Dose assessment in Nuclear Medicine Therapy

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Importance of patient dosimetry

- **What is it?**
  
  It is a technique to simulate the radionuclide therapy of a patient and to assess the internal doses to organs and lesions.

- **What the aim?**
  
  At present to establish the highest dose to OARs with no damage.
  
  In the future it will be more and more oriented to define the ratio between tumour dose and OAR dose.
State of the art following the original schema of MIRD16 and MIRD 21

- Planar conjugate view counting is the most widespread method.
- Hybrid planar + quantitative SPECT (or better if SPECT-CT)
- Fully 3D SPECT-CT based dosimetry

State of the art following the MIRD17 schema

- Non uniform activity distribution dosimetry at the voxel level or voxel dosimetry

Average dose to organs/lesions

Uniform activity distribution

Radiopharmaceuticals of excellence for PRRT of NET

- $^{90}\text{Y}/^{177}\text{Lu}$-DOTATOC
- $^{90}\text{Y}/^{177}\text{Lu}$-DOTATATE
- $^{90}\text{Y}/^{177}\text{Lu}$-DOTA-lanreotide

Analogues of somatostatin

The future PRRT of NET?

Alpha emitter labelled peptides: $^{213}\text{Bi}$-DOTATOC

Dik J Kwekkeboom et al. Semin Nucl Med 2010

## Physical properties of beta emitters in radionuclide therapy of NET

<table>
<thead>
<tr>
<th></th>
<th>$^{131}$I</th>
<th>$^{177}$Lu</th>
<th>$^{90}$Y</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Half-life</strong></td>
<td>8.04 d</td>
<td>6.71 d</td>
<td>64 h</td>
</tr>
<tr>
<td><strong>Radiation</strong></td>
<td>$\beta^-\gamma$ (100%)</td>
<td>$\beta^-\gamma$ (17%)</td>
<td>$\beta^-$</td>
</tr>
<tr>
<td><strong>Maximum beta energy</strong></td>
<td>182 keV</td>
<td>133 keV</td>
<td>933 keV</td>
</tr>
<tr>
<td><strong>Range in water</strong></td>
<td>3.6 mm</td>
<td>1.9 mm</td>
<td>11.8 mm</td>
</tr>
<tr>
<td><strong>Range in perspex</strong></td>
<td>3.1 mm</td>
<td>1.6 mm</td>
<td>10.3 mm</td>
</tr>
<tr>
<td><strong>Range in aluminium</strong></td>
<td>1.6 mm</td>
<td>0.8 mm</td>
<td>5.2 mm</td>
</tr>
<tr>
<td><strong>Range in lead</strong></td>
<td>0.5 mm</td>
<td>0.3 mm</td>
<td>1.6 mm</td>
</tr>
</tbody>
</table>

Lesions’ diameter <2cm → $^{177}$Lu-DOTATOC is preferred
Lesions’ diameter >2cm → $^{90}$Y-DOTATOC is preferred

Gabriel M et al. Q J nucl Med Mol Imaging 2010
How to simulate PRRT?

Directly with $^{90}$Y-DOTATOC in course of therapy

Bremsstrahlung from beta particles of $^{90}$Y


With $^{111}$In-DOTATOC (185MBq)

$\gamma$ emission at 173keV and 247keV ($T_{1/2phys} = 67.4$ h)

Planar imaging and/or SPECT-CT
How to simulate PRRT?

Directly with $^{177}$Lu-DOTATOC in course of therapy

$\beta/\gamma$ isotope

Planar imaging and/or SPECT-CT

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The role of PET-CT imaging

$^{68}$Ga / $^{177}$Lu DOTATOC for dosimetry?

$^{68}$Ga / $^{177}$Lu DOTATOC for diagnostics?
Pharmacokinetics of $^{90}$Y-DOTATOC

Urinary excretion

Blood clearance

$D_{\text{media \ RM}(^{90}\text{Y})} = 0.148 \text{Gy/GBq}$

$D_{\text{media \ KIDNEYs}(^{90}\text{Y})} = 30 \times D_{\text{media \ RM}(^{90}\text{Y})}$
Results of $^{111}$In planar dosimetry for therapy with $^{90}$Y-DOTATOC

- OAR par excellence are **kidneys**
- High doses are absorbed also by:
  - Liver
  - Spleen

Kidneys protection reduces uptake (-25% to -65%)
Estimates of tumour and OAR doses per unit activity in patient undergoing PRRT trial

Cremonesi M et al QJ Nucl Med Mol Imaging 2010
Fully 3D dosimetry: gamma-camera characterization for quantitative purpose

Results of SPECT-CT dosimetry for therapy with $^{90}\text{Y} / ^{177}\text{Lu}$-DOTATOC

Specific counts-to-activity calibration curves for all isotopes

Calculation of specific S-voxel for your case by Monte Carlo simulation for voxeldosimetry

Other…

…a physicist for implementation!
A study of dosimetric accuracy

111In dosimetry

<table>
<thead>
<tr>
<th>Residence Time (h)</th>
<th>Heart</th>
<th>Lung</th>
<th>Liver</th>
<th>Kidney</th>
<th>Spleen</th>
<th>Marrow</th>
<th>Vessels</th>
</tr>
</thead>
<tbody>
<tr>
<td>C-planar</td>
<td>20 ± 2%</td>
<td>-2 ± 0.8%</td>
<td>29 ± 1%</td>
<td>-21 ± 3%</td>
<td>-12 ± 1%</td>
<td>-24 ± 1%</td>
<td>-36 ± 1%</td>
</tr>
<tr>
<td>Q-planar</td>
<td>-6.5 ± 1%</td>
<td>10 ± 1%</td>
<td>-4 ± 1%</td>
<td>-7 ± 3%</td>
<td>-5 ± 3%</td>
<td>-1 ± 2%</td>
<td>-3.5 ± 3%</td>
</tr>
<tr>
<td>Q-SPECT</td>
<td>-3.6 ± 0.5%</td>
<td>2 ± 0.8%</td>
<td>-4.6 ± 0.4%</td>
<td>-5 ± 1%</td>
<td>-3 ± 1%</td>
<td>-0.5 ± 0.8%</td>
<td>6.4 ± 0.8%</td>
</tr>
<tr>
<td>C-planar/Q-SPECT</td>
<td>-9 ± 1%</td>
<td>-10 ± 0.8%</td>
<td>-8 ± 0.7%</td>
<td>-21.5 ± 3%</td>
<td>-17 ± 3%</td>
<td>-18 ± 1.3%</td>
<td>-9 ± 2%</td>
</tr>
<tr>
<td>Q-planar/Q-SPECT</td>
<td>-5 ± 1%</td>
<td>-0.6 ± 1%</td>
<td>-5 ± 1%</td>
<td>-3 ± 0.5%</td>
<td>-2.5 ± 3%</td>
<td>-0.5 ± 2%</td>
<td>5 ± 3%</td>
</tr>
</tbody>
</table>

90Y dosimetry

<table>
<thead>
<tr>
<th>A₀ (Gbq)</th>
<th>T₁/₂ eff (h)</th>
<th>CF (cps/MBq)</th>
<th>A/A₀ (MBq × h/MBq)</th>
<th>Mass (g)</th>
<th>MIRD (1)</th>
<th>3D voxel (2)</th>
<th>Difference % (2) versus (1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidneys (right)</td>
<td>2.2</td>
<td>31.7</td>
<td>1.31</td>
<td>1.07</td>
<td>139.5</td>
<td>3.9⁹</td>
<td>4.2 (±0.8)</td>
</tr>
<tr>
<td>Lesion pancreas</td>
<td>2.2</td>
<td>37.1</td>
<td>1.13</td>
<td>1.16</td>
<td>73.3</td>
<td>8⁹</td>
<td>8.7 (±1.4)</td>
</tr>
</tbody>
</table>

⁹Calculated by OLINDA by using the mean phantom, correcting for the individual mass of the kidney (CT derived).
⁹Calculated by OLINDA by using the sphere model corrected by exponential fitting for the correspondent mass.
Dose limits for kidneys

- From external radiation therapy it is:
  - TD$_{5,5}$ = 23 Gy and TD$_{5,50}$ = 27 Gy
- In internal radiation therapy the best quantity is the estimate of the Biological Effective Dose (BED) and the Equivalent Uniform Dose (EUD)
  - BED can be evaluated by simple dosimetry technique (mean value), even if a better estimate of both BED and EUD is furnished by voxel dosimetry (BED and EUD maps)

\[
BED = \sum_i D_i + \frac{\beta}{\alpha} \times \frac{T_{1/2\text{rep}}}{(T_{1/2\text{rep}} + T_{1/2\text{eff}})} \times \sum_i D_i^2
\]

α/β = 2.6 Gy for healthy renal tissue

Renal mono-exp decay assumption

Repair from sub-lethal damage (2.8h for kidneys)

Oehme L et al Nuklearmedizin 200
Radiobiological aspects

- BED map → DVH of dose values
  → DVH of BED values

$P(\Psi)$: the probability distribution of BED values where $\Psi$ covers all possible values for BED

$EUD = -\frac{1}{\alpha} \ln \left( \int_{0}^{\infty} P(\Psi) e^{-\alpha \Psi} d\Psi \right)$

The mean absorbed dose required to yield a surviving fraction equal to that arising from the probability distribution of dose values (absorbed dose or BED) given by the normalized DVH.

Sgouros G et al Semin nucl Med 2008
Combining dosimetry for target radionuclide and external beam therapies for organs and tumours

Combination between two dose distribution data

Information regarding the spatial variability of radiosensitivity within a tumour

BED map using full patient-specific data.

Conclusions

- The role of dosimetry is fundamental to optimize the individual activity chosen for treatment
- The dosimetric studies should improve the effective dose delivered to the tumour mass without increasing toxicity
  - The empirical approach should be left

- **What’s the future?**
  - To reach a more accurate computation level
  - To optimize the tumours quantification through a more precise imaging
  - To implement standard software for 3D dosimetry calculation and radiobiological considerations
  - To implement new Monte Carlo based techniques
Thanks for your attention!