New Technology in Nuclear Medicine

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Objectives

1. Discuss current gamma camera & SPECT technology
2. Understand semiconductor-based detection
3. Discuss current PET technology
4. Understand time-of-flight PET and affect on SNR
5. Understand the role of photodiodes
6. Discuss organ-specific and total body PET
7. Discuss new image reconstruction techniques
Gamma Camera Detection

- NaI(Tl) scintillation crystals
  - Optically coupled to photomultiplier tubes (PMTs)
- Collimation
  - Small holes or long holes = high resolution, low sensitivity
- Energy Discrimination
  - Eliminate scatter
PMT Array

Rectangular gamma camera with PMTs mounted to NaI crystal. Photo from *Physics in Nuclear Medicine*, Cherry et al. 3rd Edition
PMT Construction
Methods to Improve Gamma Detection?

• Increase sensitivity
  – Increase detection efficiency
    • Geometric efficiency: detector intercepts gammas
    • Intrinsic efficiency: absorb gamma (attenuation) and convert to light
      – Effective atomic number (high Z)
      – High light yield per keV

• Improve spatial and energy resolution
  – Remove scatter, smaller PMTs, increase SNR

• Reduce response time (rise time)
  – Reduce dead time and increase count rate
From *Physics in Nuclear Medicine*, Cherry et al. 3rd Edition
Properties of Scintillators and Semiconductors

<table>
<thead>
<tr>
<th>Property</th>
<th>NaI(Tl)</th>
<th>BGO</th>
<th>LSO(Ce)</th>
<th>GSO(Ce)</th>
<th>CsI(Tl)</th>
<th>LuAP(Ce)</th>
<th>LaBr₃(Ce)</th>
<th>Plastic*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Density (g/cm³)</td>
<td>3.67</td>
<td>7.13</td>
<td>7.40</td>
<td>6.71</td>
<td>4.51</td>
<td>8.34</td>
<td>5.3</td>
<td>1.03</td>
</tr>
<tr>
<td>Effective atomic number</td>
<td>50</td>
<td>73</td>
<td>66</td>
<td>59</td>
<td>54</td>
<td>65</td>
<td>46</td>
<td>12</td>
</tr>
<tr>
<td>Decay time (nsec)</td>
<td>230</td>
<td>300</td>
<td>40</td>
<td>60</td>
<td>1000</td>
<td>18</td>
<td>35</td>
<td>2</td>
</tr>
<tr>
<td>Photon yield (per keV)</td>
<td>38</td>
<td>8</td>
<td>20-30</td>
<td>12-15</td>
<td>52</td>
<td>12</td>
<td>61</td>
<td>10</td>
</tr>
<tr>
<td>Index of refraction</td>
<td>1.85</td>
<td>2.15</td>
<td>1.82</td>
<td>1.85</td>
<td>1.80</td>
<td>1.97</td>
<td>1.9</td>
<td>1.58</td>
</tr>
<tr>
<td>Hygroscopic</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Slightly</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Peak emission (nm)</td>
<td>415</td>
<td>480</td>
<td>420</td>
<td>430</td>
<td>540</td>
<td>365</td>
<td>358</td>
<td>Various</td>
</tr>
</tbody>
</table>

W = average energy expended to create an ion pair

CZT is CdTE with some zinc replacing some telluride
Energy Resolution

**Ideal Spectrum**
- Pulse amplitude (energy deposited in detector)
- Compton region
- Compton edge, $E_{ce}$
- Multiple Compton scattering
- Photopeak, $E_y$

**Actual Spectrum, without pulse pileup**
- 137Cs
- FWHM (%): $\frac{\Delta E}{E_\gamma} = \frac{46}{662} \times 100% = 7%$
- $\Delta E = 46$ keV
- Maximum height
- $1/2$ Maximum height
- Energy (keV)
- Relative number of counts
- Relative number of counts
Compare NaI, Ge, and CZT

NaI(Tl) detector resolution, 18.3 keV (13.1%) FWHM

Ge(Li) detector resolution, 0.6 keV (0.42%) FWHM

CZT

FWHM = 4.7 keV (3.4%)
# CZT Semiconductor Detectors

<table>
<thead>
<tr>
<th>Benefits</th>
<th>Drawbacks</th>
</tr>
</thead>
<tbody>
<tr>
<td>High atomic number – greater stopping power</td>
<td>Thinner crystals – best for low energy detection</td>
</tr>
<tr>
<td>Smaller detectors – higher spatial resolution</td>
<td>Low mobility of charge carriers – poor timing performance</td>
</tr>
<tr>
<td>Higher sensitivity – lower dose or faster scans</td>
<td>Expensive, which leads to small field of view</td>
</tr>
<tr>
<td>Less dead space at edge of detector, No PMTs</td>
<td></td>
</tr>
<tr>
<td>Better energy resolution – better scatter rejection (dual isotope imaging)</td>
<td></td>
</tr>
<tr>
<td>Can be operated at room temps, unlike Ge or Si semiconductors</td>
<td></td>
</tr>
</tbody>
</table>
Cardiac SPECT CZT

• Example
  – Spectrum Dynamics D-SPECT
    • Pixelated CZT detector arrays, multiple vertical columns (6-9)
    • Parallel hole collimators
    • Sensitivity: 850 cps/MBq (conventional is ~130 cps/MBq)
    • Resolution: 8.6 mm (conventional is 15 mm)

From Imbert et al, Compared performance of high-sensitivity cameras dedicated to myocardial perfusion SPECT: A comprehensive analysis of phantom and human images, J of Nuc Med, Vol 53;12
GE Discovery NM/CT 670 CZT

- First commercially available general purpose SPECT/CT with CZT detectors
  - 39 x 51 cm FOV with 2.46 mm pixels (spatial resolution of 2.8 mm)
    - Collimator holes aligned and registered with detectors
  - 1.4x higher count rate
  - 6.3% energy resolution
    - Can detect multiple tracers simultaneously
  - Improved SNR allows reduction in dose or scan time (25%)

Dual Isotope Imaging

Overlay of $^{99m}$Tc and $^{123}$I spectra, showing greater crosstalk between the two peaks for the NaI detector with its poorer energy resolution and wider energy window.

From GE Healthcare white paper, “CZT Technology: Fundamentals and Applications”
Dual Isotope Imaging

HMPAO (Tc-99m)  DaTSCAN (I-123)

Example from Gehealthcare.co.uk, Rambam Health Care Campus, Haifa, Israel
Basics of PET Imaging

- PET imaging is based on coincidence detection of two 511 keV photons
  - Must distinguish true counts from random and scatter counts and to correct for attenuation, decay, and prompt gammas
  - Without collimation, PET depends on coincidence timing window (6-10 nsec)
    - Only counts interactions if within timing window
Pair Annihilation

- Positron-emitting radionuclide
- Effective positron range
- Actual positron range
- Positron path
- Annihilation event
- 511 keV photon
Coincidence Detection

- True coincidence
- Scatter coincidence
- Random coincidence
Random & Scatter Counts

• Random counts:
  – Increase with total activity administered
    • Can use septa to separate detectors (collimation)
    • Random/true ratio about 0.2 for brain and 1.0 for body
  – Decrease as timing window narrows (12 nsec to 6 nsec)

• Scatter counts: from patient and scanner
  – Septa between detectors to decrease scatter
  – Scatter/true ratio about 0.2 for brain and 0.4 for body (2.0 for 3D imaging, no septa)
Correction for non-Trues

• Randoms
  – Estimate and subtract by using a delayed timing window (64-70 nsec)
  – Computed based on continuous monitoring of single rates

• Scatter
  – Model based on extrapolation of projection data or from CT/transmission data
Other Corrections

• Attenuation correction
  – Use transmission source or CT scan

• Dead time correction
  – Use empirical dead time models based on a range of activities, object sizes, and energy thresholds
  – Is a function of activity administered (like randoms) and detector response

• Prompt gamma correction
  – Narrower energy window or scaled random estimate or modeled mathematically
Detector Selection

<table>
<thead>
<tr>
<th>Scintillator</th>
<th>$\mu_t (511 \text{ keV}) \text{ cm}^{-1}$</th>
<th>$\varepsilon (2 \text{ cm})$</th>
</tr>
</thead>
<tbody>
<tr>
<td>NaI(Tl)</td>
<td>0.34</td>
<td>0.49</td>
</tr>
<tr>
<td>BGO</td>
<td>0.95</td>
<td>0.85</td>
</tr>
<tr>
<td>LSO, LYSO</td>
<td>0.88</td>
<td>0.83</td>
</tr>
<tr>
<td>GSO</td>
<td>0.70</td>
<td>0.75</td>
</tr>
<tr>
<td>BaF$_2$</td>
<td>0.44</td>
<td>0.58</td>
</tr>
</tbody>
</table>

- Efficiency is greater for BGO and LSO, LYSO
- LSO is less efficient but higher light yield and faster response
- Improved energy resolution for LSO
- 2.6% of Lu is radioactive Lu$^{176}$ (long-lived)
  - Problem for low activity measurements (Y$^{90}$)
Time-of-Flight (TOF)

- Conventional – Line of response (LoR)
- TOF – position window is a function of timing window on LoR
  - Reduction in randoms
  - Increase in SNR

Timing Resolution

<table>
<thead>
<tr>
<th>Timing Resolution (window)</th>
<th>Position Resolution (window)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 nsec</td>
<td>90 cm</td>
</tr>
<tr>
<td>3 nsec</td>
<td>45 cm</td>
</tr>
<tr>
<td>1 nsec</td>
<td>15 cm</td>
</tr>
<tr>
<td>500 psec</td>
<td>7.5 cm</td>
</tr>
<tr>
<td>100 psec</td>
<td>1.5 cm</td>
</tr>
<tr>
<td>50 psec</td>
<td>0.75 cm</td>
</tr>
<tr>
<td>20 psec</td>
<td>0.375 cm (&lt; 4mm)</td>
</tr>
</tbody>
</table>

Increase in SNR as timing window decreases since reconstruction is constrained to a smaller region.
TOF and Noise

SNR is proportional to square root of object size divided by system timing resolution (TOF). From 500 psec to 50 psec, 10-fold increase in SNR.
# Comparing PET Scanners

<table>
<thead>
<tr>
<th></th>
<th>Philips Ingenuity TF</th>
<th>GE Discovery IQ (5-ring)</th>
<th>Siemens Biograph mCT</th>
<th>Toshiba Celesteion</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Timing Resolution</strong></td>
<td>540 psec</td>
<td>N/A</td>
<td>540 psec</td>
<td>411 psec</td>
</tr>
<tr>
<td><strong>Detector Resolution</strong></td>
<td>4 mm LYSO and PMTs</td>
<td>6.3 mm BGO and PMTs</td>
<td>4 mm LSO and PMTs</td>
<td>4 mm LYSO and PMTs</td>
</tr>
<tr>
<td><strong>Sensitivity (cps/kBq)</strong></td>
<td>7.3</td>
<td>22.8</td>
<td>10.2</td>
<td>3.8</td>
</tr>
<tr>
<td><strong>Peak NECR, kcps @ kBq/ml</strong></td>
<td>124 @ 20.3</td>
<td>124 @ 9.1</td>
<td>186 @ 30.1</td>
<td>70 @ 29.6</td>
</tr>
</tbody>
</table>
Noise Equivalent Count Rate (NECR)

$\text{NECR} = \frac{T^2}{T+S+R}$
Photodiodes

- Silicon photodiodes (semiconductors) can replace PMTs
- Can be very small and thin
- No signal gain, unlike PMTs
  - Small signal, need low noise electronics
- Avalanche photodiodes (APDs) apply internal electric fields for signal amplification/gain (100-1000)
  - Gain is a function of bias voltage and temp
Silicon Photomultipliers (SiPMs)

- Matrix of parallel micro-APDs
  - Signals from single APDs are summed
    - Gains similar to PMTs ($1 \times 10^6$)
  - SiPM response depends on
    - Total # of APD cells
    - APD recovery time
    - Decay time of light pulses (depends on crystal)
- Small active areas up to 6 x 6 mm$^2$
- Used in PET/MRI and small animal imaging
- GE, Philips, and Siemens clinical scanners
## Advanced PET

<table>
<thead>
<tr>
<th></th>
<th>Philips Vereos</th>
<th>GE Discovery MI</th>
<th>Siemens Vision*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Timing Resolution</strong></td>
<td>325 psec</td>
<td>375 psec</td>
<td>249 psec</td>
</tr>
<tr>
<td><strong>Detector Resolution</strong></td>
<td>4 mm LYSO and SAPD array</td>
<td>4 mm LYSO and SiPMs</td>
<td>3.2 mm LSO and SiPMs</td>
</tr>
<tr>
<td><strong>Sensitivity (cps/kBq)</strong></td>
<td>22.1</td>
<td>13.7</td>
<td>84</td>
</tr>
<tr>
<td><strong>Peak NECR, kcps @ kBq/ml</strong></td>
<td>157.6 @ 52.8</td>
<td>193 @ 21.9</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

*Not FDA approved, currently under development*
Philips Vereos

- Digital Photon Counter (DPC)
  - Couples LYSO detectors directly to DPC consisting of 3200 single APDs
  - 1:1 coupling, completely digital acquisition chain = photon counting
  - High sensitivity = lower dose or faster scans
  - High NECR = reduced image noise

Images courtesy of Philips
Siemens Biograph Vision – not FDA approved

• Optiso Ultra Dynamic Range (UDR) detector
  – Smallest LSO detectors (3.2 mm) with SiPMs
    • Highest spatial resolution
  – Best timing resolution (249 psec)
  – 100% detector coverage, no dead space
  – Low dead time
  – Highest sensitivity (86 cps/kBq)
Organ-Specific Technology

- Brain PET consortium goal
  - 50 psec timing resolution
  - 1.5 mm spatial resolution
  - < 4 mm depth of interaction resolution
  - Use scintillators with optically polished sidewalls wrapped with Teflon and dual-ended SiPMs
  - LSO or LaBr$_3$

Eric Harmon et al, Proc of SPIE Vol 10578, 2018
Brain Biosciences, CerePET™ (not FDA approved)

- Detector: LYSO
  - 2x2x13 mm
  - Coupled to PMTs
- Spatial resolution
  - 2 mm axial and transaxial
- Portable
- Increased sensitivity (2-fold)
Total-Body PET

- Increase geometric efficiency by covering the entire body
  - Extend from 20 cm axial FOV to 200 cm
  - 4 to 5-fold gain in sensitivity for organ
  - 24-fold gain for eyes to thighs (melanoma)

From Cherry et al, J Nucl Med 2018; 59:3-12
Total-Body PET - Explorer

- Explorer PET scanner under construction
  - Increased sensitivity can be used to:
    - Reduce dose or faster scanning
    - Image at later time points (lower activity)
  - Image-derived input functions (major vessels in FOV)
  - 2.76 mm LYSO with analog SiPM
  - 400 psec timing resolution
  - Stream single events offline, large dataset
2\textsuperscript{nd} Prototype

- Detectors based on digital SiPMs from the Philips Vereos
  - 3.9 mm LYSO with digital SiPMs with 1:1 coupling
  - Timing resolution of 250 psec

- Further advances can improve sensitivity
  - Thicker crystals, reduction in dead space, greater efficiency, improve timing resolution (< 100 psec)
Image Reconstruction

- Improvements over simple backprojection
  - Filtered Backprojection (FBP)
    - Corrects for $1/r$ blurring
Filtered Backprojection (FBP)

Apply ramp filter or Hann or Shepp-Logan filters, which roll-off at higher freq
Shepp-Logan FBP

Simulation phantom shown with Shepp-Logan FBP with different cut-off frequencies (% of kmax):

1) Top left: 1.0 kmax
2) Top right: 0.8 kmax
3) Bot left: 0.6 kmax
4) Bot right: 0.2 kmax

Noise vs smoothing
Iterative Reconstruction

- Object $f(x,y)$
- ECT system
- Measured projection data sinogram $p(r,\phi)$
- Image estimate $f^*(x,y)$
- Forward projection
- Calculated projection data $p(r,\phi)$
- Compare converged?
  - Yes
  - No
- Update image estimate
- Reconstructed image
Iterations

Iteration 1
Iteration 3
Iteration 5

Iteration 10
Iteration 20
Iteration 30
Ordered Subsets and Expectation-Maximization

- Only a small number of projections, ordered subsets (OS), are used to determine the initial iterations
  - Speeds up algorithm
- Expectation-Maximization (EM)
  - Uses stats to compute most likely source distribution (ML-EM)
  - Assigns greater weight to higher count elements
Iterations

From Alessio and Kinahan, faculty.washington.edu
Newer Recon Techniques

• Preconditioned Alternating Projection Algorithm (PAPA)
  – Relaxed ordered subsets (ROS) with a non-smooth penalty function (acceleration)
  – Higher order total variation (HOTV) regularizer
  – PAPA-ROS-HOTV improves image quality, spatial resolution, noise, and contrast
  – Similar images acquired to OSEM but at 1/3 signal – 1/3 DOSE or TIME
(a) FDG Brain PET
  • Upper row: OSEM
  • Bottom row: PAPA-ROS-HOTV
(b) FDG whole body PET, non-Hodgkin’s lymphoma
  • Left: OSEM
  • Right: PAPA-ROS-HOTV
(c) ImmunoPET: $^{89}$Zr-Df-IAB2M whole body PET
  • Left: OSEM
  • Right: PAPA-ROS-HOTV

Red arrows show lesions not observed on OSEM images

Schmidtlein and Lin et al, Med Phys, 44(8) 2017
Summary

Several new technologies to improve image quality, reduce patient dose, or reduce scan time

• CZT detectors for SPECT imaging
  • Improve spatial and energy resolution and sensitivity (1.4 fold)
  • Dual isotope imaging

• Improve TOF for PET imaging
  • Increase sensitivity and SNR (3 to 10-fold)

• Replace PMTs with analog or digital SiPMs
  • Increase sensitivity and SNR

• Total-body PET imaging
  • Increase sensitivity 20-fold (body) or 4 to 5-fold for organs

• New image recon techniques
  • Increase sensitivity for low counts (3-fold)
Impact

• Increasing SNR
  – Reduce imaging time and increase throughput
  OR
  – Reduce dose (30-100-fold), which will allow repeated use of nuc med imaging
    • 6 mSv to 0.06 mSv (6 mrem) per study