6: Positron Emission Tomography

1. What is the principle of PET imaging?
   - Positron annihilation
   - Electronic collimation – coincidence detection
2. How are the effects of scatter and attenuation corrected for?
3. What factors can affect resolution?
4. 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.

Positron Emission Tomography (PET)
Cancer detection (metastasis) in patients

PET/CT
**Pet BioImag 2013**

**6-3**

**Positron Emission Tomography Scanner**

PET is similar to SPECT but different (detection principle and instrumentation).

**6-4**

**PET of animal models**

transgenic mice, cancer detection

- **micro PET scanner**
- **Positioning of the rodent**
- **Imaging gene expression (HSV)**
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

- $^{18}$Fluoro-deoxy-glucose

**What does one want to measure with PET?**

**Annihilation photons**

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

Conservation of linear momentum is not possible with one photon ($p=E/c$) → 2 photons

**Energie of photons?**

$$h\nu = m_e c^2 = 511 \text{keV}$$

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

**Annihilation coincidence detection:**

- two events detected at same time
- → annihilation event along a line (defined by detector)
- ⇒ NO need for a collimator

**NB.** Light travels 1m in 3ns:

$$1 \text{m}/3 \cdot 10^8 \text{m/s} = 3 \text{ns}$$
What is coincidence detection?

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

What defines simultaneity (coincidence)?

Electronic signal

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

Bi$_4$Ge$_3$O$_{12}$ (BGO): $\tau \approx 10$ ns.

Elimination of collimator material is a major source of sensitivity increase (why?)

What is measured with PET?

What is really measured with PET?

$Y_{ab} = N_{ab} (A_{ab} T_{ab} + S_{ab} + R_{ab})$

Trues

Normalization

Attenuation

Scatter

Randoms
6-2. Why are Random and Scattered Events bad?

**Random**
emissions from unrelated nuclear transformations interact simultaneously with the detectors

**Scatter**
At least one annihilation photon is (Compton) scattered

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)
\( \tau \): coincidence time window.

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 / E_i )</th>
<th>511 (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>

Measure \( E_i \) → identify severely scattered photons

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?**

simpler for PET than SPECT

**Attenuation**

Probability of detecting the photon pair

\[
P_1P_2 = e^{-\mu L} e^{-\mu(d-x)} \quad S = C_T^*(x)e^{-\mu d}
\]

\[
S = P_1P_2 \cdot C_T^*
\]

Compare to geometric average of SPECT (Lesson 5)

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**What are the steps in Attenuation Correction for PET?**

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

\[HVL = 0.693/\mu \quad \Rightarrow HVL \leq 7\,\text{cm}\]

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 (662keV, why is this good enough?)

Comparison with blank scan i.e. subject removed

Correction factor for each Radon transform \((\mu\text{ homogeneous})\)
Why is PET/CT the industry standard?

PET-Attenuation correction using CT-Data

CT + PET = PET/CT

PET/CT: Two separate scanners in one package

Soft tissue
Bone

P / U (cm/g)

Energy (keV)

m / p (cm/keV)

CT ~70 keV

PET 511 keV

scatter & attenuation correction

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6-4. Why is Resolution never perfect?

Annihilation Range and photon non-collinearity

Collinearity: Assumed for Reconstruction

Background: At time of annihilation, e-p pair has non-zero kinetic energy

\[ E_+ + E_- = 511 \text{ keV} \]

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

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

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>^15O</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>^68Ga</td>
<td>68</td>
<td>1.9</td>
<td>1.7</td>
</tr>
<tr>
<td>^82Rb</td>
<td>1</td>
<td>3.2</td>
<td>1.7</td>
</tr>
</tbody>
</table>

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How does the detector affect PET spatial resolution?

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

True coincidence count rate \( R_T \)
\[
R_T = 2C^*T\gamma e^{-2}
\]
1. \( C^* \): tissue activity of a voxel
2. \( \gamma e^{-x} \): the intrinsic detector efficiency
3. \( G \): the geometric efficiency (solid angle defined by the detector surface/4\(\pi\)).

NB. \( \gamma = 0.9 \rightarrow 81\% \) 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 and neuroscience

<table>
<thead>
<tr>
<th>Tracer</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>(^{18})Fluoroethyl-Tyrosine (FET)</td>
<td>Amino acid transport</td>
</tr>
<tr>
<td>Deoxy-(^{18})fluoro-thymidine (FLT)</td>
<td>Proliferation</td>
</tr>
<tr>
<td>(^{18})Fluoromisonidazole (FMISO)</td>
<td>Hypoxia</td>
</tr>
<tr>
<td>(^{11})C-Methionine</td>
<td>Amino acid transport and metabolism</td>
</tr>
<tr>
<td>(\text{H}_2\text{O}^{15})</td>
<td>Blood flow</td>
</tr>
<tr>
<td>(^{18})Fluoro-Deoxyglucose (FDG)</td>
<td>Glucose metabolism</td>
</tr>
<tr>
<td>(^{18})FDOPA</td>
<td>Presynaptic dopaminergic function</td>
</tr>
<tr>
<td>(^{15})O-Butanol</td>
<td>Blood Flow</td>
</tr>
<tr>
<td>(^{11})C-Flumazenil</td>
<td>Benzodiazepine-receptor mapping</td>
</tr>
</tbody>
</table>

Neuroscience

<table>
<thead>
<tr>
<th>Tracer</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>FDG or (^{18})fluorodeoxyglucose</td>
<td></td>
</tr>
<tr>
<td>(\text{O}_{15}) Water</td>
<td></td>
</tr>
</tbody>
</table>
**PET: Neuroscience**

Pseudo-color display:
- red, yellow: high activity
- green, blue: low activity

**FDG PET Stomach carcinoma**
Early detection of response to treatment

Response-Prediction

Day 14

3 M. after CTx

responder

non-responder
**Whole-body FDG PET**

- Brain
- Kidney
- Bladder

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**X-ray imaging modalities. Overview**

CT, SPECT, PET

- **Measurement of signal integrated along line of incidence (LOI)** (Radon transform)
  1. CT: attenuated incident x-ray beam (direction of beam given by source)
  2. SPECT: emitted single photon (need collimation to determine ray direction)
  3. PET: annihilation photon pair (directionality by electronic collimation)

- **Apply correction to measured Radon transform** (attenuation, scatter, etc.)
- **Backprojection or central slice theorem:**
- **Finally an image!**

<table>
<thead>
<tr>
<th></th>
<th>CT</th>
<th>SPECT</th>
<th>PET</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Projection Encoding</strong></td>
<td>Defined by incident x-ray (collimation to reduce scatter)</td>
<td>Collimator essential (electronic collimation)</td>
<td>Coincidence detection (electronic collimation)</td>
</tr>
<tr>
<td><strong>Spatial Resolution</strong></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><strong>Attenuation</strong></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><strong>Radionuclides</strong></td>
<td>None (contrast agents)</td>
<td>Any with hν = 60-200keV</td>
<td>Positron emitters only</td>
</tr>
</tbody>
</table>