Step 1: Inject Patient with Radioactive Drug

- Drug is labeled with positron ($\beta^+$) emitting radionuclide.
- Drug localizes in patient according to metabolic properties of that drug.
- Trace (pico-molar) quantities of drug are sufficient.
- Radiation dose fairly small ($<1$ rem).
Ideal Tracer Isotope

- **Interesting Biochemistry**
  Easily incorporated into biologically active drugs.

- **1 Hour Half-Life**
  Maximum study duration is 2 hours.
  Gives enough time to do the chemistry.

- **Easily Produced**
  Short half life ⇒ local production.

\[
\begin{align*}
^{18}\text{F} & \quad \text{2 hour half-life} \\
^{15}\text{O}, \; ^{11}\text{C}, \; ^{13}\text{N} & \quad \text{2, 20, & 10 minute half-lives}
\end{align*}
\]
Step 2: Detect Radioactive Decays

- Radionuclide decays, emitting $\beta^+$. 
- $\beta^+$ annihilates with $e^-$ from tissue, forming back-to-back 511 keV photon pair. 
- 511 keV photon pairs detected via time coincidence. 
- Positron lies on line defined by detector pair (known as a chord or a line of response or a LOR).
Multi-Layer PET Cameras

- Can image several slices simultaneously
- Can image cross-plane slices
- Can remove septa to increase efficiency ("3-D PET")

Planar Images "Stacked" to Form 3-D Image
Step 3: Reconstruct with Computed Tomography

By measuring all 1-dimensional projections of a 2-dimensional object, you can reconstruct the object.
• Use external $\beta^+$ source to measure attenuation.

• Attenuation (for that chord) same as for internal source.

• Source orbits around patient to measure all chords.

• Measure Attenuation Coefficient for Each Chord

• Obtain *Quantitative* Images
Time-of-Flight Tomograph

- Can localize source along line of flight.
- Time of flight information reduces noise in images.
- Time of flight tomographs have been built with BaF$_2$ and CsF.
- These scintillators force other tradeoffs that reduce performance.

Not Compelling with Present Technology...
PET Images of Cancer

Treated Tumor Growing Again on Periphery

Metastases Shown with Red Arrows

Normal Uptake in Other Organs Shown in Blue
PET Camera Design

- Typical Parameters
- Detector Module Design
PET Cameras

- Patient port ~60 cm diameter.
- 24 to 48 layers, covering 15 cm axially.
- 4–5 mm fwhm spatial resolution.
- ~2% solid angle coverage.
- $1 – $2 million dollars.

Images courtesy of GE Medical Systems and Siemens / CTI PET Systems
Early PET Detector Element

BGO Scintillator Crystal
(Converts $\gamma$ into Light)

Photomultiplier Tube
(Converts Light to Electricity)

10 — 30 mm high (determines axial spatial resolution)

3 — 10 mm wide (determines in-plane spatial resolution)

30 mm deep (3 attenuation lengths)
Modern PET Detector Module

BGO Scintillator Crystal Block
(sawed into 8x8 array, each crystal 6 mm square)

- Saw cuts direct light toward PMTs.
- Depth of cut determines light spread at PMTs.
- Crystal of interaction found with Anger logic (i.e. PMT light ratio).

Good Performance, Inexpensive, Easy to Pack
Crystal Identification with Anger Logic

- Uniformly illuminate block.
- For each event, compute X-Ratio and Y-Ratio, then plot 2-D position.
- Individual crystals show up as dark regions.
- Profile shows overlap (i.e. identification not perfect).

Can Decode Up To 64 Crystals with BGO
Fundamental Limits of Spatial Resolution

- Dominant Factor is Crystal Width
- Limit for 80 cm Ring w/ Block Detectors is 3.6 mm

<table>
<thead>
<tr>
<th>Factor</th>
<th>Shape</th>
<th>FWHM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detector Crystal Width</td>
<td><img src="image" alt="Detector Crystal Width" /></td>
<td>d/2</td>
</tr>
<tr>
<td>Anger Logic</td>
<td><img src="image" alt="Anger Logic" /></td>
<td>0 (individual coupling)</td>
</tr>
<tr>
<td>Photon Noncollinearity</td>
<td><img src="image" alt="Photon Noncollinearity" /></td>
<td>2.2 mm (Anger logic)*</td>
</tr>
<tr>
<td>Positron Range</td>
<td><img src="image" alt="Positron Range" /></td>
<td>*empirically determined</td>
</tr>
<tr>
<td></td>
<td></td>
<td>from published data</td>
</tr>
<tr>
<td>Reconstruction Algorithm</td>
<td>multiplicative factor</td>
<td>1.25 (in-plane)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.0 (axial)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.3 mm (head)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.8 mm (heart)</td>
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<tr>
<td></td>
<td></td>
<td>0.5 mm (18F)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4.5 mm (82Rb)</td>
</tr>
</tbody>
</table>

*empirically determined from published data
Radial Elongation

- Penetration of 511 keV photons into crystal ring blurs measured position.
- Effect variously known as Radial Elongation, Parallax Error, or Radial Astigmatism.
- Can be removed by measuring depth of interaction.
PET Front End Electronics

Custom ASIC

Off the Shelf

PMT A
PMT B
PMT C
PMT D

Analog ASIC

Energy

X

Y

Time

ADC

ADC

ADC

TDC

FPGA

RAM

“Singles” Event Word

- Position
- Time

- Digitize Arrival Time (latch 500 MHz clock — 2 ns accuracy)
- Identify Crystal of Interaction & Measure Energy
- Correct Energy and Arrival Time (based on crystal)
- Maximum “Singles” Event Rate is 1 MHz / Detector Module

If Energy Consistent with 511 keV,
Send Out “Singles” Event Word (Position & Time)
PET Readout Electronics

From Each Camera Sector

Singles 0

Singles n

Search for “Singles” in Time Coincidence (~10 ns window)
Strip Off Timing Information
Format “Coincidence” Event Word (chord location)
Maximum “Coincidence” Event Rate is 10 MHz / Camera

Off the Shelf

FPGAs

Fiber Optic Interface

“Coincidence” Event Word

Search for Coincidences, Send Out “Coincidence” Event Word (Position of Chord)
PET Detector Requirements

Detect 511 keV Photons With (in order of importance):

- >85% efficiency
- <5 mm spatial resolution
- “low” cost (<$100 / cm²)
- “low” dead time (<1 µs cm²)
- <5 ns fwhm timing resolution
- <100 keV fwhm energy resolution

Based on Current PET Detector Modules
New Scintillators Developed Recently

- Approximately 10 years of R&D before large scale production.
- Development efforts driven by end users, but included efforts of luminescence scientists, spectroscopists, defects scientists, materials scientists, and crystal growers.

Very Strong Parallels...
### Scintillator Properties

<table>
<thead>
<tr>
<th></th>
<th>PbWO₄</th>
<th>Lu₂SiO₅</th>
</tr>
</thead>
<tbody>
<tr>
<td>Density (g/cc):</td>
<td>8.3</td>
<td>7.4</td>
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<tr>
<td>Attenuation Length (cm):</td>
<td>0.9</td>
<td>1.2</td>
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<tr>
<td>Light Output (phot/MeV):</td>
<td>200</td>
<td>25,000</td>
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<tr>
<td>Decay Time (ns):</td>
<td>10</td>
<td>40</td>
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<tr>
<td>Emission Wavelength (nm):</td>
<td>420</td>
<td>420</td>
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<tr>
<td>Radiation Hardness (Mrad):</td>
<td>&gt;10</td>
<td>10</td>
</tr>
<tr>
<td>Dopants:</td>
<td>Y, Nd</td>
<td>Ce</td>
</tr>
<tr>
<td>Cost per cc:</td>
<td>$1</td>
<td>&gt;$25</td>
</tr>
</tbody>
</table>

**Different Tradeoffs Required**
Avalanche Photodiode Arrays

Advantages:
• High Quantum Efficiency ⇒ Energy Resolution
• Smaller Pixels ⇒ Spatial Resolution
• Individual Coupling ⇒ Spatial Resolution

Challenges:
• Dead Area Around Perimeter
• Signal to Noise Ratio
• Reliability and Cost