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Thyroid Neoplasms: Incidental Findings on Extent of Disease Evaluation CT for Other Pediatric Malignancies

William J. Hammond, MD¹, Todd E. Heaton, MD¹, Benjamin A. Farber, MD¹, Usman A. Mahmood, MS², Jill S. Gluskin, MD³, Suzanne L. Wolden, MD⁴, Michael P. La Quaglia, MD¹, Charles A. Sklar, MD⁵, and Anita P. Price, MD³

¹Pediatric Surgical Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, NY, USA

²Department of Medical Physics, Memorial Sloan Kettering Cancer Center, New York, NY, USA

³Department of Radiology, Memorial Sloan Kettering Cancer Center, New York, NY, USA

⁴Department of Radiation Oncology, Memorial Sloan Kettering Cancer Center, New York, NY, USA

⁵Department of Pediatrics, Memorial Sloan Kettering Cancer Center, New York, NY, USA

Abstract

Purpose—We performed a retrospective analysis to evaluate the risk of thyroid cancer in incidental thyroid nodules (ITNs) discovered on CT in patients with a history of pediatric cancer.

Methods—With IRB approval we reviewed the records of pediatric oncology patients age ≥ 21 y with newly detected thyroid nodules on surveillance CT of the neck, chest, chest/abdomen/pelvis, or PET/CT performed between April 2008 and March 2015. Patients with <6 months of follow-up after incidental findings, a history of primary thyroid malignancy, or incomplete records were excluded.

Results—The final cohort (N=68) included 35 females and 33 males (mean age 16.0 ± 4.3 [SD] years) with a mean follow-up time of 3.7 ± 1.9 [SD] years after CT detection of ITN(s). Twenty patients (29.4%) received a follow-up thyroid ultrasound, eleven (16.2%) of whom underwent fine needle aspiration (FNA) for cytopathologic diagnosis. Among these, six (8.8%) underwent thyroid resection, with final pathology demonstrating papillary carcinoma in five (7.4%) and benign pathology in one.

Corresponding Author: Todd E. Heaton, MD, Department of Surgery, Pediatric Surgical Service, Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, New York, NY 10065, Phone 1-212-639-7002/Fax 1-212-717-3373, heatont@mskcc.org.

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Level of Evidence: Level IV, retrospective study with no comparison group

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Conclusions—Despite the low incidence of thyroid nodules and low risk of thyroid malignancy in the general pediatric population, we found a significant rate of malignancy in CT-detected ITNs in our pediatric oncology patients, and recommend ultrasound and FNA of these nodules in this high-risk population.

Keywords

Papillary carcinoma; Thyroid nodule; Children; Adolescents; Incidentaloma; CT; Ultrasound

1. Introduction

Increasing use of CT imaging in the pediatric population has increased the rate of “incidentaloma” findings including thyroid nodules, necessitating guidance on appropriate workup. Survivors of childhood malignancy are a population in whom surveillance CT imaging is believed to outweigh the risk from exposure to ionizing radiation. Incidental thyroid nodules are encountered in this population, but long-term outcomes are unknown. As such, much of the management of incidental thyroid nodules in the pediatric cancer population is deduced from studies of normal adults.

Long-term follow-up studies on childhood cancer survivors demonstrate a clear risk of secondary malignant neoplasms (SMNs). Comparative analysis on the risk of thyroid malignancy using data from The Childhood Cancer Survivor Study (CCSS) cohort versus age, sex, and race matched general population data from the United States Surveillance, Epidemiology, and End Results (SEER) Program indicated a SMN standardized incidence ratio (SIR) of 11.3 for thyroid cancer with a median time to occurrence of 13.3 years after the primary malignancy [1]. In a more focused study, The Late Effects Study Group, followed childhood survivors of Hodgkin lymphoma, and reported a SIR of 32.7 for a thyroid SMN [2]. Compilation of long-term and late effects data has been used to validate a risk model for thyroid SMNs to guide clinician management of childhood cancer survivors [3]. However, extrapolating data from these studies to patients under current treatment protocols is not straightforward as newer chemo- and radiotherapies for childhood cancers increasingly aim to balance toxicity and efficacy.

Across all cancer survivors, increased risk of a SMN is associated with female sex, younger age at diagnosis of primary malignancy, ionizing radiation, and exposure to alkylating agents [4]. A standardized definition of the interval after primary malignancy treatment to SMN does not exist, but common cutoffs include 1 and 5 years [1, 5]. Thyroid SMNs have demonstrated clustering with primary malignancies including: Hodgkin lymphoma (HL), non-Hodgkin lymphoma (NHL), leukemia, neuroblastoma and central nervous system (CNS) tumors, but analyses of associations with more rare childhood cancers lack sufficient statistical power to draw conclusions [2–4, 6]. Radiation exposure is a well-documented hazard for thyroid malignancy [7–10], and among childhood cancer survivors, increased risk of a thyroid SMN is dose-dependent, with maximal risk in the 2000–2499 cGy range and decreasing as doses exceed 3000 cGy [4, 11, 12]. Childhood cancer survivors treated with radiation therapy develop nodules at a rate of 2% annually with a peak incidence occurring 15 to 25 years after exposure [13].

Although the pediatric cancer survivor population is known to be at increased risk of thyroid SMNs, the incidence of these malignancies among thyroid nodules detected incidentally on surveillance imaging in this cohort is unknown. A recent study on a mixed pediatric population comprised of otherwise healthy children and oncology patients reported a 1.4% rate of thyroid incidentalomas on a contrast enhanced CT (CECT) of the chest, but did not evaluate SMNs. In this retrospective study, we evaluated the characteristics and risk of carcinoma in incidental thyroid nodules among pediatric cancer survivors.

2. Patients and methods

2.1 Patients and data collection

With IRB approval, a retrospective review of all pediatric patients (age ≥ 21 yr) who received a CT-based (CT or PET/CT) scan of the neck, chest, or the chest, abdomen and pelvis from April 21, 2008 to March 2, 2015 was performed. All final CT reports were searched using the software Montage™ (Montage Healthcare Solutions, Inc., Philadelphia, PA) for the term: “thyroid.” A total of 421 patients were identified. Patients with less than 6 months of follow-up after incidental finding, incomplete records, a primary diagnosis of thyroid cancer, or a genetic syndrome predisposing the patient to thyroid cancer were excluded. For a patient with multiple surveillance scans, only the initial scan showing a positive finding was included. All CT scans were evaluated by a pediatric radiologist to confirm the presence of thyroid nodule(s).

Cytopathology and surgical pathology data were collected from the electronic medical record. Follow-up from primary malignancy, follow-up from incidental thyroid nodule, and time from primary malignancy diagnosis to diagnosis of the incidental nodule were calculated for each patient.

2.2 CT and PET/CT Imaging Techniques and Evaluation

All imaging was completed on the following CT or PET/CT scanners: LightSpeed 16 or LightSpeed HD750 and LightSpeed Discovery 690 or LightSpeed Discovery STE (GE Healthcare, Milwaukee, WI). All scans were acquired using size and weight based kilovoltage (kVp), pediatric specific tube currents, and reconstructed using 5mm thick slices. The coverage area on diagnostic CT scans was from the frontal sinus to the aortic arch for CT of the neck, top of the shoulders to adrenal for CT of the chest, and top of the shoulders to the pubic symphysis for CT of the chest, abdomen, and pelvis. Area of CT coverage in PET, non-diagnostic CT exams vary with primary malignancy. Appropriate weight-based pediatric contrast dosing was used in scans requiring contrast.

The volume CT dose index (CTDIvol) was recorded from the patient dose records. All CTDIvol data pertain to the 32cm poly (methyl methacrylate) (PMMA) dosimetry phantom. Organ dose software, VirtualDose™ (Virtual Phantoms, Inc., Albany, NY), was used to calculate the dose delivered to the thyroid from CT chest and CT chest, abdomen and pelvis exams. VirtualDose™ consists of a database of organ doses calculated from Monte Carlo (MC) simulations [14]. The MC simulations incorporate a library of 25 anatomically realistic phantoms that represent patients of different ages, body morphology, and sizes. The

phantoms that most closely matched the pediatric patient's age, weight, and height were used to determine thyroid organ dose. The scan range used for organ dose estimation was based on the scan range found in the patient image sets. The CT chest and CT chest, abdomen and pelvis scans partially included the thyroid gland. The average thyroid organ dose from the imaging studies and the expected increase in organ dose if the full thyroid had been included within the scan range were both calculated for each patient.

2.3 Thyroid Ultrasound Techniques and Evaluation

Thyroid ultrasounds were performed on Siemens S2000 scanners using a high frequency 18MHz linear transducer with color Doppler. A pediatric radiologist retrospectively reviewed all ultrasounds and correlated the findings with the final reports. Evaluations documented the number of nodules, size (largest dimension), echogenicity (anechoic, hypo-, iso-, hyperechoic), content (cystic, solid, or mixed), shape (taller than wide or absence of the feature), margin (ill-defined or well circumscribed), intranodular vascularity (absent, mild, moderate, or hypervascular), presence of microcalcifications, and presence of halo sign for each nodule.

2.4 Cytopathology and Pathologic Analysis

FNA specimens were categorized according to The Bethesda System for Reporting Thyroid Cytopathology. Final pathologic staging was performed using the American Joint Committee on Cancer (AJCC) TNM classification system. Patients with papillary thyroid cancer were stratified into The American Thyroid Association (ATA) Pediatric Thyroid Cancer Risk Levels.

2.5 Definitions of Surgical Procedure and Treatment

Patients underwent either a partial or total thyroidectomy. Patients with nodal disease received a central neck dissection (CND, level VI) or CND with lateral neck dissection (levels II, III, IV) depending on the extent of disease.

2.6 Statistical Analysis

Two sample Student's t-tests were used to analyze means. Non-normally distributed values are reported using median and 95% confidence interval and compared using the Wilcoxon signed-rank test. Univariate analysis was completed using Pearson's Chi-square test. Fisher's exact test was employed for small sample size comparisons. All analyses used two-tailed tests with a P-value of <0.05 and were performed using R version 3.2.4 (The R Foundation for Statistical Computing®, Vienna, Austria; www.r-project.org).

3. Results

3.1 Patient characteristics

During the study interval, there were 16,368 CT or PET/CT scans of the neck, chest, or chest, abdomen and pelvis. There were 997 CT studies corresponding to 421 unique pediatric patients for whom "thyroid" was reported on the final CT neck, chest, or chest, abdomen and pelvis readings. We eliminated 353 patients from analysis using the described

selection criteria, leaving 68 patients. Of these, 68 patients (35 females, 33 males; mean age 16.0 ± 4.3 [SD] years, range 3.9–21.0 years) met inclusion criteria with mean follow-up after incidentaloma finding of 3.7 ± 1.9 [SD] years (range 6 months–7.7 years). The most common primary diagnoses for the 68 patients included: Hodgkin lymphoma (n=17; 25%), non-Hodgkin lymphoma (n=13; 19.1%), neuroblastoma (n=7; 10.3%), rhabdomyosarcoma (n=3; 4.4%), desmoplastic small round cell tumor (n=3; 4.4%), osteosarcoma (n=3; 4.4%), and Sertoli-Leydig tumor of the ovary (n=3; 4.4%). Mean age at diagnosis of the primary malignancy among all patients was 13.6 ± 5.4 [SD] years (range: 1 month–20.8 years). Mean follow-up after primary malignancy was 6.1 ± 3.6 [SD] years (range 1.0–16.5 years). The mean time from primary malignancy diagnosis to diagnosis of a thyroid nodule on CT imaging was 2.4 ± 2.8 [SD] years (range: 1 month–14.2 years). Of the 68 patients identified, 37 (54.4%) had a history of radiation therapy, 20 of whom (29.4%) had radiation to the neck. Overall, there were 11 deaths amongst the 68 patients, all attributable to the primary malignancy.

3.2 Thyroid Imaging Findings

Of the 68 patients, 20 (29.4%) had follow-up ultrasound of their thyroid nodule(s) with a median time to ultrasound of 90 days (95% CI: 22–356 days). All ultrasound studies of the thyroid were performed after a CT study. The remaining 48 patients (70.6%) were followed clinically without a thyroid ultrasound, but no justification for foregoing the ultrasound was found. The CT and ultrasound characteristics of the 20 patients who received a follow-up thyroid ultrasound are summarized in Table 1.

3.3 Cytopathology and Pathology Findings

Eleven patients (16.2%) underwent FNA of their thyroid nodule(s) with a median time from diagnosis on CT to FNA of 69 days (95% CI: 9–373 days). Characteristics of patients undergoing FNA are provided in Table 2. Nodule size on ultrasound was, on average, larger in patients having FNA (1.5 ± 0.6 [SD] cm, range 0.7–2.5 cm) than among patients not biopsied (0.8 ± 0.3 [SD] cm, range 0.3–1.3 cm; $P < 0.01$). FNA cytopathology (listed in Table 1) was negative for malignancy in five patients (Bethesda II), atypical lymphoid proliferation in a background of Hürthle cells in one (Bethesda IV), suspicious for malignancy in two (Bethesda V), and positive for malignancy in three (Bethesda VI). Six patients underwent thyroid resection. The median time from incidental finding to resection was 207 days (95% CI: 72–2127 days) and a median time from FNA to resection of 62 days (95% CI: 6–70 days).

3.4 Characteristics of Patients Diagnosed with Thyroid Carcinoma

Final pathology confirmed papillary carcinoma in 5 of the 68 patients (7.4%), each of whom had Bethesda V–VI cytopathology on FNA. The sixth patient who underwent resection was diagnosed with a benign Hürthle cell adenoma. The mean age at resection of thyroid malignancy was 19.2 years (range 16.0–25.2 years), with a mean time from primary malignancy diagnosis to resection of 7.0 years (range 4.2–10.9 years). The primary diagnoses of the 5 patients with thyroid malignancy were Hodgkin lymphoma (n=3), myelodysplastic syndrome-monosomy 7 (n=1), and non-Hodgkin lymphoma (n=1). Four of the 5 patients with papillary carcinoma were male, 3 of the 5 had lymph node involvement,

and one had lung metastases confirmed on separate biopsy. The ATA Pediatric Thyroid Cancer Risk Levels of the 5 patients with thyroid malignancy were: low (n=2), intermediate (n=2), and high (n=1). Two of 3 patients with intermediate or high-risk disease were treated with ^{131}I therapy post-operatively. None of those 3 had any evidence of thyroid malignancy at last follow-up. Mean follow-up after thyroidectomy for patients with papillary carcinoma was 3.4 years (range: 1.5–4.3 years). Subgroup analysis of patients with pathologically confirmed papillary thyroid cancer demonstrated a younger age at primary malignancy (mean=6.9 $\pm$ 3.2 [SD] years), longer follow-up from primary malignancy (mean=10.4 $\pm$ 2.9 [SD] years), and a longer time from primary malignancy to incidental thyroid nodule (mean= 5.3 $\pm$ 2.9 [SD] years) compared to the cohort as a whole (P-values: 0.01, 0.01, 0.02, respectively) as shown in Figure 1. Three of 5 patients (60%) with thyroid malignancy had a history of radiation to the neck with the average dose of 2100 cGy $\pm$ 0 [SD]. There were no instances of thyroid malignancy recurrence in those 5 patients. Common ultrasound features of patients with final pathology of thyroid malignancy included: solid component, mild intranodular vascularity, calcium, halo sign, and taller than wide feature. Figure 2 illustrates the imaging findings in one patient with pathologically confirmed papillary cancer.

4. Discussion

The current ATA Guidelines Task Force on Pediatric Thyroid Cancer and the Children's Oncology Group (COG) Long-Term Follow-Up Guidelines prescribe annual thyroid palpation as the screening method in childhood cancer survivors [13, 15]. The ATA panel recommends neither for nor against the use of routine ultrasound in high-risk children as there are no data on its impact on long-term outcomes [13]. The committees advise ultrasound for cases of a palpable nodule, thyroid asymmetry, and/or cervical lymphadenopathy and FNA for nodules with concerning sonographic features [13, 15]. There are currently no recommendations or data on the workup of incidental thyroid nodules in children undergoing surveillance CT-based imaging for a previous malignancy. Additionally, the ATA Task Force on Pediatric Thyroid Cancer seeks to limit their recommendations to those age $\geq$ 18 years, which is problematic when treating this group of patients, a majority of whom are in late adolescence. Given the appreciable risk of malignancy demonstrated in this study and the absence of guidance, we recommend ultrasound follow-up of thyroid incidentalomas in childhood cancer survivors with FNA for nodules with concerning sonographic features.

A recent study on a mixed pediatric population of healthy patients and oncology patients reported the likelihood of a thyroid incidentaloma being a malignancy on a CECT of the chest was 5.7% (2/35 patients) [16]. Of these 2 cases, one was a thyroid primary malignancy and the other was a metastatic focus of Burkitt lymphoma in a patient with active disease—neither of which represents a SMN. However, this study focuses on patients undergoing CT for surveillance after a primary malignancy and specifically evaluates the risk of thyroid cancer.

In agreement with data from the CCSS, our data suggest that a thyroid SMN is associated with both a younger age at diagnosis and longer follow-up from primary malignancy. In our cohort, there were 5 patients (7.4%) in whom an incidental thyroid nodule was found to be

thyroid cancer. Our study showed earlier detection of the thyroid malignancy compared to larger childhood cancer survivor studies [1, 2, 5]. In our data, larger nodules were more likely to undergo FNA, but the study is underpowered to evaluate ultrasound or CT imaging characteristics predictive of thyroid malignancy. Furthermore, in 22 patients (32.4%) an incidental nodule was discovered within the first 6 months after diagnosis of primary malignancy, and in 30 patients (44.1%) the incidental nodule was discovered within the first year. Given the short interval between primary diagnosis and nodule discovery, we assumed that such thyroid nodules did not result from treatment. A subanalysis of the data excluding these patients resulted in an increased incidence of SMN, from 7.4% to 10.9% (5/46 patients) using a 6-month exclusion and from 7.4% to 13.2% (5/38 patients) using a 1-year exclusion. This subanalysis shows the trend toward increasing incidence of thyroid SMN as patients are further from treatment.

In the literature we reviewed, the protocol for most CTs of the chest did not include imaging of the entire thyroid. Therefore, we evaluated the difference in radiation to the organ if the cephalad limit of the CT chest was changed from the thoracic inlet, which usually images half of the thyroid, to become inclusive of the entire thyroid. If the protocol had been changed to include the entire thyroid, the simulated mean dose increases for the 3–9, 10–16, and 17–20 year-old age ranges would be: 7.7 mGy, 12.2 mGy, 22.5 mGy per scan, respectively. However, these calculated values would be expected to decrease with application of angular tube current modulation and/or organ dose modulation by an amount anywhere between 20% and 28% [14, 17]. Further dose reduction would be expected with scanners equipped with advanced model-based iterative reconstruction technologies.

This is the first study to examine the risk of thyroid carcinoma in a nodule incidentally noted on CT surveillance for another malignancy in the pediatric population. Given the 7.4% risk of thyroid carcinoma in all patients with incidental nodules, increasing to 13.2% if only including patients 1 year out from their primary diagnosis, we believe that these nodules merit further work-up. Many of these patients do not fit into the COG Long-Term Follow-Up or ATA Guidelines Task Force on Pediatric Thyroid Cancer protocols, as they are still on active surveillance for their primary malignancy and most age out of the ATA guidelines before they finish surveillance. While we understand the limitation of this single-center, retrospective data, we think that any nodule >1cm in size discovered in a patient more than 1 year after their diagnosis of their primary malignancy should be evaluated with US, and recommend FNA for nodules with concerning ultrasound characteristics. We further recommend inclusion of the entire thyroid in ongoing surveillance CTs, as the added radiation exposure is relatively small and additional important information can be easily obtained in the same scan.

5. Conclusion

Given the sizable risk of malignancy in thyroid nodules found on surveillance CT in pediatric oncology patients we believe an evaluation with ultrasound and possible FNA is merited. We have proposed preliminary guidelines for evaluation of these nodules and recommend a minor change in the surveillance CT scan protocol, which could increase the

likelihood of detecting thyroid SMNs. Further study with a prospective registry of these patients is warranted to validate these recommendations.

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Abbreviations

AJCC	American Joint Committee on Cancer
ATA	The American Thyroid Association
CCSS	Childhood Cancer Survivor Study
CECT	contrast enhanced CT
CND	central neck dissection
COG	Children's Oncology Group
FNA	fine needle aspiration
SEER	United States Surveillance, Epidemiology, and End Results Program
SIR	standardized incidence ratio
SMN	secondary malignant neoplasm

References

1. Neglia JP, Friedman DL, Yasui Y, et al. Second malignant neoplasms in five-year survivors of childhood cancer: childhood cancer survivor study. *J Natl Cancer Inst.* 2001; 93:618–629. [PubMed: 11309438]
2. Bhatia S, Robison LL, Oberlin O, et al. Breast cancer and other second neoplasms after childhood Hodgkin's disease. *N Engl J Med.* 1996; 334:745–751. [PubMed: 8592547]
3. Kovalchik SA, Ronckers CM, Veiga LH, et al. Absolute risk prediction of second primary thyroid cancer among 5-year survivors of childhood cancer. *J Clin Oncol.* 2013; 31:119–127. [PubMed: 23169509]
4. Meadows AT, Friedman DL, Neglia JP, et al. Second neoplasms in survivors of childhood cancer: findings from the Childhood Cancer Survivor Study cohort. *J Clin Oncol.* 2009; 27:2356–2362. [PubMed: 19255307]
5. Wolden SL, Lamborn KR, Cleary SF, et al. Second cancers following pediatric Hodgkin's disease. *J Clin Oncol.* 1998; 16:536–544. [PubMed: 9469338]
6. Robison LL, Mertens AC, Boice JD, et al. Study design and cohort characteristics of the Childhood Cancer Survivor Study: a multi-institutional collaborative project. *Med Pediatr Oncol.* 2002; 38:229–239. [PubMed: 11920786]
7. Ito M, Yamashita S, Ashizawa K, et al. Childhood thyroid diseases around Chernobyl evaluated by ultrasound examination and fine needle aspiration cytology. *Thyroid.* 1995; 5:365–368. [PubMed: 8563473]
8. Ron E, Lubin JH, Shore RE, et al. Thyroid cancer after exposure to external radiation: a pooled analysis of seven studies. *Radiat Res.* 1995; 141:259–277. [PubMed: 7871153]

9. Ronckers CM, Sigurdson AJ, Stovall M, et al. Thyroid cancer in childhood cancer survivors: a detailed evaluation of radiation dose response and its modifiers. *Radiat Res.* 2006; 166:618–628. [PubMed: 17007558]
10. Schneider AB, Bekerman C, Leland J, et al. Thyroid nodules in the follow-up of irradiated individuals: comparison of thyroid ultrasound with scanning and palpation. *J Clin Endocrinol Metab.* 1997; 82:4020–4027. [PubMed: 9398706]
11. Bhatti P, Veiga LH, Ronckers CM, et al. Risk of second primary thyroid cancer after radiotherapy for a childhood cancer in a large cohort study: an update from the Childhood Cancer Survivor Study. *Radiat Res.* 2010; 174:741–752. [PubMed: 21128798]
12. Veiga LH, Bhatti P, Ronckers CM, et al. Chemotherapy and thyroid cancer risk: a report from the childhood cancer survivor study. *Cancer Epidemiol Biomarkers Prev.* 2012; 21:92–101. [PubMed: 22028399]
13. Francis GL, Waguespack SG, Bauer AJ, et al. Management guidelines for children with thyroid nodules and differentiated thyroid cancer. *Thyroid.* 2015; 25:716–759. [PubMed: 25900731]
14. Ding A, Gao Y, Liu H, et al. VirtualDose: a software for reporting organ doses from CT for adult and pediatric patients. *Phys Med Biol.* 2015; 60:5601–5625. [PubMed: 26134511]
15. Children's Oncology Group. Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers. Version 4.0. Monrovia, CA: Children's Oncology Group; 2013. <http://www.survivorshipguidelines.org/pdf/LTFUResourceGuide.pdf> [Accessed December 15, 2016]
16. Baez JC, Zurakowski D, Vargas SO, et al. Incidental thyroid nodules detected on thoracic contrast-enhanced CT in the pediatric population: prevalence and outcomes. *AJR Am J Roentgenol.* 2015; 205:W360–W365. [PubMed: 26295673]
17. Dixon MT, Loader RJ, Stevens GC, et al. An evaluation of organ dose modulation on a GE Optima CT660-computed tomography scanner. *J Appl Clin Med Phys.* 2016; 17:5724. [PubMed: 27167255]

Figure 1.

Analysis of all patients (N=68) and in the subgroups undergoing FNA (n=11) and with a pathologic diagnosis of thyroid cancer (n=5). ITN = incidental thyroid nodule, NS = not statistically significant, P-value <0.05 statistically significant.

Figure 2.

Papillary carcinoma in 16-year-old male (patient 4 in Table 1) noted in surveillance imaging for Hodgkin lymphoma. (A) Axial contrast enhanced CT neck demonstrates a well-defined hypodense lesion in the right lobe of the thyroid. (B) Transverse sonographic image of right lobe of the thyroid shows a circumscribed solid nodule with taller than wide feature and punctate foci representing calcification (arrow). (C) Longitudinal ultrasound image of the right lobe of the thyroid demonstrate halo sign (arrows). (D) Longitudinal ultrasound image with Doppler demonstrating mild intranodular vascularity.

Characteristics determined on initial CT and ultrasound in follow-up of thyroid nodules incidentally detected on extent of disease CT imaging, FNA cytopathology, and final surgical pathology diagnosis (n=20).

Table 1

Patient No.	No. of Nodules	Size ^a (cm)	CECT Characteristics			Ultrasound Characteristics						FNA Cytopathology	Final Pathology
			Margin	Radiodensity	Taller* Than Wide	Margin	Content	Calcium	Echogenicity ^b	Halo Sign	Intranodular Vascularity	Taller* Than Wide	
1	Single	2.0	Well defined	Hypodense	No	C	Solid	Yes	Hypoechoic	Yes	Mild	No	Papillary carcinoma, sclerosing variant, 10/10 LN pos.
2	Single	0.8	Well defined	Hypodense	Yes	C	Solid	Yes	Isoechoic	Yes	Mild	Yes	Papillary carcinoma, classic type
3	Single	1.6	Well defined	Hypodense	Yes	C	Solid	No	Hypoechoic	Yes	Moderate	No	Hürthle cell adenoma (benign)
4	Multiple (2)	1.0	Well defined	Hypodense	No	C	Solid	Yes	Hypoechoic	Yes	Mild	Yes	Papillary carcinoma, classic type, 14/34 LN pos. ^{##}
5	Multiple (5)	1.4	Well defined	Hypodense	Yes	C	Solid	No	Isoechoic	Yes	Mild	Yes	Papillary carcinoma, follicular variant (2 foci)
6	Multiple (2)	0.7	Well defined	Hypodense	Yes	C	Solid	Yes (poss. colloid)	Hypoechoic	No	Mild	Yes	Papillary carcinoma, solid variant, 1/1 LN pos.
7	Single	1.5	Well defined	Hypodense	Yes	C	Mixed	Yes (prob. colloid)	Hyperchoic (s) Anechoic (c)	No	Hyper	No	NA
8	Single	2.5	Heterogeneous	Hypodense	Yes	C	Mixed	No	Isoechoic (s) Anechoic (c)	No	Moderate	No	NA
9	Single	1.9	Well defined	Isodense	No	C	Mixed	Yes	Isoechoic (s) Anechoic (c)	No	Moderate	No	NA
10	Single	1.1	Well defined	Isodense	No	C	Solid	No	Isoechoic	Yes	Mild	No	NA
11	Multiple (>5)	2.0	Well defined	Hypodense	No	C	Mixed	No	Isoechoic (s) Anechoic (c)	Yes	Mild	No	NA
12	Multiple (2)	0.7	Well defined	Hypodense	No	I	Solid	No	Hyperchoic	No	Mild	No	NA
13	Single	0.7	Well defined	Hypodense	No	C	Solid	No	Isoechoic	Yes	Avascular	No	NA
14	Multiple (<5)	0.7	Well defined	Hypodense	Yes	I	Cystic	No	Hypoechoic	No	Avascular	No	NA
15	Multiple (2)	0.8	Well defined	Hypodense	Yes	C	Cystic	No	Anechoic	No	Avascular	No	NA
16	Single	1.0	Well defined	Hypodense	No	C	Cystic	No	Anechoic	No	Avascular	No	NA
17	Multiple (3)	0.9	Well defined	Hypodense	No	C	Cystic	No	Anechoic	No	Avascular	No	NA
18	Multiple (>5)	1.0	Well defined	Hypodense	No	C	Mixed	No	Isoechoic (s) Anechoic (c)	No	Avascular	No	NA
19	Multiple (<5)	1.3	Ill defined	Hypodense	No	I	Mixed	No	Isoechoic (s) Anechoic (c)	No	Avascular	No	NA
20	Multiple (2)	0.3	Well defined	Hypodense	No	C	Cystic	No	Anechoic	No	Avascular	No	NA

Note—NA= not applicable because FNA or surgical resection were not performed. The number of nodules, if less than or equal to 5, is specified in parentheses.

^aIn patients with multiple nodules, the size of the largest nodule is listed. Margin status: C = circumscribed, I = Ill-defined.

^bIn nodules with mixed content, echogenicity of solid (s) and cystic (c) components. LN = lymph node in patients with metastatic disease.

^{##}patient with metastatic disease to lung.

Table 2

Patients undergoing FNA of thyroid nodule(s) incidentally detected on extent of disease CT imaging. Mean $\pm$ standard deviation, and range.

	Lesions Not Biopsied (n=57)	Lesions Biopsied (n=11)	P-value*
Age at ITN (y)	15.8 $\pm$ 4.6 [3.9–21.0]	17.0 $\pm$ 2.0 [14.2–20.2]	0.19
Age at primary cancer diagnosis (y)	14.2 $\pm$ 5.1 [0.1–20.8]	10.7 $\pm$ 6.0 [2.6–19.6]	0.10
Sex (Male:Female)	26:31	7:4	0.27
Nodule size on ultrasound (cm)	0.8 $\pm$ 0.3 [0.3–1.3]	1.5 $\pm$ 0.6 [0.7–2.5]	<0.01
History of radiation to neck	17	3	1.00
Radiation dose to neck (cGy)	2585 $\pm$ 1458 [1200–6900]	2100 $\pm$ 0	0.58

* P<0.05 is statistically significant.