Dosimetry in radionuclide therapy

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The Radionuclide Therapy Committee of the European Association of Nuclear Medicine states correctly in the introduction to its protocols that therapeutic effects of radionuclides in the management of disease are due to the amount absorbed radiation energy and to the radiosensitivity of the irradiated tissue [1]. Absorbed radiation dose (= Gy), however, is frequently replaced in practical Nuclear Medicine by “mCi” or “MBq” as dose units, even as certainly the amount of activity applied is certainly not the only factor in delivery of an absorbed radiation dose. Radiation dose to an organ or tumor is defined by the simple equation:

\[ \text{Gy} = \frac{\text{activity} \times \text{residence time (t)} \times S}{\text{volume}} \]

[2]. The specific S-value of a radionuclide refers to linear energy transfer of its radiation including also relative biological weighting factors. It would seem logical to establish a clear dose response relationship for Nuclear Medicine therapy (Table 1), so that adequate clinical results could be expected. Specific modalities especially of systemic radionuclide therapy, however, make dosimetry and therefore an estimate of the dose response relationship quite difficult.

<table>
<thead>
<tr>
<th>radiation dose</th>
<th>radiation effect</th>
<th>clinical effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>80 - 100 Gy</td>
<td>moderate atrophy</td>
<td>metabolic activity significantly reduced, growth potential impaired, moderate volume reduction of irradiated tissue</td>
</tr>
<tr>
<td>100 - 150 Gy</td>
<td>significant atrophy</td>
<td>metabolic activity severely reduced, growth potential blocked, significant volume reduction of irradiated tissue</td>
</tr>
<tr>
<td>200 - 300 Gy</td>
<td>severe atrophy</td>
<td>metabolic activity and growth potential blocked, volume of irradiated tissue: almost gone</td>
</tr>
<tr>
<td>500 Gy</td>
<td>necrosis</td>
<td>tissue dead and gone</td>
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Table 1. Estimated correlation of radiation dose with degree of radiation atrophy

In Nuclear Medicine there is only one therapeutic method which allows a dosimetric calculation as in other forms of radiotherapy: This is radioembolization of hepatoma with $^{90}$Y-particles [3]: The tumor (= target) volume is known from CT-scans, 100 % of the selectively intraarterially applied activity are in the tumor, no metabolic break-down of the labeled particles occurs for several physical half-lives of $^{90}$Y so that “residence time” equals physical halflife. Even intratumoral application of radioactive colloids which should stay in the tumor does not fit in this model, as intratumoral distribution is variable.

Also in all other therapeutic methods (intracavitary, systemic) such assumptions are not correct: Definition of target volume, residence time can vary and in systemic therapy also the amount of activity delivered to the target. Target volume can be assessed by sonography, CT, MRI, SPECT and PET for solid lesions, its assessment in intracavitary therapy is almost impossible. Target volume can also not be assessed in cases with diffuse bone marrow involvement (bone metastases with “superscans”, patients with neuroblastoma in bone marrow etc.). Residence time can easily be registered when the radiopharmaceutical emits $\gamma$-radiation.
by serial activity measurements over the target. It is impossible to evaluate this parameter when pure β-emitters are used. The same situation exists when activity delivered to the target should be estimated. For β-emitters identical γ-emitting radiotracers can be used for this purpose (e.g. $^{85}\text{Sr}$ for $^{89}\text{Sr}$, $^{111}\text{In}$-Octreotide for $^{90}\text{Y}$-Octreotide). Activity delivered to the target can be estimated for γ-emitters (e.g. $^{131}\text{I}$, $^{153}\text{Sm}$, $^{186}\text{Re}$) by quantitative scans and SPECT [4] or by substitution of such radionuclides with PET-tracers (e.g. $^{124}\text{I}$). For pure β-emitters one can again substitute a PET-tracer (e.g. $^{86}\text{Y}$ for $^{90}\text{Y}$). Overall therefore, we do have possibilities to estimate uptake of the radiopharmaceutical, target volume (Fig. 1) and residence time for many therapeutic methods and we should make use of them to achieve some gross dosimetry. $^{86}\text{Y}$ would even provide a possibility to measure target volume for intracavitary therapy. Similar dosimetric approaches should also be applied to predict side effects of radionuclide therapy due to irradiation of bone marrow and critical organs. Recent insights of microdosimetry, however, including effects of Auger electrons and α-emitters cannot adequately be used in clinical therapy in general as yet. The mentioned dosimetric methods are not very popular in large parts of the Nuclear Medicine Community as it is known that simple empirical strategies such as “fixed dose”-applications (e.g. $^{131}\text{I}$, $^{89}\text{Sr}$, $^{32}\text{P}$) have been quite successful also. This discrepancy between results of scientific dosimetry and clinical outcome without it can partly be explained by differences in individual radiosensitivity.

The assessment of specific radiosensitivity of a lesion is still an unsolved problem. Studies using Palladium-islets or well plates were done [5] but results so far show, that it still is almost impossible to register e.g. radiosensitivity of a certain tumor in an individual patient. While the efforts to improve registration of specific radiosensitivity by ex-vivo assays should be encouraged in the future one should also try to overcome the old habit of using only amounts of radioactivity as “doses” especially as new and exciting therapeutic applications of radionuclides are being developed. In this situation one should try at least to estimate absorbed radiation dose (≡ Gy) in therapy, which could improve results of our therapeutic approaches significantly.

Fig. 1. SPECT-slices as used for estimate of volume and regional uptake in bone metastases (number of pixels, cts. Per pixel)

References