Increased Risk of Second Primary Malignancy in Pediatric and Young Adult Patients Treated with Radioactive Iodine for Differentiated Thyroid Cancer

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Introduction: The long-term sequelae of radioactive iodine (RAI) for differentiated thyroid cancer (DTC) in pediatric and young adult patients are not well-defined. Epidemiologic analyses of second primary malignancy (SPM) risk have only been performed in the adult population. Existing data are limited to case series with limited follow-up. The objective of this study was to analyze the elevated risk of SPM attributable to RAI in young patients treated for DTC.

Methods: Population-based analysis of 3850 pediatric and young adult patients (<25 years old) undergoing treatment with surgery with/without RAI for DTC, followed in the Surveillance, Epidemiology, and End Results cancer registry (1973–2008), equating to 54,727 person-years at risk (PYR). The excess risk of SPM was calculated relative to a reference population and expressed as standardized incidence ratio (SIR) and excess absolute risk (EAR) per 10,000 PYR. Excess risk was compared in RAI-treated and non-RAI-treated patients.

Results: A total of 1571 patients (40%) received RAI. The percentage of patients treated with RAI increased over time, from 4% in 1973 to 62% in 2008 ($p < 0.001$). Among patients who received RAI, 26 SPMs were observed, and 18.3 were expected. The relative risk of SPM at any site was significantly elevated ($SIR = 1.42$), corresponding to 4.4 excess cases per 10,000 PYR. SPM risk was not elevated in the non-RAI-treated cohort ($SIR = 1.01$, $EAR = 0$). Patients treated with RAI were at dramatically elevated risk for development of a salivary malignancy ($SIR = 34.1$), corresponding to 1.7 excess cases per 10,000 PYR. The risk of leukemia in RAI-treated patients was elevated ($SIR = 4.0$, $EAR = 0.9$) but did not reach statistical significance. There was no elevated risk of salivary cancer or leukemia in the non-RAI-treated cohort.

Conclusions: Pediatric and young adult patients who receive RAI for DTC experience an elevated risk of SPM, mainly salivary gland cancer. These risks appear to be only slightly higher than in adult patients. Over a decade, approximately 1 in 227 RAI-treated patients will develop an SPM, and 1 in 588 RAI-treated patients will develop a salivary cancer, attributable to RAI. Because the expected survival time for young DTC patients is long, it is critical to weigh the benefits of RAI carefully against the small, but real, increase in SPM risk.

Introduction

THYROID CANCER IS UNCOMMON in children and young adults, with only 2% of cases occurring in patients younger than 20 years of age (1). This corresponds to an incidence in the United States of 1 in 200,000 children and young adults (1). As in adults, the vast majority of thyroid cancers are of papillary histology (85%), with a minority of cases comprising follicular (10%) and medullary (5%) histologies (1).

In contrast to adults, pediatric thyroid cancer patients are more likely to present with advanced stage disease. Young

patients more frequently present with nodal metastases (46–78%), distant metastases (6–8%), and extrathyroidal extension (18%) (1,2). Despite the tendency to present with more advanced disease, metastatic disease is usually radioiodine avid. The rate of mortality from thyroid cancer in children and young adults is low—<2% (3). This is likely attributable to more favorable biologic behavior, as well as generally high iodine avidity of tumor cells.

The use of radioactive iodine (RAI) therapy for regional and distant metastases is usually effective in pediatric patients, and partial or complete clinical responses are observed

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in most patients treated with RAI. Demidchik *et al.* observed durable complete responses in 29% of young patients with metastatic differentiated thyroid cancer (DTC) treated with RAI (4). However, in pediatric patients with thyroid cancer who do not have distant metastases, the evidence for the benefit of routine adjuvant (postoperative) RAI is unclear and limited to data drawn from small retrospective analyses. Because disease-specific survival is excellent in children and young adults treated for DTC—approximately 98% at 40 years—it is difficult to identify a clear survival benefit associated with the routine administration of postoperative RAI for all cases of DTC (2,3). The published literature is inconsistent with respect to the efficacy of RAI therapy on reducing the risk of recurrence in young patients with DTC (2,5–8).

As with any intervention, it is critical to quantify risk and benefit as accurately as possible. There are well-described toxicities of RAI, most of which are limited, but late effects do occur in a subset of patients, including chronic sialadenitis, oligospermia, and ovarian failure (9,10). Most concerning, in studies of adult patients, the use of RAI has been associated with an excess risk of development of second primary malignancies (SPMs). Rubino *et al.* calculated the excess risk of SPM associated with RAI as 27%, a figure that escalates with higher doses of RAI (10). We have previously reported that an excess second cancer would be observed in approximately 1 in every 200 adult patients with DTC followed for a decade after treatment with RAI (11).

The risks of SPM after treatment with RAI have not been well-defined in the pediatric and young adult population due to the limited statistical power available in the necessarily small cohorts of this uncommon cancer. There is reason to speculate that the risk of SPM due to RAI may be higher in young patients compared to adults due to the increased sensitivity to radiation of cells in younger patients and the longer life-span in which an SPM may be diagnosed. Here, we analyzed data relating to the use of postoperative RAI in thyroid cancer patients younger than 25 years old in the United States, describing utilization trends over time and analyzing the excess risk of SPM associated with RAI use. Data are drawn from a population-based cohort recorded in a U.S. national cancer registry in which patients are actively followed after cancer treatment for the development of SPMs.

Materials and Methods

Data sources

Data on thyroid cancer incidence, patient age, tumor characteristics, and treatment details are from the National Cancer Institute (NCI) Surveillance, Epidemiology, and End Results (SEER) program. Started in 1973, this is a population-based cancer registry that has grown to now capture cancers diagnosed in 28% of the U.S. population.

SEER collects details on demographics, tumor characteristics, therapy, and survival of cancer patients. RAI therapy is recorded if it is received as part of the initial course of cancer-directed therapy, generally within one year of surgery. Strict quality control is an integral part of the SEER program (12–15). Because SEER is a de-identified data set, the NCI does not require institutional review board oversight; a data use agreement was signed. The SEER 17 data set, capturing new

diagnoses from 1973–2008, was accessed using SEER*Stat, release 7.1.0 (July 2012; NCI Division of Cancer Control and Population Sciences, Bethesda, MD).

Definitions

The SEER 17 registry was queried for individuals who had initial treatment at 0–24 years of age for a DTC, and had no prior history of other cancer. DTC included papillary and follicular thyroid cancer histologies, defined as International Classification of Diseases for Oncology, third edition histology codes 8050, 8052, 8130, 8260, 8290, 8330–8332, 8335, 8340–8344, 8450, and 8452. Additional parameters analyzed were age, sex, year of diagnosis, tumor size, presence of extrathyroidal extension, extent of disease (defined using SEER historic staging as local, regional or distant), nodal status, and administration of RAI.

There were 3850 actively followed patients who presented at younger than 25 years of age with DTC. A total of 213 patients (5.5%) were excluded due to incomplete RAI data. The cohort with available data encompassed 54,727 total person-years at risk (PYR), and median follow-up time of 15.5 years. The extent of disease data have been expanded several times during the SEER program, such that nodal and distant metastasis statuses were available for 3536 patients. Information on tumor size has been recorded consistently since 1983 and was available for 2950 patients. The SEER program defines patients as N0 based on pathologic criteria, or clinical and radiographic criteria if a lymph node dissection was not performed.

Risk of SPM

For this study, a SPM was defined as any nonthyroid cancer (solid or hematologic) arising in any of 194 body sites that developed more than six months after the diagnosis of DTC. The definition of SPM in SEER data is according to NCI-modified Warren and Gates criteria (16,17).

The risk of SPM is expressed as excess risk beyond the expected number of SPM. The number of expected cancers is calculated in a reference noncancer cohort with matched age, sex, race (as defined by SEER), and time period. Excess SPM risk is calculated for both RAI-treated and non-RAI-treated individuals, and is expressed in both relative and absolute terms. Relative risk increase is expressed as the standardized incidence ratio (SIR), which is the relative increase in risk of SPM compared to the reference cohort (18,19). The SIR is similar to a risk ratio, defined as the ratio of observed to expected cancers. Absolute risk increase is expressed as the excess absolute risk (EAR). It is calculated as the excess (observed – expected) number of second malignancies in patients per 10,000 PYR (20).

Excess risk figures, both SIR and EAR, were calculated and compared in RAI-treated and non-RAI-treated patients. SPM sites were then filtered to include those with a SIR > 1.0 in only the RAI-treated cohort to identify SPMs putatively associated with the administration of RAI. SIR confidence intervals were calculated using Byar's approximation to the Poisson distribution. The statistical power to detect an elevated SPM in RAI-treated patients was calculated based on the Poisson rate in the reference cohort, and 17,505 PYR in the RAI-treated cohort. For any cancer type, the sample size of RAI-treated patients had 80% power to detect a SIR of 1.9

at one-sided $\alpha=0.05$. For a less common cancer (leukemia), the cohort had 80% power to detect a SIR of 11.

Of note, undercounting of RAI administration is possible, due to two possible sources of misclassification in SEER data. First, prior to 1987, RAI therapy was routinely coded as “other radiation,” which could include other forms of radiation such as brachytherapy. However, since brachytherapy is rarely used in thyroid cancer patients, and since 1988 there have been no cases of “other radiation” since the RAI category was introduced, these cases of “other radiation” prior to 1987 were categorized as RAI. Second, delayed administration of RAI may not be reliably captured; patients are not specifically followed for RAI use after the first postoperative year. In both instances, these possible misclassification errors would have conservative effects on the analyses, in that they would attenuate the differences between groups, and therefore understate the excess risk of SPM attributed to the RAI-treated cohort.

In the analysis of RAI utilization trends, rates were regressed over time using linear and polynomial least squares regression models. Survival was analyzed using the Kaplan–Meier method. Statistical analyses were performed using the SAS statistical software package (v9.2; SAS Institute, Inc., Cary, NC).

Results

A total of 3637 pediatric and young adult patients were identified who were diagnosed with DTC at younger than 25 years of age, between 1973 and 2008, and who did not have a prior diagnosis of any cancer. These patients were actively followed for the development of a SPM for a median follow-up time of 15.5 years—in total 54,727 PYR.

The majority of pediatric and young adult patients presented at 15–24 years of age: 266 patients (7.3%) were diagnosed with DTC at younger than 15 years old, and no patients younger than one year of age were diagnosed with DTC. Across the United States during 1973–2008, the incidence of thyroid cancer per 100,000 population was 0.1 for patients 5–9 years old, 0.4 for patients 10–14 years old, 1.6 for patients 15–19 years old, and 3.8 for patients 20–24 years old.

The majority of thyroid cancers (82.2%) in pediatric and young adult patients measured >1 cm in size. At presentation, 43.9% of patients had nodal metastases, and 4.7% of patients had distant metastases. At the time of pathologic

analysis, extrathyroidal extension was identified in 15.5% of tumors. Patient and tumor characteristics are detailed in Table 1.

A total of 1587 pediatric and young adult patients (43.6%) received postoperative RAI. As detailed in Table 1, RAI use was more common in younger patients and patients with larger tumors, nodal metastases, distant metastases, and extrathyroidal extension.

The percentage of young patients receiving postoperative RAI has increased over time, rising from 4% in 1973 to 62% in 2008 ($p<0.001$; Fig. 1). During this time period, the proportion of thyroid cancers with high-risk features declined. In 1983–1987, microcarcinomas constituted 11% of diagnosed cancers, increasing to 18% in 2004–2008. Larger tumors measuring ≥ 4 cm comprised 25% of patients in 1983–1987, and decreased to 19% in 2004–2008. The proportion of patients presenting with nodal metastases decreased from 47% in 1983–1987 to 39% in 2004–2008. The proportion of patients with distant metastases has not changed over time, ranging between 4.5% and 5.0%.

Overall survival and disease-specific survival rates were comparable among patients who were treated with RAI and those who were not. Overall survival at 20 years was 98.5% [CI 97.5–99.2] among RAI-treated patients, and 97.3% [CI 96.4–98.0] among non-RAI-treated patients. Disease-specific survival at 20 years was 99.7% [CI 98.8–99.9] among RAI-treated patients, and 99.9% [CI 99.6–99.9] among non-RAI-treated patients. These rates have been similar over time, with patients diagnosed in 1973–1981 experiencing a 20-year disease-specific survival of 99.7% [CI 99.0–99.9], and patients diagnosed in 2000–2008 experiencing a 20-year disease-specific survival of 99.8% [CI 99.5–99.9]; Fig. 2).

As RAI use has become more common over time, the relative risk of developing an SPM has also increased in parallel. For young patients diagnosed with DTC in 1973–1981, a period in which fewer than 20% received postoperative RAI, the risk of developing an SPM was not elevated: SIR 0.92 [CI 0.66–1.25]. In contrast, for young patients diagnosed in 1992–2008, the period in which more than 20% received RAI, the risk of SPM was elevated with a SIR of 1.36 [CI 1.00–1.78]; Fig. 2).

Examining patients treated with RAI in all years (1973–2008; $n=1486$ actively followed patients), a total of 26 SPMs were observed, and 18.3 would be expected in a comparable noncancer reference population. This represents a SIR of 1.42 [90% CI 1.00–1.97], $p=0.037$ for RAI-treated patients,

TABLE 1. PATIENT AND TUMOR CHARACTERISTICS

	<i>All patients</i>	<i>RAI-treated</i>	<i>No RAI</i>	<i>p-Value</i>
Number of patients	3637 (100%)	1587 (44%)	2050 (56%)	
Age 0–14 years	266 (7%)	133 (50%)	133 (50%)	0.035
Age 15–24 years	3371 (93%)	1454 (43%)	1917 (57%)	
Tumor ≤ 1 cm	434 (18%)	159 (37%)	275 (63%)	<0.0001
Tumor > 1 cm	2011 (82%)	1114 (57%)	867 (43%)	
Nodal metastases	1569 (44%)	897 (57%)	672 (43%)	<0.0001
Extrathyroidal extension	415 (16%)	272 (67%)	143 (34%)	<0.001
Distant metastases	166 (4.7%)	114 (69%)	52 (31%)	0.047

Univariate comparisons made with the chi-squared test. Data from the Surveillance, Epidemiology, and End Results cancer registry, July 2012.

RAI, radioactive iodine.

FIG. 1. Trend in the use of radioactive iodine therapy in pediatric and young adult patients (age <25 years) with differentiated thyroid cancer from 1973 to 2008. The trend line reflects polynomial least squares regression line with best fit ($r^2=0.92$; $p<0.001$). Data from the Surveillance, Epidemiology, and End Results cancer registry, July 2012. RAI, radioactive iodine.

indicative of a 42% excess relative risk of SPM. In comparison, the SIR for non-RAI-treated patients was 1.01. In absolute terms, this represents an EAR of 4.4 excess cases per 10,000 PYR. In other words, one excess SPM would be observed in every 227 RAI-treated patients followed over a decade.

Increased risk of SPM in patients who received RAI

Excess second primary cancers occurring in patients treated with RAI, but not in patients not receiving RAI, comprised three cancer types (Fig. 3). These were mostly salivary cancers, and smaller numbers of leukemias and renal cancers. A total of three salivary gland cancers were observed, and 0.9 were expected, corresponding to a SIR of 34.12 ([90% CI 9.1–69.9], $p=0.0007$). The EAR was 1.66 per 100,000 PYR, or one excess salivary SPM for every 588 RAI-treated patients followed over a decade. The median latency for the development of a second cancer in the salivary gland was 10 years. Two of the cases were mucoepidermoid

cancers and one was an acinic cell carcinoma. Two of the salivary cancers were localized, and one had distant metastases at the time of presentation. No patients had died of salivary cancer at most recent follow-up.

Smaller numbers of excess SPM cases did not reach statistical significance for leukemias and kidney cancers. Two leukemias (one acute myeloid leukemia [AML] and one chronic myeloid leukemia [CML]) were observed, and 0.5 were expected, corresponding to a SIR of 3.98 ([90% CI 0.7–9.5], $p=0.09$) and an EAR of 0.86 per 100,000 PYR. The median latency for the development of leukemia was 10 years, and one patient died of AML. One renal cancer was observed, and 0.32 were expected, corresponding to a SIR of 3.09 ([90% CI 0.2–9.4], $p=0.27$) and an EAR of 0.39 per 100,000.

Excess risks in younger (age ≤ 18 years) members were compared to older (age 19–24 years) members of the RAI-treated cohort. Due to small numbers in these subsets, statistical power was limited, and observed differences were not statistically significant. The risk of SPM at any site was higher in patients ≤ 18 years old (SIR=1.85 vs. 1.26, $p=0.39$), a difference that appeared most pronounced for salivary cancers (SIR=76.00 vs. 16.67, $p=0.76$). However, these sample sizes were small, and the differences were not statistically significant.

SPM risk in patients who did not receive RAI

SPM risk was not elevated in the non-RAI-treated cohort. Fifty-eight cases of SPM were observed, and 57.8 were expected, corresponding to a SIR of 1.01 [CI 0.76–1.3] and an EAR of 0. There was no elevated risk of salivary cancer or leukemia in the non-RAI-treated cohort.

Discussion

The use of adjuvant RAI therapy in patients with thyroid cancer is known to be associated with an escalated risk of SPMs. This risk has been quantified in several large studies of adult patients. Risks have not been well-defined in the pediatric population due to the relative rarity of this cancer in this population. Given that children and young adults are significantly more sensitive to radiation-induced carcinogenesis,

FIG. 2. Comparison of pediatric and young adult patients (age <25 years) treated for DTC in an early (1973–1981) and later (2000–2008) time period in the United States, focusing on (A) the percentage of patients receiving treatment with RAI, (B) the 20-year DSS, and (C) the relative risk of developing an SPM. DTC, differentiated thyroid cancer; DSS, disease-specific survival; SPM, second primary malignancy.

FIG. 3. The risk of SPM in pediatric and young adult patients (age <25 years) treated for DTC, with or without RAI therapy. SIRs of SPM in RAI-treated patients were elevated for cancers arising in all sites (1.42), kidney (3.09), leukemia (3.98), and salivary gland (34.12). SIR, standardized incidence ratio.

and have a longer remaining life-span in which SPMs may develop, it has been hypothesized that the risks of SPM may be higher in young patients (21–23).

Here, we analyzed data relating to the use of postoperative RAI in 3637 thyroid cancer patients younger than 25 years old, describing utilization trends over time and analyzing the excess risk of SPM associated with RAI use. Data are drawn from a national cancer registry in which patients are actively followed after cancer treatment for the development of SPMs. We report a dramatic increase in the utilization of RAI in young patients with DTC, corresponding to an escalating risk of SPM development.

Between 1973 and 2008, the percentage of pediatric and young adult DTC patients receiving postoperative RAI treatment increased by a factor of 15, from 4% to 62%. In parallel, there has been a contemporaneous increase in the incidence of SPM among pediatric and young adult DTC patients, with a SIR rising over time from 0.92 to 1.32. This indicates that as RAI use has become more common, the diagnosis of DTC in young patients has now become associated with a risk of developing a second cancer, and that this risk, in relative terms, is now 32% more than a comparable person with no history of cancer.

This increased risk of SPM was only observed among patients treated with RAI (SIR = 1.42). Patients who did not receive RAI have not experienced an increased risk of SPM (SIR = 1.01). Over the period of the study, patients who received RAI experienced a significantly increased risk of developing salivary carcinoma (SIR = 34.12, $p = 0.0007$), and a statistically nonsignificant increase in the incidence of leukemia (SIR = 3.98, $p = 0.09$). Of the three patients who developed salivary gland cancer, one developed distant metastases. One of two leukemia patients died of disease. Overall, the excess risks of SPM in young patients were found to be similar to—or slightly increased compared to—those observed in adults. We have previously reported that adult patients have an excess risk of SPM associated with RAI treatment, with a SIR of 1.2 for all cancer types, and a SIR of 3.8 for salivary cancer (11). RAI concentrates in the salivary glands, can exert bone marrow toxicity, and is excreted by the kidneys. An increased risk of SPM was observed in these sites, in both this study and in a previous study of adult patients (11). This is likely due to expression of the

sodium–iodide symporter (NIS) in salivary ductal cells and other sites (24).

An important caveat concerning these data is that when studying second primary cancers, it is most informative to consider both relative and absolute measures of excess risk. In adults, the use of postoperative RAI is associated with a 20–30% excess *relative* risk of developing a SPM. These increased risks are associated with solid tumors, salivary gland carcinomas, and leukemia (10,11,25). However, the *absolute* excess risks are generally low—approximately 0.5% over 10 years. Results in the cohort of children and young adults were similar, in that one excess case of cancer would be observed for every 227 RAI-treated patients followed over a decade (0.44%). An excess case of salivary cancer would be expected in 1 of every 588 RAI-treated patients over a decade. The risk of leukemia was increased fourfold in relative terms. However, the absolute risk is low, as only two cases were observed in 1486 patients (17,505 person-years under surveillance), compared to 0.5 that would be expected to develop in a comparable population, translating to an excess of only 1.5 cases. Therefore, these data indicate that the risks of SPM in young patients treated with RAI are not substantially different from the risks in adult patients.

A limitation of this study, as with any study of pediatric thyroid cancer, is limited statistical power. Although the use of a high-quality national cancer registry provided the largest cohort to date of patients with DTC of young age, the available cohort of RAI-treated patients with active follow-up was 1486 patients. This provided statistical power to identify a doubling of SPM risk reliably. For less common cancer types such as leukemia, this cohort was only powered to identify a 10-fold increase in SPM risk reliably (see Methods). While the risk of SPM did appear to trend higher in a younger subset (age ≤ 18 years), the differences were not large, and should be interpreted with caution due to limited statistical power.

Since RAI use is only coded if given within a year of surgery, it is possible that some patients in the “non-RAI” group may indeed have ultimately received RAI at some point in their treatment at a later date. This misclassification bias would be a conservative bias in that it would tend to attenuate the difference between the RAI and non-RAI groups. Because RAI dose is not recorded in SEER, an association between dose and SPM risk could not be examined.

RAI is likely to offer benefit for some young patients with well-differentiated follicular-derived thyroid cancers. In young patients, DTC metastases tend to be more iodine-avid and therefore more likely to respond to RAI treatment. However, the benefit of routine adjuvant RAI treatment is unknown for pediatric and young adult patients with intermediate risk disease, such as patients presenting with large thyroid cancers or low-volume neck nodal metastases. In adult patients, the American Thyroid Association guidelines now advise “selective use” of RAI for this risk group (26). Of five published retrospective series of adjuvant RAI use in young patients, with cohort sizes ranging from 170 to 566 patients, no studies have demonstrated a survival benefit, and the majority (four of five) have demonstrated no decrease in the risk of recurrence (2,5–8).

The risks of RAI include often-transient conditions such as nausea and vomiting, sialadenitis, xerostomia, xerophthalmia,

ovarian failure, oligospermia, and bone marrow suppression. Pulmonary fibrosis can also occur, and the risk of SPM must also be considered.

In adults, SPMs occurring after RAI therapy for DTC have been reported to occur as various types of solid tumors, including salivary gland, bone, soft tissue, and colorectal cancers, as well as leukemia (10,25,27,28). In a meta-analysis, Sawka *et al.* estimated that the increased risk of SPM due to RAI is 1.19 in relative terms, and approximately 1% in absolute terms (27).

Data in pediatric and young adult patients are more limited. Most studies have been too limited in size to measure excess risks of SPM effectively, based on cohorts of 60–350 patients (25,29,30). Hay *et al.* from the Mayo Clinic reported the largest retrospective experience of pediatric patients with thyroid cancer (2). Of 215 patients younger than 21 years of age with thyroid cancer, only two died of thyroid cancer (2). At 30–50 years of follow-up, the leading cause of mortality (68%) was SPM (2). Of the patients who died, 73% had received RAI (2).

In this study, a population-based cohort of 3637 pediatric and young adult patients was used to demonstrate elevated risks of SPM after treatment with RAI in young patients. The three sites at potentially elevated risk included organs known to concentrate radioiodine—the salivary glands and the kidneys—as well as leukemia, reflecting radiation exposure to the bone marrow. The increase in risk was largest and only statistically significant for the salivary glands. Overall, absolute increases in risk were low, with 1 of 227 patients followed over a decade developing a second cancer.

It is critical to weigh risks and benefits of RAI therapy carefully in young patients. This is a decision that needs to be considered in light of both patient and tumor characteristics on a case-by-case basis. In young patients with distant metastases or high-volume, extensive nodal metastases that are likely to be iodine-avid, the benefits of RAI therapy probably outweigh the risks of SPM described here. However, in many cases, such as patients with intrathyroidal, node-negative tumors, or patients with low-volume central compartment nodal micrometastases, who have an excellent long-term prognosis and low risk of locoregional recurrence, the risks of developing SPM may outweigh the minimal benefits of RAI therapy. The American Thyroid Association DTC guidelines have provided useful guidance on the benefits of RAI based on risk group. In adults, the routine use of RAI therapy for all patients with DTC is no longer justifiable. It is suggested that these guidelines are also a useful starting point when carefully weighing the risks and benefits of RAI therapy in young patients with DTC, most of whom have excellent thyroid cancer-specific survival and many years in which to develop a radiation-induced malignancy.

Author Disclosure Statement

The authors of this manuscript have no commercial or competing financial interests to disclose.

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