PARATHYROID IMAGING
Imaging of the parathyroid glands revolves around the detection of parathyroid adenomas and hyperplastic parathyroid glands in the setting of primary hyperparathyroidism. Arguments for and against imaging and about which imaging modality to use have been hotly debated in the radiology and surgery literature.

I Anatomy
The lower parathyroid glands are derived from the third pharyngeal pouch and the upper parathyroid glands from the fourth pharyngeal pouch of the branchial apparatus. Most people have four glands (a pair at the upper and lower poles of the thyroid gland), however 25% of individuals have more than four (1, 2). The parathyroid glands may be aberrantly located anywhere from the carotid bifurcation to the anterior mediastinum, with inferior migration occurring most frequently (3). The vascular supply to the parathyroid glands is usually through the superior and inferior thyroidal arteries, with drainage to thyroidal veins. The glands are innervated through the cervical sympathetic plexus.

I Hyperparathyroidism
Hyperparathyroidism has an incidence of 0.037% per year in the United States (4). Patients may present with the classic findings of bones (demineralization or arthritis), stones (renal calculi), groans (abdominal pain), or moans (psychiatric disturbances). Primary hyperparathyroidism is caused by a solitary parathyroid adenoma in 80%–85% of cases (5–9). The remaining 15%–20% of patients with hyperparathyroidism have either hyperplastic parathyroid glands (12%–15%), multiple adenomas (2%–3%), or parathyroid carcinoma (<2%) (5–9).

Parathyroid adenomas are ecotopic (not around the thyroid bed) in 10%–20% of cases (6–8, 10).

Options for imaging the parathyroid glands are many and include ultrasound (US), computed tomography (CT), magnetic resonance (MR) imaging, angiography, and nuclear medicine scintigraphy. The advantages and disadvantages of the various cross-sectional imaging techniques are summarized in Table 1 (3, 11–14). The choices for scintigraphic localization of parathyroid adenomas include thallium-201–technetium-99m pertechnetate subtraction scanning, Tc-99m sestamibi (hexakis-2-methoxy-isobutyl-isonitrile) subtraction imaging with iodine-123 or Tc-99m pertechnetate, and Tc-99m sestamibi imaging without subtraction. The subtraction techniques allow tracers that are concentrated in the thyroid gland (pertechnetate and iodine) to be subtracted from ones (thallium and sestamibi) that accumulate in both thyroid glands and parathyroid adenomas. Thallium is a potassium analog that may concentrate in parathyroid adenomas due to changes in potassium turnover in active cells. Thallium emits low-energy, low-penetrating, 80-keV photons that make penetration from the mediastinum variable. In addition, thallium washes out of adenomas relatively rapidly. The mechanism for sestamibi uptake is not well understood but may relate to mitochondrial density in oxyphil cells, blood flow within adenomas, or potassium turnover.
(15,16). Tc-99m sestamibi has 140-keV photons that penetrate the anterior neck and mediastinal soft tissues better and is concentrated at a higher rate and for a longer time within an adenoma than thallium. Because sestamibi uptake in parathyroid adenomas persists after thyroid gland wash-out, it can be used without subtraction techniques if one performs delayed imaging. The difficult task of patient immobilization and accurate superimposition of subtracted images, required with thallium-pertechnetate studies, is obviated with delayed sestamibi imaging. Single photon-emission CT (SPECT) scanning can also be combined with high-dose Tc-99m sestamibi scintigraphy for more accurate localization of parathyroid adenomas (15).

In most institutions, preoperative localization of the parathyroid glands with imaging is not performed before the first surgery (for patients who have previously undergone surgery, see below). This stems from the early surgical literature that suggests that surgical time, morbidity, and mortality are not substantially influenced by preoperative localization of parathyroid adenomas for hyperparathyroidism (17–19). Surgical exploration entails bilateral dissection of the perithyroidal region, emphasizing the inferior poles where most parathyroid adenomas occur. In experienced hands, this surgical procedure can be performed quickly and accurately with success rates of more than 90% (8,19–22).

Proponents of preoperative localization of parathyroid adenomas even in previously unoperated cases cite (a) the need for only unilateral dissection when an adenoma is evident at imaging; (b) the identification of ectopic adenomas preoperatively, allowing better planning and patient education; (c) detection of other head and neck masses that may require treatment at the same time (eg, thyroid masses); and (d) the reduction in operating room time, recurrent laryngeal nerve paralysis, and postoperative hyperparathyroidism when preoperative imaging is performed (22–26). In studies by Russell et al (25) and Casas et al (27), the difference between mean operating times with (71 and 135 minutes, respectively) and without (97 and 180 minutes, respectively) preoperative imaging justified the expense of the study. The operative success rate also improved from 90% to 100% with preoperative imaging (27). Uden et al (28) also noted that the time for surgery and anesthesia decreased with preoperative imaging; however, when a cost-benefit analysis was performed, they found that the cost of the imaging procedure outweighed its benefit. A reduction of 28 minutes of operating room time in the study by Roe et al (19) did not justify the $901.00 mean cost of localization. Other surgeons take a centrist position regarding bilateral or unilateral neck explorations. They will perform unilateral neck dissection if imaging studies are definitive, but convert to bilateral surgery if (a) imaging is equivocal or shows a multifocal abnormality, (b) more than one enlarged gland is identified at surgery, (c) the patient has a multiple endocrine neoplasia (MEN) syndrome (often associated with parathyroid hyperplasia), or (d) a unilateral exploration is unrevealing (25).

When a parathyroid adenoma is not identified in a stereotypical perithyroidal location, the surgeon may empirically explore the anterior mediastinum, deep cervical space, periesophageal grooves, or carotid sheath region. The yield of surgery in this scenario is much lower (less than 70% successful) than that expected for those adenomas in a perithyroidal location, and the surgical complication rate increases with such blind explorations (20). The intrathyroidal parathyroid adenoma (which accounts for a small percentage of cases) cannot be readily distinguished from thyroid adenomas and poses a particularly difficult problem (8,29). To make matters more confusing, thyroidal abnormalities occur in up to 40%–48% of patients with hyperparathyroidism (21,30). These factors have led less experienced surgeons and those who have had a less successful track record to opt for preoperative localization of all parathyroid adenomas.

It is fairly well accepted that the risks associated with surgery in a patient who has previously undergone surgery outweigh the cost of preoperative imaging. In those patients who undergo repeat surgery, the risk of vocal cord injury due to damage to the recurrent laryngeal nerve or vagus nerve is approximately 7%, compared with the initial operating room risk of 1.3% (18). When imaging is not performed before repeat surgery for hyperparathyroidism, surgery is approximately 60% successful; when imaging is performed before repeat surgery, the success rate increases to 80%–90% (7). At repeat surgery of previously operated cases, 30%–75% of abnormal parathyroid glands are found in a perithyroidal location, overlooked or missed at the time of initial operation (18,20,29,31). In patients in whom the initial surgery fails, parathyroid adenomas are located in the anterior mediastinum in 20%–38%, in a paraesophageal or deep cer-

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<td><strong>Modality</strong></td>
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<tr>
<td>CT</td>
<td>Examines head, neck, and chest; easy detection of calcification; biopsy capable</td>
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<td>Nuclear medicine</td>
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<td>US</td>
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Figure 1. Parathyroid adenoma. T1-weighted MR image demonstrates a parathyroid adenoma (arrow) on the right side of the trachea just behind the carotid artery. The contralateral "nodule" (*) is the esophagus.

Figure 2. Initial and delayed Tc-99m sestamibi scans of parathyroid adenoma. (a) Initial 15-minute scan shows tracer accumulation both in the thyroid gland (T) and a nodule (arrow) below the right lobe of the thyroid gland. (b) Two-hour delayed image shows that the tracer accumulation in the thyroid gland has largely cleared; the parathyroid adenoma (arrow) remains evident.

Parathyroid Adenomas

At US, parathyroid adenomas appear as oval, oblong, or bulbous lesions with an echogenicity less than that of the thyroid gland (21,33). With high-resolution US, sensitivities of 60%-70% and specificities of 90%-96% have been achieved for adenomas (5,6,11,21,33). Of those glands greater than 1 g in size, US has a detection rate of 95% (21). When Stark et al (33) compared the accuracies of high-resolution CT and US in the detection of parathyroid adenomas, they found the sensitivity of CT to be 70% with a specificity of 90%, an improvement from their experience with US. Sommer et al (34) also found CT to be more accurate than US by more than 10%; combining the studies yields a detection rate of 89% in patients who have not previously undergone surgery.

Spritzer et al (14) were one of the first groups to report on the accuracy of MR imaging in the detection of parathyroid adenomas. Seventeen patients had adenomas; MR imaging correctly depicted 14 of them (82.3%). Two false-positive and three false-negative studies for adenomas were reported; given the possibility of 72 glands, this yields an accuracy of 92% for MR imaging of adenomas (Fig 1).

Currently, most centers have embraced Tc-99m sestamibi imaging without subtraction as the technique of choice for nuclear scintigraphy of the parathyroid glands. Ten to 30 mCi of Tc-99m sestamibi is injected, with scanning at 15-minute intervals up to 2-4 hours after injection (35). Because the agent washes out of the thyroid gland rapidly but is retained by parathyroid (and thyroid) adenomas, delayed images are the most useful for localization (Fig 2). One need not sacrifice accuracy with the simpler sestamibi study. The overall sensitivity of T1-Tc-99m pertechnetate subtraction scintigraphy for parathyroid adenoma detection (75%-85%) (36,37) is substantially less than that of Tc-99m sestamibi, which is about 90%-100% (16,37-40). A recent article by Lee et al (41) has shown a specificity of 98% for double-phase sestamibi imaging.

When Price (7) reviewed the pre-sestamibi literature up to 1993, he found that MR imaging had the highest sensitivity for the detection of adenoma (74%), followed by nuclear medicine studies (72%), CT (63%), and US (63%). The false-positive rate of nuclear medicine (11%) was lower than that of MR imaging (14%), CT (16%), and US (18%). Sestamibi data over the past 3 years suggest that it surpasses all other techniques in sensitivity and accuracy. Unfortunately, the high rate of thyroid abnormalities (40%-48%) that coexist with parathyroid adenomas may lead to false-positive scintigrams because some thyroid lesions may concentrate radiotracers to the same degree as parathyroid adenomas (16,29,37). Reports of Tc-99m sestamibi in thyroid cancers and their nodal and distant metastases signal the possibility for false-positive studies (42).

More invasive studies have a high yield, but are more demanding. The study by Miller et al (43) found parathyroid venous sampling (80%), intraoperative US (78%), and arteriography (49%-60%) to have higher sensitivities than the noninvasive imaging studies. The expense and technical difficulty in performing these invasive examinations preclude their routine utilization, but they may be held in abeyance for cases with equivocal or non-revealing noninvasive studies.

In the patient in whom prior surgery for a parathyroid adenoma has failed, both imaging and surgery must contend with scar tissue in and around the thyroid glands, loss of tissue planes, postoperative inflammation, lymphadenopathy simulating parathyroid
adenomas, and distortion of landmarks. False-negative images (due to obscured anatomy) tend to occur in the perithyroid or perithymic operative beds. The frequency of false-positive examinations (usually due to lymphadenopathy) is lowest with nuclear medicine studies, followed by MR imaging, US, and CT (29). In patients who have undergone repeat surgery, the sensitivities of US (36%-76%) (7,29,33,44), scintigraphy (26%-90%) (7,12,29,44), CT (46%-63%) (7,29,33,44), and MR imaging (50%-91%) (3,7,12,29,44) have ranged widely. Price (7) concluded in a review of the literature that MR imaging was the best cross-sectional imaging study to perform in this scenario and nuclear scintigraphy the best functional examination. The latest figures on sestamibi scintigraphy have shown sensitivities and accuracies in the 80%-90% range (45,46). Sestamibi scintigraphy is therefore probably the most accurate and affordable study; its disadvantage is that the surrounding anatomy is not visualized for surgical orientation. When combined with US, the accuracy does not increase; however, the accuracy of sestamibi and MR imaging combined reaches 92% (47). Alternatively, one can perform the most accurate (although most expensive) cross-sectional imaging technique, MR imaging, which provides good anatomic detail, while running the small risk of mistaking a lymph node for an adenoma. Because a third surgery is an anathema to the surgeon, multiple studies are not uncommonly performed if one is not definitive. The idea of using a morphologic test (CT, US, or MR imaging) as well as a functional test (Tc-99m sestamibi) is appealing. Use of this algorithm will increase the success rate of repeat surgery by more than 30% (18).

I Parathyroid Hyperplasia
About 30% of patients with parathyroid hyperplasia have familial hyperparathyroidism, including variants of the MEN syndrome (Table 2). As noted earlier, 12%-15% of patients with hyperparathyroidism have hyperplasia. CT is reported to have a sensitivity of 45%-88% (7,33), US 30%-69% (5-7,33,47), and MR imaging 40%–63% (7,14) for detecting hyperplastic glands. Parathyroid hyperplasia is detected in 43%-45% of cases with thallium subtraction and in 55%-75% of cases with technetium sestamibi (5-7,37,48). The added accuracy in identifying hyperplastic glands has led a growing consensus in support of the use of Tc-99m sestamibi as the optimal agent for parathyroid adenoma and hyperplasia localization (16,37,40).

I Parathyroid Carcinoma
In all patients with hyperparathyroidism, the frequency of parathyroid carcinoma is only 1%-2%; however, parathyroid carcinoma causes hyperparathyroidism in 8%-90% of cases (1,2). Metastases to lymph nodes occur in one-third of cases, and distant metastases occur in 21%-28% of patients. Men and women are affected equally. Edmonson et al (49) noted that a parathyroid carcinoma may have the same sonographic appearance as a benign large adenoma (hypoechoic with or without heterogeneity); only the presence of local invasion into the thyroid gland, muscles, or vessels or nodal metastases would suggest this diagnosis. Parathyroid carcinomas have been reported to accumulate Tc-99m sestamibi (45,50).

I Secondary and Tertiary Hyperparathyroidism
The evaluation of patients with secondary or tertiary hyperparathyroidism is rarely centered around the parathyroid glands because the kidneys are the source of the abnormality in these diseases. Parathyroid glandular hyperplasia usually occurs in association with chronic renal failure and renal osteodystrophy. Tc-99m sestamibi has been able to help identify bilateral uptake in hyperplastic glands and residual parathyroid tissue in those individuals treated surgically in the neck for secondary hyperparathyroidism (48).

THYROID IMAGING
I Anatomy
The thyroid gland sits anterolateral and superficial to the larynx and trachea and is fixed to the airway by fibrous septa. Although no true lobes of the gland exist, it is enveloped by portions of the deep cervical fascia. The thyroid isthmus is the midline portion of the gland, and from it may arise a pyramidal "lobe" (in 50%-80% of patients) lying superficial to the thyroid cartilage (51). The vascular supply to the thyroid gland is derived from paired superior thyroid arteries (branches of the external carotid arteries) and inferior thyroidal arteries (branches of the thyrocervical trunks of the subclavian arteries). The incon-
Figure 3. US scan shows a calcified thyroid mass. Note the acoustic shadowing (*) behind the echogenic focus (arrow), signifying calcification within this thyroid gland. Unfortunately, the presence or absence of calcification is not very useful for distinguishing benign from malignant thyroid lesions.

The thyroid gland drains into superior, middle, and inferior thyroidal veins, which pass to internal jugular and brachiocephalic veins. Vagal and sympathetic plexus branches provide innervation.

I Imaging of Masses

US.—The main role of cross-sectional thyroid imaging (US, CT, MR imaging) is to evaluate thyroid masses for potential malignancy. US, because of its simplicity, low cost, and ability to help distinguish cystic from solid lesions is often the first modality employed to evaluate a thyroid mass in the euthyroid patient. When a solid lesion is hyperechoic, the frequency of malignancy is only 4% (52). If a solid lesion is isoechoic, the frequency of malignancy increases to 26% and, if hypoechoic, malignancy occurs in 63% (52). Papillary carcinoma most commonly is seen as a solid hypoechoic (77%) or isoechoic (14%) mass with or without calcification (calcifications are hyperechoic but cause acoustic shadowing that is hypoechoic [Fig 3]) (52). If a cancer is hyperechoic at US, it is usually due to the sclerosing form of papillary carcinoma (10).

If one looks at the margins of tumors at US, one finds that 16% of malignant lesions have sharply margined, well-defined borders whereas irregular or ill-defined borders occur in approximately 60% of cancers (52). Unfortunately, irregular or ill-defined borders also occur in approximately 45% of benign lesions (52). When a mass has a complete halo of echopenia around it, the lesion is 12 times more likely to be benign than malignant. If the halo is incomplete, a benign origin is still approximately four times more likely than a malignant one (52). Lesions meeting the absolute criteria for cysts (well-demarcated, smooth-walled, anechoic, and demonstrating enhanced through-transmission) are usually benign (10). A cystic lesion with punctate, calcified mural nodules is worrisome for papillary carcinoma.

Nuclear medicine.—The common agents used for thyroid imaging include I-123, I-131, and Tc-99m pertechnetate. Because the radiation energy of I-131 is so high (364 keV), it is the preferred agent for imaging subternal thyroid glands or for performing whole-body imaging after thyroid ablation in order to detect metastatic foci of thyroid cancer. The other agents have energies of 140 keV (Tc-99m) and 159 keV (I-123) (53). The major role of scintigraphy in the evaluation of a thyroid mass is the determination of whether the lesion is hot (more uptake than the normal thyroid gland), warm (some activity but not as much as the normal gland), or cold (little to no uptake). The risk of cancer is 1%—4% for a hot nodule, 8%—10% for a warm nodule, and 15%—25% for a cold nodule (7,54,55). In a patient with a prior history of head and neck irradiation, the risk of malignancy in a cold nodule doubles to 30%—50% (7). Cold nodules in men have a higher rate of malignancy because women have a greater frequency of benign cold nodules from degenerated adenomas. If one performs dynamic injection Tc-99m pertechnetate scintigraphy, one may find that hypoperfused lesions (less vascularity than that of the native thyroid gland) are virtually never cancers whereas most malignancies are “euperfused” or hyperperfused (55). Rarely, a lesion is cold at I-123 scintigraphy but hot or warm at Tc-99m pertechnetate scanning (a “discordant nodule”). It is believed that this phenomenon is caused by a lesion that traps iodine (assessed with pertechnetate) but does not organify it. The differential diagnosis includes malignancy, goiter, or follicular adenoma. Often a biopsy is required in this situation.

CT.—Enhanced CT has a major drawback in the evaluation of thyroid lesions. Because of the iodine uptake from the contrast agent, thyroid localization with nuclear scintigraphy and radioactive iodine treatment must be delayed 4—8 weeks after administration of iodinated contrast agents. The presence of calcification, cysts, hemorrhage, hypo- or hyperattenuation, or well-defined borders in a solitary mass at CT does not exclude a carcinoma. Peripheral eggshell-like calcification and large multiple chunks of calcium are suggestive of benignity, whereas fine punctate calcifications are more worrisome for malignancy (Fig 4) (56). Calcification occurs in 13% of all thyroid lesions, including 17% of all malignancies and 11% of all benign processes (52). In a similar fashion, cystic areas occur in many thyroid masses; 38% of malignancies have cystic components and 62% of benign masses may be wholly or partly cystic (52). Hemorrhage may be found in papillary carcinomas or goiters. Multiplicity of nodules in an enlarged thyroid gland usually is suggestive of a benign process (or metastases).

The presence of lymphadenopathy or infiltration of adjacent tissues suggests malignancy. More than 50% of patients with papillary carcinoma have nodal spread at presentation, and 22% have occult thyroid tumors (57). Curiously, the lymph nodes of thyroid papillary carcinoma may themselves show calcification, cyst formation, colloid accumulation, hemorrhage, or necrosis (Fig 5) (58,59). Sometimes the wall of a cystic node may be unidentifiable, thereby simulating a branchial cleft cyst. Papillary carcinoma of the thyroid may metastasize to posterior triangle, submandibular, retropharyngeal,
or jugular chain lymph nodes (58,59). The nodes may enhance uniformly and dramatically or, as in the case of cystic or calcified nodes, not at all (58,59). Any lymph node seen in a patient with papillary carcinoma is suspected of being malignant, no matter the size, because of the relatively high rate of lymphatic spread.

**MR imaging.**—Histologic specificity of thyroid lesions is not improved with MR imaging. The key to the diagnosis of thyroid cancer at MR imaging is the presence of malignant lymphadenopathy. Irregular margination and clustered nodularity is characteristic, but not specific, for carcinoma (60). Lesions that have an intact and symmetric pseudocapsule are usually benign, whereas those with pseudocapsules that are penetrated or destroyed are usually cancers (Fig 6) (60,61). Lesions that have capsules with irregular thicknesses may be malignant or benign. At MR imaging, the nodes of papillary carcinoma may have high or low signal intensity on T1- and T2-weighted images, possibly related to the presence of intranodal hemorrhage or colloid accumulation (Fig 7).

Postoperatively, thyroid carcinoma recurrences usually have medium to high signal intensity on T2-weighted images, whereas scars in the operative bed usually have low signal intensity (62). Postoperative edema, infection, or hemorrhage may simulate recurrent tumor. I-131 scintigraphy is the best modality to evaluate the operative bed and to screen for distant metastases after thyroidectomy. MR imaging, in conjunction with I-131 radioisotope scanning, has been recommended for confusing postoperative cases (63).

**Fine-needle aspiration (FNA).**—Intimately associated with any imaging technique is FNA cytology. Many palpable lesions of the thyroid gland may be aspirated without imaging guidance, but US is the most common modality used to guide aspirations because it images in real time. Aspiration cytology in good hands shows outstanding results. In a series of 11,000 guided and unguided samples obtained at the Mayo Clinic, Rochester, Minnesota, the sensitivity of the technique was found to be 98% with a 99% positive predictive value for cancer (64). Nondiagnostic specimens were present in 21% of cases, however. With US-guided FNA, sensitivity approaches 100%, specificity approaches 90%, and the number of nondiagnostic samples is reduced (10).

### I Malignancies of the Thyroid Gland

Thyroid cancers are a mixed group of lesions. The most common histologic subtype is papillary carcinoma, which accounts for 55%–80% of thyroid malignancies (1,7,65). Follicular elements in a papillary carcinoma are common, and this has led to a "mixed papillary-follicular" or "follicular variant" histologic classification; ultimately, however, the "mixed cancer" behaves like a papillary carcinoma (vide infra). Purely follicular carcinoma accounts for 5%–15% of thyroid malignancies. Anaplastic carcinoma represents 3%–10% of all malignancies, with medullary or Hürthle cell carcinoma accounting for 4%–5% (1,64). Medullary carcinoma may be present in association with the multiple endocrine neoplasia syndromes and, serologically, may express calcitonin. The other histologic diagnoses to consider in thyroid malignancies are non-Hodgkin lymphoma and metastases.

Imaging has a well-defined role in the work-up of the patient with a solitary nodule in the thyroid gland. Invariably, however, unless a classic appearance of a benign condition is present, pathologic sampling is required. Imaging should also evaluate for infiltration of the adjacent soft tissue, aerodigestive tract, paraspinal musculature, and carotid arteries. The presence or absence of adenopathy is also important for prognostic implications with thyroid cancer.

**Papillary carcinoma.**—The presence of psammoma bodies (laminated calcific spherules in 25%–40% of
Figure 6. Carcinoma and goiter. T1-weighted MR image (repetition time msec/echo time msec = 600/11) shows bilateral diffuse enlargement of the thyroid gland. On the right side, there is a fairly well-encapsulated mass (M) with high signal intensity. This right thyroid nodule had been increasing in size and represents the unusual occurrence of a well-defined papillary adenocarcinoma of the thyroid gland arising within the multinodular goiter (note the heterogeneity of the left lobe of the thyroid gland).

Figure 7. Coronal T1-weighted MR image (600/11) shows a chain of high-signal-intensity lymph nodes (n) of papillary carcinoma. At MR imaging, nodes that are hypervascular and markedly enhancing or hyperintense on T1-weighted MR images are possible with metastatic papillary carcinoma.

Figure 8. Anaplastic carcinoma. CT scan shows that this thyroid lesion (L) has invaded the tracheal cartilage and caused thickening of the subglottic and tracheal mucosa (+) on the right side. The tracheoesophageal groove on the right side is also infiltrated by this anaplastic carcinoma of the thyroid gland.

cases), ground-glass nuclei, and a branching pattern with a fibrovascular papillary stroma are the histologic signatures of papillary carcinoma of the thyroid gland (1). As noted earlier, follicular growth patterns may coexist. Cyst formation (cystadenocarcinoma), encapsulation, multifocality, and anaplasia may be present within a thyroid gland with papillary carcinoma. Papillary carcinoma is the thyroid malignancy with the greatest likelihood of spread to lymph nodes, and the nodes may be tiny, cystic, hemorrhagic, or calcified. The prevalence of nodal metastases at the time of diagnosis is 50%, whereas distant metastases are reported to occur in 4%–7%, usually to the lungs, bone, or central nervous system (1). Despite these features, the 20-year survival rate is reported to be as high as 90%. Approximately 10% of papillary carcinomas are bilateral (66).

Follicular carcinoma.—Pure follicular carcinoma is relatively uncommon when one excludes the follicular variant of papillary carcinoma. The tumor may be diffusely invasive or well-encapsulated. Follicular carcinoma spreads to lymph nodes less frequently (2%–10%) than does papillary carcinoma, but disseminates hematogenously more readily (1). No distinguishing features on imaging studies suggest this diagnosis as opposed to other cancers, although at US follicular carcinoma is isoechoic in 52% and hyperechoic in 44% (5,52). As opposed to papillary carcinoma, follicular carcinoma rarely becomes cystic and more frequently invades vessels (1).

Anaplastic carcinoma.—This cancer is one of the most aggressive malignancies of the head and neck, with prognoses marked in months rather than years. Older patients are usually affected. Anaplastic thyroid carcinomas occur within a substrate of goiters in 47% of cases (1) and often coexist with other forms of better-differentiated thyroid cancer. At US, these carcinomas are most commonly hypoechoic (5,52,67), whereas at CT, anaplastic carcinomas show evidence of dense amorphous calcification in 58% of cases and necrosis in 74% (68). Metastatic lymph nodes are present in 74%–80% of cases and show necrotic areas in 50% of the time (68,69). Invasion into carotid arteries or adjacent aerodigestive structures occurs in 34%–55% of patients, and in 25% the primary tumor...
or calcification in only 1–2% of cases (19%–51%). Yousem (19%–51%). Invasion of the carotid sheath enhances CT scans and shows necrosis hypoattenuating on unenhanced and differential diagnosis. The tumor is hypoproliferative (leukemia) and granulomatous (eg, sarcoidosis) diseases show increased activity. Other lymphomas may be seen as a solitary mass (80%–90%) or as multiple nodules (10%–20%) (70). An antecedent history of Hashimoto thyroiditis is suggestive of lymphoma. Most are B-cell neoplasms (1). The patient usually presents with a slowly growing neck mass. The imaging features of toxic adenomas are nonspecific at noncritigraphic modalities. The lesions are usually solid and enhancing.

Nonfunctioning thyroid adenomas.—A cold (nonfunctioning) nodule is approached more aggressively than a hot nodule because of the higher rate of malignancy, especially in young patients.

Figure 9. Goiter. Nuclear medicine Tc-99m pertechnetate thyroid scan shows multiple areas of decreased tracer uptake with some areas of avid tracer activity. The gland appears enlarged. This is the characteristic appearance of a multinodular goiter. The differential diagnosis could be an active phase of thyroiditis.

Figure 10. Multinodular goiter. US scan shows multiple echopenic masses (*) in the left and right lobes of an enlarged thyroid gland.
The gland is enlarged with homogeneous high signal intensity at T1-weighted examinations (54). However, this finding is not specific to colloid cysts because areas of hemorrhage, which also have high signal intensity on T1-weighted images, can be seen in goiters, adenomas, and traumatized cysts. Even thyroglossal duct cysts (wide infra) may be hyperintense due to high protein content.

**Teratomas.**—Teratomas are rare neoplasms of the thyroid gland. As in other locations in the body, thyroid teratomas may demonstrate fluid, fat, calcification, and osseo-dental densities in various combinations. They usually occur in the midline.

**Multinodular goiter.**—Another common palpable thyroid abnormality is the multinodular goiter. A goiter is simply an enlarged thyroid gland that may be seen with hyper- or hypothyroidism. In the United States, the common vernacular is to imply a nontoxic goiter when the term is used. A euthyroid or hypothyroid goiter is the most common thyroid lesion in this country. In rare instances, a previously nonfunctioning multinodular goiter may evolve into one with hyperfunctioning nodules and cause hyperthyroidism. Patients, usually older women, present because of hypothyroidism, neck masses, or tracheal-esophageal compression. The frequency of carcinoma in a multinodular goiter is very low (less than 3%), and the characteristic appearance of multiple cold areas interspersed with hot areas in a large gland will usually obviate the need for aggressive biopsy of a palpable nodule (Fig 9) (54). A large, dominant, hard, or growing mass amidst a goiter should probably still be sampled for biopsy (74).

**Nontoxic multinodular thyroid glands** show minimal to moderate heterogeneity with nodularity and mildly increased signal intensity at T1-weighted MR examinations (60, 61). Hemorrhagic foci are noted in 60% of cases, and the lesions are often heterogeneous at T2-weighted examination (61). Goiters usually do not have pseudocapsules (61). At CT and US, mixed solid and cystic zones within an enlarged, nodular thyroid gland with or without calcification is the characteristic appearance of a multinodular goiter (Fig 10).

**Hyperthyroidism.**—The three most common causes of hyperthyroidism are Graves disease (diffuse toxic goiter), toxic multinodular goiter, and toxic adenomas. The toxic adenomas (see above) are separated into those that are TSH responsive or TSH independent (autonomous). Occasionally, inflammation of the thyroid gland (thyroiditis) may produce a transient state of hyperthyroidism. On rare occasions, ectopic thyroid tissue (lingual or ovari-
tinguishing Graves disease, which shows homogeneous diffuse intense uptake (70%-85%) in a large gland, from the thyroiditides (Fig 11). Thyroiditis is less homogeneous and the uptake may be normal, high, or low depending on the state of the inflammatory process. Because some thyroiditides (see below) may revert to euthyroid activity with time, the implications for therapy are important: Graves disease requires antithyroid medication, radioactive iodine obliteration of the gland, or surgery. Thyroiditides are treated conservatively. Diffuse glandular enlargement with avid enhancement may be noted at CT and MR imaging in patients with Graves disease. A large pyramidal lobe often coexists. Carcinoma of the thyroid gland in a patient with Graves disease is rare, reported in 0.15%-0.5% of patients (76).

Hypothyroidism.—Patients with hypothyroidism have cold intolerance, fatigue, apathy, weight gain, bradycardia, constipation, edema, macroglossia, and poor condition of the hair, nails, and skin. Women are affected more frequently than men. The response to thyroid hormone replacement is excellent. Hashimoto thyroiditis is the most common cause of hypothyroidism in the United States (see below). Worldwide, iodine deficiency (endemic goiter) is another cause of hypothyroidism but is infrequently seen in developed countries. Other causes include the other chronic thyroiditides. Postoperative and postradiation therapy (be it I-131 or external beam irradiation) patients also account for a great number of hypothyroid patients. It is common for patients treated with radioactive iodine for hyperthyroidism to develop hypothyroidism after several years.

Congenital hypothyroidism occurs more commonly in the Japanese population (one in 5,500 newborns) (77). Possible causes include thyroid aplasia, hemiaplasia (the left gland is absent more commonly than the right), ectopia, dyshormonogenesis, pituitary or hypothalamic deficiency, and autoimmune diseases. Prompt replacement of thyroid hormone is crucial because mental retardation is a possible complication of undiagnosed neonatal hypothyroidism (77). Both US and scintigraphy are used to identify thyroid tissue in this population.

**Figure 12.** Thyroglossal duct cyst. T2-weighted MR image (3,000/80) shows that the cyst (+) is off midline and infrahyoid, yet embedded in the strap muscles. A tract to the midline (arrows) is evident.

**I Congenital Lesions**

**Thyroglossal duct cysts.**—The thyroglossal duct cyst is a congenital lesion in which the tract of migration of the thyroid gland from the foramen cecum of the tongue (located in the midline at the circumvallate papillae level) to the normal position of the thyroid gland is persistent. Although a congenital lesion, 50% of cases present after age 10 years. One sees a midline cystic mass that is located in an infrahyoid level in 65%, hyoid level in 15%, and suprahyoid level in 20% of cases (78). It may occur in a paramedian position in 25% of cases, usually in the infrahyoid compartment. The stereotypical locations of the thyroglossal duct cyst are embedded in the strap muscles below the hyoid bone or at the midline junction of the hyoid bone above the strap muscle insertions (Fig 12).

Because the fluid in the thyroglossal duct cyst may have a high protein content, it may appear cystic with some internal echoes at US. It moves with swallowing or when sticking the tongue out. At CT, the noninfected thyroglossal duct cyst varies in intensity from markedly hypointenueating (with no protein content) to slightly hyperintenseating (with high protein or hemorrhage within). At MR imaging, the thyroglossal duct cyst may have either low or high signal intensity on T1-weighted images but is typically hyperintense on T2-weighted images. Enhancement is uncommon in thyroglossal duct cysts unless the lesion has been traumatized or infected. In those instances, peripheral rim enhancement may occur.

Ectopic thyroid tissue is found in roughly 25%-33% of thyroglossal duct cysts (78,79). The incidence of carcinoma within the thyroid tissue of a thyroglossal duct cyst is less than 1% (78,79). When it occurs, it is usually papillary carcinoma. Rarely the tract of the thyroglossal duct may serve as conduit for acute suppurative thyroiditis (79).

**Lingual thyroid glands.**—Lingual thyroid tissue occurs in one in 3,000 patients with thyroid disease and represents the most common form of functioning ectopic thyroid tissue (51). It is also the most common benign mass found at the circumvallate papillae. The lingual thyroid gland represents arrest of migration of the thyroid tissue within the tongue, usually in the midline between the circumvallate papillae and the epiglottis. This may be a complete arrest or incomplete arrest of migration. Lingual thyroid glands are associated with absence of thyroid tissue in the neck in 70%-80% of cases and are much more commonly seen in women (51,63,80). Patients often present in puberty, during which time the tissue may expand rapidly. Variation in size may occur with menstruation.

The primary role of imaging is to identify whether there is normal thyroid tissue in the lower neck so that complete excision or transplantation of the lingual thyroid tissue may be contemplated. If no other thyroid tissue is present, the patient is consigned to life-long thyroid replacement therapy if the lingual thyroid gland is totally removed. A nuclear medicine study to determine whether a lingual mass represents thyroid tissue, as well as to search for other (ectopic) thyroid tissue, is favored over cross-sectional imaging. A malignancy arising within a
Inflammatory Lesions

There are no specific scintigraphic, sonographic, CT, or MR imaging appearances that enable differentiation among the various inflammatory processes involving the thyroid gland. The value of imaging studies pales in comparison to that of serologic tests for distinguishing among the various inflammatory lesions of the thyroid gland. Conversely, if imaging is to be used as a map for surgical correction or resection of the thyroid gland, then MR imaging and US seem to be of particular benefit. In some instances, the administration of iodine at contrast-enhanced CT might precipitate thyroid storm (acute outpouring of thyroid hormone), so CT is usually avoided.

Suppurative thyroiditis.—Patients with acute suppurative thyroiditis present with acute onset of pain and swelling in the thyroid gland associated with fever, odynophagia, and dysphagia (81). The role of imaging is to exclude a pyriform sinus or thyroglossal duct fistula as a cause for the acute suppurative thyroiditis. This entity may occur in association with a fourth branchial cleft anomaly and has a left-sided predominance (81). Imaging may depict leakage from the pyriform sinus to the lateral neck at the thyroid gland level. Acute suppurative thyroiditis is the rarest form of thyroiditis but has the most fulminating clinical presentation.

Hashimoto thyroiditis.—Most of the other forms of thyroiditis are subacute or chronic diseases. Hashimoto (chronic lymphocytic) thyroiditis is the most common of the chronic thyroiditides, being five to 10 times more frequent than subacute thyroiditis (7). It is the most common thyroiditis in children. The diagnosis is based on serologic tests because the disease is an autoimmune process with antigenic stimulation to thyroglobulin, colloid, and other thyroid cell antigens. Serum levels of antimicrosomal antibodies are elevated, and FNA may reveal a preponderance of lymphocytes, centroblasts, and Hürthle cells (82). Women are affected almost 20 times more frequently than men, and the chief complaint is usually enlargement and tenderness of the thyroid gland. Hypothyroidism is present at presentation or develops later in 50% of cases.

With Hashimoto thyroiditis, the gland is enlarged and shows multinodularity and heterogeneous increased or decreased uptake of radioisotopes. Although there may be increased uptake of iodine on nuclear medicine studies early in the disease, the usual response is diminished or normal thyroid uptake at imaging (82). Patients who trap more tracer have a greater chance of returning to a euthyroid state than those who do not. At US, the thyroid gland is symmetrically enlarged and hypoechoic but may have nodules within it. Calcification is seen in the chronic stages. On T2-weighted MR images, the gland has shown increased signal intensity, sometimes with linear low intensity bands thought to represent fibrosis (60,73). Hashimoto thyroiditis shows no greater risk for carcinoma but seems to predispose to non-Hodgkin lymphoma (70). Hashimoto thyroiditis in the presence of thyroid lymphoma is seen in 25%–67% of cases (69,70). Hashimoto disease has also been associated with other autoimmune entities such as pernicious anemia, Sjögren syndrome, lupus, rheumatoid arthritis, Addison disease, and Graves disease.

Riedel thyroiditis.—Riedel thyroiditis (struma thyroideum) is an uncommon chronic inflammatory lesion of the thyroid gland and neck. The disease may be bilateral or unilateral and is more common in women than men. Patients present with evidence of mass effect with compression of the trachea, hoarseness, and difficulty in swallowing. Usually, the patients have hypothyroidism. At imaging, Riedel thyroiditis is homogeneously hypoechoic at US and is usually hypoechogenic to normal thyroid tissue at CT (5,73). The lesion may be isoechogenic to muscle at unenhanced CT. Riedel thyroiditis may spread outside the thyroid gland, infiltrating and obliterating adjacent tissue planes. The characteristic finding on MR images is hypointensity at T1- and T2-weighted imaging, with infiltration of adjacent structures of the neck (73). The low signal intensity at MR imaging is thought to be due to the fibrotic nature of the disorder. This lesion may be associated with retroperitoneal fibrosis, mediastinal fibrosis, sclerosing cholangitis, and orbital pseudotumor. It is distinguished from Hashimoto thyroiditis, which has high signal intensity on T2-weighted MR images.

de Quervain thyroiditis.—de Quervain thyroiditis (subacute thyroiditis) is a disease of middle age occurring most commonly in women after an upper respiratory infection. Coxsackie, ECHO, and mumps viruses have been implicated (1). Pain, fever, and fatigue are common presenting symptoms. Patients with subacute thyroiditis may present (50% of cases) with acute toxic hyperthyroidism, with subsequent return to an euthyroid state after 1–2 months (51). Hypothyroidism occurs approximately 2–4 months after onset and, typically, the patient returns to euthyroidism within 6 months of the acute onset (7). Patients are typically treated medically, as the prognosis is good for return of normal thyroid function. Subacute thyroiditis is hypoechoic at US, although there may be
atrophy of thyroidal tissue with time (5). Nuclear medicine studies show heterogeneous uptake that will vary in degree according to the stage of the disease. 

Miscellaneous.—External beam radiation may cause a chronic thyroiditis associated with fibrosis. In low doses (used in years past for irradiating the thymus, adenoids, acne, or ringworm), radiation predisposes to papillary carcinoma. Radioactive iodine treatment also causes severe fibrosis and atrophy of the gland. Amyloidosis and hemosiderosis may affect the thyroid gland and lead to decreased signal intensity on T2-weighted MR images. Tuberculosis, sarcoidosis, and fungal infections may cause a granulomatous inflammation of the thyroid gland but are uncommon conditions (36).

References

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