LECTURE 6: Pre-Processing for Nuclear Medicine Images

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Outline

1. The use of PET/SPECT, PET/CT and MRI/PET Images
2. What to measure from Nuclear Medicine Images?
3. Denoising Nuclear Medicine Images
4. Partial Volume Correction
I. the use of PET/SPECT, PET/CT and MRI/PET Images
Nuclear Medicine Imaging Modalities

- **Scint**: Scintigraphy, two-dimensional images
- **PET**: Positron Emission Tomography
- **SPECT**: Single Photon Emission Tomography
- ...

**PET and PET-CT Sites in the US**

<table>
<thead>
<tr>
<th></th>
<th>2008</th>
<th>2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fixed PET</td>
<td>215</td>
<td>120</td>
</tr>
<tr>
<td>Fixed PET-CT</td>
<td>715</td>
<td>1030</td>
</tr>
</tbody>
</table>

**1,744,000 Clinical PET and PET-CT Studies in 2011 (US Statistics)**

- Oncology: 95%
- Cardiology: 3%
- Neurology: 2%
Where we use them?

1,650,000 Clinical PET and PET-CT Studies in 2010 (US Statistics)

- Diagnosis: 33%
- Staging: 19%
- Treatment Planning: 38%
- Therapy Followup: 10%
Basics of PET/SPECT Imaging

• Uses short-lived positron emitting isotopes (produced by collimators)
• Two gamma rays are produced from the annihilation of each positron and can be detected by specialized gamma cameras
• Resulting image show the distribution of isotopes
• An agent is used to bind into isotopes (glucose, …)
PET/CT and PET/MRI
PET/CT and PET/MRI

MRI/PET (or should I say PET/MRI?)
-superior soft tissue contrast resolution
-minimized radiation

PET/CT
choice of modality for oncological applications
SPECT Imaging

- PET and SPECT are distinguished by the type of radioisotope incorporated in the tracer.
SPECT Imaging

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  - PET => radioisotope emission
  - SPECT => gamma-ray photon emission
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(credit: M. Wernick and J. Aarsvold)
SPECT Imaging

- Myocardial perfusion imaging
  - Illustrates the function of the heart muscle

(Credit: wikipedia)
SPECT Imaging

- Myocardial perfusion imaging
- Functional brain imaging
- Bone diseases
- Neuroendocrine or neurological tumors
- White cell scan
- …
II. What to Measure?
What to Measure in PET/SPECT/.. Images?

- **SUV** (standardized uptake value: voxel-wise or region-wise) (SUVpeak, SUVmax, SUVlbm)
What to Measure in PET/SPECT/.. Images?

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  - **FDG** is widely used radiotracer in PET, and glucose analog.
  - It accumulates in (preferentially) malignant cells due to higher glucose metabolism.
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  - The SUV is a semi-quantitative measure of normalized radioactivity concentration in PET images:

\[
SUV = \frac{\text{activity concentration in the tissue}}{\text{injected activity/body size}}
\]
What to Measure in PET/SPECT/.. Images?

Axial fused FDG PET/CT image shows tumor contours automatically generated with diagnostic software (XD3 Multi-Modality Diagnostic Software; Mirada Medical, Oxford, England) by using percentages of the maximum SUV (20%, 30%, 40%, and 50%) and a fixed SUV cutoff of 2.5.

A sample histogram – PET image
A sample histogram – PET image

Eur J Nucl Med Mol Imaging
DOI 10.1007/s00259-013-2484-x

EDITORIAL

\( \text{SUV}_{\text{max}} \) of 2.5 should not be embraced as a magic threshold for separating benign from malignant lesions

Thomas C. Kwee • Gang Cheng • Marnix G. E. H. Lam • Sandip Basu • Abass Alavi
What to Measure in PET/SPECT/.. Images?

- Metabolic lesion/tumor volume (MTV)
What to Measure in PET/SPECT/.. Images?

- Metabolic lesion/tumor volume (MTV)
  - Requires precise delineation/segmentation of lesion(s)
  - Should be distinguished its meaning from GTV (gross Tumor volume)

Patient with multiple melanoma,
MTV = 77.2 mL
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Patient with multiple melanoma, MTV=77.2 mL

What to Measure in PET/SPECT/.. Images?

- Metabolic lesion/tumor volume (MTV)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Patients who died (n = 9)</th>
<th>Survivors (n = 38)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>SUVmax (g/mL)</td>
<td>14.1 ± 1.7</td>
<td>10.6 ± 1.4</td>
<td>0.2492</td>
</tr>
<tr>
<td>Mean SUVmax</td>
<td>8.7 ± 1.5</td>
<td>7.7 ± 1.1</td>
<td>0.6841</td>
</tr>
<tr>
<td>(g/mL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean SUVmean</td>
<td>4.9 ± 0.8</td>
<td>3.8 ± 0.4</td>
<td>0.2445</td>
</tr>
<tr>
<td>(g/mL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TLG (g)</td>
<td>707.3 ± 198.9</td>
<td>197.4 ± 45.1</td>
<td>0.0004</td>
</tr>
<tr>
<td>MTV (mL)</td>
<td>123.2 ± 30.6</td>
<td>28.9 ± 4.2</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

Data are mean ± SE.

Patient with multiple melanoma, MTV=77.2 mL
What to Measure in PET/SPECT/.. Images?

- Shape information of (functional) lesion (spiculated vs focal)
What to Measure in PET/SPECT/.. Images?

- spiculated
- focal
What to Measure in PET/SPECT/.. Images?

- Texture information of lesion (heterogeneous vs homogeneous)
What to Measure in PET/SPECT/.. Images?

• Texture information of lesion (heterogeneous vs homogeneous)

TEXTURE ANALYSIS?

• Technique used in image processing to identify, characterize, and compare regions with distinct patterns

• Measure and capture local image properties which are not necessarily based on intensity properties
What to Measure in PET/SPECT/.. Images?

- Texture information of lesion (heterogeneous vs homogeneous)

TEXTURE ANALYSIS?

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- Measure and capture local image properties which are not necessarily based on intensity properties
What to Measure in PET/SPECT/... Images?

- Texture information of lesion (heterogeneous vs homogeneous)

A spatial arrangement of a predefined number of voxels allowing the extraction of complex image properties.

Credit to:
Example Texture Analysis Strategy

### A. Global features

- **Intensity histogram**
  - Minimum (1)
  - Mean (2)
  - Maximum (3)

### B. Regional features

- **Homogeneous areas size**
  - Size-zone variability
  - Intensity variability
- **Intensity size-zone matrix**

### C. Local features

- **Concurrence matrix**
  - Distance = 1
  - Direction = →

---

Credit to: M. Hatt, JNM
Complete responder, non-responder, and partial responder tumors?
Complete responder, non-responder, and partial responder tumors?
### Global features

<table>
<thead>
<tr>
<th></th>
<th>11.7</th>
<th>11.0</th>
<th>9.6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum intensity</td>
<td>8.2</td>
<td>7.3</td>
<td>5.3</td>
</tr>
<tr>
<td>Mean intensity</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Regional features

<table>
<thead>
<tr>
<th></th>
<th></th>
<th>0.15</th>
<th>0.17</th>
</tr>
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<tbody>
<tr>
<td>Intensity variability</td>
<td>0.07</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Size-zone variability</td>
<td>0.27</td>
<td></td>
<td></td>
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</table>

### Example Texture Analysis in PET Images

The images show different textures analyzed using PET imaging techniques. The table below provides quantitative measures of texture analysis, including global and regional features.
Example Texture Analysis in PET Images

<table>
<thead>
<tr>
<th></th>
<th>Complete Responder</th>
<th>Partial Responder</th>
<th>Nonresponder</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Global features</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
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<td>Maximum intensity</td>
<td>11.7</td>
<td>11.0</td>
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<td></td>
<td></td>
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</tr>
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<td>0.07</td>
<td>0.15</td>
<td>1</td>
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What to Measure in PET/SPECT/.. Images?

- Number and distribution of the lesions (focal, multi-focal)

**Ex.** Infections diseases such as in TB (tuberculosis), we often see multi-focal uptake
What to Measure in PET/SPECT/.. Images?

- Number and distribution of the lesions (focal, multi-focal)
III. Denoising Nuclear Medicine Images
Noise in PET Images

PET images have low SNR
Noise in PET Images

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Noise affects qualitative and quantitative evaluations
Noise in PET Images

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- Noise affects qualitative and quantitative evaluations
- To model noise distribution, Gauss. assumption is often made
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  - GAUSSIAN distribution
  - POISSON distribution
  - Mixed POISSON GAUSSIAN
Noise in PET Images

- PET images have low SNR
- Noise affects qualitative and quantitative evaluations
- To model noise distribution, a Gaussian assumption is often made
  - SUV
  - MTV
  - TLG and other metrics are affected
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Noise in PET Images

PET images have low SNR. Noise affects qualitative and quantitative evaluations.

To model noise distribution, Gauss. assumption is often made:
- GAUSSIAN distribution
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Current Methods:
- Signal-dependent Noise models
- Gaussian Smoothing
- Adaptive Filtering (Perona-Malik)
- Anatomy Guided (wavelet, etc.)

• SUV
• MTV
• TLG and other metrics are affected
Realistic Approach to PET Denoising

- A mixed Gaussian-Poisson distribution should be considered as noise model
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  – $O = P.I + n$
  – (O: observed image, I: clean image, P: Poisson noise, n: Gaussian noise)
Realistic Approach to PET Denoising

- A mixed Gaussian-Poisson distribution should be considered as noise model
  - $O = P \cdot I + n$
  - (O: observed image, I: clean image, P: Poisson noise, n: Gaussian noise)
  - How can we Gaussianize above equation?
Realistic Approach to PET Denoising

- A mixed Gaussian-Poisson distribution should be considered as noise model
  - $O = P.I + n$
  - $(O$: observed image, $I$: clean image, $P$: Poisson noise, $n$: Gaussian noise)
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    • Anscombe’s Transformation
    • Generalized Anscombe’s Transformation (GAT)
Realistic Approach to PET Denoising

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Realistic Approach to PET Denoising

\[ f_\sigma(x) = \begin{cases} 
\frac{2}{\alpha} \sqrt{\alpha x + \frac{3}{8} \alpha^2 + \sigma^2 - \alpha \mu} & \text{if } x > -\frac{3}{8} - \sigma^2 \\
0 & \text{otherwise.} 
\end{cases} \]
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Poisson distribution
Realistic Approach to PET Denoising

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Poisson distribution

\[ n_i^* \approx N(\mu_i, \sigma_i^2) \]

Gaussian distribution
Realistic Approach to PET Denoising

\[
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\[ p_i \approx P(\lambda_i) \]

\text{Poisson distribution}

\[ x_i^* = \alpha p_i + n_i^* \]

\[ n_i^* \approx N(\mu_i, \sigma_i^2) \]

\text{Gaussian distribution}
Realistic Approach to PET Denoising

\[ f_\sigma(x) = \begin{cases} \frac{2}{\sigma} \sqrt{\alpha x + \frac{3}{8} \alpha^2 + \sigma^2 - \alpha \mu} & \text{if } x > -\frac{3}{8} - \sigma^2 \\ 0 & \text{otherwise.} \end{cases} \]

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Poisson distribution

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Gaussian distribution

Inverse (exact) transform of GAT:

\[ \int_{-\infty}^{+\infty} \sqrt{x + \frac{3}{8} + \sigma^2} \sum_{k=0}^{+\infty} \left( \frac{\lambda^k e^{-\lambda}}{k! \sqrt{2\pi \sigma^2}} e^{-\frac{(x-k)^2}{2\sigma^2}} \right) dx. \]

(Proof: Anscombe, 1948 Biometrika)
Example Results

• After Gaussianization, proper smoothing methods can be used, followed by inverse GAT!
Example Results

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• Following results show Gaussian, Perona-Malik (anisotropic), Bilateral/Trilateral Filtering,
Example Results

- After Gaussianization, proper smoothing methods can be used, followed by inverse GAT!
- Following results show Gaussian, Perona-Malik (anisotropic), Bilateral/Trilateral Filtering.

(mansoor, bagci, et al, MICCAI 2014)
Wavelet and shrinkage-based methods

- Wavelet methods decompose signals into low and high frequency components
- Noise is localized in the high frequency components
- Removing high frequency components (some parts) will denoise the images
Wavelet and shrinkage-based methods

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- Removing high frequency components (some parts) will denoise the images

- How do we know what proportion of the coefficients (high frequency) should be zero?
Wavelet and shrinkage-based methods

**Possible Answer:**
- Most of the wavelet coefficients are zero or very small. (called SPARSE)
- Noise is localized in the high frequency component.
- Finding a threshold value that set all the small coefficients into 0 will denoise the image!
Segmentation Based Denoising (after using GAT)

Xu, bagci, et al. MICCAI 2014
Segmentation Based Denoising (after using GAT) (we will revisit this after teaching segmentation methods)
IV. Partial Volume Correction (PVC)
Partial Volume Effect (PVE)

- PVE is a general problem that cause a source of image degradation in medical images.

(a) Ideal  
(b) PVE

(credit to: Dawood et al,
Partial Volume Effect (PVE)

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- The causes of PVE lie in the limited resolution of the respective imaging devices.
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\[ I = I_u * P + N \]

- Observed Image
- Uncorrupted image
- Point Spread Function
- noise
PVE Model

- $P$ denotes the point spread function which is, in general, the imaging system's response to a point source, i.e., how the system depicts an object smaller than the system's resolution.
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- PVE has two reasons
  - TF: Tissue Fraction
  - Spill-over
PVE Model - TF

**TF:** Tissue Fraction

Blurry edges as a result of sampling!
PVE Model - Spill-Over

- The largest contribution to PVE is caused by the spill-over effect.
PVE Model - Spill-Over

- The largest contribution to PVE is caused by the spill-over effect.
- Spilling of the measured tracer concentration of a voxel into its surrounding region.
The spill-over effect affects a voxel's intensity twofold: first, a voxel distributes part of its own signal to the surrounding region. Secondly, the voxel gets signal intensity from its neighbors:

\[ I(x) = I_u(x) - I_{out}(\Omega_x) + I_{in}(\Omega_x) \]

- Actual intensity
- Spill-out intensity to neighbor
- Spill-in from neighbor
PVE Model - Spill-Out/In

A. Actual activity distribution
B. Spill-out
C. Spill-in
D. Measured image
PVE Model

**RC**: recovery coefficient
85% for this example
How to correct PVE?

Point-spread function (PSF)
Typical spatial response function.
FWHM=6mm (conventional way for representing spatial resolution)
How to correct PVE?

In order for the object D (dashed) to exhibit 100% of true activity (solid), its dimension needs to be greater than $2 \times \text{FWHM} = 12\text{mm}$.
PVC Methods

• **Deconvolution**: tries to reverse the convolution of a clean image with the PSF.
  – In practice, noise is amplified with this operation and PSF may not be known exactly.
PVC Methods

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  - In practice, noise is amplified with this operation and PSF may not be known exactly.

**Van-Cittert deconvolution:**
- If PSF is known approximately, then iteratively we can estimate PV as

\[
I_0 = I \\
I_{j+1} = I_j + \alpha(I_0 - P * I_j)
\]

Where \( I \) is the given PET image, \( \alpha \) is relaxation parameter, and \(*\) denotes convolution operation.
PVC Methods

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When to stop iteration?
PVC Methods

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\[
I_0 = I
\]

\[
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\]

Where I is the given PET image, alpha is relaxation parameter, and * denotes convolution operation.

**When to stop iteration?** Small changes btw iterations (noise affects too)
PVC Methods

- **Richardson-Lucy deconvolution:**
  - is a statistical approach. The PSF is assumed to be known.
  - Correct the observed image towards a maximum likelihood solution.
PVC Methods

- Richardson-Lucy deconvolution:
  - is a statistical approach. The PSF is assumed to be known.
  - Correct the observed image towards a maximum likelihood solution.

\[
I_0 = C(>0),
\]

\[
I_{j+1} = I_j \cdot (P^T \ast \left( \frac{I_u}{P \ast I_j} \right))
\]

- When no additive noise N, \( I = P \ast I_u \)
PVC Methods

• Blind deconvolution:
  – For an unknown PSF, estimate PSF iteratively (or use additional knowledge such as anatomy information).
  – Then use one of the existing algorithm such as RL or Wiener filtering.
Qualitative Comparison of RL and BD

(a) Ideal  (b) PVE  (c) RL  (d) BD
Qualitative Comparison of RL and BD

(a) Ideal
(b) PVE
(c) RL
(d) BD

(a) Original
(b) RL
(c) BD
PVC of SPECT data using MR images

- The idea is to use prior knowledge (anatomical information)
- MRI provides high resolution anatomic detail

Credit: Matsuda, et al. JNM 2003
PVC of SPECT data using MR images
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- Registration
- Convolution with PSF
- Skull is excluded
PVC of SPECT data using MR images

Simulated WM SPECT

GM SPECT (subtract Simulated WM SPECT From original SPECT)

Convolution With PSF

registration

WM

Convoluted GM

Convolution With PSF

Skull is excluded
PVC of SPECT data using MR images

1. Skull is excluded
2. Registration
3. Convolution With PSF
4. Simulated WM SPECT
5. GM SPECT (subtract Simulated WM SPECT From original SPECT)
6. Deconvolution
7. Binary mask
8. Convolution With PSF
9. GM
10. WM

PVC of SPECT data using MR images

1. Registration
2. WM SPECT
3. GM SPECT (subtract Simulated WM SPECT From original SPECT)
4. Deconvolution
5. Binary mask
6. GM PVC SPECT Image
7. Skull is excluded
More methods (assumptions)

• Partition based methods. The true activity distribution can be segmented into a series of $n$ non-overlapping compartments with a known uniform uptake.
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- **Partition based methods.** The true activity distribution can be segmented into a series of $n$ non-overlapping compartments with a known uniform uptake.
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- **Partition based methods.** The true activity distribution can be segmented into a series of n non-overlapping compartments with a known uniform uptake.

- **Multi-resolution approach.** Gray level of high resolution image (CT or MRI) should be positively correlated with those of the functional image to be corrected.

- **Fitting method.** Tumor can be considered as a sphere with an unknown diameter and with uniform uptake and that the background level is uniform.
Summary

• Nuclear medicine imaging modalities (PET & SPECT) are useful in many diagnostic and therapeutic tasks
• Smoothing is required to clean images, improve both visualization and interpretations
• Quantitative markers are needed to evaluate nuclear medicine imaging modalities
• PVE is a major confounding factor in PET/SPECT imaging that cannot be ignored.