

ACR Appropriateness Criteria® Thyroid Disease

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Abstract

There are a wide variety of diseases that affect the thyroid gland ranging from hyperplastic to neoplastic, autoimmune, or inflammatory. They can present with functional abnormality or a palpable structural change. Imaging has a key role in diagnosing and characterizing the thyroid finding for management. Imaging is also essential in the management of thyroid cancer.

The American College of Radiology Appropriateness Criteria are evidence-based guidelines for specific clinical conditions that are reviewed annually by a multidisciplinary expert panel. The guideline development and revision include an extensive analysis of current medical literature from peer reviewed journals and the application of well-established methodologies (RAND/UCLA Appropriateness Method and Grading of Recommendations Assessment, Development, and Evaluation or GRADE) to rate the appropriateness of imaging and treatment procedures for specific clinical scenarios. In those instances where evidence is lacking or equivocal, expert opinion may supplement the available evidence to recommend imaging or treatment.

Key Words: Appropriateness Criteria, Appropriate Use Criteria, AUC, Hyperthyroidism, Medullary, Papillary, Thyroid, Thyroid malignancy, Thyroid nodule

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Disclaimer: The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists, and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

Variant 1. Palpable thyroid nodule. Not goiter. Euthyroid. Initial imaging.

Procedure	Appropriateness Category	Relative Radiation Level
US thyroid	Usually Appropriate	0
CT neck with IV contrast	May Be Appropriate	⚠⚠⚠
CT neck without IV contrast	May Be Appropriate	⚠⚠⚠
MRI neck without and with IV contrast	Usually Not Appropriate	0
MRI neck without IV contrast	Usually Not Appropriate	0
I-123 radionuclide uptake and scan neck	Usually Not Appropriate	⚠⚠⚠
I-131 radionuclide uptake and Tc-99m pertechnetate scan neck	Usually Not Appropriate	⚠⚠⚠⚠
CT neck without and with IV contrast	Usually Not Appropriate	⚠⚠⚠
FDG-PET/CT neck	Usually Not Appropriate	⚠⚠⚠⚠

Variant 2. Suspected goiter. Initial imaging.

Procedure	Appropriateness Category	Relative Radiation Level
US thyroid	Usually Appropriate	0
CT neck without IV contrast	Usually Appropriate	⚠⚠⚠
CT neck with IV contrast	May Be Appropriate	⚠⚠⚠
I-123 radionuclide uptake and scan neck	May Be Appropriate	⚠⚠⚠
I-131 radionuclide uptake and Tc-99m pertechnetate scan neck	May Be Appropriate	⚠⚠⚠⚠
MRI neck without and with IV contrast	May Be Appropriate	0
MRI neck without IV contrast	May Be Appropriate	0
CT neck without and with IV contrast	Usually Not Appropriate	⚠⚠⚠
FDG-PET/CT neck	Usually Not Appropriate	⚠⚠⚠⚠

Variant 3. Thyrotoxicosis. Initial imaging.

Procedure	Appropriateness Category	Relative Radiation Level
US thyroid	Usually Appropriate	0
I-123 radionuclide uptake and scan neck	Usually Appropriate	⚠⚠⚠
I-131 radionuclide uptake and Tc-99m pertechnetate scan neck	Usually Appropriate	⚠⚠⚠⚠
CT neck with IV contrast	Usually Not Appropriate	⚠⚠⚠
CT neck without IV contrast	Usually Not Appropriate	⚠⚠⚠
MRI neck without and with IV contrast	Usually Not Appropriate	0
MRI neck without IV contrast	Usually Not Appropriate	0
CT neck without and with IV contrast	Usually Not Appropriate	⚠⚠⚠
FDG-PET/CT neck	Usually Not Appropriate	⚠⚠⚠⚠

Variant 4. Primary hypothyroidism. Initial imaging.

Procedure	Appropriateness Category	Relative Radiation Level
CT neck with IV contrast	Usually Not Appropriate	⚠⚠⚠
CT neck without and with IV contrast	Usually Not Appropriate	⚠⚠⚠
CT neck without IV contrast	Usually Not Appropriate	⚠⚠⚠
FDG-PET/CT neck	Usually Not Appropriate	⚠⚠⚠⚠
I-123 radionuclide uptake and scan neck	Usually Not Appropriate	⚠⚠⚠
I-131 radionuclide uptake and Tc-99m pertechnetate scan neck	Usually Not Appropriate	⚠⚠⚠⚠
MRI neck without and with IV contrast	Usually Not Appropriate	0
MRI neck without IV contrast	Usually Not Appropriate	0
US thyroid	Usually Not Appropriate	0

Variant 5. Preoperative evaluation of differentiated thyroid cancer.

Procedure	Appropriateness Category	Relative Radiation Level
US thyroid	Usually Appropriate	0
CT neck with IV contrast	Usually Appropriate	⚠⚠⚠
MRI neck without and with IV contrast	May Be Appropriate	0
CT neck without IV contrast	May Be Appropriate	⚠⚠⚠
MRI neck without IV contrast	May Be Appropriate	0
FDG-PET/CT whole body	Usually Not Appropriate	⚠⚠⚠⚠
CT neck without and with IV contrast	Usually Not Appropriate	⚠⚠⚠
I-123 scan whole body	Usually Not Appropriate	⚠⚠⚠
I-131 scan whole body	Usually Not Appropriate	⚠⚠⚠⚠
In-111 somatostatin receptor scintigraphy whole body	Usually Not Appropriate	⚠⚠⚠⚠

Variant 6. Early imaging after treatment of differentiated thyroid cancer.

Procedure	Appropriateness Category	Relative Radiation Level
US thyroid	Usually Appropriate	0
I-123 scan whole body	May Be Appropriate	⚠⚠⚠
CT neck with IV contrast	May Be Appropriate (Disagreement)	⚠⚠⚠
I-131 scan whole body	May Be Appropriate (Disagreement)	⚠⚠⚠⚠
MRI neck without and with IV contrast	May Be Appropriate	0
CT neck without IV contrast	Usually Not Appropriate	⚠⚠⚠
MRI neck without IV contrast	Usually Not Appropriate	0
FDG-PET/CT whole body	Usually Not Appropriate	⚠⚠⚠⚠
CT neck without and with IV contrast	Usually Not Appropriate	⚠⚠⚠
In-111 somatostatin receptor scintigraphy whole body	Usually Not Appropriate	⚠⚠⚠⚠

Variant 7. Suspected recurrence of differentiated thyroid cancer.

Procedure	Appropriateness Category	Relative Radiation Level
CT neck with IV contrast	Usually Appropriate	⚡⚡⚡
US thyroid	Usually Appropriate	0
I-123 scan whole body	Usually Appropriate	⚡⚡⚡
MRI neck without and with IV contrast	Usually Appropriate	0
CT chest with IV contrast	May Be Appropriate	⚡⚡⚡
CT chest without IV contrast	May Be Appropriate	⚡⚡⚡
FDG-PET/CT whole body	May Be Appropriate	⚡⚡⚡⚡
I-131 scan whole body	May Be Appropriate	⚡⚡⚡⚡
CT neck without IV contrast	May Be Appropriate	⚡⚡⚡
MRI neck without IV contrast	May Be Appropriate	0
CT chest without and with IV contrast	Usually Not Appropriate	⚡⚡⚡
CT neck without and with IV contrast	Usually Not Appropriate	⚡⚡⚡
In-111 somatostatin receptor scintigraphy whole body	Usually Not Appropriate	⚡⚡⚡⚡

Variant 8. Suspected recurrence of medullary thyroid cancers.

Procedure	Appropriateness Category	Relative Radiation Level
US thyroid	Usually Appropriate	0
CT neck with IV contrast	Usually Appropriate	⚡⚡⚡
CT chest with IV contrast	Usually Appropriate	⚡⚡⚡
MRI neck without and with IV contrast	Usually Appropriate	0
CT abdomen with IV contrast	May Be Appropriate	⚡⚡⚡
CT abdomen without and with IV contrast	May Be Appropriate	⚡⚡⚡⚡
MRI abdomen without and with IV contrast	May Be Appropriate	0
MRI complete spine without and with IV contrast	May Be Appropriate	0
Tc-99m bone scan whole body	May Be Appropriate	⚡⚡⚡
CT chest without IV contrast	May Be Appropriate	⚡⚡⚡
CT neck without IV contrast	May Be Appropriate	⚡⚡⚡
FDG-PET/CT whole body	May Be Appropriate	⚡⚡⚡⚡
MRI abdomen without IV contrast	May Be Appropriate	0
MRI complete spine without IV contrast	May Be Appropriate	0
MRI neck without IV contrast	May Be Appropriate	0
CT abdomen without IV contrast	Usually Not Appropriate	⚡⚡⚡
CT chest without and with IV contrast	Usually Not Appropriate	⚡⚡⚡
CT neck without and with IV contrast	Usually Not Appropriate	⚡⚡⚡
Ga-68 DOTATATE PET/CT skull base to mid-thigh	Usually Not Appropriate	⚡⚡⚡⚡
I-123 scan whole body	Usually Not Appropriate	⚡⚡⚡
I-131 scan whole body	Usually Not Appropriate	⚡⚡⚡⚡
In-111 somatostatin receptor scintigraphy whole body	Usually Not Appropriate	⚡⚡⚡⚡

Table 1. Appropriateness category names and definitions

Appropriateness Category Name	Appropriateness Rating	Appropriateness Category Definition
Usually Appropriate	7, 8, or 9	The imaging procedure or treatment is indicated in the specified clinical scenarios at a favorable risk-benefit ratio for patients.
May Be Appropriate	4, 5, or 6	The imaging procedure or treatment may be indicated in the specified clinical scenarios as an alternative to imaging procedures or treatments with a more favorable risk-benefit ratio, or the risk-benefit ratio for patients is equivocal.
May Be Appropriate (Disagreement)	5	The individual ratings are too dispersed from the panel median. The different label provides transparency regarding the panel's recommendation. "May be appropriate" is the rating category and a rating of 5 is assigned.
Usually Not Appropriate	1, 2, or 3	The imaging procedure or treatment is unlikely to be indicated in the specified clinical scenarios, or the risk-benefit ratio for patients is likely to be unfavorable.

Table 2. Relative radiation level designations

RRL	Adult Effective Dose Estimate Range (mSv)	Pediatric Effective Dose Estimate Range (mSv)
0	0	0
⊕	<0.1	<0.03
⊕⊕	0.1-1	0.03-0.3
⊕⊕⊕	1-10	0.3-3
⊕⊕⊕⊕	10-30	3-10
⊕⊕⊕⊕⊕	30-100	10-30

Note: Relative radiation level (RRL) assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (eg, region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "varies."

SUMMARY OF LITERATURE REVIEW

Introduction/Background

There are a wide variety of diseases that affect the thyroid gland and range from hyperplastic to neoplastic, autoimmune, or inflammatory. They can present with functional abnormality or a palpable structural change. Imaging has a key role in diagnosing and characterizing the thyroid finding for management. Imaging is also essential in the management of thyroid cancer.

Thyroid nodules are the most common finding in the thyroid gland. The majority of thyroid nodules are benign [1,2]. Initiating workup is costly for the patient and health care system as biopsy is frequently followed by repeat imaging and surgery [3], despite the fact that the majority of small thyroid cancers are indolent [1,2]. Vaccarella et al [4] estimated that "overdiagnosis," or identifying cancer that otherwise would be indolent, accounts for 77% of thyroid cancer cases in the United States. The radiology community has proactively addressed issues of thyroid nodule biopsy and unnecessary surgery [5]. The ACR formed committees [6] that published guidance regarding the incidental

thyroid nodule detected on imaging [7] and ACR Thyroid Imaging Reporting and Data System (TI-RADS) was conceived to aid management of thyroid nodules detected on ultrasound (US) [8].

When biopsy reveals the diagnosis of thyroid cancer, imaging has several roles, depending on the type of cancer. Papillary and follicular carcinomas arise from the follicular epithelial cells are known as differentiated thyroid carcinomas (DTC), representing 84% and 11% of all thyroid malignancies, respectively [2]. DTC have an excellent prognosis, with a 10-year survival rate of 99% for papillary carcinoma and 95% for follicular type [2]. DTCs are treated primarily with surgery and may have radioiodine ablation depending on the stage of disease. Medullary thyroid carcinoma (MTC) arises from parafollicular cells and is more aggressive, with a survival rate of 82% at 10 years [2]. MTC is also treated with surgery. Anaplastic carcinoma is an aggressive undifferentiated tumor typically occurring in the elderly with a 10-year survival of 8% [9]. Treatment of anaplastic carcinoma does not significantly impact survival. Other malignancies, such

as thyroid lymphoma, sarcoma, and metastases, are rare. Imaging is used in operative planning, routine tumor surveillance, and further evaluation of suspected recurrence.

Imaging also plays a role in evaluation of non-neoplastic disease entities, such as goiter and thyrotoxicosis. Goiter refers to abnormal growth and enlargement of the thyroid gland. It typically occurs over many years and is more common in women in their fifth and sixth decades of life. Enlargement of the gland can occur with or without nodules and can involve the whole gland symmetrically or predominantly affect one lobe. Thyrotoxicosis is a condition of elevated thyroid hormone production. The most common causes are intrinsic to the thyroid and include Graves disease, toxic adenoma, toxic multinodular goiter, and subacute thyroiditis. Pituitary causes of thyrotoxicosis are rare and are addressed in the ACR Appropriateness Criteria® topic on “Neuroendocrine Imaging” [10].

Special Imaging Considerations

Use of iodinated intravenous (IV) contrast for CT helps to delineate invasive tumor and morphological abnormalities in small nodal metastases. In the past, there were concerns about iodinated contrast agents delaying subsequent whole-body scans or radioiodine ablation; however, this has now been shown to be unfounded. Recent studies show that water-soluble iodinated contrast agents are generally cleared within 4 to 8 weeks in most patients; therefore, post-thyroidectomy patients requiring radioiodine therapy can be scanned with radioactive iodine (RAI) within 1 month of the contrast-enhanced CT [11,12].

Iodinated contrast has also been associated with hyperthyroidism and hypothyroidism. A case control study matched 391 incident thyroid dysfunction patients with 1,434 euthyroid controls [13]. Iodinated contrast media exposure was associated with incident overt hyperthyroidism (odds ratio, 2.50; 95% confidence interval, 1.06-5.93) and incident overt hypothyroidism (odds ratio, 3.05; 95% confidence interval, 1.07-8.72) occurring at a median time of 9 months after the administration. However, there are no studies that establish causality and mechanism of effect, and the prevalence of the thyroid dysfunction after contrast is not known. Contrast media should be judiciously used for all indications whether or not the indication of imaging is related to the thyroid.

More information about thyroid scintigraphy, thyroid uptake examinations, and whole-body imaging for

thyroid carcinoma can be found in the ACR–SPR Practice Parameter for the Performance of Scintigraphy and Uptake Measurement for Benign and Malignant Thyroid Disease [14].

DISCUSSION OF PROCEDURES BY VARIANT

Variant 1: Palpable Thyroid Nodule. Not Goiter. Euthyroid. Initial Imaging

Screening for thyroid cancer by palpation is not recommended by the US Preventive Task Force [15]. However, if a patient presents with a palpable neck nodule, the goal of imaging is to determine if the palpable abnormality corresponds to a thyroid nodule and to characterize the nodule for malignancy risk. Thyroid function tests should be performed first. If the serum thyroid-stimulating hormone (TSH) is subnormal, then the patient has thyrotoxicosis (Variant 3). This variant refers to a palpable thyroid nodule in the setting of a euthyroid patient.

US Thyroid. US provides high-resolution imaging to show that the palpable abnormality is within the thyroid and is the best study to characterize the nodule for the risk of malignancy. Certain sonographic features are more prevalent in malignancies. The combination of these features and the nodule size guide the decision to biopsy under the ACR TI-RADS and other risk stratification criteria [8,16].

CT Neck. There is no evidence that CT can differentiate between malignant and benign nodules unless there is gross invasion or metastatic disease [7]. There may be a role for this cross-sectional imaging modality if the nodule is part of a goiter that is suspected to extend substernally or there is a suspicion of invasive thyroid cancer. Dual-phase CT imaging with and without IV contrast does not provide any additional information.

MRI Neck. There is no evidence that MRI can differentiate between malignant and benign nodules unless there is gross invasion or metastatic disease. There may be a role for this cross-sectional imaging modality if the nodule is part of a goiter that is suspected to extend substernally or there is a suspicion of invasive thyroid cancer. CT is preferred since there is less respiratory motion artifact.

FDG-PET/CT Neck. There is no evidence to support the use of PET using the tracer fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG)/CT in the setting of palpable thyroid nodule.

Radionuclide Uptake and Scan. In euthyroid patients, radioisotope scanning is not helpful in determining malignancy and decision to biopsy. Although cold nodules are more likely to be malignant, the majority of nodules are cold, and the majority of cold nodules are benign, resulting in a low positive predictive value.

Variant 2: Suspected Goiter. Initial Imaging

A goiter is suspected based on a diffuse palpable abnormality or obstructive symptoms, such as dyspnea, orthopnea, obstructive sleep apnea, dysphagia, and dysphonia. These symptoms are related to mass effect on the trachea or esophagus.

The role of imaging is to confirm the diagnosis of goiter and document the size and extent of the goiter. If obstructive symptoms are present, imaging can quantify the degree of compression on the trachea. This information is valuable in deciding if surgery will improve obstructive symptoms and planning operative approach.

US Thyroid. US is the preferred first-line imaging modality for suspected goiter. It confirms that the neck mass is arising from the thyroid and characterizes the size and morphology of the goiter. If the goiter is nodular, US can also evaluate for suspicious features in nodules (see [Variant 1](#)).

CT Neck. CT is superior to US for evaluating substernal extension and deep extension to the retropharyngeal space [17]. CT can also define the degree of tracheal compression more effectively than US. Performing a CT with iodinated contrast is not necessary for goiter evaluation unless there is concern for an infiltrative neoplasm. Dual-phase CT imaging with and without IV contrast does not provide any additional information.

MRI Neck. MRI is an alternative to CT for characterizing the goiter, but CT is preferred because there is less respiratory motion artifact. Performing an MRI with IV contrast is not necessary for goiter evaluation unless there is concern for an infiltrative neoplasm.

FDG-PET/CT Neck. FDG-PET/CT imaging is not recommended as the initial imaging for the evaluation of suspected goiter.

Radionuclide Uptake and Scan. Radionuclide uptake may have a role if the goiter is associated with thyrotoxicosis. The radionuclide uptake and scan confirms that the entire goiter consists of thyroid tissue. Iodine-123 (I-123) is preferred over iodine-131 (I-131) because of its superior imaging quality [18]. In addition

to confirming the entire goiter is made of thyroid tissue, in a multinodular goiter the scan should be compared to an US to identify hypofunctioning or isofunctioning nodules to be targeted for biopsy [16].

Variant 3: Thyrotoxicosis. Initial Imaging

Thyrotoxicosis may present with symptoms of hyperthyroidism, such as heat intolerance, tachycardia, anxiety, and weight loss, or be subclinical and found as an incidental laboratory abnormality (low TSH). The most common causes of thyrotoxicosis are Graves disease, toxic adenoma, toxic multinodular goiter, and subacute thyroiditis. Rare causes include trophoblastic disease, thyroid hormone resistance, amiodarone-induced thyroiditis, iatrogenic thyrotoxicosis, factitious ingestion of thyroid hormone, and struma ovarii [19].

Graves disease is diagnosed by laboratory tests, including measurement of TSH receptor antibodies [20], but in ambiguous cases or where toxic adenoma or multinodular goiter is suspected [19], imaging with an iodine uptake and scan can help confirm the cause for thyrotoxicosis. Imaging also has a role in planning therapy with RAI.

US Thyroid. US is the best imaging study to evaluate thyroid morphology and can be a helpful adjunct study to a radioiodine uptake. When a radioactive uptake scan shows nodules from toxic multinodular goiter or toxic adenoma, US can confirm presence of nodules and also evaluate for suspicious features of malignancy (see [Variant 1](#)). US also provides thyroid dimensions for planning RAI treatment [19].

Doppler US may be an alternative to nuclear medicine for separating thyrotoxicosis that is due to an overactive thyroid, such as Graves disease and toxic adenoma, from thyrotoxicosis, which is due to destructive causes such as subacute or lymphocytic thyroiditis. On Doppler US, these two causes of thyrotoxicosis have increased and decreased thyroid blood flow, respectively [21,22]. Although one study found similar sensitivity and specificity for Doppler US (95% and 90%) and radionuclide uptake studies (90% and 100%) [23], a radionuclide uptake study is still preferred because it directly measures thyroid activity rather than inferring it based on blood flow [24].

Among rarer causes of thyrotoxicosis, US can also distinguish between the two types of amiodarone-induced thyrotoxicosis. Type I (iodine-induced hyperthyroidism) has an enlarged or nodular thyroid gland, whereas type II (destructive) has a normal or small diffuse goiter with

decreased blood flow [24]. Other causes also have characteristic features. Postpartum destructive thyroiditis has decreased blood flow. Findings of acute thyroiditis on US are hypoechoic lesions in and near the thyroid, tissue destruction, and abscesses. Painless thyroiditis has inhomogeneous hypoechogenic texture with decreased blood flow [19].

CT Neck. CT is usually not used in the workup of thyrotoxicosis.

MRI Neck. MRI is usually not used in the workup of thyrotoxicosis.

FDG-PET/CT Neck. FDG-PET/CT imaging is not recommended as the initial imaging for the evaluation of a palpable thyroid nodule.

Radionuclide Uptake and Scan. Radioiodine uptake and scan can distinguish between high-uptake causes of thyrotoxicosis, such as Graves disease, toxic adenoma, and toxic multinodular goiter, and low-uptake causes, such as subacute thyroiditis and exogenous thyroid hormone [19,25]. The scan component is also helpful in differentiating between high-uptake causes, such as toxic adenoma, toxic multinodular goiter, and Graves disease (diffuse uptake) [19], as well as rarer causes, such as Marine-Lenhart syndrome (toxic nodule plus Graves) [26]. If radioiodine therapy is planned, the uptake component of the scan can then help determine the dose. Either I-123 or I-131 plus pertechnetate can be used [19]. If nodularity is present, I-123 is preferred so as to identify any hypofunctioning or isofunctioning nodules to target for biopsy [16]. In postpartum thyrotoxicosis, I-131 should be avoided [19].

Variant 4: Primary Hypothyroidism. Initial Imaging

Hypothyroidism is a condition of low thyroid hormone that is due to an underactive gland. Hypothyroidism can present with symptoms such as weight gain, cold intolerance, constipation, weakness, and fatigue, or be diagnosed as a laboratory abnormality. The treatment of hypothyroidism is thyroid hormone replacement. The most common etiology in the developed world (where dietary iodine supply is adequate) is Hashimoto thyroiditis, also known as chronic lymphocytic thyroiditis. Other etiologies include thyroidectomy, radioiodine therapy, external neck irradiation, iodine deficiency or excess, and drugs.

There is no role for imaging in the workup of hypothyroidism in adults. Imaging for thyroid morphology

does not help differentiate among causes of hypothyroidism, and all causes of hypothyroidism will have decreased radioiodine uptake.

US Thyroid. There is no role for US imaging in the workup of hypothyroidism in adults. Imaging for thyroid morphology does not help differentiate among causes of hypothyroidism.

CT Neck. There is no role for CT imaging in the workup of hypothyroidism in adults. Imaging for thyroid morphology does not help differentiate among causes of hypothyroidism.

MRI Neck. There is no role for MRI in the workup of hypothyroidism in adults. Imaging for thyroid morphology does not help differentiate among causes of hypothyroidism.

FDG-PET/CT Neck. There is no role for FDG-PET/CT imaging in the workup of hypothyroidism in adults.

Radionuclide Uptake and Scan. There is no role for radioiodine uptake and scan in the workup of hypothyroidism in adults. Imaging for thyroid morphology does not help differentiate among causes of hypothyroidism, and all causes of hypothyroidism will have decreased radioiodine uptake.

Variant 5: Preoperative Evaluation of Differentiated Thyroid Cancer

Surgery for DTC involves resection of the primary tumor and clinically significant lymph nodes. The goals of preoperative imaging are to evaluate for extrathyroidal invasion into surrounding structures (airway, esophagus, muscles) and for vascular encasement, and to identify lymph nodes in the lateral compartment >8 to 10 mm. Of note, the resection of larger nodal metastases, not micrometastases, is associated with improved survival, especially in patients <45 years of age [27].

In addition to the American Joint Committee on Cancer staging, which provides prognosis for survival, thyroid cancers are categorized by the American Thyroid Association into low, intermediate, and high risk, which provides risk for recurrence [16]. Preoperative staging and risk of recurrence both determine the need for RAI therapy after surgery and the protocol for tumor surveillance (Variant 6).

US Thyroid. US is a routine preoperative study in all patients with thyroid cancer. The role of US is to stage the primary tumor and cervical lymph nodes. In a retrospective study of patients who had primary surgery

for thyroid cancer, US detected additional sites of metastatic disease not appreciated on physical examination in 20% of patients [28]. Compared to CT, US is more accurate in predicting early extrathyroidal tumor extension and multifocal bilobar disease [29]. US has excellent resolution for lymph node morphology. Most studies find US has higher diagnostic accuracy compared to CT for preoperative evaluation of nodal disease, especially for lateral compartment nodes [29-33]. Some centers use US for routine preoperative lymph node mapping and fine-needle aspiration of suspicious lymph nodes >8 to 10 mm [31].

CT Neck. Preoperative CT with IV contrast is recommended as an adjunct to US for patients with clinical suspicion for advanced disease, including invasive primary tumor or clinically apparent multiple or bulky lymph node involvement [16]. CT is a better modality than US for delineating the extent of laryngeal, tracheal, esophageal, or vascular involvement [30,33]. CT is useful in defining the inferior border of disease and in determining the extent to which mediastinal structures are involved in cases with significant caudal spread. These inferior sites cannot be visualized on US.

CT can also delineate bulky nodal disease and extra-nodal extension that involves muscle and blood vessels [34]. In particular, CT has higher sensitivity than US in detecting lymph node metastases in the central compartment and retropharyngeal space [32].

CT should be performed with iodinated contrast in order to better assess for tumor vascular encasement and small nodal metastases with hyperenhancement and necrosis. Contrast is not contraindicated for DTC based on new studies on iodine retention [11,12] (see Special Imaging Considerations section). Dual-phase CT imaging with and without IV contrast does not provide any additional information.

MRI Neck. MRI of the neck and mediastinum has the same role as CT in evaluating sites that are limited on US. The performance of MRI for imaging the neck and mediastinum has not been directly compared with CT on large numbers of thyroid cancer patients. Contrast is valuable for local staging and assessing suspicious lymph nodes. MRI has disadvantages of motion artifact in the lower neck from respiration and swallowing and is less sensitive than CT scan for the detection of small pulmonary nodules.

FDG-PET/CT Whole Body. A small prospective study compared diagnostic accuracy of FDG-PET/CT with US

and contrast-enhanced CT. The sensitivity of PET for the detection of cervical lymph node metastases at all nodal levels is lowest for PET (30% versus 41% for US and 35% for CT) [35]. In general, because of the low avidity of well-differentiated thyroid cancers, FDG-PET/CT is not useful. Sensitivity of FDG-PET/CT scanning for malignancy may be slightly increased with TSH stimulation with recombinant human TSH but not enough to change management in most patients [36].

Whole-Body Scintigraphy. Whole-body scintigraphy (WBS) has no role in the preoperative staging for DTC since the normal thyroid has very high iodine uptake and will take up most of the tracer.

In-111 Somatostatin Receptor Scintigraphy. There is no role for indium-111 (In-111) somatostatin receptor scintigraphy at any stage of evaluation of DTC.

Variant 6: Early Imaging After Treatment of Thyroid Cancer

After surgery, an early postoperative US within 6 to 12 months should be performed on all patients. Additional imaging depends on the extent of disease and surgery. In patients with total thyroidectomy, extent of residual disease cannot be determined at surgery or on US, so WBS helps to decide if and how much RAI the patient should receive. WBS is also performed after RAI therapy.

Imaging combined with serum thyroglobulin and thyroglobulin antibodies helps to categorize patients into risk groups according to response to therapy. Thyroglobulin testing with different cutoffs can be used to define response to therapy in patients after thyroidectomy with or without RAI and in those with lobectomy alone [37]. The choice of further imaging depends on the response to therapy based upon results from serum thyroglobulin testing and US performed in the first year after definitive treatment [15]. An excellent response to therapy is associated with a low recurrence risk (<5%) in patients with low- or intermediate-risk tumors. For these patients, if the serum thyroglobulin remains low, additional imaging is not indicated. For patients with thyroidectomy and RAI ablation, a low serum thyroglobulin is defined as a level of <0.2 ng/mL on thyroid hormone therapy in a sensitive assay or <1 ng/mL after TSH stimulation in patients who have undergone thyroidectomy and radioiodine ablation [16]. For patients with thyroidectomy or lobectomy but no RAI therapy, a low serum thyroglobulin is defined as a level of <0.2 ng/mL or <30 ng/mL, respectively [37]. However, if

the serum thyroglobulin is elevated above the appropriate cutoff or if thyroglobulin antibodies are present and especially if they are rising, additional surveillance imaging is performed (see [Variant 7](#) if there is concern for residual/recurrent disease on this basis).

US Thyroid. US of the neck is the first-line imaging investigation for DTC after initial therapy and includes evaluation of the thyroid bed and cervical nodes. It can characterize palpable abnormalities in the neck and detect deeper neck masses that are not palpable. It is performed at 6 to 12 months and then periodically, depending on the patient's risk for recurrent disease and thyroglobulin status [16]. Periodic US may not be necessary in low-risk patients who have had remnant ablation, normal initial US, and a low serum thyroglobulin [16].

CT Neck. CT is not recommended as the initial imaging study after treatment. See [Variant 7](#) if there is concern for residual/recurrent disease.

MRI Neck. MRI is not recommended as the initial imaging study after treatment. See [Variant 7](#) if there is concern for residual/recurrent disease.

FDG-PET/CT Whole Body. FDG-PET/CT scanning is not recommended for routine surveillance if there is no residual disease.

Whole-Body Scintigraphy. If the patient receives RAI therapy, a post-therapy WBS should be performed to evaluate for residual disease. WBS is not utilized in low-risk patients without suspicion for recurrence and normal thyroid US [16]. It has no role in low-risk patients who have had a lobectomy.

In intermediate- and high-risk patients, WBS has a role in evaluating initial response to radioiodine ablation. If there has been excellent response to therapy, WBS is usually not performed for ongoing surveillance. An uptake in the thyroid bed is sometimes performed to aid in detection of local recurrence and guide therapy. Either I-123 or I-131 can be used if a pretherapy scan is desired [16], as rates of successful remnant ablation are similar after I-123 and I-131 [38,39]. If the choice exists, I-123 has better image quality [40,41]. Note that a post-therapy scan after radioiodine ablation using the radioactivity from the radioiodine ablation is recommended, as it upstages disease in 6% to 13% of cases [42-44].

In-111 Somatostatin Receptor Scintigraphy. There is no role for In-111 somatostatin receptor scintigraphy at any stage of evaluation of DTC.

Variant 7: Suspected Recurrence of Differentiated Thyroid Cancer

Suspected recurrence of DTC may present with a palpable neck abnormality or symptoms related to the organ of distant metastasis. More commonly, there may be no symptoms, but the patient may have a persistently elevated or rising thyroglobulin or rising thyroglobulin antibodies. After imaging, these patients can be categorized as elevated thyroglobulin with structural disease or elevated thyroglobulin with no detectable abnormality on imaging. The latter is thought to be due to small nodal metastases and can remain untreated for years.

The three American Thyroid Association risk categories of recurrence help to guide imaging. After initial excellent response, the risk for recurrence is 1% to 2% in low-risk patients, 2% to 4% in intermediate-risk patients, and 14% in high-risk patients [45-47]. In general, more imaging modalities are used to pursue recurrence in high-risk patients because distant metastases are more likely in these patients and negatively impacts on survival. Recurrence with a structural abnormality can be treated with neck dissection, repeat RAI therapy, external beam radiotherapy, and systemic therapy [16].

US Thyroid. US of the neck is the first imaging investigation for suspected DTC recurrence and includes evaluation of the thyroid bed and cervical nodes. It can characterize palpable abnormalities in the neck and detect deeper neck masses that are not palpable [28].

CT Neck. CT of the neck complements US of the neck for detection of additional metastases in the central compartment, in the mediastinum, and behind the trachea [29,33,48] or for assessment for invasive recurrent disease into the aerodigestive tract.

CT should be performed with iodinated contrast in order to better assess for tumor vascular encasement and small nodal metastases with hyperenhancement and necrosis. Contrast is not contraindicated for DTC based on new studies on iodine retention [11,12] (see Special Imaging Considerations section). Dual-phase CT imaging with and without IV contrast does not provide any additional information.

CT Chest. CT imaging of the chest should be considered in high-risk DTC patients with elevated serum thyroglobulin (>10 ng/mL) or rising thyroglobulin antibodies with negative imaging studies in the neck. CT chest is favored over MRI chest because it is able to detect small pulmonary metastases [16]. Contrast CT is not

necessary for pulmonary metastases but adds to evaluation of metastatic nodes and the thyroid bed.

MRI Neck. MRI of the neck and mediastinum has the same role as CT. The performance of MRI for imaging the neck and mediastinum has not been directly compared with CT on large numbers of thyroid cancer patients. MRI has disadvantages of motion artifact in the lower neck from respiration and swallowing and is less sensitive than CT scan for the detection of small pulmonary nodules. Using IV contrast is valuable for detecting recurrence in the surgical bed and assessing suspicious lymph nodes.

FDG-PET/CT Whole Body. FDG-PET/CT is primarily considered in high-risk DTC patients with elevated serum thyroglobulin (>10 ng/mL) with negative WBS and US. It is frequently positive when radioiodine uptake is negative and vice versa [49]. This is because radioiodine-negative tumor represents differentiated disease that is no longer able to concentrate iodine. FDG-PET/CT is also more sensitive in patients with aggressive histological subtypes, including poorly differentiated, tall cell, and Hürthle cell thyroid cancer. FDG-avid nodal and distant metastatic disease is typically not responsive to radioiodine and has a worse prognosis [6,49,50]. The sensitivity of FDG-PET/CT scanning for malignancy may be slightly increased with TSH stimulation with recombinant human TSH, but the benefit of detecting small foci does not change management in most patients [36].

In-111 Somatostatin Receptor Scintigraphy. There is no role for In-111 somatostatin receptor scintigraphy at any stage of evaluation of DTC.

Whole-Body Scintigraphy. If the US is negative, radioiodine WBS can be performed for suspected recurrence of DTC. WBS may be performed as a first-line investigation in high-risk DTC patients, such as those who initially had macroscopic invasion, gross residual disease, or iodine avid distant metastases. An uptake is sometimes performed to aid in detection of local recurrence and guide dosage of local therapy. I-123 is preferred over I-131 if possible [16], as image quality is higher [40,41].

Variant 8: Suspected Recurrence of Medullary Thyroid Cancers

Surveillance for MTC involves monitoring tumor markers, calcitonin, and carcinoembryonic antigen. Imaging of the neck is the preferred initial study. If there is suspicion of recurrence in a body site because of localizing

signs or symptoms and elevated tumor markers, the specific body site is imaged. If the patient is asymptomatic, imaging depends on the calcitonin level.

US Thyroid. US of the neck is the first imaging investigation for suspected MTC recurrence and includes evaluation of the thyroid bed and cervical nodes. It can characterize palpable abnormalities in the neck and detect deeper neck masses that are not palpable. Imaging with US of the neck alone is generally adequate with calcitonin levels <150 pg/mL, as disease is usually limited to the neck [51]. Overall, per-person sensitivity is similar to CT with much greater specificity for cervical nodes (sensitivity 75% and specificity 92% for US versus sensitivity 80% and specificity 25% for CT) [52], and detection rate is greater than PET (US finds nodes in 56% of patients versus 32% for PET) [53].

CT Neck. CT has greater specificity than US for evaluation of cervical nodes (sensitivity 75% and specificity 92% for US versus sensitivity 80% and specificity 25% for CT) [52]. For calcitonin levels >150 pg/mL, the risk of metastases outside the neck is higher. In these patients, imaging is appropriate, starting with neck and chest CT [54]. Dual-phase CT imaging with and without IV contrast does not provide any additional information.

CT Chest. For calcitonin levels >150 pg/mL, the risk of metastases outside the neck is higher. CT chest is more sensitive than PET alone for lung nodules (detection rate, 35% for CT versus 20% for PET) and mediastinal nodes (detection rate, 31% for CT versus 20% for PET) [53]. CT should be performed with iodinated contrast in order to better assess for tumor in the surgical bed, vascular encasement, and morphology of small nodal metastases.

CT Abdomen. For calcitonin levels >150 pg/mL, the risk of metastases outside the neck is higher. Three-phase contrast CT of the liver is an alternative to MRI [54].

MRI Neck. MRI has the same role as CT in evaluating sites that are limited on US. The performance of MRI for imaging the neck and mediastinum has not been directly compared with CT on large numbers of thyroid cancer patients. MRI has disadvantages of motion artifact in the lower neck from respiration and swallowing and is less sensitive than CT scan for the detection of small pulmonary nodules. Using IV contrast is valuable for detecting recurrence in the surgical bed and assessing suspicious lymph nodes.

MRI Abdomen. MRI of the abdomen is performed for evaluation of liver metastases, and one study reports that

it is more sensitive than CT, US, or PET (with a detection rate of 49% versus 44% for CT, 41% for US, and 27% for PET) [53]. A meta-analysis of CT versus MRI for liver metastases of various origins (not MTC) suggests MRI with liver-specific agents is more sensitive than CT [55]. If MRI is used, diffusion-weighted imaging sequences should be included [56].

MRI Complete Spine. MRI of the complete spine may be more sensitive than bone scan for bone metastases (100% versus 72% in one study of patients on immunotherapy) [57]. However, another study concluded they were complementary, with equal overall detection rates but bone scintigraphy having the advantage of detecting additional lesions in the extremities (and MRI in the axial skeleton) [53]. Using IV contrast is valuable for detecting bone lesions in this case.

FDG-PET/CT Whole Body. Medullary cancer is challenging to image with nuclear medicine because it lacks the iodine avidity of DTC while still not being aggressive enough to take up FDG in many cases. FDG-PET/CT has suboptimal detection for MTC in most patients, with 59% sensitivity according to a meta-analysis of 25 studies [58]. However, the sensitivity increases to 75% in patients with more aggressive disease, as indicated by calcitonin levels >1,000 pg/mL and with a calcitonin doubling time <12 months [58-60]. In these patients, FDG-PET/CT may be a first-line study or performed after other imaging studies are negative [61,62]. In countries where the tracer FDOPA (3,4-dihydroxy-6-18F-fluoro-L-phenylalanine) is available, it should be used in place of FDG as it is more sensitive for MTC [63-65].

Tc-99m Bone Scan Whole Body. Bone scan has a role in imaging for patients with symptoms of bone pain with elevated tumor markers and in asymptomatic patients with calcitonin levels >150 pg/mL [16]. There is no conclusive evidence that bone scan performs better than MRI, but it does survey the entire skeleton rather than body regions on MRI.

In-111 Somatostatin Receptor Scintigraphy. In-111 somatostatin receptor scintigraphy, radioiodine uptake and WBS, and DOTATATE have no role for imaging of MTC; pentetreotide is insensitive, and MTC cells do not take up iodine [61,62,66].

Whole-Body Scintigraphy. WBS has no role in the imaging of MTC, and MTC cells do not uptake iodine [61,62,66].

Ga-68 DOTATATE Skull Base to Mid-Thigh. There is some early evidence gallium-68 (Ga-68) DOTATATE is more sensitive than FDG-PET/CT [67], although results are mixed, and the studies may be complementary [68]. In any event, it is more sensitive than pentetreotide [69]. It would not be recommended until further work is done.

SUMMARY OF RECOMMENDATIONS

- **Variante 1:** US thyroid is usually appropriate for the initial imaging of palpable thyroid nodule, without goiter and in a euthyroid state.
- **Variante 2:** US thyroid is usually appropriate for the initial imaging of suspected goiter. CT neck without IV contrast is usually appropriate if there is suspicion for substernal extension.
- **Variante 3:** US thyroid, I-123 radionuclide uptake and scan neck, or I-131 radionuclide uptake and Tc-99m pertechnetate scan neck are usually appropriate for the initial imaging of thyrotoxicosis. The nuclear medicine studies are procedures that are equivalent alternatives and complementary with US.
- **Variante 4:** Imaging is not recommended for the initial imaging of primary hypothyroidism.
- **Variante 5:** US thyroid is usually appropriate for the preoperative evaluation of differentiated thyroid cancer. CT neck with IV contrast is usually appropriate if there is higher stage disease.
- **Variante 6:** US thyroid is usually appropriate for early imaging after treatment of differentiated thyroid cancer. The panel did not agree on recommending CT neck with IV contrast or I-131 scan whole body in this clinical scenario. There is insufficient medical literature to conclude whether or not these patients would benefit from these procedures. The use of CT neck with IV contrast or I-131 scan whole body in this patient population is controversial but may be appropriate.
- **Variante 7:** US thyroid and I-123 scan whole body are usually appropriate for the suspected recurrence of differentiated thyroid cancer. These procedures are complementary. CT neck with IV contrast or MRI neck without and with IV contrast are second-line studies that are usually appropriate and alternatives depending on clinical findings.

■ **Variant 8:** US thyroid, CT neck with IV contrast, CT chest with IV contrast, or MRI neck without and with IV contrast is usually appropriate for the suspected recurrence of medullary thyroid cancers. These procedures are equivalent alternatives and the choice of modality depends on clinical findings.

SUPPORTING DOCUMENTS

The evidence table, literature search, and appendix for this topic are available at <https://acsearch.acr.org/list>. The appendix includes the strength of evidence assessment and the final rating round tabulations for each recommendation.

For additional information on the Appropriateness Criteria methodology and other supporting documents go to www.acr.org/ac.

RELATIVE RADIATION LEVEL INFORMATION

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, because of both organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared with those specified for adults (see [Table 2](#)). Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® Radiation Dose Assessment Introduction document [70].

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