Gamma-ray imaging in medicine

Introduce a gamma-emitting radioisotope into body (attached to a biologically interesting molecule) and observe how it distributes through different organs.

"Diagnostic nuclear medicine"

"Functional imaging" – shows how organs are working, not just their structure ("physiology" not just "anatomy")

Can be used to learn about normal physiology (e.g. brain activity) in volunteers, or more commonly to diagnose illness:

- Tumours
- Heart defects
- Kidney problems, etc etc etc





Gamma camera (Anger 1957)

Consists of thin sheet (~10mm thick) of NaI(TI) scintillator, backed by an array of PMTs.

Gamma-ray interacting in scintillator produces a flash of light which is seen by several PMTs.

From the relative intensities in the different PMTs the coordinates of the centre of the flash can be determined

- original analogue cameras used a resistor circuit to perform linear mappings
- in a modern digital camera each PMT has its own ADC and from the digitized outputs a computer calculates the coordinates – this means that non-linear corrections can be applied.

Although the PMTs are typically 50mm diameter, the coordinates of the gamma-ray interaction can be determined to within a few mm ("intrinsic unsharpness").

As well as the position-sensitive detector, a camera also needs some way of forming an image (the equivalent of a lens).

In the case of the Gamma Camera, this is achieved by collimating the incident gamma-rays so that only those travelling in certain directions can hit the detector.

One could use a pinhole collimator, but a parallel hole collimator is much more efficient.

Parallel hole collimator

This consists of a thick lead plate (~20mm) with many parallel holes drilled through it.

The holes only transmit γ -rays close to normal incidence, so image is same size as object (magnification = 1)



Collimator transmits a cone of gamma-rays. Maximum angle transmitted is $\theta=w/L$, where *w* is width and *L* length of holes.

Each point in object contributes a circular image on detector, of diameter 2D0, where D is distance from object to detector.

Geometrical unsharpness increases linearly with distance from source.

Sensitivity (fraction of photons transmitted) is independent of distance D.

Septum penetration

The walls between the holes are called septa. For the collimator to work properly, we need the probability of a gamma-ray passing through a septum to be small. The worst case is as shown:



A bit of trigonometry gives

$$s = t \sqrt{1 + \frac{L^2}{\left(2w + t\right)^2}}$$

where s is the shortest path length through septa of thickness t.

Photon attenuation is $exp(-\mu s)$. Effective attenuation is often taken as $s=3/\mu$ [exp(-3)=0.05]. Since μ decreases rapidly with photon energy, higher energies need much thicker septa: For a collimator with L=20mm and w=1mm, the required septum thickness t would be:

Energy	μ	3/µ	t
100 keV	63 cm ⁻¹	0.48 mm	0.05 mm
200 keV	11.3 cm ⁻¹	2.7 mm	0.3 mm
500 keV	1.83 cm ⁻¹	16.4 mm	6.3 mm

Most collimators are designed to work with energies up to 300 keV.

Examples of radionuclides for diagnostic imaging

^{99m}Tc

- half-life 6 hours
- emits 140 keV gamma-ray
- no other harmful radiations simply decays by isomeric transition to ground state (essentially stable – half-life 10⁵ years)
- obtained from parent ⁹⁹Mo generator (half-life 66 hours)
- attached to various biologically-interesting molecules

^{81m}Kr

- half-life 13s
- Emits 190 keV gamma-ray
- No other harmful radiations daughter essentially stable (10⁵ years)
- obtained from decay of parent ⁸¹Rb (half-life 4.6 hours)
- gas used to image lung function

²⁰¹Tl

- half-life 73 hours
- emits mainly 167 keV gamma-rays
- decays by EC to stable ²⁰¹Hg
- cyclotron produced
- chemical analogue of potassium used for cardiac studies over a few hours.

Comparison of ^{99m}Tc-MAA [macroaggregated albumin] and ^{81m}Kr [gas] images. The gas is inhaled and provides a "ventilation study". The MAA is injected into the vein leading to the lungs and provides a "perfusion study" showing how good the blood supply to the lungs is. In a healthy person the two should match. Mismatches in blood supply indicate pulmonary embolisms (blockages in blood vessels serving lungs)



3D distribution of tracer can be found by rotating camera about body, measuring projected views at all angles, and using tomographic reconstruction

"Single Photon Emission Computed Tomography – SPECT"



Tomography (slice imaging)

In 2D, tomography involves measuring a complete set of line integrals through a slice of an object (for example, the total X-ray attenuation along each line through a slice of the body). Then image reconstruction is used to determine the contribution (eg attenuation coefficient) at each point within the slice.



The line is specified by its angle θ and its offset x'. In terms of the (x,y) coordinate system within the slice, the equation of the line is $x\cos\theta+y\sin\theta=x'$ The set of measurements (at varying offset x') for a particular angle. θ is called the parallel projection of the

particular angle θ is called the parallel projection of the object at angle θ .

The data consists of a complete set of parallel projections at angles 0 to π

(or 0 to 2π , but often the projection at angle θ + π is just the mirror image of the projection at angle θ).

Suppose we want to determine the value for each pixel in an NxN image (e.g. 256x256), then we need to make measurements at N points across each of N independent projections around body – gives N² independent equations for N² unknowns (but noise etc. means they are not exact) SPECT is similar, but gamma camera measures 2D projections of total activity at angles around a 3D region of body – then reconstruct specific activity at each point

Complications:

- Gammas are attenuated increasingly with depth need to correct for this, but don't know depth of source.
- Unsharpness increases linearly with depth.

SPECT image of brain (one slice) showing the uptake of methyltyrosin (amino acid) labelled with ¹²³I (EC, half-life 13 hours, gamma-ray 160 keV) compared with an MRI image of the same slice of the brain. SPECT clearly shows the presence of a brain tumour.



Positron Emission Tomography (PET)

Use a radionuclide that decays by $\beta^{\scriptscriptstyle +}$, emitting a positron. Positron annihilates with electron giving two back-to-back 511 keV photons.



Detecting both photons in coincidence defines a line of response (LOR) through the point of annihilation – "electronic collimation".

Because there is no collimator, sensitivity is higher than SPECT - dose to patient can be less.

Also, problems of attenuation, unsharpness can be solved – can make quantitative measurements of specific activity.

There are positron-emitting isotopes of biologically-important elements: ¹¹C (20 min), ¹³N (10 min), ¹⁵O (2 min) but most PET uses ¹⁸F because of the convenient half-life (110 mins) – can be attached to many organic molecules – in particular fluoro-deoxyglucose (FDG) is used to follow glucose metabolism

PET

Ed Hoffman (1942-2004) and Michael Phelps (1939-)



"Modern" PET scanner – 1987

Consists of one or more rings of detector blocks Typically two rings, each of 64 detector blocks. Records data only if two blocks detect γ -rays within interval τ

Detector block consists of single crystal of high-Z scintillator (e.g. bismuth germanate "BGO") ~40mmx40mmx30mm thick. 511 keV γ -ray has high probability of interacting in crystal. Crystal is divided by slots into 8x8 array of elements and is viewed by 4 PMTs (2x2 array)

By comparing the light intensity seen by the 4 PMTs, computer can determine which of the 64 elements the γ -ray interaction was in.

Elements are ~5mm x 5mm - determines intrinsic unsharpness.

In terms of elements, the scanner shown has 16 rings each of 512 elements [8192 elements in total].





Modern PET scanner consists of rings of thousands of small detectors



Also small animal PET scanners giving 1mm resolution



Provides very fine functional images



Unsharpness in PET

- 1/ Fundamental physics limits:
- positron range before annihilation: ~1mm (depends on nuclide)
- acollinearity electron momentum means photons deviate from 180° apart by ~0.5° – for a 1m diameter ring means line deviates by ~2 mm at centre

2/ In practice unsharpness is limited by "size" of detector elementsbest for human scanners is ~4mm

(there are dedicated small animal scanners that approach 1 mm resolution)

Attenuation correction



Probability that either of the two gammas is attenuated is $exp(-\mu s_1).exp(-\mu s_2)=exp(-\mu S)$

- depends only on total path through body, and can be measured using an external transmission source
- true even if attenuation within body is non-uniform

PET measurements can be fully quantitative

Background in PET images

Random coincidences

For a pair of detectors operating at singles rates S_1 , S_2 get random coincidences at rate $2\tau S_1 S_2$ where τ is coincidence resolving time.

For PET scanner $\tau \sim 10$ ns.

Can explicitly measure the overall randoms contribution by introducing a delay into one half of the timing circuit, and can then subtract this from the image – but increases statistical noise.

Scattered photons

511 keV gammas interact mainly by Compton scattering. Scattered photons may be detected (in coincidence). Energy resolution of scintillator too poor to discriminate scattered photons.

2D vs 3D PET

Scattered γ -rays contribute background to images, reducing contrast and making quantitative measurements hard.

Earlier scanners included collimating septa (thin lead rings, shown in blue below) between the detector rings, which effectively divided the scanner into a stack of separate rings, each producing a 2D tomographic image of a single slice.



Since the probability of one of the γ -ray pair scattering and remaining in the same plane is small, the septa discriminate against scattered γ -rays.

But they also block a lot of unscattered γ -rays, reducing the sensitivity. Modern scanners can usually operate without septa

Reconstruction of the resulting 3D image is more complex.

Time of flight

If one could measure the relative arrival times of the two photons accurately enough one could determine how far along the line the decay was. To locate to within a few mm would need picosecond timing resolution. With 0.5ns resolution one can start to localise decay and may improve images a bit.

PET/CT

X-ray CT is used to image structure of body (for reference, and to calculate attenuation corrections). Previously patients had to move between CT scanner and PET scanner. Now combined PET/CT scanners perform near-simultaneous CT and PET scans.

Examples of uses of PET:

Finding tumours and examining recurrence of tumours after treatment

Studying viability of heart muscle after heart attack

Studying brain activity and diagnosing abnormalities

Drug uptake studies







Compton camera

An alternative to a gamma camera with a collimator would be a Compton camera, with two planar detectors.

Gamma ray scatters in first, depositing part of its energy, then scattered photon is absorbed in second. From these two measured energies one can calculate the scattering angle, then relative to the line defined by the two points the source must lie on a cone.



Nice idea:

- would extend imaging to higher energy gammas
- large field of view

But

- need to measure energies and positions very accurately
- reconstruction of complex distributions complicated!