REGION-BASED MAXIMUM LIKELIHOOD RECONSTRUCTION IN POSITRON EMISSION TOMOGRAPHY FOR QUANTITATIVE ONCOLOGICAL ANALYSIS

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\( ^{18}\text{F-FDG} \) PET in clinical oncology:

- cancer diagnosis
- cancer staging
- response to therapy assessment

\( ^{18}\text{F-FDG} \) uptake in tissues: index of cellular metabolic activity

PET is an intrinsically quantitative technique because of:

- radiotracer nature
- attenuation correction
Reconstruction from projections: problem formulation

Acquisition process LSV modeling:

\[ \bar{Y} = E\left[ Y_i \right] = \iiint_{FOV} f(x, y, z) h_i(x, y, z) \, dx \, dy \, dz \]

\[ i = 1, \ldots, I \]

Poisson variable

integration kernel
Reconstruction from projections: D-D approach

- Approximation of \( f(x,y,z) \) as a linear combination of \( J \) basis functions \( b_j(x,y,z) \) with unknown weights \( \lambda_j \):
  \[
  \tilde{f}(x,y,z) = \sum_{j=1}^{J} \lambda_j b_j(x,y,z)
  \]

- System matrix coefficients computation:
  \[
  a_{ij} = \iiint_{\text{FOV}} h_i(x,y,z)b_j(x,y,z)\,dx\,dy\,dz
  \]

Reconstruction process: iterative search of \( \lambda \) values optimizing an objective function of the acquired data
Maximum Likelihood iterative reconstruction (MLEM)

- maximization of measured data likelihood function
- expectation maximization algorithm

\[ \lambda_{j}^{n+1} = \frac{ \sum_{i} a_{ij} \sum_{k} y_{i} a_{ik} \lambda_{k}^{n} } { \sum_{i} a_{ij} } \]

\( i^{th} \) LOR error
\( i^{th} \) LOR estimated counts
weighted average of the errors
Main factors affecting PET accuracy in clinical practice

- **Scanner spatial resolution**

The PSF of a PET scanner is **anisotropic** and **spatially variant** (FWHM typically ranges from 4 to 9 mm)

- **Noise component**

- **Reconstruction algorithm characteristics**
Scanner PSF modeling and inclusion in MLEM reconstruction
Scanner PSF modeling and inclusion in MLEM reconstruction

Line sources

PSF not included

PSF included

Off axis

@1 cm

@5 cm

@10 cm

@15 cm

@20 cm

@23 cm

@26 cm
Scanner PSF modeling and inclusion in MLEM reconstruction: results

Maximum likelihood algorithm drawbacks:

- maximum likelihood solution noisy due the problem ill-conditioning: stopping rules and/or post filtering required
- convergence slow and object-dependent

→ object dependent bias/noise compromise

Effects of PSF inclusion:

- improvement of contrast and quantitative accuracy
- noise component reduction
- Gibbs-like artifacts
- worsening of the object dependent convergence

→ detectability/quantification trade-off: a more correct quantification of small objects is necessarily associated with larger noise level and larger computation time.
Scanner PSF modeling and inclusion in MLEM reconstruction: results

**Lung cancer patient data:** 35 mm tumor, large TBR, 3D mode

**Without PSF**

**With PSF**

Clinical noise level

Uptake +28%

Metabolic volume -39%
Scanner PSF modeling and inclusion in MLEM reconstruction: results

**Lung cancer patient data:** 15 mm tumor, low TBR, 2D mode

**Without PSF**

**With PSF**

Clinical noise level

**Uptake** +39%

**Metabolic volume** -33%
**Region-based MLEM with PSF inclusion for lesion quantification: the idea**

- **Local quantification tool based on a standard smooth clinical image (STD-CI)**

- **Definition of regional basis functions on STD-CI:**
  - the lesion of interest is properly segmented into regional basis functions
  - the image outside the area to be quantified is “frozen” and therefore handled as an unique basis function.

- **The ML convergence can be locally achieved without noise increasing** (reduced unknown variables; a priori information)
Region-based MLEM: analytical formulation

• STD-CI obtained with a standard voxel-based reconstruction process:

\[ I_{STD-CI}^{STD-CI}(x, y, z) = \sum_{j=1}^{J} \lambda_{j}^{STD-CI} b_{j}(x, y, z) \]

• Approximation of \( f(x,y,z) \) as linear combination of \( R \) regional basis functions \( \beta_{r}(x,y,z) \) with unknown weights \( \mu_{r} \):

\[ \tilde{f}(x, y, z) = \sum_{r=1}^{R} \mu_{r} \beta_{r}(x, y, z) \]

• Basis functions definition:

\[ \beta_{r}(x, y, z) = \begin{cases} 
T_{r}(x, y, z)E_{T_{r}} \left[ I_{STD-CI}^{STD-CI}(x, y, z) \right] & r = 1..N \\
T_{r}(x, y, z)I_{STD-CI}^{STD-CI}(x, y, z) & r = bkg 
\end{cases} \]
Region-based MLEM: analytical formulation

- Model of the data collection process:
  \[
  \bar{Y}_i = \sum_{j=1}^{J} a_{ij} \lambda_j = \sum_{r=1}^{R} \tilde{a}_{ir} \mu_r
  \]

- System matrix coefficients of the region-based problem:
  \[
  \tilde{a}_{ir} = \sum_{j \in T_r} a_{ij} \bar{\lambda}_j
  \]
  with \( \bar{\lambda}_j = \) value assumed by the basis function \( \beta_i(x,y,z) \) in the \( j^{th} \) voxel.

\[
\mu_r^{n+1} = \mu_r^n \cdot \frac{\left( \sum_{i} \tilde{a}_{ir} \sum_{k} \frac{y_i}{\tilde{a}_{ik} \mu_k^n} \right)}{\sum_{i} \tilde{a}_{ir}}
\]

\( n^{th} \) iteration of region-based MLEM reconstruction
Region-based MLEM: preliminary evaluations

Choice of the number of regional basis functions for “uniform” lesions:

- R1: internal region;
- R2: transition region; activity underestimated for partial volume effect;
- R3: external region; activity overestimated for spillout effect
Region-based MLEM: preliminary evaluations

Experimentally acquired sphere phantom

**D=9.5mm**
**TBR=7.5**

**D=28mm**
**TBR=7.5**

### 20 iterations

STD-CI Basis functions

voxel based region based
The algorithm

STD-CI

Initial lesion segmentation

Volume Of Interest (VOI) identification

Volume Of Interest (VOI) segmentation ($T_r(x,y,z)$)

Regional basis functions ($\beta_r(x,y,z)$)

MLEM reconstruction

- volume estimate
- FDG uptake estimate

isotropic dilatation of segmented lesion by PSF max (spillout)
Experimentally scanned sphere phantom: results

Activity contrast=7.5

<table>
<thead>
<tr>
<th>STD-CI</th>
<th>voxel-based</th>
<th>region-based</th>
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</thead>
</table>

% contrast

% volume

sphere diameter (mm)
Experimentally scanned sphere phantom: results

Activity contrast=4

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% volume

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<tbody>
<tr>
<td>sphere diam (mm)</td>
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<td>10</td>
<td>15</td>
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% volume

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<th>320%</th>
<th>270%</th>
<th>220%</th>
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The algorithm (2)

STD-CI

Lesion segmentation → VOI identification → VOI segmentation

Regional basis functions

MLEM reconstruction

VOI identification

PSF filtering

VOI segmentation

Change?

Exit

No → Yes
Experimentally scanned sphere phantom: results

Activity contrast = 7.5
Experimentally scanned sphere phantom: results

Activity contrast=4

- first iteration
- last iteration

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- voxel-based
- region-based

sphere diameter (mm)

% contrast

% volume
Errors in sphere segmentation: robustness evaluation

**TBR 7.5**

- Correct initialization
- Error +30%
- Error -30%

**TBR 4**

- Correct initialization
- Error +30%
- Error -30%
Experimentally acquired sphere phantom: results

TBR 7.5

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<table>
<thead>
<tr>
<th>diameter (mm)</th>
<th>one object segmented</th>
<th>all objects segmented</th>
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<tbody>
<tr>
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<tr>
<td>28.0</td>
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One object segmented

All objects segmented

POLITECNICO DI MILANO
Open problems and brainstorming

1. Uniform, small, low-contrast objects:
   • initial lesion segmentation with acceptable error (±30%)
   • VOI segmentation in connected $T_r(x,y,z)$

2. Contiguous objects:
   • VOI identification
   • VOI segmentation in $Tr(x,y,z)$

3. Inhomogeneous objects:
   • VOI segmentation in $Tr(x,y,z)$