Dose-response Relationship in Differentiated Thyroid Cancer Patients Undergoing Radioiodine Treatment Assessed by Means of $^{124}$I PET/CT

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Dose-response-analysis in DTC using $^{124}$I
Abstract

The dose-response relationship in a fixed-activity approach generally applied in the treatment of differentiated thyroid cancer is assessed using $^{124}$I PET/CT.

Methods: Pre-therapeutic $^{124}$I PET/CT images of 47 patients scheduled for radioiodine therapy were retrospectively analyzed. $^{124}$I PET/CT images were acquired 24 and 96 hours after oral administration of approximately 28 MBq $^{124}$I-sodium iodide. Lesions were identified as thyroid remnants or metastases (lymph node, lung, bone). After applying a neoteric segmentation technique allowing accurate volume estimation down to the $^{124}$I PET spatial resolution of 0.15 mL, lesions were divided in a known-volume group and a small-volume group. For the known-volume group, average lesion absorbed dose (AD) values were calculated, whereas for the small-volume group a minimum lesion AD was estimated. Lesion response was determined based on $^{124}$I PET/CT and $^{131}$I single photon emission computed tomography/(computed tomography) (SPECT/CT) follow-up images. A lesion not detectable on any of the follow-up images was considered a completely responding lesion. Differences in lesion AD estimations between completely and incompletely responding lesions were evaluated by Mann-Whitney $U$ test. Moreover, receiver-operator-characteristics (ROC) curves were used to test the performance of pre-therapeutic $^{124}$I PET/CT lesion AD for prediction of complete lesion response.

Results: In the approach of fixed radioiodine activity (3.0 ± 1.0 GBq), 89% of thyroid remnants and 69% of metastases responded completely. Except for the small-volume groups, the lesion AD of completely responding lesions was significantly higher compared to that of incompletely responding lesions. Using ROC curve analysis, it was shown that for the known-volume group, pre-therapeutic $^{124}$I PET/CT
lesion dosimetry can be used as a prognostic tool to predict lesion-based $^{131}$I therapy response with an area under the curve of 0.76 for remnants and 0.97 for metastases. The corresponding lesion AD threshold value maximizing correct complete response prediction was 90 Gy for remnants and 40 Gy for metastases.

**Conclusion:** In a fixed-activity approach, a statistically significant dose-response relationship for both thyroid remnants and metastases using pre-therapeutic $^{124}$I PET/CT lesion dosimetry was found. The findings may be useful in patient management.

**Key words:** radioiodine therapy; thyroid carcinoma; lesion-response relationship; $^{124}$I; dosimetry
INTRODUCTION

Radioiodine therapy is the standard adjuvant therapy, after total thyroidectomy in patients with differentiated thyroid cancer (DTC) (1,2). The purpose of radioiodine therapy is twofold: ablation of thyroid remnants and treatment of radioiodine avid metastases.

The generally accepted threshold for lesion absorbed dose (AD) to achieve high therapy response is 85 Gy for metastases and 300 Gy for thyroid remnants, respectively (3,4). To predict therapy response, a reliable AD estimation requires, inter alia, accurate lesion volume determination, which is hampered by the often small lesion volumes with respect to the spatial resolution of 131I scintigraphy and lesion segmentation difficulties encountered in ultrasonography (US), computed tomography (CT) or other imaging modalities (1,5). As a result, personalized radioiodine therapy based on lesion dosimetry is not globally adopted. In general, a fixed 131I activity is administered based on disease characteristics and patient age with the risk of under- or overtreatment (6).

Several groups have concluded that quantitation of 124I positron emission tomography (PET) images is feasible (7-11). Compared to 131I single photon emission tomography (SPECT), 124I PET imaging offers a higher image spatial resolution, increased count rate sensitivity, and higher quantitative capacity. This has resulted in the application of pre-therapeutic 124I PET(CT)-based lesion dosimetry (12-17).

To date, the only study assessing the dose-response relationship using 124I PET/CT in a larger number of patients was recently published by Jentzen et al. (17). Pre-therapeutic 124I PET/CT lesion AD estimation and toxicity assessment were taken into consideration in patient management, allowing the administration of an
optimized therapeutic activity (8.0 ± 4.3 GBq). However, using a fixed activity approach in the absence of toxicity assessment generally results in lower administered 131I activity than the optimized therapeutic activity. Consequently, it is expected that the lesion AD in the fixed-activity approach are lower than the values published by Jentzen et al. (17), possibly resulting in more lesions that receive a lesion AD below the established threshold values.

Therefore, the aim of this study was to assess the dose-response-relationship in an approach of a fixed therapeutic 131I activity in a large group of patients using pre-therapeutic 124I PET/CT lesion dosimetry. Moreover, a new segmentation technique allowing volume estimation down to the PET spatial resolution of 124I was used (18). In addition, we assessed the feasibility of performing pre-therapeutic 124I PET/CT lesion dosimetry as a prognostic tool to predict therapy response in DTC patients in a fixed-activity approach.

MATERIALS AND METHODS

Patient Population

This study was approved by the institutional review board and the requirement to obtain informed consent was waived. In the Maastricht University Medical Centre, pre-therapeutic imaging with 124I has been introduced as a clinical standard in 2007. A retrospective analysis of DTC patients who underwent 124I PET/CT examinations, followed by 131I therapy, between January 2007 and December 2012 was performed. All patients had histologically confirmed papillary or follicular DTC and underwent total thyroidectomy prior to 124I PET/CT examinations. None of the
patients received additional treatment such as surgery or external-beam radiation therapy. Patients were included if (post-therapy) follow-up imaging with, either (pre-therapeutic) $^{124}$I PET/CT or $^{131}$I planar whole body scintigraphy ($^{131}$I WBS) and $^{131}$I SPECT/CT as part the radioiodine therapy, was available. For patients who underwent multiple radioiodine therapies preceded by $^{124}$I PET/CT examinations, only the data of the first radioiodine therapy were included. Patient TNM status was characterized in 4 stages according to the AJCC Cancer Staging Atlas (19). Moreover, the maximum thyroglobulin (Tg) value recorded within one year after $^{131}$I ablation therapy was reported. Until March 2011, Tg was measured using a time-resolved fluoroimmunoassay (Autodelfia, PerkinElmer) with a limit of detection (LOD) of 0.5 pmol/L. From March 2011, Tg was measured using a time-resolved amplified cryptate emission assay (Brahms GmbH, Thermo Fisher ) with a LOD of 0.25 pmol/L. Abnormal (positive) results were recorded if Tg > 1.5 pmol/L. In case of incomplete recovery of the antibody used in the assay, additional testing was done for specific anti-thyroglobulin antibodies.

Patient preparation was done by thyroid hormone withdrawal or recombinant human thyroid-stimulating hormone (rhTSH) and similar for the pre- and follow-up $^{124}$I PET/CT examinations. In case of thyroid hormone withdrawal, patients were withdrawn from thyroxine medication for 4-6 weeks, or remained without medication post-operatively. In cases of rhTSH preparation, 0.9 mg thyrotropin alfa or rhTSH (Thyrogen®, Genzyme Ltd., Suffolk, U.K.) was injected intramuscularly on day 1 and 2, afterwards $^{124}$I was orally administered on day 4, and $^{124}$I PET/CT performed on day 5 (24 hours after $^{124}$I administration) and day 8 (96 hours after $^{124}$I administration). For radioiodine therapy, a fixed-activity protocol was performed according to the Dutch
guidelines, employing 2.8 GBq (75 mCi) for simple thyroid remnant ablation and 5.6 GBq (150 mCi) for regional nodal disease or distant metastases.

**Image Acquisition and Reconstruction**

Acquisition of $^{124}$I PET/CT was performed in 3D-mode using a PET camera equipped with time-of-flight (Gemini TF PET/64-slice CT scanner, Philips, Best, The Netherlands) at 24 and 96 hours after oral administration of $28.0 \pm 3.3$ MBq $^{124}$I-sodium iodide. $^{124}$I radioactivity measurements were performed using a 3 ml syringe filled with approximately 1 ml of $^{124}$I solution that was placed in a validated dose calibrator (Isomed 2000, Nuklear Medizin Technik GmbH, Dresden, Germany). $^{124}$I PET scans were acquired from head, neck and thorax comprising 4-5 bed positions of 4 minutes each. In selected cases imaging was continued until the pelvis. A low-dose spiral CT scan from head to thigh was performed (tube voltage 120 kVp, effective tube current 30 mAs, slice thickness 4 mm), followed by the PET acquisition and supplementary high-dose CT without contrast (neck: 120 keV, 150 mAs, slice thickness 2 mm, increment 1.8; thorax: 120 keV, 175 mAs, slice thickness 5 mm, increment 4.0). All CT images were reconstructed using the filtered backprojection algorithm. PET images were reconstructed using the line of response based, time-of-flight (Blob OS-TF) reconstruction algorithm provided by the manufacturer with a voxel size of 4x4x4 mm$^3$. In addition, for accurate lesion volume assessment and quantification purposes, PET images were retrospectively reconstructed with a voxel size of 2x2x2 mm$^3$. For all PET images, standard corrections for attenuation-, scatter-, decay-, and dead-time were performed.
The $^{131}$I WBS was made as a total-body scan from top till toe using a table speed of 10 cm/min. SPECT/CT was acquired immediately after WBS. Acquisition of $^{131}$I SPECT/CT was performed using a standard SPECT/CT camera, (Precedence SPECT/6-slice CT scanner, Philips, Best, The Netherlands) equipped with dual 1.6 cm $\gamma$-detectors with high-energy general-purpose collimators. SPECT data were obtained by a non-circular orbit, a 128x128 matrix (voxel size: 4.7 x 4.7 x 4.7 mm$^3$) and 32 angles over 180 degrees and 45 seconds per stop, using a 364-keV photo peak with 10% window (total acquisition time 24 min). Reconstruction space and width was 3 mm using the Philips Astonish algorithm.

**Lesion Volume Calculation**

The volume of each lesion with focal uptake, present on both of the pre-therapeutic $^{124}$I PET images (24 and 96 h after administration) was semi-automatically determined using an in-house-built software algorithm (Matlab, The Mathworks) based on a recently published iterative thresholding method (18). The method assumes a spherically shaped lesion with homogeneous $^{124}$I uptake. Accounting for the reconstructed $^{124}$I PET spatial resolution of 6.7 mm (expressed as full-width-at-half-maximum), background-corrected relative boundary-reproducing values used for lesion delineation were calculated. The smallest diameter or volume that can be determined using this method corresponds to the PET spatial resolution or its equivalent sphere volume of 0.15 mL. Consequently, lesions were classified into two groups in line with a previous study (17): lesions with reliable volume estimation larger than 0.15 mL, the so-called known-volume group, and lesions with a volume smaller than 0.15 mL, the small-volume group. For the known-volume group, the
lesion volume was calculated as the average value of the lesion volume determined on the 24-h and 96-h $^{124}$I PET images. Lesions for which the average lesion volume differed more than 30% with respect to the 24-h or 96-h volume were excluded. Lesions for which either the 24-h or 96-h volume was smaller than 0.15 mL were classified into the small-volume group. For the small-volume group, the lesion volume used for lesion AD estimation was assumed to be equal to the PET spatial resolution volume of 0.15 mL.

**Lesion Absorbed Dose Estimation**

For each $^{124}$I PET image, lesion uptake was calculated as the average activity concentration (AC) of the segmented volume, corrected for partial volume effect, using measured (absolute) recovery coefficients (18), which effectively corrects for prompt gamma coincidence effect as well (20). Assuming identical $^{124}$I and $^{131}$I pharmacokinetics, half-life correction was performed on the $^{124}$I AC to assess the projected $^{131}$I AC. $^{131}$I residence time was determined according to the adapted 2-points approach (21). In case the effective half-life was less than the physical $^{131}$I half-life, the lesion time-activity curve was parameterized using a combination of a linear uptake function and a mono-exponential decay function (interception time at 8 h after $^{131}$I administration). In case the effective half-life was greater than the $^{131}$I physical half-life, physical decay was assumed beyond the 96 h time point. The (self-irradiation) lesion AD was calculated using the sphere model in the Olinda software package (Olinda version 1.1, Vanderbilt University) (22). For all lesions, a density of 1.0 g/ml was used. This resulted in an average and a minimum lesion AD per administered $^{131}$I activity for the known-volume and small-volume group, respectively.
The predicted average and minimum lesion AD delivered in radioiodine therapy were estimated by multiplication with the therapeutic $^{131}$I activity.

**Therapy Response Assessment**

**Lesion-based Analysis**

Lesions were classified as either thyroid remnant or metastases including lymph node or distant metastases (lymph node, lung, bone). Both the thyroid remnants and metastases were subdivided into a known-volume group and a small-volume group. Each individual lesion was either defined as *completely* or *incompletely* responding by an experienced nuclear medicine physician and medical physicist. Specifically, the *completely* responding lesion did not show $^{124}$I uptake on subsequent follow-up scan within 1 year and no $^{131}$I uptake on subsequent post-therapeutic planar and SPECT/CT scanning. In contrast, the *incompletely* responding lesion did show focal $^{124}$I or $^{131}$I uptake on day 4 scan (in absence of significant level of background noise), not contributable to physiological uptake according to visual assessment. For each lesion group, the predicted lesion AD in radioiodine therapy of the completely responding lesions was compared to that of the incompletely responding lesions. Moreover, the performance of pre-therapeutic $^{124}$I PET/CT to predict complete lesion response was assessed using receiver operating characteristic (ROC) curve analysis (23).

**Patient-based Analysis**
Patients were classified as incompletely responding if persisting disease after radioiodine therapy was demonstrated, either by functional imaging ($^{124}$I PET/CT, $^{131}$I SPECT/CT, $^{18}$F-FDG), anatomical imaging (US, MRI), histology or increased Tg value. Otherwise patients were classified as completely responding. The average patient-based lesion AD was calculated as the mean lesion AD of all radioiodine avid lesions observed per patient.

Statistics

Statistical analysis was performed using SPSS version 22 (IBM Corp, Armonk, NY, USA). Descriptive data are shown as mean ± standard deviation (median; range). Differences between two groups were assessed using the Mann-Whitney U test. Values for $P < 0.05$ were considered statistically significant. ROC curves were used to test the performance of pre-therapeutic $^{124}$I PET/CT lesion AD for prediction of complete lesion response.

RESULTS

Patient and Lesion Characteristics

Detailed patient characteristics are provided in Table 1. Out of the in total 67 patients satisfying the inclusion criteria, one patient was excluded as this patient received a diagnostic CT with iodine containing contrast agent prior to the $^{124}$I PET/CT scan. Three patients were excluded due to the lack of either the 24-h or 96-h $^{124}$I PET/CT examination. Furthermore, twelve patients were excluded due to unavailability of the PET raw data required for the additional retrospective 2x2x2 mm$^3$ voxel image reconstruction. Four patients did not show any visible lesions on the $^{124}$I
PET images. Of the remaining 47 patients, 29 patients were classified as completely responding and 18 patients as incompletely responding.

Detailed lesion characteristics are given in Table 2. In total, 168 lesion were suitable for AD estimation. Nine lesions were excluded because of lesion volume discrepancies between the 24-h and 96-h scans. For the thyroid remnants and metastases, 89% (109/123) and 69% (31/45) of the lesions showed a complete response, respectively.

Lesion-based Therapy Response

Figure 1 illustrates the calculated lesion AD in radioiodine therapy for both thyroid remnants and metastases for all lesions (including known- and small-volume group), the known-volume group and the small-volume group. Statistically significant higher lesion AD was observed for the completely responding lesions compared to the incompletely responding lesions for all lesions and the known-volume group, but not for the small-volume remnants group. Since there were only 2 incompletely responding lesions in the small-volume metastases group, no statistical tests were performed for this group. Detailed lesion data are provided in the supplemental material.

Figure 2 shows the ROC curves for both the thyroid remnants and metastases. Except for the metastatic small-volume group, all area under the curve (AUC) values were significantly higher than 0.5. The AUC values were highest for the known-volume group. The arrow in Figure 2 corresponds to the established threshold values for the lesion AD of 300 Gy for thyroid remnants and 85 Gy for metastases (3,4). For the known-volume group, these threshold values resulted in sensitivity values of 0.69
and 0.67, and specificity values of 0.75 and 0.92 for the thyroid remnants and metastases, respectively. The Youden index (24), defined as the value that gives the maximum correct classification, was calculated as being 90 Gy for thyroid remnants and 40 Gy for metastases, resulting in respective sensitivity values of 0.85 and 1.0, and specificity values of 0.75 and 0.92.

**Patient-based Therapy Response**

In Table 1, it can be derived that the incompletely responding patients had a higher TNM status and considerably more radioiodine-avid metastases than the completely responding patients. The median patient-based thyroid remnant lesion AD was higher for the completely responding patients (370 Gy) than the incompletely responding patients (180 Gy) but this was not statistically significant. For metastases, the median patient-based lesion AD was higher for the incompletely responding patients (63 Gy) compared to the completely responding patients (39 Gy), but also not statistically significant. It should be noted that in 7 patients a complete response of all radioiodine-avid lesions was seen at the lesion-based analysis. However, in the patient-based analysis these did not have a complete response as during follow-up new lesions in other anatomical areas were detected with FDG PET/CT, $^{124}$I PET/CT and/or ultrasound in combination with cytology.

**DISCUSSION**

Maxon et al. (3,4) demonstrated that a lesion AD threshold of 300 Gy for thyroid remnants and 85 Gy for lymph node metastases was associated with a high complete lesion response rate of 80–90%, establishing the lesion AD as an important
quantity for prediction of lesion response in radioiodine treatment. Several groups have identified $^{124}$I PET/CT as a promising modality for performing lesion-based dosimetry (12-17). Applying an empirically fixed radioiodine activity approach, Flower et al. (12) were the first to assess lesion AD in 3 patients using $^{124}$I PET. In agreement with our findings, they reported that the administration of fixed activities (3.0–5.5 GBq) resulted in a large variation of lesion AD to both thyroid remnants (16–400 Gy) and involved neck nodes (2.5–33 Gy). In contrast, Erdi et al. (13) developed a method to estimate lesion AD of thyroid remnants based on pre-therapeutic $^{124}$I PET imaging at maximum-tolerated activity (MTA) of $^{131}$I using a dose constraint of 2 Gy to blood. Performing this method in 3 patients, they observed a large lesion AD range (5–248 Gy) at MTA (10–15.5 GBq). Indeed, an approach of MTA applying a maximum blood dose of 2 Gy has been reported to be safe and well-tolerated (25-27). Alternatively, several groups have reported on an optimal activity approach using pre-therapeutic $^{124}$I PET/CT lesion AD calculations (14-16). In this approach, $^{131}$I therapeutic activity was chosen to achieve lesion AD values above the established threshold values, considering toxicity estimations. Although this approach has been reported to result in change in patient management in 25–50% of DTC patients (14, 16), the biological effectiveness of dosimetry-guided approaches is not proven yet (1).

To date, the only study assessing the dose-response relationship by means of $^{124}$PET/CT in a larger number of patients was recently published by Jentzen et al. (17). Adopting an optimum activity approach, therapy response for thyroid remnant and metastatic lesions above the accepted lesion AD was assessed. This approach resulted in relatively high therapeutic $^{131}$I activity (median 10 GBq, range 2–20 GBq) and the vast majority of lesions, as expected, received an AD above the established threshold.
values. In our study therapeutic activity was almost 4 times lower (median 2.8 GBq, range 1.1 – 5.5 GBq) and the estimated lesion AD range extended to the lower lesion AD values. As a result, we observed a statistically significant dose-response relationship confirming a higher calculated lesion AD of completely responding lesions than the incompletely responding lesions. Interestingly, for thyroid remnants we observed a complete lesion response of 89% which is in good agreement with a complete response of 91% found by Jentzen et al (17), whereas for metastases our study showed a complete lesion response of 69% compared to 88%. These findings suggest that an optimized activity approach might be most beneficial in DTC patients presenting with metastatic disease.

Using ROC curve analysis, we showed that for lesions larger than 0.15 mL, pre-therapeutic $^{124}$I PET/CT lesion dosimetry can be used as a prognostic tool to predict lesion-based $^{131}$I therapy response. For these lesions, the optimal threshold value was 90 Gy for thyroid remnants and 40 Gy for metastases. These values are considerably lower than the accepted threshold values of 300 Gy and 85 Gy. However, it is important to note that these optimum lesion AD thresholds are defined as the values that give the maximum correct classification combining both sensitivity and specificity. In DTC patient management, a correct prediction of incompletely responding lesions is important. Consequently, for patient’s management decision-making, higher AD threshold values may be preferred.

Reliable lesion dosimetry requires accurate radioactivity quantification and volume estimation which are affected by the finite spatial resolution of current nuclear medicine imaging equipment (28), in particular for the small lesion volumes often encountered in DTC patients. In addition, high spatial resolution images
obtained by US or CT are considered unreliable due to a lack of differentiation between thyroid tissue and hematoma on these modalities (1). As a result, lesion AD calculations are considered unreliable for small lesions. Using an established PET-based thresholding method yielding reliable volume estimation for lesions larger than 0.80 mL, Jentzen et al. (17) were able to accurately calculate lesion AD for 24% and 27% of all analyzed thyroid remnants and metastases, respectively. In our study, we used a more advanced segmentation technique allowing volume estimation down to the $^{124}$I PET spatial resolution volume of 0.15 mL. Consequently, reliable lesion AD estimation was obtained in 38% of thyroid remnants and 40% of metastases. Despite the improved volume segmentation technique, for the majority of lesions only the minimum lesion AD could be calculated. In the future, further developments in PET/MRI might contribute to further improvements of the dosimetry in small-volume disease (29).

Using voxel-based 3D dose distribution calculations, several studies have reported on the AD distribution heterogeneity within lesions (13-14). In these studies, substantial variability in intratumoral AD was observed, possibly resulting in underdosing of tumour subregions and ultimately therapy failure (13). Although in our study correction for partial volume effect was performed by means of the recovery coefficient, heterogeneity of the lesion AD distribution was not considered since the majority of lesions included in our study were small compared to the $^{124}$I PET spatial resolution.

A limitation of our study was its retrospective nature. However, a high concordance with other studies using $^{124}$I likely confirms the validity of our results. In fact, to date, no prospective randomized study addressing the optimal activity
approach has been published and the optimal therapeutic activity is not established yet (1,2). The results of our study indicate that pre-therapeutic $^{124}$I PET/CT lesion dosimetry can be used as a prognostic tool to predict lesion response. Therefore, we would strongly advocate cooperative efforts to establish a multi-center prospective $^{124}$I trial to confirm our findings.

**Conclusion**

This study provides evidence of a statistically significant dose-response-relationship assessed by means of pre-therapeutic $^{124}$I PET/CT dosimetry in both thyroid remnants and metastases. This will be a clinically useful contribution in patient management.

**Disclosure**

No potential conflict of interest relevant to this article was reported.
References


FIGURE 1. Boxplots of lesion AD for both remnants (A,B,C) and metastases (D,E,F).

Boxplots are provided for all lesions (A,D), the known-volume group (B,E) and the small-volume group (C,F). Statistically significant differences are characterized by $P < 0.05$. Numbers close to whiskers represent the number of lesions.
FIGURE 2. ROC curves for both remnants (A,B,C) and metastases (D,E,F). ROC curves are provided for all lesions (A,D), the known-volume group (B,E) and small-volume group (C,F). The arrows correspond to a threshold value of 300 Gy for remnants and 85 Gy for metastases. The dashed line represents the line of equality.
TABLE 1. Patient Characteristics of the Analyzed (N=47) Patients. Descriptive Data are Shown as Mean ± Standard Deviation (Median; Range).

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<tr>
<th>Characteristic</th>
<th>Completely responding</th>
<th>Incompletely responding</th>
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<tr>
<td>Age (years)</td>
<td>51 ± 11 (52; 23–70)</td>
<td>50 ± 18 (53; 18–79)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>Female</td>
<td>25</td>
<td>11</td>
</tr>
<tr>
<td>Number of lesions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thyroid remnants</td>
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<tr>
<td>Metastases</td>
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<tr>
<td>Variant</td>
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<td>11</td>
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<tr>
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<tr>
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<tr>
<td>2</td>
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<td>3</td>
<td>12</td>
<td>4</td>
</tr>
<tr>
<td>4</td>
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<td>6</td>
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<tr>
<td>Max. Tg value in FU (pmol/L)</td>
<td>11 ± 55</td>
<td>2.5·10³ ± 7.0·10³</td>
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<td></td>
<td>(&lt;0.5; 0.25–290)</td>
<td>(5.7; &lt;0.2 –2.510⁴)</td>
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<td>First ¹³¹I radionuclide therapy</td>
<td></td>
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<tr>
<td>Yes</td>
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<td>16</td>
</tr>
<tr>
<td>No</td>
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<td>2</td>
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<tr>
<td>Single therapeutic ¹³¹I activity (GBq)</td>
<td>3.0 ± 0.7 (2.8; 2.8–5.5)</td>
<td>3.0 ± 1.0 (2.8; 1.1–5.5)</td>
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<tr>
<td>Follow-up period (months)</td>
<td>19 ± 16 (10; 4.5–61)</td>
<td>17 ± 17 (9; 3.5–64)</td>
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### TABLE 2. Overview of the Analyzed Lesions.

<table>
<thead>
<tr>
<th>Lesion Type</th>
<th>Completely responding</th>
<th>Incompletely responding</th>
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<td><strong>Thyroid remnants</strong></td>
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<td></td>
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<tr>
<td>- Known volume group</td>
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<tr>
<td>- Paratracheal</td>
<td>12</td>
<td>5</td>
</tr>
<tr>
<td>- Thyroid bed</td>
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<tr>
<td>- Small volume group</td>
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<tr>
<td>- Paratracheal</td>
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<tr>
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<td>4</td>
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<td><strong>Metastases</strong></td>
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<td>14</td>
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<td>12</td>
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<tr>
<td>- Thyroid bed</td>
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<td>-</td>
</tr>
<tr>
<td>- Neck lateral (II-V)</td>
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<td>1</td>
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<tr>
<td>- Cervical high</td>
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<td>- Cervical low (VI)</td>
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<td>11</td>
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<td>- Small volume group</td>
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<td>- Thyroid bed</td>
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<td>- Neck lateral (II-V)</td>
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