J of Nuclear Medicine Technology, first published online June 14, 2022 as doi:10.2967/jnmt.121.263502

Analysis of residence time, effective half-life and internal dosimetry prior to radioiodine therapy

Caio Vinicius de Oliveira[1]

Tatiane Sabriela Cagol Camozzato[1]

Patricia Fernanda Dorow[1]

Jéssica Pasqueta[1]

[1]**Federal Institute of Education, Science, and Technology of Santa Catarina – IFSC, Florianópolis, Santa Catarina, Brazil**

Corresponding author: Tatiane Sabriela Cagol Camozzato, PhD.

Federal Institute of Education, Science, and Technology of Santa Catarina

950, Mauro Ramos Avenue, Centro, Florianópolis, 88020-300, Santa Catarina, Brazil

Word Count:

ABSTRACT

Introduction: Radioiodine therapy has been widely used for ablation of remnant tissue after a surgical procedure for treatment of differentiated thyroid carcinoma (DTC). The use of internal dosimetry provides a new approach in choosing the activity to be administered considering the distribution and retention of ^{131}I individually per patient. This study aims to assess the accumulated activity, internal bone marrow dosimetry and effective half-life of cases undergoing treatment for DTC using clinical techniques of internal dosimetry. **Methods:** This is a quantitative retrospective study with analysis of diagnostic documents and images. The internal dosimetry method used consists of calculating the dose absorbed by the bone marrow per administered activity of ^{131}I. The calculation of the absorbed dose takes into account the accumulated activity obtained through measurements of whole-body images acquired at 4 intervals over a period of 5 days. **Results:** Dosimetry presented the values of absorbed dose by the bone marrow per administered activity, with a median of 0.117 mGy/MBq (min.: 0.043 - max.: 0.152). The median whole-body residence time is equal to 22.0 hours (min: 12.6 – max: 39.4). The median effective half-life equal to 15.6 hours (min.: 7.6 and max.: 28.2). **Conclusion:** Internal dosimetry provides information relevant to safe dose limits for application to DTC radioiodine therapy, especially in advanced cases of the disease where the use of greater activities may be necessary.

Keywords: Nuclear medicine; Dosimetry; Radiometry; Thyroid gland neoplasms; Iodine radioisotopes.

1. Introduction

Thyroid cancer is the most common of the head and neck region and affects three times as many women as men. The most indicated treatment for differentiated thyroid carcinomas (DTC) is partial or total thyroidectomy, complemented by radioactive iodine therapy (1). This treatment is indicated due to the fact that DTC and its metastases maintain the biological characteristics of a healthy thyroid, including the expression of sodium iodide transport protein, the main cell responsible for specific iodine uptake (2). Thus, radioiodine therapy is indicated for the ablation of remaining tissue that is not resected or incompletely surgically resected. For treatment of thyroid disease, the use of ^{131}I-NaI corresponds to the majority of radionuclide treatments currently (3).

In ablation of remnant thyroid tissue after surgery, the activity of ^{131}I-NaI usually prescribed is between 1 and 5 GBq in a single administration and may be higher in more advanced cases of the disease (2). These amounts of activity were selected empirically, with no consensus, varying between authors and nuclear medicine centers that perform this therapeutic procedure (4).

When considering fixed activities, it is not considered that the accumulated activity, hence the absorbed dose, can change considerably from patient to patient. The characteristics that alter iodine distribution are age, sex, renal function, injury extension, among others (5). The administered activity individualization is carried out through a therapeutic planning using dosimetric procedures. Internal dosimetry provides information on the distribution of iodine in patients' body, allowing the estimation of the activity to be used, preventing the biological effects of ionizing radiation (6).

This study aimed to assess the accumulated activity, internal bone marrow dosimetry and effective half-life of patients undergoing treatment for DTC using clinical internal dosimetry techniques.

2. Materials and methods

The study retrospectively assessed the pretherapeutic internal dosimetry of 5 cases diagnosed with DTC undergoing total or quasi-total thyroidectomy. Dosimetry

was used as a strategy for therapeutic planning of radioiodine therapy for ablation of remnant tissue and metastases. The study was conducted in a private nuclear medicine service located to the state in southern Brazil. The research was submitted to a Brazilian ethics committee for evaluation, receiving approval according to report number 3.988.505. Written informed consent was obtained from each patient prior to participation in the study. Three internal dosimetry techniques are performed for radioiodine therapy, one or all of which can be chosen depending on the indication. The techniques are: I. Bone marrow-based dosimetry; II Lung-based dosimetry; III. Organ-based dosimetry. All use diagnostic images to determine the accumulated activity.

The preparation of patients for dosimetry reproduces the preparation for therapy, introducing a diet with restriction of foods that contain iodine. Patients also suspended medications and preparations that contain iodine (up to 4 weeks). In 4 cases hormonal suspension was performed and in one the use of recombinant human TSH (rhTSH). This choice between the two methods is due to the need to reproduce the method foreseen for the therapy in the dosimetry. Some authors show that residence time can change between hormone withdrawal and the use of rhTSH (7,8).

I. Acquisition of whole-body images

The oral solution of ^{131}I-NaI with 74 MBq activity was administered. The activity was measured with the Capintec CRC-15R radioisotope dose calibrator (Capintec, Inc., Ramsey, NJ, USA).

Following ^{131}I-NaI administration, whole body conjugate images were acquired using a Siemens Symbia T2 SPECT/CT gamma camera. The equipment has two detectors with 5/8” NaI:Tl crystal, equipped with high-energy collimators that are required due to photon energy of ^{131}I (364 keV). The acquisition mode is whole-body scan and table speed 12 cm/min.

A total of 4 images were acquired at predefined time intervals of 2, 6, 48 and 120 hours after the tracer administration, ensuring that the patient did not empty his bladder for the first image. Thus, the whole-body counting of a 2-hour image is

considered to be 100% of the administered activity.

For image acquisition, the triple energy window (TEW) scatter correction method was used to correct the scatter due to ^{131}I gamma radiation energy and use of a high-energy collimator (9,10). With three energy windows simultaneously, the 15% main window was centered on the 364 keV (336.7-391.3 keV) photopeak and two of 6% immediately below and above the main window, with 314.9-336.7 keV and 391.3-413.1 keV, respectively.

II. Data processing

The acquired images were exported in DICOM format and assessed in ImageJ processing software (NIH, Bethesda, MD, USA). Each acquired image series, per interval, consists of 6 images: anterior and posterior, scattering in the inferior anterior and posterior window, and scattering in the superior anterior and posterior window. In each image, a region of interest (ROI) was drawn outlining the patient's whole body. For the ROI, the total counts are measured and the values are recorded as $C_{pp,ant}$, $C_{pp,post}$, $C_{ls,ant}$, $C_{ls,post}$, $C_{us,ant}$, and $C_{us,post}$, as shown in Figure 1.

The TEW scatter fraction determination is described in Equation 1, considering the measured counts for images with energy window shifted below (C_{ls}) and above (C_{us}) (9).

Equation 1

$$C_{scatt} = \left(\frac{C_{ls}}{w_{ls}} + \frac{C_{us}}{w_{us}}\right)\frac{W_{pp}}{2}$$

W_{pp} is width centered on photopeak window, W_{ls} is width of lower window and W_{up} is width of upper window.

The total count is a result of the image counts with the main energy window (C_{pp}) subtracted from the total scattering (C_{scatt}) (2). Both counts are the geometric

mean of the anterior and posterior projection.

Equation 2

$$C_{total} = \sqrt{C_{pp,ant} \,.\, C_{pp,post}} - \sqrt{C_{scatt,ant} . C_{scatt,post}}$$

III. Accumulated activity determination

Given the total counts of each image set, $C_{total,2h}$, $C_{total,6h}$, $C_{total,48h}$ and $C_{total,120h}$ values are plotted on a chart, thus the activity-time curve was determined. The curve adjustment results in an equation of the double exponential format shown in Equation 3.

Equation 3

$$Activity(t) = Ae^{-at} + Be^{-bt}$$

A, B, a and b are curve adjustment coefficients.

The accumulated activity (Ã) is the total number of disintegrations over a period. Its determination is carried out by activity integration by time. The calculation is expressed by Equation 4. In the activity chart by time, the accumulated activity is determined by the area below the curve.

Equation 4

$$\tilde{A} = \int_0^\infty A(t)\, dt = \int_0^\infty Ae^{-at} + Be^{-bt}\, dt$$

Alternatively, the concept of residence time (τ) can be used, and the accumulated activity per administered activity.

IV. Absorbed dose estimation

The absorbed dose of the bone marrow is calculated by a adptation of the European Association of Nuclear Medicine protocol (11), where sample of blood is

not used. In this line, the assessed compartment is blood, considering that activity concentration in blood and bone marrow is similar (12). For this symmetrical approach, two components are assessed: blood self-irradiation and blood irradiation by ^{131}I concentration in the whole body. The absorbed dose per unit of activity administered in the bone marrow is defined by the sum of these two components, described in Equation 5.

Equation 5

$$\frac{D_{blood}}{A_0} = S_{blood \leftarrow blood} \cdot \tau_{blood}(h) + S_{blood \leftarrow body} \cdot \tau_{body}(h)$$

D is the absorbed dose; A_0 is the administered activity; S is the mean absorbed dose per unit of accumulated activity; and τ is residence time. The $S_{blood \leftarrow blood}$ value, using beta radiation decay, is equal to 108 Gy.ml/GBq.h. The component for the dose coming from the whole body $S_{blood \leftarrow body}$ is equal to 0.0188 * $m^{-2/3}$ Gy/GBq.h, which is depends on the body mass (m) (11). S values replaced in Equation 5 are described in Equation 6.

Equation 6

$$\frac{D_{blood}}{A_0}\left(\frac{Gy}{GBq}\right) = 108\ \left(\frac{Gy}{GBq.h}\right) \cdot \tau_{ml\ blood}(h) + \frac{0{,}0188\ \left(\frac{Gy\ .kg}{GBq\ .h}\right)}{m^{2/3}\ (kg)} \cdot \tau_{body}(h)$$

The first component, blood←blood dose ($D_{blood \leftarrow blood}$), is traditionally measured by the blood sample density counts over time (11). Hänscheid et al., in 2009 (13), through the considerations initially made by Thomas et al. in 1993 (14), propose the determination of $D_{blood \leftarrow blood}$ through, exclusively, analysis of body residence time (τ_{body}), i.e., τ_{blood} is determined indirectly. In their studies, τ_{blood} represents 14 ± 3% of τ_{body}. Therefore, the proposed relationship can be expressed by Equation 7.

Equation 7

$$\tau_{ml\ blood}(h) = \frac{0.14}{BV\ (ml)} . \tau_{body}(h)$$

BV is the blood volume in ml. BV is expressed in Equation 8 for men and in Equation 9 for women. (15).

Equation 8

$$\mathrm{BV_{male}\ (ml)} = 31.9\,.\,\mathrm{h} + 26.3\,.\,\mathrm{m} - 2402$$

Equation 9

$$\mathrm{BV_{female}\ (ml)} = 56.9\,.\,\mathrm{h} + 14.1\,.\,\mathrm{m} - 6460$$

h is height in centimeters and m is the mass in kilograms.

Equation 6 and Equation 7 can be combined and is expressed in Equation 10, which was used to determine the total absorbed blood dose.

Equation 10

$$\frac{D_{blood}}{A_0}\left(\frac{Gy}{GBq}\right) = \left[\frac{15{,}12\ \left(\frac{Gy.ml}{GBq.h}\right)}{BV\ (ml)} + \frac{0{,}0188\ \left(\frac{Gy\,.kg}{GBq\,.h}\right)}{m^{2/3}\ (kg)}\right] . \tau_{body}(h)$$

Comparatively, D_{blood}/A_0 was calculated using OLINDA/EXM, version 1.0 (Vanderbilt University, Nashville, Tennessee, USA). In the software, ^{131}I was selected as radionuclide and the phantom chosen between a woman or an adult man. In biokinetic data entry, τ_{body} was used for the whole-body ("Tot Body/Rem Body") and τ_{blood}, for the bone marrow ("Red Mar"); however, as τ_{blood} was calculated to 1 ml. it is necessary to be multiplied by the organ mass. For the phantom used, the bone marrow mass is equal to 1,300 and 1,120g for females and males, respectively.

V. Maximum activity

V.I- Maximum dose-based activity in the bone marrow

The maximum activity is determined by Equation 11. The maximum dose of 2 Gy is used considering the bone marrow as the target organ. Bone marrow is the

critical organ when radionuclide therapy is used. In dosimetry studies, alterations in the hematopoietic system were observed in the subgroup that received doses higher than 2 Gy in the bone marrow (16).

Equation 11

$$A_{max}(GBq) = \frac{2\ (Gy)}{D\ (Gy/GBq)}$$

The maximum activity was also evaluated for the maximum dose of 1.3 Gy, considering the uncertainties in the measurement method without the use of a blood sample (13).

V.II- Maximum dose-based activity on the lung dose limit

In the case where there was diffuse pulmonary metastasis, the maximum activity to be administered was determined considering that the activity in the lungs after 48 hours is not higher than 2.96 GBq (17,18,19). An ROI is drawn by the lungs and count density is measured in the conjugated images and applied to the scattering correction as the whole-body ROI. Count density in the lungs after 48 hours ($C_{lung,48h}$) is compared to whole body density counts of 2-hour image ($C_{total,2h}$). Being the relationship expressed by Equation 12.

Equation 12

$$\mathrm{C_{lung,relative}} = \frac{\mathrm{C_{lung,48h}}}{\mathrm{C_{total,2h}}}$$

The activity maximum of ^{131}I-NaI to be administered preventing radiation effects is determined by Equation 13.

Equation 13

$$\mathrm{A_{max}(GBq)} = \frac{2.96\ (\mathrm{GBq})}{\mathrm{C_{lung,relative}}}$$

VI. Effective half-life

Activity concentration in the patient's organism is dependent on the physical and biological half-life of ^{131}I. The physical half-life is equal to 8.02 days, while the biological life is dependent on multiple variables related to individuals. Through accumulated activity analysis, the activity curve as a function of time was calculated for each patient in the study.

VII. Organ-based dosimetry

For criteria of comparison between the limit of bone marrow toxicity and the activity necessary for thyroid remnant treatment, one of the cases was selected to perform dosimetry based on the injury. The determination of the absorbed dose in the organ by administered activity was performed using the total volume dosimetry method. (20,21).

Acquisition with SPECT/CT protocol used in dosimetry was as follows: 60 projections (30 per detector), 6th step, 60 seconds, matrix 128x128 and TEW as described above. Iterative OSEM reconstruction protocol was used with 10 iterations and 5 subsets.

The partial volume effect correction was experimentally determined using the Image Quality IEC 61675-1 simulator. The simulator spheres with a volume of 28.7, 16.8, 8.6, 3.6, 2.1 and 1.1 ml were filled with a constant ^{131}I concentration, thus the recovery coefficient (RC) was projected. The RC correlates the difference between the actual and measured value of both activity and volume as described in Equation 14.

Equation 14

$$\mathrm{RC} = \frac{[\mathrm{A}]_{\mathrm{measured}}}{[\mathrm{A}]_{\mathrm{actual}}} = \frac{\mathrm{v_o}}{\mathrm{v_a}} = \frac{\mathrm{c_m}}{\mathrm{c_o}}$$

$[A]_{measured}$ is the measured activity concentration, $[A]_{actual}$ is the actual activity concentration, v_0 is the object's actual volume, v_a is the apparent volume, c_m is the measured count density, and c_0 is the actual count density. The apparent volume (v_a) was measured in the image with a volume of interest (VOI) positioned on the structure with a threshold of 5% and determined by Equation 15.

Equation 15

$$v_a = v_{vx} \frac{C}{c_{max}}$$

V_{vx} is the voxel volume, C is the count density measured in VOI and C_{max} is the highest intensity voxel count density.

The accumulated activity is determined by assessing ^{131}I concentration over time by means of SPECT images performed in sequence of scanning images used in bone marrow dosimetry. The activity for each image series is determined calculated by Equation 16.

Equation 16

$$A_i = \frac{C_{30}}{\varepsilon f_{30}}$$

A_i is the activity measured for each interval, C is the total count with the threshold of 30% of the image; f_{30} is the measurement correction factor in threshold 30% to 5%; and ε is the activity calibration factor per count (MBq/cnt) experimentally determined for imaging equipment with a volume with known activity. F_{30} is necessary for the use of 30% threshold for target area measurement, avoiding the interference of background radiation in the target volume.

Equation 17 describes the absorbed dose in the sphere that is determined by the product sphere residence time. S value is calculated for the actual sphere volume corrected by tissue density. $S = 0.110 \times v_{sphere}^{-0.974}$ Gy/MBq.h and $\rho = 1.05$ g/cm³. (20).

Equation 17

$$\frac{D}{A_0} = \tau_{sphere} \cdot S_{sphere \leftarrow sphere}(v_{sphere}) / \rho_{thyroid}$$

Equation 18

$$v_{sphere} = RC_{v_a} \cdot v_a$$

3. Results

Internal dosimetry had as indication cases that presented advanced conditions of the disease and cases in retreatment with suspicion or confirmation of metastases.

Table 1 lists sex, age, height, mass, body mass index (BMI), estimated body blood volume (BV) of the assessed group, total body residence time (τ_{body}) and blood residence time (τ_{blood}).

The residence time determined for the whole-body presented a median equal to 22.0.

Count density behavior over time is illustrated in Figure 1. Figure 2 illustrates the activity-time curve of the assessed group curve adjustment coefficients obtained through Fit Data application of the software OLINDA/EXM.

I. Bone marrow-based dosimetry

D_{blood}/A_0 was determined with τ_{body} and τ_{blood} using adapted from EANM protocol without blood sampling (Equation 10) and OLINDA/EXM. There was no significant difference between the methods, analyzing by paired t-test p= 0.564.

Figure 3 presents the comparison between the methods OLINDA/EXM and EANM protocol.

The dose in blood per administered activity (D_{blood}/A_0) individual and maximum activity (A_{max}) considering the red bone marrow toxicity in 2 Gy and 1.3 Gy are expressed in Table 2.

Table 3 presents the data of time required for decay of half and a quarter of the

initial activity, both effective and biological. The median time of the first effective half-life was equal to 15.6 hours (min: 7.6 - max: 28.2 hours) and the second half-life was equal to 12.8 hours (min: 5.5 – max: 24.9 hours). The preparation of the one used in case P3 was performed with the use of rhTSH.

II. Lung dosimetry

From the group assessed, one case presented pulmonary metastasis. $C_{lung,relative}$ was equal to 0.0246, i.e., after 48 hours 2.46% of iodine concentration is retained in the lung compared to the whole-body measurement measured in the 2 hour image. Therefore, the maximum calculated activity is equal to 120.5 GBq. Maximum activity based on dose limits in bone marrow and lung are compared, with the lowest prevailing. The dosimetry of this case considering the dose limit equal to 2 Gy in the bone marrow determines the maximum activity of 27.4 GBq. Thus, the limit for the bone marrow is prioritized.

III. Organ-based dosimetry

The activity ratio measured by the actual activity designated as RC is expressed in Figure .

The dosimetry of one case of the studied group was assessed. The injury was characterized as remaining tissue in the thyroid bed, illustrated in Figure 5a.

The volume was estimated at 1.9 cm^3. Factor f_{30} was determined at 0.59 for a point source illustrated in Figure 5a and the equipment ε calibration factor was calculated at 15,604 cnt/MBq. The residence time was calculated at 0.995 hours, activity-time curve expressed in Figure 5b.

Through residence time, volume and S value, the dose absorbed by the organ per unit of ^{131}I administered was equal to 0.0584 Gy/MBq, calculated by Equation 17.

Considering the dose of 300 Gy, necessary for ablation of the remaining thyroid tissue, proposed by Maxon et al. (1992) (22), the administered activity required to reach this dose threshold would be equal to 4.89 GBq. The maximum activity of ^{131}I for bone marrow toxicity prevention in this case was calculated at 11.11 GBq (P5 - Table 3).

The determination of small volumes is limited by the spatial resolution of the system. The spatial resolution at full width at half maximum (FWHM) was equal to 13.6 mm obtained by axial reconstruction of a point source of ^{131}I.

Figure 7 illustrates the result obtained from the acquisition of a cylinder with a volume of 22 ml and 0.74 MBq of ^{131}I with the described protocol. The apparent volume (v_a) was calculated at 23.47 ml, with a difference of 6.3% of the actual volume (v_o). In Figure 6, the red VOI represents the actual volume, the green and yellow VOI the apparent volume measured with threshold of 5% and 30% respectively.

4. Discussion

Preparation for dosimetry should be the same as that normally used in therapy to ensure reproducibility of ^{131}I-NaI distribution (11). Imaging exams using iodine as a contrast agent cannot have been performed within a period of 6 to 8 weeks (23). To perform dosimetry, the patient's metabolic status must be the same as that of the therapy, as it affects the renal function and, thus the clearance rate and residence time (19,24).

The activity administered for dosimetry represents a small amount compared to what will be used in therapy. However, this amount cannot be large enough to alter the tumor's ability to capture and retain iodine called stunning. Studies show that even small activities can induce stunning (25). It should be limited to 4 Gy in the remaining thyroid tissue to avoid this effect. The ^{131}I activity for the recommended diagnostic imaging is 10-20 MBq (19,26). The activity used in this study was 74 MBq. Activity reduction can be performed to prevent stunning; however, it is necessary to reduce the image scanning speed so that the counting rate is not reduced, making

quantification impossible.

When acquiring the 4 series of whole-body images, it is necessary to guarantee the same geometry as the exam. The table elevation and the detector distance from the patient must be the same. Patient positioning should be as close as possible between images and that the patient's whole body is in the detector's field of view (11). The equipment's auto-contour systems must be deactivated. The immobilization of the arms close to the body attached with the auxiliary straps was important because the total imaging time is relatively long.

Intervals between acquisitions must be consistent with the physical and biological half-life of iodine. The image with an interval of 2 hours is considered as the maximum activity concentration (100%) which is used as a reference for other measurements (6). For this consideration to be satisfactory, it is necessary that the patient does not urinate after iodine administration until the end of the acquisition of this image. From the samples assessed, a significant amount of radioactive material is eliminated in the first hours. The activity concentration after a 6-hour interval from administration of the sample in this study had a mean of 78±15%.

The 48-hour image showed that the tissue avid for Iodine-131 still maintains considerable material retention while the background (other tissues) has almost completely eliminated the iodine. This provides a contrast between these tissues, providing a better visualization of the structures. Acquisition at this interval allows the assessment of pulmonary metastasis. At 120 hours, the delayed image contributes to the adjustment of the accumulated activity curve. This image commonly shows the accumulation of less than 2% of the initial activity. The interval can be adopted with 96 hours; however, if concentration is higher than 5%, an image with 144 hours must be performed (11).

In cases where there is diffuse pulmonary metastasis, the absorbed dose in the lung should be assessed. Pulmonary dosimetry plays an important role in preventing pulmonary fibrosis (19). Lung dosimetry studies define that after 48 hours ^{131}I activity concentration in the lung should be less than 2.96 GBq. Activities higher than this value can provide doses that exceed the limits for radiotoxicity effects in the lung (17,18,19). Thus, the image previously acquired within 48 hours is used to

calculate the maximum activity and maintain the dose limits in the lungs.

As blood residence time is estimated through the whole-body's residence time, where blood samples are not analyzed, it is necessary to consider the uncertainties in the calculations. Hanscheid *et al*., in 2009 (13), propose a conservative approach in estimating maximum activity. At work, τ_{blood} represents 14 ± 3% of the τ_{body} (min: 8 and max: 24%). Considering Equation 16 and Equation 19 in cases that present τ_{blood} greater than 14% of τ_{body}, the values of absorbed dose per activity can change considerably between the estimated and the real. Therefore, the author proposes the limit of absorbed dose in the marrow to be equal to 1.3 Gy instead of 2 Gy. In this way, even in cases of extreme variation between the real and measured values, the radiotoxicity limit in the hematopoietic system will not be exceeded. Assessing the data published by Willegaignon et al. (27,28) τ_{blood} is 10.3 ± 4% of τ_{body} (range: 2 to 18 %). In this work, if τ_{blood} had not been measured directly, the adoption of the limit as 1.3 Gy would have fulfilled the role of preventing the dose limit extrapolation.

The half-life concept is applied to the decay portrayed by an exponential function with a single term. Therefore, the time required for the decay of half of the initial activity will not necessarily be the same as the second half-life, i.e., a quarter of the initial activity. Compared with recent studies, there is an agreement between the results. Barros, in 2019, measuring the dose rate of 98 hospitalized patients after the therapeutic dose of iodine for DTC therapy, obtained as a result the mean effective half-life of 10.7 ± 4.5 hours. Considering only the subgroup that underwent hormone suspension preparation, i.e., not using rhTSH, the mean was 12.5 ± 5 hours. The author also reports that the subgroup of patients over the age of 65 years had a mean effective half-life of 13.3 ± 4.7 hours, approximately 30% higher than those of middle-aged 10.3 ± 4.6 hours.

The influence of spatial resolution on image quantification error is described as the partial volume effect. As the size of a structure decreases, the measured concentration is reduced and the apparent volume increased relative to the actual value (29). Organ-based dosimetry estimates the dose absorbed by the tumor by providing a targeting of the amount of ^{131}I activity to reach therapeutic levels. Organ dosimetry is dependent on tissue mass (volume). For DTC this process becomes

even more challenging because it is remnant tissue and, in some cases, micro metastases (20).

Cervical uptake exams and whole-body research prior to therapy with low doses of radioiodine are provided for in Clinical Protocol and Therapeutic Guidelines for Differentiated Thyroid Carcinoma, approved by the Ministry of Health (30). The objectives of these tests were to estimate the volume of remaining tissue or metastatic disease and iodine avidity of these tissues. However, the ordinance concludes that patients considered to be at low and intermediate risk, due to the low potential for distant metastases, may not need to undergo PCI. This measure also aims to prevent the induction of a stunning effect, which may harm the therapy.

5. Conclusion

Internal dosimetry takes into account the physiological characteristics in an individualized way, patient by patient, providing important data regarding ^{131}I absorption and retention. Through the dosimetric techniques employed, it was possible to determine the maximum activity of ^{131}I to be administered, considering the limits of radiotoxicity in the bone marrow and in the lungs described in the literature. In advanced cases of DTC, in which patients are classified as being at high risk, the Organ-based approach to dosimetry associated with toxicity in healthy tissues enables assessment of the administration of larger activities, in order to eliminate the disease with a single dose. The methodology involved in each dosimetric technique was described in detail, aiming at therapy planning reproduction and dissemination, considering the individual metabolic response.

6. DISCLOSURE

No potential conflicts of interest relevant to this article exist.

7. KEY POINTS

Highlight to assess the accumulated activity, internal bone marrow dosimetry and effective half-life of cases undergoing treatment for of differentiated thyroid carcinoma (DTC).

Dosimetry presented the values of absorbed dose per administered activity, with a mean of 0.101 mGy/MBq. The mean whole-body residence time is equal to 23.1 hours e effective half-life equal to 16.0 hours.

Internal dosimetry provides information relevant to safe dose limits for application to DTC radioiodine therapy, especially in advanced cases of the disease where the use of greater activities may be necessary.

8. References

1. Instituto Nacional de Câncer (INCA). **Câncer de tireoide**. 2022. Disponível em: https://www.inca.gov.br/tipos-de-cancer/cancer-de-tireoide. Acesso em: 02 abril. 2019.

2. Luster M, et al. **Guidelines for radioiodine therapy of differentiated thyroid cancer.** SI: European Journal of Nuclear Medicine and Molecular Imaging; 2008 Ago. V. 35(10), 1941-1959 p.

3. Sapienza MT, et al. **Radionuclide therapy: current status and prospects for internal dosimetry in individualized therapeutic planning.** S.I: Clinics; 2019. V. 74(8), 1-8 p.

4. Hacksaw A, et al. **^{131}I Activity for Remnant Ablation in Patients with Differentiated Thyroid Cancer: a systematic review**. S.I: The Journal Of Clinical Endocrinology & Metabolism; 2007 Jan. V. 92(1), 28-38 p.

5. Tuttle RM, et al. **Empiric Radioactive Iodine Dosing Regimens Frequently Exceed Maximum Tolerated Activity Levels in Elderly Patients with Thyroid Cancer**. SI: Journal of Nuclear Medicine; 2006 Jul. V. 47(10), 1587-1591 p.

6. Smilys B. **Radioiodoterapia do câncer diferenciado de tireoide com dosimetria personalizada simplificada.** S.I: Dissertação (Mestrado) - Curso de Ciências na área de Oncologia, Universidade Estadual de Campinas; 2018. 84 f.

7. Luster M, et al. **Comparison of radioiodine biokinetics following the administration of recombinant human thyroid stimulating hormone and after thyroid hormone withdrawal in thyroid carcinoma.** S.I: European Journal Of Nuclear Medicine And Molecular Imaging; 2003 Out. V. 30(10), 1371-1377 p.

8. Plyku D, et al. **Recombinant Human Thyroid-Stimulating Hormone Versus Thyroid Hormone Withdrawal in 124 I PET/CT–Based Dosimetry for ^{131}I Therapy of Metastatic Differentiated Thyroid Cancer.** S.I: Journal Of Nuclear Medicine**,** 2017 Jan. V. 58(7), 1146-1154 p.

9. Dewaraja YK, et al. **Quantitative ^{131}I SPECT with Triple Energy Window Compton Scatter Correction**. S.I: IEEE Transactions on Nuclear Science, 1998 Dez. V. 45(6).

10. Dewaraja YK, et al. **MIRD Pamphlet No. 24: Guidelines for Quantitative ^{131}I SPECT in Dosimetry Applications.** S.I: Journal of Nuclear Medicine, 2013 Out. V. 54(12), 2182-2188 p.

11. Lassmann M, et al. **EANM Dosimetry Committee series on standard operational procedures for pre-therapeutic dosimetry I: blood and bone marrow dosimetry in differentiated thyroid cancer therapy.** S.I: European Journal of Nuclear Medicine and Molecular Imaging, 2008 Mai. V. 35(14), 1405-1412 p.

12. Sgouros G. **Blood and bone marrow dosimetry in radioiodine therapy of thyroid cancer.** S.I: Journal of Nuclear Medicine, 2005. V. 46, 889-900 p.

13. Hänscheld H, et al. **Blood dosimetry from a single measurement of the whole body radioiodine retention in patients with differentiated thyroid carcinoma.** S.I: Endocrine-Related Cancer, 2009. V.16, 1283-1289 p.

14. Thomas SR, et al. **Predictive estimate of blood dose from external counting data preceding radioiodine therapy for thyroid cancer.** S.I: Nuclear Medicine and Biology, 1993. V.20, 157-162 p.

15. Retzlaff JA, et al. **Erythrocyte volume, plasma volume and lean body mass in adult men and women.** S.I: Blood, 1969. V. 33, 649-667 p.

16. Benua RS, et al. **The relation of radioiodine dosimetry to results and complications in the treatment of metastatic thyroid cancer.** S.I: American Journal of Roentgenology**,** 1962 jun. N. 87, 171-182 p.

17. Song H, et al. **Lung dosimetry for radioiodine treatment planning in the case of diffuse lung metastases.** S.I: Journal of nuclear medicine, 2006 Dez. V. 47, 1985-1994 p.

18. Sgouros G, et al. **Lung toxicity in radioiodine therapy of thyroid carcinoma: development of a dose-rate method and dosimetric implications of the 80-mCi rule.** S.I: Journal of nuclear medicine, 2006 Dez. V. 47, 1977-1984 p.

19. Luster M, et al. **Radioiodine Therapy.** Seminars In Nuclear Medicine, 2017 Març. V. 47(2), 126-134 p.

20. Mínguez P, et al. **Whole-remnant and maximum-voxel SPECT/CT dosimetry in ^{131}I-NaI treatments of differentiated thyroid cancer. S.I: Medical Physics**, 2016 Set. V. 43(10), 5279-5287 p.

21. Mínguez P, et al. **Analysis of activity uptake, effective half-life and time-integrated activity for low- and high-risk papillary thyroid cancer patients treated with 1.11 GBq and 3.7 GBq of ^{131}I-NaI respectively.** S.I: Physica Medica, 2019 Set. V.65, 143-149 p.

22. Maxon HR, et al. **Radioiodine-131 therapy for well-differentiated thyroid cancer--a quantitative radiation dosimetric approach: outcome and validation in 85 patients.** S.I: J Nucl Med, 1992. V. 33(6), 1132-1136 p.

23. Silberstein EB, et al. **The SNMMI Practice Guideline for Therapy of Thyroid Disease with ^{131}I 3.0.** S.I: Journal of Nuclear Medicine, 2012 Jul. V. 53(10), 1633-1651 p.

24. Bhat M, et al. **Dosing of radioactive iodine in end-stage renal disease patient with thyroid cancer.** S.I: Endocrinology, Diabetes & Metabolism Case Reports, 2017 Nov. V. 2017.

25. Lassmann M, et al. **Impact of ^{131}I diagnostic activities on the biokinetics of thyroid remnants.** S.I: Journal Of Nuclear Medicine, 2004 Abr. V. 4(45), 619-625 p.

26. Medvedec M. **Thyroid stunning in vivo and in vitro.** S.I: Nuclear Medicine Communications**,** 2005 Ago. V. 26(8), 731-735 p.

27. Willegaignon J, et al. **Estimating ^{131}I biokinetics and radiation doses to the red marrow and whole body in thyroid cancer patients: probe detection versus image quantification.** São Paulo: Radiologia Brasileira, 2016 Jun. V. 49(3), 150-157 p.

28. Willegaignon J, et al. **Prediction of iodine-131 biokinetics and radiation doses from therapy on the basis of tracer studies.** S.I: Nuclear Medicine Communications, 2016 Mai. V. 37(5), 472-479 p.

29. Krempser AR, et al. **Avaliação do efeito de volume parcial na quantificação de atividade em imagens de PET/CT.** S.I: Revista Brasileira de Física Médica, 2012 Nov. V.6(2), 35-40 p.

30. Brasil. Ministério da Saúde. Portaria nº 7, de 3 de janeiro de 2014. **Aprova o Protocolo Clínico e Diretrizes Terapêutica do Carcinoma Diferenciado da Tireoide**. SAS/MS nº 7 - Jan. 2014.

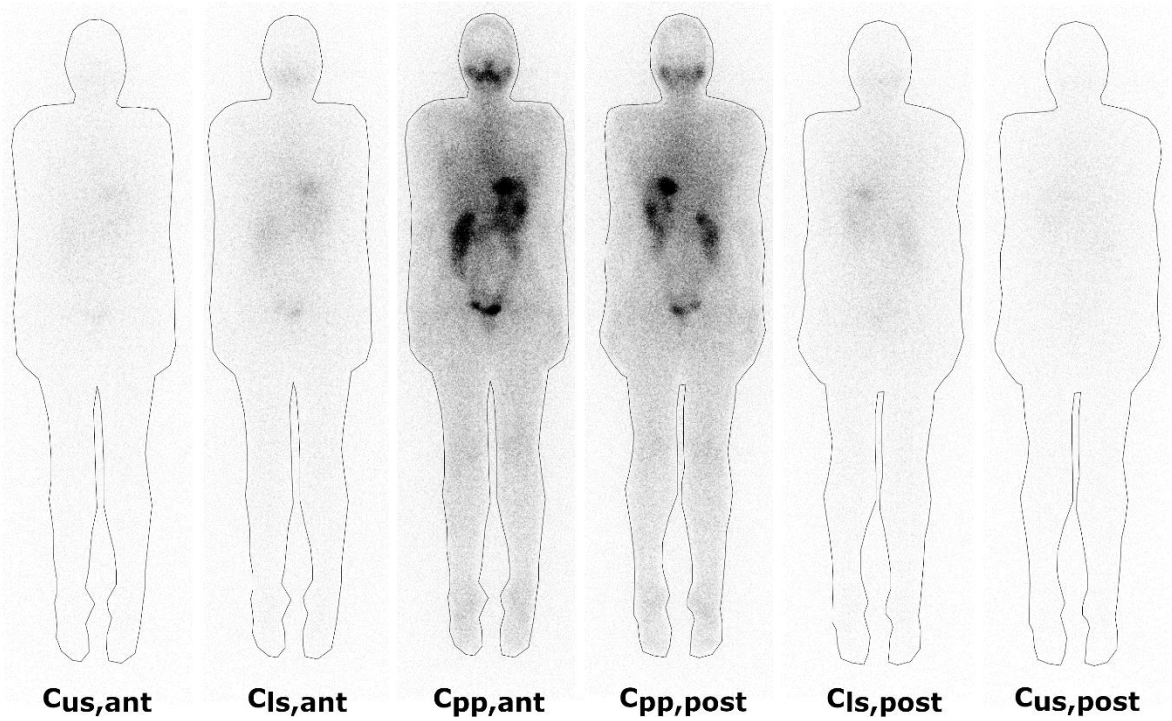

Figure 1- Measurement of the regions of interest (ROI) of the set of anterior and posterior conjugate images and their respective images for scattered radiation correction

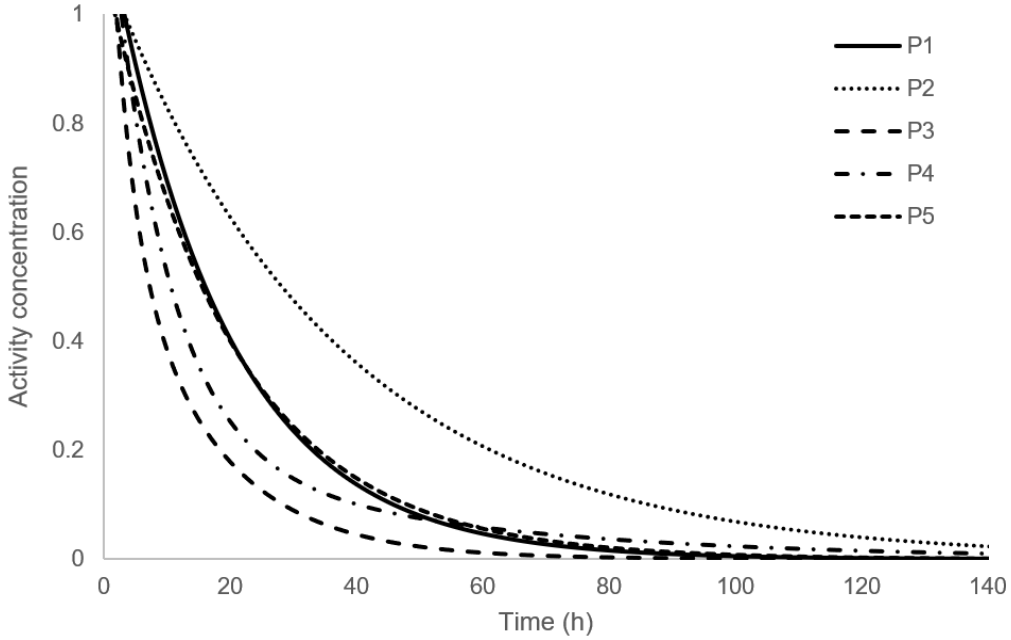

Figure 2 – Activity-time fitted curve of the assessed group

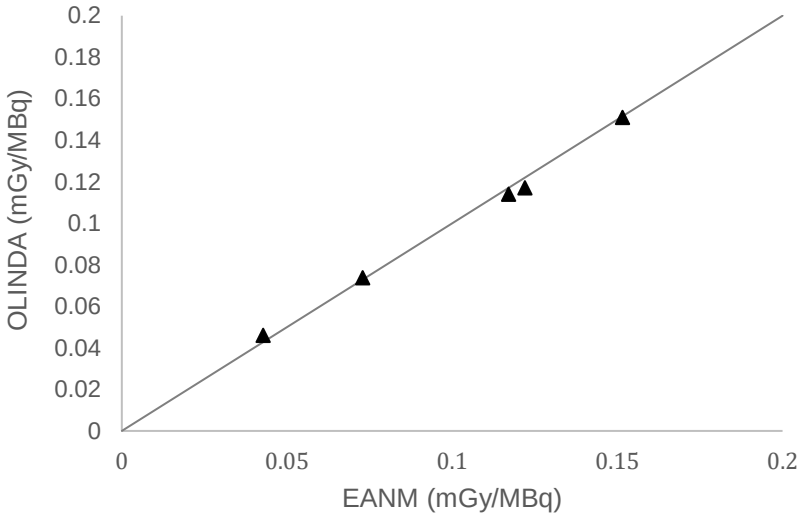

Figure 3 - Comparison of the absorbed dose by activity calculated by OLINDA/EXM and MIRD

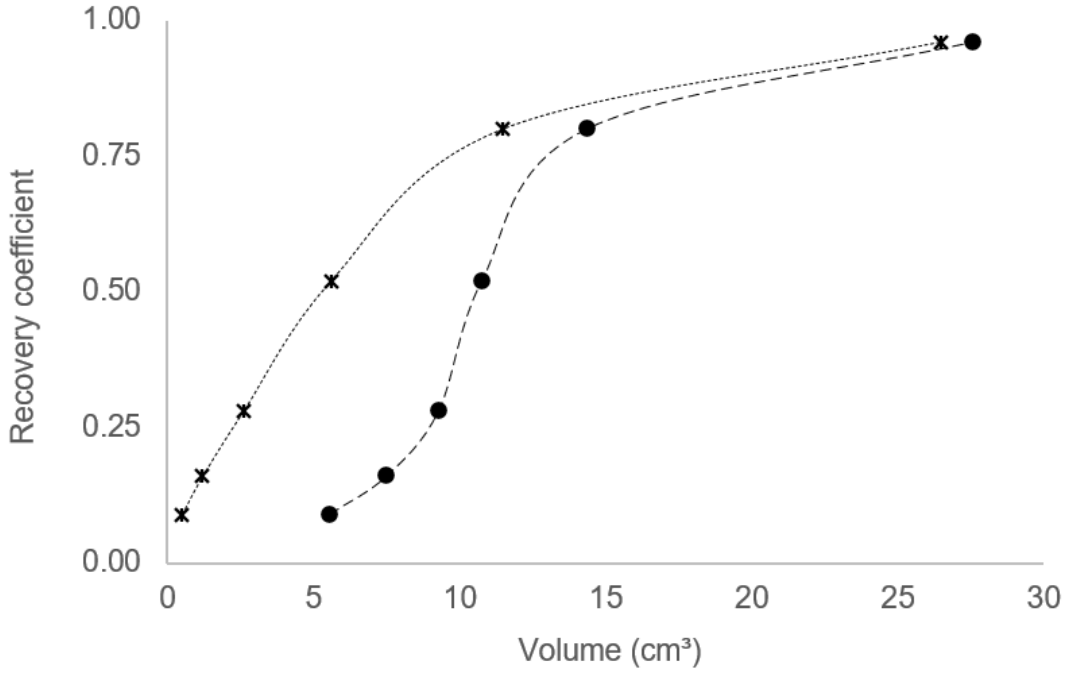

Figure 4 – Recovery Coefficient of definitive experimentally. Circle symbols indicate the apparent volumes and x symbols the true sphere volume.

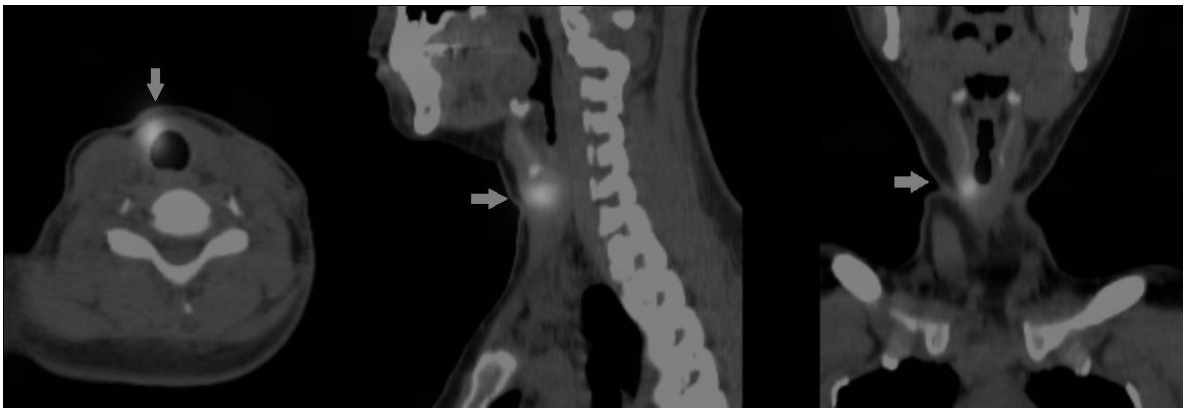

Figure 5a - Axial, sagittal and coronal SPECT/CT reconstruction of the remaining thyroid tissue

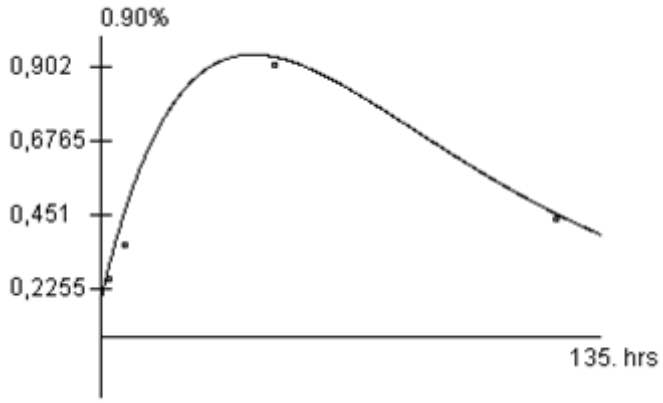

Figure 5b - Activity concentration function in organ target

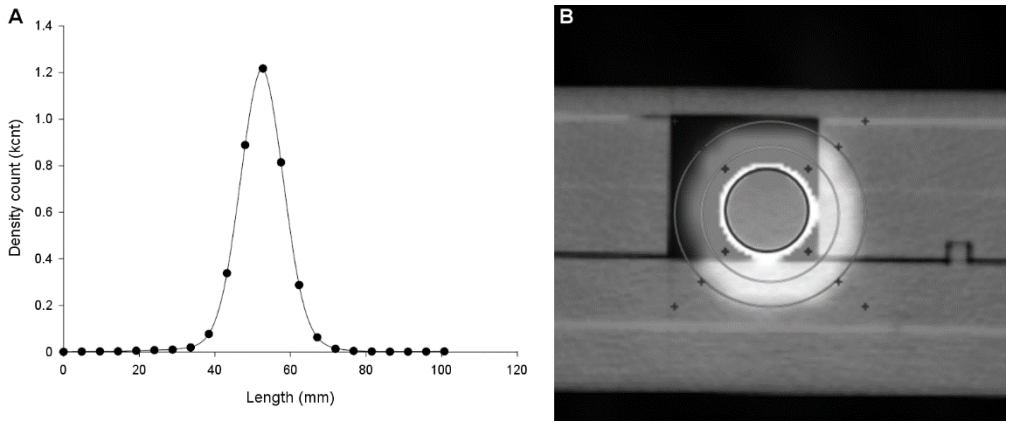

Figure 6 - Tomographic image point scattering function and apparent volume compared to actual volume

Table 1 - List of variables of internal dosimetry cases

ID	Sex	Age [years]	Height [cm]	Weight [Kg]	BMI	BV [ml]	τ_{body}	$\tau_{blood\ -ml}$
P1	F	50	161	59	22.8	3532.8	22.1	0.00088
P2	M	71	182	76	22.9	5402.6	39.4	0.00102
P3	M	36	187	95	27.2	6061.8	12.6	0.00029
P4	M	28	178	82	25.9	5432.8	19.3	0.00050
P5	F	29	165	57	20.9	3732.2	22.0	0.00083

Table 2 - Maximum activity determined for the assessed case group.

ID	D_{blood}/A_0 (mGy/MBq)	A_{max} - Limit 2 Gy (GBq)	A_{max} - Limit 1.3 Gy (GBq)
P1	0.122	16.39	10.66
P2	0.152	13.20	8.58
P3	0.043	46.72	30.37
P4	0.073	27.42	17.82
P5	0.117	17.09	11.11

Table 3 - Effective and biological time calculated for half and a quarter of the initial activity of ^{131}I

ID	effective (h)		biological (h)	
	T1/2	T1/4	T1/2	T1/4
P1	16.1	28.9	17.6	31.3
P2	28.2	53.1	33	61.6
P3	7.6	13.1	7.9	13.6
P4	12.5	23.2	13.3	24.7
P5	15.6	29.5	16.9	32

Graphical Abstract