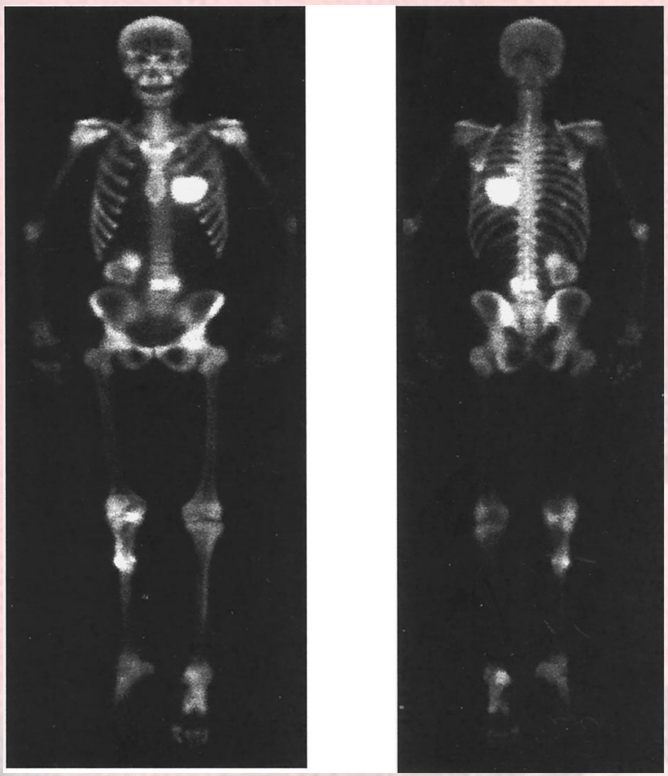
Nuclear Medicine



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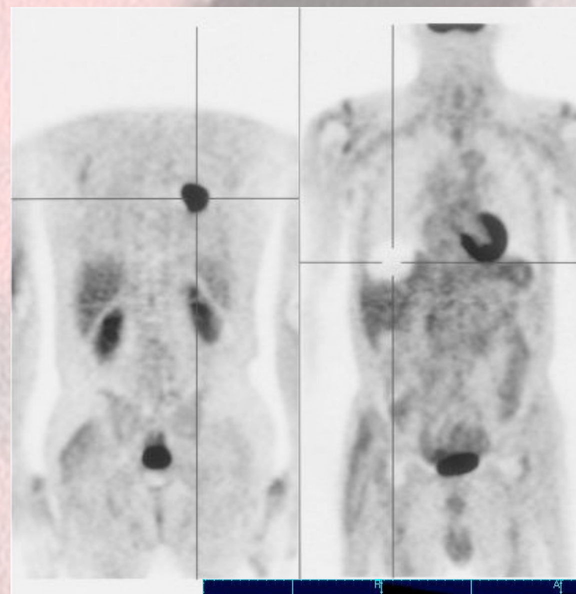
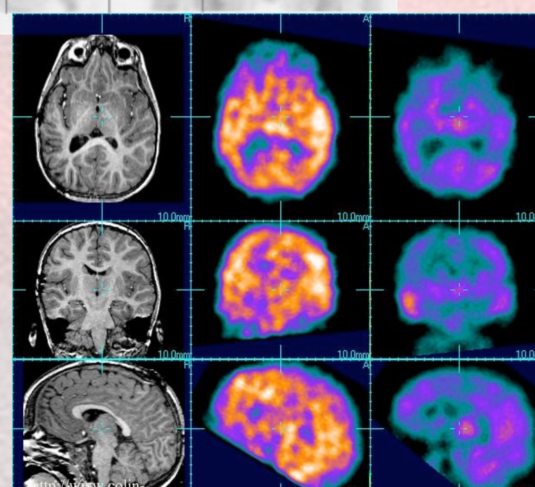




http://www.colin-studholme.net/research/ipag/mrdspect/mrspect3.html

Background Image courtesy of Dr. Bill Moore, Dept. of Radiology, Stony Brook Hospital

Nuclear Medicine
– Gamma Ray Imaging

- The ionizing radiation employed in most diagnostic nuclear medical imaging is no different from that employed in x-ray imaging.
- Both involve the detection of photons emerging from the patient's body however it depends on where the source is located with respect to the patient.
- X-rays are high energy photons that originate in an *extranuclear* source.
- However, the gamma rays used in nuclear medicine are *intranuclear* or produced by the decay of unstable atomic nuclei inside of you.
- Ernest Rutherford (1897) discovered that the emissions of certain radioactive elements could be detected using a zinc sulfide screen, producing tiny flashes of light called scintillations.
- Applied medically, it became possible to use isotopes that could be introduced into a patient, where the are photons emitted could be identified by newer scintillation detectors, and an image could be produced of the distribution of the isotope within the body.

Nuclear Medicine
– Gamma Ray Imaging

- The basics of using gamma rays to image is a nuclear medical technique called a gamma camera.

- The gamma camera consists of three basic parts
  1. Collimators
  2. Scintillation detector (Scintillator or Photomultiplier tube (PMT)).
  3. Electronics & computer elements

http://www.paec.gov.pk/kiran/images/800by600/dual-head-gamma-camera.jpg

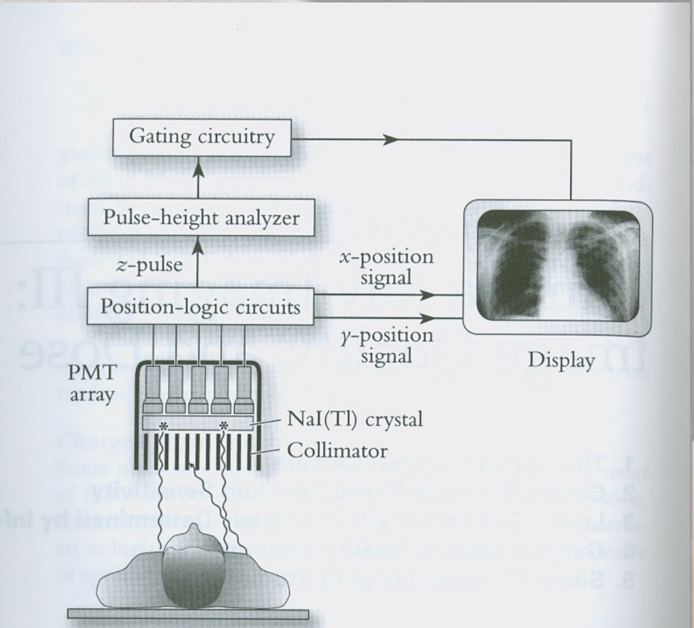
The Gamma Camera

- The gamma camera was invented by H. Anger in the1960s and is often referred to as the Anger camera
- An Anger camera consists of a collimator, placed between the detector surface and the patient, and the collimators are made from a highly absorbing material such as lead. This suppresses gamma rays that deviate substantially from the collimator openings and acts as a kind of "lens". The simplest collimators contain parallel holes.
- Depending on the position of the radiation event, the appropriate phototubes are activated. The positional information is recorded onto film as an analog image or onto a computer as a digital image.
- This set-up yields relatively accurate positional information. The intrinsic resolution of two radiation sources placed immediately on the crystal surface without the collimator is in the order of 1 mm.

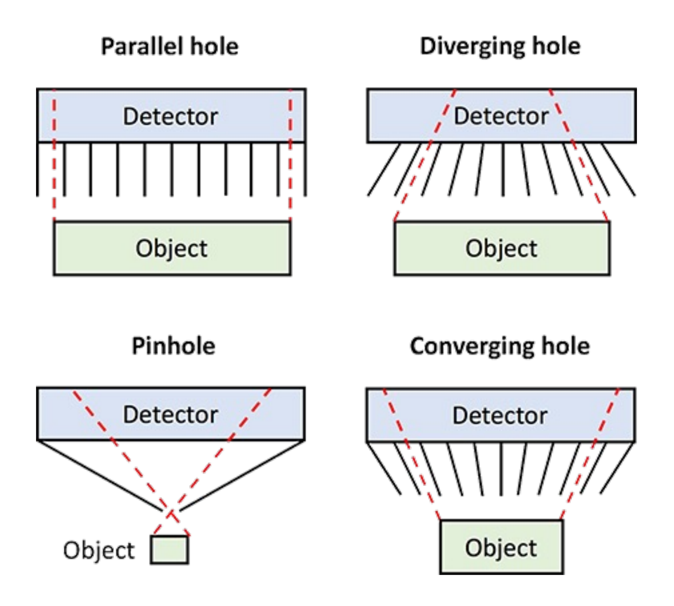
The Gamma Camera

-Collimators

- In an ordinary photographic camera, a lens diverts light rays by refraction to form an image on the film or detector.
- For gamma rays, the image is formed by a component called a collimator
- The collimators are usually made from a thick sheet of a heavy material usually lead, that is perforated like a honeycomb by long thin channels.
- The collimator forms an image by selecting only the rays traveling in (or nearly in) a specific direction, in which the channels are oriented.
- Gamma rays traveling in other directions are either blocked by the channel walls or miss the collimator entirely.



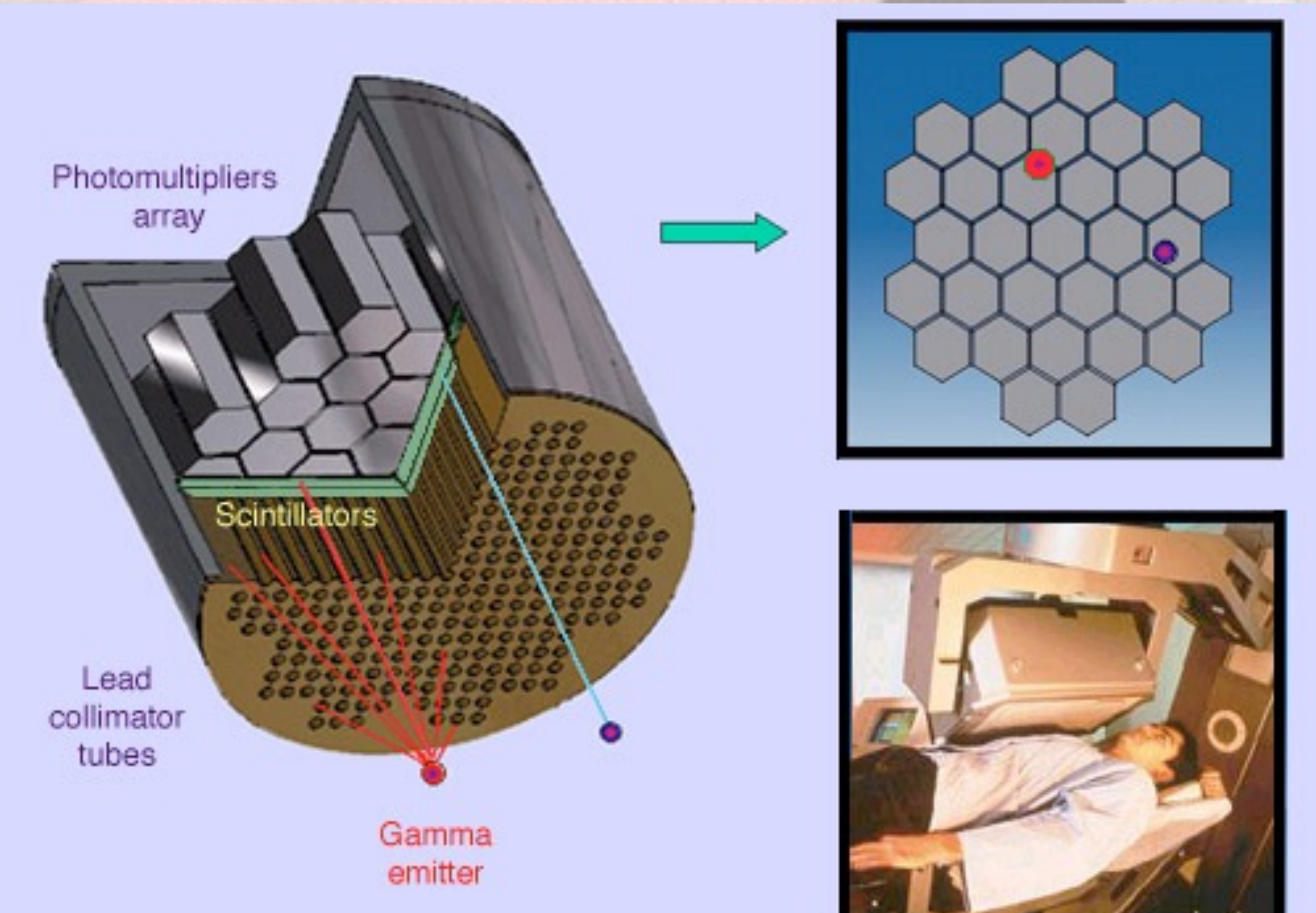
Wolbarst, Physics of Radiology, Ch. 42



https://www.radiologycafe.com/frcr-physics-notes/molecular-imaging/gamma-camera/

The Gamma Camera

-Collimators



http://www.radioactivity.eu.com/site/pages/Principe_GammaCamera.htm

The Gamma Camera

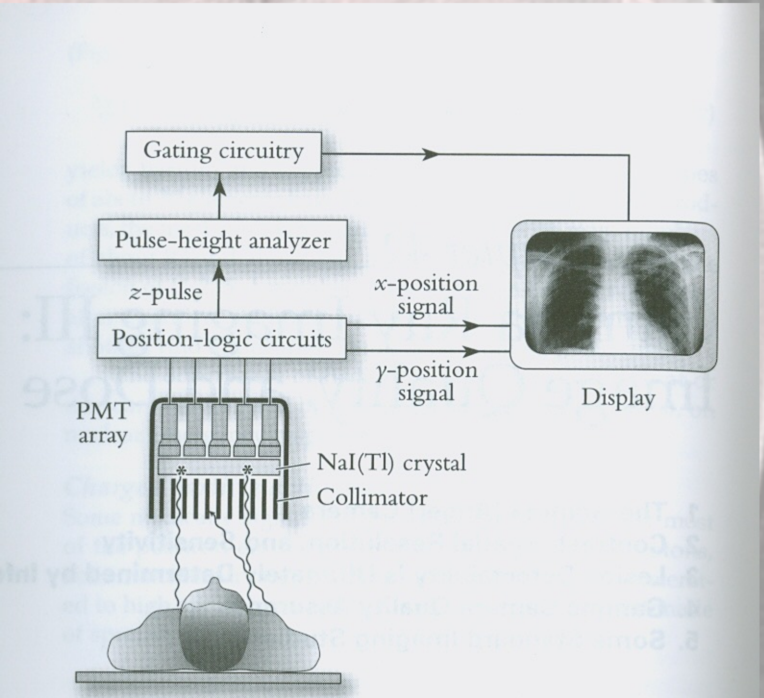
-Collimators

- Collimators are “rated” with respect to their photon energy and resolution/sensitivity.

Low-energy, or “technetium,” collimators, are “all purpose” collimators (LEAP) or “low energy high resolution” (LEHR), image gamma rays less than 200 keV in energy.
^{99m}Tc , ^{201}Tl , ^{123}I and ^{57}Co

Medium-energy, or “gallium,” collimators for gamma rays 200–300 keV in energy.
^{67}Ga and ^{111}In

High-energy, or “iodine,” collimators for gamma rays greater than 300 keV in energy. ^{131}I



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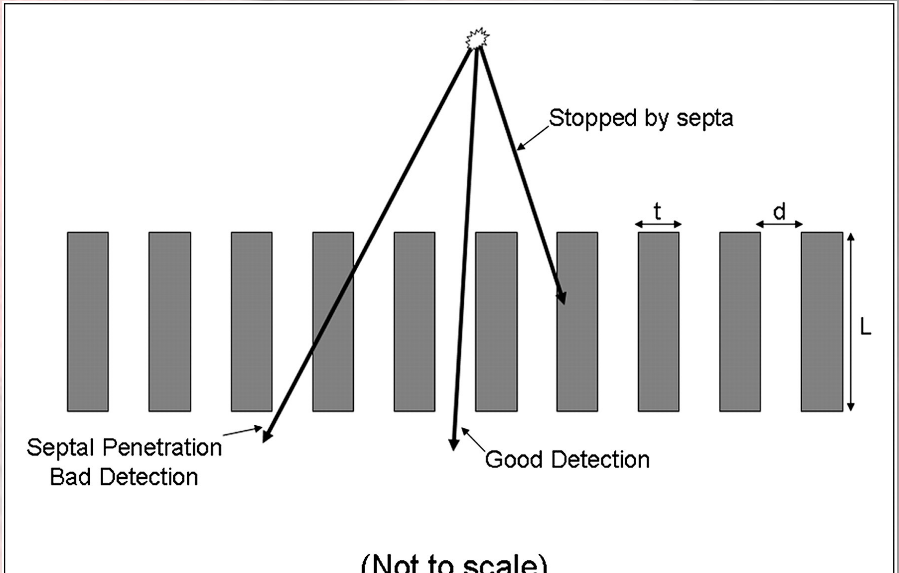
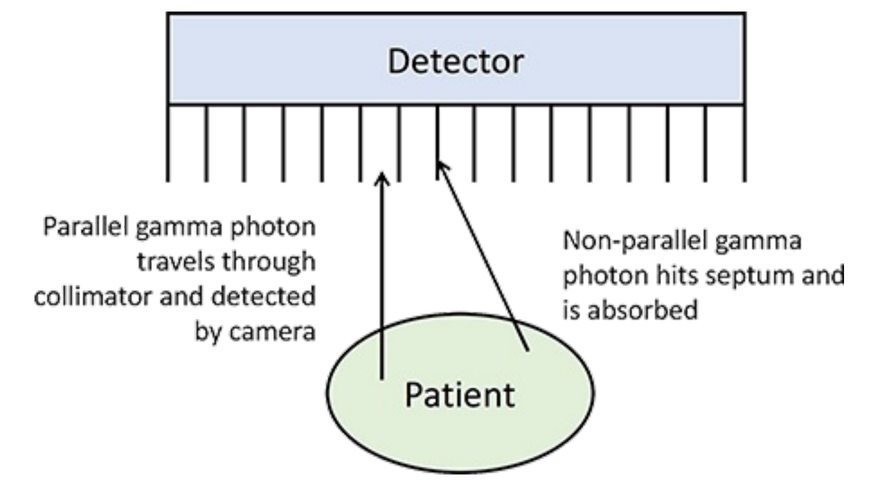
The Gamma Camera

-Collimators

- The collimator preferentially selects the direction of the incoming radiation.
- Gamma rays traveling at an oblique angle to the axes of the holes will strike the lead walls (septa) and not reach the crystal to be detected.
- This allows only radiation traveling perpendicular to the crystal surface to pass and contribute to the resulting image.
- A certain fraction (about 5%) of photons striking the septa will pass through them and reach the crystal; this phenomenon, which degrades image quality, is known as *septal penetration*.



http://tech.snmjournals.org/content/39/2/100/F1.large.jpg



https://www.radiologycafe.com/frcr-physics-notes/molecular-imaging/gamma-camera/

The Gamma Camera

-Collimators

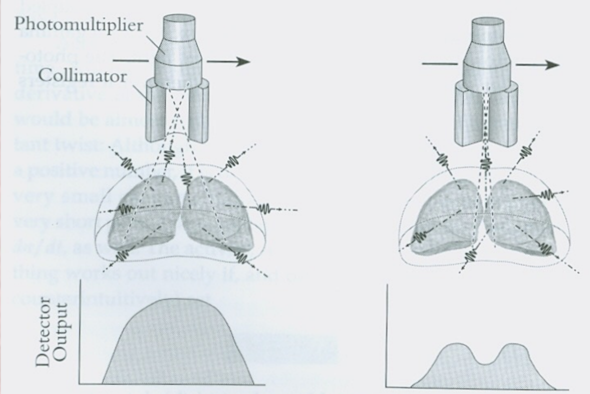
- For low-to-medium-to-high-energy collimation, the collimators are made longer and the septa thicker to maintain *septal penetration* at or below an acceptably low level, (5%).

- This, in turn, reduces the overall fraction of emitted gamma rays reaching the crystal.

- To compensate for the resulting lower sensitivity, the apertures are typically made wider in progressing from low-to-medium-to-high energy collimators. This, however, degrades spatial resolution.

- Therefore, gamma camera images are progressively poorer in quality for radionuclides whose gamma rays are emitting low-to-medium-to-high energy because of a combination of :

    1. increased septal penetration with increasing photon energy,
    2. lower sensitivity because of the longer collimation, and
    3. coarser resolution because of the wider apertures.



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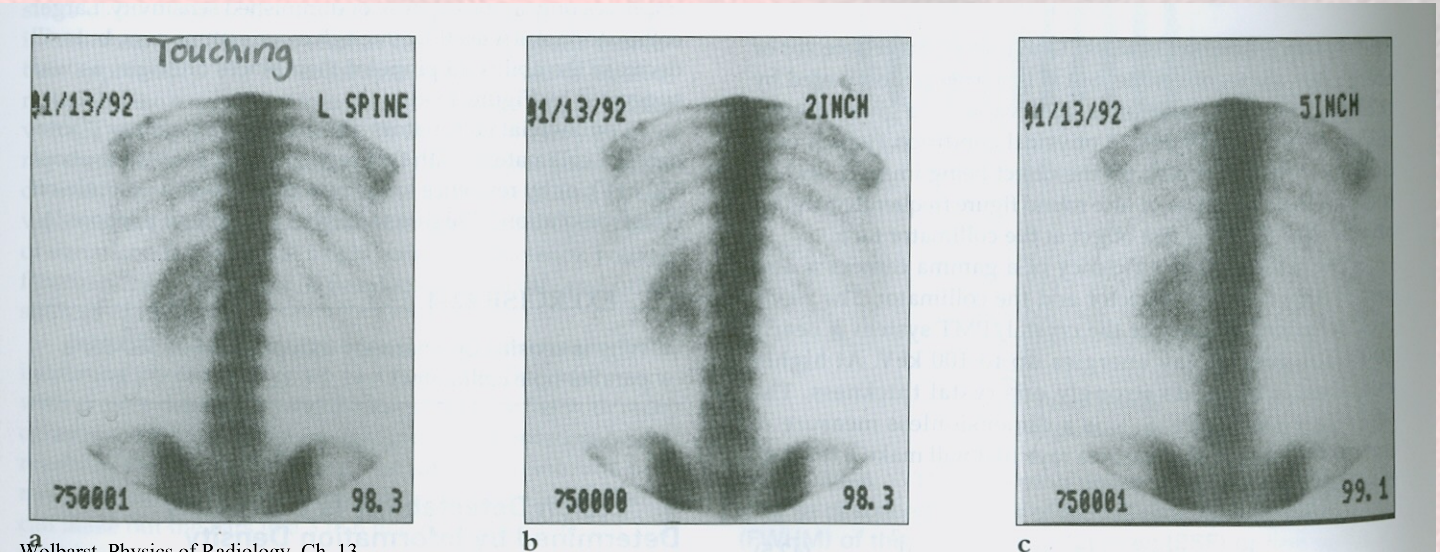
The Gamma Camera

-Collimators

Source to camera distance



Wolbarst, Physics of Radiology, Ch. 13

^{99m}Tc bone scans with about ¾ of a million counts detected.   In A the patient was touching the camera face (right at the collimators). B was 2 inches in front of the camera and C is 5 inches from the camera. As the source gets farther away, the image quality decreases.

The Gamma Camera

-Detectors

- The detectors are generally made of a reflective material so that light emitted toward the sides and front of the crystal are reflected toward a photomultiplier tube and get counted.

- This maximizes the amount of light collected and therefore the overall sensitivity of the detector.

- This also ensures that the amount of light detected is proportional to the energy of the absorbed gamma ray photon.

Fiber optic light pipe:

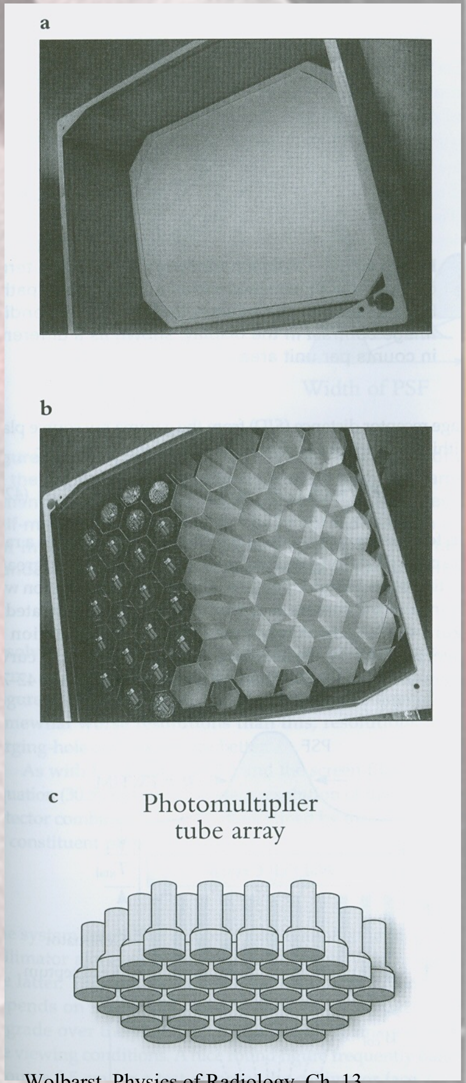
- Interposed between the back of the crystal and the entrance window of the PMT (thin layer of transparent optical gel).

- It optically couples the crystal to the PMT and thus maximizes the transmission (>90%) of the light signal from the crystal into the PMT.

The Gamma Camera

-Detectors

- PMT crystals vary in thickness from 1/4” - 1”
- ¼” provides the best spatial resolution but lowest sensitivity.
- 1” provides the highest sensitivity but coarsest resolution mostly used for imaging the photons of ^{18}F.
- 3/8”provides the optimum balance between sensitivity and resolution and is the most widely used for general gamma camera imaging. ~95% of the photons from ^{99}Tc are absorbed in a 3/8” crystal.
- The resulting light signal is spread out among the PMTs in a two-dimensional array on the back of the crystal.
- These photons are detected by (PMTs) and based on the photoelectric effect, from a single photon, a PMT can produce a cascade of electrons, which yields a measurable electrical current.



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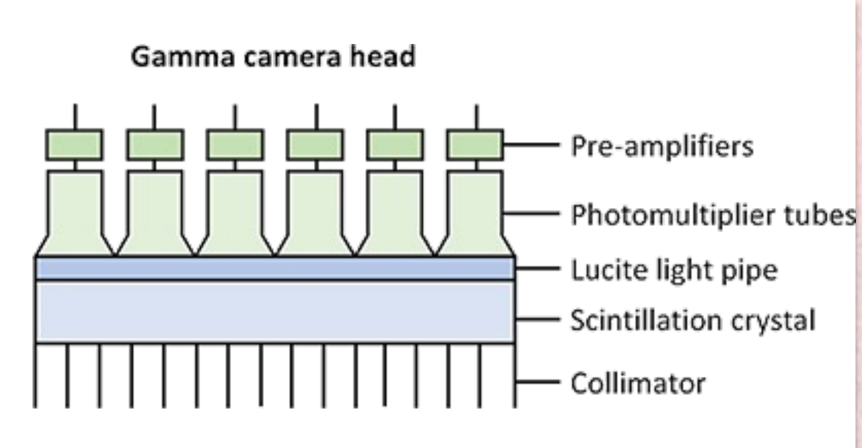
The Gamma Camera

-Detectors



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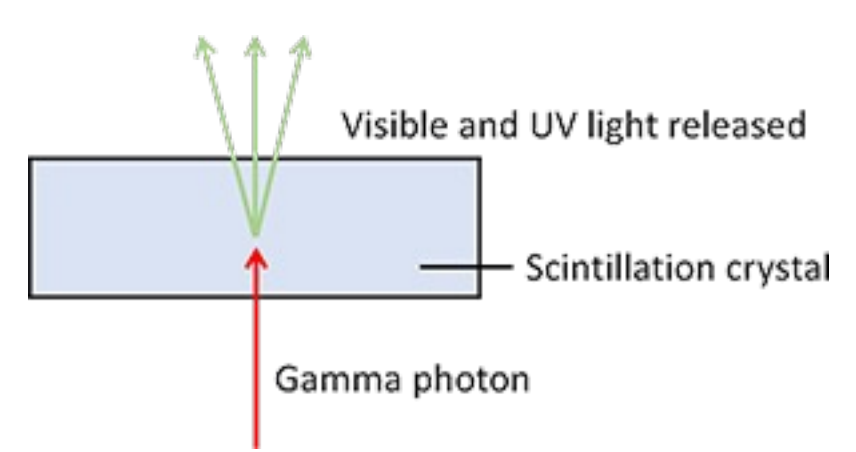

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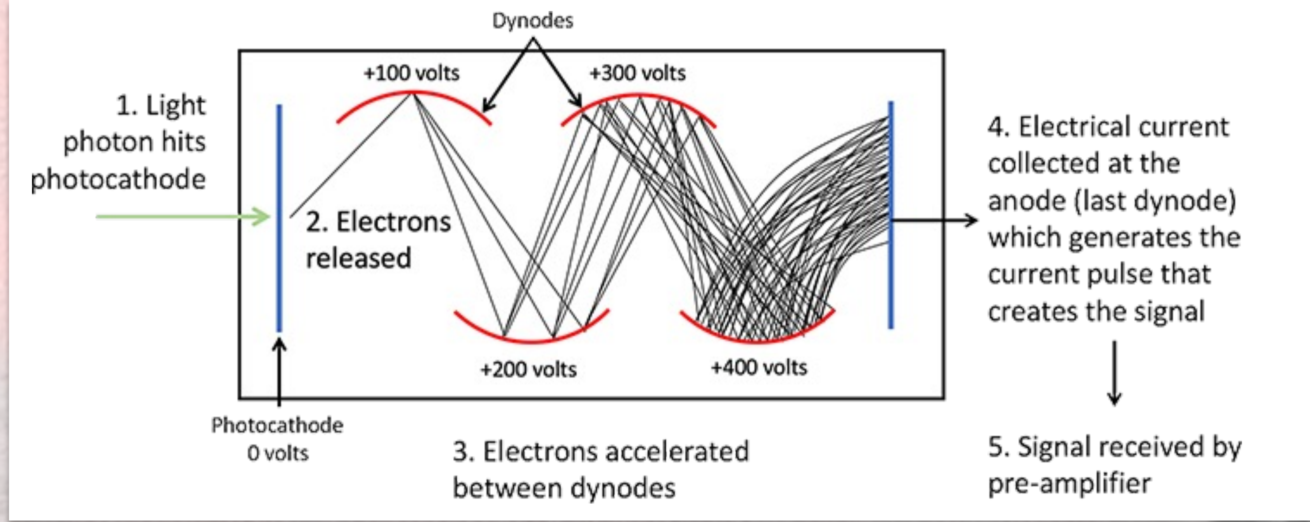


https://www.radiologycafe.com/frcr-physics-notes/molecular-imaging/gamma-camera/

The Gamma Camera

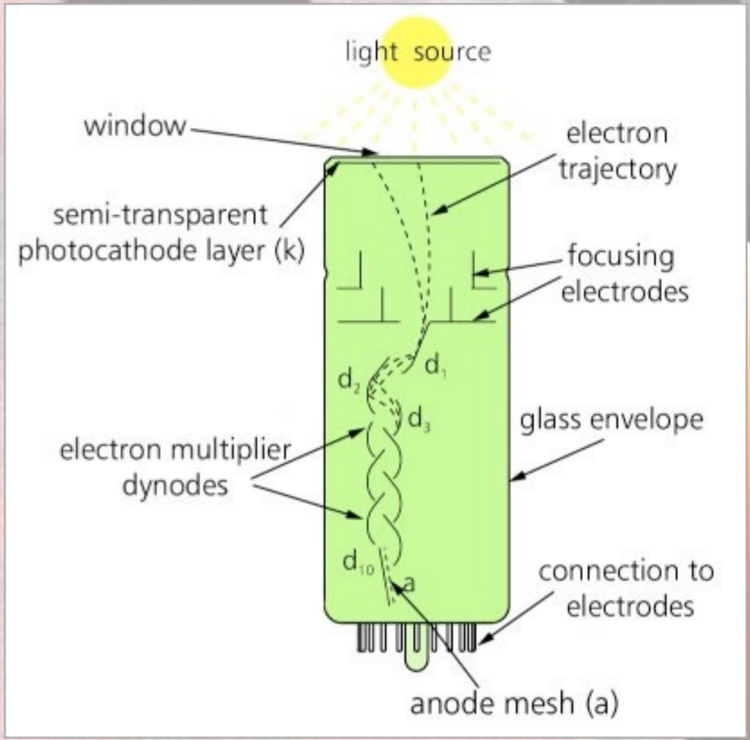
-PMTs

- The photomultiplier is an extremely sensitive light detector providing a current output proportional to light intensity.

- Photomultipliers are used to measure any process which directly or indirectly emits light. Large area light detection, high gain and the ability to detect single photons give the photomultiplier distinct advantages over other light detectors.

- The photomultiplier detects light at the photocathode (k) which emits electrons by the photoelectric effect.

- These photoelectrons are electrostatically accelerated and focused onto the first dynode (d_1) of an electron multiplier.



http://www.et-enterprises.com/photomultipliers/understanding-photomultipliers

The Gamma Camera

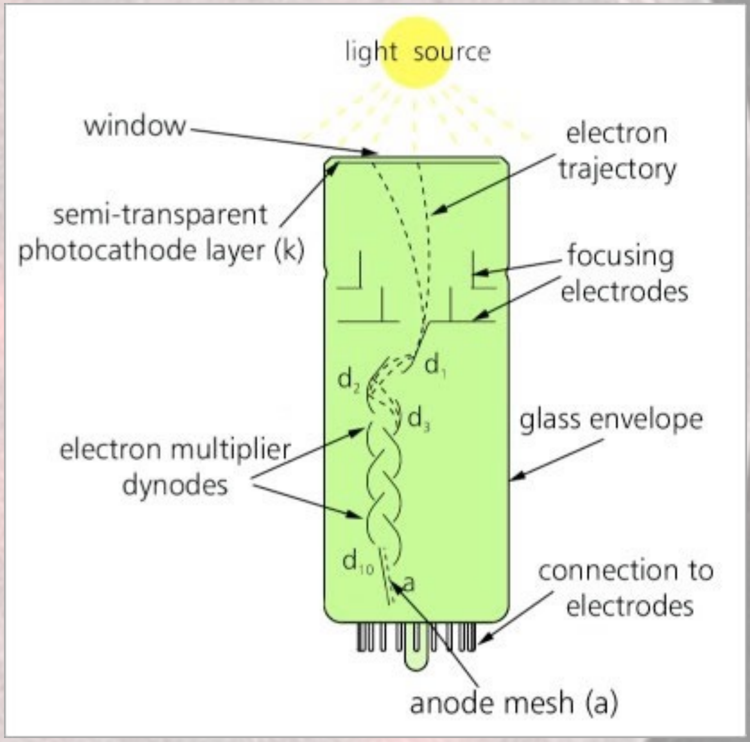
-PMTs

- On impact with d_1, each incident electron liberates several secondary electrons which are in turn, electrostatically accelerated and focused onto the next dynode (d_2).

- The process is repeated at each subsequent dynode and the secondary electrons from the last dynode are collected at the anode (a).

- The ratio of secondary to primary electrons emitted at each dynode depends on the energy of the incident electrons and is controlled by the inter-electrode potentials.

- By using a variable high voltage supply and a voltage divider network, to provide the inter-electrode voltages, the amplitude of photomultiplier output can be varied over a wide dynamic range.



http://www.et-enterprises.com/photomultipliers/understanding-photomultipliers

The Gamma Camera

-PMTs

A scintillator is a device that converts high energy photons into visible photons. Suppose that a scintillator sits on top of a strontium vanadate ($SrVO_3$) cathode. The work-function of strontium vanadate is $1.79eV$.

- What wavelength should the photons emitted from scintillator have so that they can just be detected by the strontium vanadate cathode?

- Assuming that one of these photons is incident on the strontium vanadate photocathode and liberates an electron, what must the minimum voltage be on the first dynode? Assume that each incident electron produces say $z = 2$ secondary electrons.

- If the PMT is made of $N = 10$ dynodes in total arranged in such a way that the same number of secondary electrons is produced from each incident electron, how long does it take the signal to reach the anode if the separation between each dynode is $0.5cm$?

- Notice that for every gamma ray incident we got 2^N electrons out, or $N_e = z^N N_\gamma$.

The Gamma Camera

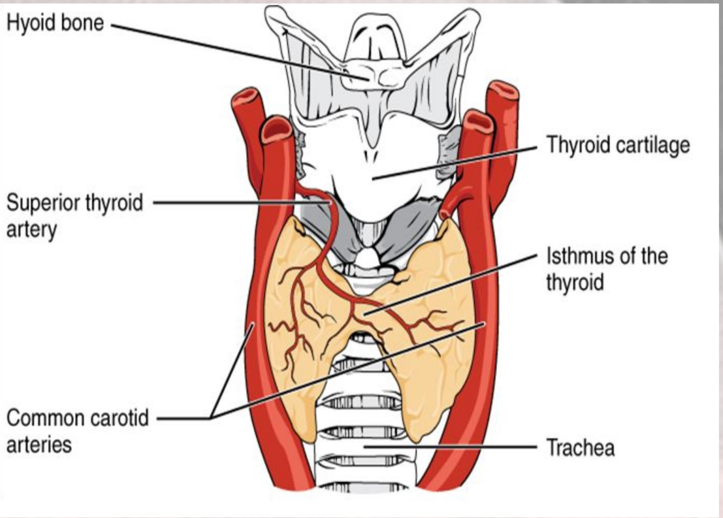
-Thyroid Imaging

The thyroid is a gland that makes and stores essential hormones that help regulate the heart rate, blood pressure, body temperature, and the rate of chemical reactions (metabolism) in the body.

It is in the anterior neck.

The thyroid gland is the main part of the body that takes up iodine.

In a thyroid scan, radioactive iodine is given to the patient and a gamma camera is used to measure how much iodine has been absorbed from the bloodstream by the thyroid gland. If a patient is allergic to iodine, technetium can be used as an alternative.



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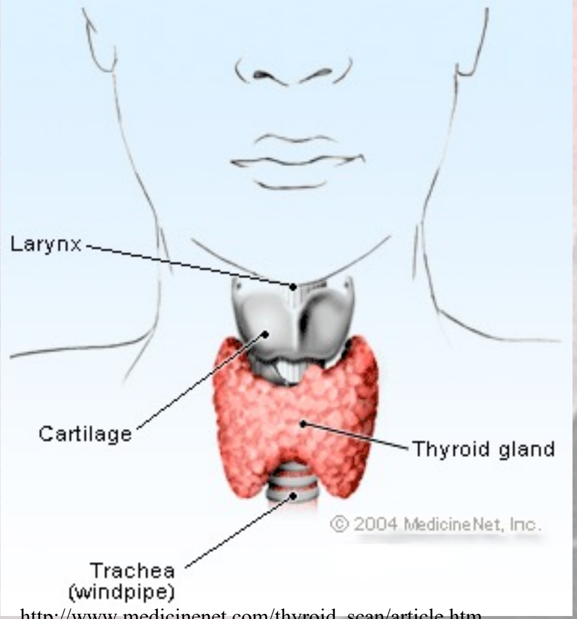
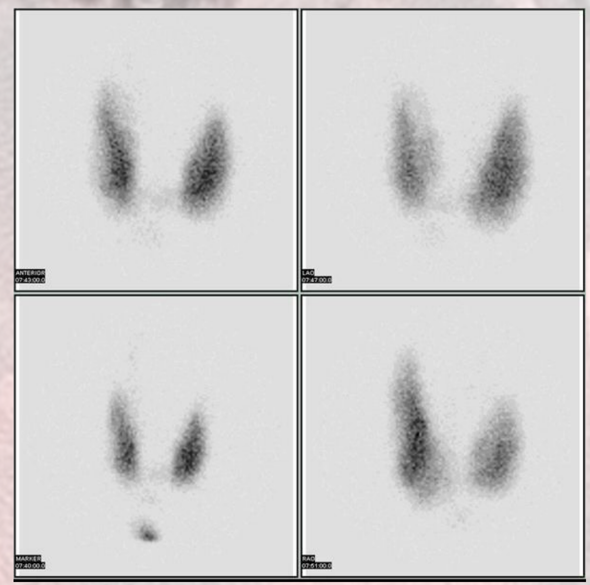


http://www.medicinenet.com/thyroid_scan/article.htm

The Gamma Camera

-Thyroid Imaging

https://slideplayer.com/amp/9521838/



https://s3.amazonaws.com/healthtap-public/ht-staging/user_answer/reference_image/8948/large/Thyroid_scan.jpeg?1349479012

The Gamma Camera

- Osteosarcoma

- Osteosarcoma is the most common cancerous bone tumor in kids. The average age at diagnosis is 15 and both sexes are just as likely to get this tumor until the late teen years, when it is more often seen in boys.

- Osteosarcoma is also more commonly seen in people over age 60.

- Osteosarcoma tends to occur in the bones of the:

    - Shin (near the knee – proximal tibia)
    - Thigh (near the knee – distal femur)
    - Upper arm (near the shoulder – proximal humerus)

- This cancer occurs most commonly in larger bones and in the area of bone with the fastest growth rate. An osteosarcoma can occur in any bone.

http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0002616/figure/A001650.B9714/?report=objectonly

Human Skeletal System - Bones

- The human skeletal system showing the major bones of the body.

Main sites for Osteosarcoma

Jaw – *Mandible*

Upper Arm - *Proximal Humerus*

Upper Shin – *Proximal Tibia*

Lower Thigh – *Distal Femur*

Human Skeletal System
- Bones & Sarcoma

- Bones of the human body fall into two basic classes:

  Flat bones are designed to protect vital organs. Some examples are the skull bones, breast bone (sternum), and ribs.

  Long bones make a framework for our muscles that aid movement. Some examples are those in the arms and legs.

- Bones make new blood cells. This is done in the soft, inner part of some bones called bone marrow, which contains blood-forming cells. New red blood cells, white blood cells, and platelets are made in bone marrow.

- Bones also provide the body with a place to store minerals such as calcium.

- Osteosarcoma is a primary bone cancer meaning that it originates in the bones.

- Other types of bone metastases can occur, and these are secondary bone cancers because they arose somewhere else in the body.

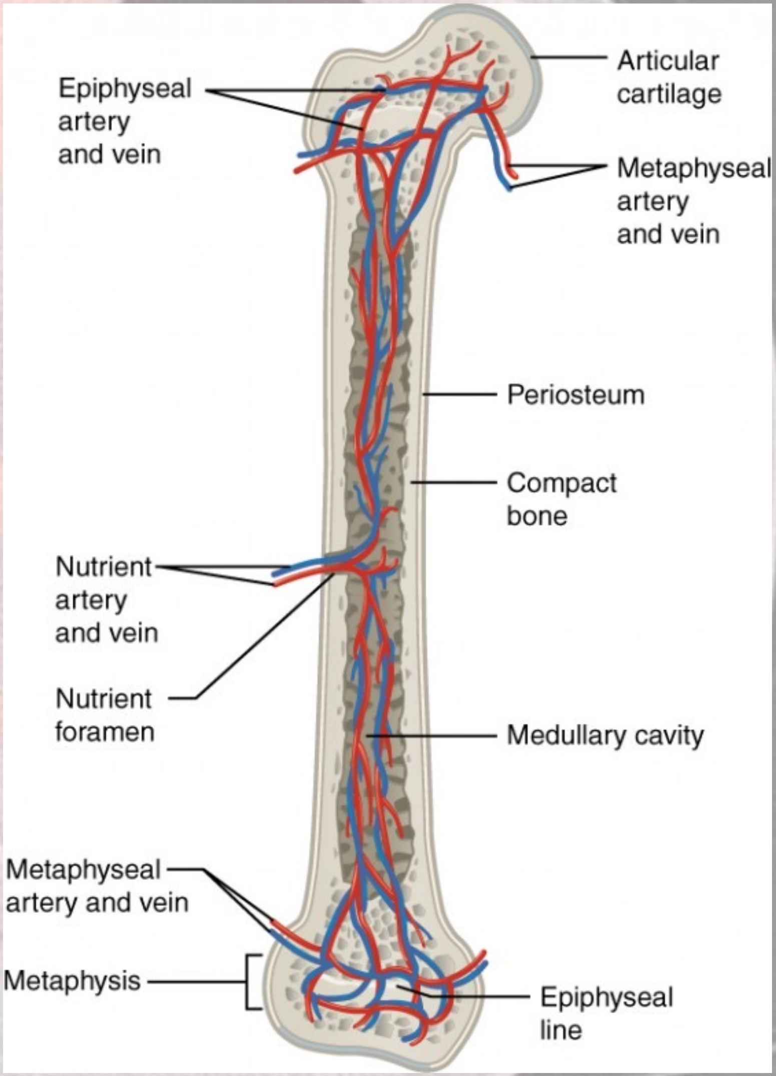
- For example, breast cancer cells that metastasize in the bone are still breast cancer cells thus they are secondary as a bone cancer.

Human Skeletal System
- Bone Structure

- Bone is living tissue made up of calcium and various proteins that make it strong and rigid. It contains cells that continuously break down and remove old bone (***osteoclasts***), and other cells that build up new bone to maintain its strength (***osteoblasts***).

- Each bone consists of a compact outer shell of the bone (the *cortex*) and a spongy inside (*cancellous tissue*). The inside contains the bone marrow, which produces blood cells

- The joints of the bones are covered in cartilage - a tough, flexible material like gristle. Cartilage is more elastic than bone, and it allows the bones to move freely at the joints. It also cushions the bones at the joint to stop them rubbing against each other.



https://www.coursehero.com/study-guides/cuny-csi-ap-1/bone-structure/

Osteosarcoma

- Osteosarcoma is the most common type of cancer that develops in bone.
- Like the osteoblasts in normal bone, the cells that form this cancer make bone.
- But the bone matrix of an osteosarcoma is not as strong as that of normal bones.
- Most osteosarcomas occur in children and young adults. Teens are the most commonly affected age group, but osteosarcoma can occur at any age.
- In children and young adults, osteosarcoma usually develops in areas where the bone is growing quickly, such as near the ends of the long bones.
- Most tumors develop in the bones around the knee, either in the distal femur (the lower part of the thigh bone) or the proximal tibia (the upper part of the shinbone).
- The proximal humerus (the part of the upper arm bone close to the shoulder) is the next most common site.
- However, osteosarcoma can develop in any bone, including the bones of the pelvis (hips), shoulder, and jaw. This is especially true in older adults.

Osteosarcoma

Sarcomas fall in to two categories

- **Soft tissue sarcomas.** These develop from soft tissues, such as muscles, fat, nerves, blood vessels, fibrous tissues, or deep skin tissues. Most sarcomas begin in soft tissues.

- **Bone cancers.** Bone cancers, also called osseous sarcomas, start in the bone. Bone cancers are much less common than benign (noncancerous) bone tumors or secondary cancers that spread to the bone from other locations (such as the lung or breast).

  There are three types of bone sarcoma:

  Osteosarcoma – primary cancer of the bone
  Ewing’s sarcoma – secondary cancer of the bone
  Chondrosarcoma – cancer in cartilage

- Bone sarcomas very rare with approximately 2,890 new cases diagnosed in the United States each year, and approximately 1,410 deaths.

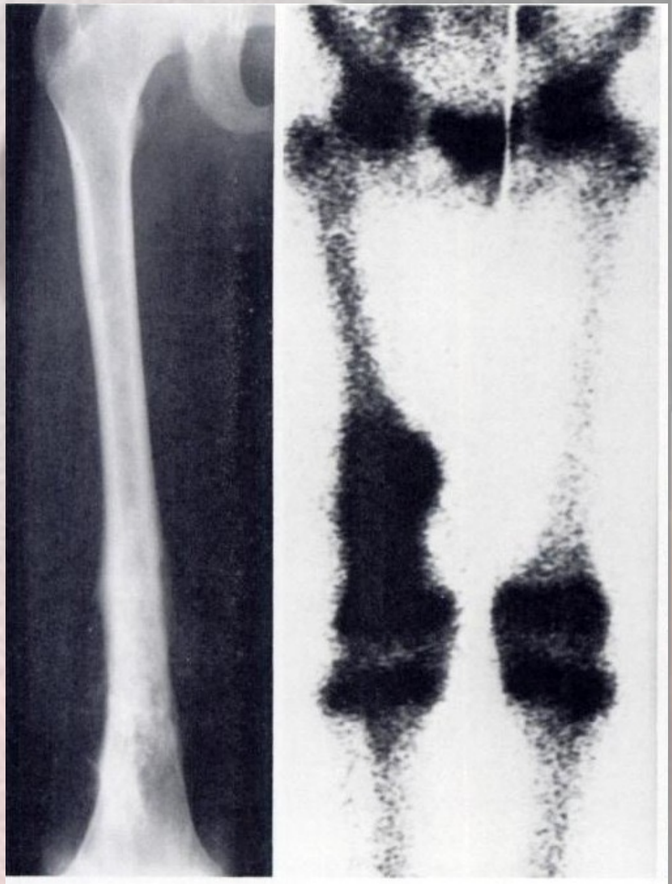
- The incidence is slightly higher in males than females and no race has a higher incidence than another.

The Gamma Camera

-Osteosarcoma

How is an Osteosarcoma detected:

- X-ray – used to confirm the presence of a tumor in the bone
- Magnetic Resonance Imaging (MRI) or Computed Tomography (CT) scans ar used to determine the extent of the tumor
- Radionuclide Bone scan – uses primarily a Gamma Camera to confirm primary sites and identify any additional sites of bone involvement
- Positron Emission Tomography (PET), gamma camera, or a Single Photon Emission CT (SPECT) scan -- to find small tumors or check if treatment is working effectively
- Biopsy -- to remove tissue from the tumor for microscopic examination by an expert pathologist



Chew & Hudson Radionuclide Bone Scanning of Osteosarcoma, *AJR 139:49-54, July 1982*

Image of the right femur using an x-ray and part of a whole-body gamma camera imaging of a pyrophosphate radiolabeled using ^{99m}Tc.

The left is an image of a suspected osteosarcoma

The right is the gamma camera image showing uptake in both knees as well as the distal femur.

The Gamma Camera

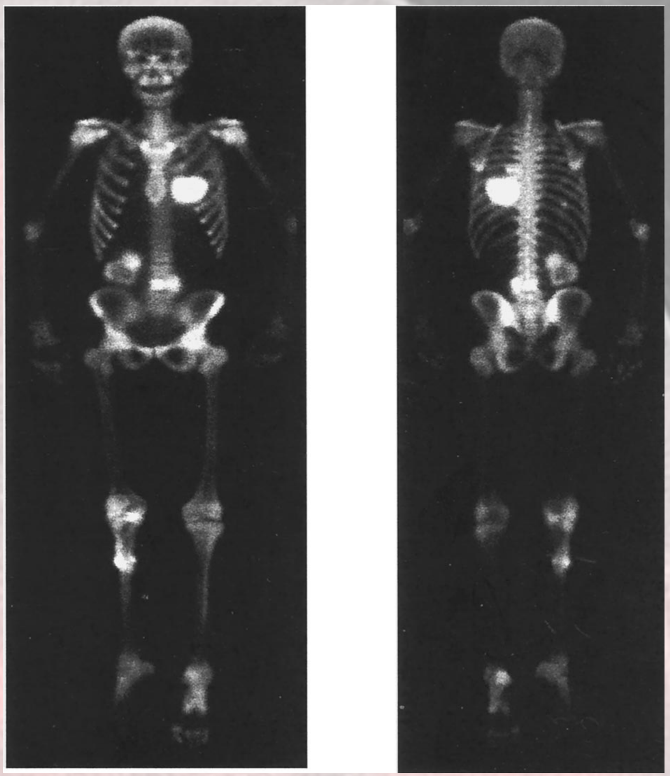
-Osteosarcoma

- The bone scan is a well-established procedure in nuclear medicine.

- Areas of bone injury or bone destruction are usually associated with ongoing bone repair and consequent increased metabolic activity.

- The radionuclides which mimic the metabolic behavior of calcium will localize in this region of bone repair in increased concentration relative to normal bone. In the past ${}^{85}_{38}Sr$ and ${}^{18}_{9}F$ were the primary radionuclides used.

- However, various phosphate compounds labeled with ${}^{99m}_{43}Tc$ are mostly the radionuclides of choice today.



http://jco.ascopubs.org/content/20/1/189.full.pdf+html

- Technetium is metastable and decays by emitting a $140keV$ gamma ray with a physical half-life of 6 hours and a biologic half life of 1 day.

$$ {}^{99m}_{43}Tc \rightarrow {}^{99}_{43}Tc + \gamma $$

The Gamma Camera

- Osteosarcoma

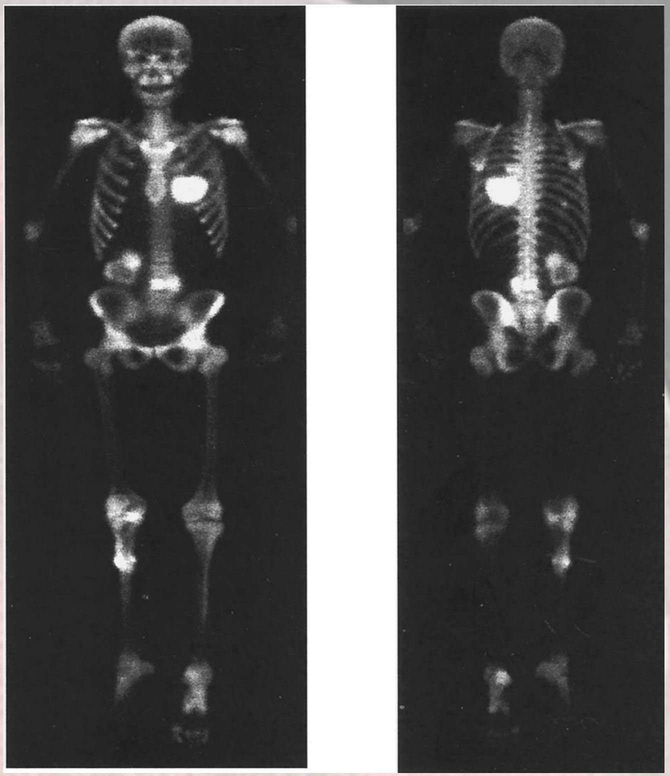
- However not all bone scans are done with ^{99m}Tc.

- Here is a gamma camera image of a bone scan that was done with ^{153}Sm (Samarium.)

- Samarium is a bone-seeking radiopharmaceutical that provides both diagnostic (gamma ray emitter) and therapeutic (beta emitter) irradiation to osteoblastic bone metastases with an ~ 2day half life.

- This is a theranostic procedure.

- The injected radionuclide is ^{153}Sm-EDTMP (^{153}Sm ethylene diamine tetramethylene phosphonate), has a high bone uptake due to the phosphorus concentration in the bones.



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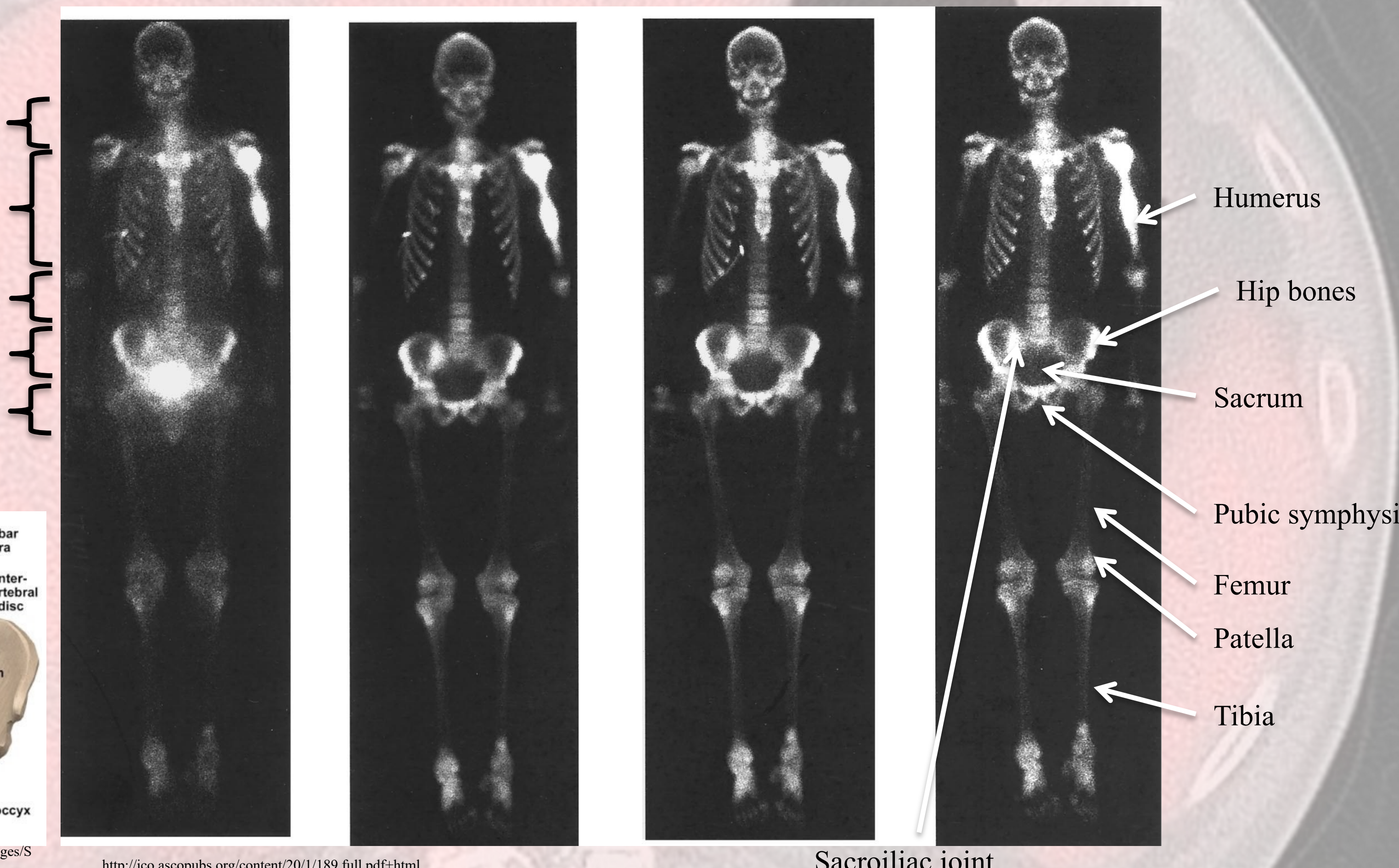
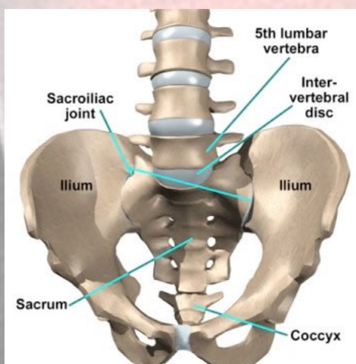
Variable uptake of ^{153}Sm-EDTMP in metastatic osteosarcoma

Anterior and posterior gamma camera imaging 24 hours after administration of 3 mCi/kg. Note the more avid radioisotope uptake of the left chest mass adherent to the pericardium compared with the spine and right renal metastases.

The Gamma Camera

- Osteosarcoma





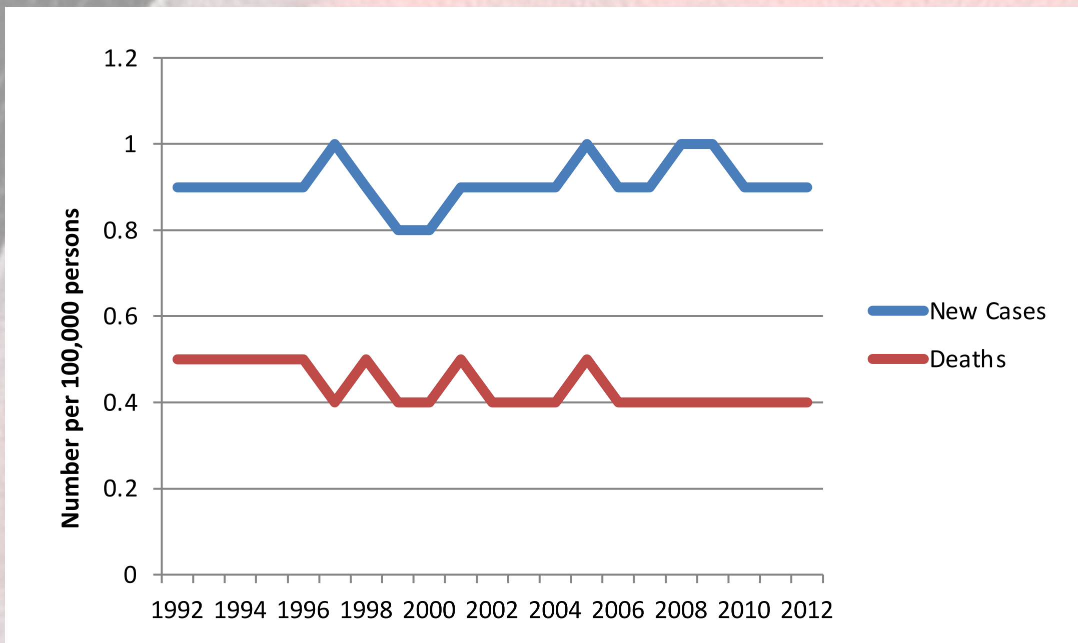
http://nasachiropractic.com/clients/4013/images/SI_joint.jpg

http://jco.ascopubs.org/content/20/1/189.full.pdf+html

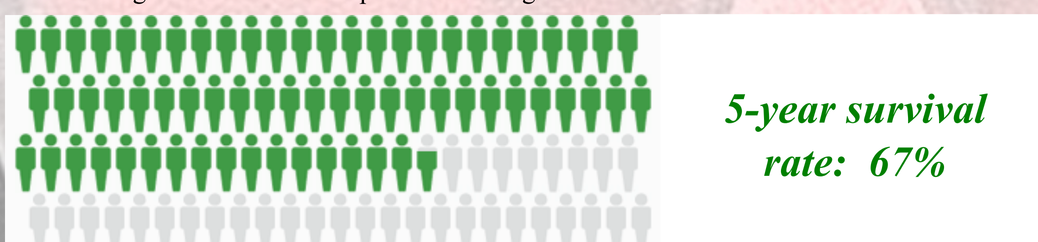
Whole-body anterior gamma camera imaging of osteosarcoma of the left humerus and additional bone metastases (left rib, right sacroiliac joint, L5 spine) at 2, 24, 48, and 120 hours (right to left) after 6 mCi/kg of ^{153}Sm-EDTMP.

Osteosarcoma

-Statistics



Data and figure below from: http://seer.cancer.gov/statfacts/html/bones.html



Number of New Cases and Deaths per 100,000

The number of new cases of bone and joint cancer was 0.9 per 100,000 men and women per year. The number of deaths was 0.4 per 100,000 men and women per year. These rates are age-adjusted and based on 2008-2012 cases and deaths.

Lifetime Risk of Developing Cancer: Approximately 0.1 percent of men and women will be diagnosed with bone and joint cancer at some point during their lifetime, based on 2010-2012 data.

Summary:

- The radioactive decay of unstable elements allows for medical imaging and detection of metabolically active sites in the body.

- Radiolabeled drugs are injected into the body and travel to glucose active sites and subsequent *PET* or gamma camera scans are performed to locate the activity.

- *PET* scans are a non-invasive imaging technique and are fused with CT (or MRI) scans to given anatomical information.

- *PET* scans make use out of coincident coupled gamma rays from the annihilation of positron-electron pairs.

- Gamma camera scans provide effective imaging of uptake in bones.