Radioiodine Therapy of Hyperthyroidism
-Consequences of Not Using Individual Biokinetic Data

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Abstract. Radioiodine therapy of hyperthyroidism using $^{131}$I has been performed for more than five decades. For the calculation of the activity to be administered for giving a certain absorbed dose to the thyroid, the mass of the thyroid and the individual biokinetic data, uptake and biologic half-time, have to be determined. Different protocols to determine the administrated activity of $^{131}$I are in use, but not all of them determine the absorbed dose to the thyroid. In order to receive information about the practice in Sweden a questionnaire was sent to all nuclear medicine clinics. The results showed large methodological differences. Nine out of twenty-three hospitals calculate the administered activity using the individual uptake of iodide in the thyroid and the individual biologic half-time. Nine hospitals use the individual uptake of iodide, but not the individual biologic half-time. Five hospitals do not use the individual biokinetic data at all for the determination of the administered activity to the patient. In total seventeen different protocols at twenty-three hospitals are in use. Protocols not using the individual biologic half-time can result in a variation of administered activity to the patient, with a range of 50 % to 160 %, compared to protocols using the individual biologic half-time. Protocols not using the individual biokinetic data will in general administer 240 % higher activity to the patient, with a range of 70 % to 770 %. In Sweden five out of twenty-three hospitals used fixed administered activity, but if all hospitals in Sweden used a protocol considering the individual biokinetic data the total administrated activity of $^{131}$I would decrease with 10 %. Correspondently, the radiation dose to the patient, the family members, the staff and the environment would be reduced. For a number of patients the dose reduction would be considerably larger, while still getting the desired clinical effect. Hospitals have performed radioiodine therapies for a long time using their own protocols. Due to local traditions they lack motivation to change their protocol to a protocol considering the individual biokinetic data. More effort should be made, worldwide, to conform these protocols in use, to protocols considering the individual biokinetic data, and thus decrease unnecessary radiation dose to individual patients and their families.

Introduction
Radioiodine therapy using $^{131}$I is a world wide used therapy for benign thyroid diseases. It has been performed for almost 60 years, but still there is no consensus in what level of dosimetry that is needed. For all types of radiotherapy the goal is to deliver an absorbed dose to pathological tissue for an effective treatment without causing undesired effects in healthy tissues. Different protocols are used to determine the activity of radioiodine needed for the intended therapy. The category of protocol that considers most number of parameters when calculating the mean absorbed dose to the thyroid considers the active thyroid mass/volume, the uptake and biologic half-time of radioiodine in the individual patient’s thyroid.

Some hospitals simplify the method and measure the uptake and estimate the weight of the thyroid, but do not consider the biologic half-time of radioiodine in the thyroid of the individual patient. Others simplify the method even more and give a standard activity for all sizes of the gland. None of the simplified protocols above has the possibility to estimate the absorbed dose to the thyroid, since the biologic half-time and/or uptake measurements of radioiodine are not performed. These protocols are not in agreement with internationally accepted radiation protection principles and national regulations. The best from a radiation protection point of view is to use as small amount of activity as possible to get the desired effect and benefit to the patient [1]. This is in accordance with the ALARA principle (“all exposure shall be kept As Low As Reasonable Achievable, economic and social factors taken into account”) recommended by the ICRP [2]. The use of radiation is restricted and controlled by legislation and recommendations. The council of the European Union says in the directive on health protection of individuals against dangers of ionising radiation in relation to medical exposures [3] that “For all medical exposure of individuals for radiotherapeutic purposes, ...., exposures of target
volumes shall be individually planned; taking into account that doses of non-target volumes and tissues shall be as low as reasonably achievable and consist with the intended radiotherapeutic purpose of the exposure.” The directive has been implemented into the legislation of each member country [4]. Both in legislation and recommendations are expressed the requirements for radioiodine therapy with an individually determined administered activity. A questionnaire was distributed [5] to Swedish hospitals to see whether they fulfil the legislation and recommendations or not.

Protocols in Sweden

Twenty-three hospitals currently perform radioiodine therapy for hyperthyroidism in Sweden. To calculate the activity to be administered for giving a certain absorbed dose to the thyroid, the mass of the thyroid and the individual biokinetic data, that is the individual uptake of iodide in the thyroid and the individual biologic half-time, have to be determined. Three different categories of protocols could be seen, Table 1. The administered activity was calculated in nine hospitals, using all the three parameters mentioned above. Nine hospitals use the individual uptake of iodide, but not the individual biologic half-time. Five hospitals do not use the individual biokinetic data and/or the volume of the thyroid for the determination of the administered activity to the patient. In each category several different protocols were in use and in total seventeen different protocols are in use at twenty-three hospitals in Sweden.

Table I. Methodological differences in radioiodine therapy of hyperthyroidism in Swedish hospitals.

<table>
<thead>
<tr>
<th>Number of hospitals</th>
<th>Number of different protocols</th>
<th>Parameters considered when calculating administered activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>5</td>
<td>Uptake of $^{131}$I and biologic half-time, thyroid volume</td>
</tr>
<tr>
<td>9</td>
<td>7</td>
<td>Uptake of $^{131}$I and thyroid volume</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>None</td>
</tr>
</tbody>
</table>

Comparing the different categories of protocols

The differences in absorbed dose to the thyroid using different protocols were studied [6]. Data from 187 radioiodine treatments for Graves’ disease at Malmö University Hospital were analysed. The therapy given was based on individual absorbed dose calculations considering both volume of the thyroid and individual uptake and biologic half-time of $^{131}$I, Equation 1, with a prescribed absorbed dose to the thyroid of 80 Gy for all patients.

\[
\frac{D}{A} = 0.043 \times U_0 \times \frac{T_{eff}}{V}
\]  

(1)

$D/A$: absorbed dose per administered unit activity (Gy/MBq), $U_0$: extrapolated initial uptake at time zero (%), $T_{eff}$: effective half-time (d) and $V$: estimated volume of the thyroid (cm$^3$). A density of the thyroid of 1 g/cm$^3$ was assumed.

The activity, which should have been administered at other hospitals applying 3.7 MBq/g corrected for uptake (not considering individual biologic half-time) or 370 MBq (fixed activity to all patients), was calculated for the individual patients, as was the corresponding absorbed dose to the thyroid according to Equation 1.

Protocols not considering the individual biologic half-time results in a distribution of administered activity to the patient, with a range of 50 % to 160 %, compared to protocols using Equation 1, Table II and FIG 1. The protocol with a fixed administered activity of 370 MBq will in general administer 240 % higher activity to the patient, with a range of 70 % to 770 %.

Table II. The relative distribution of the mean absorbed dose to the thyroid using three different protocols of calculating the administered activity compared to calculation according to Equation 1. Comparison to prescribed 80 Gy.

<table>
<thead>
<tr>
<th>Protocol</th>
<th>Median (Gy)</th>
<th>Range (Gy)</th>
</tr>
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<tbody>
<tr>
<td>3.7 MBq/g (corrected for uptake)</td>
<td>83 (105 %)</td>
<td>36 – 129 (45 % – 160 %)</td>
</tr>
<tr>
<td>370 MBq</td>
<td>194 (240 %)</td>
<td>58 – 617 (70 % – 770 %)</td>
</tr>
</tbody>
</table>
FIG. 1. The relative distribution of the mean absorbed dose to the thyroid using 3.7 MBq/g (corrected for uptake) or a fixed activity of 370 MBq to all patients. Comparison to an absorbed dose to the thyroid of 80 Gy according to Equation 1.

For the individual patient the risk of a second treatment would be reduced if a protocol considering the individual parameters were used, as well as the risk of being exposed to unnecessary radiation. If all hospitals in Sweden used a protocol considering the individual parameters, the total administrated activity of $^{131}$I would decrease with 10%, while still achieving the desired therapeutic effect.

**Discussion/Conclusion**

Less activity will be needed for therapy if the absorbed dose to the thyroid is calculated, using the parameters individual uptake, biologic half-time of $^{131}$I and the volume of the thyroid, compared to if one or all parameters are disregarded. Using all individual parameters will optimize the therapy and decrease unnecessary radiation dose to individual patients, their families and contamination of the environment. The risk of a second treatment will be reduced as well. However, when treating hyperthyroidism with radioiodine, there is no clear consensus on what dosimetry that is needed. The choice of treatment is likely to be influenced by local traditions and other subjective biases, cost, convenience, and patient preferences. In Sweden fourteen out of twenty-three hospitals do not consider the individual biokinetics and/or the volume of the thyroid. If all hospitals in Sweden used a protocol considering these parameters the total amount of administrated activity of $^{131}$I would decrease and patients, staff and family members would be exposed to a lower radiation dose. This will benefit the restrictions for the family members since they will not be so strict and will last for a shorter period of time. The need for isolation of the patient due to radiation protection reasons will be reduced, which will reduce the cost for the hospital, since treating an outpatient is more cost-effective. For the patient there are significant social benefits being treated as an outpatient.

Hospitals have performed radioiodine therapies for a long time using their own protocols. Due to local traditions they lack motivation to change their protocol into a protocol considering the individual biokinetic data. More effort should be done, worldwide, to conform the protocols in use, into protocols considering the individual biokinetic data, and thus decrease unnecessary radiation dose to individual patients and their families, in agreement with internationally accepted radiation protection principles and national regulations. Estimating the mean absorbed dose to the thyroid is also a step forward to understand and control the clinical outcome and the effects of radioiodine therapy.
References


