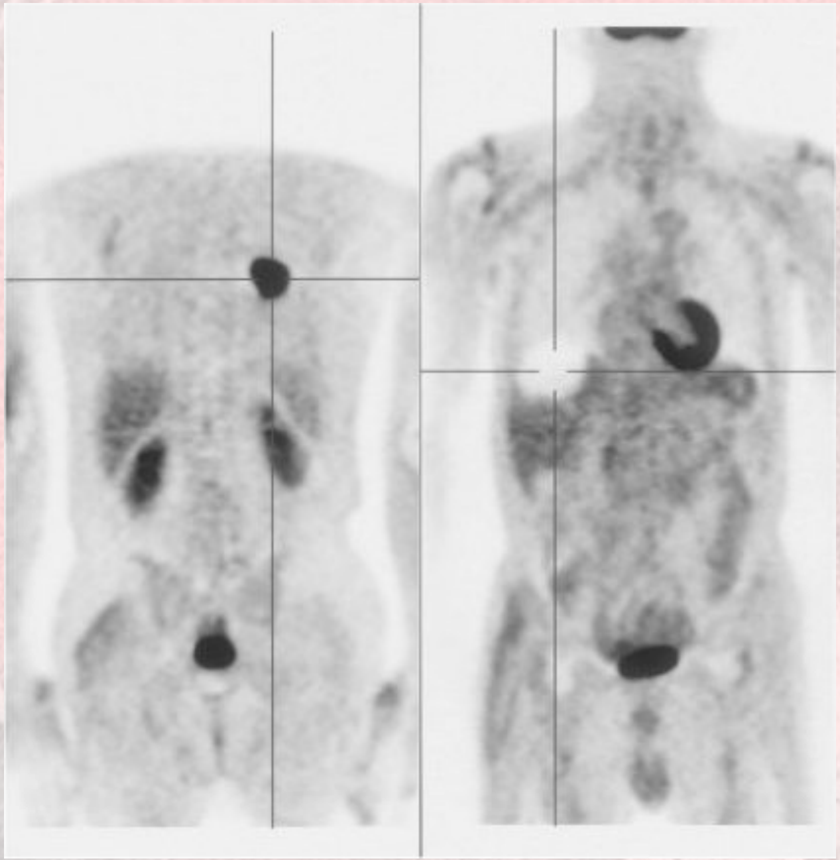
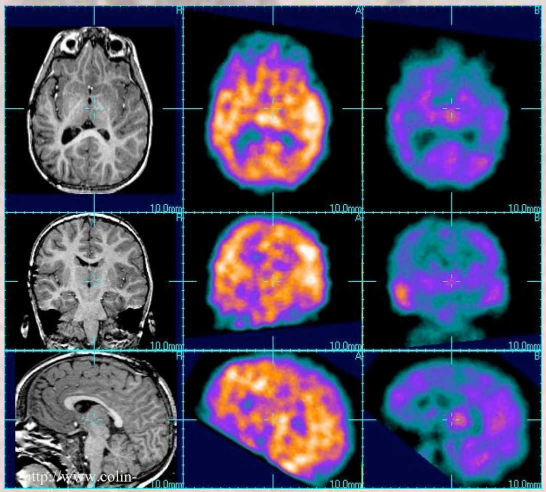
Radioactivity, Nuclear Medicine & PET Scans





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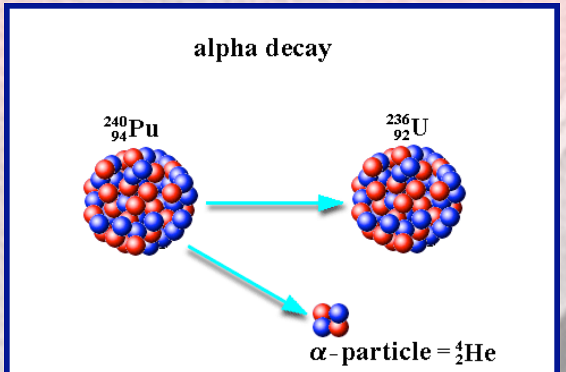


http://www.mwit.ac.th/~Physicslab/applet_04/atom2/Alphae.gif

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

Introduction & Motivation

- Nuclear Medical Imaging: images of the body using the decay of radioactive nuclei.
- Why do we need another imaging technique especially when we have so many others that work well?
- What are the problems associated with…

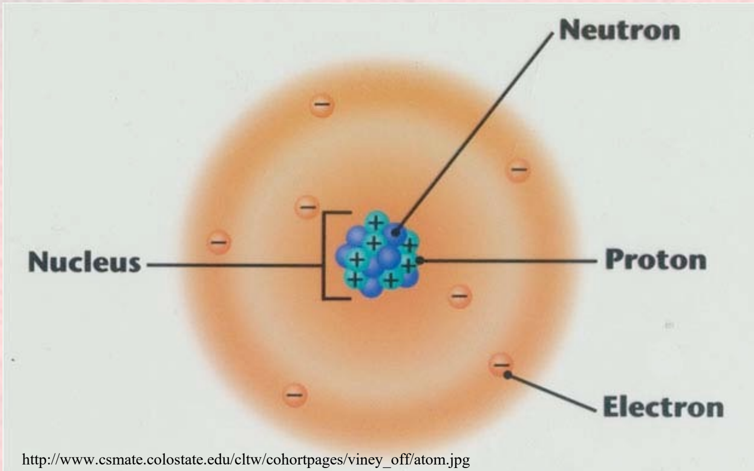
Optical fiber scopes?	• Can only image cavities and not solid organs.
Ultrasound?	• Can image solid organs but imaging the brain is limited due to reflection of sound at the skull. • Some tissues remain indistinguishable to US.
X-rays?	• Have restricted ability to image body function. • Low contrast for resolving soft tissue.

- Radionuclide imaging does not offer much spatial resolution (details much smaller than about a centimeter are blurred.)

- Radionuclide imaging does offer great contrast, and this gives information about body functions.

- Coupled with diagnostic CT, anatomical and metabolic activity information about a structure can be determined.

Basic Nuclear Physics



http://www.csmate.colostate.edu/cltw/cohortpages/viney_off/atom.jpg

$$\rightarrow \; {}^{A}_{Z}X$$

- Nucleons (protons & neutrons) are held together by the strong nuclear force.
- The strong nuclear force is a short-range force (extends over a few proton diameters.)
- Strong nuclear force is an attractive force, much larger than the repulsive Coulomb force (a long-range force.)
- A is the atomic mass (number of protons & neutrons expressed in atomic mass units) and Z is the electric charge of the nucleus (due to the number of protons.)

Basic Nuclear Physics

- The nucleus is generally stable when the number of protons equals the number of neutrons (with of course slight variations).

- Isotopes of elements can be formed by varying the number of neutrons in the nucleus.

- For example: Carbon
  - has two stable isotopes: $^{12}_{6}C$ & $^{13}_{6}C$
  - and several unstable (*radioactive*) isotopes: $^{10}_{6}C$, $^{11}_{6}C$, & $^{14}_{6}C$

- The nucleus generally becomes unstable when the number of neutrons generally increases well beyond the number of protons.

- To become more stable (*lower in energy*) the nucleus can decay with an emission of radiation (light), particles with mass, or through a series of both.

- For a given radioactive sample, the activity of the sample, number of radioactive atoms, or mass of radioactive atoms in the sample decreases exponentially with time.

Radioactive Decay Processes

- Conserve mass and charge

- *Alpha Decay*: The emission of a massive particle that resembles a helium nucleus (2 protons & 2 neutrons.)

$$ {}^{A}_{Z}X \rightarrow {}^{4}_{2}He + {}^{A-4}_{Z-2}Y \rightarrow Q = (m_X - m_Y - m_\alpha)c^2 $$

- *Beta Minus Decay*: The emission of a high energy (near the speed of light) electron from the decay of an unstable neutron.

$$ {}^{A}_{Z}X \rightarrow {}^{0}_{-1}e + {}_{Z+1}^{A}Y + \bar{\nu}_e \rightarrow Q = (m_X - m_Y)c^2 $$

- *Beta Plus Decay*: The emission of a high energy (near the speed of light) positron (a positively charged electron) from the decay of an unstable proton.

$$ {}^{A}_{Z}X \rightarrow {}^{0}_{+1}e + {}_{Z-1}^{A}Y + \upsilon_e \rightarrow Q = (m_X - m_Y - 2m_e)c^2 $$

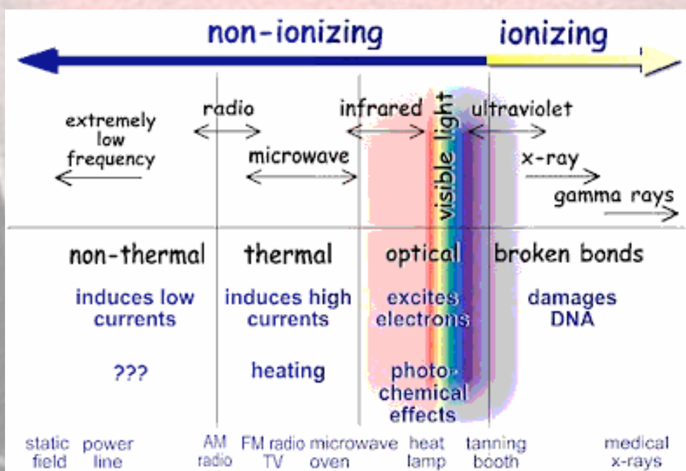
- *Gamma Decay*: The emission of a high energy photon by protons or neutrons transitioning to lower energy levels inside of the nucleus.

$$ {}^{A}_{Z}X^* \rightarrow {}^{0}_{0}\gamma + {}^{A}_{Z}X $$

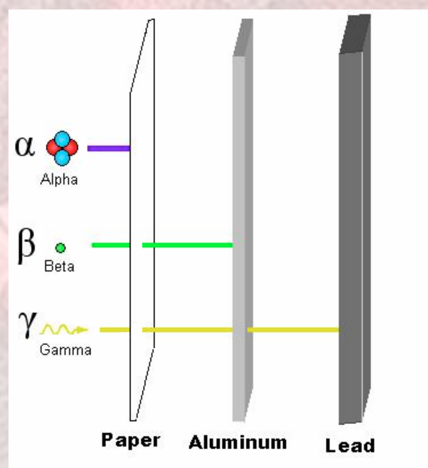
Radioactive Decay

- Ionizing radiation

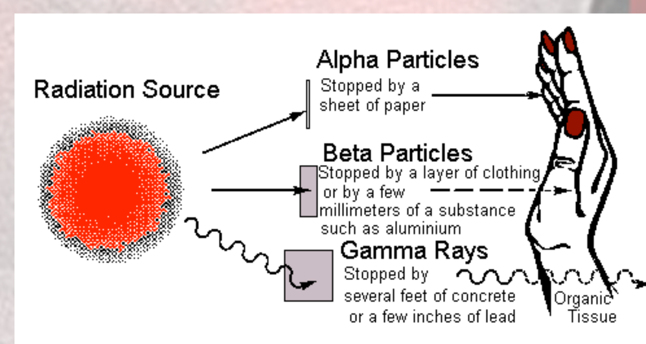
- Most radionuclides do not become stable with one decay.
- There is usually a chain of radioactive decays that the radioactive element undergoes to become stable, and this radioactive decay chain process is called *transmutation*.
- The energies associated with these decays are usually in the MeV range and are capable of breaking chemical bonds.
- These decay products are called *ionizing radiation* since they can interact with matter and produce ions in the body.



http://upload.wikimedia.org/wikipedia/en/3/33/EM-spectrum.png



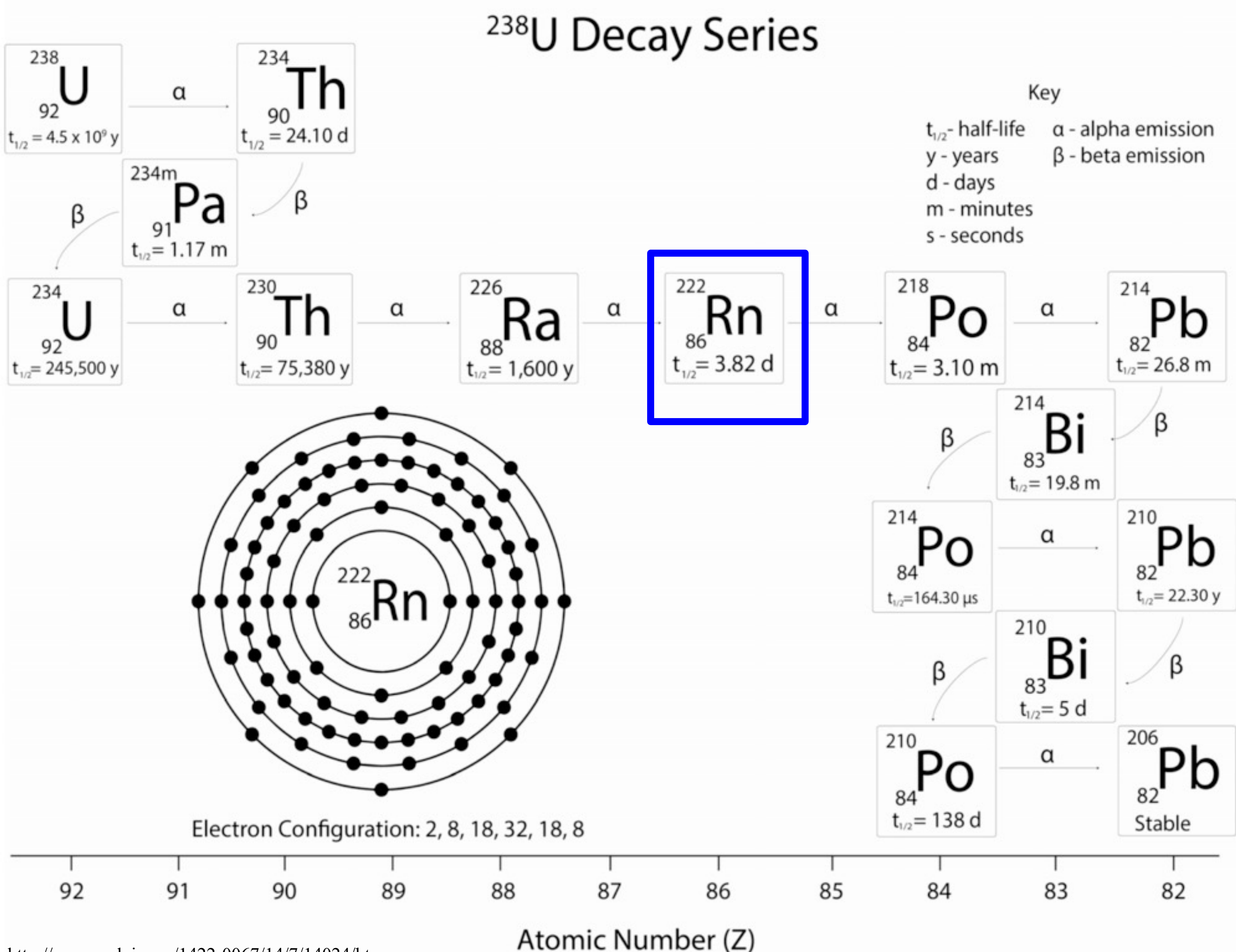
http://upload.wikimedia.org/wikipedia/commons/a/ae/RadiationPenetration2-pn.png



http://www.ims.uaf.edu/orion/physicsweb/images/ionize2.gif

Radioactive Decay

- Ionizing radiation



http://www.mdpi.com/1422-0067/14/7/14024/htm

Radioactive Decay

- The Radioactive Decay Law

- For a given radioactive sample the number of radioactive atoms that decay (to form something more stable) is proportional to the number of radioactive atoms present.

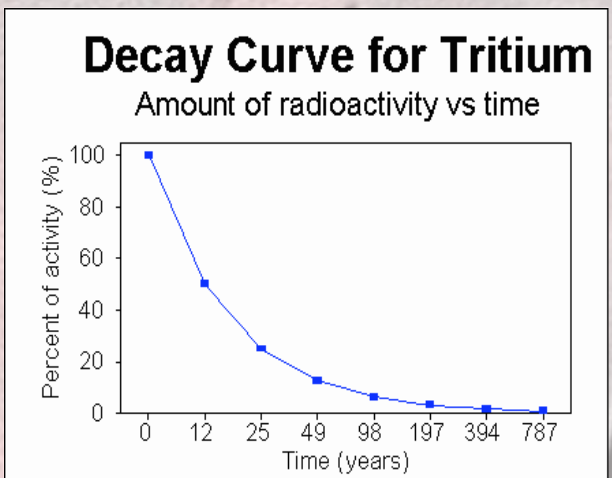
- The decrease in the number of radioactive atoms, mass of radioactive atoms, or activity of radioactive atoms is experimentally found to be exponential in time.

- The radioactive decay law is written as:

$$N = N_0 e^{-\lambda t}$$

$$m = m_0 e^{-\lambda t}$$

$$A = A_0 e^{-\lambda t}$$



http://wwwchem.csustan.edu/chem3070/images/tritium.gif

- Where N, m, & A are the number, mass, and activity of radioactive sample as a function of time.

- λ is called the decay constant and varies for each radioactive element.

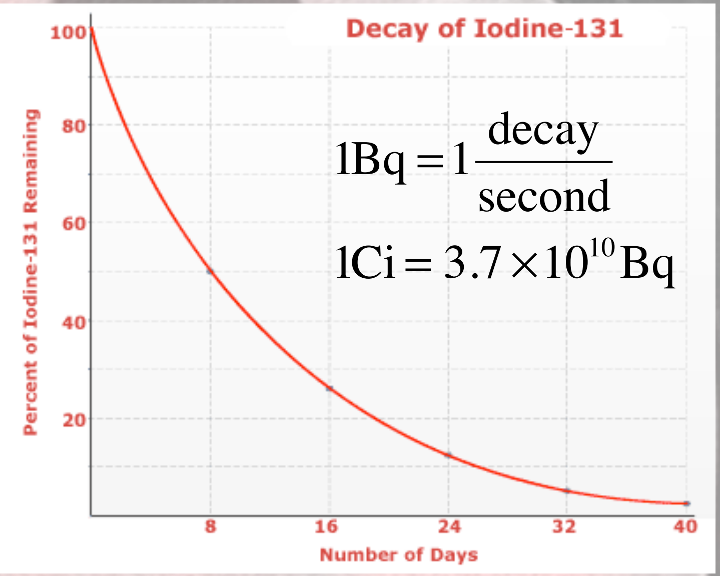
Radioactive Decay

- The Radioactive Decay Law

- The most useful quantity to measure is the activity of the sample.

- From the decay curve you can determine the *half-life* of the radioactive sample and the radioactive decay constant can be determined since it is related to the *half-life*.

- The *half-life* is the time it takes for the activity of a radioactive sample to decrease to ½ of its initial value.



$$1\text{Bq} = 1\frac{\text{decay}}{\text{second}}$$

$$1\text{Ci} = 3.7\times10^{10}\,\text{Bq}$$

http://wps.pearsoned.ca/wps/media/objects/4050/4148005/i_decay_curve.gif

- Activities are usually measured in units called a *Becquerel* (Bq) or a *Curie* (Ci).

- What is the half –life of the $^{131}_{53}I$ sample?

- What is the decay constant for $^{131}_{53}I$?

- A large λ means that the radioactive sample is very active.

Radioactive Decay

- The Radioactive Decay Law

- If you were to inject a patient with $75\,mCi$ of radioactive iodine ${}^{131}_{53}I$. How long would you have to wait for the activity to decrease to 0.05% of the initial injection amount? A Curie is a unit of activity, and it is related to the number of radioactive decays per second, the Becquerel by the relation $1Ci = 3.7{\times}10^{10}Bq = 3.7{\times}10^{10}\frac{decay}{s}$.

- Suppose that the half life of ${}^{40}_{19}K$ is $1.25Gyr$, the ratio of radioactive potassium to stable potassium $\frac{{}^{40}_{19}K}{{}^{39}_{19}K} = 0.012\%$, and that the amount of potassium in an average banana is $450mg$. What is the activity of an average banana if we assume that average mass of a potassium atom is $39.962767\frac{g}{mol}$?

Radioactive Decay

- Radiolabeling and the effective half-life

- Most radionuclides are introduced into the body attached to a molecule or drug.
- This process is called *radiolabeling* and falls under the heading of *radiopharmacology or radiopharmaceuticals*.
- The time the body retains a radiolabeled chemical may be very different from the physical half-life of the substance.
- The biological half-life is defined as T_B and the nuclear half-life of an isolated element is defined as $T_{\frac{1}{2}}$.
- T_B depends on the chemistry and the physiology of the body processes.
- The effective half-life of a radiolabeled drug is given as: $\frac{1}{T_E} = \frac{1}{T_{\frac{1}{2}}} + \frac{1}{T_B}$.
- The effective half-life is the time it takes the body to clear ½ of the radiolabeled drug.

Radiopharmaceuticals & Radiopharmacology

- Radiopharmaceuticals fall into one of two fundamental categories:
  - diagnostic or therapeutic.
- The ideal diagnostic radiopharmaceutical is one that:
  - is a pure gamma (photon) emitter,
  - has an energy in the range of 100 to 250 keV,
  - has a half-life in the body of 1 to 2 times the duration of the test,
  - exhibits a high target–nontarget ratio (meaning that it is especially concentrated by the organ or tissue of interest),
  - involves a minimal radiation dose to the patient,
  - is inexpensively produced and can be safely produced and handled.

Positron Emission Tomography (PET)
- The basic idea

- *PET* scans are a non-invasive imaging technique.

- *PET* scans differ from some other imaging techniques in that *PET* scans are based upon metabolic activity.

- *PET* scans require the injection of a small amount of biologically relevant material like oxygen or glucose (sugar) which have been labeled with radionuclides such as ${}^{11}_{6}C$, ${}^{13}_{7}N$, ${}^{15}_{8}O$, and ${}^{18}_{9}F$ (${}^{18}_{9}F$ being the most common).

- ${}^{18}_{9}F$ is very useful because of its long half-life (109 min), and because it decays be emitting positrons having the lowest positron energy, which generally allows for the sharpest images with a high-resolution *PET*. (*PET* scan times ~ 15 to 30min WB with a wait time after drug administration of about 60 min.)

- Once introduced into the body, organs and tissues process these radioactive agents as part of their normal metabolic function.

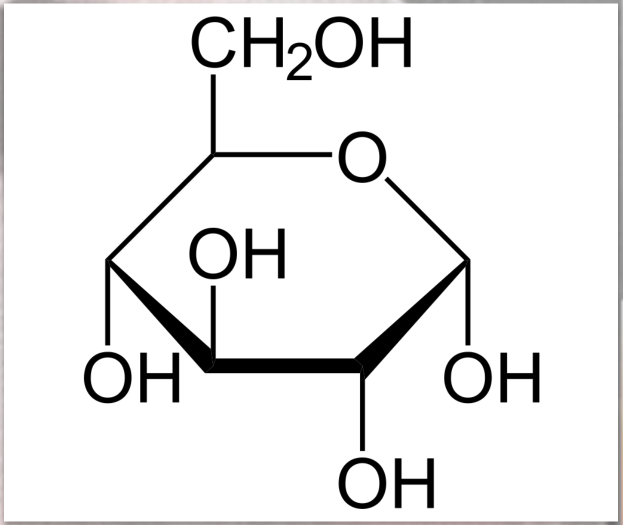
- For example, brain cells need sugar in the form of glucose to operate; the more they operate, the more glucose they require.

- The more metabolically active an area the more glucose that is needed there.

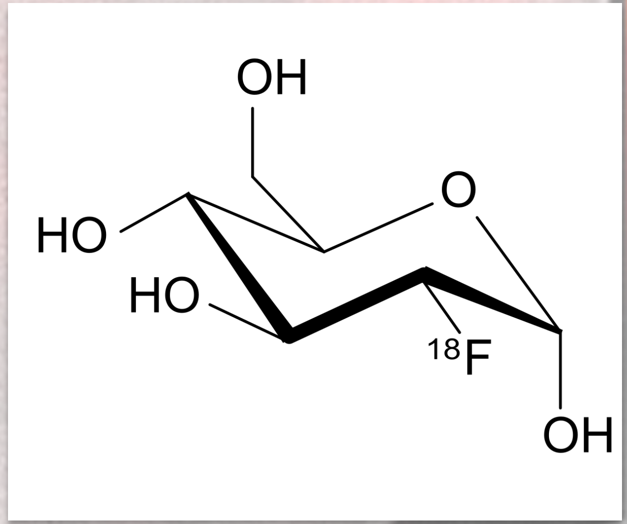
Positron Emission Tomography (PET)

- The basic idea

- *2-fluoro-2-deoxy-D-glucose* (*FDG*) is a radiolabeled drug that contains $^{18}_{9}F$.
- This drug has the radioactive fluorine substituted for a hydroxyl group (OH^{-}).
- FDG follows the same transport route as glucose.
- Glucose, once inside the cell, undergoes glycolysis to produce energy.
- FDG once inside of the cell, cannot undergo glycolysis since it is missing the OH^{-}.
- This traps the FDG in the cell and FDG is a good reflection of the glucose uptake in cells.
- Malignant cells replace oxygen respiration by fermentation of sugar, so they accumulate FDG at a higher rate than normal cells and the uptake can be measured.



https://en.wikipedia.org/wiki/Glucose



https://en.wikipedia.org/wiki/Fluorodeoxyglucose_(18F)

Positron Emission Tomography (PET)
- The basic idea

- The $^{18}_{9}F$ is a positron emitter and the positron that is emitted travels a small distance (maybe a few millimeters) before encountering an electron.

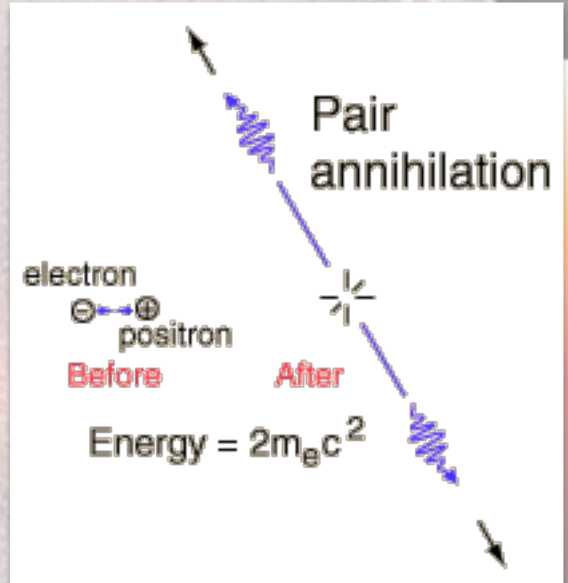
- The system is "at rest" at the time of annihilation.

- The electron-positron pair annihilates and to conserve momentum and energy produces two high energy gamma rays at almost 180^0 from each other.

- Created are two $511keV$ photons that are detected coincidently.

- The detector only detects coincident pulses, and the photons are allowed to lag in time due to different distances of travel out of the body.

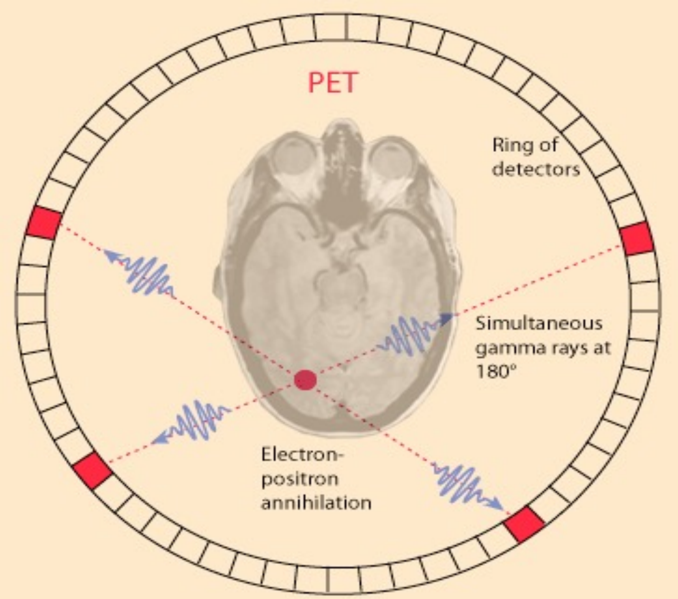
- If two gamma ray photons are detected, separated in time by $\Delta t = 0.1ns$, what resolution ΔL of the detection?



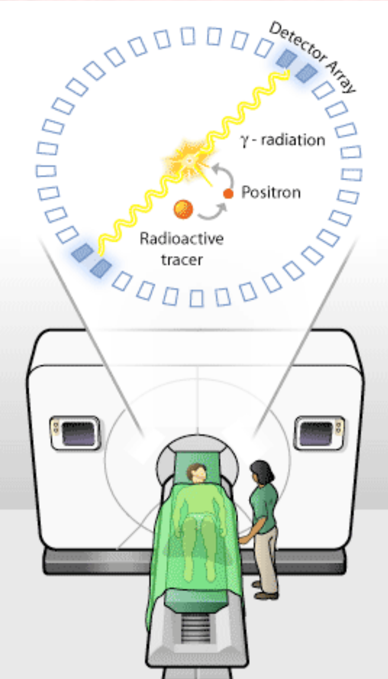
http://hyperphysics.phy-astr.gsu.edu/hbase/Particles/imgpar/annih.gif

Positron Emission Tomography (PET)

- Gamma ray detectors surround the patient and detect the coincident gamma rays.
- These detected gamma rays give spatial information about the active metabolic site.



http://hyperphysics.phy-astr.gsu.edu/HBASE/NucEne/imgnuk/petscang.gif



http://www.csulb.edu/~cwallis/482/petscan/pet_lab.html

- From the differences in detection times, a time-of-flight analysis can be used to determine where the annihilation occurred.
- Spatial uncertainty in the annihilation localization sets the limit to the detection precision of the scanner.
- *PET* scans do not give anatomical information only metabolic activity in each area.

A Combination PET and CT Scanner

https://www.gehealthcare.com/products/molecular-imaging/pet-ct/discovery-mi-gen-2

Positron Emission Tomography (PET)

- A case study

- Normal distribution of FDG. Anterior reprojection emission FDG *PET* image shows the normal distribution of FDG 1 hour after intravenous administration.

- Intense activity is present in the brain (straight solid arrows) and the bladder (curved arrow).

- Lower-level activity is present in the liver (open arrow) and kidneys (arrowheads).

- *i* is the site of FDG injection.

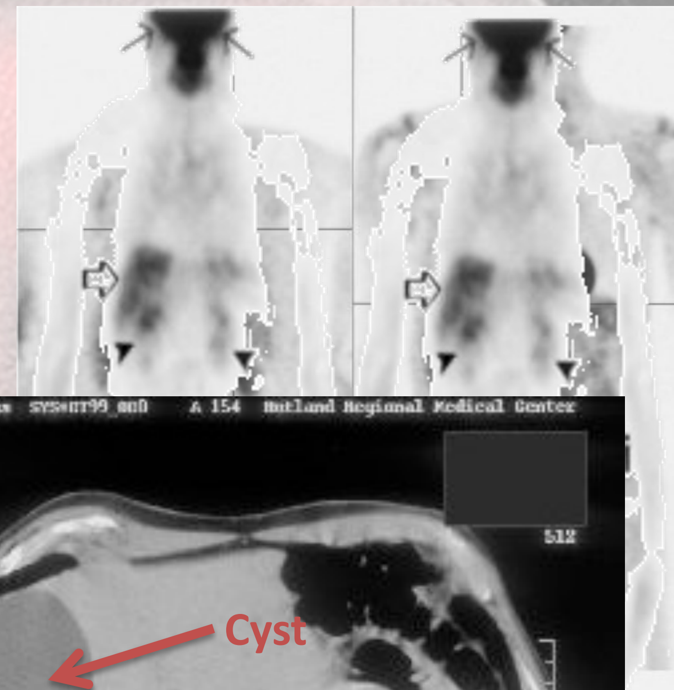
Shreve P D et al. Radiographics 1999;19:61-77

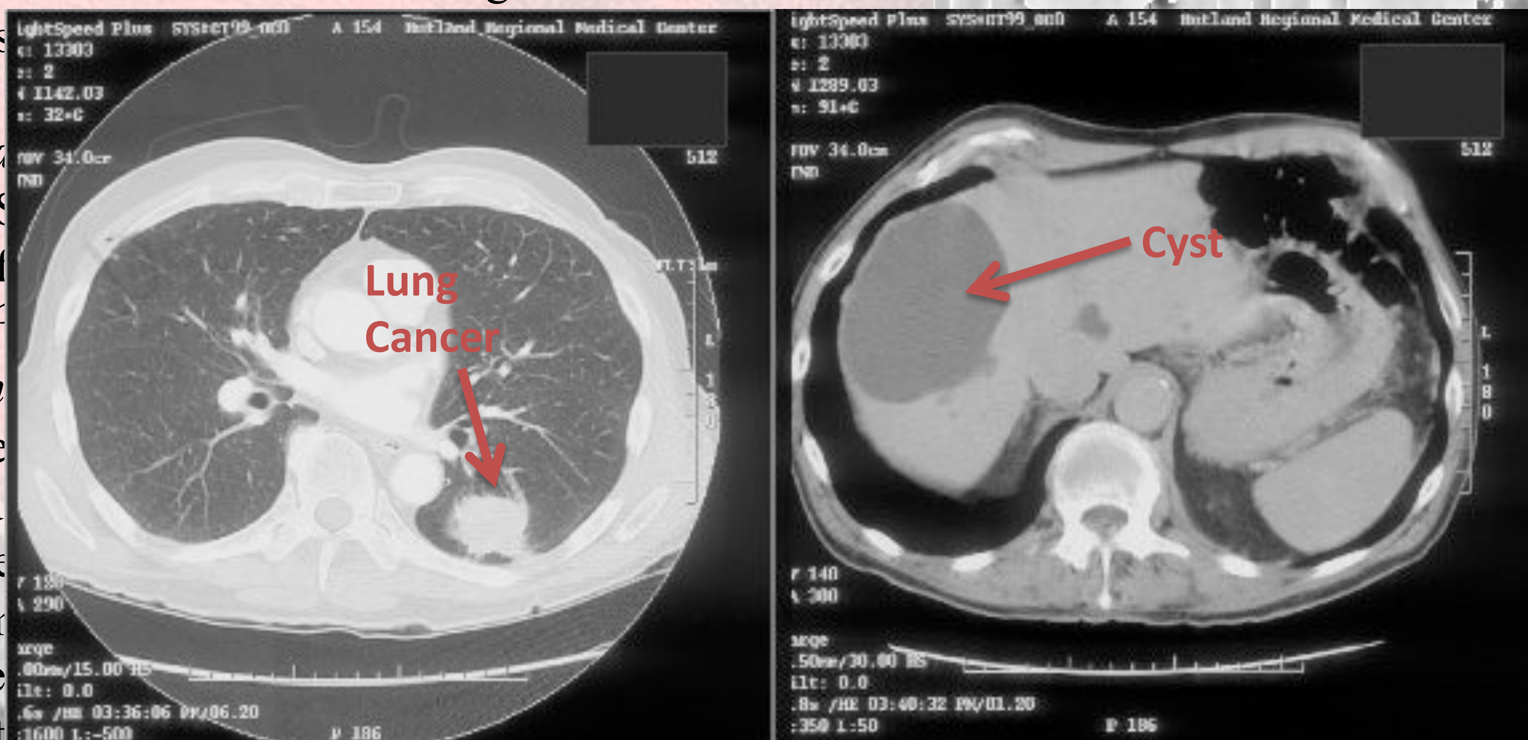
Positron Emission Tomography (PET)

- A case study

Clinical data

- A 75-year-old man had an abnormality detected on a routine chest x-ray. A subsequent CT scan of the chest and then a PET scan were performed. On the right are two sets of coronal images from the PET s





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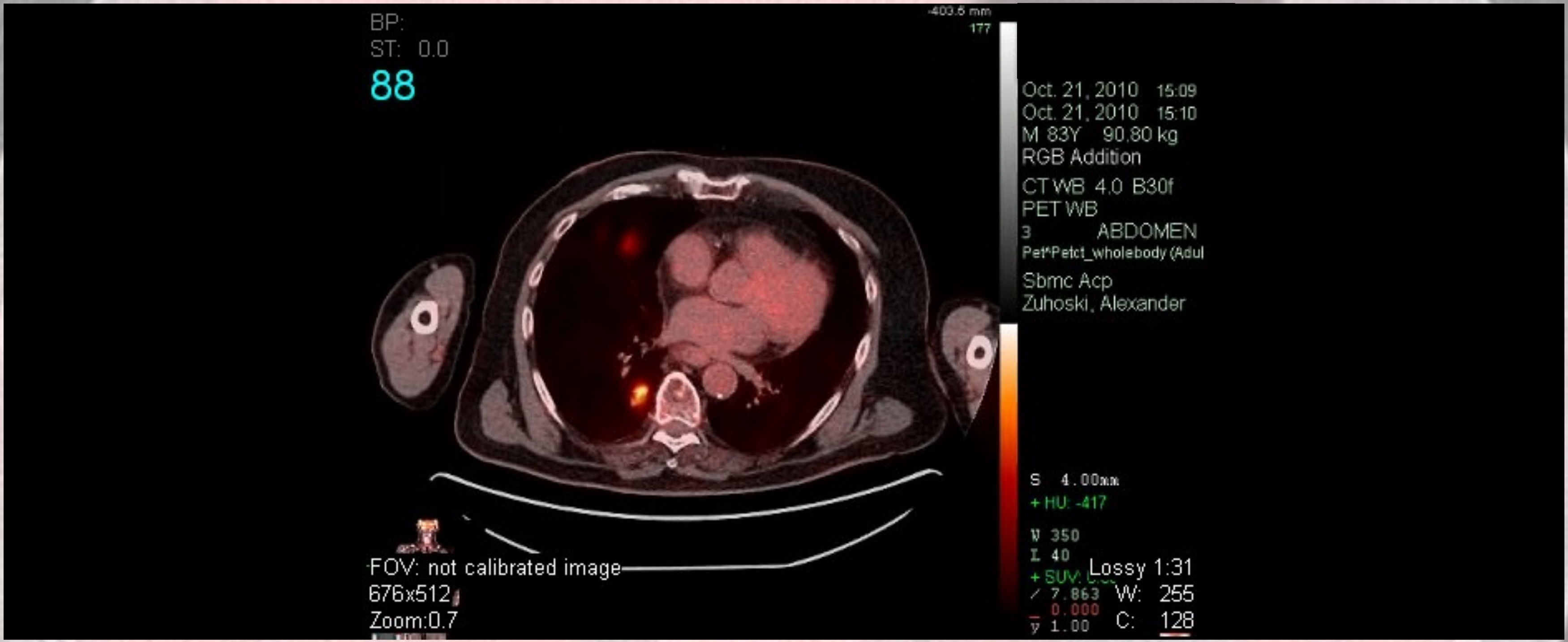
hepatic (liver) cyst.

Case study: http://www.dhmc.org/webpage.cfm?site_id=2&org_id=72&morg_id=0&sec_id=0&gsec_id=1508&item_id=15997

PET-CT Fusion

- A case study in lung cancer



- A 75-year-old male history of smoking. Whole body CT and whole-body PET imaging showed several lesions on the lung consistent with lung cancer.
- To see the anatomy and the metabolic activity a fusion of the WB CT and WB PET images was performed.

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* 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.

- *PET*-CT fusions offer the spatial resolution of the CT (to determine anatomy) and the metabolic activity from the PET scan to offer a better and more comprehensive patient diagnosis.