Absolute quantification of ^{131}I uptake in thyroid carcinoma metastases using xSPECT Quant for absorbed dose prediction

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History

An 82-year-old female patient with a history of thyroid cancer presented with multiple lung lesions detected on a chest CT, which were regarded as suspicious for metastases. Twenty years ago, the patient was diagnosed with primary thyroid carcinoma and underwent a near-total thyroidectomy and large-dose ^{131}I therapy for ablation of residual thyroid tissue. She was treated with a total of 24 GBq of ^{131}I and achieved complete ablation of the residual thyroid.

Given the suspicion of lung metastases, diagnostic ^{131}I scintigraphy was performed. A dosage of 597 MBq (16 mCi) of ^{131}I was administered orally, and planar and SPECT/CT images were acquired 40 hours post-administration.

The study was performed on a Symbia Intevo™ 16 SPECT/CT using a high-energy collimator. Following the initial planar acquisition, a SPECT/CT study of the thorax was completed, with an initial CT acquisition (130kV, 40 eff mAs and 16 x 1.2 mm collimation) followed by a SPECT acquisition at 60 stops per detector and 21 seconds per stop, which resulted in 120 projections over 360°. Absolute quantification of ^{131}I uptake was derived using xSPECT Quant™ [a], which is based on system calibration using a NIST-traceable ^{113}Sn source. SPECT and CT data were fused, and lesion volumes and absolute tracer concentration were evaluated using *syngo*®.via.

Findings
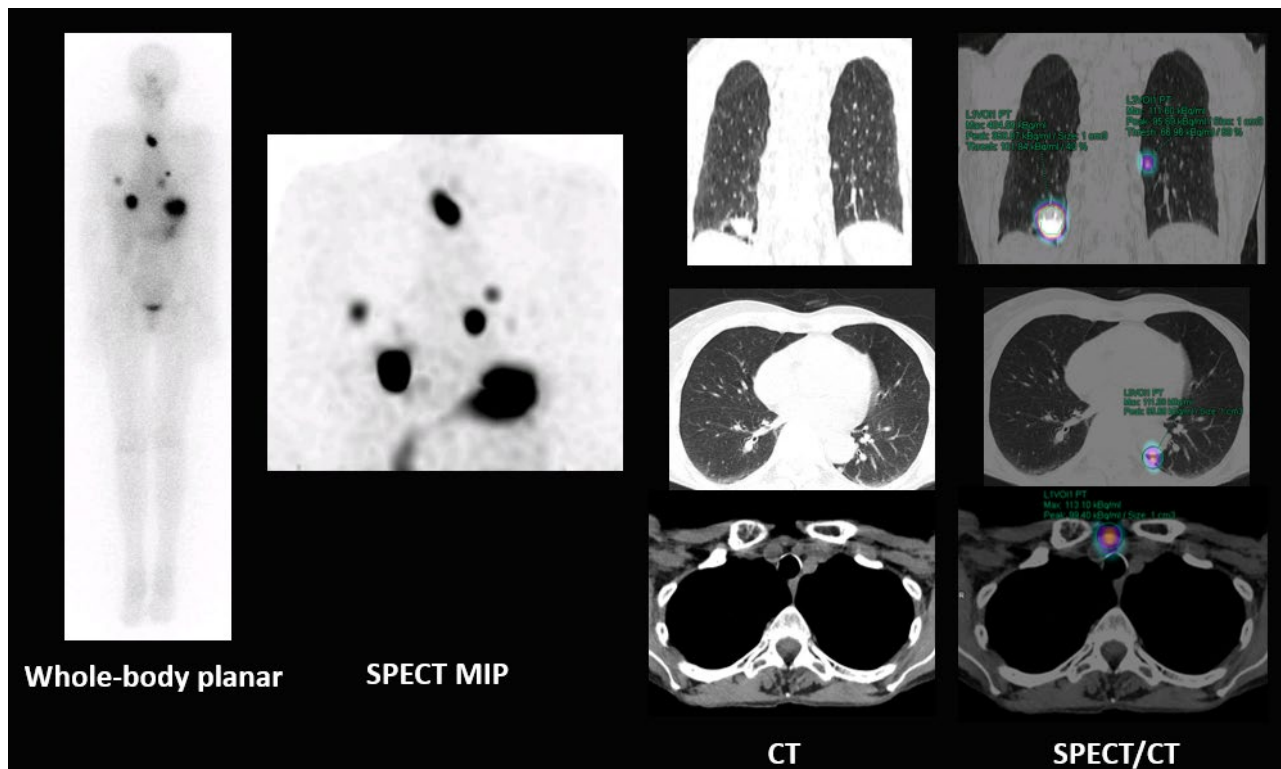
1 Whole-body planar, SPECT MIP and CT, and fused SPECT/CT images show multiple radioiodine-avid metastases in the lungs and anterior mediastinum. The stomach reflects a high amount of physiological tracer retention. Bladder and intestinal activity are low and within physiological limits. Absence of focal uptake in the neck reveals ablation of residual thyroid secondary to the large-dose ^{131}I therapy administered 20 years ago.

Figure 1 notes multiple ^{131}I-avid metastatic lesions in the lung and superior mediastinum on the planar whole-body image along with significant physiological retention of tracer in the stomach and a low level of tracer in the bladder and intestine.

The SPECT and SPECT/CT images show a large metastatic lesion in the right lung base with a maximum dimension of 2 cm, along with several smaller metastatic lesions located in the right lung within the lateral aspect of the upper lobe, posterior paravertebral aspect of the left lung attached to the pleura, anterior aspect of the upper lobe of the left lung, and the anterior-superior mediastinum just below the sternum anterior to the trachea, which is likely a lymph nodal metastasis.
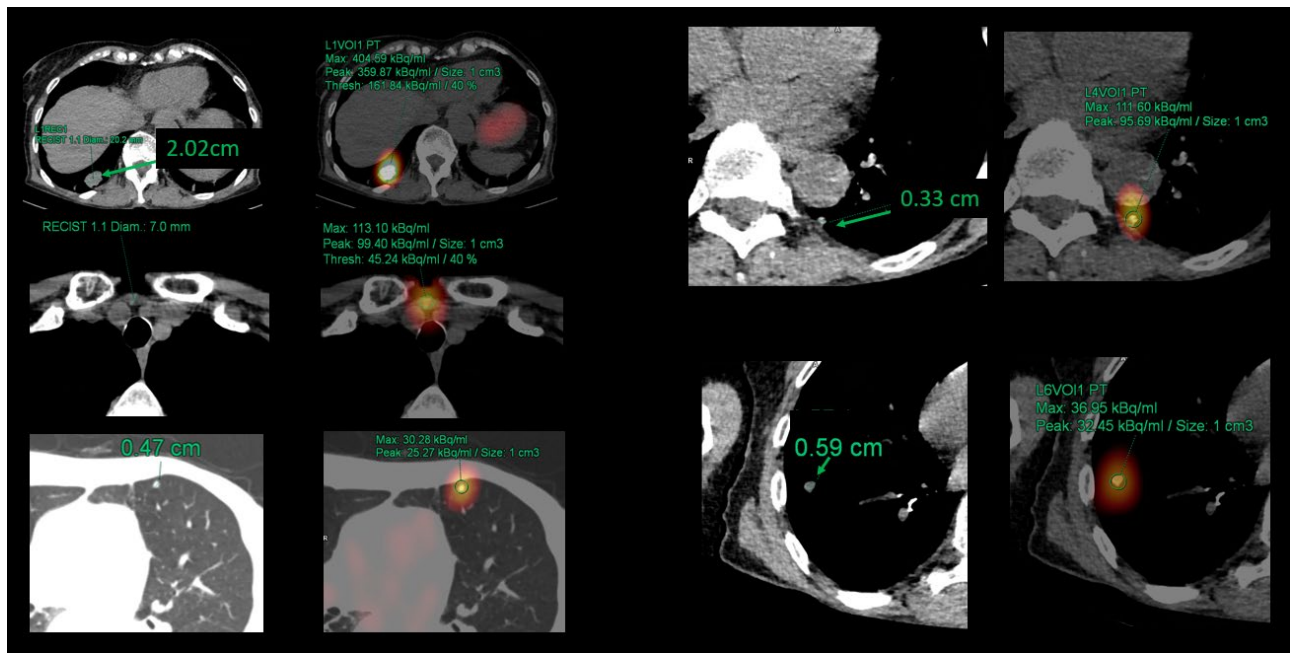
2 CT and fused SPECT/CT images of focal metastatic lesions with the lesion size and absolute tracer concentration in kBq/ml obtained using xSPECT Quant and *syngo*.via.

Figure 2 denotes the lesion size along with maximum and peak absolute concentration of tracer, which were obtained using [131]I xSPECT Quant. The largest lesion, with a maximum dimension of 2 cm, shows a maximum concentration of ^{131}I of 404 kBq/ml. The smallest lung metastasis, which is in the paravertebral space of the left lung attached to pleura (top left) and 3.3 mm in size, shows a lower maximum tracer concentration of 111 kBq/ml. A 6 mm lung nodule in the right lung (bottom right) shows maximum tracer concentration of 36 kBq/ml. The 5 mm lung nodule in the left upper lobe also showed similar maximum tracer concentration (bottom left). The increased intensity of tracer uptake in the small, 3 mm left lung metastasis, as compared to the 6 mm right lung metastases, is visually obvious in the planar as well as the SPECT images, and the absolute tracer concentration also correlates with the visual estimation, even though the lesion is small, which invites partial volume effects. The focal retrosternal nodal lesion in the anterior superior mediastinum also appears highly iodine-avid on both planar and SPECT, and the maximum absolute concentration of 113 kBq/ml reflects the visual impression. No bone lesions were seen on the SPECT/CT images. The single retrosternal nodal lesion also reflected high radioiodine avidity.

From this single-time-point, pre-therapy study following administration of a diagnostic dose of ^{131}I, the number, size, and uptake intensity of lung and mediastinal lesions are well determined. The high uptake in the lung metastases, especially in the large metastases in the right lung base and the small lesion in the left lung attached to the pleura, suggests the possibility of high lesion-absorbed dose and a positive response following large-dose ^{131}I therapy. However, in view of the need to predict the efficacy of large-dose ^{131}I therapy and decide on the amount of ^{131}I to be administered, the absorbed dose to lesions needs to be calculated from the quantitative values of the absolute tracer concentration, which are generated from the xSPECT Quant data along with the lesion volume estimation derived from CT.

Time-integrated activity coefficient was obtained by assuming a linear accumulation from administration until time of imaging (40 hours post administration), along with a mono-exponential decay with a half-life taken from literature. The time-integral activity curves (TIAC) were then multiplied with S-values extrapolated from the OLINDA solid-sphere model, which resulted in an absorbed dose in [Gy] and [Gy/GBq]. Activity in the lesions was taken from quantitative SPECT and segmented using an iso-contour (10% of maximum) in order to mitigate the impact of partial volume effect affecting the relatively small volumes of interest. The volumes of the lesions were determined from hand segmentation of the CT portion of the SPECT/CT acquisition.
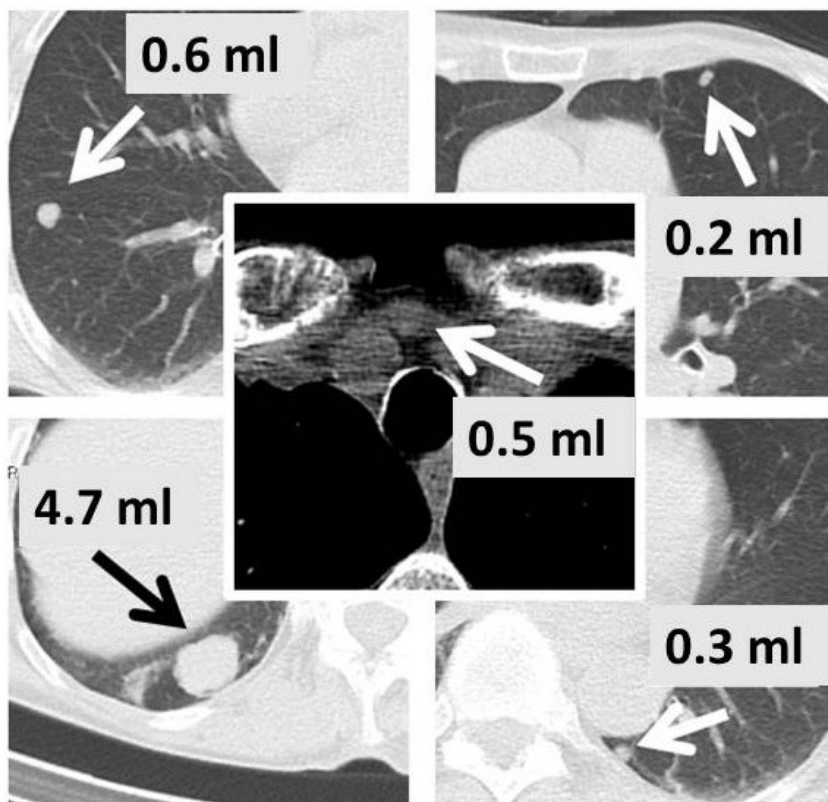
3 Volumes of individual lung and mediastinal metastatic lesions calculated from CT images derived from SPECT/CT. Small lung metastases with volumes of 0.2, 0.3, and 0.6 ml are susceptible to partial volume effects.

Although sequential multi-time-point acquisitions are necessary to measure change in absolute tracer concentration within lesions in order to accurately calculate time-activity curves for absorbed dose estimations, in this patient, only a single time-point acquisition 40 hours post dose administration was available for dosimetry calculations. Thus, the half-life of the tracer within the metastatic lesions that was used for dosimetry was derived from published literature. Two half-life values of 48 hours and 67 hours noted as representing an acceptable range of half-lives[1] were used to calculate a dose range for each metastatic lesion.
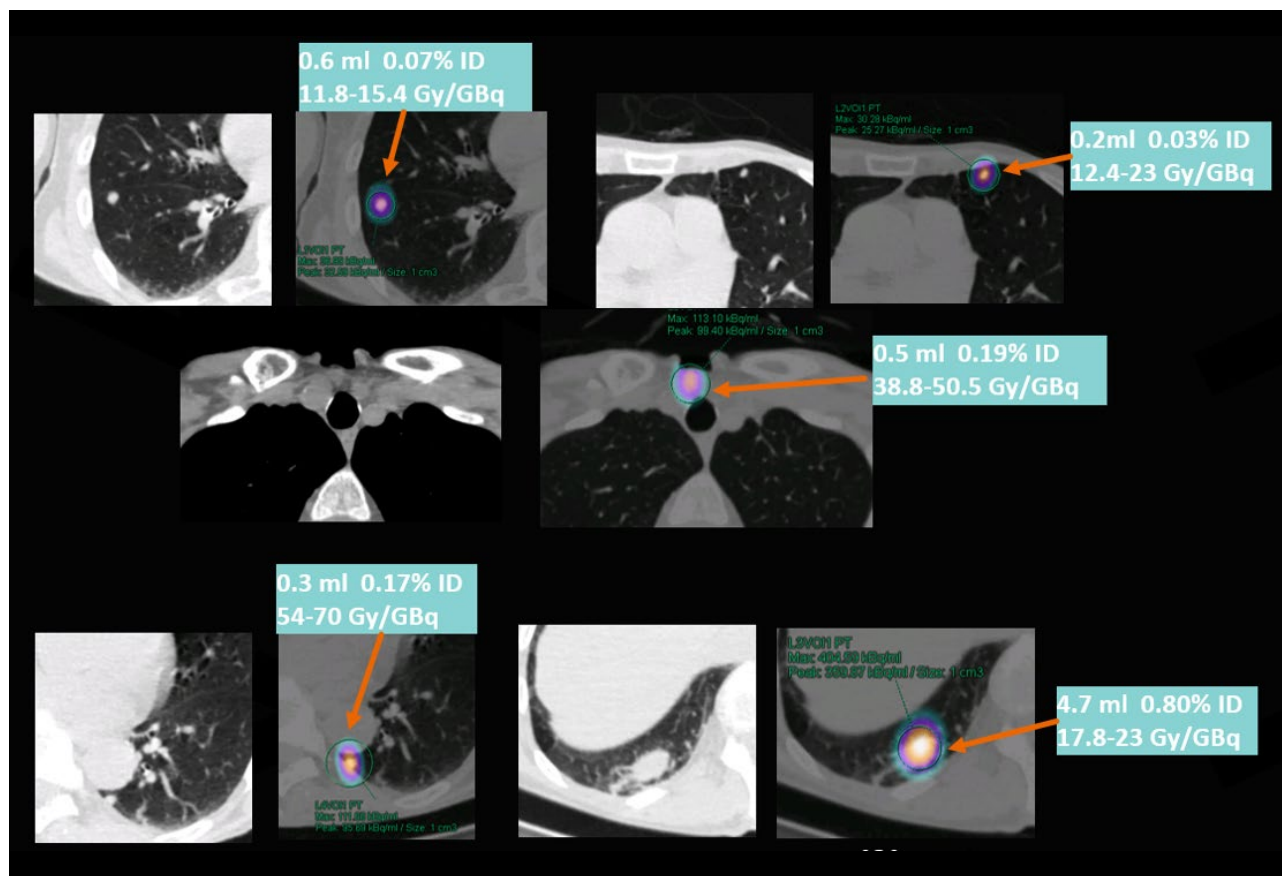
4 Lesion volume, percentage of administered ^{131}I dose, and range of absorbed dose in Gy/GBq calculated using a publication-derived half-life of 48 hours and 67 hours for ^{131}I within lesions.

As Figure 4 shows, the largest lung metastasis with a volume of 4.7 ml and tracer retention of 0.8% of total administered dose was calculated to receive an absorbed dose of 17.8 Gy/GBq, if the half-life is considered to be 48 hours, and 23 Gy/GBq, if the half-life is considered to be 67 hours. For the small 0.3 ml paravertebral lesion attached to the pleura in the left lung with relatively high tracer concentration as shown on quantitative SPECT/CT, the absorbed dose ranges from 54-70 Gy/GBq, depending on the half-life considered. From the dosimetry calculations, it would require 4.34 GBq (approx. 110 mCi) of ^{131}I to be able to deliver 100 Gy to the largest lung metastases considering 67 hours as half-life. Some of the smaller lesions may even be responsive to lower levels of administered activity.

Discussion

This case example illustrates the value of accurate estimation of absolute tracer concentration within lesions following diagnostic and post-therapeutic ^{131}I administration in patients with metastatic thyroid carcinoma for absorbed dose calculation. Accurate volume estimation using diagnostic CT acquired as part of SPECT/CT and calculation of absorbed tracer concentration using xSPECT Quant based on system calibration using a NIST-traceable-[113]Sn source are key inputs for absorbed dose calculation. In this example, due to lack of sequential imaging, the effective half-life of the tracer within the lesions was based on a range (48 to 67 hours) obtained from literature and the time-activity curves derived from the absolute tracer concentration and the accepted half-life range. These inputs were then used with OLINDA-based S-values to derive the range of absorbed dose for each lesion.

Studies have shown that absorbed dose higher than 300 Gy to the residual thyroid tissue and 80 Gy to metastases are required for effective response: Maxon et al.[2] demonstrated that 98% of tumors with an absorbed radiation dose of more than 80 Gy responded, while only 20% of tumors receiving less than 80 Gy showed significant response. A tumor dose <35 Gy was always associated with an absence of any response.

Pre-therapy dosimetry for a prediction of absorbed dose to critical organs and lesions following large dose ^{131}I therapy was performed by Dorn et al[3] with sequential whole-body planar acquisitions starting immediately after tracer administration and continued at daily intervals up to 4-5 days. The geometric mean of the anterior and posterior counts in multiple ROIs over lesions were used to generate time-activity curves, from which residence time and absorbed dose calculations were made. The objective of pre-therapy dosimetry was to enable the largest and safest dose without crossing the absorbed dose thresholds of 3 Gy for bone marrow and 30 Gy to the lungs.

Based on dosimetry studies, 41 therapy doses were delivered with curative intent since absorbed dose to metastatic lesions was calculated to be >100 Gy on pre-therapeutic dosimetry. Of these, 44% of patients could achieve >100 Gy tumor dose without crossing bone marrow or lung dose thresholds. The calculated dose to the metastases ranged from 100 Gy to >1,000 Gy. Most lesions receiving >100 Gy showed significant response on follow-up. Forty-six percent of patients had lowering of administered dose due to marrow and lung absorbed-dose estimations, which would have been higher than toxicity thresholds with doses required to achieve adequate tumor dose. There was a wide range of the administered ^{131}I activity required to

achieve a 3 Gy bone marrow dose (range: 7.4 GBq to 37.9 GBq) from the pre-therapy dosimetry. The authors concluded that higher initial ^{131}I doses can be administered based on pre-therapy dosimetry in order to achieve significantly higher tumor-absorbed doses without exceeding critical-organ thresholds with significant tumor response whenever tumor-absorbed dose exceeded 100 Gy, as was seen in 44% of cases. No significant bone marrow or lung toxicity was seen in the entire patient group, reflecting the fact that pre-therapy dosimetry-based dose adjustment ensured no patient exceeded dose thresholds for these organs.

The calculation of absorbed dose based on a single-time-point quantitative SPECT/CT using literature-derived effective half-life of the tracer within lesions reflect a simplified approach to aid decision-making for large-dose ^{131}I therapy in order to deliver adequate lesion dose. In this case, only the pre-therapy scan performed with 16 mCi of ^{131}I at 40 hours post administration was used for absorbed-dose estimation and predicted a dose of 110 mCi of ^{131}I to deliver 100 Gy to the largest lung metastases. Although SPECT data at multiple time points would have been optimal for calculating the absorbed dose estimate, it was unfortunately not available in this case. Nevertheless, the calculations in this case were regarded as sufficient for guiding further therapy decisions. This approach could be easily extended to multiple-time-point scans. The accuracy of the quantification based on xSPECT Quant using a highly accurate NIST-traceable-[113]Sn source for system calibration together with attenuation correction using diagnostic CT as well as scatter correction is key to optimal dosimetry accuracy, which should be the major driver for therapy decision-making.

Conclusion

xSPECT Quant-based measurement of absolute concentration of ^{131}I in thyroid carcinoma metastases in a patient who underwent a diagnostic ^{131}I SPECT/CT study was instrumental in tumor-absorbed dose calculation based on literature-derived effective tracer half-life and helped guide further large-dose ^{131}I therapy decisions. ●

Examination protocol

Scanner: Symbia Intevo 16

SPECT		CT	
Injected dose	597 MBq (16 mCi) [131]Iodine	Tube voltage	130 kV
Scan delay	40-hour post oral administration	Tube current	40 eff mAs
Acquisition	60 stops, 21 sec/stop	Slice collimation	16 x 1.2 mm

[a] *xSPECT Quant ^{131}I is not commercially available in all countries. Due to regulatory reasons, its future availability cannot be guaranteed. Please contact your local Siemens organization for further details.*

The outcomes achieved by the Siemens customers described herein were achieved in the customer's unique setting. Since there is no "typical" hospital and many variables exist (e.g. hospital size, case mix, level of IT adoption) there can be no guarantee that others will achieve the same results.

References

1 de Keizer B, Brans B, Hoekstra A, et al. Tumour dosimetry and response in patients with metastatic differentiated thyroid cancer using recombinant human thyrotropin before radioiodine therapy. *Eur J Nucl Med Mol Imaging* 2003; 30: 367-373.

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3 Dorn R, et al. Dosimetry-guided radioactive iodine treatment in patients with metastatic differentiated thyroid cancer: largest safe dose using a risk-adapted approach. *J Nucl Med.* 2003 Mar; 44(3): 451-6.

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