglucose ($C_6H_{11}FO_5$, FDG):
  - Used primarily for the study of metabolism in the brain and heart.
- ^{18}F-Fluorothymidine (FLT):
  - Thymidine is incorporated into DNA.
  - Measures cell proliferation. Used in in vivo tumor diagnosis and characterization in humans.
- ^{15}O-water:
  - Produced in cyclotron from $^{15}N(p,n)^{15}O$.
  - Used for cerebral and myocardial perfusion studies.
- ^{11}C-Raclopride (synthetic compound, $C_{15}H_{20}Cl_2N_2O_3$):
  - Used to detect various neurological and psychiatric disorders, such as Parkinson's and schizophrenia.

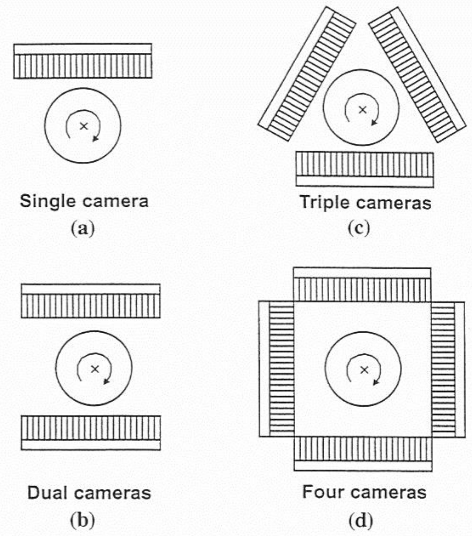
Properties of PET Positron Emitters

Properties of positron emitters used in PET.

Positron Emitters	Half Life (min)	Maximum Positron Kinetic Energy (MeV)	Positron Range (mm)	Production Reaction	Means of Production
C-11	20.3	0.97	2.06	$^{14}N(p, \alpha)^{11}C$	Cyclotron
N-13	9.96	1.19	3	$^{16}O(p, \alpha)^{13}N$ $^{13}C(p, n)^{13}N$	Cyclotron
O-15	2.07	1.7	4.5	$^{14}N(d, n)^{15}O$ $^{15}N(p, n)^{15}O$ $^{16}O(p, pn)^{15}O$	Cyclotron
F-18	109.8	0.635	1.4	$^{18}O(p, n)^{18}F$ $^{20}Ne(d, \alpha)^{18}F$	Cyclotron
Rb-82	1.27	3.15	13.8	$^{82}Sr \rightarrow {}^{82}Rb$	Generator
Ga-68	68.3	1.88	5.4	$^{68}Ge \rightarrow {}^{68}Ga$	Generator

Single Photon Emission Computed Tomography

- **SPECT** is a nuclear medicine tomographic imaging technique using gamma rays.
  - Similar to conventional nuclear medicine planar imaging using a gamma camera.
  - It is able to provide true 3D information as cross-sectional slices through the patient.
- A gamma camera acquires multiple 2-D images (also called projections), from multiple angles.
  - The gamma camera is rotated around the patient (360 deg.)
  - Projections are acquired at defined points during the rotation, typically every 3-6 degrees
  - The time taken to obtain each projection is also variable, but 15 – 20 seconds is typical. This gives a total scan time of 15-20 minutes.
- A computer is used to apply a tomographic reconstruction algorithm to the multiple projections, yielding a 3-D dataset.
- Same radiopharmaceuticals as for γ-camera may be used.
  - Possible to reconfigure the camera for SPECT image acquisition while the patient remains on the table.
- Multi-headed gamma cameras can provide accelerated acquisition.



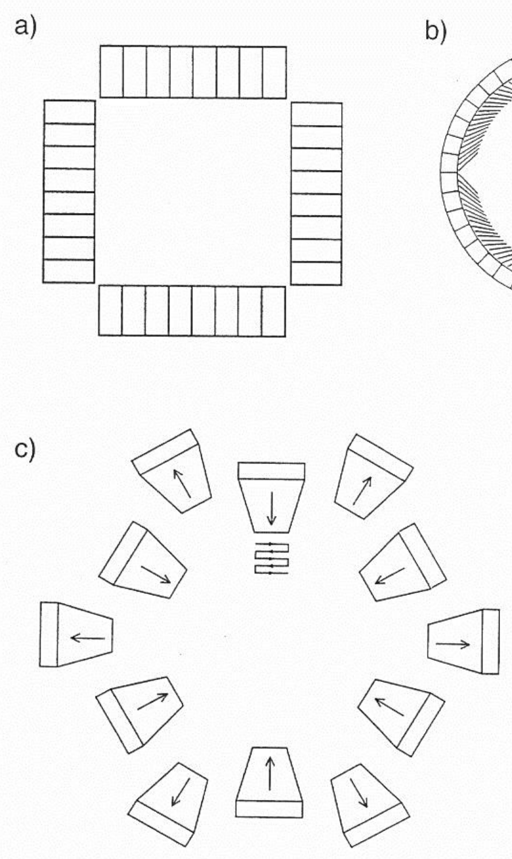
Schematic diagrams show typical configurations of commercial SPECT imaging systems that are based on single or multiple rotating scintillation cameras. The increased number of scintillation cameras around the patient results in increased detection efficiency or improved spatial resolution. [*From: Tsui, BMW, Physics of SPECT. RadioGraphics* **16(1)**,173–183, 1996]

http://www.schmerzklinik.de/html/cluster-ks-schule.html

SPECT: Images

- Reconstructed images typically have resolutions of 64x64 or 128x128 pixels (36 mm).
- Reconstructed images have lower resolution and increased noise than planar images, and are susceptible to artifacts:
  - Patient movement.
  - Uneven distribution of radiopharmaceutical
  - Attenuation of the gamma rays within the patient can lead to significant underestimation of activity in deep tissues, compared to superficial tissues.

- Modern SPECT equipment is available with an integrated X-ray CT scanner:
  - X-ray CT images are an attenuation map of the tissues.
  - This data can be incorporated into the SPECT reconstruction to correct for attenuation.
  - Precisely registered CT image which can provide additional anatomical information.

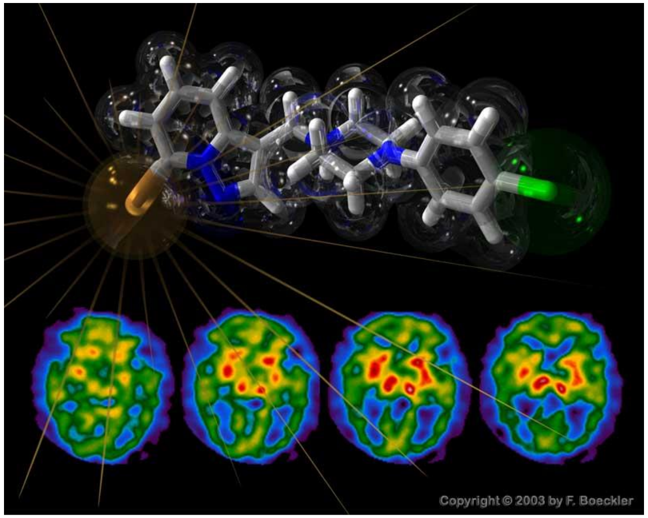


Examples of multi-detector based SPECT systems. (a) The MARK IV system consists of four arrays of eight individual NaI(Tl) detectors arranged in a square configuration. (b) The Headtome-II system consists of a circular ring of detectors. A set of collimator vanes that swings in front of the discrete detector is used to collect projection data from different views. (c) A unique Cleon brain SPECT system consists of 12 detectors that scan both radially and tangentially. [*From: Tsui BMW. SPECT (Single-Photon Emission Computed Tomography). (In) Biomedical Engineering Handbook, J. Bronzino, Ed., (CRC Press, Inc., Boca Raton, FL), pp. 1055–1076, 1995*]

SPECT: Common Protocols

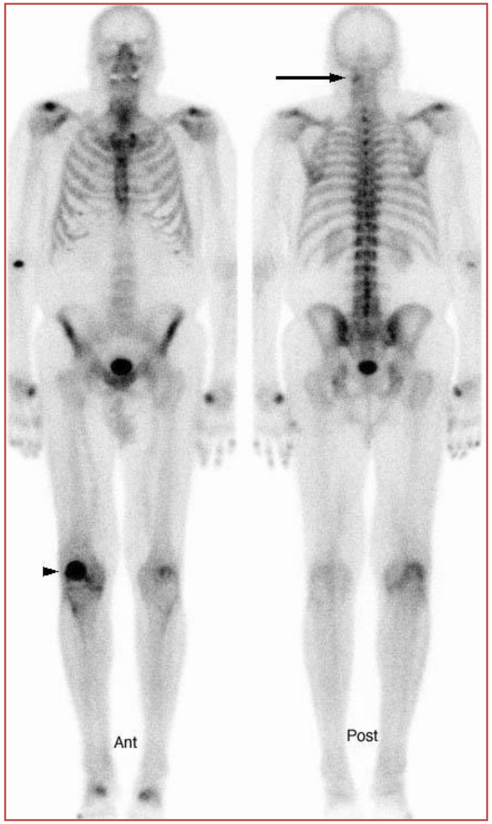
Study	Radioisotope	Emission energy	Half-life	Radiopharmaceutical	Activity (MBq)	Rotation (degrees)	Projections	Image resolution	Time per projection
Bone scan	Technetium-99m	140 keV	6 h	Phosphonates/ Biphosphonates	800	360	120	128x128	15 s
Brain scan	Technetium-99m	140 keV	6 h	HMPAO; ECD	555-1110	360	64	128x128	30 s
Tumor scan	Iodine-123	159 keV	13 h	MIBG	400	360	60	64x64	30 s
White cell scan	Indium-111	171 & 245 keV	67 h	In vitro labeled leukocytes	18	360	60	64x64	30 s

Using advanced brain-imaging techniques, researchers have been able to conclusively demonstrate that there are chemical, anatomical, and functional changes in the brains of substance-addicted persons, similar to the changes in other neurobiological disease processes. For example, the colorful images here depict SPECT scans (from Amen 2001) demonstrating that addictions (to heroin or alcohol, in this case), as well as mental disorders, affect brain function similarly to a neurological impairment such as stroke. Single-photon emission computed tomography (SPECT) uses small doses of radioisotope tracers to study regional cerebral blood flow and thus, indirectly, brain function during health and disease states.
http://www.pain-topics.com/faqs/index1.php



Combination of Imaging Techniques

Tc-99m MDP planar imaging



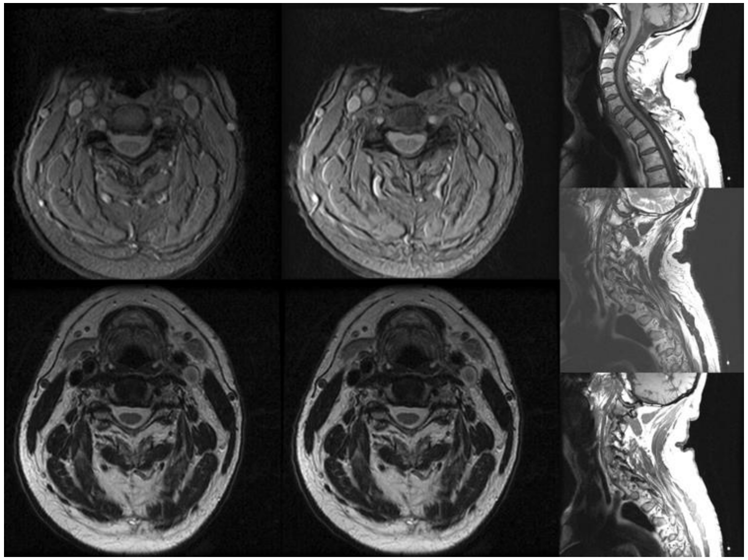
Tc-99m MDP planar imaging is correlated with patient symptomatology.

CASE

A 65-year-old male with history of prostate cancer presented with neck pain upon rotation.

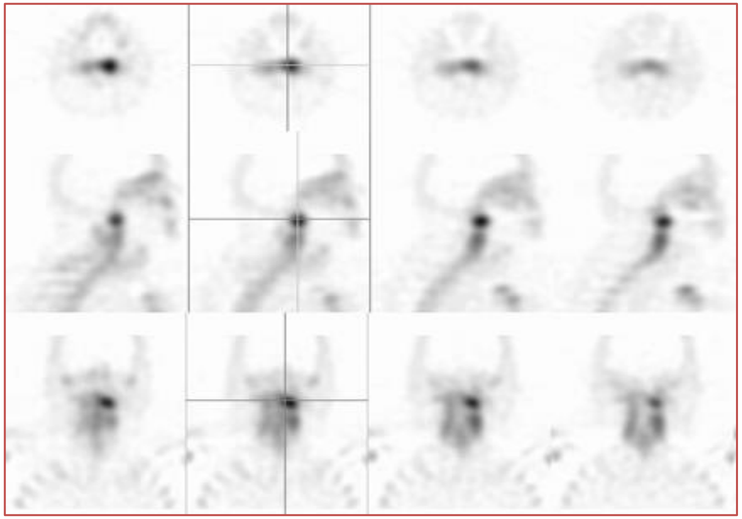
DIAGNOSIS

Left C3/4 facet disease, which is the likely cause of the patient's symptomatology and clinical history.



Plain films, CT scan, and MRI demonstrate anatomic correlation of hypertrophic changes at the facet joint.

Tc-99m MDP SPECT imaging improves the sensitivity of bone scanning for patients with back pain. SPECT imaging of the cervical spine confirms abnormal uptake overlying the approximate left C3/4 level (shown by arrows).



http://www.med.harvard.edu/JPNM/TF03_04/Oct14/WriteUp.html

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