Dramatic improvements in ultrasound resolution, coupled with the superficial location of the thyroid gland, have made ultrasound the primary imaging modality in the evaluation of focal and diffuse thyroid disease. Ultrasound is widely available, relatively inexpensive, painless, free of ionizing radiation, and does not require intravenous contrast. High-resolution transducers allow ultrasound penetration up to 5 cm and create high-definition images with a spatial resolution of 0.7 to 1.0 mm.1

A wide spectrum of diffuse diseases affects the thyroid gland (Table 1). The most common cause of diffuse thyroid disease is autoimmune thyroid disease (AITD): Hashimoto’s thyroiditis and Graves disease are the most common autoimmune diseases, but the rarer subacute lymphocytic thyroiditis is also placed within the AITD spectrum. Thyroiditis is a generic term referring to a group of several common inflammatory conditions of the thyroid gland; it is characterized by lymphocytic infiltration of the gland leading to parenchymal destruction. If the thyroid follicles are destroyed slowly, as in Hashimoto’s thyroiditis, hypothyroidism eventually results. If follicles are rapidly destroyed, as in subacute granulomatous and subacute lymphocytic thyroiditis, the release of preformed thyroid hormone stores into the blood stream causes transient thyrotoxicosis. Thyrotoxicosis is followed by a period of hypothyroidism until the thyroid recovers and thyroid hormone production resumes. On the other hand, hyperthyroidism in the setting of Graves disease and hyperfunctioning autonomous adenoma is caused by increased production of thyroid hormone. It is important to distinguish between these entities because they may have similar clinical presentation but their treatment varies. Graves disease must be treated with antithyroid drugs, radioisotope therapy, or subtotal thyroidectomy, whereas patients with destruction-induced thyrotoxicosis are treated conservatively.

The histology of autoimmune disease (lymphocytic parenchymal infiltration and follicular destruction) results in fewer sound reflectors, and thus accounts for the characteristic decreased echogenicity of the thyroid at ultrasound.2,3 The clinical diagnosis is usually based on an algorithm of presenting symptoms, laboratory analysis of thyroid function, immunology, and occasionally radioactive iodine uptake scans.4 Ultrasound is not generally required for the diagnosis of diffuse thyroid diseases; however, Hashimoto’s thyroiditis is primarily a subclinical disease,5 and ultrasound can detect this subset of patients before they come to clinical attention, when typical ultrasound findings are present. In addition, ultrasound has a role in excluding focal thyroid disease and in assessing the size of the thyroid.

In the classic imaging paradigm, ultrasound is useful to evaluate structure and radionuclide thyroid scintigraphy is used to assess function. Recently, color and spectral Doppler have also been used to assess function by measuring thyroid vascularity. Despite the seeming similarity in the imaging...
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<tr>
<td>Graves thyroiditis</td>
<td>Enlarged, mildly hypoechoic, and heterogeneous</td>
<td>Markedly ↑</td>
<td>Markedly hyperemic; proptosis; hyperthyroid; +antithyroid antibodies</td>
</tr>
<tr>
<td>Hashimoto’s thyroiditis</td>
<td>Enlarged, heterogeneous with lobular margins; hypoechoic and micronodular, septal lines</td>
<td>Highly variable: both ↑ and ↓ flow possible</td>
<td>+Antithyroid antibodies, hypothyroidism; cervical adenopathy</td>
</tr>
<tr>
<td>Subacute lymphocytic thyroiditis (painless)</td>
<td>Hypoechoic</td>
<td>*</td>
<td>+Antithyroid antibodies; postpartum; transient</td>
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<tr>
<td>De Quervain thyroiditis (subacute granulomatous)</td>
<td>Painful patchy areas of hypoehogenicity</td>
<td>↓ in the hypoechoic patch</td>
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<td>Acute suppurative thyroiditis</td>
<td>Abscess or infected linear tract in the thyroid</td>
<td>Normal background; no flow within an abscess</td>
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</tr>
<tr>
<td>Riedel thyroiditis</td>
<td>Large hypoechoic thyroid with course parenchyma</td>
<td>*</td>
<td>Large, rock-hard gland; encases adjacent structures</td>
</tr>
<tr>
<td>Medication-induced (ie, amiodarone) (AIT)</td>
<td>Type 1: abnormal thyroid Type 2: normal thyroid</td>
<td>Type 1: ↑ Type 2: absent</td>
<td>History of current or recent amiodarone use; hyperthyroid</td>
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<tr>
<td>Atrophic thyroiditis</td>
<td>Small, hypoechoic thyroid</td>
<td>↓</td>
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<td>Thyroid lymphoma</td>
<td>Large, ill-defined markedly hypoechoic nodules or masses with ↑ through transmission on background of Hashimoto’s thyroiditis</td>
<td>↓ in the hypoechoic mass</td>
<td>Rapidly enlarging neck mass in patient with history of Hashimoto, ± adenopathy</td>
</tr>
<tr>
<td>Multinodular goiter</td>
<td>Closely opposed or interspersed, similar-appearing nodules replace parenchyma, course calcifications, variable cystic changes in nodules</td>
<td>Variable</td>
<td>Confluent nodules in a normal or enlarged thyroid; ± abnormal thyroid function tests</td>
</tr>
</tbody>
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Abbreviations: AIT, amiodarone-induced thyrotoxicosis; ESR, erythrocyte sedimentation rate.

* Insufficient data.
features of diffuse thyroid diseases, it is important for the radiologist to be aware of the spectrum of imaging appearances of common thyroid diseases and the distinctive imaging appearance of rare conditions affecting the thyroid gland.

**THYROID ANATOMY AND ULTRASOUND SCANNING TECHNIQUE**

The thyroid is a butterfly-shaped, highly vascular gland located in the anterior neck superficial to the trachea and esophagus. It is surrounded by a pencil-thin echogenic capsule on ultrasound. The thyroid plays a critical role in the regulation of many metabolic functions, such as cardiac rate and output, lipid metabolism, and skeletal growth, as well as heat production.\(^5\) The thyroid bed is confined by strap muscles anteriorly, sternocleidomastoid muscles anterolaterally, carotid and jugular vessels laterally, and trachea, esophagus, and longus colli muscles posteriorly (Fig. 1). The normal thyroid parenchyma has a characteristic homogeneous, medium-level to high-level echogenicity speckle pattern created by sound waves interacting with normal follicles.\(^7\) The gland appears darker than the surrounding hyperechoic adipose tissue and brighter than adjacent hypoechogenic neck muscles.

Thyroid size can be influenced by many factors, such as alcoholic cirrhosis, renal failure,\(^8\) smoking, parity, iodine intake, and serum thyroid-stimulating hormone (TSH) concentration, use of oral contraceptives, gender, age, body mass index (BMI, calculated as weight in kilograms divided by the square of height in meters),\(^9\) and treatment with thyroxine or radioactive iodine. It has been reported that lean body mass and body surface area are the major determinants of thyroid size\(^10,11\) in non–iodine-deficient areas. In most adults, the thyroid measures between 4 and 6 cm in length and between 1.3 and 1.8 cm at the thickest anteroposterior dimension. A generous estimation of normal thickness of the thyroid isthmus is up to 4 to 6 mm.\(^12\) The thyroid gland may be considered enlarged when the anteroposterior diameter of the lobe is more than 2 cm or if the isthmus is thicker than a few millimeters.\(^1,13\) Calculation of the thyroid volume is based on the ellipsoid model.\(^14\) The height, width, and depth of each lobe are multiplied, the product is then multiplied by a correction factor of 0.529, and both lobe volumes are added together.\(^15,16\) The normal thyroid volume is 18.6 ± 4.5 mL (± standard deviation), with mildly greater volume in males (19.6 ± 4.7) compared with females (17.5 ± 4.2).\(^17\) If available, three-dimensional ultrasound has been shown to be more accurate compared with two-dimensional ultrasound for measurement of thyroid gland volume,\(^18\) particularly if the thyroid is large and irregular (as in patients with multinodular goiter).

The clinical history and previous relevant imaging studies should be reviewed before starting the ultrasound study. Ultrasonographic examination of the thyroid is performed in accordance with the practice guidelines published by the American Institute of Ultrasound in Medicine\(^19\) and the American College of Radiology.\(^20\) The patient is placed in a supine position with a rolled towel placed underneath the shoulders to hyperextend the neck and better delineate the substernal space. Scanning is performed with a high-resolution linear-array 12-MHz to 15-MHz transducer. The frequency of the transducer can be changed during the study; a tradeoff is made between selecting the highest possible frequency to optimize spatial resolution and still maintain adequate sound penetration at the necessary tissue depth. A lower-frequency (5–7 MHz) curved transducer may be used to obtain a more accurate volumetric assessment when the thyroid is markedly enlarged and extends beyond the field of view attainable on the screen.\(^21\)

Both lobes and isthmus of the thyroid gland should be scanned in a sequential manner. Appropriate images should be documented in axial and sagittal planes. Applying slight compression with the transducer improves visualization of microcalcifications and cystic areas in thyroid nodules; compression may also improve visualization of the deep tissues in the central compartment. Saving images in cine mode maximizes anatomic coverage of the neck and allows images to be viewed close to real time for later review. Panoramic images simultaneously depict both lobes for comparison of vascularity and echogenicity and allow the entire volume to be displayed on the monitor for accurate size determination.\(^22\)
Doppler optimized for flow detection should be deliberately used to assess vascularity of the thyroid gland, any suspicious lymph nodes, and any detected focal nodules. Color Doppler may also increase the conspicuity of isoechoic thyroid nodules. Focal nodules are measured in 3 dimensions and studied for the level of echogenicity compared with normal parenchyma, presence and type of calcifications, cystic change, margins, presence of a halo, and the amount and distribution of blood flow.\(^{13}\)

All patients should undergo an evaluation of the cervical lymph nodes as part of a routine thyroid ultrasound. Enlarged but morphologically normal-appearing cervical lymph nodes are common in patients withAITD (particularly Hashimoto’s thyroiditis and can even be the first clue of this diagnosis. Lymph node mapping is particularly helpful when thyroid cancer has already been established\(^{23}\) or when performing surveillance screening for recurrence after thyroidectomy. The likelihood that a suspicious-appearing thyroid nodule is thyroid cancer dramatically increases if malignant-appearing cervical nodes are detected.\(^{24}\) In rare cases of aggressive papillary microcarcinoma, the only clue to the presence of thyroid cancer is detection of cervical adenopathy.\(^{25}\) Thyroid cancer most commonly metastasizes to ipsilateral cervical lymph nodes but contralateral metastases are present up to 20% of the time; hence, both lateral nodal stations need to be examined.\(^{26,27}\)

Tissues deep and inferior to the thyroid are also assessed for round or oval hypoechoic, hypervasculard nodules when evaluating for enlarged parathyroid glands. Asking the patient to swallow and observing them in real time may help to elevate the lower aspect of a thyroid goiter or reveal a parathyroid gland lying deep to the clavicles.\(^{28}\) It is also important to have the patients turn their head away from the side being imaged to sweep the deep cervical tissues and esophagus to the side being evaluated to improve detection of tracheoesophageal groove lesions. Occasionally, it is necessary to transiently decrease the transducer frequency (7–10 MHz) to improve sound penetration when the retrothyroid tissues are at an increased distance from the skin. Once a suspect nodule is detected, returning to higher frequencies allows better characterization.

**Sonographic Technique Advances**

**Grayscale**

The resolution of current ultrasound scanners is superb but such detailed resolution is a 2-edged sword. As smaller and smaller nodules are resolved, the clinical dilemma of how to manage this growing pool is being debated. A study performed by Guth and colleagues\(^{29}\) showed that 35% more nodules were detected in a similar iodine-deficient population when imaging with a higher-resolution transducer (13 MHz) compared with 7 MHz.\(^{30}\)

Several technical improvements have contributed to improved image quality. Compound imaging is a technique that averages images obtained simultaneously from different scanning angles. The images are combined into a single improved image in real time (as opposed to conventional scanning, in which images are generated from 1 angle of insonation). This technique reduces artifacts and speckle noise (the grainy appearance of the image), and improves contrast resolution. The increased contrast-to-noise ratio in thyroid images results in improved nodule conspicuity (Fig. 2).\(^{31,32}\) Tissue harmonic imaging uses integral multiples of the transmitted frequency for image formation and results in images with improved signal-to-noise, reduced reverberation and side-lobe artifacts, and improved lateral resolution.\(^{33,34}\) As with compound imaging, tissue harmonic imaging improves nodule border definition and contrast.\(^{35,36}\) Although not truly a technical improvement, it is the investigators’ opinion that the ability to record portions of sonographic examinations in a cine mode is indispensible. The cine mode is a series of rapidly recorded multiple images taken at sequential cycles of time. The images can be displayed in a dynamic movie format or they can be viewed as individual frames on the workstation. The thyroid (or thyroidectomy bed in patients with thyroid cancer) and the lateral compartment are captured in cine mode in the transverse, and when necessary, in the sagittal plane to improve

![Fig. 2. Compound imaging. Side-by-side transverse views of the thyroid show a solid thyroid nodule without (A) and with (B) compound imaging. Image (B) is less grainy.](image-url)
detection of pathologic lymph nodes and subtle thyroid nodule contour irregularity and microcalcifications. Cine virtual convex scanning may further improve anatomic coverage of the neck and thyroid. Captured cine sweeps are useful for the follow-up of a multinodular goiter when measurements of nodules are often difficult to accurately reproduce on static images alone.

**Color and power Doppler**

Color and power Doppler are both used to assess the degree of vascularity in the thyroid parenchyma and in nodules. Color Doppler is direction sensitive. Power Doppler may be more sensitive for detecting slow flow and it is independent of flow direction. Advanced dynamic flow (ADF) is a new technology in color flow imaging that provides superior spatial and temporal resolution, allowing more accurate measurement of blood flow. Quantitative measurement of thyroid blood flow (TBF) has been shown to be a promising method for distinguishing Graves from thyroiditis.37

**Microbubbles**

Microbubble contrast agents have been used in other organ systems. Results of studies assessing the role of microbubble contrast in the assessment of thyroid nodules have been mixed.38 No benefit for microbubble assessment of diffuse thyroid disease has been shown.39

**Elastography**

Ultrasound elastography (USE) is a method for qualitative and quantitative estimation of tissue elasticity. It is analogous to physical palpation for evaluation of tissue stiffness of benign and malignant nodules. The rationale behind elastography is that a cancerous nodule is stiffer and that it deforms less than surrounding tissue. Elastography measures the amount of tissue deformation under applied stress. Stress can be created by external compression with a specially designed ultrasound transducer or by physiologic strain produced by a pulsating carotid artery. Depending on the method used, the data are either processed and displayed with a color map in real time in the former or postprocessed offline for the latter (Fig. 3). Offline postprocessing may take several hours.

Recent studies have shown the potential of USE in distinguishing between benign and malignant thyroid nodules. Rago and colleagues40 showed a specificity and a sensitivity as high as 100% and 97%, respectively, with a positive predictive value (PPV) of 100% and negative predictive value (NPV) of 98% using external compression in 98 consecutive patients with a single thyroid nodule. USE has the potential to substantially reduce the number of fine-needle aspirations (FNAs) by 60.8%41 because of the high specificity and NPV that can be achieved identifying benign nodules.42 Vorlander and colleagues43 achieved a 100% NPV in all the nodules stratified as soft using the strain index (in 96 of 309 patients, strain >0.31) in patients referred for surgery with dominant, nontoxic thyroid nodules. This technique may also play a role in selecting nodules that need to undergo biopsy in a multinodular thyroid as well as managing patients with nondiagnostic or indeterminate FNA (constituting approximately 30% of all FNAs). Promising work has recently been published by Rago and colleagues,40 who looked at 195 nodules in 176 patients who were found to have indeterminate or nondiagnostic cytology on FNA and were able to undergo USE prior to surgical resection. The investigators reported an overall 94.9% sensitivity, 90.3% specificity, PPV of 71.1%, NPV of 98.6%, and an accuracy of 91.3% of USE in predicting malignancy. Soft nodules with high elasticity, which represent the largest proportion (73%) of nodules with indeterminate or nondiagnostic cytology, were highly associated with a benign histology. Although many patients with inconclusive biopsies currently

![Fig. 3. Elastogram (A) and conventional ultrasound images (B) show a 7-mm left-lobe irregular solid papillary microcarcinoma, showing a homogeneously hard blue pattern.](image-url)
receive surgical resection, presurgical risk stratification may reduce the number of benign thyroidectomies. A recent abstract from a meta-analysis including 8 studies with overall 639 thyroid nodules showed a mean sensitivity and specificity of 92% and 96% for the diagnosis of malignant thyroid nodules, whereas mean sensitivity and specificity of FNA has been reported to be 83% and 92%, respectively. Although this emerging technique is promising, it has limitations related to nodule selection. Rim or coarsely calcified nodules, those with cystic areas greater than 25% and isthmus nodules (when measuring carotid-artery–induced strain) are not amenable to USE. Because the nodule to be examined must be clearly distinguishable from other nodules, multinodular goiters with coalescent nodules are not suitable for this analysis. These encouraging feasibility studies suggest that sonoelastography may play a pivotal role in a cost-effective strategy to stratify ultrasound (and potentially FNA) indeterminate nodules in a noninvasive way. Additional validation with prospective studies is needed. There is no established role for elastography in the diagnosis of diffuse thyroid diseases.

DIFFUSE THYROID DISEASE
Hashimoto’s Thyroiditis
Hashimoto’s thyroiditis, synonymous with chronic lymphocytic thyroiditis (CLT), is the most common form of thyroiditis and is the most common cause of hypothyroidism in the United States. As with other autoimmune diseases, women are more commonly affected than men, with an 8 to 9:1 female/male ratio. Up to 2% of all women are affected. The disease usually develops in young or middle-aged women who are genetically predisposed and leads to progressive thyroid failure at a rate of 4% per year in women with positive antithyroid antibodies and increased serum TSH. Patients typically present with a painless, lobular, diffusely enlarged thyroid gland, often in the setting of hypothyroidism; the diagnosis is confirmed by the presence of serum autoantibodies to thyroglobulin and thyroid peroxidase. The pathologic hallmark of allAITDs is thyroid infiltration by cytotoxic T cells and B-cell lymphocytes as well as plasma cells. Infiltration results in the typical histopathologic changes of Hashimoto’s thyroiditis: lymphoplasmacytic aggregates with germinal centers, atrophic thyroid follicles, oxyphilic change of the epithelial cells (Hurthle cells), and variable fibrosis. Because not all patients have antithyroid antibodies and many are euthyroid at the time of diagnosis, ultrasound is a useful adjunct to suggest the diagnosis when it is clinically unsuspected.

Histopathologic changes of diffuse lymphocytic infiltration and severe thyroid follicle destruction lead to reduced thyroid echogenicity at ultrasound. In Hashimoto’s thyroiditis, diffuse thyroid hypoechogenicity is highly predictive of either current or future hypothyroidism. Studies using an objective quantitative analysis of the degree of hypoechogenicity of the thyroid in patients with Hashimoto’s thyroiditis compared with normal subjects showed that the degree of hypoechogenicity correlates positively with the likelihood and severity of hypothyroidism. Although hypoechogenicity of the thyroid is a well-established parameter for detecting AITD, it has poor specificity in morbidly obese patients. Thyroid hypoechogenicity was believed to be present in 64.8% of clinically and biochemically euthyroid patients with BMI of more than 40 who underwent thyroid ultrasound.

Ultrasound features of Hashimoto’s thyroiditis parallel the varied clinical presentation and histopathologic changes. Hence, sonographic appearances vary based on severity of follicular disruption, lymphocytic infiltration, chronicity of disease and extent of thyroid involvement. Several characteristic sonographic features have been described in patients with Hashimoto’s thyroiditis. The parenchyma is heterogeneous and coarsened compared with normal thyroid. The color Doppler appearance is highly variable but either normal or increased vascularity may be shown early in the disease. Deceased vascularity may be shown later in the disease course. The increase in hypervascularity seems to be associated with development of hypothyroidism, which may be caused by trophic stimulation of the thyroid by TSH. The presence of innumerable hypoechogenic solid micronodules ranging in size from 1 to 7 mm surrounded by an echogenic rim of fibrosis is highly specific for this disease, with an almost 95% PPV. At histology, these nodules correspond to parenchymal lymphocytic and plasma cell infiltrates. As thyroid parenchyma is progressively destroyed, the thyroid develops echogenic linear bands of parenchymal fibrosis, which can become confluent and thicker. Occasionally, involvement of the thyroid is asymmetric with preferential involvement of the anterior aspect of the gland. Eventually in end-stage disease, the gland becomes atrophic and diffusely hypoechogenic, similar to that of strap muscles.

Several enlarged, and occasionally atypical-appearing, central compartment lymph nodes are usually found adjacent to the lower
poles of both lobes. These reactive lymph nodes are easily recognized and are a useful clue to the diagnosis. However, in those with Hashimoto’s thyroiditis and coexisting hyperparathyroidism, detection of potential parathyroid adenomas becomes more difficult, because the grayscale appearance of a parathyroid adenoma and reactive central compartment nodes can be similar. The use of color Doppler to identify a vascular arch around a parathyroid adenoma as opposed to central hilar flow typical of a lymph node is useful, although a nuclear medicine sestamibi parathyroid scan becomes indispensible in this circumstance. Although reactive lymph nodes seen in Hashimoto’s thyroiditis are mildly enlarged and hypoechoic, the presence of microcalcifications, cystic change, peripheral vascularization on color Doppler, echogenic lymph node cortex, loss of fatty hilum, and round shape are features concerning for malignant lymph node metastases, particularly from thyroid cancer.

Occasionally, Hashimoto’s thyroiditis can present as a focal nodule (Fig. 10) or nodules within a diffusely altered parenchyma or within a sonographically normal thyroid gland. This form of nodular thyroiditis is found in 5% of all nodule biopsies. No distinguishing sonographic features of nodular Hashimoto’s thyroiditis permit a specific diagnosis. Nonetheless, one study has suggested that the most common pattern observed was that of a hyperechoic solid nodule (Fig. 13). The so-called “white-knight” likely represents a regenerative nodule of Hashimoto’s thyroiditis. However, caution should be exercised not to assume a nodule is benign simply based on hyperechogenicity, since a small subset of thyroid cancer can appear echogenic on ultrasound. Ill-defined margins, cystic changes, and intranodular calcifications were also occasionally observed. It is not known whether this represents a less severe form of Hashimoto or a separate subtype.

Fig. 4. Hashimoto’s thyroiditis. (A) Transverse image through the midline shows a coarsened, hypoechoic, and heterogeneous gland. Thyroid parenchyma is isoechoic compared with the strap muscles (asterisk), and the margins appear lobular. Parenchyma is coarsened because of bright fibrous linear bands separating the hypoechoic parenchyma into patchy areas and micronodulation. Both lobes and isthmus are thickened. (B) Color Doppler of the thyroid in the same patient shows moderately to markedly increased flow. Vascular flow on color Doppler is variable in Hashimoto.

Fig. 5. Micronodular pattern in Hashimoto’s thyroiditis. (A) Sagittal image of the thyroid shows diffuse, ill-margined innumerable small hypoechoic nodules (arrow) surrounded by echogenic stroma termed “micronodulation,” a finding specific for Hashimoto’s thyroiditis. (B) Sagittal image of the thyroid in another patient with Hashimoto’s thyroiditis shows Swiss-cheese appearance. Diffuse small hypoechoic lesions (arrow) in the thyroid create pseudocystic appearance.
Thyroid lymphoma is uncommon; it accounts for less than 5% of all thyroid malignancies but when present it almost always develops in patients with underlying Hashimoto’s thyroiditis. It has been established that Hashimoto’s thyroiditis is a risk factor for development of thyroid lymphoma. One study showed that the relative risk of malignant thyroid lymphoma in these patients is 67 times increased compared with baseline. The patient with thyroid lymphoma classically presents with a rapidly enlarging thyroid gland. Ultrasound reveals a solid, markedly hypoechoic, ill-marginated mass in a background of chronic thyroiditis. Lymphoma can be classified into nodular, diffuse, and mixed subtypes on ultrasound; however, the key diagnostic finding in all subtypes is enhanced through transmission posterior to the lesion. Thyroid lymphoma can be diagnosed on fine-needle aspiration biopsy (FNAB) with flow cytometry and immunohistochemistry. Core biopsy, open surgical biopsy or thyroidectomy is reserved for cases

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**Fig. 6.** Coarse septations in Hashimoto’s thyroiditis. (A) Sagittal images of the thyroid in a patient with Hashimoto’s thyroiditis show multiple coarse echogenic linear septations (arrow), representing fibrous bands. These septal lines are mostly oriented in the long axis of the gland. (B) Another case of Hashimoto’s thyroiditis with thicker echogenic bands of fibrosis (F) separating coarse hypoechoic parenchyma. Thin septal lines are also present in the background. (C) “Bag of marbles” appearance; innumerable hyperechoic nodules represent areas of fibrosis.

**Fig. 7.** Hashimoto’s thyroiditis. Sagittal view shows patchy hypoechogenicity preferentially involving the anterior aspect of the thyroid (marked by the calipers). This area was more hypervascular on color Doppler (not shown) than the deeper aspect. Note the scattered micronodules in the remainder of the gland surrounded by normal background thyroid.

**Fig. 8.** Long-standing Hashimoto’s thyroiditis. Small, markedly hypoechoic thyroid gland in a patient on long-term thyroid hormone replacement for hypothyroidism. Variable amount of echogenic fibrosis and lobular thyroid margins can be seen.
in which FNAB is unavailable or the diagnosis cannot be confirmed by FNA alone.\textsuperscript{67} Surgical treatment of thyroid lymphoma is performed only if the trachea is markedly compressed by tumor; otherwise, thyroid lymphoma is the only thyroid malignancy treated nonsurgically: a combination of chemotherapy and external beam radiation is used.\textsuperscript{68} When disease is confined to the thyroid gland, the prognosis is good.

Although still controversial, numerous studies have shown an increased frequency of papillary thyroid cancer in patients with Hashimoto.\textsuperscript{69,70} It is unclear if this apparent increase may be because of increased detection of cancer in this population\textsuperscript{71} or if there is a pathologic and causative link between differentiated thyroid cancer andAITD.\textsuperscript{72} A recent single-center prospective study in patients newly diagnosed with thyroid nodules found no significant difference between the malignancy rate of 1.0% in a cohort of 164 patients with underlying Hashimoto’s thyroiditis. The incidence of thyroid cancer in the 551-person control group was 2.7%, using cytopathologic correlation.\textsuperscript{73} The sonographic features of benign and malignant nodules within a gland affected by diffuse Hashimoto’s thyroiditis are generally similar to their counterparts in the general population.\textsuperscript{74} However, when diffuse thyroid abnormalities are present, detection of focal nodules, particularly thyroid carcinoma, is more difficult. A solid hypoechoic papillary cancer could be masked in a hypoechoic, heterogeneous thyroid gland containing pseudonodules from lymphocytic infiltrates and fibrosis. Nonetheless, a higher percentage of malignant nodules in glands with background Hashimoto have calcifications. All types of calcifications (microcalcifications, tiny nonspecific nonshadowing bright reflectors, macrocalcifications, and peripheral eggshell calcifications) (Fig. 13) are observed with greater frequency in this patient subset.\textsuperscript{74} The frequency of psammoma bodies is lower, whereas the presence of dense calcifications is higher in papillary thyroid cancer in a Hashimoto’s thyroid compared with papillary thyroid cancer in a normal thyroid.\textsuperscript{75} Not only can the parenchymal heterogeneity and hypoechogenicity characteristic of Hashimoto’s thyroiditis lead to false-negative studies (a malignant nodule is obscured because of surrounding parenchymal distortion) (Fig. 14), false-positive ultrasound examinations (nodule is perceived

**Fig. 9.** Hashimoto’s thyroiditis with hyperplastic adenopathy. Longitudinal (A) and transverse (B) images of the inferior thyroid in 2 different patients show enlarged, hyperplastic central compartment nodes (arrows) with thick, hypoechoic cortex inferior or deep to the lower pole. When present, these are often a clue to the diagnosis. Enlarged lateral compartment nodes can also be seen. Notice decreased echogenicity in the inferior aspect of the imaged thyroid gland (asterisk).

**Fig. 10.** Nodular Hashimoto’s thyroiditis. This type of nodule has been recognized as a benign pattern seen in Hashimoto’s thyroiditis. It was described by Bonavita and colleagues\textsuperscript{63} as looking like a giraffe hide, consisting of bright blocks separated by dark bands. The background thyroid is hypoechoic and coarsened with micronodularity typical of diffuse Hashimoto’s thyroiditis. FNA biopsy showed CLT. This nodule is a variation of the homogeneously echogenic nodule referred to as “white-knight” (see Fig. 13).
within surrounding heterogeneous parenchyma) (Fig. 15) also occur. Careful, real-time examination, the use of cine images to differentiate true nodules from background heterogeneity, and actively searching for parenchymal calcifications is essential when evaluating for thyroid cancer. The Society of Radiologists in Ultrasound (SRU) consensus guidelines are then applied to triage each individual nodule.71 FNA biopsy can be used in cases in which the distinction cannot be made. Rapidly enlarging and markedly hypoechoic masses in this patient subset should be evaluated with biopsy to exclude lymphoma. The use of USE may soon have a larger role to play in evaluating the gland for thyroid cancer in the difficult cases.

Graves Disease

Graves disease is a common autoimmune disorder; it occurs in 1.5–2.0% of women in the United States.76 The disease is caused by binding of thyroid autoantibodies to the thyrotropin receptor on the follicular cells. Autoantibody binding stimulates the cells as though TSH triggered the receptor. The result is increased hormone synthesis and secretion, and growth of the thyroid gland. Diffuse hypertrophy and hyperplasia of follicular cells with colloid depletion and lymphoid infiltration are shown at histology.76 The diagnosis is typically made in the hyperthyroid patient who presents with diffuse thyroid enlargement (diffuse toxic goiter). Secondary findings (ie, orbitopathy) may be identified in a small subset of patients with long-standing disease. There are no specific grayscale ultrasound findings of Graves disease; findings suggestive of the

Fig. 11. Hashimoto’s thyroiditis with lymphoma. (A) Profoundly hypoechoic large expansile masses were found in both lobes because of mixed type pattern of B-cell lymphoma in this patient presenting with rapidly enlarging thyroid mass. Cervical adenopathy was present (not shown). Masses were low density on computed tomography (B) and were intensely hypermetabolic on fluorodeoxyglucose-positron emission tomography scan (C).

Fig. 12. Hashimoto’s thyroiditis. Nodular type of B-cell lymphoma in the isthmus shows relative hypovascularity on color Doppler with typical increased through-transmission, an important finding that suggests lymphoma. Background thyroid shows micronodules. (Courtesy of Mitchell E. Tublin, MD, Pittsburgh, PA.)

Fig. 13. Hashimoto’s thyroiditis with coexistent papillary thyroid cancer and benign focal Hashimoto nodule. Lower pole focal nodule is solid and hypoechoic with course internal calcification and fine bright reflector (arrow) that proved to be a papillary thyroid cancer. The asterisk denotes an echogenic solid nodule with hypoechoic halo that has been referred to as “white-knight” and is thought to be a regenerative nodule in Hashimoto’s thyroiditis.
disease include diffuse enlargement, convex bowing of the anterior gland margin, and mild textural coarsening (Fig. 16). The echogenicity of the gland can be normal but it is often decreased to variable degrees because of increased intra-thyroidal blood flow, functional changes in thyroid follicles with increased cellularity and decreased colloid content (resulting in reduction of cell/colloid interfaces), and lymphocytic infiltration. While the grayscale appearance of the thyroid in goitrous Hashimoto’s thyroiditis is similar to Graves disease, the latter thyroid parenchyma typically is less heterogenous and the contour is less lobular.

Early color Doppler studies suggested that the thyroid inferno pattern\textsuperscript{77} could be useful to differentiate between Graves and Hashimoto disease. Further work has suggested that color and spectral Doppler ultrasound might distinguish thyrotoxicosis caused by hormone overproduction from Graves disease from those with gland destruction related to thyroiditis.\textsuperscript{78–80} Although thyroid scintigraphy still plays a critical role in the diagnostic workup of hyperthyroidism,\textsuperscript{81} color and spectral Doppler interrogation has been shown to differentiate Graves disease from the other causes of hyperthyroidism with high specificity. An added advantage of ultrasound is that it may also identify nodules.\textsuperscript{82–86} Normal thyroid parenchyma shows occasional spots of flow on color Doppler; peak systolic velocities between 15 and 30 cm/s in the inferior thyroid artery and 3 to 5 cm/s in the intra-thyroid arteries are considered within the range of normal.\textsuperscript{87} Patients with untreated, active Graves disease show markedly increased vascularity at color Doppler, approximately 15-fold higher TBF measured in mL/min compared with normal,\textsuperscript{88} and high peak systolic velocity flow on spectral Doppler in the medium-sized perithyroid and intra-thyroid arteries. Saleh and colleagues\textsuperscript{85} found that a threshold peak thyroid artery systolic velocity of more than 60 cm/s had a 100% specificity and 80% sensitivity for distinguishing Graves from other causes of diffuse toxic goiter. This increased flow is believed to be caused by thyroid stimulation from activation of the TSH receptor rather than increased levels of thyroid hormone.\textsuperscript{89,90} Another study found that peak systolic velocity in the perithyroid artery was significantly higher in Graves disease than in Hashimoto’s thyroiditis (48 ± 12.3 vs 21.7 ± 8.4 cm/s).\textsuperscript{83} The investigators did not suggest a cutoff value for their differentiation. Advanced dynamic flow is a recently developed high-resolution power Doppler mode that can be used as a quantitative method for calculating TBF. Special software is used to calculate the percentage of flow in a region of interest. Using this technique, TBF was significantly higher in Graves disease than in patients with painless thyroiditis, subacute thyroiditis, or normal

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**Fig. 14.** Hashimoto’s thyroiditis with papillary thyroid cancer. Calipers denote a subtle hypoechoic nodule in a patient with background Hashimoto that proved to be a papillary thyroid cancer. The nodule was more discrete in real time but easily blends in to the adjacent hypoechoic parenchyma on the sagittal view.

**Fig. 15.** Hashimoto’s thyroiditis with pseudonodules. Thin and thicker fibrous septa separating the hypoechoic thyroid into lobules create the appearance of pseudonodules, causing parenchymal coarsening seen in this disease. When it is unclear if a nodule is present, FNA may be needed.
controls. Hence, all patients with Graves disease showed a TBF greater than 4%, whereas TBF in all other patients was less than 4%, signifying that 4% could be used as the discriminatory cutoff for distinguishing Graves disease from destruction-induced thyrotoxicosis. These findings correlated with radioactive iodine uptake scans. 37

Thyroid vascularity and thyroid artery volumetric flow have been shown to be significantly higher when the disease was most active as determined by clinical and laboratory criteria, suggesting color Doppler imaging may be a useful marker for disease activity to monitor treatment response. 79 A significant decrease in flow velocities in the superior and inferior thyroid arteries after medical treatment has been reported. Low thyroid echogenicity and high flow in the thyroid artery and glandular parenchyma before starting medical therapy were also shown to be specific for the prediction of relapse of hyperthyroidism at the end of the treatment. Thyroid glands with low initial echogenicity showed a 93% relapse rate after treatment with methimazole was completed. The relapse rate dropped to 55% when initial thyroid echogenicity was normal. 91

Treatment options include antithyroid medications and thyroid ablation with radioactive iodine. Radioiodine ablation should not be performed if a malignant lesion is suspected, and ultrasound-guided FNAB should precede treatment. 45 Surgical resection is reserved for patients who have contraindication to other options or when there is significant mass effect on surrounding structures. 92 Radioiodine therapy results in marked scarring and atrophy of the thyroid gland. 93 The ablated thyroid appears small and heterogeneous at ultrasound (Fig. 17) and is referred to as radiation thyroiditis.

De Quervain Thyroiditis

De Quervain thyroiditis also known as de Quervain’s thyroiditis, subacute granulomatous thyroiditis, nonsuppurative thyroiditis or subacute thyroiditis, is an uncommon, self-limiting, inflammatory thyroid disease. It is most commonly seen in middle-aged women and often follows a viral upper respiratory tract infection. Patients with subacute granulomatous thyroiditis typically

Fig. 16. Graves disease. (A) Diffusely enlarged, hypoechoic thyroid gland with mild heterogeneity on grayscale is not specific for Graves. (B) Thyroid scintigraphy shows increased tracer accumulation consistent with Graves disease. (C) Color Doppler reveals marked increase in hypervascularity in the parenchyma termed thyroid inferno. (D) Peak systolic velocity measured in the inferior thyroid artery in a different patient with long-standing untreated Graves disease measures 74 cm/s. Peak systolic velocity measurements greater than 60 cm/s are reported to be specific for Graves disease.
present with an enlarged, painful thyroid gland, low-grade fever, occasional dysphagia, suppressed levels of TSH, and an increased erythrocyte sedimentation rate. Pain is believed to be caused by stretching of the thyroid capsule from the underlying inflammation and edema. During the initial inflammatory phase, microabscesses form as follicles are replaced with neutrophils. Later, the macrophages and multinucleated giant cells that surround damaged follicles stimulate a granulomatous process. Thyrotoxicosis occurs with follicular disruption and hormone release. A transient period of hypothyroidism often ensues. Follicles regenerate in the healing phase; hence, most patients usually recover complete thyroid function and return to a euthyroid state. If thyrotoxicosis is the presenting symptom, a radioiodine scan may be needed to confirm thyroiditis by showing diminished or absent uptake.

Ultrasound is useful to confirm the initial diagnosis and for follow-up of patients with subacute thyroiditis. The ultrasound examination is also helpful because it may identify focal nodules and help exclude other causes of neck pain. The imaging manifestations of the disease parallel the disease course: abnormalities detected by all modalities tend to resolve when the clinical symptoms abate. The characteristic ultrasound findings for this disorder are ill-defined, moderately, or markedly patchy hypoechoic areas of thyroid parenchyma that show little to no vascular flow on color Doppler interrogation (Figs. 18 and 19). Hypoechoic areas tend to elongate along the long axis of the thyroid; these regions can involve one area or both thyroid lobes and extend across the isthmus. Half of patients presenting with unilateral thyroid pain have bilateral hypoechoic areas of involvement. When the condition is severe, affected regions can expand the capsule. A presumptive diagnosis may be made when ill-defined hypoechoic lesions on ultrasound correspond to the patient’s area of pain. Ultrasound features of malignancy (microcalcifications and taller-than-wide shape) are absent. Localized pain is also atypical in thyroid malignancy. FNAB is useful in those cases in which the hypoechoic areas cannot be distinguished from thyroid malignancy; histologic findings in thyroiditis characteristically shows multinucleated giant cells and mononuclear infiltrate. The imaging differential diagnosis includes other causes that create decreased parenchymal echogenicity although they are usually painless, such as lymphocytic thyroiditis, Graves disease, lymphoma, multinodular goiter, or occasionally thyroid malignancy. Short-term follow-up ultrasound may be useful to document regression or resolution.

On computed tomography (CT), the involved areas of subacute thyroiditis show decreased attenuation because of follicular disruption and loss of iodine concentration (physiologic thyroid iodine concentration is responsible for thyroid attenuation between 80 and 100 HU at CT). Low radiiodine uptake is shown at scintigraphy; however, uptake returns to normal when the patient returns to a euthyroid state. Magnetic resonance (MR) imaging findings reported in small series include ill-marginated areas of mild T1 signal hyperintensity with corresponding T2-weighted signal marked hyperintensity compared with the normal background thyroid signal. A single case report suggested that the focal fluorodeoxyglucose uptake with subacute thyroiditis may mimic thyroid malignancy. Patients are treated conservatively with antiinflammatory medications and corticosteroids.
Subacute Lymphocytic Thyroiditis

Subacute lymphocytic thyroiditis is a self-limited, autoimmune disorder that comprises 29% to 50% of all cases of thyroiditis.\textsuperscript{47} It occurs most often in women 30 to 50 years of age with increased thyroid peroxidase antibodies,\textsuperscript{100,101} although on average the antibody levels are lower than that in Hashimoto’s thyroiditis.\textsuperscript{102} Subacute lymphocytic thyroiditis is believed to be a less severe transient, or subacute, form of Hashimoto’s thyroiditis. Subacute lymphocytic thyroiditis occurring sporadically is termed painless thyroiditis or silent sporadic thyroiditis, but when it occurs within 1 year after parturition it is termed painless post-partum thyroiditis (PPT) or postpartum thyroiditis. Geographic and methodological differences probably account for a wide range of reported rates, but the mean prevalence of postpartum thyroiditis is 7.2% to and the mean incidence is 7.8% of

Fig. 18. De Quervain’s thyroiditis. Elderly woman presented with neck pain and new-onset atrial fibrillation with transient hyperthyroidism 1 month after a viral upper respiratory tract infection. Transverse (A) and sagittal (B) ultrasound showed a poorly circumscribed, masslike enlargement of the upper left thyroid lobe extending into the isthmus with bulging of the overlying capsule.\textsuperscript{123} I scan (not shown) showed markedly low iodine uptake and 2 FNA biopsies showed no malignant cells but were interpreted as lesion of undermined significance. (C) Repeat ultrasound approximately 5 months later showed complete sonographic resolution, supporting the diagnosis of subacute thyroiditis.

Fig. 19. De Quervain’s thyroiditis. (A) Panoramic ultrasound of the thyroid shows bilateral broad bands of hypoechogenicity in the ventral aspect of the gland (arrows) in this patient who presented with tenderness of the larger left lobe lesion. (B) Color Doppler view of the left lobe shows typical decreased perfusion in the area of thyroiditis. (Courtesy of Mitchell E. Tublin, MD, Pittsburgh, PA.)
women. The prevalence rate triples in women with type 1 diabetes. Postpartum thyroiditis is believed to occur as a consequence of the immunologic flare after the immune suppression of pregnancy in genetically susceptible women. The disease recurs in 69% of women in subsequent pregnancy. Postpartum thyroiditis is believed to occur as a consequence of the immunologic flare after the immune suppression of pregnancy in genetically susceptible women.

The disease is characterized pathologically by lymphocytic infiltration of the thyroid similar to Hashimoto’s thyroiditis, with the main difference being relative lack of oncocytic metaplasia, minimal to absent follicular atrophy and mild to no fibrosis. Clinically, patients present with transient thyrotoxicosis followed by hypothyroidism or any combination of the two 1 to 6 months (usually 4–6 weeks) after childbirth. Symptoms usually resolve clinically and radiographically by the end of the first postpartum year. There may be thyroid enlargement. Although most patients regain normal thyroid function, up to one-quarter to one-third develop permanent hypothyroidism within the next 10 years.

Although the role of ultrasound in this entity is limited, the characteristic ultrasound appearance is thyroid hypoechogenicity (Fig. 20), as in other forms of autoimmune thyroid disease. A prospective study showed that thyroid-antibody–positive women who developed PPT were more likely to show typical sonographic findings of thyroid hypoechogenicity compared with both antibody-positive women who did not develop PPT and a control group composed of antibody-negative women. In a subset of patients with PPT, thyroid gland hypoechogenicity preceded hypothyroidism, suggesting it may be useful for identifying patients at increased risk. The usefulness of thyroid ultrasound as an independent predictor of long-term thyroid dysfunction in patients with PPT is still unclear. As with De Quervain thyroiditis, when patients present with thyrotoxicosis, thyroid scintigraphy showing low radioidine uptake is useful in distinguishing PPT from Graves disease.

**Acute Suppurative Thyroiditis**

The abundant blood supply of the thyroid, its excellent lymphatic drainage, encapsulation, and high iodine content make the gland resistant to bacterial infection. Acute suppurative thyroiditis is therefore an uncommon but potentially life-threatening infectious diseases of the thyroid. It usually affects children and young adults who have congenital fourth branchial pouch sinus tracts, especially when they present with recurrent suppurative thyroiditis. These usually extend from the left (92%) pyriform recess to the thyroid gland. Elderly, immunocompromised, and debilitated patients can be affected by hematogenous or lymphatic seeding, or direct spread from pharyngeal or other regional infections. The most common predisposing factor in adults seems to be underlying thyroid disease (ie, multinodular goiter, Hashimoto’s thyroiditis, or thyroid carcinoma). Infection is most often caused by a bacterial organism such as *Staphylococcus* or *Streptococcus* species, but polymicrobial infection is also common. Acute suppurative thyroiditis presents with rapid onset of thyroid pain, fever, dysphagia, dysphonia, and compressive symptoms. Leukocytosis and increased erythrocyte sedimentation levels are often present.

Contrast-enhanced CT is useful in the acute setting to evaluate the extent of infection within and beyond the thyroid gland and depict the presence of an abscess. Unlike sonography, CT has the advantage of being able to evaluate the pharynx and superior mediastinum. The main role of sonography is to identify and provide guidance for percutaneous drainage of thyroid abscesses. Sonographic findings are generally nonspecific. The thyroid may appear enlarged and hypoechoic secondary to inflammation. Focal accumulation of complex fluid containing bright echoes from gas suggests an abscess. An infected sinus tract to the pyriform sinus is suspected when a left-sided, irregular tubular tract containing complex echoes extends from the thyroid gland superiorly into the neck (Fig. 21). Patients with suspected pyriform sinus fistulae should undergo a barium esophagram when the infection is quiescent or direct inspection by endoscopic hypopharyngoscopy. Fistulae are usually managed surgically, although there has been a trend toward less invasive treatment such as chemocauterization with trichloroacetic acid into the fistula opening on direct endoscopy. The remaining cases are treated with aggressive antibiotics and drainage of any formed abscess.
Simple/multinodular Goiter

Goiter refers to generalized enlargement of the thyroid. It can be seen with most diffuse (or nodular) thyroid diseases. Simple diffuse nontoxic goiter refers to diffuse, nonnodular thyroid enlargement in a euthyroid patient (Fig. 22), which may eventually progress to multinodular goiter in the absence of underlying thyroid disease. The cause of simple goiter is multifactorial and involves complex interactions between environmental (iodine intake), genetic, and endogenous (female gender) factors. The most common cause of goiter outside the United States is dietary iodine deficiency. To compensate for inadequate thyroid hormone output, follicular epithelium undergoes compensatory hypertrophy to achieve a euthyroid state. Pathologically, the nodularity observed in multinodular goiter consists of ordinary, polyclonal follicles that expand in a nodular fashion because they replicate within a mold made out of a poorly distensible network of connective tissue resulting from scarring caused by hemorrhagic necrosis over the course of goiter growth. It is reminiscent to the development of round regenerative nodules in a cirrhotic liver.

On ultrasound, multinodular goiter, also known as adenomatous (although nodules are not true adenomas) or colloid goiter, is characterized by focal or diffuse replacement of the thyroid parenchyma by closely opposed, isoechoic solid nodules containing variable amount of cystic change, without normal intervening parenchyma and background heterogeneity (Fig. 23).

Fig. 21. Acute suppurative thyroiditis. This 17-year-old woman presented with repeated episodes of acute neck pain with fever requiring hospital admission. (A) Transverse and (B) longitudinal ultrasound images through the upper pole and axial (C) and coronal oblique (D) reconstructed contrast-enhanced neck CT images showed a tubular tract extending laterally from the hypopharynx into the left thyroid substance (arrow) containing complex fluid representing an infected pyriform sinus-thyroid fistula. Culture of the fine-needle aspirate fluid grew methicillin-resistant Staphylococcus aureus. Because of recurrent symptoms after antibiotic therapy, the patient required left thyroid lobectomy. (Courtesy of Ka-Kai Ngan, MD, Pittsburgh, PA.)

Fig. 22. Simple diffuse goiter. A transverse ultrasound image through the isthmus of a euthyroid patient shows a moderately to markedly enlarged thyroid gland with normal homogenus thyroid echogenicity. Notice that both thyroid lobes extend lateral to the carotid artery.
Parenchymal nodularity and inability to reproduce the borders of individual nodules in 3 dimensions is often accentuated during real-time examination. In other cases, multiple discrete nodules can be seen throughout an otherwise normal-appearing gland. When involvement is asymmetric, the lower lobes are often preferentially affected. Similar-appearing nodules with borders that blend together can be difficult to distinguish from one another. Over time, the nodules undergo a varying degree of cystic or complex cystic changes because of necrosis, colloid accumulation, or hemorrhage; this accounts for the varying size and composition of the nodules in multinodular goiter. Dystrophic calcifications are common; the calcifications are typically coarse and cause posterior acoustic shadowing. The internal matrix of the nodules may be obscured by shadowing from rim calcifications. When all nodules appear similar, representative nodules, or nodule clusters when involvement is focal, can be selected for measurement with emphasis on the ones that are most reproducible for follow-up purposes. Nodules that appear dominant, enlarging, or different, or those that have malignant sono-graphic features (microcalcifications, hypoecho-genicity, tall configuration) are targeted for ultrasound-guided FNA.

CT and MR imaging can also reveal multiple variably sized nodules containing complex cystic change, but they are better suited than ultrasound to assess the intrathoracic extension of a substernal goiter, compression of adjacent trachea and esophagus, and mass effect on surrounding vessels. Although ultrasound is the modality of choice for evaluating patients with mild to moderate thyroid enlargement, its inability to penetrate through lung and bone limit the usefulness of ultrasound for evaluating the mediastinal extension of goiter. T2-weighted MR images show heterogeneous signal, and T1-weighted images show high signal foci, representing colloid-containing or hemorrhage-containing cysts. Parenchymal calcifications are better shown on ultrasound or CT. Treatment is focused on maintaining or restoring normal thyroid function and reducing gland volume in patients whose main symptoms are related to mass effect. Reduction of thyroid volume may be achieved by levothyroxine suppression, surgical resection, or ¹³¹I radioiodine ablation.

Multiple studies have shown that the risk of thyroid cancer in each patient is the same, and independent of the number of thyroid nodules present. Therefore, the risk of malignancy in each individual nodule within a multinodular gland decreases by a rate proportional to the number of nodules. In a prospective study by Deandrea and colleagues in a cohort of 402 patients with nonpalpable or single palpable nodules, it was shown that 22% of malignant thyroid nodules evaluated by FNA were found in multinodular thyroids, whereas 33% were found in a uninodular goiter. Not only should the presence of multiple nodules not be dismissed as a sign of benignity but each nodule should be scrutinized for the presence of suspicious features. Both the SRU and American Thyroid Association recommend analyzing the sono-graphic features of individual nodules in a multinodular gland to triage the nodules rather than using nodule size as the primary criteria for biopsy in patients with multiple nodules. A study by Frates and colleagues found that among 120 patients with multiple nodules, the nodule harboring the thyroid cancer was in the largest nodule only 72% of the time. The likelihood that the largest nodule was malignant decreased as
the number of nodules increased. Many laboratories consider nodules that are sonographically similar to be histologically similar. When nodules with different sonographic features are present, each nodule should be evaluated individually by applying the criteria established for solitary nodules, discussed in the subsequent article. The nodules with more suspicious features should be selected for biopsy first, followed by other nodules that are representative of the remaining nodules.120,123–126 Nodules that are not biopsied and do not seem suspicious can be followed to evaluate for rapid growth or other features that cause concern.71

**Riedel Thyroiditis**

Riedel thyroiditis, or Riedel's thyroiditis, is a rare, local manifestation of a systemic form of systemic fibrosclerosis. Its cause is obscure but it is characterized at histology by a fibroinflammatory process that destroys all or portions of the thyroid gland. Fibrosis and inflammation may extend beyond the capsule into the surrounding tissues128,129; the adjacent carotid artery and jugular vein may be encased by fibrosis. Riedel thyroiditis may occur in isolation, or as part of a systemic fibro-sclerosing process that may include retroperitoneal fibrosis, mediastinal fibrosis, orbital pseudotumor, and sclerosing cholangitis.

Most patients are between 30 and 50 years old at the time of diagnosis. Riedel thyroiditis is rare: the estimated incidence of Riedel thyroiditis among thyroidectomy specimens has been reported to be between 0.04% and 0.30%.130,131 The patients typically present with an enlarged, fixed, rock-hard, painless goiter. Tracheal and esophageal compression by periglandular fibrosis may cause dysphagia and dyspnea.46 Most patients are euthyroid at the time of diagnosis, but in 30–40% hypothyroidism eventually develops when the thyroid becomes nearly completely replaced by fibrosis.132 Forty-five percent of patients have increased thyroglobulin and thyroid peroxidase antibodies,132 although it is unclear if this is a cause or the effect of fibrotic destruction. Riedel thyroiditis should be distinguished from the fibrotic form of Hashimoto. The fibrotic form of Hashimoto’s thyroiditis seen in up to 13% of patients with Hashimoto’s thyroiditis,133 and also results in a rock-hard thyroid gland on palpation, was previously believed to represent a variation of Riedel thyroiditis but they are now considered separate entities but in earlier correction it was as is. In contrast to the fibrous form of Hashimoto, Riedel shows extrathyroid extension and loss of normal thyroid lobulation.128

The rarity of Riedel thyroiditis accounts for the paucity of literature describing its imaging appearance. The radiographic findings reflect the fibrotic and locally aggressive nature of the process. Sonographic findings include an enlarged, hypoechoic gland or coarsened echotexture with fibrous septations resulting in pseudonodular morphology.132,134,135 Involvement of the neck and thyroid gland can be focal or diffuse. CT shows an enlarged, hypodense to normal attenuation gland, which slightly enhances after the administration of intravenous contrast.131 MR may be more useful than CT in that fibrous tissue shortens T2 relaxation times and results in characteristic low T1-weighted and T2-weighted signal intensity (Fig. 24).135,136 Both minimal and marked enhancement after contrast administration have been described.136,137 CT and MR imaging are better suited than ultrasound to determine the extent of tracheal and esophageal compression, and extrathyroidal soft-tissue involvement but either modality may show encasement of jugular vessels.

![Fig. 24. Riedel thyroiditis. The thyroid is diffusely enlarged and hypodense on CT (A) and low signal on T1-weighted and T2-weighted MR imaging (B and C) consistent with fibrosis. The thyroid is encircling the trachea and esophagus posteriorly.](image-url)
Extracapsular extension is neither a sensitive nor specific finding of Riedel thyroiditis. Periglandular fibrosis may be absent in early stages of Riedel disease and when present the differential diagnosis expands to include thyroid lymphoma and anaplastic thyroid carcinoma. Anaplastic thyroid cancer is expected to show more heterogeneous echogenicity on ultrasound and higher T2 signal intensity on MR imaging because of tumor necrosis. FNAB is typically inconclusive; the ultimate diagnosis of Riedel thyroiditis is usually made by surgical wedge resection. The treatment may involve surgical resection for compressive symptoms if medical therapy fails.

Amiodarone-associated Thyroid Disease

Amiodarone is an iodine-rich antiarrhythmic cardiac drug used to treat certain arrhythmias refractory to standard therapy. Although most patients remain euthyroid, 15% to 20% develop either amiodarone-induced thyrotoxicosis (AIT) or amiodarone-induced hypothyroidism. There is no role of imaging for the latter because these patients are all generally treated with thyroid hormone replacement. There are 2 main types of AIT. Type 1 is a form of iodine-induced hyperthyroidism that develops in abnormal glands (multinodular goiter or latent Graves disease). The thyrotoxicosis in type 1 AIT is caused by excessive thyroid hormone synthesis and is treated with antithyroid drugs. The more common type 2 AIT occurs in patients without underlying thyroid disease. Thyrotoxicosis in these patients is caused by amiodarone-induced destructive thyroiditis; the disease is treated with steroids.

Although there are mixed forms, classifying patients with AIT into the correct subtype is vital for determining appropriate therapy. Ultrasound with color Doppler has an important role to play in this regard. Ultrasound in patients with type 1 AIT reveals a diffuse or nodular goiter. On the other hand, a normal thyroid or small diffuse goiter is shown in patients with type 2 AIT. Color Doppler is particularly useful in distinguishing between the 2 types of AIT. Mildly to markedly increased flow is shown within the thyroid in patients with type 1 AIT, whereas flow within the thyroid is markedly diminished or absent in patients with type 2 AIT. Therefore, the presence of vascular flow on color Doppler suggests type 1 AIT. Color Doppler flow evaluation should be directed at the thyroid parenchyma and not discrete nodules, if present. Thyroid radioactive iodine uptake values are likewise usually low to absent in type 2 AIT and are normal or increased in type 1 AIT. Preliminary work by Piga and colleagues has found that thyroid technetium 99m methoxyisobutylisonitrile scintigraphy may also be a useful tool in differentiating the different forms of AIT and potentially identifying the mixed form. In this study, diffuse retention of the radioactive tracer was present in all patients with type 1 AIT, which indicates hyperfunctioning tissue, whereas no significant uptake was found in type 2 AIT, suggestive of a destructive process. Other
drugs that are associated with thyroid abnormalities include lithium, interferon alfa, and interleukin 2.

**Atrophic Thyroiditis**

Atrophic thyroiditis is an AITD characterized by a small (atrophic) thyroid gland with lymphocytic infiltration, fibrosis, and parenchymal destruction, leading to clinical hypothyroidism. Serum autoantibodies to thyroid peroxidase and thyroglobulin are present, similar to Hashimoto’s thyroiditis. The main distinction from Hashimoto’s thyroiditis is the absence of a palpable goiter. A higher percentage of patients with atrophic thyroiditis have also been found to have antibodies blocking the TSH receptor compared with classic goiterous Hashimoto.\(^{146}\) TSH receptor blockade (as opposed to the TSH stimulation of Graves disease) is believed to cause thyroid atrophy and hypothyroidism.\(^{147}\) The typical sonographic appearance of atrophic thyroiditis is a small, hypoechoic thyroid (Fig. 26). Whether atrophic thyroiditis represents a separate disease entity from Hashimoto, end stage of Hashimoto, or is simply an extreme within a normal distribution of thyroid volume has been a topic of continued debate.\(^{148,149}\)

**Thyroid Amyloid**

Systemic amyloidosis can affect any organ of the body including the thyroid. Although this condition is rarely encountered in clinical practice, specific sonographic appearances have been described. In 1 small series, in which histopathologic examination of the thyroid was performed, distinctive sonographic findings included enlargement of 1 or both lobes of the thyroid, high echogenicity approaching that of the connective tissue of the neck, decreased ultrasound penetration, and a very fine homogenous echotexture (Fig. 27) suggestive of ground glass appearance. Tiny cystic cavities within the thyroid believed to be dilated follicles were occasionally observed.\(^{150}\)

**Metastatic Disease**

Most thyroid metastases are clinically silent and most nodules in patients with known malignancy are still benign. Although detection of clinically apparent palpable metastatic disease to the thyroid is uncommon (5% of 188 in 1 autopsy series),\(^{151}\) when meticulous autopsy is performed, the incidence is as high as 24%.\(^{152}\) Lymphoma, melanoma, renal cell carcinoma, lung, colorectal carcinoma, and breast cancer metastases to the
thyroid have been described, seen in association with diffuse metastatic disease elsewhere. Although thyroid metastases have highly variable imaging appearances, sonographic findings in a series of 11 patients showed all metastasis to be either hypoechoic or markedly hypoechoic, most with well-defined margins and lack of a halo and calcifications (Figs. 28 and 29). It is not unexpected that most metastases were hypodense compared with the usually hyperdense, iodine-rich, thyroid gland on CT. Signal characteristics on MR imaging were variable.153 Multiple, similar appearing solid nodules are the most common presentation; but a single nodule or a heterogenous pattern can also occur when the thyroid is diffusely involved. Multiple markedly hypoechoic thyroid nodules with concurrent cervical adenopathy may suggest lymphoma.152 Tissue sampling with FNA is used to establish the diagnosis.

**SUMMARY**

Optimized technique, improved scanner platforms, and color Doppler have made it possible to quickly evaluate thyroid anatomy and perfusion. Thyroid hypoechogenicity and parenchymal heterogeneity are easily appreciated and are the hallmark ofAITD. A wide range of diffuse thyroid diseases are often first evaluated with ultrasound; although the imaging features of these diseases often overlap, a reasonable differential diagnosis can often be made when clinical and laboratory values are considered. Color Doppler may play an ancillary role in assessing disease activity in several causes of thyrotoxicosis. The potential role of recent ultrasound advancements (elastography, microbubbles) in the assessment of thyroid disease is under investigation.

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