## **Supplemental material**

# Examples of the different approaches employed to calculate either the thyroid-targeted activity or the thyroid-absorbed dose

A practical approach adopted in several centers is to start with an estimate of the desired <sup>131</sup>I activity necessary/sufficient to destroy the hyperfunctioning thyroid tissue, for example 5.55 MBq/gram (or 150  $\mu$ Ci/gram. The 24-h RAIU value is then used to estimate the activity that must be administered to the patient, according to the general equation:

$$A_{tot} = \frac{A_{tar} \times M}{RAIU}$$

where A<sub>tot</sub> is the total activity <sup>131</sup>I-iodide to be administered, A<sub>tar</sub> is the desired activity per gram of the target tissue, M is the mass of the target tissue, and RAIU is the 24-h value expressed as fraction of "1" (see examples in BOX-1 here below).

Total activity of <sup>131</sup>I-iodide ( $A_{tot}$ ) to be administered with the aim of delivering to the target tissue a desired activity ( $A_{tar}$ ) of 5.55 MBq (or 150 µCi) per gram, as calculated for two different patients with identical thyroid mass (M, as estimated by ultrasound), but with different 24-h uptake value (RAIU, expressed as fraction of 1).

General equation:

$$A_{tot} = \frac{A_{tar} \times M}{RAIU}$$

Patient #1: thyroid mass 35 grams; RAIU 75%:

$$A_{tot} = \frac{5.55 \times 35}{0.75} = 279 \, MBq$$

Patient #2: thyroid mass 35 grams; RAIU 50%:

$$A_{tot} = \frac{5.55 \times 35}{0.50} = 389 \, MBq$$

Despite an equal thyroid mass, different RAIU values dictate different activities to be administered to these two patients.

#### BOX-1

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The 24-h RAIU provides an approximation of the radiation dose. In fact, reliable dosimetric estimates require sequential RAIU measurements up to 5, or even 7–8 days to accurately define the radioiodine residence time in the thyroid. Since this procedure is impractical in a busy clinic, the RAIU is commonly measured at 3–4 h and at 24 h, assuming that radioactivity in the thyroid gland at 24 h declines with an average effective half-time of ~6 days (*1*,*2*). However, this approach may introduce errors exceeding a factor of two in the dosimetry estimates (*3*,*4*).

An alternative approach assumes that residual thyroid function after radioiodine therapy is proportional to the final volume (or mass) of the thyroid parenchyma according to the equation:

$$M_f = M_0 \times e^{-0.0038D}$$

Where  $M_f$  is the final thyroid mass following radioiodine therapy (desired target of treatment),  $M_0$  is the pre-treatment thyroid mass, and D is the thyroid-absorbed dose (calculated according to MIRD formalism (5) (see examples in the box-2 here below).

Effect of the same thyroid-absorbed dose, D, in two patients with different pre-treatment thyroid mass,  $M_0$ . For each value of the estimated thyroid-absorbed dose, the final post-treatment thyroid mass,  $M_f$  (with the associated post-treatment thyroid function) depends on the pre-treatment thyroid mass according to the general equation:

$$M_f = M_0 e^{-0.0038 \times D}$$

Patient #1: thyroid mass 10 grams; D = 500 Gy

$$M_f = 10 e^{-0.0038 \times 500} = 0.7 grams$$

In this patient ablation of the functioning thyroid mass is virtually complete.

Patient #2: thyroid mass 50 grams; D = 500 Gy

 $M_f = 50 e^{-0.0038 \times 500} = 7.5 grams$ 

Despite the same tyhyroid-absorbed dose, in this patient there will be some residual thyroid mass/ function post-treatment.

### BOX-2

This approach (the "volume algorithm") is as effective as the fixed 400 Gy thyroid-absorbed dose approach (6), but with administration of 26% less activity than with the fixed 400 Gy dose method. The "volume algorithm" delivers a lower radiation burden to the thyroid (296 Gy versus 400 Gy) and to the remainder of the body.

## **References to this supplemental material**

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