Advanced quantification in oncology PET

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Two steps

Radiotracer concentration (kBq/mL)

• Glucose metabolism
• Metabolically active tumor volume
• etc…
Quantification issues in oncology PET

• Tumor segmentation

• Identification of indices that best characterize the tumor in a specific context

• Interpretation of tumor changes during therapy

• Understanding the relationship between macroscopic parameters (from PET images) and microscopic tumor features
Quantification issues in oncology PET

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Current quantification in oncology PET

Tracer uptake (kBq/mL)

SUV (Standardized Uptake Value)

\[
SUV = \frac{\text{Tracer uptake}}{\text{Injected activity} / \text{patient weight}}
\]

SUV ~ metabolic activity of tumor cells
Comparing 2 PET scans: current approach

- Need to identify and possibly delineate the tumors
- Each tumor = 1 single SUV
- Change compared to an empirical threshold (provided in recommendations such as EORTC, PERCIST)
- Tedious when there are many tumor sites

~12 weeks
A novel parametric imaging approach

Goal: Get an objective \textit{voxel-based} comparison of 2 PET/CT scans

PET1

PET2

\sim 12 \text{ weeks}
Main steps

1. PET image registration based on the CT associated with the PET scans

2. Voxel-based subtraction of the 2 image volumes

\[ PET_{1} - T_{21} \rightarrow PET_{1} - PET_{2}' \]

3. Identification of voxels in which SUV significantly changed between the 2 scans using a biparametric analysis
Step 1

VOI selection

Identification of the transformation needed to realign the 2 CT

\[ T_{21} \] (rigid transform using Block Matching)

Registration of the PET volumes using the \( T_{21} \) transformation

realigned with
Step 2

Subtraction of the 2 realigned PET scans

\[ T_{21}^{\text{PET2/CT2}} - \text{PET1/CT1} = T_{21}^{\text{PET2}} - \text{PET1/CT1} \]

Each point corresponds to a voxel
Step 3

Identification of the significant tumor changes in the 2D-space by solving a Gaussian mixture model

$$f(x_i | \theta) = \sum_{k=1}^{K} p_k \phi(x_i | \mu_k, \Sigma_k)$$

$x_i$ : vector of parameters (PET1(i)-PET2(i), PET1(i))

θ : vector of parameters ($p_1$, ..., $p_K$, $\mu_1$, ..., $\mu_K$, $\Sigma_1$, ..., $\Sigma_K$)
Step 3: results

- **ΔV**: volume with a significant change
- **ΔSUV**: change magnitude

**Parametric image**

Nb of voxels

- Background
- Tumor voxels
- Physiological changes

**Graph:**

- X-axis: [PET1] SUV
- Y-axis: (PET1 - T2) SUV
- Z-axis: Nb of voxels

**Legend:**

- PET1
- T2
- ΔSUV

**Note:**

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Example

Identification of small tumor changes (lung cancer)

PET1  T_{21}(PET2)  T_{21}(PET2) - PET1 after solving the GMM  PET3

PET1  T_{21}(PET2)  T_{21}(PET2) - PET1 after solving the GMM  PET3
Clinical validation: 28 patients with metastatic colorectal cancer

78 tumors with 2 PET/CT (baseline and 14 days after starting treatment)

<table>
<thead>
<tr>
<th></th>
<th>NPV</th>
<th>PPV</th>
<th>Sensitivity*</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>EORTC</td>
<td>91%</td>
<td>38%</td>
<td>85%</td>
<td>52%</td>
</tr>
<tr>
<td>PI</td>
<td>100%</td>
<td>43%</td>
<td>100%</td>
<td>53%</td>
</tr>
</tbody>
</table>

* for detecting lesions

- All tumors identified as progressive tumors at D14 were confirmed as such 6 to 8 weeks after based on CT (RECIST criteria)
- Among the 14 tumors identified as progressive tumors by RECIST criteria, 12 were identified as such at D14 using PI while only 2 were identified using EORTC criteria (SUVmax)

Necib et al, J Nucl Med 2011
Comparing more than 2 PET/CT scans

Longitudinal study

Problem: characterize the tumor changes
No method, each scan is usually compared only to the previous one
A parametric imaging solution

First step: PET image registration based on the associated CT

Use of the transformation identified based on the CT to register the PET scans
Model: a factor analysis model

$$\text{SUV (i, t)} = \sum_{k=1}^{K} I_k(i).f_k(t) + \varepsilon_k(t)$$

- **SUV units**
- **voxel $i$**
- **SUV**
- **time**

$\text{SUV (i, t)} = I_1(i) + I_2(i) + I_3(i)$

- Stable uptake over time: $f_1(t)$
- Decreasing uptake over time: $f_2(t)$
- Increasing uptake over time: $f_3(t)$
Solving the model

\[
\text{SUV} \ (i, t) = \sum_{k=1}^{K} I_k(i) . f_k(t) + \varepsilon_k(t)
\]

**Priors:**
- Non-negative \( I_k(i) \) coefficients
- Non-negative \( f_k(t) \) values
- In each voxel, the variance of the voxel value is roughly proportional to the mean

**Iterative identification of \( I_k(i) \) et \( f_k(t) \)** (Buvat et al Phys Med Biol 1998) using a Correspondence Analysis followed by an oblique rotation of the orthogonal eigenvectors
Sample results

Lung cancer patient with 5 PET/CT scans

Normalized SUV
Why is such an approach useful?

Heterogeneous tumor responses can be easily identified
Sample results: early detection of tumor recurrence (1)

Images showing tumor progression and treatment outcomes over different cycles and time periods.
Sample results: early detection of tumor recurrence (2)

EORTC: no tumor recurrence detected at PET3

PET scan

SUVmean

PI: tumor recurrence detected at PET3
Discussion / conclusion

- No need to precisely delineate the tumors
- Makes it possible to detect small changes in metabolic activity
- Summarizes changes between two or more scans in a single image
- Shows heterogeneous tumor response within a tumor or between tumors
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