Direct Reconstruction of Kinetic Parameter Images from Dynamic PET Data

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• PET accumulates/averages the emissions of voxels.

• Time resolution can be achieved by dividing the data into time frames.
  – Heart perfusion
  – Brain activation
  – Glucose utilization rate
  – Receptor-ligand

• Time response of voxels are governed by ODEs

• Parameters of these ODEs are clinically important
Current Method for Estimation of Compartment Model Parameters

- SNR is low
- Some parameters are nearly unidentifiable
- Current techniques reconstruct time sequences of images and perform parameter estimation on large regions.

![Diagram of Current Method](image)
Limitation of Current Approach

- Requires high SNR
- Depends on accurate ROI
- Does not yield dense parametric estimate
- “Partial Volume” effect is a problem
- Requires reconstruction of many low SNR images
Extensions to Dense Parameter Estimation Methods

- Pixelwise Weighted Least Squares (PWLS):
  - Each voxel parameter is estimated independently
  - no a priori information

- Pixelwise Weighted Least Squares with regularization (PWLSR):
  - Same as PWLS but with spatial regularization
Our Approach: Parametric Image Reconstruction

Advantages:
- Directly reconstructs parameters from sinogram data
- Improves SNR
- Dimensionality reduction
- Produces a single full image of parameter vector
- Point spread function and system geometry can account for “Partial Volume” effects
Parametric Reconstruction Model

\[ \varphi = \begin{bmatrix} K_1 \\ k_2 \\ k_3 \\ k_4 \end{bmatrix} \rightarrow \text{2-tissue Compartment Model} \rightarrow F(\varphi) \rightarrow LL(y|\varphi) \rightarrow \text{Scanner Geometry} \]

- \( \varphi_s \) parameter vector of voxel \( s \)
  \[ f(t_1, \varphi_s) \]
  \[ \vdots \]
  \[ f(t_K, \varphi_s) \]

- \( f(\varphi_s) = \) time response at voxel \( s \)

- \( F(\varphi) = [f(\varphi_1), f(\varphi_2), \ldots, f(\varphi_N)] \) time response of all voxels

- \( y \) is the sinogram data

- Log likelihood has the form \( LL(y|F(\varphi)) \)
Compartmental Models

- Models needed to quantify processes
- Parameters of the model correspond to clinically important information
- Compartmental models,
  - use compartments for physical spaces and states of tracer
  - use rate of tracer exchange between compartments as its parameters
  - can be described by first order ODEs
- Complex processes can be modeled by adding more compartments into the model
2-tissue Compartment Model

- Used in:
  - FDG studies
  - Receptor studies

- $C_P$, plasma compartment: Tracer concentration inside the arterial blood vessels
- $C_F$, free compartment: Tracer concentration in the tissue that is not metabolized or bounded
- $C_B$, bound compartment: Tracer concentration in the tissue that is metabolized or bounded
2-tissue Compartment Model Equations

- \( C_P \) is measured by sampling blood from the patient during the scan
- Tracer concentration at other compartments
  \[
  \frac{dC_F(t)}{dt} = K_1 C_P(t) - (k_2 + k_3) C_F(t) + k_4 C_B(t) \tag{1}
  \]
  \[
  \frac{dC_B(t)}{dt} = k_3 C_F(t) - k_4 C_B(t) \tag{2}
  \]
- PET signal,
  \[
  C_T(t) = C_F(t) + C_B(t) \tag{3}
  \]
  \[
  f(K_1, k_2, k_3, k_4) = [(1 - V_B) C_T(t) + V_B C_P(t)] S_A e^{-\lambda t} \tag{4}
  \]
2-tissue Compartment Model: Important Parameters

- For receptor-ligand imaging binding potential (BP) and volume distribution (VD) are clinically important parameters.

\[
BP = \frac{k_3}{k_4} \quad (5)
\]

\[
VD = \frac{K_1}{k_2} \left( 1 + \frac{k_3}{k_4} \right) \quad (6)
\]
MAP Estimate of Parametric Image

\[ C(y|\varphi) = LL(y|\varphi) + S(\varphi) \]  \hspace{1cm} (7)

\[ \hat{\varphi} = \arg \max_{\varphi} C(y|\varphi) \]  \hspace{1cm} (8)

- How do we efficiently compute this
PICD - Parametric Iterative Coordinate Descent

- Efficient implementation of ICD for reconstruction with kinetic models
- Sequentially update parameter $\varphi_s$ vector at each voxel
- $LL(y|\varphi) + S(\varphi)$ will increase with each PICD iteration
- Efficient when $F(\varphi)$ is a nonlinear function
- Works with MRF prior
PICD - Update Strategy

- For each voxel update, make approximation

\[ LL(y|\varphi_s) - LL(y|\tilde{\varphi}_s) \approx \sum_k (\theta_{1k} \Delta f_{sk} + \frac{1}{2} \theta_{2k} \Delta f_{sk}^2) \]  \hspace{1cm} (9)

where \( \Delta f_{sk} = f(t_k, \varphi_s) - f(t_k, \tilde{\varphi}_s) \)

- \( \theta_{1k} \) and \( \theta_{2k} \) can be recursively updated using same algorithm as in conventional ICD [Bouman and Sauer 96]

- We re-parametrize using \( \varphi_s = [a_s, b_s, c_s, d_s] \)

- Then the time response is

\[ f(t_k, \varphi_s) = [(1 - V_B)((ae^{-ct} + be^{-dt}) \otimes C_P(t_k)] + V_B C_P(t_k)] S_A e^{-\lambda t} \]  \hspace{1cm} (10)
PICD - Pixel Vector Update

- Estimation of $a_s$ and $b_s$ parameters
  - linear parameters
  - closed form update for fixed values of $c_s$ and $d_s$
  - dependence on $a_s$ and $b_s$ is removed
- Estimation of $c_s$ and $d_s$ parameters
  - nonlinear parameters
  - $\Delta f_{sk}(c_s, d_s)$

\[
\begin{bmatrix}
  c_s \\
  d_s
\end{bmatrix}
\xrightarrow{\text{Parametric Model}}
\begin{bmatrix}
  \Delta f_{sk} \\
  \Delta LL
\end{bmatrix}
\]

\[
c_n \leftarrow \arg\max_{c_s \geq d_s} \Delta LL(y|c_s, d_s) + S(\varphi) \tag{11}
\]

\[
d_n \leftarrow \arg\max_{d_s \geq 0, d_s \leq c_s} \Delta LL(y|c_s, d_s) + S(\varphi) \tag{12}
\]
Multiresolution Reconstruction

- Multiresolution reconstruction
  - Coarsest scale initialized to constant value
  - Coarse scale solutions are used to initialize fine scale solutions
  - Used 3 scales (32×32, 64×64 and 128×128)
Simulations - Phantom

- Rat phantom with seven separate regions is used to assess the estimation methods

<table>
<thead>
<tr>
<th>Region</th>
<th>$k_1$</th>
<th>$k_2$</th>
<th>$k_3$</th>
<th>$k_4$</th>
<th>$a$</th>
<th>$b$</th>
<th>$c$</th>
<th>$d$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Background</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>CSF</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Nonbrain (NB)</td>
<td>.1836</td>
<td>.8968</td>
<td>0</td>
<td>0</td>
<td>.1836</td>
<td>0</td>
<td>.8968</td>
<td>0</td>
</tr>
<tr>
<td>Whole brain (WB)</td>
<td>.0918</td>
<td>.4484</td>
<td>0</td>
<td>0</td>
<td>.0918</td>
<td>0</td>
<td>.4484</td>
<td>0</td>
</tr>
<tr>
<td>Striatum (STR)</td>
<td>.0918</td>
<td>.4484</td>
<td>1.2408</td>
<td>.1363</td>
<td>.02164</td>
<td>.07016</td>
<td>1.7914</td>
<td>0.0312</td>
</tr>
<tr>
<td>Cortex (COR)</td>
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<td>.4484</td>
<td>.141</td>
<td>.1363</td>
<td>.0607</td>
<td>.0311</td>
<td>.628</td>
<td>.09725</td>
</tr>
<tr>
<td>White matter (WM)</td>
<td>.02295</td>
<td>.4484</td>
<td>0</td>
<td>0</td>
<td>.02295</td>
<td>0</td>
<td>.4484</td>
<td>0</td>
</tr>
</tbody>
</table>

- Regions are obtained by segmenting MRI scans of a rat

- Total scan time is 60 min., divided into 18 time frames: $4 \times 0.5$ min, $4 \times 2$ min and $10 \times 5$ min
Simulations - Assumptions

- Raclopride with $^{11}C$ is used as tracer.
- The blood function, $C_{P}(t)$ was generated as described in [Wong et. al. 01]
- Activity scaled to are scaled 10M counts
- 180 projection angles each with 200 projection and 0.875 mm spacing
- Used 4 mm. wide triangular PSF
- Poisson noise model with accidental coincidences
- Comparison methods use FBP
Reconstructed Emission Images

Original phantom

FBP reconstruction

Parametric reconstruction
Parametric Images of $a$, $b$, $c$ and $d$

(1) Original Phantom

(2) Pixelwise Weighted Least Squares
(3) Pixelwise Weighted Least Squares with Regularization

(4) Parametric Image Reconstruction
Parametric Images of $K_1$, $k_2$, $k_3$ and $k_4$

(1) Original Phantom
(2) Pixelwise Weighted Least Squares
(3) Pixelwise Weighted Least Squares with Regularization

(4) Parametric Image Reconstruction
Parametric Images of $BP$ and $V_D$

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<th>Pixelwise Weighted Least Squares</th>
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<td>Pixelwise Weighted Least Squares with Regularization</td>
<td>Parametric Image Reconstruction</td>
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Normalized RMSE of the Parametric Images

Pixelwise WLS
Pixelwise WLS with regularization
Parametric Image Reconstruction
Conclusions

- Propose direct reconstruction of parametric image
- Advantages
  - Higher SNR
  - Dense parameter estimates
  - Reduced “Partial Volume” effect
- Demonstrated improved quality on realistic simulation data
References
