Cardiac Physiology using: Positron Emission Tomography (PET)

-What it can do

-How it works

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How is PET (and conv. Nuc med) different?

- Mammography, CT, US, (MRI):
  - Gives image of morphology (anatomy)
- PET (Positron Emission Tomography):
  - Image of *physiology*
  - Images of Biochemical Function

Nuclear Imaging

- Uses a tracer to follow biochemical Reactions
- In Nuc imaging
  - Attach a radioactive element (a "tracer") to the biochemical
    - "Label" the biochemical
  - Often ^{99m}Tc, or ^{131,123}I or with PET, other isotopes
  - Inject it (or swallow or breath it)
  - Image the radiation emitted (with Gamma Camera or PET camera)
  - Sensitive so am't injected is so small it does NOT influence physiology

Goal of Nuclear Imaging

- Trace fate of biochemical compounds
  - Static image of their distribution in organ(s)
  - Set of dynamic images: images as a function of time
    - Uptake by organ/tissue
    - Metabolism
    - clearance

Problems with conventional Gamma Camera (non PET) nuc imaging

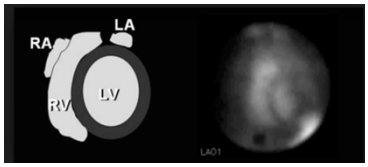
- Tc (etc) not naturally present
  - Usually must chelate it (e.g. DTPA, etc)
- Labeled biochemical -> not exactly same behaviour as unlabeled form
- Gamma Camera is Sensitive, but not as sensitive as we'd like
  - Conventional nuc imaging
    - Still many 100s of times more sensitive than MRI
- Can't measure absolute amounts of tracer – only relative

Two kinds of images of cardiac "function"

- Biochemical function
- Mechanical function
  - Fraction of blood pumped at each beat
  - Track edges of LV with time
    - Compute volume from area of each slice
  - OR (with nuc) directly measure blood volume with time

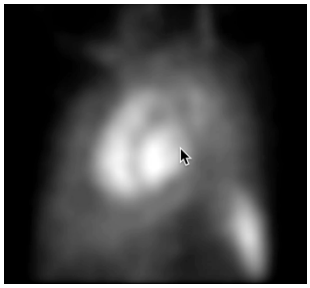
Mechanical Function by Gated Blood Pool (MUGA)

- Label blood with tracer
  - Many ways to do this (RBCs or even albumin)
- Am't radn emitted Prop to Blood Volume
  - #photons emitted prop to blood volume
- Draw contour including LV (doesn't have to be that accurate)
- Plot #photons detected vs time
- No need to make it tomographic! So only 1 contour total, or 1 per time point.

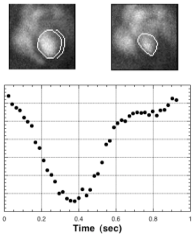


ED ES

Intensity prop to blood volume



photons vs time gives relative LV volume over time



From this curve can measure

- Ejection Fraction
- Ejection Rate
- Filling Rate
- Length of Diastasis
- % filling due to atrial contraction

Remember:

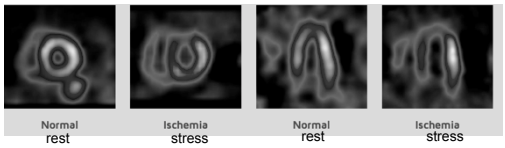
Doesn't depend on accurate edge definition

Only need a small number (usually only 1 or 2) contours

In addition to mechanical function

- Can measure relative perfusion to heart muscle.

(Non-PET) Myocardial Perfusion scan



- See relative perfusion at rest and stress
- Angiography (CT or Catheterization Lab)
  - Get estimates of degree of blockage
  - %stenosis
- Myo perfusion
  - Visualize SIGNIFICANCE of stenoses
- (Not absolute flow)

How is PET different?

- Image of *physiology*
- Images of Biochemical Function
- Can make absolute measurements
- *Can measure actual ngm/ cc of biochemical*

ONE reason PET can do this

PET Radioisotopes (positron emitters)

- Biochemically Important Atoms
  - ^{11}C (20 min.) - cyclotron
  - ^{13}N (10 min.) -cyclotron
  - ^{15}O (2 min.) -cyclotron
  - ^{18}F (2 hours) -nearby (few 100 Km) cyclotron
  - ^{82}Rb (1.3 min) -generator - no cyclotron

PET

For Example:

- replace a Carbon atom with *radioactive* Carbon atoms
  - Labeled biochemical behaves IDENTICALLY to original
- Inject biochemical into blood
- PET "traces" the biochemical as it is used by the body.
- PET makes images of the biochemical within the body
  - At one time point
  - As a function of time.

Cardiac Metabolism

- Glucose (^{18}FDG) – routine clinical
  - ^{18}FDG readily available for puchase
- Acetate (11-C-Acetate)
  - regional oxygen utilization (?)
- Fatty acids (11-C Palmitate)
- Amino Acids (13-N Glutamate)

Myocardial Blood Flow

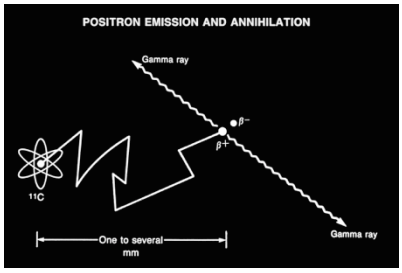
- ^{15} O-Water
- ^{13}N-ammonia
- ^{82}Rb (routine clinical PET)
  - Is a potassium analog
  - No cyclotron
  - Generator produces it for about 4 weeks.

What is a positron?

- Its given off by the nucleus of the PET radionuclide
- Its just like an electron but + charged
- It's the ANTI-matter of an electron

What does positron do in body?

- Just like an electron, bounces around off other atoms
- Travels a fraction of a mm or up to a few mm as it slows down
- Slows down and eventually spends too much time near its anti-matter sister, the electron

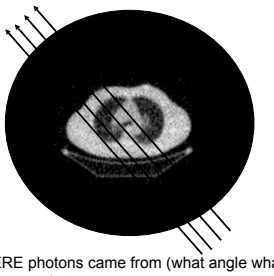


How can we use this phenomenon to make tomographic images?

How does PET work?

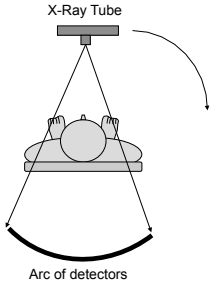
- (nearly) All tomography works the same way
  (CT, SPECT, MR, our eye-brain…)
- Need "views" of the object from all angles
- Reconstruct those views into tomographic slices

Need "views" (projections) from all angles



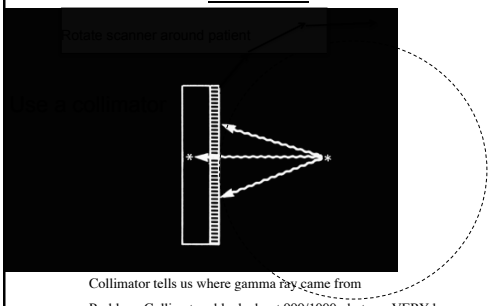
Tomography:
Need to know WHERE photons came from (what angle what position)
Need to know how many photons

CT scanner



- Need to know WHERE photons came from
- Along line between detector and Xray Tube

SPECT (Single Photon Emission…)
Need to Know WHERE Photons Came From

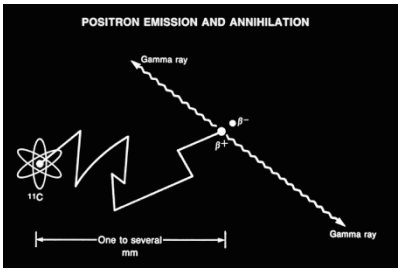


Collimator tells us where gamma ray came from

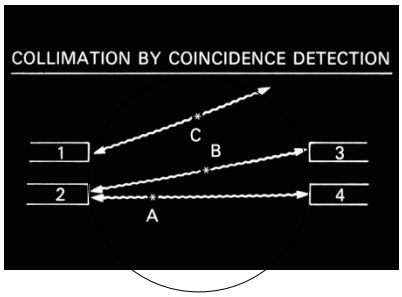
Problem: Collimators block about 999/1000 photons. VERY low sensitivity device.

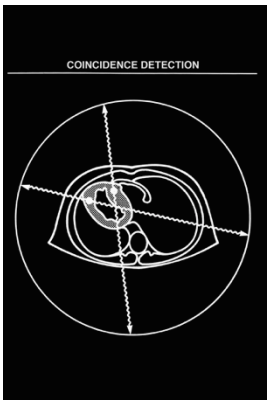
PET scanners

- How do they work??
  - How do they tell where photons came from??



PET doesn't need a collimator to tell direction gammas came from





PET Sensitivity

- 10^{-10} - 10^{-11} atoms
- Sub Picogram/cc quantities

PET is Quantitative

- PET can measure *absolute* [biochemical] in ngm/cc

PET Scanners

- 30 - 60 slices over >15 cm FOV
- 4-6 mm resolution in plane
- 4-10 mm resolution axially (2-5 mm slice separation)
- ~ 50-100 x more sensitive than 2 headed SPECT and 1000's of times more sens than most MRI
- Combined with CT scanners (not so imp for heart)
- (more recently, combined with MRI scanners)

By labeling appropriate biochemicals

PET Can Measure

- **Metabolism** (glucose, fatty acids, oxidative metabolism, [amino acids],...)
- **Blood flow** (absolute - ml/min/gm or relative)
- **Blood volume** (ml/gm)
- **Receptor concentrations**
- **Absolute [biochemical compounds] (n-gm/cc)**

Using PET to measure Physiology

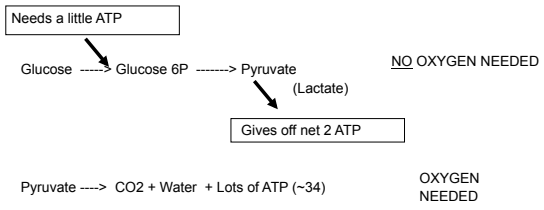
Two examples

- Tissue energy consumption
- Blood flow

Glucose Metabolism

- Why is it important in cardiology?

Aerobic vs anaerobic glucose metabolism



Note: Just Bacharach's version of biochemistry - don't trust details

Metabolism of Glucose (one molecule)

- 1st steps (called "glycolysis")
  - Don't require oxygen
  - Produce 2 ATP's of energy
  - DOES require "spark" of energy
- 2nd steps
  - DO require lots of oxygen
  - Produces 34 more ATP's of energy
- Therefore:
  - Very LITTLE energy produced/molecule w/o oxygen
  - LOTS of energy producec/molecule with oxygen
- A cell needs certain amount of E
  - If there is Oxygen -> don't need much glucose
  - If no oxygen -> need LOTS of glucose

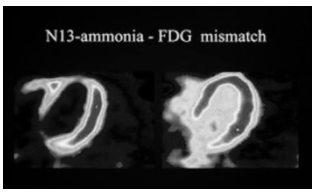
Cardiac cells vs Cancer Cells

- Tumors are often oxygen starved
  - Grow fast
  - in places with no capillary supply
- Normal cardiac cells have lots of oxygen
  - Can make lots of E for small amount of glucose
- Myocardial cells may be oxygen starved
  - Coronary vessel blockage
  - still need energy to survive & pump blood
  - Switch from aerobic burning of glucose to anaerobic
  - Produces 15 x less energy per glucose molecule
  - So must burn LOTS of glucose
  - OR go into "hibernation" – don't contract much, don't use too much E
- Tumor OR ischaemic myocardium both will burn more gluose than normal tissue for same E consumption
  - Increased uptake of glucose (and of FDG)

Can use these facts to determine:

Cardiac Viability

- Surgeon does NOT want to try a bypass if the muscle is already dead
- Glucose metabolism
  - needs initial ATP to start the process
    - ATP is produced only by LIVING cells
  - Therefore if there is glucose uptake, tissue is alive

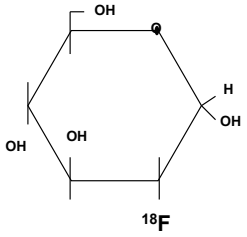


What is "FDG" and why is it a good PET tracer?

Why not just :

- Label glucose with ^{11}C
  - Bad idea
  - The $^{11}C0_2$ goes all over the place
- Can't image where the glucose was when it was metabolized

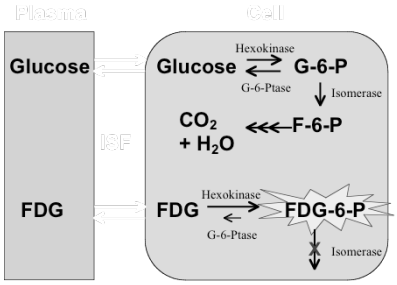
^{18}F-Fluoro-Deoxy-Glucose (FDG)



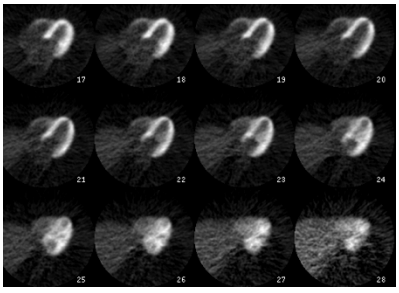
'Molecule of the Century'
- Henry Wagner

Patient injected activity: 10 mCi ~ 1 nano-gram
($6.4*10^{-12}$ moles = $3.8*10^{12}$ molecules)

How Cells "burn" Glucose and F-DeoxyGlucose

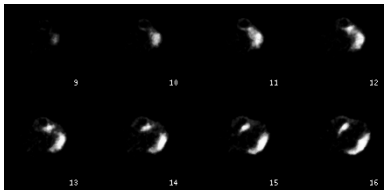


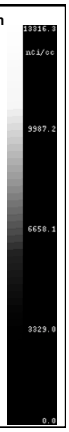
FDG Static Images (5 mCi, "3-D" mode)



GE Advance, 5 mCi FDG, 28 min post inj., 30 min scan

4.25mm/slice



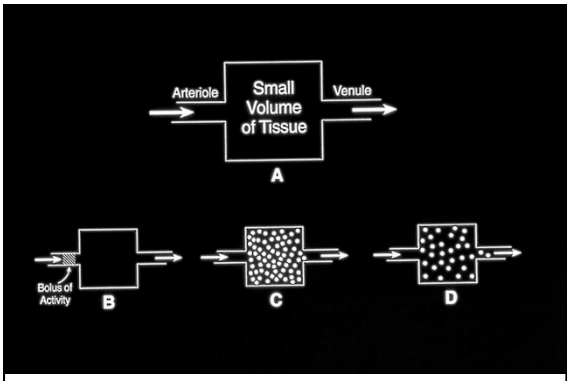


TO get absolute flows/metabolic rates Need Physiologic/mathematical model

- Physiologist/physician/physicist work together
- Make model of what happens to biochemical
  - It may depend on blood flow, metabolism, etc
- Take PET data over time (wash-in/out)
- Use model to measure absolute quantities of blood flow, metabolism….

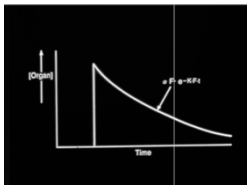
Some tracers

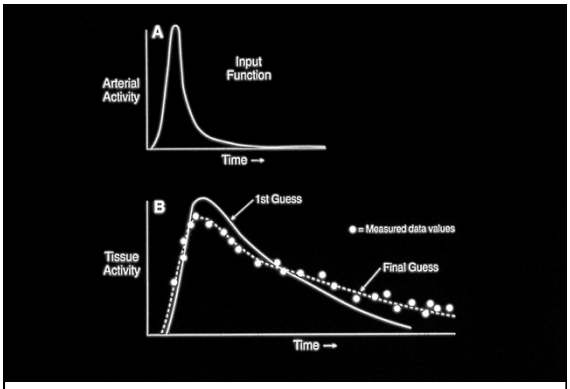
- Not metabolized at all
- Have a simple model
- Water is good example ($H_2{}^{15}O$) – can be used to measure blood flow



In this simple model:

- tracer washes out exponentially with time
- exp constant = flow



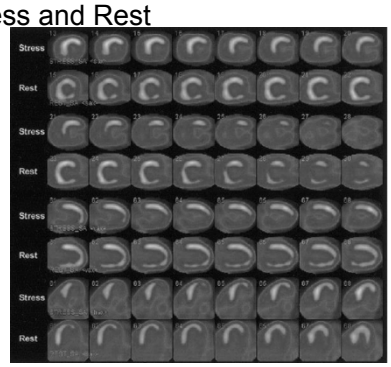


Other Models

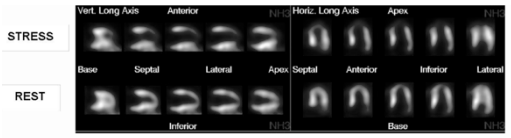
- Let you measure absolute myocardial blood flow from:
  - $^{13}NH_3$ or ^{15}O-water (requires a cyclotron)
  - ^{82}Rb (Routine clinical -no need for cyclotron)
- Absolute metabolic rates (e.g. of glucose)
- Other physiologic parameters from a variety of labeled biochemicals

^{82}Rb at Stress and Rest

- DiCarli et al
- In Obese women
  - Sens: 95%
  - Spec: 90%



Absolute flow from $^{13}NH_3$

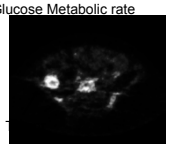


(Schindler TH et al, JACC Cardiovasc Imaging 2010)

Physiologic Imaging with PET

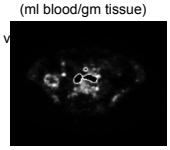
(1 Slice of 35)

Glucose Metabolic rate

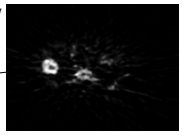


Blood Volume Image
(ml blood/gm tissue)

Small v

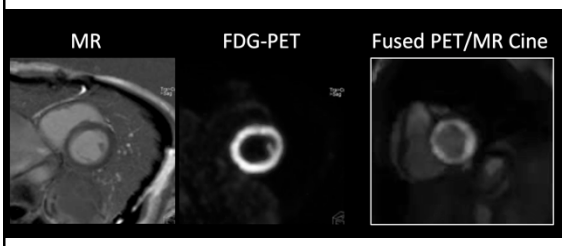


Blood Flow



Avg. tumor blood
flow = 3.6ml/min/gm

Combining PET and MR
PET Glucose + DCE MR
for “perfusion”



Lau et al Wash. Univ. Delayed Contrast enhancement + FDG)