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# OPTIMIZATION OF $^{131}$I DOSES FOR THE TREATMENT OF HYPERTHYROIDISM

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**Abstract –** Several methods can be used to determine the activity of $^{131}$I in the treatment of hyperthyroidism. However, many of them do not consider all the parameters necessary for optimum dose calculation. The relationship between the dose absorbed by the thyroid and the activity administered depends basically on three parameters: organ mass, iodine uptake and effective half-life of iodine in the thyroid. Such parameters should be individually determined for each patient in order to optimize the administered activity. The objective of this work is to develop a methodology for individualized treatment with $^{131}$I in patients with hyperthyroidism of the Grave's Disease. A neck-thyroid phantom developed at the IRD was used to calibrate a scintillation camera and a uptake probe SCT-13004 at the Nuclear Medicine Center of the University Hospital of Rio de Janeiro and a uptake probe SCT-13002, available at the Nuclear Medicine Institute in Goiânia. The biokinetic parameters were determined based on measurements performed in eight voluntary patients. It is concluded that the use of the equipment available at the hospital (scintillation camera and uptake probe) has shown to be a suitable and feasible procedure for dose optimization in terms of effectiveness, simplicity and cost.

**Key words:** Nuclear medicine, hiperthyroidism, I-131

## INTRODUCTION

The first studies of the thyroid function were carried out with $^{131}$I. This procedure continues to be applied in Nuclear Medicine Centers for hyperthyroidism and cancer treatment and ablation of thyroid residues. The therapeutic doses of $^{131}$I are administered orally, in liquid form or in capsules (5). The advantage of radioactive iodine includes easy administration, efficacy, low cost and absence of pain. When administered orally in the form of sodium iodide solution, iodine is promptly absorbed, concentrated and incorporated by the thyroid in specific sites of the organ, with effective half-life of five days. According to data published by the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) (6), $^{131}$I is used in about 90% of the therapeutic procedures in Nuclear Medicine.

The activity present in the thyroid after administration of a single dose of $^{131}$I varies significantly among patients, depending on various factors such as: iodine uptake, thyroid mass, effective half life of iodine in the organ, distribution of activity in the tissue and radiosensitivity of organ cells. However there is little comprehensive information available in the literature related to radiation doses delivered to patients.

The risk of developing cancer in other healthy organs and tissues is directly proportional to the activity of iodine-131 administered to the

**Abbreviations: IRD,** Institute for Radioprotection and Dosimetry; **IMEN,** Nuclear Medicine Institute**; UNSCEAR,** United Nations Scientific Committee on the Effects of Atomic Radiation

patient. In the case of women in reproductive age the possibility of undesired effects on the progeny should also be considered. A realistic evaluation of such risks relies on the knowledge of iodine biokinetic in human body, followed by the calculation of the dose delivered to the patient.

There is still no consensus among physicians about the best protocol for the treatment of hyperthyroidism and the method to determine the activity to be administered for the treatment of thyroid diseases. In hyperthyroidism therapy, for example, not all the protocols consider the dose absorbed by the thyroid. Some of them use standard values without considering organ volume, effective half-life and thyroid uptake of each subject. Depending on individual parameters, the administration of a standard activity of 10 mCi to a patient for Graves' disease treatment can lead to an absorbed dose in the thyroid in the range of 60 to 600 Gy. In the case of patients with short effective half-life receiving a low dose, such treatment will probably be unsuccessful, demanding a subsequent therapy. On the other hand, high doses administered to patients with long effective half-lives will lead to unnecessary over exposure (2).

Even though among the physicians who defend the importance of the application of individualized dose calculation procedures, many of them take into consideration only a few parameters: thyroid volume and uptake, uptake only and volume only. Those professionals believe that for the calculation of the effective half-life the patient would have to show up at the hospital several times before the treatment. This would increase significantly the cost of the treatment. The most usual causes of hypethyroidism are: graves disease, toxic multinodular goiter and toxic adenoma, Graves' disease being the most frequent (80%) (4). It is well known that the effective half-life of iodine in the thyroid of patients with Graves' disease is low, while the uptake is high if compared to multinodular and uninodular goiter (3).

The typical retention curves of iodine in the thyroid show that a constant uptake value in patients with diffuse toxic goiter occurs about twelve hours after administration of the radionuclide. This phenomenon is of paramount importance for the calculation of the effective half-life in the time period between 14 and 30 hours after administration. The use of available equipment and the routine procedures carried out in nuclear medicine centers makes this methodology simple, effective and of low cost.

## MATERIALS AND METHODS

### *Production of neck-thyroid phantom*

The experimental part of this work was developed initially at the Laboratory for In Vivo Monitoring of IRD where the thyroid phantom has been produced using a 110 mm diameter filter paper cut in the size and shape of the thyroid gland (1). This phantom was contaminated with 241.86 mg of solution containing 3.075 MBq/g (83.1μci/g) of 131I with 1.1% uncertainty. An activity of 744 kBq (20 μci) was uniformly distributed over the surface of the paper. The phantom used in this study is based on a model previously available in IRD and used for occupational radiation protection purposes (Figure 1).

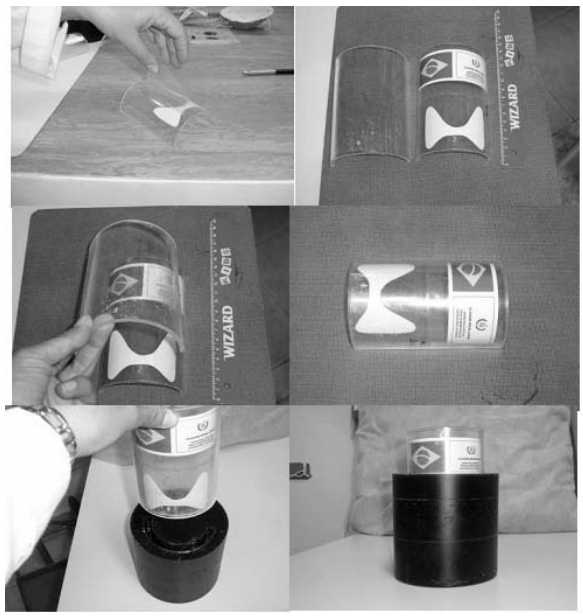



**Figure 1.** Production sequence of the neck-thyroid phantom developed in IRD.

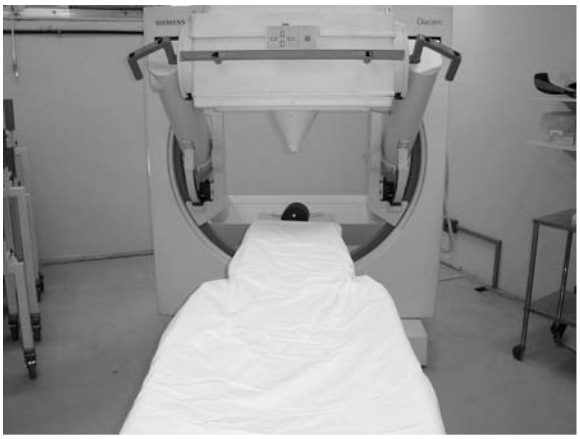
### *Hospital instruments*

The Federal University of Rio de Janeiro Hospital uses a DIACAM scintillation gamma camera containing a 2" NaI(Tl) crystal optically connected to 59 photo-multiplier tubes and equipped with a pinhole-type lead collimator for image diagnostic and a SCT-13004 probe for uptake measurements (Figure 2).

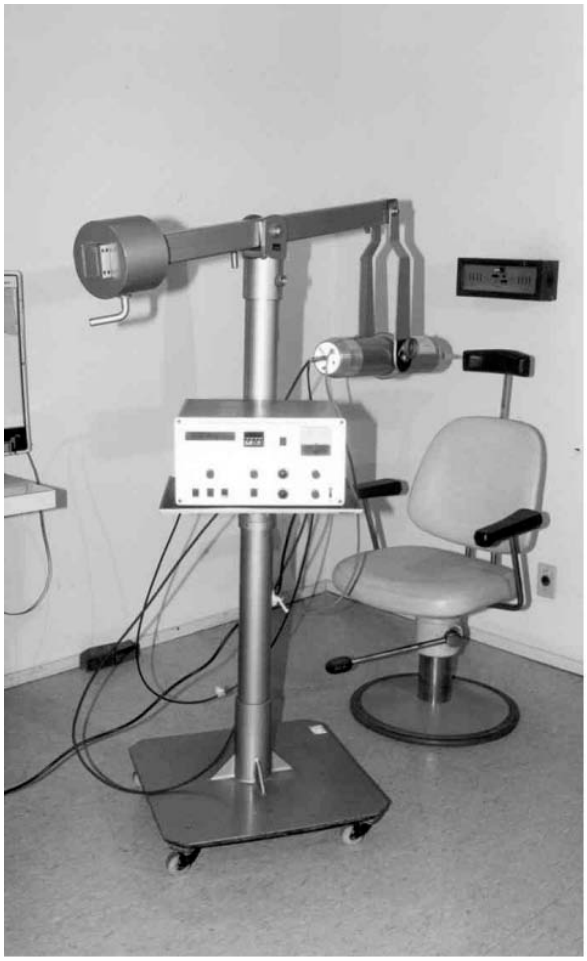
### *Calibration of the collimator-detector assembly*

Aiming to establish the best distance between the detector and the calibration phantom, it was built characteristic curves of iso-counts and iso-outputs to represent the view angle of the collimator-detector assembly. Such curves were obtained by positioning the detector at different distances from a 131I point source and selecting the 364 keV window of the scintillation camera. The source was positioned on a table over a milimetric paper in position "zero", representing the central axis of the collimator. The point source was then moved left and right in steps of 1 cm up to a final distance of 10 cm (Figure 3). For each position, 3 consecutive measurements of 30 seconds were performed. The average count value in each position was used to calculate the relative count rate. A similar procedure was carried out at the distances of 42.8, 43.8, 44.8, 45.8 and 46.8 cm in order to determine the view angle of the collimator-detector assembly without the

reduction ring. In this experiment it was used a plastic spacer developed in specifically for this application.



**a**

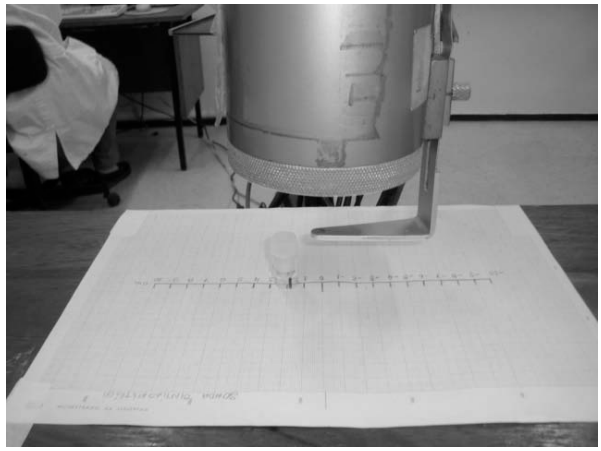


**b**

**Figures 2.** Scintillation camera with pinhole collimator **(a)** and Uptake probe model SCT-13004 **(b)** in operation at the Nuclear Medicine Center of the Federal University Hospital of Rio de Janeiro

For the calibration of detector-collimator assembly SCT-13004, the calibration source was positioned with the scale at 3 different distances (20, 25 and 30cm) relative to the detection system (Figure 3). The objective of the scale and the spacer in this type of calibration procedure is to guarantee precision and reproducibility of the measurements.

**a**



**b**

**Figure 3.** View angle isocount curves (**a** and **b**) for the detector-collimator assembly

*Calibration of the scintillation camera and uptake probe*

The calibration of the scintillation camera was performed with the neck-thyroid phantom described previously. The phantom was measured three times for 5 minutes by positioning the detection system at 42.8, 43.8, 44.8, 45.8 and 46.8 cm. The same procedure was applied to obtain the calibration factor of the uptake probe. In this case the distances from the phantom to the detector were 20, 25 and 30 cm.

*Determination of biokinetics parameters*

A mathematic simulation of data available in the literature (2,7) describing iodine retention curves (Figure 4) in the thyroid of patients with Graves' disease allowed to evaluate the most convenient time intervals to calculate activity values to estimate the effective half-life of iodine in the thyroid gland.

The declivity observed after the 14th hour suggests a conveniently time interval of two activity values.

In vivo measurements of the effective half-life of radioiodine in the thyroid were peformed in eight patients treated at IMEN during 2007 and 2008 for the validation of the proposed methodology using an appropriate time interval between 14 and 30 hours. The instrumentation was calibrated following the technique described previously.

The relationship between the dose absorbed by the organ and the necessary activity to be administered for the

therapy is calculated by using the Marinelli-Quimby (3) formula:

$$D/A = 0.043\ Uo\ Tef/V \quad (1)$$

Where D/A is the dose absorbed by unit of activity administered (Gy/MBq), Uo is the initial uptake extrapolated to time zero (%), Tef is the effective half-life (days) and V is the volume of the thyroid estimated for each patient (cm3).

The biokinetic parameter Tef is estimated by measuring the 131I count rate (with the scintilation camera or the uptake probe) in two consecutive uptake tests in a time interval (t). The initial and final activities (A0 and A) are calculated for the time interval selected using the specific calibration factor determined with the neck-thyroid phantom. Such values are applied in equation 3 to obtain the parameter λef, and subsequently in equation 2, to calculate the effective half-life of iodine in the thyroid gland.

$$Tef = \ln 2/\lambda ef \quad (2)$$

$$\lambda ef = \ln(Ao/A)/t \quad (3)$$

The initial uptake (U0) is calculated by extrapolation using the values of the uptake obtained previously. The organ volume can be estimated using a Thyrus Scintillation Camera (Figure 5) or using an ultra-sound device.

In order to facilitate the calculations, it was created a spreadsheet were data can be conveniently introduced and the related therapeutic dose is calculated to obtain the desired absorbed dose for each individual patient.

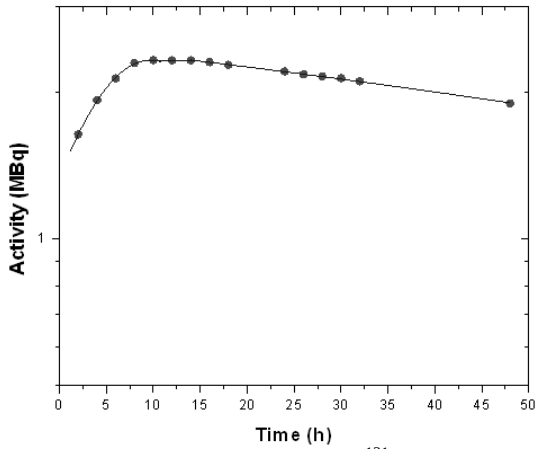



**Figure 4.** Activity (MBq) curves of $^{131}I$ in thyroid as a function of time, obtained through the mathematical simulation of real data available in the literature

**Figure 5.** Thyrus Scintillation Camera of the IMEN-Go

## RESULTS

### *View angle of the collimator-detector assembly*

The curves presented in Figure 6 permit to establish the view angle of the collimator-detector assembly of the equipment used in this experiment indicating the ideal distance between detector and source. The most suitable method to demonstrate the characteristics presented to each equipment consists on the use of the iso-counts or iso-outputs (Figure 6).

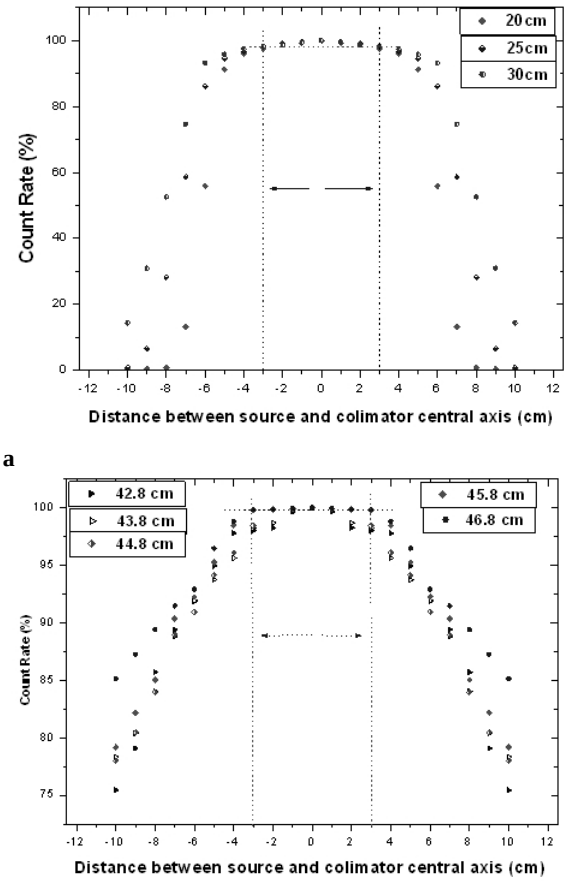



**Figure 6.** View angle isocount curves for the DIACAM Scintilation Camera (a) and uptake probe model SCT-13004 (b)

It can be verified in Figure 6 that the curves present a small flat region, where the detection system will present an equivalent count rate. Such flat region increases in diameter as the distance between source and detector window is increased.

For the iodine uptake test using the scintillation camera, the distance of 45.8 cm, between source and detector was the one which presented the best count rate output, since it presents a view angle compatible with the thyroid size of approximately 6 cm in patients with Graves' corresponding to a calibration

factor of (4.3 ± 0.2) cpm/kBq. It can also be observed in the isocount curves presented in Figure 6 that the best response with the SCT-13004 system was obtained at distances of 25 cm.

### *Calibration of the uptake probe SCT-13004*

A distance of 25 cm between the uptake probe and patient is the most usual in routine procedures in nuclear medicine centers. At such distance it was obtained a calibration factor of (39.3 ± 0.8) cpm/kBq for the uptake probe SCT-13004

Such distance is recommended since the patient is more confortably positioned and the sensitivity of the system is higher than the obtained at 30 cm. This geometry presents a field of vision compatible with the size of the gland.

### *Calibration of the uptake probe SCT-13002*

The determination of the Calibration Factor for the uptake probe SCT-13002 was made only at the distance of 25 cm between detector and phantom, considering that both present the same basic characteristics. The value obtained was (16.3 ± 0.26) cpm/kBq.

### *Biokinetic parameters of patients*

The patients listed by code in Table 1 were treated for hyperthyroidism of the Graves' disease at the IMEN-Go Nuclear Medicine Service in the months of November and December of 2007 and January and February of 2008.

The volume of the gland was estimated during the cintilografic examination with software installed in the Thyrus Scintillation Camera.

Values were compared with ultra-sound measurements requested by the endocrinologist responsible for conducting the patients to the clinic for cintilography diagnosis.

The uptake value at 2 hours and the count rates have been obtained with the uptake probe SCT-13002 for all patients studied. The effective half life of $^{131}$I in the thyroid was calculated through appropriate physical and mathematical equations, using the countings between two or more time intervals between 14 and 30 hours, as shown in Table I.

The values of effective half-life of the eigth patients studied (Table1) are in accordance to the value found in literature for patients with hyperthyroidism of the Graves' disease (4,9 ± 0.1) (2). The values of iodine uptake (%) in the thyroid in two hours and the volume (cm$^3$) found are also within the average values expected for this type of patient.

**Table I – Patients anthropometric data**

| Patient | Age | Sex | $^{131}$I (μCi) | $T_{1/2}$ (days) | $U_{2h}$ (%) | Volume (cm$^3$) |
|---|---|---|---|---|---|---|
| 1 | 32 | F | 52.0 | 4.1 | 32.0 | 36.2 |
| 2 | 43 | F | 59.1 | 5.5 | 28.1 | 41.3 |
| 3 | 29 | M | 50.6 | 4.0 | 36.9 | 31.4 |
| 4 | 61 | M | 55.8 | 5.8 | 32.3 | 35.9 |
| 5 | 46 | F | 60.3 | 4.8 | 30.8 | 37.6 |
| 6 | 41 | F | 50.0 | 3.8 | 28.7 | 40.3 |
| 7 | 41 | F | 51.0 | 5.1 | 31.5 | 36.8 |
| 8 | 45 | M | 100.0 | 4.7 | 33.0 | 35.1 |
| Average values | | | | 4.7 | 31.6 | 40.7 |

## DISCUSSION

The calibration protocol developed in this work have shown to be of easy execution and more reliable than usual procedures since it uses all biokinetic parameters necessary for dose optimization. It is also important to point out that both the scintillation camera and the uptake probe can be used for the determination of the activity of $^{131}$I in the thyroid of the patients.

This procedure can be applied for the individualized optimization of $^{131}$I dose to be administered to each patient. Furthermore, this protocol presents additional advantages of convenience and reduced cost, since the patient will have to show up at the hospital only two times: a first one to perform the uptake test and a second to receive the therapeutic dose.

### ACKNOWLEDGEMENT

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## REFERENCES

1. International Commission on Radiological Protetion (ICRP), GeneralPrinciples for the Radation Protection of Workers. ICRP Publication 75, Pergamon Press, Oxford, 1997.

2. Jönsson, H., Radiodine Therapy of Hyperthyroidism-Simplified patient-specific absorbed dose planning(PhD Thesis), Department of Radiation Physics, Malmö, 2003.

3. Marinelli, L.D., Quimby, E.H., Hine, G.J., Dosage determination with radioactive isotopes, pratical considerations in therapy and protection. *Am J Roentgenol*. 1948**, 2**:260-281.

4. Nyström, E., Berg, G., Jansson, S., Lindstedt, G., Törring, V.S, Warin, B., Thyreotoxikos hos vuxna, Klippan, Sweden, 1999.

5. Thompson, M.A., Radiation Safety Precautions in the Management of the Hospitalized 131I Therapy Patient, *Journal of Nuclear Medicine Technol*. 2001, **2**: 29.

6. United Nations Scientific Committee on the Effects of Atomic Radiation. UNSCEAR 2000 Report to the General Assembly, IAEA, Vienna, 2000.
7. Willians,RH. Textbook of Endocrinology. W.B.SaundersCompany. Philadelphia. London. Toronto. Fourth Edition, 1968.
8. Santos A. M. and Vieira J. W., 'Voxelization' of alderson-rando phantom for use in numerical dose measuring. *Cell. Mol. Biol*. 2009, **55**: 7-12.
9. Cardoso J. C. S., Berti e. A. R. and Xavier M., Whole-body measurements at IPEN, Brazil. *Cell. Mol. Biol*. 2009, **55**: 13-15.
10. Vieira J. W. and Lima F. R. A., a software to digital image processing to be used in the voxel phantom development. *Cell. Mol. Biol*. 2009, **55**: 16-22.
11. Holanda C. M. C. X., Silva-Júnior m. F., Alves R. C., Barbosa V. S. A., Silva R. P., Rocha L. G. and Medeiros A. C., The effect of the rochagan™ on radiolabeling with $^{99m}$Tc. *Cell. Mol. Biol*. 2009, **55**: 23-28.
12. Oliveira C. M., Dantas A. L. A. and Dantas B. M., A methodology to evaluate occupational internal exposure to fluorine-18. *Cell. Mol. Biol*. 2009, **55**: 29-33.