RESEARCH

Clinical experience following implementation of routine SPECT-CT imaging following 131-iodine administration for thyroid cancer

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Abstract

Background: Planar scintigraphy has long been indicated in patients receiving I-131 therapy for thyroid cancer to determine the anatomic location of metastases. We studied our experience upon implementing additional single-photon emission (SPECT)-CT scanning in these patients.
Method: We performed a retrospective study of consecutive adult patients with newly diagnosed thyroid cancer treated with I-131 between 2011 and 2017. Radiologic findings detected with planar scintigraphy alone vs those identified with SPECT-CT scanning were primary endpoints.
Result: In this study, 212 consecutive patients with thyroid cancer were analyzed in two separate cohorts (107 planar scintigraphy alone and 105 planar scintigraphy with SPECT-CT). The addition of SPECT-CT resulted in more findings, both thyroid-related and incidental. However, we identified only 3 of 21 cases in which SPECT-CT provided an unequivocal additional benefit by changing clinical management beyond planar scintigraphy alone. No difference in the detection of distant metastatic disease or outcome was identified between cohorts.
Conclusion: Synergistic SPECT-CT imaging in addition to planar nuclear scintigraphy adds limited clinical value to thyroid cancer patients harboring a low risk of distant metastases, while frequently identifying clinically insignificant findings. These data from a typical cohort of patients receiving standard thyroid cancer care provide insight into the routine use of SPECT-CT in such patients.

Key Words

- SPECT-CT imaging
- 131-iodine treatment
- planar scintigraphy
- thyroid cancer

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Introduction

The past two decades have witnessed a dramatic rise in the incidence of newly diagnosed thyroid cancer (1), primarily attributable to the detection of incidental or small-volume disease. Simultaneous to this, practitioners have also increasingly individualized their approach to thyroid cancer care. While near-total thyroidectomy was historically the operative norm for well-differentiated thyroid carcinoma, data now confirm that many are adequately treated with hemithyroidectomy (2, 3). In parallel, uniform administration of adjunctive radioactive iodine (I-131) has been abandoned as data demonstrate limited or no benefit to those with low-risk diseases (4, 5, 6). Critical to this evolution of thyroid cancer care has been the ability to personalize care decisions based upon individualized risk assessment. This occurs through improving the specificity and sensitivity of data received,

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specifically radiologic and imaging findings, as well as a cutting-edge molecular understanding of the disease.

In patients receiving I-131 therapy for well-differentiated thyroid carcinoma, a post-treatment nuclear medicine scintigraphy scan is recommended 3–7 days following isotope administration (7). This radiologic procedure provides planar imaging of the whole body, specifically determining the anatomic location of remnant thyroid tissue or metastatic thyroid cancer. While anterior neck uptake is most commonly seen, the distant metastatic disease can also be confirmed. With the use of post-treatment scintigraphy scanning, the staging of thyroid cancer can be finalized, while also documenting areas of concern for spread or persistent disease.

However, nuclear scintigraphy scanning affords only a modest resolution in comparison to other means of anatomic imaging. This detriment led to the development and use of single-photon emission CT (SPECT) with integrated CT, as a means of improving the three-dimensional characterization of post-treatment findings. Over the past several years, the integrated use of SPECT-CT scanning together with planar nuclear scintigraphy has gained widespread adoption as part of the radioiodine therapy protocol for patients with thyroid cancer. Several studies have supported the apparent incremental diagnostic value that accompanies SPECT-CT in this setting (8, 9, 10, 11, 12).

Yet, routine use of SPECT-CT leads to increased exposure to ionizing radiation, as well as additive cost. Greater use of cross-sectional imaging also increases the chance of incidental findings and their downstream ramifications. Thus, in totality, there are both perceived benefits as well as detriments to this additional imaging process. To date, no investigation has fully examined such endpoints in a real-world setting, allowing a broader understanding of the overall utility of SPECT-CT in the treatment of a typical group of thyroid cancer patients. Beginning in 2014, our institution gradually increased the use of SPECT-CT in the setting of post-treatment radioiodine imaging, culminating in near-universal use from 2016 onward. This afforded us a unique ability to perform a retrospective clinical utility study investigating both the benefits and detriments in comparison to planar scintigraphy alone.

Methods

We performed an investigation of consecutive cohorts of comparable patients with well-differentiated thyroid cancer, all receiving adjunctive I-131 therapy. The two cohorts were separated only by time, with the control population consisting of patients treated between 2009 and 2015 who received only post-treatment planar scintigraphy following radioiodine administration. In contrast, the comparison cohort received post-treatment SPECT-CT in addition to planar scintigraphy between the years 2011 and 2017. The use of SPECT-CT was phased in over several years, thus explaining the overlap of the above groups. To avoid selection bias, this study enrolled all consecutive patients evaluated at Brigham and Women's Hospital for thyroid cancer care between 2009 and 2017(13).

Our thyroid nodule and cancer center represent a single point of care for all nodule and cancer evaluation within our healthcare system, thus further reducing sampling or selection bias. For the purposes of this analysis, we only studied consecutive patients from 2009 to 2017 who were newly diagnosed with well-differentiated thyroid cancer. All patients were recommended by a thyroid specialist to receive I-131 treatment. Typically, I-131 doses ranged from 30 to 150 mCi at the discretion of the provider based upon applicable guideline recommendations for the time (7, 14). Preparation for I-131 therapy was either by thyroid hormone withdrawal or by rh-TSH injection. A low-iodine diet was administered for 1 week prior to treatment in all cases. Planar scintigraphy and SPECT-CT were performed 5–7 days after radioactive iodine treatment. All patients receiving I-131 therapy had undergone near-total thyroidectomy as the primary treatment of the disease. Imaging was performed on the Siemens Inc. Symbia Intevo imaging system in all cases.

Demographic data were collected including sex and age at the time of I-131 treatment. Thyroid cancer staging was profiled using the AJCC 7th or 8th edition (concurrent to the current period). We also collected histopathology, response to therapy at 6–12 months following initial treatment, and final outcome. A patient's response to therapy was defined per the American Thyroid Association (ATA) clinical guidelines (7).

We reviewed all post-treatment scintigraphy reports, as well as available concurrent SPECT-CT reports for each patient. Primary endpoints included detection of local or distant metastatic disease identified by either modality, as well as detection of incidental non-thyroidal findings on SPECT-CT. This was defined as any finding reported by the radiologist in his/her impression that was not thyroid or thyroid cancer-related. From this, we sought answers to three principal study questions: Did SPECT-CT improve the detection of thyroid cancer-related findings beyond that obtained with planar scintigraphy? How did any improved specificity from SPECT-CT scanning impact the

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care of patients? And, what non-thyroid cancer-related (incidental) findings were detected on SPECT-CT, leading to unintended but necessarily follow-up or further testing?

This investigation was evaluated and approved by the Mass General Brigham Investigational Review Board. Statistical comparisons were performed using chi-square analysis for categorical data and using the Mann–Whitney *U* test for continuous data. *P*-values < 0.05 were considered significant. Descriptive data are shown using absolute numbers and percentages of the total study population.

Results

We studied 212 patients with thyroid cancer consecutively treated with I-131 therapy between 2009 and 2017. The median age was 47.2 years in the planar scintigraphy cohort and 46.2 years in the SPECT-CT cohort, while 77 and 75% were female, respectively. Here, 195 patients (91.1%) were diagnosed with papillary thyroid carcinoma, while 16 (7.5%), and 1 (0.5%) were diagnosed with follicular thyroid carcinoma/Hurthle cell carcinoma and poorly differentiated thyroid carcinoma, respectively. The distribution of AJCC staging was comparable between cohorts ($P = 0.25$). The study population demographics are shown in Table 1.

In the entire study population ($n = 212$), post-I-131 radiologic findings questioning local or metastatic disease were identified in 16 (7.5%) patients, with more noted in the SPECT-CT cohort (5 of 107 (5%) planar scintigraphy cohort vs 11 of 105 (10.5%) SPECT-CT cohort). In the planar scintigraphy cohort, four (3.7%) of findings were of suspected local metastatic disease confirmed with ultrasound and one (0.9%) suspected distant metastases, while in the ‘SPECT-CT cohort’, five (4.6%) findings on planar scintigraphy demonstrated suspected local disease, while six (5.7%) were of suspected distant metastatic disease. In summary, SPECT-CT combined with planar scintigraphy identified a greater percentage of abnormal findings following I-131 therapy.

However, of these 11 abnormal findings in the SPECT-CT cohort, only 3 led to a change in clinical management. In five separate cases, SPECT-CT scanning provided more precise data than that obtained with planar scintigraphy alone (e.g. such as size measurement or precise location), though led to no change in clinical management or new unique identification. SPECT-CT scanning did identify three additional new findings reported as a local disease not identified on planar scintigraphy scanning. However, all three cases (100%) were either false-positive findings or proved clinically insignificant and did not modify care. In summary, SPECT-CT scanning, in addition to planar scintigraphy, resulted in three cases of clinical benefit, five cases of greater precision though no change in clinical management, and three cases of false or clinically insignificant findings. Details explaining the impact on clinical management are provided in Table 2. In the planar scintigraphy cohort, stimulated thyroglobulin (Tg) was available in 43 (40%) patients (mean Tg = 15.8, S.D. 9.4), while 51 (47%) patients had positive thyroglobulin antibodies. In the SPECT-CT cohort, stimulated thyroglobulin was available in 63 (60%) patients (mean 9.1, S.D. 16.5), while 21 (20%) had positive TG antibodies.

Comparing study cohorts, there was no significant detection of distant metastatic disease or detection of thyroid cancer-related findings using SPECT-CT scanning compared to planar scintigraphy alone. Similarly, at a mean follow-up of 3.4 years in SPECT-CT group and 5.7 years in planar scintigraphy group, there was no difference in final outcome between cohorts ($P = 0.07$, Table 3).

Table 1 Study population ($P = 0.25$).

Planar scintigraphy alone ($n = 107$)	**Planar scintigraphy plus SPECT-CT** ($n = 105$)
Female (*n*): 77 (72%)	Female: 75 (71%)
Age (mean, range): 47.2 years (19–82)	Age: 46.2 years (18–79)
RAI dosage (mean, range): 59.8 mCi (30–200)	RAI dosage: 66.5 mCi (30–150)
Type of thyroid cancer	
Papillary carcinoma	
Classical variant: 56 (52%)	Classical variant: 50 (47.6%)
Follicular variant: 24 (22.4%)	Follicular variant: 17 (16.1%)
Tall-cell variant: 7 (6.5%)	Tall-cell variant: 13 (12.4%)
Classical w/ tall cell features: 10 (9.3%)	Classical w/ tall cell features: 9 (8.6%)
Other PTC[a]: 5 (4.7%)	Other PTC[b]: 4 (3.8%)
Follicular thyroid carcinoma: 5 (4.7%)	Follicular/Huthle thyroid carcinoma: 11 (10.5%)
	PDTC: 1 (1%)

[a]Warthin-like, oncocytic variant PTC and PTC with high-grade features. [b]Solid variant, sclerosing variant, columnar variant.
FVPTC, follicular variant of PTC; PTC, papillary thyroid carcinoma; RAI, radioactive iodine treatment; TCVPTC, tall-cell variant of PTC.

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Table 2 Detailed descriptions of 11 cases in which additional SPECT-CT findings were noted separate from planar scintigraphy alone. Results are categorized as being false-positives, showing improved precision but without modifying care or as improving management.

Case (years) **M/F**	**Pathology**	**SPECT-CT findings**	**Final outcome**
Cases where SPECT-CT findings were found to be false-positive results (*n* = 3)			
56 M	6.0 cm PTC, tall-cell variant; +gross ETE; +LVI; +N1a, largest LN 0.9 cm	SPECT-CT identified an additional level 2 lymph node suspected to be metastases	Follow-up ultrasound identified no suspicious findings. No recurrent disease confirmed. Patient with excellent response to treatment. Presumed false-positive finding.
21 F	2.5 cm PTC, multifocal, +vascular invasion; +LN involvement, largest 4.2 cm (N1b)	SPECT-CT identified an 8 mm lymph node in the left neck and 7 mm lymph node in the right supraclavicular area suspected to be metastases	Follow-up ultrasound identified no suspicious findings. No recurrent disease identified. Patient with excellent response to treatment. Presumed false-positive finding.
54 F	1.6 cm PTC with tall-cell features, no ETE, no LVI; no LN involvement	SPECT-CT identified a 5 mm cervical lymph node suspected to be metastases	Follow-up ultrasound identified no suspicious findings. No recurrent disease identified. Patient with excellent response to treatment. Presumed false-positive finding.
Cases where SPECT-CT findings provided greater precision but did not change management (*n* = 5)			
35 F	2.3 cm PTC, follicular variant; encapsulated; no LN involvement	SPECT-CT identified an area of concerning uptake corresponding to a 9 mm soft tissue in the post-surgical thyroid bed	Patient with delayed RAI treatment 4 years after surgery. SPECT-CT clarified area of uptake was soft tissue/remnant thyroid and not metastatic LN. Patient with excellent response to treatment.
19 F	3.4 cm classic PTC, focal capsular but extensive vascular invasion; minimal ETE; no LN involvement	SPECT-CT confirmed intense uptake in right lateral neck corresponding to lymph node	SPECT-CT improved localization, though no additional treatment was required. Patient with excellent response to therapy.
55 M	4.8 cm PTC, follicular variant; encapsulated; no capsular or vascular invasion; no LN involvement	SPECT-CT identified focal uptake in right posterior pharyngeal wall, questioned as lymph node metastases	SPECT-CT finding proved to be a false-positive finding. Patient with excellent response to treatment.
30 F	Multifocal, diffuse sclerosing variant PTC, extensive LVI, +ETE, N1b, with largest LN 1.2 cm	Iodine avid focus seen in the right upper neck, SPECT-CT identified this an enlarged submental lymph node	SPECT-CT finding proved to be a false-positive finding. Subsequent recurrence identified on left neck and removed surgically. Patient with excellent response to treatment.
56 F	2.1 cm PTC, macroscopic ETE, extensive LVI, +ETE, N1b with largest lymph node 1.0 cm	Planar scintigraphy confirmed area of radiotracer uptake in right neck, SPECT-CT reported suspicious supraclavicular lymph node	SPECT-CT helped with localization. Without further treatment, neck ultrasound 6 months thereafter was negative. Patient with excellent response to therapy.
Case where SPECT-CT proved to be beneficial in addition to planar imaging (*n* = 3)			
33 F	1.2 cm PTC, multifocal w/4 foci; no ETE	Planar scintigraphy identified abnormal pelvic uptake suggesting bone metastases	SPECT-CT helped management, clarifying that pelvic uptake was a false-positive finding. No further treatment provided. Patient with excellent response to therapy and no evidence of disease during follow-up.
44 F	Multifocal PTC, largest 1.5 cm	Planar scintigraphy identified abnormal uptake in the skull	SPECT-CT helped management clarifying that skull uptake was false-positive.
49 F	1.2 cm FVPTC	Planar scintigraphy identified liver uptake concerning for liver metastases	SPECT-CT helped management clarifying that it was false-positive.

ENE, extra-nodal extension; ETE, extra-thyroidal extension; F, female; FVPTC, follicular variant papillary thyroid carcinoma; HT, Hashimoto's thyroiditis; LN, lymph nodel; LVI, lymphovascular invasion; M, male; PTC, papillary thyroid carcinoma; RAI, radioactive iodine treatment; TCVPTC, tall-cell variant papillary thyroid carcinoma; Tg, thyroglobulin.

Separately, a total of 28 of 105 patients (26.7%) in the SPECT-CT cohort were found to have at least one incidental SPECT-CT finding that was non-thyroid-related, as shown in Table 4. All findings led to follow-up recommendations, though none impacted thyroid cancer care.

In total, routine SPECT-CT imaging, in addition to planar scintigraphy led to 3 (2.8%) findings beneficial to thyroid cancer care, 5 (4.8%) findings in which greater precision was provided though did not change management, 28 (26.7%) findings that were incidental, and 3 (2.8%) false-positive findings.

Discussion

The utility and benefits of synergistic SPECT-CT when applied to baseline planar scintigraphy following I-131 therapy have been proposed by many (8, 9, 15, 16), but few data have provided evidence of the broad clinical utility (e.g. risks and benefits) in the real-world setting of thyroid cancer care. Our study provides evaluation of such clinical utility, comparing two consecutive and comparable cohorts differing primarily by the year of their treatment following the institution of routine SPECT-CT imaging from 2015 onward. We confirmed three cases (2.8%) where synergistic SPECT-CT proved beneficial and five (4.8%) where greater precision was obtained. However, SPECT-CT detected 21 non-thyroid-related incidental findings. Together, these data provide insight into the benefits as well as the predicted complexities of implementing such testing into routine practice. These data may allow clinicians to thoughtfully choose which imaging modality if favored in low-risk populations of thyroid cancer patients post-I-131 therapy.

Our data parallels and yet differs from other analyses. In a retrospective analysis of 94 patients with thyroid cancer, Wang reported that SPECT-CT changed the precise localization in 14 of 65 patients with neck uptake, 2 of 31 patients with lung uptake, and 4 of 17 patients with bone uptake. Notable to this article is the extent of advanced disease, as the author also reported that SPECT-CT detected 10 new metastases leading to changes in clinical decision-making for I-131 therapy in 22 of 94 patients as SPECT-CT changed the staging (17). It is possible that our cohort is more representative of typical low-risk thyroid cancer as among 105 patients who underwent post-treatment planar scintigraphy plus SPECT-CT, we only identified 3 new local metastases not seen on planar scintigraphy. Surprisingly, and perhaps unique to our investigation, all were found to be either false-positive or clinically insignificant results and SPECT-CT did not identify any additional new distant metastatic disease. In contrast, we found benefit in only three cases where planar scintigraphy had suggested distant metastases, but SPECT-CT clarified these as false-positive areas of bone uptake but with no ultimate disease.

In the same line with our study were the findings in the retrospective study of Garger *et al*. The authors concluded that SPECT-CT was not required in 85% of 564 subjects as the whole-body scan was able to determine the extent of local residual disease and metastases in nearly all such patients (18). Similarly, Jeong *et al.* reported that SPECT-CT provided additional information in only 8.6% of patients with neck uptake using planar scintigraphy (19). Finally, Avram *et al.* found that pre-ablation SPECT-CT could impact TNM staging (10) as well as initial ATA risk stratification (11). Our data are among the first to investigate the important endpoints of final outcome as well as change in clinical care based on results. Neither were significantly impacted by use of SPECT -CT scanning.

Separate factors associated with SPECT-CT, such as cost and additional radiation exposure, should also be

Table 3 Association between SPECT and final outcome.

	Final outcome		
	No evidence of disease	Persistent disease	*P*
Scintigraphy alone	96	11	0.07
Scintigraphy plus SPECT-CT	85	20	

Table 4 21 Incidental non-thyroid cancer-related findings reported on SPECT-CT scanning in 28 separate patients following I-131 administration.

Renal cyst
Mild dilation of mid to distal appendix
T3 bone island
Atelectasis
Sinusitis
Calcification of aortic valve
Sub-centimeter lung nodule
Nephrolithiasis
Hiatal hernia
Cholelithiasis
Hepatic steatosis
Renal angiomyolipoma
Reactive mediastinal lymph node
Sinus polyp vs cyst
Gynecomastia
Atherosclerosis
Odontogenic disease
Sialoadenitis
Thymic hyperplasia
Emphysema
Congenital rib abnormality

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considered, especially for an illness where analyses have correlated a high cost of thyroid cancer treatment even without SPECT-CT itself (20, 21). The cancer-related financial burden has been reported to be associated with lower quality of life and even increased mortality (22, 23, 24, 25). Notably, in a large study of nearly 500,000 patients with thyroid cancer, psychological financial burden experienced by patients appears greater than for other types of cancers (12). Thus, for many patients with low-risk diseases, it may be reasonable and cost-effective to avoid further intervention or advanced imaging.

We acknowledge several limitations to this study. First, we note that this is a retrospective cohort assessment. However, the two cohorts nonetheless appear logically separated by time as SPECT-CT was implemented. We separately acknowledge that the use of I-131 for thyroid cancer during this decade trended toward application to higher-risk disease. Thus, outside the setting of a randomized controlled trial, precise comparisons between cohorts cannot be assumed based on extent of disease. Nonetheless, AJCC staging was not significantly different between the two cohorts in our study.

In conclusion, performing routine post-therapy SPECT-CT scanning in conjunction with planar nuclear scintigraphy offers some benefit, yet also significant burden of incidental findings, in a typical cohort of thyroid cancer patients with low risk of distant metastases receiving radioactive iodine therapy. SPECT-CT imaging led to some additional findings that were beneficial to thyroid cancer care while also detecting a significant proportion of false and incidental findings usually not impacting an individual's thyroid cancer care.

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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Statement of ethics

This investigation was evaluated and approved by the Mass General Brigham Investigational Review Board.

Author contribution statement

All authors listed in this manuscript contributed to the design of the work and the acquisition and interpretation of data for the work. They all reviewed the manuscript, helped with revision and approved the final version to be published. All authors agree to be accountable of the work. Sara Ahmadi MD and Erik Alexander contributed to data collection and analysis.

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