Outline

• SPECT Imager Design
  – Imaging optics for gamma rays
  – Design tradeoffs
  – Calibration techniques
• Data Acquisition Systems
  – Architectures
  – Signals and conditioning
  – Event detection
  – De-randomization
  – Communication
• A survey of small-animal SPECT imagers

SPECT Imager Properties and Main “Knobs”

<table>
<thead>
<tr>
<th>Property</th>
<th>Detectors, Optics</th>
<th>Detectors, Electronics</th>
<th>Optics, Detectors</th>
<th>Detectors, Electronics</th>
<th>Electronics</th>
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</thead>
<tbody>
<tr>
<td>Spatial Resolution</td>
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<td>Energy Resolution</td>
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<td>Temporal Resolution</td>
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<td>Sensitivity</td>
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<td>Count-rate Capability</td>
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<td>Calibration</td>
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<td>Synchronization</td>
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</table>

Physical Limits

Counting statistics

$kT$

Real materials

Complexity of underlying physics

Imaging Optics for Gamma Rays

• Refraction?
  – Lenses
• Reflection?
  – Mirrors
• Diffraction?
  – Gratings & crystals
• Absorption?
  – Pinholes & collimators
Refraction

- The bending of light rays towards the normal in transitions from less to more optically dense media
  \[ n = 1 - \delta i \]
- Problem is at gamma-ray energies for most materials:
  \[ \delta \approx 10^{-6} \]
- Snell’s law:
  \[ \sin \theta_1 / \sin \theta_2 = n_2/n_1 \approx 1 \]
- So gamma-ray lenses are physically impossible…

- Or are they?
  - A compound refractive X-ray lens was invented in 1996
    - Practical up to 40 keV
  - But,
    - Long focal lengths (~ 1 m)
    - Small apertures (~ 1 mm)
    - Uses with collimated beams (synchrotrons) and microscopes
  - Another variant is the sawtooth lens:
    - (demonstrated to 80 keV!)

Reflection

- The redirection of light rays about the normal at interfaces between media of different \( n \)
- Occurs when no real solution to Snell’s law:
  \[ \sin \theta_2 = (n_2/n_1) \sin \theta_1 \]
- Problem is at gamma-ray energies for most materials:
  \[ \Delta \delta \approx 10^{-6} \]
- So gamma-ray mirrors are physically challenging…
Reflection

- Total reflection for x- and gamma rays occurs only at small angles
- Hence grazing-incidence aspheric optics:

\[ n' = 2d \sin \theta \]

Polycapillary Optics

- Hollow glass rods allow propagation of x-rays/\gamma-rays via total internal reflection
- Tapered capillaries used for focusing in the synchrotron community
- Turned into a demonstration SPECT/CT instrument by Ritman et al

Diffraction

- The redirection of light based on constructive interference of reflections from a periodic structure
- If \( \alpha \) is small, then \( \sin \alpha \) is small
- So still glancing geometries and very small acceptance angles

\[ \alpha \approx \sin \alpha \]

Diffraction

- Multilayer mirrors
- Fresnel zone plates
- Bent crystals
- All work at low energies (up to 30 keV) but are impractical for \( h\nu > 100 \) keV
  - Small fields of view
  - Fabrication issues
  - Low efficiencies
**Multilayer Mirror Optics**

- A single mirror has low collection efficiency
- NASA has pioneered multi-shell mirrors made up of arrays of metal foils
- Practical up to 35 keV
  - Above these energies, low reflectivity and finish errors limit efficiency
  - Long focal lengths (> 1 m)

**Reflection/Diffraction**


**Absorption**

- Imaginary portion of complex index of refraction
- \( \frac{I(E)}{I_0(E)} = e^{-\mu(E)x} \)
- At 140 keV:

<table>
<thead>
<tr>
<th>Element</th>
<th>Z</th>
<th>Absorption Coef. (cm(^{-1}))</th>
<th>Absorption Length (mm)</th>
<th>Transmittance (1/16&quot; material)</th>
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<tbody>
<tr>
<td>H(_2)O</td>
<td>1</td>
<td>15</td>
<td>67</td>
<td>99/100</td>
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<tr>
<td>Pb</td>
<td>82</td>
<td>36.825</td>
<td>373</td>
<td>1/15,000</td>
</tr>
<tr>
<td>W</td>
<td>74</td>
<td>36.335</td>
<td>275</td>
<td>1/150,000</td>
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<tr>
<td>Au</td>
<td>79</td>
<td>42.829</td>
<td>235</td>
<td>1/1,000,000</td>
</tr>
<tr>
<td>Pt</td>
<td>78</td>
<td>33.521</td>
<td>208</td>
<td>1/10,000,000</td>
</tr>
</tbody>
</table>

**Absorption**

- Pinholes
- Collimators
- Multi-pinholes & coded apertures
Absorption

- Other techniques
  - Rotating slits and camera
  - Scanning slit and camera

S.D. Metzler, R. Accorsi, A.S. Ayan, and R.J. Jaszczak
"Slit-Slat and Multi-Slit-Slat Collimator Design and Experimentally Acquired Phantom Images"
From a Rotating Prototype

G.L. Zeng and D. Gagnon
"CdZnTe strip detector SPECT imaging with a slit collimator"

S. Walrand, F. Jamar, M. de Jong, and S. Pauwels
"Evaluation of Novel Whole-Body High-Resolution Rotated SPECT System Based on a Novel 2D Photon Counting Detector: Monte Carlo Simulations"

P. Edholm, G.T. Herman, and D.A. Roberts
"Range Surface-Dependent Image Reformation and Evaluation"

Ideal pinhole
- \( Z = \infty \)
- \( D \sim 0 \)

Typical
- \( Z = 80 \)
- \( D \sim 3 \text{ mm} \)

Leakage
- Gold or platinum inserts
- Pb, W or Cerrobend® shields
- Shapes are a compromise between aperture thickness, acceptance angles, and vignetting at image edges
- Keel edges to reduce leakage

Multiple Pinholes: To Multiplex or Not to Multiplex

- Definitely don’t want pinhole arrangement symmetric with respect to rotation axis
- Multiple lobes in PSF can give some reconstruction artifacts – false lesions
- More iterations of reconstruction algorithm typically required
- Benefit depends on object and tracer distribution


"A prototype coded-aperture detector for small animal SPECT"

Intentional Vignetting
- Entrance side normal clearance angle
- Exit side shaped to scrape in order to define projection area

Adaptive, Anamorphic Projection

- Crossed-slit collimator decouples axial and transaxial magnifications
- Make full use of detector area regardless of object shape

Pinhole Clusters

- Replace a single pinhole with an array of smaller pinholes
- Keep angles shallower to reduce keel edge penetration
- Good for higher energies (511 keV)

Absorption

- Collimators - 4 basic flavors
- We use for our solid-state detectors:
  - Parallel hole
  - Laminated photoetched W
  - 180 layers - 7 mm thick
  - 380 µm bore spacing, 120 µm septa
  - Efficiency $= 5 \times 10^{-5}$
  - Manufactured to our spec by Tecomet of Woburn, MA

Absorption

There is ample literature on the design and analysis of single and multiple pinhole systems. Good entry points are the following papers and the literature they cite.


Understanding the Tradeoffs Between FOV, Sensitivity, Magnification, and Resolution

Geometric efficiency for a single pinhole on axis is given by:

\[ E = \pi \frac{r^2}{4b^2} \]

\( E \) is the ratio of the pinhole area to the area of the sphere with radius defined by the object to pinhole distance.

Magnification is given by:

\[ M = \frac{a}{b} \]

\( M \) is the ratio of the image to pinhole and object to pinhole distances.

The field of view (FOV) is proportional to:

\[ \text{FOV} \propto \frac{b}{a} \]

\( \text{FOV} \) is the face of the gamma camera projected back through the pinhole.

The contribution to image blur by pinhole blur is given by:

\[ R_{\text{pinhole}} = \frac{2r(a+b)}{a} \]

\( R_{\text{pinhole}} \) is the projection of the pinhole onto the camera face by marginal rays.
Understanding the Tradeoffs Between FOV, Sensitivity, Magnification and Resolution

The contribution to image blur by the intrinsic camera resolution is given by:

\[ R_{\text{camera}} = R_{\text{intrinsic}} \frac{b}{a} \]

ie the projection of the camera pixel element back through the pinhole.

Gamma camera

Parallel-hole collimators

\[ E = \frac{A_h}{4\pi L_b^2} F_{\text{packing}} \]

\[ R = D_b \frac{(L_0 + L_b)}{L_b} \]

Conclusion: Have to work close to collimator face for high resolution. Sensitivities tend to be low.

Key Points

- Magnification: as large as the required field-of-view and camera size permits.
- Obliquity: if the object to pinhole distance is very short, then vignetting by the pinhole and depth-of-interaction effects become problematic at the edges of the detector.
- Design needs to consider the imaging experiment to be performed – and there will in general be a need for different pinhole sizes and locations for different imaging tasks.

One (or a few) Camera Design Options

- Stationary camera(s)
  - Mouse rotates about vertical axis
  - Pros: Simplest arrangement
  - Cons: Abnormal position for mouse
  - Measured or modeled PSF must be rotated during reconstruction

- Stationary mouse
  - Camera rotates about horizontal axis
  - Pros: Mouse in normal position
  - Cons: High precision motion required with possibly heavy camera(s)
  - PSF probably needs to be modeled
Multi-Camera or Annular Camera Design Options

• Stationary cameras
  • Pros:
    – Mouse in normal position
    – High sensitivity
    – All data acquisition in parallel – dynamic capability
    – PSF can be accurately measured
  • Cons:
    – Imager size and complexity

Commercial Pre-Clinical Imager Examples

- Mediso/Bioscan NanoSPECT/CT
- MILabs USPECT
- Gamma Medica FLEX Triumph
- Siemens Inveon
- Scintillation detectors – pixelated or monolithic
- Solid-state detectors - CZT
- Resolution from magnification
- Sensitivity from multiple pinholes

Summary of SPECT Imager Design Decisions

• Camera type
  – Technology, size, number of resolvable elements, sensitivity, energy resolution, count-rate capability
• Number of cameras
  – Acquisition time
• What, if anything, moves and how
• Aperture type
  – Collimator or pinhole(s) or other
• Sensitivity, magnification, and field of view
• Next:
  – Calibration
  – Acquisition

Calibration

Directly measure camera and imager response.
Calibrates optical performance and corrects for mechanical tolerances, electronic variations, and detector material imperfections.

• PSF or System Matrix
  – Exhaustive: scan point source in regular 3-D grid throughout object volume
  – Parametric: scan to tune modeling/compensation parameters
• MDRF
  – Scan collimated source in regular 2-D grid across every camera face
  – Shadow grid
Calibration Stages

Rotation and secondary translation makes it easy to scan the source precisely above each camera face.

Mean Detector Response Function (MDRF) Calibration

Calibration References

F. van der Hee, B. Vesterhage, M. Rentmeester, and F.J. Beekman
"System Calibration and Statistical Image Reconstruction for Ultra-
High Resolution Stationary, Pinhole SPECT"

Y-C. Chen, L.R. Furenlid, D.W. Wilson, and H.H. Barrett,
"Calibration of Scintillation Cameras and Pinhole SPECT Imaging"

And references therein.

Trends

- Data processing and acquisition benefit from the rapid pace of technology development in:
  - Fast, low-noise op amps and A/D converters
  - Readout ASICs
  - GPUs and FPGAs
  - Networking and communications
  - Computing power and storage capacities
Photomultipliers and Multi-Anode PMTs

- Standard detectors in gamma-ray imaging

Scintillator (monolithic or segmented) and Lightguide

Asynchronous Solid-State Detectors

- A good semiconductor detector
  - Fast
  - Linear
  - No gain unless avalanche
  - Low photon energy cost per charge carrier pair

• A good semiconductor detector
  - Fast
  - Linear
  - No gain unless avalanche
  - Low photon energy cost per charge carrier pair

Integrating Readouts

Synchronous (clocked) devices

- Gated-integrator readouts
  - CZT pixel arrays
- Charge storing detectors
  - CCDs

Gated Integrators

- Applicable to all kinds of detectors
- Convenient for big arrays and implementation in ASICs
- However, integrate leakage current
- kT/C noise from the reset
- Work around - CDSH

B.W. Miller, H.B. Barber, H.H. Barrett, I. Shestakova, S. Singh, V.V. Nagerkar,
"Single-photon spatial and energy resolution enhancement of a columnar CsI(Tl)/EMCCD gamma-camera using maximum likelihood estimation"

G.A. de Vree, A.H. Wiedra, I. Moody, F. van der Have, K.M. Ligocki, and F.J. Seelkman,
"Photon-Counting Gamma Camera Based on an Electron-Multiplying CCD"
Gated Integrator Unit Cell

- Reset Switch
- CDSH Buffer
- Bump Bond
- From Detector Electrode
- To Bus

Amplifier Output versus Time

- Voltage
- Time (ms)
- baseline
- w/ gamma-ray

Pixel Array Detectors

- 2-D array scanned and processed externally
- Can read entire raster into buffer and scan with DSP/CPU
- Double buffer to prevent loss of data
- Better: on the fly detection with gate array
  - Need data from 2-D sub-pixel area
  - Pipeline processing
    - Rastered readout must be run through multi-tap shift register to access pixels from adjacent rows

Data-Acquisition Architectures

- List-mode: raw data is maintained as an ordered list
  - benefits
    - Can apply new statistical algorithms to any data
    - No information loss
    - Can reconstruct on different attributes - image, fluence, raw list
    - Can add physiological signals as entries in list
  - drawbacks
    - Data lists occupy large amounts of memory
- Image mode: data is processed and stored as a bitmap
  - benefits
    - Data have fixed size, typically modest
    - Data can quickly be visualized
  - drawbacks
    - Original observations not available for further processing
Data-Acquisition Architectures

- List-mode acquisition strategy makes it possible to design a common data-acquisition architecture to support a wide variety of camera technologies and imager designs
  - Modular cameras
  - CZT cameras with readout ASICS
  - PSFMT cameras
  - CCD's and other devices

![Diagram of data-acquisition architecture]

Modular Camera Acquisition System

- 16 cameras in 2 rings of 6 with adjustable radial position
- 5 axis robotic stage for calibration and imaging subject positioning
- Exchangeable cylindrical imaging apertures for choice of magnification/field-of-view

![Diagram of modular camera acquisition system]

FastSPECT II Imager

Key Features:
- List-mode data acquisition architecture
- Full dynamic imaging capability for periodic and non-periodic processes

![Diagram of FastSPECT II imager]
Modular Apertures

- Gold insert pinholes
  - currently 3 sizes: .1, .5, and 1 mm dia
- 1/2" Pb cylinder with cast cerrobend end cap
- Imaging geometry has pinholes located on lines between camera centers and imager center point
- Efficiency ~ 4 \times 10^{-4}

Fast Position Estimation

- Raw list-mode data
- Cameras fully calibrated with exhaustive scanning of highly collimated source
- Maximum-likelihood estimation of gamma-ray interaction position and energy.

Very Efficient ML Search Algorithm

- Can be reduced to integer math only with use of look-up tables
- Suitable for parallel computing, pipelining and implementation in GPU or gate array

Resolution Phantom Image on FSII

- Bore diameters and separations
  - 1.0 mm diameter w/ 3 mm center-to-center distance
  - 1.5 mm diameter w/ 4.5 mm center to center distance
  - 2.0 mm diameter w/ 6 mm center to center distance

Volume Rendering
FSII: Dynamic Image Sequence

18 mm
5 second time steps, 1 axial slice

99mTc Glucarate Uptake in Xenograft Tumor on Mouse Mammary Fat Pad

Challenge: How to Best Configure Instrument

Resolution
Sensitivity
Field of View

16X Magnification
3X Magnification

High-resolution SPECT Imaging of Bone Invasion by Neuroblastoma in the Mouse Knee

Axial
Coronal
Sagittal

Left: volume rendering
Right: CT indicating FOV

BazookaSPECT Camera

CdWO₄ Scintillator Crystal 10 mm × 10 mm thick
Scan direction

511 keV lead collimator

Bazooka CMOS Sensor
Image intensifier

Graduate student Brian Miller
511 keV γ-Photon Scintillation Imaging

Acquisition Mode
- Photon counting (fast frames with few events)
- Integrating (slow frames with lots of events)

Distance between beam axis and scintillator front face

Beam direction

FastSPECT III
Third generation high-resolution dynamic SPECT imager

Graduate student
Brian W. Miller

FSIII – Front End LM Processor

Processes events from 4 simultaneous data streams each with up to 200 640 × 480 frames per second with 7.4 µm × 7.4 µm pixels.

Frame Processing of all cameras in real time at 200 fps = 4000 fps to give ~1.23 Gpix/s

Easily handled with GPU programming

CGIR Graduate
Stephen Moore

Rapid Prototyping

Objet Geometries: Connex350™
- 16 micron slices
- 42 micron lateral resolution
- Multiple Materials
- 35 x 35 x 20 cm³ build volume
New Line of SPECT/PET-MRs

Non-overlapping Projections

Conclusions

- On-going rapid developments: imaging principles, detectors, systems and computing resources (GPUs)
- List-mode architectures have advantages, including ability to support new camera technologies without having to reinvent software and data links
- Careful calibration critical for optimal system performance
- Stationary imager designs permit dynamic and high-throughput studies
- System design process can/should be thoroughly guided by simulations with realistic digital phantoms.
Path to Higher Resolution Small-Animal SPECT

- 2-3 mm intrinsic-resolution Anger camera + 1-2 mm bore parallel-hole collimator
- + filtered back projection reconstruction
- Move to pinhole aperture with magnification
- Develop analytical forward model and switch to statistical reconstruction (ML-EM, etc.)
- Add additional pinholes and cameras to acquire projections in parallel
- Calibrate system for more accurate forward model – measured H matrix
- Make pinholes smaller and move closer to object, trading FOV for magnification
- Improve camera intrinsic resolution, add DOI to reduce parallax errors
- Gate acquisition to reduce respiratory and cardiac motion
- Eliminate events with non-local energy deposition in detector
- Combine with high-resolution anatomical modality
- Incorporate scatter and attenuation in object-specific H matrix
- Reconstruct in photon-by-photon list-mode form