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.

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}\text{F}luoro-deoxy-glucose

\[\text{F-18 FDG}\]
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 two photons.

**Energie of photons?**

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

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

NB. Light travels 1m in 3ns: \( 1 \text{m}/3 \times 10^8 \text{[m/s]} = 3 \text{ns} \)

**Annihilation coincidence detection:**

two events detected at the same time

- annihilation event along a line (defined by detector)
- \( \Rightarrow \) NO need for a collimator

**What is coincidence detection?**

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

- **Electronic signal**
- **What defines simultaneity (coincidence)?**

**Leading edge defines time of detection** (sharper, i.e., higher 1st derivative)

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

**Position logic electronics**

- **Photomultipliers**
- **Light guide**
- **Scintillating crystal**

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

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

**What is measured**

- True coincidences
- Random coincidences
- Scattered coincidence

**Normalization** (Instrument imperfection)

**Scatter**

**Attenuation**

**Randoms**

**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)

**Scatter**

- At least one annihilation photon is (Compton) scattered
- Erroneous Line of incidence (LOI) \( \Rightarrow \) assignment to wrong Radon transform

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

**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/Ei</th>
<th>511 (keV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>482</td>
</tr>
<tr>
<td>45</td>
<td>396</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>

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

6-10

6-3. How is attenuation correction performed?

simpler for PET than SPECT

Attenuation:
Probability of detecting the photon pair

\[ P_1 P_2 = e^{-\mu d} e^{-\mu (d-x)} \]

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

\[ S = P_1 \cdot P_2 \cdot C_T^* \]

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/\( \mu \) \( \Rightarrow \) 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?)

\[ e^{-\int \mu(x) dx} \]

Comparison with blank scan i.e. subject removed

Correction factor for each Radon transform (\( \mu \) homogeneous)

Why is PET/CT the industry standard?

PET-Attenuation correction using CT-Data

\[ \mu/\rho (\text{cm/g}) \]

0.3

0.2

0.1

0.1

0

0 100 200 300 400 500

Energy (keV)

CT + PET = PET/CT

CT

PET 511 keV

Bone

Soft tissue

CT ~70 keV

scatter & attenuation correction

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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 H2O (FWHM, mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{18}$F</td>
<td>110</td>
<td>0.6</td>
<td>1</td>
</tr>
<tr>
<td>$^{11}$C</td>
<td>21</td>
<td>1.0</td>
<td>1.2</td>
</tr>
<tr>
<td>$^{18}$O</td>
<td>2</td>
<td>1.7</td>
<td>1.5</td>
</tr>
<tr>
<td>$^{13}$N</td>
<td>10</td>
<td>1.2</td>
<td>1.4</td>
</tr>
<tr>
<td>$^{68}$Ga</td>
<td>68</td>
<td>1.9</td>
<td>1.4</td>
</tr>
<tr>
<td>$^{82}$Rb</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

- Conservation of momentum

\[
\text{Photon momentum with zero momentum e-p}
\]

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

\[
\begin{align*}
\times &= 0.5 \times D \times \tan(0.25^\circ) \\
60 &\quad 1.3 \\
80 &\quad 1.7 \\
100 &\quad 2.2
\end{align*}
\]

How does the detector affect PET spatial resolution?

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

True coincidence count rate $R_T$

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

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

NB. $\epsilon = 0.9 \rightarrow 81\%$ 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**

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

**Neuroscience**

- FDG or $^{18}$F fluorodeoxyglucose
- $^{15}$O Water

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### X-ray imaging modalities. Overview

**CT, SPECT, PET**

<table>
<thead>
<tr>
<th></th>
<th>CT</th>
<th>SPECT</th>
<th>PET</th>
</tr>
</thead>
<tbody>
<tr>
<td>Projection Encoding</td>
<td>Defined by incident x-ray (collimation to reduce scatter)</td>
<td>Collimator essential</td>
<td>Coincidence detection (electronic collimation)</td>
</tr>
<tr>
<td>Spatial Resolution (rodent)</td>
<td>100μm-mm (μm)</td>
<td>Typical 10mm (Variable and complex) (1.5-3 mm)</td>
<td>4.5-5mm at center (1mm)</td>
</tr>
<tr>
<td>Attenuation</td>
<td>= measurement variable (Varies with energy)</td>
<td>Complex correction (Varies with photon energy)</td>
<td>Accurate correction (transmission method)</td>
</tr>
<tr>
<td>Radionuclides</td>
<td>None (contrast agents)</td>
<td>Any with $hν$ = 60-200keV</td>
<td>Positron emitters only</td>
</tr>
</tbody>
</table>