Quantification in emission tomography: challenges, solutions, performance and impact

Irène Buvat
U678 INSERM, Paris

buvat@imed.jussieu.fr
http://www.guillemet.org/irene
What is quantification in emission tomography?

Extracting *physiologically meaningful values* from PET or SPECT images

Density of dopaminergic transporters

C kBq/ml

SPECT image
Why do we need quantification?

Physiological parameters are richer than visual assessment

- Differential diagnosis
- Prognosis
- Therapeutic management
- Treatment monitoring
- Radiotherapy

Supraglottic squamous cell carcinoma

Cumulative survival of patients with T1–T4 laryngeal carcinomas ($n = 34$)

PSR: protein synthesis rate from C11-TYR PET

$\text{PSR} < 2$ (5y survival, 67%)

$\text{PSR} \geq 2$ (5y survival, 34%)

de Boer et al, J Nucl Med 2004
Is quantification easy?

No

Density of dopaminergic transporters

Find $C = f(N)$

$N \neq k\, C$

Radiotracer concentration

Find $\phi = g(C_i, P_n)$

$C \neq k'\, \phi$

ET image

Radiotracer concentration

Density of dopaminergic transporters
Deriving radiotracer concentration from ET images

What should be accounted for

- patient motion
- photon attenuation
- photon scatter

- limited spatial resolution
- [randoms (PET)]
- [deadtime]

- tomographic reconstruction

- measurement procedure
Patient and organ motions

Spurious or physiological (cardiac, respiratory)

Lung FDG PET

• Reduce scan duration
• Gating (cardiac, respiratory, or both) and further processing

Increase of lesion size from 10% to 30%

Decrease of $\text{SUV}_{\text{max}}$ from 5% to $> 100%$


$\text{Li et al, Med Phys 2006:1288-1298}$

Hot topic!
Photon attenuation

Attenuation introduces activity underestimation > 70% in SPECT and PET!

1. Measure tissue density (e.g., using a CT)
2. Pre or post correction, or model attenuation in reconstruction

\[ p = R_\mu f \]

Very efficient
Fine tuning stage (motion, contrast medium, aso)
Photon scatter

20 to 50% of detected photons can be scattered (hence mislocated) in ET

Decrease contrast

- Better: towards relocation of scattered events

\[ p = R_s f \]

Tc99m cardiac SPECT

- Subtraction of scattered photons after modelling scatter distribution

20% projection

unscattered

scattered (37%)

Relocation under investigation (much less non zero elements in \( R_s \), out of the FOV activity)
Limited and non stationary spatial resolution

Introduces non stationary partial volume effect

In SPECT

Partial volume effect in ET

\[
\text{max} = 100 \\
\times = \text{max} < 100
\]

severely affects structures < 3 FWHM in size

- Multiply measured values by a recovery coefficient
- Invert a cross-contamination matrix

Definitely useful
But all methods assume that functional contours same as anatomical contours

\[
\begin{align*}
\text{spatial resolution} & \quad 12 \text{ mm} \\
\text{infinite contrast} & \quad 0 \quad 0.5 \\
\text{Structure diameter (mm)} & \quad 2 \\
\text{RC}^{-1} & \quad 1
\end{align*}
\]
Tomographic reconstruction

Indirectly affects quantitation

FBP, MLEM, OSEM, conjugate gradient? Does that change quantitative accuracy?

- Control spatial resolution, so that partial volume effect can be predicted
- Control noise level, which affects measurement variability

Need for more systematic report on the spatial resolution / noise trade-off achieved by the reconstruction to determine quantitative accuracy

Boellaard et al, J Nucl Med 2001:808-817
Measurement procedure

Significant impact of VOI drawing

In PET, therapeutic follow-up based on TNR

- Empirical work so far
- Home-made approaches

Large room for improvement

Need for optimization and standardization

Hot topic: Definition of functional regions

Feuardent et al, SNM 2005
How accurate can one be in SPECT?

Brain SPECT of dopaminergic system (no motion)

binding potential = \( \frac{(A_p - A_{bgd})}{A_p} \)

restored activity (%)

- true
- no correction
- attenuation
- attenuation + scatter
- attenuation + DD spatial resolution
- attenuation + scatter + DDSR
- attenuation + scatter + DDSR + partial volume

Need for accurate quantification in SPECT

Brain SPECT of dopaminergic system

Binding potential (BP) estimate

W/o PVE correction

With PVE correction

Differential diagnosis in presymptomatic patients

Soret et al., Eur J Nucl Med Mol Imaging 2006
Example: quantification in FDG-PET

True tumor/bgd ratio = 8

Clinical conditions (CPET!)
- 6 min acquisition
- Cs137 transmission scan for attenuation correction
- No PVE correction
- mean count value in the tumor region

<table>
<thead>
<tr>
<th>Lung spheres diameter (in mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10.5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tumor/bgd ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
</tr>
</tbody>
</table>

Different conditions

<table>
<thead>
<tr>
<th>Lung spheres diameter (in mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10.5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>18 min acquisition</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CT att correction</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.7</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PVE correction</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Max in tumor region</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.6</td>
</tr>
</tbody>
</table>

2nd step: deriving physiological parameters

Density of dopaminergic transporters

Radiotracer concentration

C kBq/ml
General and appropriate approach

- Dynamic image sequence
- Blood sampling
- Biochemical knowledge

Tracer kinetic in regions of interest
Arterial input function
Model

Fitting measurements to model

Region-dependent physiological parameters
  e.g., glucose metabolic rate, blood flow, blood volume, mean transit time
Practical trade-off

- Simplifying the whole procedure to achieve some reasonable trade-off between feasibility and index usefulness

Example of FDG-PET

Glucose metabolic rate

Full compartmental modeling

<table>
<thead>
<tr>
<th>SUV</th>
<th>SKA</th>
<th>Patlak</th>
</tr>
</thead>
</table>

Physiological meaning
Example of F18-FDG PET

Tumor FDG (t) = $K_i \int_0^t AIF(\theta)d\theta$ + unmetabolized FDG (t)

FDG made available to tumor
Glucose metabolic rate

SUV = $\frac{Tumor (t) - unmetabolized \text{ FDG}}{\int_0^t AIF(\theta)d\theta}$

~ injected dose / dilution volume
~ injected dose / patient weight
Accuracy depends on complexity

• SUV versus $K_i$

FDG-PET in acute lung injury

Quantitative accuracy depends on the relevance of the model used for physiological parameter estimates

Conclusions

• Quantification is feasible in PET and SPECT

• Quantification is a complicated process, requiring tissue density map, perfectly controlled acquisition and processing protocols, high resolution anatomical information, accurate kinetic modeling

• Accurate quantification is easier in PET than in SPECT, just because attenuation correction is more accessible, and mostly because spatial resolution is better

• SPECT/CT and PET/CT scan could make quantification a clinical reality

• Partial volume effect and motion are currently the toughest effects to deal with
Conclusions

• Quantification accuracy **highly depends on the acquisition and processing protocols**, and should be characterized

• Meta-analyses are often impossible - or meaningless - given the variety and lack of information regarding acquisition and processing

• Comparing quantitative values (e.g. for therapeutic follow-up, malignancy indices) requires **highly controlled protocols** to ensure constant acquisition and processing conditions
Thank you for your attention

Slides available on
http://www.guillemet.org/irene