Dosimetry:
Guidelines and Case Study

B. Vanderlinden, S. Gnesin
## Dosimetry? : Why?

<table>
<thead>
<tr>
<th>Dosimetry?</th>
<th>Why?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Legal obligation</td>
<td>Standardized therapy</td>
</tr>
<tr>
<td>Prediction of treatment</td>
<td>Not yet proven</td>
</tr>
<tr>
<td>Quality assurance =&gt; accreditation</td>
<td>Sounds good</td>
</tr>
<tr>
<td>Standardisation and reproducibility</td>
<td>Guidelines</td>
</tr>
</tbody>
</table>
Accuracy vs Precision/Reproducibility
Standard Operational Procedures: SOP

- All procedures must be reproducible (systems, methodology...)
- Everything must be reported (patient position, measurement time,...)
  - activity is always given with the time of measurement, administration and instrument used
  - know what and when it was done (not what and when it was planned)
- QA & QC of radionuclide calibrator, SPECT/CT, Probe,...
Dosimetric concepts => Guidelines

- The bone marrow dose limited approach, originally described by Benua et al. (1962):
  - The generally accepted surrogate dose threshold to avoid serious myelotoxicity is a blood absorbed dose of 2 Gy.

- The lesion-based dosimetry, based mainly on the data of Maxon et al. (1983) and Maxon & Smith (1990):
  - > 300 Gy to remnants
  - > 80 Gy to iodine-avid tissue.
**Basic : MIRD**

\[
D_{[GY]}(r_T) = \sum_{r_S} \tilde{A}_{r_S} \times S_{[GY]}(r_T \leftarrow r_S)
\]

\[
\tilde{A}_{r_S} = A_0[Bq] \times TIAC_{r_S[s]}
\]

\[
S_{[GY]}(r_T \leftarrow r_S) = \frac{E_{[J]}(r_T \leftarrow r_S)}{m_{r_T[Kg]}}
\]

\[
r_T = r_S
\]

\[
D_{[GY]}(r_T) = \frac{A_0[Bq]}{m_{r_T[Kg]}} \times TIAC_{r_T[s]} \times E_{[J]}
\]
Basic: Time-Integrated Activity Coefficient

\[ A_{[Bq]}(t) = A_{0[Bq]} \times e^{-\frac{\ln(2)}{T_{1/2}}t} \]

\[ A_{0[Bq]} = \text{Constant Activity} \]

\[ \tilde{A} = \int_0^\infty A_{[Bq]}(t) \, dt \]

\[ = A_{0[Bq]} \times \int_0^\infty e^{-\frac{\ln(2)}{T_{1/2}}t} \, dt \]

\[ = A_{0[Bq]} \times \frac{T_{1/2}}{\ln(2)} \]

\[ \tilde{A} = A_{0[Bq]} \times TIAC_{[s]} \]

\[ \Rightarrow TIAC_{[s]} = \frac{T_{1/2}}{\ln(2)} \]

\[ \bar{D}_{[Gy]}(r_T) = \frac{A_{0[Bq]}}{m_{r_T[Kg]}} \times \frac{T_{1/2}}{\ln(2)} \times E_{[J]} \]
EANM Dosimetry Committee series on standard operational procedures for pre-therapeutic dosimetry
I: blood and bone marrow dosimetry in differentiated thyroid cancer therapy

Michael Lassmann · Heribert Hänscheid · Carlo Chiesa · Cecilia Hindorf · Glenn Flux · Markus Luster

Published online: 20 May 2008 © EANM 2008

EANM Dosimetry Committee Series on Standard Operational Procedures for Pre-Therapeutic Dosimetry
II. Dosimetry prior to radioiodine therapy of benign thyroid diseases

Heribert Hänscheid · Cristina Canzi · Wolfgang Eschner · Glenn Flux · Markus Luster · Lidia Strigari · Michael Lassmann

Received: 22 February 2013 / Accepted: 26 February 2013 © EANM 2013
Aim: “how to perform pre-therapeutic and/or peri-therapeutic patient-specific dose assessment^”

Criteria to tailor therapeutic administered activity:
- Blood dose < 2 Gy (accepted dose limit for bone marrow)
- at 48h post-admin. < 4.4 GBq in WB if no iodine avid lung metastases
- at 48h post-admin. < 3 GBq in Wbi if presence of iodine avid lung metastases

Patient specific dosimetry vs fixed dose approach enables:
- Maximize dose to iodine avid tissue (thyroid remnants and metastases)
- avoiding undesired side effects

**Safety:** preserve bone marrow function

**Efficacy:**
- radioablation of thyroid remnant
- treat iodine avid metastases

Pre-treatment estimation with:
- I-131 NaI
- I-123 NaI
Dose to the blood

Benua RS, Cicale NR, Sonenberg M, Rawson RW. $ 
Relation of radioiodine dosimetry to results and **complications** in treatment of metastatic thyroid cancer. 

Benua RS, Leeper RD. 
A method and rationale for treating metastatic thyroid carcinoma with the **largest safe dose** of I-131. 

---

**Accent on safety**

Self irradiation  
Blood $\leftrightarrow$ Blood 
70-80% of dose to blood 

Blood $\leftarrow$ Rest of the body 
20-30% dose to blood 

No serious side effect if 
$D_{\text{blood}} \leq 2 \text{ Gy}$

---

**Activity concentration in blood is a reasonable good estimation of the activity concentration in red-marow**

G. Sgouros. Bone Marrow Dosimetry in Radioiodine Therapy of Thyroid Cancer. J Nucl Med; **2005** vol. 46no. 5 899-900
Blood based-dosimetry

Recommendations:
- 5 blood samples (Blood ← Blood) → Blood residence time: $\bar{a}(\text{blood})$
- WB conjugate acq. (Blood ← Rest of the body) after urinary bladder voiding → WB residence time $\bar{a}(\text{WB})$

**Optional WB-5**
(>5% $A_{\text{admin}}$ at 96h p.a.)
Conjugate views from 2-head gamma Camera

High energy collimator
Camera sensitivity
Count statistic: > 10⁵ counts (WB geometric mean)
\[ \sqrt{WB_{ant} \times WB_{post}} \]

I-131, 360 kev Photon → Crystal thickness> 16 mm → A diag. > 10-15 MBq

Assessment of WB activity retention with a spectroscopic probe is also possible.
Absorbed dose calculation

\[ \frac{D_{\text{blood}}}{A_0} = S_{\text{blood}} \times \tau_{\text{ML,blood}} + S_{\text{blood}} \times \tau_{\text{WB}} R(t) = \frac{A(t)}{A_0} = A_1 \times e^{-\lambda_1 t} + A_2 \times e^{-\lambda_2 t} \]

\[ \tau(h) = \int_0^\infty \frac{A(t)}{A_0} dt = \frac{A_1}{\lambda_1} + \frac{A_2}{\lambda_2} \]

**Blood absorbed dose**

\[ \frac{D_{\text{blood}}}{A_0} = S_{\text{blood}} \times \tau_{\text{ML,blood}} + S_{\text{blood}} \times \tau_{\text{WB}} \]

Admin. Activity \( D_{\text{blood}} = 2 \text{ Gy} \)

108 Gy.mL/GBq.h

0.0188 \times (\text{bw(kg)})^{-2/3} \text{ Gy/GBq.h}

Assuming standard BM mass

\[ \frac{D_{\text{blood}}}{A_0} \left[ \frac{\text{Gy}}{\text{GBq}} \right] \times A_{\text{admin}}[\text{GBq}] = 2 \text{ Gy} \]

\[ A_{\text{admin}}[\text{GBq}] = \frac{2}{\frac{D_{\text{blood}}}{A_0} \left[ \frac{\text{Gy}}{\text{GBq}} \right]} \]
Blood based dosimetry $\rightarrow$ Increase $A_{\text{admin}}$ without risk of severe side effects

Strengths:

- Patient-specific max. $A_{\text{admin}}$
- Identification patient not safe with empiric $A_{\text{admin}}$
- Maximize single $A_{\text{admin}}$, $\rightarrow$ minimize fractionation
  $\rightarrow$ avoid biokinetic changes occurring in fractionated therapy
- Increased curative outcome with fewer therapy cycles

Limitations:

- Expected benefits but Improved outcome not clearly demonstrated
- No information about tumour dose
- Diagnostic administration of I-131 can induce ‘stunning’ effect
- Costs(?)
- Use in presence of extended metastatic bone involvement

Care to critical organ: lung especially in presence of metastases
Tumour dosimetry in I-131 radiation therapy

I-123

I-124 PET  Short half life 13h
Better resolution and sensitivity than SPECT
Longer half-life (h=4.2d) good predictor of I-131 biodistribution

124I PET/CT images were acquired 24 and 96 h after oral administration of approximately 28 MBq of 124I-sodium iodide in 47 patients.
Lesions were identified as thyroid remnants or metastases (lymph node, lung, bone)
Lesion response was determined on the basis of 124I PET/CT and 131I SPECT/CT follow-up images

In a fixed-activity approach (3.0 ± 1.0 GBq), a statistically significant dose–response relationship for both thyroid remnants and metastases using pretherapeutic 124I PET/CT lesion dosimetry was found. The findings may be useful in patient management.
Standard operational procedures
- Same as previously

How to define the mass
- Everything is suitable: CT, US, NM,... (standardized...)

How to fit and compute TIAC (=Int(RIU))
- with different number of time point
- Late point important

Beta
- \( \bar{E}_\beta = 2.654 [Gy \times g \times MBq^{-1} \times d^{-1}] \)
- For \( m[g] = 20 \), the fractional energy deposition due to \( \gamma \) is 5%
  - \( \bar{E}_{\beta+\gamma} = 2.808 [Gy \times g \times MBq^{-1} \times d^{-1}] \)

Inverse law to correct for the mass

\[
A_{0[MBq]}(r_T) = \frac{1}{E} \times \bar{D}_{[Gy]}(r_T) \times \frac{m[g](r_T)}{TIAC[d]}
\]
Dose factors: Maxon, Physics, Olinda, EANM

Maxon:

\[
A_0[MBq](r_T) = \frac{\bar{D}[Gy](r_T) \times m[g](r_T)}{T_{1/2}[d]} \times 0.248[MBq \times d \times Gy^{-1} \times g^{-1}]
\]

\[E_{\text{mean}}(\beta) = 0.192[\text{MeV} \times \text{Bq}^{-1} \times \text{s}^{-1}]
\]

\[|e| = 1.602 \times 10^{-19}[\text{C}]
\]

\[\text{Joule} = \text{Volt} \times \text{Coulomb}\]

\[\bar{E}_\beta = 0.192[\text{MeV}] \times 86.4[\text{Ms} \times \text{d}^{-1}] \times 0.16[\text{mJ} \times \text{PeV}^{-1}] = 2.654[\text{mJ} \times \text{MBq}^{-1} \times \text{d}^{-1}]
\]

\[\bar{E}_{\text{Olinda}} = S_{\text{Thyr}} \times m_{\text{Thyr}} \times 86.4[\text{s} \times \text{md}^{-1}]
\]

\[= 2.84[\text{Gy} \times \text{g} \times \text{MBq}^{-1} \times \text{d}^{-1}]
\]

\[\bar{E}_{\text{EANM}} = 2.808[\text{Gy} \times \text{g} \times \text{MBq}^{-1} \times \text{d}^{-1}]
\]

\[\frac{\ln(2)}{2.808} \times 0.247[\text{MBq} \times \text{d} \times \text{Gy}^{-1} \times \text{g}^{-1}]
\]

\[A_0[MBq](r_T) = \frac{1}{\bar{E}} \times \bar{D}[Gy](r_T) \times \frac{m[g](r_T)}{TIA C[d]}
\]
We see what we treat

At which resolution?  How deep is your activity?
Sampling inside Voxels

Activity =
Target mass ≠
Dose $\beta, \gamma =$
Dose $\alpha, \text{auger} \neq$
Spill-out/-in
Resolution loss => Partial volume effect

Correction with size-dependent recovery coefficients

Phantom-based PVE correction for spheres

What is the correct volume? The correct mass?
Dosimetry : Case Study

S. Gnesin
I-123 pre-therapy hybrid dosimetry

Administration of 154.3 MBq of I-123

Acquisitions: AP WB I-123 scans with an image of quantitative SPECT/CT

Region of interest for dosimetry: WB, Thyroid remnants, ROB

Rescale the time activity curve to quantitative values (organs activity)

Quantitative SPECT/CT
Time = 26h p.a.
Blood sample analysis for red-marrow dose exposition

<table>
<thead>
<tr>
<th>time after admin (h)</th>
<th>1.33</th>
<th>3.90</th>
<th>25.33</th>
</tr>
</thead>
<tbody>
<tr>
<td>sample activity kBq/ml</td>
<td>7.02</td>
<td>4.32</td>
<td>0.47</td>
</tr>
<tr>
<td>A/A0</td>
<td>4.55E-05</td>
<td>2.80E-05</td>
<td>3.05E-06</td>
</tr>
</tbody>
</table>

A/ml/A_admin

Blood samples (1ml)

<table>
<thead>
<tr>
<th>Teff (h) I-123</th>
<th>6.35</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tbiol (h) I-123/I-131</td>
<td>12.25</td>
</tr>
<tr>
<td>Teff (h) I-131</td>
<td>11.52</td>
</tr>
</tbody>
</table>

\[ y = 0.0000478e^{0.1091025x} \]
\[ R^2 = 0.9948714 \]

\[ A_{admin} [GBq] = \frac{2D_{blood}[Gy]}{A_0 [GBq]} \]

D_blood (Gy/GBq) \[ 0.074 \]

A admin GBq (2Gy to blood) \[ 26.9 \]

For \( A_{admin} = 3.7 \) GBq \( \rightarrow \)

\[ D_{blood} = 0.074 \text{ Gy/GBq} \times 3.7 \text{ GBq} = 0.3 \text{ Gy} \]
Therapeutic administration: 3.7 GBq (standard dose)

<table>
<thead>
<tr>
<th>ROI / Organ</th>
<th>TIAC (h)</th>
<th>mGy/GBq (I-131)</th>
<th>Dose (Gy) 3.7 GBq I-31</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total body</td>
<td>18.65</td>
<td>1.39E+02</td>
<td>5.14E-01</td>
</tr>
<tr>
<td>Thyroid rem.</td>
<td>16.38</td>
<td>3.64E+05</td>
<td>1.35E+03</td>
</tr>
<tr>
<td>Mediastinal Lesion</td>
<td>3.67</td>
<td>1.50E+05</td>
<td>5.55E+02</td>
</tr>
<tr>
<td>lungs</td>
<td>0.65</td>
<td>1.01E+03</td>
<td>3.74E+00</td>
</tr>
<tr>
<td>stomach cont</td>
<td>1.64</td>
<td>6.22E+02</td>
<td>2.30E+00</td>
</tr>
<tr>
<td>Urinary Bladder</td>
<td>0.65</td>
<td>3.30E+02</td>
<td>1.22E+00</td>
</tr>
<tr>
<td>Rest of body</td>
<td>13.61</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Post treatment I-131 hybrid dosimetry (3.7 GBq)

I-131 SPECT /CT
Carcinoma Thyr.
Avec metas. poulmon
76h p.i (3.7 GBq)
Hybrid imaging WB planar + Q. SPECT

Organ and lesion TIAC(h) calculation from emission data

Organ and lesions mass determination based on CT data

Olinda organ based dosimetry

Olinda spherical-model for dose estimation to

- Thyroid remnant
- Mediastinal lymphnode
- Lung metastases

Olinda spherical-model for dose estimation to

- Thyroid remnant
- Mediastinal lymphnode
- Lung metastases
### Post treatment I-131 hybrid dosimetry (3.7 GBq)

<table>
<thead>
<tr>
<th>Group</th>
<th>A_0/A_admin Lambda (1/h)</th>
<th>TIAC (h)</th>
<th>Mass (g)</th>
<th>Dose Gy/GBq</th>
<th>Dose tot (Gy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyroide (1)</td>
<td>0.01456479</td>
<td>0.0148</td>
<td>0.9841</td>
<td>0.3</td>
<td>500</td>
</tr>
<tr>
<td>Lesion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mediastin (1)</td>
<td>0.0311521</td>
<td>0.0164</td>
<td>1.8995</td>
<td>0.65</td>
<td>300</td>
</tr>
<tr>
<td>Stomach (1)</td>
<td>0.0299313</td>
<td>0.0131</td>
<td>2.2848</td>
<td>0.54</td>
<td>80</td>
</tr>
<tr>
<td>L1 (1)</td>
<td>0.00162256</td>
<td>0.0114</td>
<td>0.1423</td>
<td>0.2</td>
<td>80</td>
</tr>
<tr>
<td>L2 (1)</td>
<td>0.00025741</td>
<td>0.0114</td>
<td>0.0226</td>
<td></td>
<td></td>
</tr>
<tr>
<td>L3 (1)</td>
<td>0.00039513</td>
<td>0.0114</td>
<td>0.0347</td>
<td></td>
<td></td>
</tr>
<tr>
<td>L4 (1)</td>
<td>0.00048362</td>
<td>0.0114</td>
<td>0.0424</td>
<td></td>
<td></td>
</tr>
<tr>
<td>L5 (1)</td>
<td>0.0003517</td>
<td>0.0114</td>
<td>0.0309</td>
<td>0.16</td>
<td>20</td>
</tr>
<tr>
<td>L6 (1)</td>
<td>0.00083665</td>
<td>0.0114</td>
<td>0.0734</td>
<td></td>
<td></td>
</tr>
<tr>
<td>L7 (1)</td>
<td>0.00025102</td>
<td>0.0114</td>
<td>0.0220</td>
<td>0.14</td>
<td>23</td>
</tr>
<tr>
<td>L8 (1)</td>
<td>0.00014035</td>
<td>0.0114</td>
<td>0.0123</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung dx (1)</td>
<td>0.06300247</td>
<td>0.0115</td>
<td>5.4785</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung sx (1)</td>
<td>0.07075424</td>
<td>0.0115</td>
<td>6.1525</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td>0.13375671</td>
<td>0.0115</td>
<td>11.6310</td>
<td>2.61</td>
<td></td>
</tr>
<tr>
<td>FOV</td>
<td>0.5</td>
<td>0.0114</td>
<td>43.8596</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bladder</td>
<td>0.1</td>
<td>2h voiding</td>
<td>0.1993</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ROB</td>
<td>0.7</td>
<td>0.06301338</td>
<td>11.1088</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Body</td>
<td>0.06301338</td>
<td></td>
<td></td>
<td>0.097</td>
<td>0.3686</td>
</tr>
</tbody>
</table>
Conclusion

- Reproducibility:
  - keep all data
  - traceability
  - reporting

- Be aware about sources of error
  - And impact in dose estimation

- Multidisciplinary discussion and debate about whole workflow and results