Blood-based Dosimetry of Radioiodine Treatment of Differentiated Thyroid Cancer

M. Lassmann
Benua and Leeper, 1962

- “Safety limit” for the bone marrow: 2 Gy to the blood (as a surrogate for bone marrow) to avoid bone marrow suppression

- Maximum activity in the WB at 48 h 3 GBq (in patients with extensive lung involvement to avoid pulmonary fibrosis)
“This SOP gives recommendations on how to tailor the therapeutic activity to be administered for systemic treatment of differentiated thyroid cancer (DTC) such that the absorbed dose to blood does not exceed 2 Gy (a widely accepted limit for bone marrow toxicity) and, at 48 h after administration, the whole-body retention does not exceed 4.4 or 3 GBq in the absence or presence of iodine-avid diffuse lung metastases, respectively. For the blood absorbed dose estimate procedure low activities of I-131 NaI will be administered pre-therapeutically followed by a series of blood and whole-body measurements.”
Whole Body Retention

Purpose:
Determination of the area under both curves

Blood Activity

Time after administration / [h]
Blood-based Dosimetry: Calculation

\[
\frac{D_{\text{blood}}}{A_0} = S_{\text{blood}} \cdot \frac{\tau_{\text{mL of blood}}}{A_0} + S_{\text{total body}} \cdot \tau_{\text{total body}}
\]

\(S_{\text{total body}}\) only gamma contribution considered

The activity to be administered for a blood dose of 2 Gy is:

\[
A_{\text{adm.}} [\text{GBq}] = \frac{2 [\text{Gy}]}{D_{\text{blood}} / A_0 [\text{Gy/GBq}]}
\]
# Blood-based Dosimetry: Methods

<table>
<thead>
<tr>
<th>Time</th>
<th>Task</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quality control, preparation of $^{131}$I standard and tracer activity, micturition (just before administration)</td>
<td>0 Administration of $^{131}$I tracer activity</td>
</tr>
<tr>
<td>Avoid micturition or defecation</td>
<td>10 min (i.v. admin.) 2 h (oral admin) 6 h Micturition (just before whole body measurements), measurement of whole body activity, blood sampling (2 ml)</td>
</tr>
<tr>
<td>Measurement of whole body activity, blood sampling (2 ml)</td>
<td>24 h Micturition (just before whole body measurements), measurement of whole body activity, blood sampling (2 ml)</td>
</tr>
<tr>
<td>96 h Micturition (just before whole body measurements), measurement of whole body activity, blood sampling (2 ml)</td>
<td>144 h Blood sampling (2 ml)  optional: measurement of whole body activity</td>
</tr>
<tr>
<td>Evaluation of blood absorbed dose and therapeutic activity</td>
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</tbody>
</table>
Pre-therapeutic Quantification of Whole Body Retention

A dual headed gamma camera with high energy collimators and crystal thickness of 5/8” or more

• The net count rate (detection efficiency) of a non-attenuated point source should exceed 50 counts per second (cps) per MBq of I-131
• The net count rate per MBq in the field of view should be at least twice as high as the overall background count rate in the I-131 energy window.

or

A (preferably) spectroscopic probe with a large crystal (min: 3x3”)

An activity as low as 10–15 MBq will provide sufficient count statistics.
Aliquots of one millilitre (1 mL) should be prepared from each blood sample.

The activity in the blood is determined in a well counter from aliquots of heparinized blood samples. The detection limit of the well counter used should be lower than 1 Bq of I-131 per ml.

All blood activities are normalized to the administered activity in order to calculate the retention FIA(t) per mL of blood.
Blood-based Dosimetry: Calculation

Absorbed Dose to Blood Calculation Methods:
• EANM SOP Formula

\[
\frac{D_{\text{blood}}}{A_0} \left( \frac{\text{Gy}}{\text{GBq}} \right) = 108 \cdot \tau_{\text{ml of blood [h]}} + \frac{0.0188}{(\text{wt[kg]} \, ^{2/3})} \cdot \tau_{\text{total body [h]}}
\]

Absorbed Dose to Bone Marrow Calculation Methods:
• EANM SOP Formula

\[
\frac{D_{\text{Red marrow}}}{A_0} \left( \frac{\text{Gy}}{\text{GBq}} \right) = 61 \cdot \tau_{\text{ml of blood [h]}} + \frac{0.106}{\text{wt[kg]}} \cdot \tau_{\text{total body [h]}}
\]
Practical Example: How to calculate the blood absorbed dose

\[ \text{Specific Absorbed Dose: } 0.064 \text{ [mGy/MBq]; Absorbed Dose: } 0.24 \text{ Gy} \]
Example: Blood Doses after Therapeutic Dosimetry
(58 patients)

Activity: 3.7 GBq
### Blood Absorbed Doses

<table>
<thead>
<tr>
<th></th>
<th>Mean Specific Absorbed Dose Gy/GBq</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-Therapy</td>
<td>0.089 ± 0.018</td>
</tr>
<tr>
<td>Therapy</td>
<td>0.102 ± 0.045</td>
</tr>
<tr>
<td></td>
<td>Max: 0.27</td>
</tr>
</tbody>
</table>

2 Gy limit:
- mean: 20 GBq
- max: 7.4 MBq

Ratio THW:RhTSH: 1.5

Lassmann et al, EANM Congress 2007

Hänscheid et al, JNM 2004
Safety data on 10 high-dose patients

Verburg et al., unpublished results

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Blood-based Dosimetry

Limitations that need to be mentioned are:
- a benefit of the strategy is plausible but no valid clinical data exist on improved response and/or outcome rates; the absorbed dose to the tumour is not known. Higher activities might be administered without achieving a higher therapeutic effect when using this methodology.

- increased cost and inconvenience, although this may be outweighed by rendering further treatments unnecessary.

- What is the optimal dosage for ablation therapy in low-risk patients?
Why blood-based dosimetry?

The strengths of the dosimetry based approach are:
- Determination of the maximal safe activity of radioiodine for each patient individually
- Identification of patients for whom empiric fixed activities are not safe (e.g. impaired kidney function)
- The potential to administer higher activities once instead of multiple administrations of lower activities in a “fractionated” therapy in order to avoid changes in tumor/lesion biokinetics after multiple therapies that have been observed
- A long history of use in several institutions
- An expected increase in the probability of curing patients in an advanced stages of the disease with fewer courses of therapy.
Acknowledgements

➢ The Nuclear Medicine Department in Würzburg, particularly H. Hänscheid, M. Luster, Chr. Reiners
➢ The members of the EANM Dosimetry Committee
➢ The Patients
Blood-based Dosimetry of Radioiodine Treatment of DTC

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