SPECT/CT: Basics, Quality Assurance, and Clinical Applications

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Educational Objectives

1. To understand the physics principles underlying SPECT/CT image acquisition and reconstruction
2. To understand the quality assurance procedures specific to SPECT/CT systems
3. To become familiar with clinical applications of SPECT/CT imaging

SPECT

- Single Photon Emission Computed Tomography
  - Radio-pharmaceutical administration – injected, ingested, or inhaled
  - Bio-distribution of pharmaceutical – uptake time
  - Decay of radionuclide from within the patient – the source of information
  - SPECT – Gamma camera detects radionuclide emission photons
  - PET – Coincidence ring detector detects annihilation photons
  - Tomography performed to image the radio-pharmaceutical distribution within the patient

- Used for visualization of functional information based on the specific radio-pharmaceutical uptake mechanism

Gamma Camera

- NaI(Tl) is the scintillator of choice
  - High light output and high detection efficiency (~85% at 140 keV for 3/8 in. NaI)
  - Good energy resolution (~10% at 140 keV)
  - Large crystals (50 cm x 40 cm)
  - Hygroscopic!

- Intrinsic Spatial and Energy Resolution
  - # of scintillation photons, \( N \propto \Gamma \) Gamma-ray energy, \( \Gamma \)
  - Spatial Resolution \( = 100 \times \sigma / N \propto 1 / \sqrt{N} \propto 1 / \sqrt{\Gamma} \)
  - Energy Resolution \( = 100 \times \text{FWHM} / \Gamma \propto 1 / \sqrt{\Gamma} \)
Collimators

Nal Crystal

Absorptive Collimation

\( \gamma \) source

Collimator Resolution

Collimator Resolution

\[ R_s = \frac{D}{L_s} (L_s + H + B) \]

System Resolution

\[ R_t^2 = R_s^2 + R_g^2 \]

Resolution is highest closest to the collimator therefore while imaging position patients as close as possible to collimator face

Collimator Efficiency

\[ G = \theta F \quad \text{where} \quad \theta = C \left( \frac{D}{L_s} \right)^2 \]

\( \theta = \text{fraction of } 4\pi \)

\( F = \text{exposed fraction} \)

Parallel Hexagonal hole C =

\[ \text{LEHR} = 1.3 \times 10^{-4} \]

\[ \text{MELP} = 3.1 \times 10^{-4} \]
### Sensitivity versus Source Distance

- **Sensitivity**: the detected photons count rate per unit activity [cps/μCi]
  
  - Photon flux vs. distance \( \propto z^{-2} \)
  - Crystal area vs. distance \( \propto z^{2} \)
  - Overall sensitivity \( S \propto z^{-2} \cdot z^{2} \sim \text{constant} \)

\[ z = L_C + H + B \]

### Anger Logic for Event Position

- Interaction location based on relative signal between \( X^* \) and \( X \) (for \( X \) location) & \( Y^* \) and \( Y \) (for \( Y \) location)
  
  - \( X = (X^* - X)/(X^* + X) \rightarrow \text{range} \ -1 \text{ to } +1 \)
  - \( Y = (Y^* - Y)/(Y^* + Y) \rightarrow \text{range} \ -1 \text{ to } +1 \)

- Interaction Energy \( \propto \) Total Signal = \( X^* + X + Y^* + Y \)

### SPECT Acquisitions

- Emission Tomography, 2004

\[ \text{SPECT in the year 2000, JNMT 24:233, 2000} \]

- SPECT acquires 2D projections of a 3D volume

- Wernick & Aarsvold, Emission Tomography, 2004

- © Yale School of Medicine
SPECT data corrections

- Measured Projections
- INT Uniformity Correction
- EXT Uniformity Correction
- SPECT in kBq/mL
- MHR/COR
- Inter-frame decay (some)
- Scatter Correction
- FBP/IR reconstruction
- CT Attenuation Correction
- Collimator Resolution Modelling

SPECT Iterative Recon: Scatter Modeling

- Scatter compensation occurs before attenuation
  - the photopeak window contains scatter
  - attenuation accounts for the removal of photopeak photons

- Adjacent energy window based estimate (DEW and TEW): Scatter estimated as a weighted sum of adjacent energy window images, \( C_i(x,y,\theta) = \sum k_i \times C_i(x,y,\theta) \)

- Subtract scatter prior to reconstruction
  \( P_{\text{conf}}(x,y,\theta) \rightarrow P(x,y,\theta) - S(x,y,\theta) \)

- Incorporate scatter into forward projection
  \( P(x,y,\theta) \rightarrow P_{\text{conf}}(x,y,\theta) + S(x,y,\theta) \)

SPECT Acquisition Schema

- Circular versus (non-circular) body-contour orbit
- Step-and-Shoot versus Continuous Mode
SPECT violates Radon transform angular symmetry → Differential Attenuation

\[ I(\theta) = I_0 e^{-\mu_b \int L \text{d}L} \]

\[ I(\theta + \pi) = I_0 e^{-\mu_b \int L \text{d}L} \]

- Other mediating factors:
  - distance-dependent resolution
  - depth-dependent scatter

SPECT Acquisition Schema

- SPECT projections acquired over 360-degrees
  - Exception: Cardiac SPECT acquired over 180°

SPECT Iterative Reconstruction

Maximum Likelihood Expectation Maximization (ML-EM)
Ordered Subset Expectation Maximization (OS-EM)

- Accounts for the statistical nature of photon detection
- Incorporates the system response \( p(b,d) \) – the probability that a photon emitted from an object voxel \( b \) is detected by projection pixel \( d \)
- \( p(b,d) \) captures...
  1. Depth-dependent resolution
  2. Position-dependent scatter
  3. Depth-dependent attenuation
- Use a measured attenuation map along with models of scatter and camera resolution to perform a far more accurate reconstruction

SPECT Iterative Reconstruction

- True projection intensity = sum of true voxel intensities weighted by detection probabilities

\[ y(d) = \sum_{b=1}^{B} \lambda(b) p(b,d) \]

- True voxel intensity = sum of true detector intensities weighted by detection probabilities

\[ \lambda(b) = \sum_{d=1}^{D} y(d) p(b,d) \]
In clinical practice, the stopping criteria is number of iterations (a time constraint) instead of a convergence criteria.

**Hybrid SPECT/CT Motivation**

- **X-ray transmission CT**
  - Improved speed (<1 min)
  - High-resolution anatomical images
  - Higher radiation dose
- **Functional-anatomical overlay (image fusion)**
  - Improve localization of uptake regions
  - Increase confidence in interpretation

**HU-to-μ (CT-AC) Transforms**

\[
\mu(E_x) = \frac{\mu(E_{x1}) - \mu(E_{x2})}{\mu_x(E_x)} \times 1000
\]

\[
\mu_x(E_x) = \left(1 \times \frac{H_u_x}{1000}\right) \times \mu_x(E) \times \frac{\mu_x(E_{x1})}{\mu_x(E_{x2})}
\]

- Photon energies different between CT and SPECT
- K=1 for Compton Scatter dominates low Z at ECT (low HU)
- K≠1 for Photoelectric pertinent for high Z at ECT (high HU)
- HU-to-μ transform is piece-wise linear (bi- or tri-modal)
CT-based AC for SPECT/CT

- CT
- CT noise reduced
- Smooth, re-bin CT to match SPECT
- Register CT w/ SPECT
- CT\(_{AC}\)
- Apply bi-linear transform on pixel-by-pixel basis
- \(\mu\)-map
- Reconstructed SPECT
- Transition Matrix \(a_{ij}\)
- Other factors:
  - SPECT projections
  - Scatter estimates
  - Collimator response

Role of CT in SPECT/CT

- Two functions for CT as part of NM exams
- Anatomic Localization
- AC
  - Does location \((x, y, z)\) in SPECT image space spatially corresponds to location \((x, y, z)\) in CT image space?
- CT Dose Requirement
  - Higher (Diagnostic)
  - Moderate
  - Ultra-low (CT-AC only)

SPECT/CT Quality Control

- Planar (AAPM Reports 6 and 9; NEMA NU 1-1994)
  - Energy resolution (Intrinsic)
  - Spatial resolution (Intrinsic and Extrinsic)
  - Uniformity (Integral and Differential)
  - Deadtime
  - Sensitivity (\(\gamma\) collimator)
  - Pixel Size
  - Rotational Uniformity and Sensitivity Variation
  - Opposed-Head Spatial Registration
  - Multiple Energy-Window Spatial Registration
- SPECT (AAPM Reports 22 and 52)
  - Uniformity and Contrast (Image Quality)
  - Resolution
  - MHR/COR (\(\gamma\) collimator)
- SPECT/CT (AAPM TG 177: Jim Halama)
  - SPECT and CT image registration
  - Image Quality (attenuation, scatter correction, iterative reconstruction)

SPECT/CT: Image Registration

- To verify the electro-mechanical registration of the isocenter and reconstructed field-of-view between the SPECT and CT images
  - Does location \((x, y, z)\) in SPECT image space spatially corresponds to location \((x, y, z)\) in CT image space?
- SPECT/CT image registration is critical for
  - Accurate SPECT images via CT-based attenuation correction
  - Display of fused images for clinical interpretation
- Does not address mis-registration due to patient movement between SPECT and CT
Registration Test Setup A

- Acquire SPECT/CT scan of 3 point sources (capillary tubes) in air containing both CT-contrast and Tc-99m solution

Registration Test Setup B

- Use Co-57 button sources w/ SPECT Jaszczak phantom containing Tc-99m water
  - Co-57 emits 122 keV; Photopeak window 122 keV w/ 20% window
  - Tc-99m emits 140 keV; Photopeak window 140 keV w/ 15% window
- 19% of counts in $^{57}$Co energy window (110-134 keV) contained in $^{99m}$Tc energy window (129-150 keV)

Image Registration – Data Analysis

- Overlay re-sampled SPECT and CT images in fused display
- For each of the 3 points determine the shift in $(\Delta x, \Delta y, \Delta z)$ to match center of point source between SPECT and CT images
- Calculate the mean deviation between SPECT and CT images along any one direction as
  - Mean deviation along x-axis = $(\Delta x_1 + \Delta x_2 + \Delta x_3)/3$
  - Similar for y and z
- PASS criteria specifications TBD
  - Mean deviation along any axis is less than one SPECT-pixel used in routine clinical imaging
SPECT/CT: Image Quality

- ACR SPECT phantom ("Jaszczak") with cold spheres and cold wedge section
- SPECT data acquisition based on ACR or AAPM Rpt 52
- Use typical CT exam parameters used for SPECT/CT scans
- Reconstruct the SPECT data with iterative reconstruction using CT-based AC, DEW scatter correction, and other routinely used reconstruction parameters
- Establish the baseline for image quality at Acceptance Test
- Evaluate the annual test results against baseline values

Clinical SPECT/CT Imaging

- Radiopharmaceuticals available for SPECT/CT imaging
  - Stress/Rest Myocardial Perfusion Imaging
    - Stress: $^{99m}$Tc-sestamibi or $^{99m}$Tc-tetrofosmin
    - Rest: $^{99m}$Tc-labeled agents or $^{99m}$Tc-chloride
  - $^{99m}$Tc-MDP: bone diseases, bone metastases
  - $^{99m}$Tc-MAA: perfusion
  - $^{99m}$Tc-sestamibi: parathyroid adenomas
  - $^{99m}$Tc-sulphur colloid: liver/spleen, lymphoscintigraphy
  - $^{111}$In-Pentetreotide: neuroendocrine cancers
  - $^{111}$In-ProstaScint: prostate cancer
  - $^{123}$I/$^{131}$I-MIBG: pheochromocytoma, neuroblastoma
  - $^{123}$I/$^{131}$I-Nal: thyroid cancer
  - $^{99m}$Tc-CEA: colorectal cancer
  - $^{99m}$Tc-RBCs: hemangioma
  - $^{99m}$Tc-HMPAO, -ECD: brain perfusion
  - $^{111}$In-WBC: infection
  - $^{67}$Ga-citrate: inflammation, lymphoma
  - $^{201}$Tl-chloride: tumor perfusion
  - $^{153}$Sm-EDTMP: skeletal disease
  - $^{99m}$Tc/CT: skeletal mets
- Some examples of clinical SPECT/CT imaging ...
Ectopic parathyroid adenoma: What is the exact location for surgery?

- **99mTc-sestaMIBI Parathyroid Imaging**
  
  ![Images of parathyroid imaging](image1.png)

**90Y-microspheres Radioembolotherapy (Selective Internal RT)**

- Hepatocellular Ca (TheraSphere®, MDS Nordion)
- Colorectal Ca liver mets (SIR-Spheres®, SirTex)

![Images of radioembolotherapy](image2.png)

**99mTc-MAA Pre-Therapy SPECT/CT**

- **90Y dose calculation & safety assessment**
- **99mTc-MAA SPECT/CT**
  - Catheter placement
  - Extra-hepatic shunting
  - Lung shunting
  - Perfusion

![Images of 99mTc-MAA SPECT/CT](image3.png)

**99mTc-MAA SPECT/CT (~20 min)**

- Detection of Extra-Hepatic MAA Shunting

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(Ahmadzadehfar et al, JNM, 2010)

**90Y SPECT/CT (~35 min)**

- IEC phantom with SBR of 8
  
  ![Images of 90Y SPECT/CT](image4.png)

(Sinan et al, JNM 56, 2015)
Pre and Post $^{90}$Y-microsphere therapy

PRIOR
- CT 3-June-2008
- Tc-99m MAA SPECT/CT 24-June-2008

THERAPY
- CT 5-Sept-2008
- 90Y SPECT/CT 2-July-2008

POST
- Tc-99m MAA SPECT/CT 2-Sept-2008

99mTc-MAA Lung Perfusion SPECT/CT: Lung Function-based IMRT Planning

- **Goal**: lower radiation dose to functioning normal lung during IMRT of lung tumors by incorporating functional (in addition to anatomical) information in the treatment plan.

$^{153}$Sm-EDTMP Bone SPECT/CT: Internal Radionuclide Therapy

- Dosimetric imaging with 30 mCi tracer dose
  - Whole body planar images at 0, 2, 4, 24, 28, 48, and 52 hr
  - SPECT/CT of target tumor at 24 hr to estimate tumor volume and absolute uptake
  - Target tumor dose $\geq 40$ Gy (w/ bladder & kidneys < 20 Gy)

Tumor Dose Estimate:
- Mass ($M$) = 0.688 kg (1g/cc)
- Residence Time ($T$) = 10.7 h
- $A$ (GBq) = 71.6 (or 1.935 Ci)
- Dose ($D$) = $A \times T / M = 172$ Gy

Whole-body SPECT/CT

$^{99m}$Tc MDP Bone Imaging
SPECT with contrast CT
- $^{99m}$Tc Sestamibi SPECT/CT → Identification (NM)
- Multi-phase IV contrast H&N CT → Localization (Radiology)
- Synergy of SPECT/CT & contrast CT under clinical evaluation

Clinical Benefits of SPECT/CT
- Visualization, diagnosis and interpretation of primary and metastases diseases
  - Higher sensitivity and contrast than Planar imaging
  - CT scan increases confidence in interpretation of SPECT examination
- Surgical planning
- IMRT treatment planning
- $^{90}$Y-microspheres therapy planning
- Internal radio-pharmaceutical therapy planning

SPECT/CT: Limitations
- Patient motion
  - Between SPECT and CT scans
  - Respiratory and cardiac motion during SPECT acquisitions
- Contrast CT
  - Contrast introduces electron density-material mismatch
  - $\mu$ map algorithms do not yet account for contrast CT
- Absolute quantification (Bq/mL) not yet fully developed
  - Radionuclide-dependent
  - Acquisition/reconstruction technique-dependent
  - Calibration techniques not yet standardized

‘Take-home’ message

Nuclear Medicine often referred to as “unclear” Medicine
SPECT/CT and PET/CT
has changed the paradigm to ...

“New-clear” Medicine Imaging
  - von Schultess (MIB, 2004)