Positron Emission Tomography
Ahmed Qamesh
Outline

• What is PET?
• PET mechanism
• Radionuclide and its synthesis
• Detection concept and Development
  – Mathematical Model
  – Photon Detection
  – Time of flight
  – Coincidence processing
  – Detector Configuration
  – 2D Vs 3D acquisition
• Data correction
• Application
• Summary
What is PET?

Positron Emission Tomography

A molecular imaging technique used to obtain images of biological systems

How?

by measuring metabolic activity of cells.

Examples: Brain, kidney, Tumors , Heart disease, ............
What is PET?

**Method:**
- Injecting the body with a radioactive trace
- A camera is then used to monitor the distribution of the substance in the body to study accurately the organ’s function.

**Advantages:**
- 2D and 3D images.
- Resolution (5–6 mm) in all directions.
- Shows chemical functioning of organs (Not just structure like CT).
- Can show some cancers in its early stages (more than CT or MRI).
Positron Emission Tomography (Overview)
PET Mechanism

Compounds with positron emitting Radioisotopes probes as molecular probes. (Isotopes of $^{18}_9 F$)

- Fluorodeoxyglucose (FDG) is the most famous example.
  1. FDG is injected into the body (stay for 40–60 min).
  2. FDG spreads via blood stream till it enter organs.
  3. Positron Emission

\[ ^{18}_9 F \rightarrow ^{18}_8 O + e^+ \]

4. Positron will travels a short distance (0.5 mm in water) before it annihilates with an electron.

\[ e^+ + e^- \rightarrow 2\gamma \]

Mass is converted into Energy (2 photons of 511 KeV)

5. An Electronic signal (Resolving time 6–15 ns).

6. Reconstruction of images.
Radionuclide synthesis

PET probes synthesis

Probes absorption in tissues

Detection process

Image Reconstruction
Radionuclide synthesis and On-site cyclotron
**General Principles:**

1. **Radionuclide synthesis**

   **What Isotope to use?**
   - **Life time:** short enough to minimize the radiation exposure to the patient.
     long enough to allow regional distribution.
   - **Cheap.**
   - **Non Toxic.**
   - **Available in Daily life.**

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<table>
<thead>
<tr>
<th>Isotope</th>
<th>Time</th>
<th>Cost</th>
<th>Time+</th>
</tr>
</thead>
<tbody>
<tr>
<td>O-15</td>
<td>2 min</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>N-13</td>
<td>11 min</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>C-11</td>
<td>20 min</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>F-18</td>
<td>110 min</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Rb-82</td>
<td>75 s</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Ga-68</td>
<td>68 min</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Cu-62</td>
<td>9.7 min</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>On-site cyclotron</td>
<td>On-site cyclotron</td>
<td>On-site cyclotron</td>
</tr>
</tbody>
</table>
F-18 preparation (on site Cyclotron)
- By firing Protons (12 MeV) onto a target material of $^{18}$O

$$p^+ + ^{18}_8 O \rightarrow ^{18}_9 F$$

Negatively charged H (proton with 2 electrons), 2e are stripped with carbon foil

- Fluorine (Halogen element). Lies in Group 7 of periodic table (7 Electrons in the outer shell)
- **Isotopes.** $^{18}_9 F, ^{17}_9 F$
General Principles:

(2) PET probes synthesis
- The aim is to remove one Hydroxy group from Glucose Molecule and replace it with Fluorine atom

Why Glucose?
- Normal body consumes energy in the form of glucose.
- Tumor has high rate of consumption

(3) Probes absorption within tissues

$^{18}_9 F \rightarrow ^{18}_8 O + e^+$
Detection concept and Development

The Siemens Biograph, a combined PET/CT scanner (Courtesy Siemens)
Mathematical Model

Problem: If no refraction or diffraction, photon beams travel along straight lines that are not bent by the objects they pass through. Both give the same projection!!!

Solution: Use Different orientations

How can we reconstruct a known function from unknown one? Inverse problem

starts with the results and then calculates the causes. Data $\rightarrow$ Model parameters

Radon Transform

• Each slice represent a constructed line with (1-D projection)

$$ R_0(x') = \text{is the line integral of the image intensity } F(x,y) $$

$$ R(r,\theta) = \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} f(x,y) \delta(x \cos \theta + y \sin \theta - r) \, dx \, dy $$

• The collection of R at all angles is called the Radon Transform of image $f(x,y)$. 
Photon Detection

- To image the annihilation radiation one should profit from its unique properties:
  1. Two Collinear photons \((180^\circ)\).
  2. Simultaneously.
  3. Energy of each photon 511 keV.

Goal

- Measuring the total energy deposited by the photon when it traverses the detector. 6–12 ns

\[ X = ct \]

Coincidence time window \((t)\): the time interval at which two a pair of annihilated photons counted

\((X)\): The position of the tumor where the annihilation happened can be achieved.
Time of flight

To improve the quality of reconstruction, a coincidence measurement of the time difference (Time of Flight) using two detectors is included. $T.O.F=3.3\,\text{ps}$

- If two photons arising from the same annihilation and an event is attributed to the line-of-response (LOR).

- With time-of-flight PET imaging
The relative time difference ($\Delta t$) between the detection of the two annihilation photons is used to determine the most likely location ($d$) of the annihilation event along the LOR.

Field-of-view (FOV).
The sensitive volume inside the detector cylinder that a patient can occupy.
In human scanners is typically 70 cm in diameter and 16 – 18 cm in axial length.
Coincidence processing

- The detected coincidence events (called coincidences) can be classified into:
  1. True coincidences.
  2. Background events.

Accidental (or random) coincidences
The two photons did not arise from the same annihilation event

Scattered coincidences
The two photons arise from the same annihilation event, because one photon has experienced Compton scatter within the patient and therefore has had a change of direction
PET Imaging system

Scintillation detectors.

- The incident photon creates tens of thousands visible wavelength photons (about 1 eV energy each).
- The number of scintillation photons produced in the crystal is proportional to the energy deposited by the annihilation photon.

- Early PET scanners used large scintillation crystals and coupled one crystal to one PMT in a single slice. (Limits the spatial resolution)

- Increasing efficiency requires
  1. Using many small crystals for higher Resolution.
  2. Using More crystals and more PMTS for higher Sensitivity.
  3. Applying septa between the transverse slices to reduce scatter from the patient

- Recently, The common used setup is the block detector

What detector to use?

Example

Crystal/PMT = 1/4
WHAT SCINTILLATOR TO USE?

Based on the following properties:

1. The stopping power  
   Short  
   (Depend on Density and Atomic number of material Z)
   (The inverse of the mean distance traveled by photons before depositing energy in the crystal).

2. The decay constant  
   small  
   (How long the scintillation flash lasts in the crystal?).
   Small decay constant allows high photons counting rates and lower background rates.

3. A good Energy resolution  
   High  
   The energy resolution depends on the light output and the intrinsic energy resolution of the crystal.

4. The light output  
   High  
   (The number of scintillation photons produced by each incident photon).

5. Cost  
   Too much or too cheap?  
   😞 😞
   In most commercial PET scanners, the cost of the scintillator material represents 30–50% of the material cost of the scanner.
Scintillators used in PET Scanners

<table>
<thead>
<tr>
<th>Material</th>
<th>Cost</th>
<th>Light Output</th>
<th>Effective Density</th>
<th>Light Decay Time</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thalium-doped sodium iodide</td>
<td>cheap (relatively)</td>
<td>high</td>
<td>highest</td>
<td>long</td>
<td>Hygroscopic No longer used</td>
</tr>
<tr>
<td>Bismuth germinate</td>
<td>expensive</td>
<td>low</td>
<td>highest</td>
<td>long</td>
<td>Does not support TOF PET</td>
</tr>
<tr>
<td>lutetium oxyorthosilicate</td>
<td>more expensive</td>
<td>high</td>
<td>high</td>
<td>very short</td>
<td>Some patent disputes</td>
</tr>
<tr>
<td>lutetium yttrium orthosilicate</td>
<td>more expensive</td>
<td>high</td>
<td>high</td>
<td>very short</td>
<td></td>
</tr>
<tr>
<td>Gadolinium orthosilicate</td>
<td>more expensive</td>
<td>very high</td>
<td>somewhat lower than LSO</td>
<td>very short</td>
<td>No longer used</td>
</tr>
</tbody>
</table>

High atomic number \( (Z) \) is preferred

1. Gives high stopping power
2. Higher Photoelectric than Compton interaction facilities energy discrimination of scattered photons.
### 2D vs 3D crystal choice

<table>
<thead>
<tr>
<th></th>
<th>Parameter important for 2D</th>
<th>Parameters important for 3D</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Stopping power (attenuation length, cm)</td>
<td>System energy resolution (%)</td>
</tr>
<tr>
<td>BGO</td>
<td>1.05</td>
<td>18–25</td>
</tr>
<tr>
<td>NaI(Tl)</td>
<td>2.88</td>
<td>10–12</td>
</tr>
<tr>
<td>GSO</td>
<td>1.43</td>
<td>12–18</td>
</tr>
<tr>
<td>LSO/LSO</td>
<td>1.16</td>
<td>12–18</td>
</tr>
<tr>
<td>LaBr(Ce)</td>
<td>2.13</td>
<td>6–7%</td>
</tr>
</tbody>
</table>

- For **2D scanners**, scintillators with low stopping power is favored. Decay time is less important.
- For **3D scanners**, scintillators with high stopping power is favored. Decay time is important.

Resolution NaI(Tl) detector of 6–7 mm using only 6 mm PMT with crystal: PMT= 100:1.
Detector configuration

A full PET scanner is constructed as an assembly of block detectors in different designs (Rings or polygonal).

A. Dual Detector Heads
   - Gives 2D planner images (1/3 efficiency of the full ring)
   - 40% lower in cost than D.
   - Full reconstruction achieved by rotating the head to collect sufficient angular data to reconstruct.

B. Half Ring
   - better resolution than A.

C. Hexagonal Ring
   - Gives 2D and 3D planner images
   - Lower Cost than D– Low counting rate

D. Full Ring
   - Gives 2D and 3D planner images

➢ To improve the resolution
   High number of small crystals required
   More Bending towards the source
**2D versus 3D acquisitions**

Rings of detector elements *may or may not* be separated by thin annular rings or septa of photon absorptive material (*tungsten*), that provide collimation.

<table>
<thead>
<tr>
<th>2D protocol</th>
<th>3D protocol</th>
</tr>
</thead>
<tbody>
<tr>
<td>With collimation</td>
<td>Without collimation</td>
</tr>
</tbody>
</table>

- Lower sensitivity
- Improved contrast
- Easier to construct
- Higher sensitivity
- Lower contrast
- Harder to construct

Many coincidences are blocked from reaching the detector. Many events out-of-plane contribute.

Brain imaging (small activity concentrations)

Coincidences from all axial angles in the FOV.

Whole-body imaging (more activity concentration)
PET Performance and Resolution

The overall spatial resolution is expressed as the Full-Width-Half-Maximum of the spread function.

**Physical factors**

1. Range effect

   Maximum Energy: $0 < E_\gamma < E_{\text{max}}$
   
   Extrapolated range: $0 < R < R_e$

   Positron Range: $0 < R < R_e$

   $R_{\text{RMS}} << R_e$ (10 times Shorter)
PET Performance and Resolution

MonteCarlo Simulation

More dispersion

Degrading of 0.1 mm

Degrading of 0.5 mm
PET Performance and Resolution

The overall spatial resolution is expressed as the Full-Width-Half-Maximum of the spread function.

**Physical factors**

1. **Range effect**
   - Maximum Energy
   - Extrapolated range

   Spectrum Energy $0 < E_\gamma < E_{\text{max}}$ → Positron Range $0 < R < R_e$

   $R_{\text{RMS}} << R_e$ (10 times Shorter)

2. **Non Colinearity of the two photons**

   The two annihilated photons are not exactly back to back.

   **Reason**
   
   The positron has a small residual momentum and Kinetic Energy at the end of the range.

   $\Delta \theta \approx 0.25^\circ$

   $D = 80 \text{ cm} - 100 \text{ cm}$

   $\text{FWHM}_{\text{Range}} \approx \text{FWHM}_{180^\circ}$
PET Performance and Resolution

**Instrumentation factors**

Intrinsic detector resolution takes place.

The depth-of-interaction-effect.

For Small area detectors, resolution is determined by the detector width ($W$)

- Resolution increases from the middle to the other side of the detector

**Interactions in the patient**

The observed photons in a straight line decreases exponentially with increasing length of the material traversed.

- The image quality degrades rapidly as the patient weight increases.
- TOF information is recommended for heavy patient

*FWHM*$_{\text{Intrinsic}}$
PET Performance and Resolution

Coincidence factor

Spurious Coincidence
Due to an annihilation and a cascade gamma ray (scattered or unscattered) falls within the 511 eV energy window.
Data Correction

**Aim**: obtain clinically useful images and accurate quantitative information from PET studies.

## Attenuation correction

Photons that encounter more or denser material on their path from the annihilation site to the detectors are more likely to be absorbed or scattered (i.e. attenuated) than photons that travel through sparser parts of the body.

- **For example**: lung tissue and skin
  - exhibits lower attenuation
  - shows higher tracer uptake than muscle.

### Solution

Determine the attenuation through the patient for all LORs.

### How?

By inserting a thin, hollow cylinder of a positron emitting activity around the patient (transmission scan)

- In PET/CT scanners, the acquired CT image is used for PET attenuation correction.
- Another possibility of PET/MRI (Julich institute of Neuroscience and biophysics)

CT (Computerized Axial Tomography): X-ray test for cross sectional images

![Correction Factor](http://www2.aizsibimnjournal.cl/aizsibimYCDAA/imprima/6,1208,FRT%253D454,00.html)
PET/CT acquisition

CT image  PET image  PET/CT image
Applications

1. Brain
   (patients who have memory disorders of suspected or proven brain tumors)

2. Heart
   (Determine blood flow to the heart muscle, determine effects of heart attack)

3. Certain types of Cancer
   (Examine the effects of cancer therapy by characterizing biochemical changes in the cancer, spread of the cancer)

4. Alzheimer’s disease
   (there is no gross structural abnormality, but PET is able to show a biochemical change)

5. Some important body functions,
   to help doctors evaluate how well organs and tissues are functioning.
   (Blood flow, oxygen use, and sugar (glucose) metabolism)
Summary

In this talk I gave an overview about PET……..
1. Basic Concepts of PET.
2. Detection process in PET.
3. Detector Configurations and different materials used.
4. CT/PET Images.
5. PET updates for reconstruction algorithms and attenuation correction.
6. The spatial resolution PET.
7. Clinical applications for PET
Thank you
References


[2] Molecular Imaging with Positron Emission Tomography, Michael E. Phelps, Department of Molecular and Medical Pharmacy, UCLA School of Medicine, California, (2002).

