MRSC2501 – Lecture 2 – PET

Describe how a PET scanner works

- Patient is injected with a positron emitting radioisotope which is distributed throughout the patient
- Patient is placed on a flat table that moves in increments through a gantry
- Gantry contains a circular detector array which has a series of scintillation crystals connected to PM tubes
    - Radioactivity distribution is estimated by back-projections
- The radiation that is detected is the result of pair annihilation of a positron and an electron, causing 511-keV photon pairs to be produced travelling in exactly opposite directions
- Photons produced this way are detected if two detectors subtended by 180^o both detect the photons within 10^{-9} seconds (6-12 nanoseconds)
- The light is converted into an electrical signal using a PM tube which is then processed by a computer to generate an image
- The table is the moved slightly further into the gantry and the process is repeated
- This results in a series of thin axial slices of an area of interest in the body which can by assembled into a 3D representation
- The data from the detected photons are translated into a diagnostic image in a similar manner to that which is used for SPECT

Advantages of PET compared to SPECT

- Greater sensitivity
- Greater resolution
- There are positron emitting isotopes for elements of a lower atomic number

Disadvantages of PET compared to SPECT

- More expensive
- Shorter half-life

Discuss why 18F is the preferred isotope for use in PET

Production

- Radionuclides must be positron emitters = β^+
- Positron emitting radionuclides are usually produced in cyclotrons by the bombardment of stable elements (parent isotope) with protons of helium nuclei
- The radionuclides produced in this manner have an excess of protons meaning they will decay by the emission of protons

Characteristics

- PET radionuclides have hale-lives of seconds, minutes, or a few days, which include:
    - C-11
    - N-13

- O-15
- F-18
- Cu-62
- Ga-68
- Rb-82

F-18

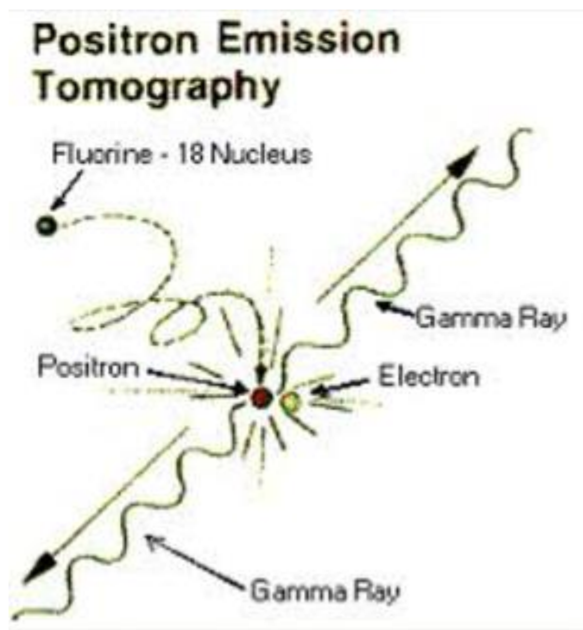
- The positron-emitting radionuclide used for whole-body PET/CT imaging is fluorine-18-deoxyglucose (FDG)
- C-11, N-13 and O-15 are all highly useful as they all replace atoms in molecules that are used in metabolism

Common Positron-Emitting Nuclides

Nuclide	Half-life (min)	Positron Yield (%)	Maximum Energy (MeV)	Method of Production
11C	20.4	99	0.96	Cyclotron
13N	9.96	100	1.19	Cyclotron
18F	110.0	97	0.64	Cyclotron
15O	2.04	99.9	1.72	Cyclotron
82Rb	1.27	96	3.35	Generator
62Cu	9.8	98	2.93	Generator
68Ga	68.1	90	1.90	Generator

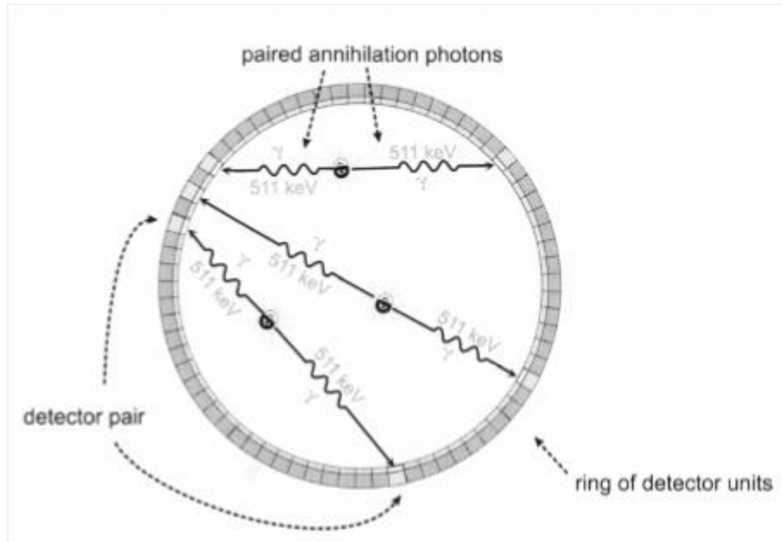
Describe annihilation coincidence detection

- when pair annihilation occurs between a positron and electron:
  - their rest masses are converted into photons ($E=MC^2$)
  - identical energies of 511 keV
  - emitted simultaneously 180° from each other (if at complete rest when they interact, otherwise the angle may slightly differ)
  - annihilation occurs between a few tenths of a mm to a few mm from the spot where the positron was emitted (this depends on the energy and the range of the positrons)



Annihilation co-incidence detection

- a detector ring works by assuming that if two photons are detected in close temporal proximity (time), by opposing detectors then it is likely that they originated from a single annihilation vent somewhere along the line between the 2 detectors
- Simultaneous detection is known as coincidence
- The detection of photons in opposing detectors defines the volumes from which they were emitted
- All coincidence events detected in an imaging period are recorded by the PET computer system as a raw data set
- This raw coincidence data is then reconstructed to produce cross-sectional images in all planes
  - if a stationary ring completely surrounds the patient then it is possible to acquire data for all projection angles simultaneously
  - allows for relatively fast dynamic studies and reduction of artifacts caused by patient motion



DETECTORS DON'T NEED TO BE EXACTLY OPPOSITE TO DETECT A COINCIDENCE

Coincidence Logic

- Coincidence logic is used to analyse the signals from opposing detectors
- Done by having the electronics attach a digital time stamp to the record of each time a photon strikes any detector
- This is done with the precision of 1-2 nanoseconds
- The processor compares the time stamp of detection events with those recorded in the opposite detector and if the difference is inside a coincidence timing window of 6-12 nanoseconds it is considered a coincidence event

Coincidence timing window

- A small window is required to allow for differences between detectors because of:
  - Signal transmit times through cables and electronics may differ
  - Different distances of travel for each photon (the event may not have occurred equidistant between both detectors)
  - Sometimes annihilation photons aren't exactly 180^{o} from each other
- A finite window width allows for other types of events to occur in coincidence

Anti-coincidence Detector

- Anti-coincidence detectors have square/rectangular sections
- The volume of the area being imaged is basically a rectangular shaped cross section with height equal to that of the detectors and length equal to that of the distance between the detectors (read about this below)

Electronic Collimation

- Sometimes only a 1 of the 2 photons will reach the detector due to the other photon in the pair being attenuated or absorbed in tissue
  - These events are called single events and are discarded
  - Single events make up a large proportion of the all the photons incident on the detector
- Because only coincidence events are detected and single events are rejected, a sort of electronic collimation is applied to the image
- This collimation makes PET scanners much more efficient than gamma cameras due to their count statistics (better signal to noise ratio) and better spatial resolution than gamma cameras

Discuss the different types of events that are registered by the detectors

True coincidence events

- Events that arise from a single positron annihilation
- Originate in the coincidence field of view (straight line connecting the 2 detectors the photon was incident on)

Scatter Events

- Originate in the patient but are detected in another detector pair's field of view
- Outside the coincidence field containing the source
- Undesirable as they contribute in an increase in image background counts, lowering the image contrast (if they are within the electronic collimation – the coincidence timing window)

Accidental (random) events

- Caused by the detection of gamma photons from different areas striking opposing detectors within the coincidence timing window
- Photons produced by independent annihilation events are detected as coincidence
- The probability of these events occurring increases significantly with the amount of radioactivity within the field of view of the scanner
- Hence these events are of most concern at high count rates

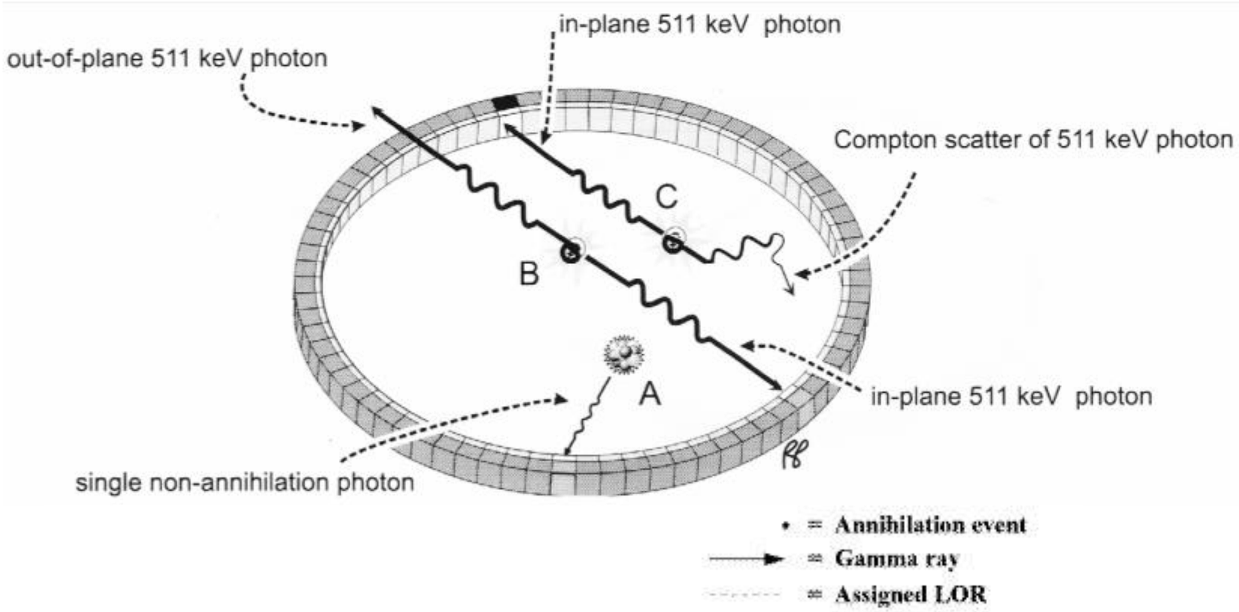
Single Events

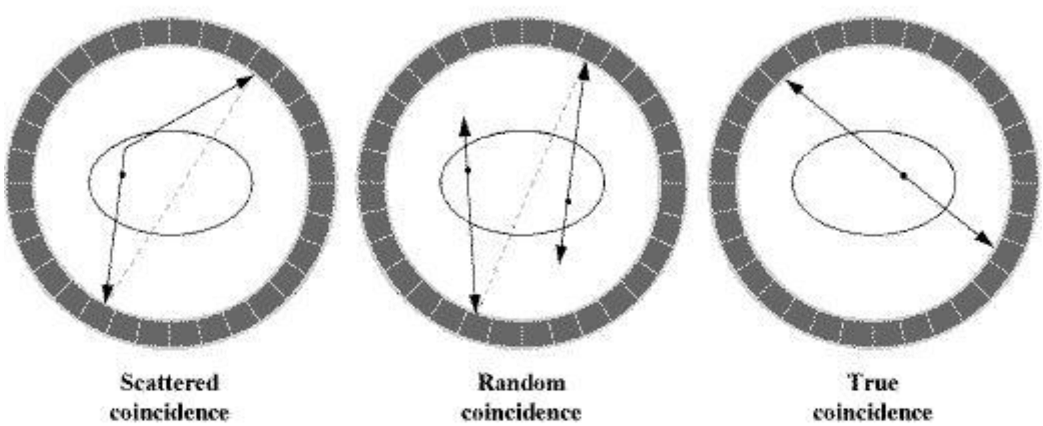
Three ways in which these occur:

- When an unpaired photon that isn't part of an annihilation event impacts a detector (A)
- When only one photon of a pair annihilation impacts on a detector and the other photon:

- Leaves the plane of detection – may hit bottom of one detect and go over the other- (B) or
- Is absorbed or scattered by the surrounding medium (C)

- These events are discarded





Time of flight techniques

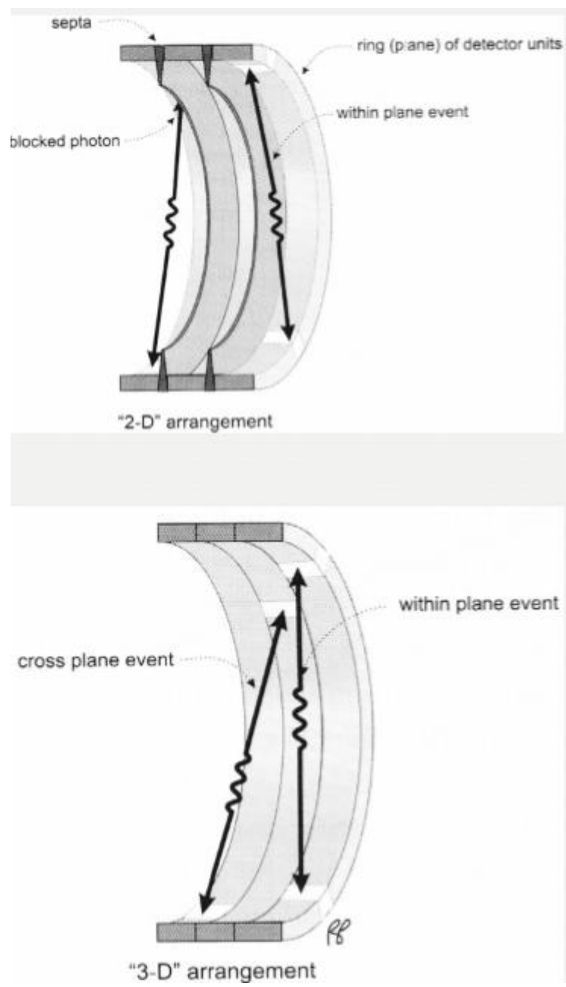
- Designed to improve the resolution of the system
- The point at which the annihilation occurs can be localized along the line of flight between the coincident photons by measuring the difference in time of arrival between the opposing crystals
- Unless the event occurs in the exact centre of the detector ring there will be difference in detected time between the detector pairs
- The time difference is proportional to the difference in distances travelled by the photons and can be used to pin point the position of the even along the line of response

Depth Resolution

- A 1cm depth resolution requires a timing resolution of ~66 picoseconds
- Electronic circuits are capable of measuring this
- The light output from scintillators are too low to provide this level of timing resolution
- The finite number of photoelectrons generated gives rise to a time jitter that adds to the uncertainty in event timing – this becomes worse with detectors of low light output
- With the fastest available scintillators and careful design of electronic components and connections, it is possible to achieve timing accuracy of a few hundred picoseconds
  - This is adequate to achieve localisation within a few cenitmetres
  - Images reconstructed with time of flight methods have a higher signal to noise ratio than those that don't

PET Attenuation

- Loss of counts due to the absorption of photons before they reach the detector
- The attenuation coefficient for 511-keV photons are nearly uniform across various kinds of body tissues
- Attenuation correction in PET is simpler and more accurate than in SPECT because of the relatively high energy of the annihilation-produced photon and coincidence detection



Describe the basic design of a PET camera

Components

- Ring of scintillator crystals
  - Rings may/may not be separated by septa
  - Each individual detector contains one or more segmented crystals or a collection of small crystals
  - A standard detector unit consists of a small crystal or small portion of a larger crystal attached to four PM tubes
- Photomultiplier tubes (4 per detector)
- Septa
  - Septal rings go along the entire length of the ring of detectors, separating each row so that photons from different rows aren't detected elsewhere
  - Septal rings improve resolution by reducing the amount of photons originating outside the plane of one ring of crystals
    - This reduces the sensitivity of the scanner as a significant fraction of true coincidence events are rejected
  - 2D scans have the septa in place
  - 3D scans don't have the septa in place

- Units have arrays of small detector elements (scintillators) as small as 4mm in size
  - Cut from blocks of BGO (bismuth germinate oxide)
  - Located in multiple rings around the patient
  - Small size gives better resolution
  - Located in front of the PM tubes
  - With this geometry, 48 slices may be scanned simultaneously

Discuss why there is a need got a different crystal detector in PET and determine what makes interactions in the detector accepted or rejected

Crystal - Material

- NaI crystals used in the rest of NM have a relatively low density compared to crystals used in PET
- This is because the NaI crystal s is lesser effective at stopping the higher energy photons, hence crystals with higher atomic number and density are required for PET which include:
  - Bismuth germinate oxide (BGO)
  - Leutetium orthosilicate (LSO)
  - Gadolinium orthosilicate (GSO)
  - Barium fluoride (BaF_2)
  - Caesium fluoride (CsF)

Crystal – Light Yield

- How much light is produced upon the gamma photon striking the scintillator
- Higher light yield is desirable
- The greater the crystal light photon output per keV, the greater the spatial and energy resolution
- Improved energy resolution improves the ability to distinguish lower energy scatter photons from high energy annihilation photons
- A larger number of light photons makes it easier to identify which crystal has been struck by the annihilation photon

Crystal – Decay Time

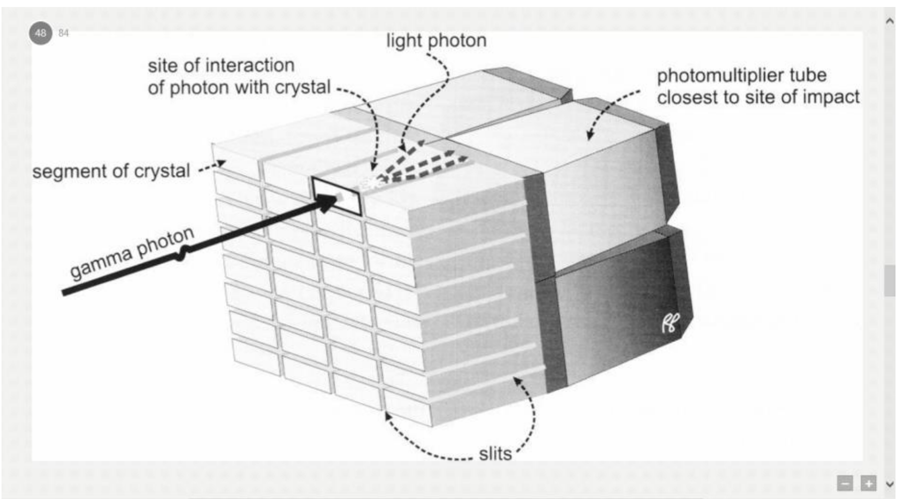
- A longer decay time results in a fewer number of photons that can be detected, and hence a lower sensitivity
- Short decay time is desirable for rapid imaging
- LSO and GSO have a shorter decay time

Properties of some scintillators used in PET scanners [adapted from Webb[2] and Ficke et al[20]]

Scintillator	Density (g/cm^3)	Effective Z	Relative Light Yield	Decay Constant (ns)	Emission Wavelength (nm)
NaI (Tl)	3.67	50	100	230	410
BGO	7.13	75	14	300	480
CsF	4.61	53	7	2.5	390
BaF_2	4.89	54	5	0.8	195, 220
			15	620	410
GSO	6.71	59	41	56	430
LSO	7.4	66	75	40	420

<u>Photomultiplier tubes</u>

- PET cameras (detectors) have many crystal subdivisions watched by a few PM tubes
- Light is channeled by the light between the crystal subdivisions
- Localisation of the site of impact of the annihilation photon upon the crystal is achieved by measuring the light detected in each PM (the closer the PM is to the site of impact, the stronger the signal generated by the PM is)



<u>Pulse Height Analyzers</u>

- Assess the energy of the interaction to see if it is within a given range, and if not it is rejected from storage
- The signals from the PMs are amplified by pre-amplifiers and amplifiers
- System electronics then determine which signals came from paired 511-keV coincident photons arising along a line of response between a pair of opposing detectors
- This is done by measuring the size of each signal, which is proportional to the energy of the photon incident on the crystal, or
- Recording the time of detection of the signal between opposing detectors

Timing discriminator

- Records the time the signal was generated

Coincidence circuit

- Examines the signals of adequate amplitude coming from opposing detectors and determines if the timing of the signals occurred within the coincided timing window
  - between 5-15ns depending on the decay time of the crystal material
- Events are only accepted if the time delay between photons striking opposing detectors is within the time window (as determined by the timing discriminator) and if the amplitudes of both pulses are within the accepted range (PHA)
- Random events are accepted as their amplitude and time discriminations are within the given range, despite being from different annihilation events and hence not detecting that the event occurred along the line of response

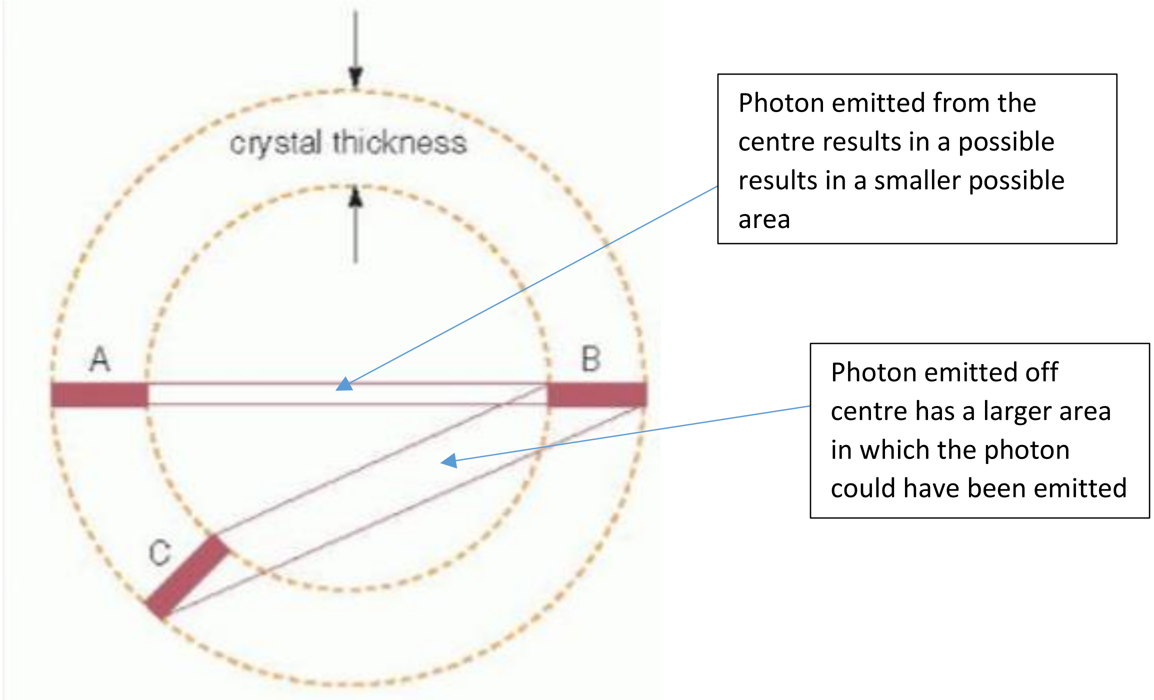
Discuss the main factors affecting spatial resolution in PET

- Modern whole body PET systems have a spatial resolution slightly better than 5-mm FWHM (full width half maximum) of the LSF (line spread function) in the centre of the detector ring
  - FWHM is the intersecting points on a graph between the y axis value that is equal to half of the amplitude of the curve and their corresponding x axis values
  - Used to measure the duration of pulse waveforms
  - Higher FWHM = lower spatial resolution
- There are 4 factors mainly affecting the spatial resolution of PET scanners:
  - Intrinsic spatial resolution of the detectors
  - Distance travelled by the positrons before annihilation
  - Annihilation photons not being emitted at exactly 180^o to each other
  - Parallax error

Detector resolution – intrinsic resolution

- Determined by the size of the detector elements
- Intrinsic resolution is the main factor affecting the spatial resolution of current scanners
- Spatial resolution of a PET system is the best in the centre of the detector ring and decreases with distances away from the centre
- This is due to the thickness of the detectors
- Uncertainty in the depth of interaction causes uncertainty in the line of response for annihilation photons that strike the detectors obliquely
- Photons emitted from the very centre of the detector ring can only strike the detector head on, as opposed to photons emitted away from the centre which strike the detectors at oblique angles
- Basically if the photons are emitted from the centre they will reach detectors EXACTLY opposite to one another and hence the area of the crystal they can strike is much smaller than if the

detector pairs are not exactly opposite to one another



- For a detector element of thickness ‘d’, a 1 dimensional slice through the response profile at mid-plane between the pair is a triangle with FWHM = d/2

Detector resolution – positron range in tissue

- The camera detects photons emitting from an annihilation event a distance from the true source
    - For low energy beta emitters such as F18, the range is fairly small ~1.2mm in water
    - For higher energy beta emitters such as Rb82, the distance travelled can be quite large ~12.4mm in water
    - Because higher energy beta emitters require a longer distance to slow down before they interact with an electron
- Because of this the resolving power is limited to the average range the positrons travel before undergoing annihilation in a specific tissue

Isotope	Max Positron Energy (MeV)	Max Positron Range (mm)	FWHM (mm)
^{18}F	0.64	2.6	0.22
^{11}C	0.96	3.8	0.28
^{68}Ga	1.90	9.0	1.35
^{82}Rb	3.35	16.5	2.60

Detector resolution – photon emission not at 180 degrees

- Known as non-co-linearity effect
- Photons don't always travel in exact 180 degrees paths due to the positron and electrons being in motion during the process of annihilation, altering the angle of ejection of the photons
  - This leads to a broadening of the angular distribution which is Gaussian with a FWHM of approximately 0.5
- The detectors assume a standard emission of 180 degrees and hence miscalculate the position of the annihilation event to occur on the line between the 2 detectors
- The amount of photon emission occurring at degrees other than 180 = 0.0022 x separation of the detectors (D)
- System resolution =
- $\sqrt{}$ (detector resolution)^2 + (positron range in tissue)^2 + (photon emission not occurring at 180^o)^2

Detector resolution – parallax (depth of interaction effect

- The resolution decreases at the periphery of the ring of detectors
- Some of the photons arising from peripheral annihilation events cross the ring of detectors at an oblique angle
- These photons may interact with one of several detectors along a long path
- When a photon interacts with a detector the annihilation event is assumed to have occurred along the line of response originating at the front of the detector since the depth of interaction is not recorded
- This effect is reduced for machines with a greater ration of detector ring size to patient size
- This is because the annihilation event will occur relatively more centrally and hence the photons will appear to cross the detector at a less oblique angle

Discuss the advantages of PET/CT imaging

Pet can detect more sites of disease than conventional anatomical imaging, however interpretation of PET can be difficult due to the lack of anatomical landmarks

Accuracy

- Localisation of the source is important as it essential for guiding biopsies, surgery and radiation therapy
- Also provides info for the stage of disease (has it penetrated the bone or is it contained in the soft tissue)
- Fusing CT/PET images helps guide biopsies by showing where the potential tumour is most metabolically active or which tumour is the most active

Guiding RT

- Combination imaging allows for better definition of planned radiation fields and sparing of normal tissues
- Tumour boundaries and metastatic spread have better definition
- CT imaging is reliant on changes in the tumour size, combining it with PET allows for us to see if the tumour size is maintained but the progression has halted or tumour necrosis has occurred as a result of successful RT treatment. Shown by changes of metabolic activity

Attenuation Correction

- CT provides more accurate and efficient attenuation correction compared to PET, making better images and faster scan times

Operation

- Modern systems use a multi-detector PET (4-16 slice) system and multi-detector CT scanner in a single couch which traverses the bore of both imaging components
- The patient is placed on the couch 30-60 minutes after intravenous FDG administration
- CT data is first acquired in ~30 seconds, followed by a repeat slower transit of the patient through the bore of the PET data acquisition for ~30-45 minutes
- The CT and PET data sets are co-registered electronically
- The data can then simultaneously be viewed as any percentage composition of these 2 data sets through superimposition

Design Features

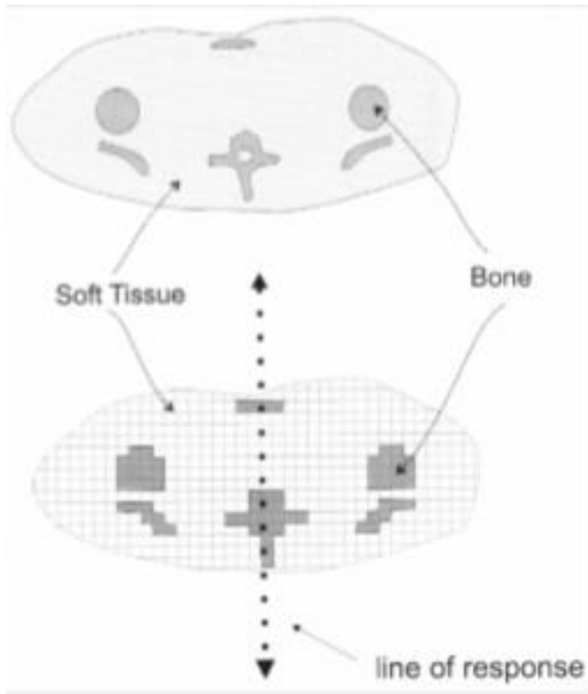
- PET-CT cameras are configured as sequential gantries with a shared bed (each machine is semi-independent and bed goes through both gantries one after the other)
  - Gantries may be completely separated to facilitate servicing of the machines
- This is done to maintain consistent positioning of the patient between the acquisitions of CT and PET data sets
- Acquisition allows for either data set to obtained first, but it is usually CT done first

Advantages

- The x-rays from the CT scan can be used as an attenuation map of density differences in the body which can then be used to correct for the absorption of photons emitted from fluorine-18-deoxyglucose (FDG) decay
- The attenuation correction essentially adds counts back into areas that are more attenuated due to the annihilation event occurring deeper in the body or surrounded by denser structures
- It also subtracts counts from areas that are attenuated much less – body surfaces, lungs…

Disadvantages

- X-ray photon energies are much lower than 511-keV photons
- The linear attenuation coefficients for bone and soft tissue must be scaled prior to being used to correct the emission data from FDG
  - The CT attenuation map is divided into pixels that correspond to bone and soft tissue
  - After the appropriate scaling factors have been applied to each pixel the attenuation along each line of response is calculated and used for the attenuation coefficient



Limitations

- Breathing artifacts due to the fact that the breath can be hold for the length of a CT scan but is not possible for the length of a PET scan
  - Misalignment near the diaphragm can cause mis-registration of images in the lower lungs and upper abdomen
  - Artifacts may be introduced in areas affected by breathing due to the CT data being used for attenuation correction
  - Can be avoided by instructing the patient to shallowly breathe for the duration of both scans
- Contrast agent artifacts can improve anatomical localisation, however it usually quite dense and can therefore affect the attenuation map
  - Greater attenuation will be detected at areas where there is more contrast, namely the colon or vascular filling with an intravenous bolus
  - PET photons are also attenuated by the contrast, however the location and distribution of the contrast may change between the 2 scans
  - The contrast will also diffuse into the soft tissues, affecting the attenuation coefficient scaling factors of soft tissues which are based on non-contrast CT x-ray attenuation