CLINICAL STUDY

Single photon emission computed tomography (SPECT)/computed tomography using Iodine-123 in patients with differentiated thyroid cancer: additional value over whole body planar imaging and SPECT

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Abstract

Objective: The aim of the study was to assess the diagnostic performance of co-registered single photon emission computed tomography (SPECT)/computed tomography (CT) compared to Iodine-123 whole body gamma camera (WBGC) imaging and to SPECT alone in patients with differentiated thyroid cancer.

Methods: WBGC and SPECT/CT ($n=85$) imaging of the neck and thorax was performed in 79 consecutive patients. Three experienced observers reviewed: i) WBGC images followed by ii) SPECT alone, and iii) co-registered SPECT/CT. Foci of increased radioiodine uptake were classified on a five-point scale. Biopsy, other imaging modalities, and clinical follow-up served as the reference standard.

Results: Twenty-two patients had local recurrence or metastatic thyroid cancer (11 were radioiodine negative), 9 had remnant thyroid tissue, and 54 had no evidence of disease. When classifying equivocal, probably, and definitely malignant findings as positive for malignancy, the sensitivity, specificity, positive predictive value, and negative predictive value were as follows: 41, 68, 31, and 77% for WBGC imaging; 45, 89, 59, and 82% for WBGC plus SPECT imaging; and 50, 100, 100, and 85% for WBGC plus SPECT/CT imaging respectively. The specificity was improved by the addition of SPECT ($P=0.0002$) and SPECT/CT ($P<0.0001$) than to WBGC imaging. SPECT/CT was also more specific than WBGC plus SPECT imaging ($P=0.016$). In a study-based analysis, SPECT/CT provided additional diagnostic information in 42% (36/85) of cases. SPECT/CT provided further characterization in 70% (63/90) of foci and improved the diagnostic confidence of all three observers.

Conclusion: The addition of SPECT/CT significantly improved the diagnostic information over Iodine-123 WBGC imaging and WBGC plus SPECT imaging alone.

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Introduction

Patients with differentiated thyroid cancer have an overall good prognosis; however, lifelong follow-up is required for many cases, since potentially curable local recurrences and distant metastases may occur even decades later (1–4). Radioiodine imaging plays a major role in the follow-up after initial surgery and ablation of residual thyroid tissue using Iodine-131 therapy, although the need for such extensive therapy for microcarcinomas has been questioned. Iodine-123 has replaced Iodine-131 at many institutions as a radio-nuclide for gamma camera imaging due to its more suitable physical characteristics (5).

However, the lack of anatomical details on planar gamma camera imaging and superimposition of areas presenting with increased radioiodine uptake can make accurate diagnosis and localization of radioiodine-avid metastatic disease challenging. This is particularly important in the neck and thorax where differentiation between physiological radioiodine accumulation, remnant thyroid tissue and residual or recurrent thyroid cancer may be difficult. Furthermore, accurate characterization and localization of thoracic radioiodine uptake to lung, bone, or lymph nodes can be equally challenging. In addition, altered anatomy, particularly in the neck and sites of physiological radioiodine accumulation such as in the esophagus, may be

misinterpreted as metastatic disease (6, 7). For example, a retrospective review of 500 radioiodine whole body scans revealed diagnostic pitfalls leading to additional imaging or diagnostic procedures in 59% of studies (8).

Single photon emission computed tomography (SPECT) provides a 3D set of gamma camera images which improve the localization of increased tracer uptake within the body. This allows one to analyze the radioiodine distribution within the body in any plane; e.g. axial, coronal, and sagittal. However, precise anatomical localization is frequently still difficult due to a lack of appropriate landmarks on SPECT images. Integrated SPECT/computed tomography (CT) enables co-registration of structural and functional data and provides patient-specific data for the correction of photon attenuation (9, 10). This often permits improved spatial localization and characterization of increased tracer uptake which should ultimately lead to improved diagnostic performance in radioiodine imaging as well.

Most studies of SPECT/CT in thyroid cancer have used Iodine-131 to further evaluate equivocal findings on planar imaging. In our study, Iodine-123 SPECT/CT of the neck and thorax was performed in consecutive patients regardless of the findings on planar imaging. At our institution, thyroid cancer patients generally undergo thyroidectomy and radioiodine ablation, followed by endogenous TSH-stimulated Iodine-123 whole body planar gamma camera imaging and serum thyroglobulin measurement in high-risk patients 6 months later. Iodine-123 gamma camera imaging is also performed in patients with rising thyroglobulin levels. The routine protocol includes whole body planar imaging and SPECT/CT of the neck and thorax at 24 h after radioiodine injection.

This study represents a detailed analysis of the incremental value of the addition of Iodine-123 SPECT/CT compared with whole body planar imaging and SPECT alone. In addition, we assessed potential changes in patient management.

Materials and methods

Patients

Consecutive patients with differentiated thyroid cancer, who underwent Iodine-123 imaging from March 2006 to February 2009, were eligible for the study. Iodine-123 gamma camera imaging was performed in patients with rising thyroglobulin levels as well as in high-risk patients 6 months following thyroidectomy and radioiodine ablation. Measurement of urinary iodine excretion was not performed prior to Iodine-123 administration. All the patients were imaged following endogenous TSH stimulation.

This retrospective analysis of patient data was performed as part of an audit, and institutional audit committee approval was obtained. The demographical

and follow-up data were collected through a combination of review of clinic/correspondence letters/multidisciplinary meeting summaries and biochemical/histopathology databases on the electronic patient record, review of patient notes and direct communication with the physician in charge of the patient's care. The information for each patient was recorded on a patient case record form.

Gamma camera and SPECT/CT imaging

Whole body planar gamma camera (WBGC) images were acquired in the anterior and posterior projections ~24 h post radiotracer injection (350–400 MBq Iodine-123 sodium iodide) on a dual-headed gamma camera (Millennium VG Hawkeye, GE Healthcare, Amersham, UK) with low energy general purpose collimators. The bed speed was 5 cm/min, and the data were acquired into a 256×1024 matrix, with a pixel size of 2.2 mm. SPECT imaging of the neck and thorax was performed following WBGC imaging with 60 s frame time, step and shoot mode 360/60 frames (6° angle step), 1.28 zoom. One patient also underwent an additional SPECT/CT of the abdomen and pelvis. SPECT data were reconstructed using an OSEM iterative reconstruction algorithm (Hermes, Nuclear Diagnostics Medical Systems, Sweden) into a 128×128 matrix, with a pixel size of 3.45 mm that incorporated the attenuation map information described below.

The CT acquisition was carried out using a fixed protocol (140 kV, 2.5 mA) resulting in forty 10 mm slices that were subsequently rebinned to produce 128 3.45 mm slices with a transverse pixel size of 1.7 mm. The CT data were also rescaled to produce an attenuation map related to attenuation coefficient values at 159 keV matching the dimensions of the reconstructed SPECT slices.

Image analysis

Gamma camera images were reviewed by three experienced observers (T B, H M, N A) in a consensus reading without knowledge of clinical data on a dedicated workstation (Hermes Medical Solutions, Nuclear Diagnostics, Stockholm, Sweden) using a linear gray scale. For analysis of SPECT/CT images, both linear gray and color scale displays were used. The three clinicians reviewed the scans first separately followed by a consensus reading. In all cases, a consensus was reached.

The whole body planar images were reviewed initially followed by the SPECT and then the SPECT/CT. For Iodine-123 whole body planar imaging, symmetrical uptake in the salivary glands, linear uptake in the region of the esophagus, and uptake in the stomach, gastrointestinal tract and bladder were considered normal. Any focal increased uptake outside these areas was considered abnormal. Radioiodine uptake in the neck which was localized in the area of the thyroid

bed was considered residual thyroid tissue following previous radioiodine ablation.

Sites of increased tracer uptake were noted along with the likelihood of the presence of disease according to the following five-point grading scale for whole body planar images, SPECT alone, and SPECT/CT:

- i) definitely normal
- ii) probably normal (more likely to be physiological)
- iii) equivocal (equally likely to be pathological or physiological)
- iv) probably abnormal (more likely to be pathological)
- v) definitely abnormal.

For SPECT and SPECT/CT, the anatomical localization of increased radioiodine uptake was taken into account when reviewing images. Although we used a low-dose CT for anatomical correlation, the lung and bone windows were also reviewed for lung nodules and bone metastases. In addition, the overall diagnostic confidence score for each patient was allocated using the same five-point scale. For subsequent analysis, definitely abnormal, probably abnormal, and equivocal findings were considered malignant. Probably normal and definitely normal findings were considered benign. Thyroglobulin levels or findings from neck ultrasound, or any other clinical information were not made available to the image reviewers.

Statistical analysis

The sensitivity, specificity, positive predictive value, and negative predictive value were calculated for whole body planar gamma camera imaging, SPECT, and SPECT/CT on a study basis. For the purpose of these calculations, equivocal findings were considered malignant. Comparison of the detection of thyroid cancer metastases by each method was performed using an exact McNemar's test with a two-tailed *P* value <0.05 being statistically significant (11). Following the exclusion of 11 studies found on follow-up to have non-radioiodine-avid disease, receiver operating characteristic (ROC) curve analysis was performed by recalculating sensitivity and specificity for each technique along the five-point grading scale. In addition, the area under the curve (AUC) was calculated.

Results

Ninety-three patients underwent Iodine-123 imaging for follow-up of thyroid cancer from March 2006 to February 2009; however, in 12 cases SPECT/CT was not performed due to logistical and/or technical reasons. In one case, neck movement resulted in substantial image misregistration, and one patient with normal planar and SPECT/CT imaging was lost to follow-up. Therefore, the study population consisted of 79 patients in whom a total of 85 Iodine-123 imaging

studies were performed. Patient characteristics are shown in Table 1.

Of these cases, 64 studies were performed as routine follow-up of high-risk patients 6 months after radioiodine ablation of residual thyroid tissue; five studies were performed 6 months after radioiodine therapy for completion of ablation (*n*=3) or for metastatic disease. Twelve studies were performed in patients with rising or elevated thyroglobulin. The remaining three cases were to exclude recurrence – one in a patient with severe shoulder pain who was found to have an osteolytic lesion and in two patients with lung nodules, one of whom had a history of breast cancer. One patient underwent Iodine-123 imaging prior to radioiodine ablation following surgery.

Following endogenous TSH stimulation after withdrawal of L-thyroxine therapy, all the patients had elevated TSH levels (TSH > 30 mIU/l) before i.v. administration of Iodine-123. SPECT/CT of the neck and thorax was performed in all the patients as per our imaging protocol, and a further SPECT/CT of the abdomen/pelvis was performed in one patient, which revealed no abnormal radioiodine uptake. The reference standard was established by clinical follow-up including thyroglobulin levels in addition to histopathology (*n*=5), neck ultrasound (*n*=18), computed tomography (*n*=17), gamma camera imaging of subsequent radioiodine therapy (*n*=10), bone scintigraphy (*n*=2), magnetic resonance imaging (MRI) of the neck (*n*=2), MRI of the spine (*n*=2), and 2-(18F)-fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography (FDG-PET/CT) (*n*=2). Mean follow-up was 13 months.

Diagnostic performance

Based on the reference standard, there was evidence for residual or recurrent thyroid cancer in 22 out of 85 Iodine-123 imaging studies, 11 of which were non-radioiodine avid. In addition, nine studies had

Table 1 Patient characteristics.

Characteristics	Number (<i>n</i> =79)
Participant age, years	
Mean	49
Range	16–85
Sex <i>n</i> (%)	
Female	60 (76%)
Male	19 (24%)
Histopathology <i>n</i> (%)	
Papillary thyroid cancer	61 (77%)
Follicular thyroid cancer	17 (22%)
Unknown	1 (1%)
Stage at diagnosis	
I	36
II	7
III	7
IV	16
Unknown	13

Table 2 Findings for whole body planar gamma camera (WBGC) imaging, with the addition of single photon emission computed tomography (SPECT) and SPECT/computed tomography (CT).

Modality	Malignant (<i>n</i> =22)					Benign (<i>n</i> =63)				
	DA	PA	E	PN	DN	DA	PA	E	PN	DN
WBGC imaging	3	3	3	6	7	0	11	9	15	28
WBGC+SPECT imaging	6	3	1	5	7	1	4	2	14	42
WBGC+SPECT/CT imaging	10	1	0	0	11	0	0	0	8	55

DA, definitely abnormal; PA, probably abnormal; E, equivocal; PN, probably normal; DN, definitely normal.

radioiodine-avid remnant thyroid tissue only; 54 studies had no evidence of disease. The diagnostic performance of WBGC imaging, SPECT, and SPECT/CT are presented in Tables 2 and 3. In a study-based analysis, SPECT/CT provided additional diagnostic information in 42% (36/85) of cases.

The sensitivity was 41% for WBGC imaging, 45% with the addition of SPECT, and 50% with the addition of SPECT/CT. However, although we observed an increase in sensitivity, this did not reach statistical significance for either WBGC imaging versus SPECT ($P=1.0$) or WBGC imaging versus SPECT/CT ($P=0.5$). When 11 cases who were found on follow-up to have non-radioiodine-avid disease were excluded, the sensitivity increased from 82% for WBGC imaging to 91% with the addition of SPECT and to 100% with the addition of SPECT/CT.

Nevertheless, there was a significant improvement in specificity from 68% for WBGC imaging to 89% ($P=0.0002$) with the addition of SPECT. The addition of SPECT/CT further increased the specificity to 100% ($P<0.0001$). The increase in specificity between SPECT and SPECT/CT also was statistically significant ($P=0.016$).

A major factor in the increased specificity of SPECT and/or SPECT/CT was the reclassification of initially equivocal findings. There were 12 WBGC scans classed as equivocal, three remained so on SPECT, but none were on SPECT/CT. Classing equivocal findings as positive for disease, WBGC imaging was false-positive in 20 cases (nine thyroid remnants; four esophageal tracer retention; four asymmetric salivary glands; and three surface contamination) and false-negative in 13 cases (11 non-radioiodine-avid metastases and 2 cervical nodal metastases).

The addition of SPECT alone correctly classified 13 false-positive findings as physiological activity or remnant, and it identified metastatic neck lymph nodes in one study and additional bone metastases in another study. Therefore, the combination of WBGC and SPECT imaging produced 7 false-positive findings and 12 false-negative findings (Figs 1 and 2).

SPECT/CT correctly assigned all false-positive findings and identified a metastatic cervical lymph node misinterpreted as submandibular gland on WBGC and SPECT imaging alone. Several additional small bone metastases were identified on the CT component of the

study in a patient already noted to have multiple bone metastases on WBGC and SPECT imaging. SPECT/CT was false-negative for 11 cases with non-radioiodine-avid disease; five of these cases had metastatic neck lymph nodes, one with additional miliary lung metastases. One case had a 2.5 cm metastatic skin lesion on the neck which was subsequently excised, and three cases had small lung metastases on diagnostic CT which were not visible on the low-dose CT component of the SPECT/CT. In two cases, the sites of disease remain occult but were classed as radioiodine negative on the basis of a persistently elevated thyroglobulin.

ROC analysis

Following the exclusion of 11 cases found on follow-up to have non-radioiodine-avid disease, ROC curve analysis revealed an AUC of 0.84 for WBGC imaging, 0.95 for WBGC plus SPECT imaging, and 1.0 for WBGC plus SPECT/CT imaging (Fig. 3).

Diagnostic confidence

On a per study basis, overall diagnostic confidence increased with the addition of SPECT and SPECT/CT to WBGC imaging. The percentage of studies classed as 'definitely normal' or 'definitely abnormal' increased

Table 3 Diagnostic performance of whole body planar gamma camera (WBGC) imaging, with the addition of single photon emission computed tomography (SPECT) and SPECT/computed tomography (CT).

	WBGC imaging	WBGC+SPECT imaging	WBGC+SPECT/CT imaging
True-positive (<i>n</i>)	9	10	11
False-positive (<i>n</i>)	20	7	0
True-negative (<i>n</i>)	43	56	63
False-negative (<i>n</i>)	13 (2)	12 (1)	11 (0)
Sensitivity (%)	41 (82)	45 (91)	50 (100)
Specificity (%)	68	89	100
PPV (%)	31	59	100
NPV (%)	77 (96)	82 (98)	85 (100)
Accuracy (%)	61 (70)	78 (89)	87 (100)

In the analysis, equivocal interpretation was considered malignant. Numbers in brackets refer to analysis of patients with radioiodine-avid disease only.

Figure 1 (a) Planar whole body Iodine-123 gamma camera imaging in anterior and posterior views shows mildly increased linear activity in projection of the esophagus but more focal activity projected over the mediastinum. This was interpreted as equivocal for either radioiodine retention in the esophagus or a mediastinal lymph node metastasis. (b) The finding remained equivocal on SPECT but clearly localises to the esophagus on SPECT/CT. Full colour version of this figure available via <http://dx.doi.org/10.1530/EJE-09-1023>.

from 46% (39/85) with WBGC imaging to 66% (56/85) with the addition of SPECT to 89% (76/85) with the addition of SPECT/CT.

Change in diagnostic findings

The addition of SPECT/CT provided further characterization in 63 (70%) of the 90 foci identified on 51 WBGC imaging studies (Table 4). A total of 41 foci initially thought to be either equivocal or pathological (false-positive) were reclassified by the addition of SPECT/CT as being thyroid remnant ($n=20$) or other sites of physiological radioiodine uptake ($n=21$). Five metastatic foci thought to be physiological (false-negative) were lymph node ($n=3$) or bone metastases ($n=2$). For 17 foci, the site of metastases was accurately localized.

Change in patient management

The addition of SPECT/CT to WBGC imaging led to a change in management in 9 (11%) out of 85 cases. In two patients, identification of cervical lymph node metastases that were not clearly identified on WBGC imaging led to surgical lymph node dissection rather than radioiodine therapy. In one patient who was thought to have both cervical and mediastinal lymph node metastases, SPECT/CT localized the mediastinal activity to the esophagus. Therefore, the patient underwent a cervical lymph node dissection. In one patient who was thought to have localized cervical nodal disease, equivocal mediastinal uptake was shown to be a mediastinal lymph node, and the patient had radioiodine therapy rather than surgery. In five patients with

elevated thyroglobulin levels, WBGC imaging was thought to be abnormal; however, SPECT/CT showed the increased Iodine-123 uptake to be physiological. These patients underwent diagnostic CT, neck ultrasound and FDG-PET/CT scans, and surgery or radiotherapy rather than radioiodine therapy.

In addition, in 11 cases who were thought to have abnormal Iodine-123 uptake on WBGC imaging, SPECT/CT did not confirm disease obviating the need for further investigations or avoiding ineffective radioiodine therapy. However, none of these patients had raised serum thyroglobulin levels, and most likely a 'watch-and-wait' policy would have been adopted. Thus, although SPECT/CT provided additional information in these cases, we did not anticipate a change in management.

Discussion

SPECT/CT improved the diagnostic performance of Iodine-123 imaging for differentiated thyroid cancer. The specificity increased from 68 to 89% with the addition of SPECT ($P=0.0002$) and to 100% with the addition of SPECT/CT ($P<0.0001$). The overall accuracy improved from 61% for planar gamma camera imaging to 78% with the addition of SPECT and to 87% with the addition of SPECT/CT. Furthermore, the diagnostic confidence of the observers improved such that we found no equivocal findings using SPECT/CT.

The accurate localization and characterization of focally increased Iodine-123 uptake is often not possible on planar gamma camera imaging, particularly in

Figure 2 (a) Whole body planar Iodine-123 gamma camera imaging in anterior view shows minor asymmetric uptake in the region of the submandibular glands thought to be probably normal. (b) SPECT/CT axial and coronal images: on SPECT there is discrete focal uptake bilaterally. On SPECT/CT this localised to several small bilateral cervical lymph nodes. (c) Axial diagnostic CT thorax (lung windows) demonstrates several small pulmonary nodules consistent with metastases, which were not apparent on SPECT. Full colour version of this figure available via <http://dx.doi.org/10.1530/EJE-09-1023>.

the neck and upper thorax. Although the addition of SPECT improved the diagnostic accuracy, it frequently remained difficult to differentiate between malignant and physiological radioiodine uptake. For example, we found it difficult to resolve between residual thyroid tissue and cervical lymph node metastases on whole body imaging with the addition of SPECT alone. Radioiodine retention in the esophagus was often recognized on planar imaging and SPECT by its typical linear configuration. However, focally increased activity is better characterized by SPECT/CT. In 13 studies, SPECT/CT enabled accurate localization of physiological radioiodine retention in the esophagus thought to be possibly pathological on planar gamma camera imaging and on SPECT. This is an important finding as in such cases the patient is spared further imaging procedures or even unnecessary radioiodine therapy (8).

The sensitivity of radioiodine whole body imaging depends on various factors including technical parameters, the activity administered and the reference standard used (12). Although we injected 350–400 MBq Iodine-123, the sensitivity was only 41% (9 out of 22), which is lower than 70–89% sensitivity figures reported by others (13–15). However, previous studies used, for example, post-radioiodine therapy imaging as the reference standard; thus, all the patients had radioiodine-avid disease. In our study, follow-up revealed 11 cases with non-radioiodine-avid disease, which when excluded, resulted in a sensitivity of 82%

for planar imaging, which compares well with these reports (13–15).

To date, there have been several studies addressing the use of radioiodine SPECT/CT in differentiated thyroid cancer (16–20). Fused SPECT/CT in 25 patients with inconclusive findings on post-radioiodine ablation imaging improved anatomical localization in 17 (44%) out of 39 foci compared with SPECT alone (18). Furthermore, image interpretation changed in 15 (38%) foci. In another study, SPECT/CT provided additional diagnostic information in 41 (57%) out of 71 patients who underwent Iodine-131 imaging post radioiodine therapy ($n=54$) or as a diagnostic procedure ($n=17$) (19). SPECT/CT particularly improved the characterization and localization of increased Iodine-131 uptake in lymph node metastases, remnant thyroid tissue, lung and mediastinal as well as bone metastases. Similar results were found by others (16, 17, 20). The additional diagnostic information of SPECT/CT over planar imaging ranged from 57 to 74% of patients (16, 17, 19). When assessing the impact of SPECT/CT on patient management, we found a change in 11% of the patients. Previous reports found a change in 24 (17), 25 (18), and 41% of the patients (19). However, these studies were limited to patients with indeterminate findings on planar Iodine-131 imaging.

To the best of our knowledge, this is the first consecutive series using Iodine-123 SPECT/CT in the follow-up of thyroid cancer regardless of the findings on

Figure 3 Receiver operating characteristic (ROC) curves of whole body gamma camera (WBGC) imaging versus WBGC + SPECT imaging versus WBGC + SPECT/CT imaging (patients with non-radioiodine-avid disease excluded). AUC, area under the curve. Full colour version of this figure available via <http://dx.doi.org/10.1530/EJE-09-1023>.

whole body imaging. However, previous studies have analyzed consecutive series of cases using Iodine-131 imaging. Spanu *et al.* prospectively performed 117 SPECT/CT of the neck and thorax demonstrating 116 foci on planar imaging (21). SPECT/CT had incremental value over planar in 67.8% positive cases (40/59) and modified management in 35.6% positive cases (21/59). This translated to an incremental value in 40/117 (34%) studies and a change in management

in 21/117 (21%) studies. Of note, patients with non-radioiodine-avid disease were excluded from their analysis. Our findings compare well with additional diagnostic information of SPECT/CT in 42% of studies. Spanu *et al.* (21) found SPECT/CT to be particularly useful in revealing nodal metastases adjacent to salivary glands occult on planar imaging (4 cases in 3 patients). Similarly, we found three cases of cervical nodal metastases in two patients. These would be potentially missed in other studies which only perform SPECT/CT in equivocal findings on planar imaging. The specific advantage of SPECT/CT for nodal assessment of the neck is also emphasized by a recent study which found a gain in information on nodal stage in 20 (35%) out of 57 patients leading to a change in risk stratification in 14 (25%) patients (22).

We found a reduction in the number of equivocal/indeterminate findings with the addition of SPECT/CT, which is supported by a recent study where positive SPECT/CT predicted persistent/recurrent disease in 9 (16%) out of 55 patients (23). Three out of nine patients (33%) had non-radioiodine-avid disease and accounted for false-negative SPECT/CT as reported for our study (23).

In common with the majority of previous studies discussed above, the CT performed as part of SPECT/CT in our study did not contribute independent diagnostic information. We used a low resolution Hawkeye-CT, which was not of diagnostic image quality although the CT images provided valuable anatomical information regarding the precise localization of abnormal radioiodine uptake. More recently, SPECT/CT systems are incorporating diagnostic multislice CT, capable of low-dose as well as diagnostic CT. Depending on the protocol used, these may permit even better lesion characterization and, as such, further reduce the need for subsequent diagnostic studies (24). It is also important

Table 4 Summary of the additional characterization of whole body gamma camera (WBGC) findings provided by single photon emission computed tomography (SPECT)/CT in 63 out of 90 foci.

WBGC findings	Number of foci	Characterization by SPECT/CT	Number of foci	Additional value	Number of foci
Not seen on planar GC imaging	4	Bone metastases	2	Metastatic foci not seen on planar GC imaging	5
Probably salivary gland uptake	1	Cervical lymph node metastases	2		
Abnormal cervical activity	5	Cervical lymph node metastasis	1		
Abnormal thoracic activity	10	Cervical lymph node metastases	5	Localization of metastases	17
		Bone metastases	4		
		Mediastinal lymph node metastases	6		
Abnormal pelvic activity	2	Bone metastases	2		
Abnormal cervical activity	35	Physiological uptake in submandibular gland	4	Exclusion of disease	41
		Physiological esophageal activity	9		
		Contamination	2		
		Thyroid bed remnant	20		
Abnormal thoracic activity	5	Physiological esophageal activity	5		
Abnormal shoulder activity	1	Contamination	1		

to consider the additional radiation exposure from the CT portion of SPECT/CT, which in our cases was ~1 mSv in addition to ~5 mSv from Iodine-123 imaging.

There are some limitations of this study which need to be considered. The diagnostic performance was patient-based. This may underestimate the fraction of 'false-negative' findings. For example, two patients had lung metastases which were negative on SPECT/CT, but the patients were considered 'true-positive' for the purpose of a patient-based analysis as cervical metastases were correctly identified. This is a general limitation as a detailed focus based analysis is challenging because histopathologic confirmation would be difficult as it is not feasible to sample all potential sites of disease.

The number of patients with radioiodine-avid disease was limited. Patients subsequently shown to have non-radioiodine-avid disease were retained in this analysis of consecutive patients. This resulted in lower sensitivities compared with previous reports. However, the primary purpose of the study was to assess the incremental value of adding SPECT and SPECT/CT to conventional planar gamma camera imaging. This analysis is not biased by the study population. For the same reason, thyroglobulin levels or findings from neck ultrasound or any other clinical information were not made available to the image reviewers.

In conclusion, our study has shown that the addition of SPECT/CT improved the diagnostic performance of Iodine-123 whole body planar imaging and SPECT alone. With the increasing availability of latest generation SPECT/CT systems, implementation into routine clinical radioiodine imaging should be considered. Future studies should assess the optimum protocol, impact on patient outcome, and cost-effectiveness.

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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