6: Positron Emission Tomography

1. What is the principle of PET imaging ?
   - Positron annihilation
   - Electronic collimation – coincidence detection
2. What is really measured by the PET camera ?
   - True, scatter and random coincidences
3. How are the effects attenuation corrected for ?
4. What factors can affect resolution ?
5. Examples: PET tracers in oncology and neuroscience

After this course you are capable of:
1. Describing the essential elements of a PET scan
2. Distinguish the principle of PET detection from that of SPECT
3. Understand the bases of scatter elimination.
4. Understand the factors affecting spatial resolution in PET.

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6-1. What is Positron Emission Tomography ?

**PET**

Positron Emission tomography: measured are x-rays emitted by annihilation of positrons emitted by exogenous substance (tracer) in body
The principle is as emission tomography, but there is one major difference ... (see later)

Two issues:
1. How to determine directionality of x-rays ?
2. Absorption is undesirable

Most widely used tracer for PET

$^{18}F$luoro-deoxy-glucose

F-18 FDG
What does one want to measure with PET?

**Annihilation photons**

**Question:** Why are two photons produced?

Conservation of linear momentum is not possible with one photon \( (p = E/c) \) but 2 photons.

Energie of photons?

\[ h\nu = mc^2 = 511 \text{keV} \]

(1 eV = 1.6 \times 10^{-19} \text{J})

\[ p = \frac{E}{c} \]

\[ 2 \text{ photons} \]

**Annihilation coincidence detection:**

- Two events detected at the same time
- Annihilation event along a line (defined by detector)
- \( \Rightarrow \) NO need for a collimator

CB. Light travels 1 m in 3 ns:

\[ 1\text{m}/3 \times 10^8 \text{[m/s]} = 3\text{ns} \]

What is coincidence detection?

**Electronic collimation** (i.e. w/o physical collimators)

**Electronic signal**

What defines simultaneity (coincidence)?

**Position logic electronics**

**Photomultipliers**

**Light guide**

**Scintillating crystal**

**PET-camera**

Bi\(_4\)Ge\(_3\)O\(_12\) (BGO): \( \tau \approx 10\text{ns} \)

Elimination of collimator material is a major source of sensitivity increase (why?)
6-2. What is really measured with PET?

What is measured:

\[ Y_{ab} = N_{ab} (A_{ab} T_{ab} + S_{ab} + R_{ab}) \]

Normalization:

(Instrument imperfection)

Attenuation

Randoms

Scattered coincidence

Trues

Why are Random and Scattered Events bad?

Random

Emissions from unrelated nuclear transformations interact simultaneously with the detectors

Rate of random coincidences:

\[ R_{\text{rand}} = 2\tau S_1 S_2 \]

S_1 and S_2: count rates on the individual detectors (singles rates)

\( \tau \): separation of singles (= coincidence time)

Reduce randoms by reducing \( \tau \) (coincidence interval)

Scatter

At least one annihilation photon is (Compton) scattered

Erroneous Line of incidence (LOI)

\( \Rightarrow \) assignment to wrong Radon transform

Does not work for scattered events (why?)
How can scattered events be distinguished from true coincidence?

Energy discrimination & background subtraction

Most scattering is by Compton

\[ E_f = \frac{m_e c^2}{2 - \cos \theta} \]

<table>
<thead>
<tr>
<th>( \theta/E_i )</th>
<th>( E_i ) (keV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>482</td>
</tr>
<tr>
<td>45</td>
<td>395</td>
</tr>
<tr>
<td>90</td>
<td>256</td>
</tr>
<tr>
<td>110</td>
<td>218</td>
</tr>
<tr>
<td>180</td>
<td>170</td>
</tr>
</tbody>
</table>

Some crystals (BGO) only allow 30% energy discrimination

Other approaches are needed:

Subtract background (= scatter + randoms) measured in signal void regions → polynomial interpolation

6-3. How is attenuation correction performed?

to PET than SPECT

[Diagram of attenuation correction]

Probability \( P_1 \):

\[ S_1 = C_T(x)e^{-\mu(d-x)} \]

\[ P_1 = S_1/C_T^*(x) \]

Probability \( P_2 \):

\[ S_2 = C_T^*(x)e^{-\mu x} \]

\[ P_2 = S_2/C_T^*(x) \]

Attenuation:

Probability of detecting the photon pair

\[ P_1P_2 = e^{-\mu x}e^{-\mu(d-x)} \]

\[ S = C_T^*(x)e^{-ad} \]

\[ S = P_1P_2C_T^* \]

Compare to geometric average of SPECT (Lesson 5)
What are the steps in Attenuation Correction for PET?

Mass attenuation coefficient $\mu/\rho$ in soft tissue = 0.095 cm$^2$/g (511 keV)

$HVL = 0.693/\mu \quad HVL \approx 7 cm$

Average path length for the photon pair longer than for a single photon different lines of response attenuate to varying degrees

Attenuation correction in practice:
- Spatially uniform attenuation coefficient assumed
- Transmission technique using e.g. Cs source (662 keV, why is this good enough?)

Transmission technique:
- Radon transform ($\mu$ homogeneous)

Correction factor for each:
- $e^{-\mu d(\phi)}$

Why is PET/CT the industry standard?

PET-Attenuation correction using CT-Data

Comparison with blank scan i.e. subject removed

$e^{-\int_{0}^{L} \mu(x) dx}$
6-4. Why is Resolution never perfect? 
Annihilation Range and photon non-collinearity

**Range:** limits spatial resolution 
(In air, \( \beta^* \) range ~ several m)

<table>
<thead>
<tr>
<th>Isotope</th>
<th>Half-life (min)</th>
<th>Max. Energy (MeV)</th>
<th>Range in H_2O (FWHM, mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>^18F</td>
<td>110</td>
<td>0.6</td>
<td>1</td>
</tr>
<tr>
<td>^11C</td>
<td>21</td>
<td>1.0</td>
<td>1.2</td>
</tr>
<tr>
<td>^13N</td>
<td>2</td>
<td>1.7</td>
<td>1.5</td>
</tr>
<tr>
<td>^13N</td>
<td>10</td>
<td>1.2</td>
<td>1.4</td>
</tr>
<tr>
<td>^82Rb</td>
<td>68</td>
<td>1.9</td>
<td>1.7</td>
</tr>
<tr>
<td>^68Ga</td>
<td>1</td>
<td>3.2</td>
<td>1.7</td>
</tr>
</tbody>
</table>

**Collinearity:** Assumed for Reconstruction

Background: At time of annihilation, e-p pair has non-zero kinetic energy
\[ \rightarrow \text{conservation of momentum} \]

\[ \text{E}^+ \text{range} \sim \text{several m} \]

\[ \text{o} \]

\[ \text{conservation of momentum} \]

\[ \text{Background: At time of annihilation, e-p pair has non-zero kinetic energy} \]

\[ \text{Collinearity: Assumed for Reconstruction} \]

\[ \text{D (detector distance)} \]

\[ \bullet \ x = 0.5 \ D \tan(0.25^\circ) \]

\[ \begin{array}{c|c}
D (cm) & x (mm) \\
60 & 1.3 \\
80 & 1.7 \\
100 & 2.2 \\
\end{array} \]

**Example:** BGO Block Detector
Coincidence window: 12 ns
Energy resolution: ~ 25%

**True coincidence count rate** \( R_T \)

\[ R_T = 2C^*T \varepsilon^2 \]

1. \( C^* \): tissue activity of a voxel
2. \( \varepsilon \): the intrinsic detector efficiency (1-e^{-ux})
3. \( G \): the geometric efficiency (solid angle defined by the detector surface/4\pi).

NB. \( \varepsilon = 0.9 \rightarrow 81\% \) of photon pairs emitted towards detectors produce coincidence

This is a reason for the 3cm thick crystals used for PET detection.
6-5. What are typical PET tracers?

**Oncology**
- $^{18}$F-Fluoroethyl-Tyrosine (FET): Amino acid transport
- Deoxy-$^{18}$fluoro-thymidine (FLT): Proliferation
- $^{18}$Fluoromisonidazole (FMISO): Hypoxia
- $^{11}$C-Methionine: Amino acid transport and metabolism
- $H_2^{15}$O: Blood flow
- $^{18}$Fluoro-Deoxyglucose (FDG): Glucose metabolism

**Neuroscience**
- $^{15}$O-Butanol: Blood Flow
- $^{18}$FDOPA: Presynaptic dopaminergic function
- $^{11}$C-Flumazenil: Benzodiazepine-receptor mapping

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X-ray imaging modalities. Overview

**CT, SPECT, PET**

<table>
<thead>
<tr>
<th>Measurement of signal integrated along line of incidence (LOI) (Radon transform)</th>
<th>Apply correction to measured Radon transform (attenuation, scatter, etc.)</th>
<th>Backprojection or central slice theorem: Finally an image!</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CT</strong></td>
<td><strong>SPECT</strong></td>
<td><strong>PET</strong></td>
</tr>
<tr>
<td>Projection Encoding</td>
<td>Defined by incident x-ray (collimation to reduce scatter)</td>
<td>Collimator essential</td>
</tr>
<tr>
<td>Spatial Resolution</td>
<td>100$\mu$m-mm (μm)</td>
<td>Typical 10mm (Variable and complex (1.5-3 mm))</td>
</tr>
<tr>
<td>Attenuation</td>
<td>= measurement variable (Varies with energy)</td>
<td>Complex correction (Varies with photon energy)</td>
</tr>
<tr>
<td>Radionuclides</td>
<td>None (contrast agents)</td>
<td>Any with $h\nu$ = 60-200keV</td>
</tr>
</tbody>
</table>