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 which imaging modality to use have been hotly debated in the radiologic and surgical literature.

Anatomy and Imaging

The parathyroid glands are derived from the third (lower parathyroid glands) and fourth (upper parathyroid glands) pharyngeal pouches. Whereas the majority of people have four glands (a pair at the upper and lower poles of the thyroid gland), 25% of individuals have more than this number. Although the parathyroid glands may be aberrantly located anywhere from the carotid bifurcation to the anterior mediastinum, inferior migration of those glands derived from the third pharyngeal pouch occurs most frequently. Of the two dominant cell types in the parathyroid glands, the chief cells and the oxyphil cells, the former are the predominant source of parathormone.

Vascular supply to the parathyroid glands is usually through the superior and inferior thyroidal arteries, with drainage to thyroidal veins. The glands are innervated by the cervical sympathetic plexus.

There are several options for imaging the parathyroid glands; these include ultrasonography, computed tomography (CT), magnetic resonance (MR) imaging, angiography, and nuclear medicine scintigraphy. The advantages and disadvantages of each of the imaging modalities described are summarized in Table 1.

High frequency (5-10 MHz) ultrasonography is the least invasive of the imaging modalities used to search for parathyroid adenomas because it does not require intravenous injections of any compounds. Unfortunately, its accuracy is less than that of the other modalities mainly because of the difficulty in identifying ectopic parathyroid adenomas that may occur throughout the neck, behind air-filled structures, or in the anterior mediastinum where acoustic impedance by bone or air prevents adequate imaging. Nonetheless, for parathyroid adenomas that are located in a perithyroidal location, ultrasonography is an excellent imaging choice.

CT offers the benefit of cross-sectional imaging for parathyroid adenoma localization. Because the entire neck from skull base to anterior mediastinum can be scanned with CT, the possibility of detecting ectopic parathyroid adenomas is increased. Distinguishing lymphadenopathy from parathyroid adenomas is a problem encountered with CT (as well as with ultrasonography and MR imaging). The other disadvantage of CT is that it requires the administration of iodinated intravenous contrast agents. These contrast agents are essential for distinguishing blood vessels from adenomas or lymphadenopathy. Moreover, the use of iodinated contrast agents prevents subsequent imaging with iodine-based nuclear medicine agents because of the uptake of contrast by the thyroid gland. It is necessary to wait at least 6 weeks after contrast-enhanced CT scans to image the thyroid gland with iodinated nuclear medicine agents.

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PARATHYROID AND THYROID IMAGING

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Table 1. ADVANTAGES AND DISADVANTAGES OF VARIOUS IMAGING MODALITIES FOR DETECTION OF PARATHYROID ADENOMAS

<table>
<thead>
<tr>
<th>Examination</th>
<th>Advantages</th>
<th>Disadvantages</th>
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<tbody>
<tr>
<td>CT</td>
<td>Examines head, neck, and chest</td>
<td>Requires iodinated contrast</td>
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<tr>
<td></td>
<td>Easy detection of calcification</td>
<td>Iodinated contrast affects thyroid imaging by scintigraphy</td>
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<td></td>
<td>Biopsy capable</td>
<td>Shoulder artifacts</td>
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<td></td>
<td></td>
<td>Difficult to differentiate node versus adenoma</td>
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<tr>
<td>MR imaging</td>
<td>Examines head, neck, and chest</td>
<td>Expensive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Difficult to differentiate node versus adenoma</td>
</tr>
<tr>
<td></td>
<td>No iodinated contrast required</td>
<td>Intravenous gadolinium agent employed</td>
</tr>
<tr>
<td></td>
<td>Excellent soft tissue discrimination</td>
<td>Requires patient cooperation, no claustrophobia</td>
</tr>
<tr>
<td>Nuclear medicine</td>
<td>Examines head and neck well</td>
<td>Very expensive</td>
</tr>
<tr>
<td>scintigraphy</td>
<td>Functional, not anatomic imaging</td>
<td>Lower yield for ectopic glands especially in chest</td>
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<tr>
<td></td>
<td>Distinguishes nodes from adenomas</td>
<td>Intrathyroidal masses indistinguishable from adenomas</td>
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<tr>
<td>Ultrasonography</td>
<td>Examines neck well</td>
<td>Smaller lesions easily missed</td>
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<tr>
<td></td>
<td>Inexpensive</td>
<td></td>
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<tr>
<td></td>
<td>Noninvasive</td>
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<tr>
<td></td>
<td>Real-time, biopsy capable</td>
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medicine agents. Contrast enhancement is not the solution to parathyroid imaging; only 25% of parathyroid adenomas demonstrate noticeable enhancement. False-negative studies with CT also may occur in the setting of poor-quality images from shoulder artifacts.

MR imaging with gadolinium enhancement is another useful study for evaluating patients with hyperparathyroidism. On T2-weighted scans and post-gadolinium T1-weighted scans, parathyroid adenomas are bright against a dark, fat-suppressed background. MR imaging is limited by the distribution and coverage of the surface coil used to detect parathyroid adenomas and also by any motion artifact that may occur during imaging. Nonetheless, with the appropriate surface coil and instructions to the patient, MR imaging is able to adequately evaluate the entire neck and anterior mediastinum. As with the other modalities listed, the potential for misdiagnosing lymphadenopathy as parathyroid adenomas also exists with MR imaging.

The choices for scintigraphic localization of parathyroid adenomas include thallium (Tl)-201–technetium (Tc)-99m pertechnetate subtraction scanning, 99mTc-sestamibi (hexakis-2-methoxy-isobutylisonitrile) subtraction imaging with iodine-123 (I-123) or 99mTc pertechnetate, and 99mTc-sestamibi imaging without subtraction. The subtraction techniques allow tracers that are concentrated in the thyroid gland (pertechnetate and iodine) to be subtracted from those (thallium and sestamibi) that accumulate in both thyroid glands and parathyroid adenomas. Thallium is a potassium analogue that may concentrate in parathyroid adenomas because of changes in potassium turnover. Because sestamibi uptake in parathyroid adenomas persists after thyroid gland washout, it can be used without subtraction techniques if one performs delayed images. The difficult task of patient immobilization and accurate superimposition of subtracted images, required by thallium-pertechnetate studies, is obviated with delayed sestamibi imaging.

Of the parathyroid agents, thallium emits low-energy, low-penetrating 80 keV photons and washes out of parathyroid adenomas relatively rapidly. 99mTc-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. 99mTc-sestamibi, therefore, produces higher signal-to-noise images than thallium subtraction scans. Single-photon emission computed tomography (SPECT) scanning also can be combined with high-dose 99mTc sestamibi scintigraphy for more accurate parathyroid adenoma localization.

Hyperparathyroidism

Hyperparathyroidism has an incidence of 0.037% in the United States. Patients may present with the classic findings of stones (renal calculi), groans (abdominal pain), bones (denomineralization or arthritis), or moans (psychiatric disturbances). Primary hyperparathyroidism is caused by a solitary parathyroid adenoma in 80% to 85% of cases. Hyperplastic parathyroid glands (12–15%), multiple adenomas (2–3%), and parathyroid carcinoma (<2%) account for the remaining 15% to 20% of cases. Parathyroid adenomas may be ectopic (not around the thyroid bed) in 10% to 20% of cases.
Parathyroid imaging is controversial not only from the standpoint of the indications for imaging but also from the issue of which modality (if any) to choose. In most institutions, preoperative localization of the parathyroid glands by imaging is not performed before the first surgery (for previously operated patients, see subsequent discussion). This stems from the early surgical literature that suggests that operative time, morbidity, and mortality is not significantly influenced by preoperative localization of parathyroid adenomas for hyperparathyroidism. The 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 over 90%. This has led Doppman to state that the best localization procedure a patient can obtain for parathyroid adenomas is to locate “an experienced parathyroid surgeon.”

Proponents of preoperative localization of parathyroid adenomas even in unoperated cases cite (1) the need for only unilateral dissections when an adenoma is evident on imaging; (2) the identification of ectopic adenomas preoperatively, allowing better planning and patient education; (3) detection of other head and neck masses that may require treatment at the same time (e.g., thyroid masses); and (4) the reduction in operating room time, recurrent laryngeal nerve paralysis, and postoperative hypoparathyroidism when preoperative imaging is performed. In two studies by Russell and Casas and their colleagues, the difference between mean operating times with (71 minutes and 135 minutes) and without (97 minutes and 180 minutes) preoperative imaging justified the cost of the imaging test. The operative success rate also improved from 90% to 100% with preoperative imaging. Uden also noted that the time for surgery and anesthesia decreased with preoperative imaging; however, when a cost–benefit analysis was performed, he 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 and colleagues did not justify the $901 mean cost of localization. Other surgeons take a centrist position regarding bilateral or unilateral neck explorations. They perform unilateral neck dissections if imaging studies are definitive but convert to bilateral surgery if (1) imaging is equivocal or shows multifocal abnormality, (2) more than one enlarged gland is identified at surgery, (3) the patient has a multiple endocrine neoplasia (MEN) syndrome (often associated with parathyroid hyperplasia), or (4) a unilateral exploration is unrevealing.

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 (<70% successful) than that expected for those adenomas in a perithyroidal location (>90% success rate), and the surgical complication rate increases with such blind explorations. 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. To confuse matters further, thyroidal abnormalities occur in as many as 40% to 48% of patients with hyperparathyroidism. These factors have led less-experienced surgeons and those who have had a less successful track record to choose preoperative localization of parathyroid adenomas.

Parathyroid Adenomas

Exactly how accurate are the imaging studies for detecting parathyroid adenomas? On ultrasonography, parathyroid adenomas appear as oval, oblong, or bulbous lesions with echogenicity less than that of the thyroid gland. Using high-resolution ultrasound in a study of more than 150 patients, a sensitivity of 64% and specificity of 94% for adenomas and hyperplastic glands was achieved. Of those glands greater than 1 g in size, ultrasonography had a detection rate of 95%. Other investigators also quote sonographic sensitivities of

Figure 1. Ultrasonogram of parathyroid adenoma. Deep to the thyroid tissue, one can see a hypoechoic mass (arrows) representing a parathyroid adenoma.
When Stark and colleagues compared the accuracy of high-resolution CT with ultrasonography for detecting parathyroid adenomas, they found the sensitivity of CT to be 70% with a specificity of 90%, an improvement over their experience with ultrasonography. Sommer and colleagues also found CT to be more accurate than ultrasonography by over 10%; combining the studies yields a detection rate of 89% in patients without previous surgery.

Spritzer and co-workers were among the first to report on the accuracy of MR imaging (Fig. 2) in detecting parathyroid adenomas. Seventeen patients had adenomas, and MR imaging correctly identified 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 MR accuracy of 92% for adenomas.

The numerous options for nuclear medicine scanning for parathyroid adenomas stem from the fact that there are no agents that are exclusively taken up by the parathyroid glands or adenomas. Therefore, agents that are taken up by parathyroid adenomas and the thyroid glands (thallium and Tc-99m sestamibi) must be subtracted from those that are only taken up by the thyroid glands (Tc-99m pertechnetate and Tc-99m sestamibi) (Fig. 3). This then allows visualization of abnormal uptake by parathyroid adenomas. Computer processing is required to enhance accuracy with subtraction techniques. At most centers, however, Tc-99m sestamibi imaging is performed without subtraction. Ten to thirty mCi of Tc-99m sestamibi are injected with scanning at 15-minute intervals for up to 2 to 4 hours after injection. Because the agent washes out of the thyroid gland rapidly but is retained by parathyroid (and thyroid) adenomas, delayed images are all that are usually necessary for good localization (Fig. 4).

It is not necessary to sacrifice accuracy with the simpler sestamibi study. The overall sensitivity of thallium-201-Tc pertechnetate subtraction scintigraphy for parathyroid adenoma detection (75-85%) is substantially less than that of Tc-99m sestamibi, which runs in the range of 90% to 100%, and ultrasonography (90%). No thallium-positive adenomas have been sestamibi-negative to date. Furthermore, in a comparative study of nonoperated patients, Kneeland and colleagues found scintigraphy (82%) to have higher sensitivity rate than MR imaging (74%), CT (74%), and ultrasonography (59%). The differences were only statistically significant between scintigraphy and ultrasonography.

When Price reviewed the presestamibi literature up until 1993 (243 to 1785 cases), he found that MR imaging had the highest sensitivity rate for the detection of adenoma (74%) followed by nuclear medicine studies (72%), CT (65%), and ultrasonography (63%). The false-positive rate of nuclear medicine (11%) was lowest compared with MR imaging (14%), CT (16%), and ultrasonography (18%). Sestamibi data over the past 2 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 thyroid lesions may concentrate radiotracers to the same degree as parathyroid adenomas. Reports of Tc-99m sestamibi uptake in thyroid cancers and their nodal and distant metastases signal the possibility for false-positive studies.

Parathyroid Hyperplasia

Approximately 30% of patients with parathyroid hyperplasia have familial hyperparathyroidism, including variants of the multiple endocrine neoplasia (MEN) syndromes (Table 2). As noted earlier, hy-

Figure 2. A and B, MR images of parathyroid adenoma. A, A small soft tissue nodule (arrow) is seen adjacent to the trachea located below the thyroid gland on the right side. This was a parathyroid adenoma in a low perithyroidal location. B, After gadolinium injection, the lesion (arrow) enhances avidly.
Figure 3. Thallium subtraction study. The thallium scan (top left) can be sequentially subtracted from the technetium pertechnetate scan of the thyroid gland (top right). On the lower set of images, note how the thyroid gland uptake is eliminated allowing visualization of the inferior pole parathyroid adenoma on the left (arrows).

Figure 4. A and B, 99mTc sestamibi scan of a parathyroid adenoma. A, Initial technetium-99m sestamibi scan of the parathyroid region demonstrates uptake in the thyroid gland and parathyroid adenoma (arrows). B, On delayed imaging, the thyroid uptake has washed out, whereas the parathyroid adenoma (arrow) has persistent tracer accumulation.
Table 2. MULTIPLE ENDOCRINE NEOPLASIA (MEN) SYNDROMES

<table>
<thead>
<tr>
<th>Feature</th>
<th>MEN I</th>
<th>MEN IIA</th>
<th>MEN IIB</th>
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<tbody>
<tr>
<td>Eponym</td>
<td>Wermer</td>
<td>Sipple</td>
<td>Mucosal neuroma syndrome</td>
</tr>
<tr>
<td>Parathyroid abnormality</td>
<td>Hyperparathyroidism (90%) due to hyperplasia more commonly than adenoma</td>
<td>Parathyroid hyperplasia in 20–30%</td>
<td>Very rare</td>
</tr>
<tr>
<td>Thyroid lesion</td>
<td>Goiter, adenomas, thyroids are rare</td>
<td>Medullary thyroid carcinoma</td>
<td>Medullary thyroid carcinoma</td>
</tr>
<tr>
<td>Pituitary lesions</td>
<td>Adenomas (20–30%)</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Pheochromocytoma</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Other manifestations</td>
<td>Pancreatic islet cell adenomas (insulinoma or gastrinoma) 30–35%</td>
<td>No</td>
<td>Mucocutaneous neuromas</td>
</tr>
<tr>
<td></td>
<td>Adrenal cortex adenomas or carcinomas</td>
<td>Yes</td>
<td>Marfanoid facies</td>
</tr>
<tr>
<td></td>
<td>Rarely glucagonomas, VIPomas, carcinoid</td>
<td>No</td>
<td>Cafe au lait spots</td>
</tr>
<tr>
<td></td>
<td>Zollinger-Ellison syndrome</td>
<td>A-D chromosome 11</td>
<td>A-D chromosome 10</td>
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<tr>
<td>Chromosomal linkage</td>
<td>A-D chromosome 10</td>
<td>A-D chromosome 10</td>
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perplasia accounts for 12% to 15% of patients with hyperparathyroidism.

CT is reported to have a sensitivity rate of 45% to 88%,
ultrasonography, 30% to 69%,
and MR imaging, 40% to 63%,
for detecting hyperplastic glands. Parathyroid hyperplasia is
detected in 43% to 65% of cases with thallium subtraction
and 55% to 75% with
The added accuracy in identifying hyperplastic glands has led to a growing consensus in support
of the use of
Parathyroid Carcinoma

Of all patients with hyperparathyroidism, the incidence of parathyroid carcinoma (Fig. 5) is only
1% to 2%, although parathyroid carcinoma causes hyperparathyroidism in 85% to 90% of cases.
Metastases to lymph nodes occur in one third of
cases, and distant metastases in 21% to 28% of pa-
tients. Men and women are affected equally.

Edmonson and colleagues noted that a parathy-
roid 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
Reoperation for Hyperparathyroidism

During reoperation of previously operated cases,
30% to 75% of abnormal parathyroid glands are
found in a perithyroidal location, presumably
overlooked or missed during the initial opera-
tion. Parathyroid adenomas in patients who
have failed initial operation are located in the ante-
rior mediastinum in 20% to 38%, in a paraesopha-
geal or deep cervical location in approximately 20%,
infrathyroidal in 8%, and parathyrmic in 2%. Supernumerary adenomatous glands are present in
15% of cases. Of those located in the chest, posterior mediastinal ectopic adenomas are one-fifth as common as anterior ones.

The risks associated with reoperation outweigh
the cost of preoperative imaging. In those patients
who are reoperated, the risk of vocal-cord injury
because of damage to the recurrent laryngeal nerve
or vagus nerve is approximately 7% compared with
the initial operating room risk of 1.3%. When im-
aging is not performed prior to reoperation for hyperparathyroidism, surgery is approximately 60% to 70% successful; when imaging is performed prior
to reoperation, the success rate increases to 80% to 90%. In reoperative cases, the sensitivities of ultrasonography (36–76%), 19, 24, 45, 56, 78 scintigraphy (26–90%), 19, 24, 45, 56, 78 CT (46–63%), 19, 45, 56, 78 and MR imaging (50–91%) 19, 24, 45, 56, 78 have ranged widely. In a review of the literature, Price concluded 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 in the range of 80% to 90%. 41, 42 Parathyroid hyperplasia is the most difficult diagnosis to make and accounts for most false-negative studies. 41, 42 Nonetheless, Majors and colleagues found that sestamibi scanning identified parathyroid tissue in all nine previously operated patients, including one with parathyroid cancer. 43

By combining ultrasonography, CT, and scintigraphy, one can increase the sensitivity rate to 78%, but at a high cost. 44 Although more invasive studies have a greater yield, they are more demanding. Miller and colleagues' study found parathyroid venous sampling (80%), intraoperative ultrasonography (78%), and arteriography (49–60%) to have higher sensitivity rates than the noninvasive imaging studies. 45 The expense and technical difficulty in performing these invasive examinations precludes their routine use, but they may be held in abeyance for cases with equivocal or nonrevealing, noninvasive studies.

In the patient who has failed prior surgery for a parathyroid adenoma, both imaging and surgery must contend with scar tissue in and around the thyroid glands, a loss of tissue planes, postoperative inflammation, lymphadenopathy simulating parathyroid glands, and distortion of landmarks. False-negative scans (caused by obscured anatomy) tend to occur in the perithyrmic or perithyroidal operative beds. The incidence of false-positive examinations (usually caused by lymphadenopathy) is lowest with nuclear medicine studies, followed by MR imaging, ultrasonography, and CT according to Miller and colleagues. 46

Therefore, which study should one perform in the previously operated patient? Two camps of opinion have formed. Sestamibi scintigraphy is probably the most accurate and affordable study currently available to identify parathyroid adenomas; its disadvantage is that the surrounding anatomy is not visualized for surgical orientation. It alone or combined with ultrasonography or CT is an effective option. Alternatively, the most accurate (and most expensive) cross-sectional imaging technique is MR imaging, which provides good anatomic detail, although it has the small risk of mistaking a lymph node for an adenoma. Because re-reoperation 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, ultrasonography, or MR imaging) and a functional test (99mTc sestamibi) is appealing. Use of this algorithm increases the reoperation success rate by more than 30%. 47

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 abnormality in these diseases. Parathyroid glandular hyperplasia usually occurs in association with chronic renal failure and renal osteodystrophy. 48 99mTc sestamibi has been able to identify bilateral uptake in hyperplastic glands and residual parathyroid tissue in those individuals treated surgically in the neck for secondary hyperparathyroidism. 49

Therapeutic Techniques

Ethanol ablation of parathyroid adenomas has been performed under ultrasound guidance by percutaneous injection of absolute ethanol. 50, 71 This technique may be used in patients with primary or secondary hyperparathyroidism who are not surgical candidates because of medical illnesses. Approximately 0.5 mL to 1 mL of ethanol (95%) may be injected at multiple sites within an adenoma with a 22-gauge needle. The success of this technique is monitored by following serial serum calcium levels; the technique may be repeated until normocalcemia is achieved.

Parathyroid Cysts

Cysts of the parathyroid glands are more common in women than in men and may be present in the neck (Fig. 6) or anterior mediastinum. At presentation, they may be very large in size, and the differential diagnosis may include thyroid cysts, thymic cysts, and necrotic lymph nodes. They usually arise in the region of the inferior pole of the thyroid gland. They are virtually never found in children; most cases present in the fourth and fifth decade of life. 41 They are usually unicocular, large, and may have hyperproteaceous contents yielding high intensity on T1-weighted MR scans. The etiology may be congenital because of remnants of pharyngeal pouches, or cysts may develop from degenerated parathyroid adenomas.

Hypoparathyroidism

The most common cause of hypoparathyroidism is iatrogenic removal of all functioning parathyroid tissue during surgery for hyperparathyroidism or thyroid disease. Primary idiopathic hypoparathyroidism
Figure 6. A and B. MR images of parathyroid cyst. A, Coronal T1-weighted scan demonstrates a rounded cystic mass (arrows) with low intensity fluid. B, The cyst (c) is bright on axial T2-weighted scan. This patient is status post-thyroidectomy.

roidism is a disease of childhood unassociated with cervical abnormalities. Pseudohypoparathyroidism may be caused by renal disease; the serum parathormone (PTH) levels are paradoxically high because of a lack of renal responsiveness to the hormone. The glands may be normal or hyperplastic. In pseudopseudohypoparathyroidism, the calcium and phosphate levels are normal, although the physical features of pseudohypoparathyroidism (coarse facies, dwarfism, mental retardation, round face, stubby fingers) may be present.

Imaging of parathyroid glands in patients with hypoparathyroidism is limited to the surveillance for congenital absence, which is best accomplished with scintigraphic methods.

THE THYROID GLAND

The thyroid gland is positioned 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" (50-80% of patients) lying superficial to the thyroid cartilage.

The vascular supply to the thyroid gland is derived from paired superior thyroidal arteries (branches of the external carotid arteries) and inferior thyroidal arteries (branches of the thyrocervical trunks of the subclavian arteries). The inconstant thyroidea ima arises directly from the aortic arch and supplies a small inferior portion of the gland. 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.

Histologically, the gland contains follicular cells that secrete the thyroid hormones and parafollicular ("C") cells that elicit thyrocalcitonin. Interspersed within the gland one finds fibrous septa and colloid deposits.

Imaging Features of Masses

Ultrasonography

The main role of cross-sectional thyroid imaging (ultrasonography, CT, MR) is to evaluate thyroid masses for potential malignancy. Ultrasonography, because of its simplicity, low cost, and ability to distinguish cystic from solid lesions is often the first modality used to evaluate a thyroid mass in the euthyroid patient. Good quality ultrasonography requires transducers that have 7.5 to 10 MHz frequencies. These allow excellent detail of the superficial portions of the gland but enough penetration to evaluate posteriorly to the level of the spine. When a solid lesion is hyperechoic, the incidence of malignancy is only 4%. If a solid lesion is isoechoic, the incidence of malignancy increases to 26% and, if hypoechoic, malignancy occurs in 63%.
illary carcinoma most commonly presents as a solid hypoechoic (77%) or isoechoic (14%) mass with or without calcification (calcifications are hyperechoic but cause acoustic shadowing that is hypoechoic) (Fig. 7). If a cancer is hyperechoic on ultrasonography, it is usually because of the sclerosing form of papillary carcinoma or medullary carcinoma. If the margins of tumors on ultrasonography are studied, 16% of malignant lesions will be found to have sharply marginated, well-defined borders.

Figure 7. A–C, Ultrasonograms of papillary carcinoma. A, A reasonably well-defined soft tissue mass (M) is present surrounded by normal thyroid tissue. The mass is hypoechoic. Fine-needle aspiration revealed papillary carcinoma. B, On transverse sonographic images of a different patient, a soft tissue mass (M) is identified that has internal heterogeneity to its echotexture. This mass was also a papillary carcinoma of the thyroid gland. C, The longitudinal sonographic view of this mass (M) shows the absence of an echopeneic halo around the lesion and ill-defined inferior borders (arrows).
whereas irregular or ill-defined borders occur in approximately 60% of cancers. Unfortunately, irregular or ill-defined borders also occur in approximately 45% of benign lesions. When a mass has a complete halo of echopenia around it, the lesion is twelve times more likely to be benign than malignant. If the halo is incomplete, a benign etiology is still approximately four times more likely than a malignant one. Lesions meeting the absolute criteria for cysts (well-demarcated, smooth-walled, anechoic, and demonstrating enhanced through-transmission) are usually benign. A cystic lesion with punctate, calcified mural nodules is indicative of papillary carcinoma (Fig. 8).

Nuclear Medicine

A nuclear medicine study may be another first-line imaging modality in a patient with a palpable thyroid mass. The agents used for thyroid imaging include 123I, 131I, 99mTc pertechnetate, and 201Tl. The half-lives, whole-body radiation doses, and thyroid radiation doses are listed in Table 3. Scanning is performed 15 minutes after administration of 5 to 10 mCi of 99mTc pertechnetate, 4 to 24 hours after administration of 100 to 400 mCi of 123I iodine, and 24 to 72 hours after administration of 30 mCi of 131I agents. With 201Tl scanning is performed 5 to 10 minutes after thallium administration. Because the radiation energy of 131I is so high (364 keV), it is the preferred agent for imaging substernal thyroid glands or to perform whole-body imaging after thyroid ablation to detect metastatic foci of thyroid cancer. The other agents have energies of 140 keV (99mTc) and 159 keV (123I).

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 in a hot nodule is between 1% and 4%, a warm nodule 8% and 10%, and a cold nodule 15% and 25% (Fig. 9). In a patient who has a prior history of head and neck irradiation, the risk of malignancy in a cold nodule doubles to 30% to 50%. Cold nodules in men have a higher rate of malignancy because women have a greater incidence of benign cold nodules from degenerated adenomas. If one performs dynamic injection 99mTc pertechnetate scintigraphy, one may find that hypoperfused lesions (less vascularity than that of native thyroid gland) are virtually never cancers, whereas most malignancies are "euperfused" or hyperperfused. Increased thallium uptake on both early and delayed scintigrams also has been anecdotally reported in thyroid malignancies.

Rarely, a lesion is cold on 123I scintigraphy but hot or warm on a 99mTc pertechnetate scan (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 iodine scan). The differential diagnosis includes malignancy, goiter, or follicular adenomas. Often, a biopsy is required in this situation.

Computed Tomography

The presence of calcification, cysts, hemorrhage, hypodensity or hyperdensity, or well-defined borders in a solitary mass on CT does not exclude a carcinoma (Fig. 10). Peripheral eggshell-like calcification and large multiple chunks of calcium suggest benignity, whereas fine punctate calcification is more indicative of malignancy. Calcification occurs in 13% of all thyroid lesions, including 17% of all malignancies and 11% of all benign processes. Similarly, cystic areas occur in many thyroid masses; 38% of malignancies have cystic components, and 62% of benign masses may be entirely or partly cystic. Hemorrhage may be found in papillary carcinomas or goiters. Multiplicity of nodules in an enlarged thyroid gland usually suggests 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. Curiously, the lymph nodes of thyroid papillary carcinoma may show calcification, cyst formation, colloid accumulation, hemorrhage, or necrosis. Sometimes the wall of a cystic node may be unidentifiable, thereby simulating a
Table 3. Scintigraphic Agents Used for Thyroid Imaging

<table>
<thead>
<tr>
<th>Agent</th>
<th>Half-life</th>
<th>Total Body Dose (rads)</th>
<th>Dose to Thyroid Gland (rads)</th>
<th>Dose Administered</th>
</tr>
</thead>
<tbody>
<tr>
<td>I-123</td>
<td>13.6 h</td>
<td>0.03</td>
<td>2–8</td>
<td>100–400 µCi PO</td>
</tr>
<tr>
<td>I-125</td>
<td>60.1 d</td>
<td>0.29</td>
<td>80–450</td>
<td>30–100 µCi PO</td>
</tr>
<tr>
<td>I-131</td>
<td>8.05 d</td>
<td>0.5</td>
<td>30–100</td>
<td>30–100 µCi PO</td>
</tr>
<tr>
<td>Tc-99m</td>
<td>6.02 h</td>
<td>0.02</td>
<td>0.04–2.0</td>
<td>5–10 mCi IV</td>
</tr>
<tr>
<td>Tl-201</td>
<td>3 d</td>
<td>0.21</td>
<td>0.92</td>
<td>2–3 mCi IV</td>
</tr>
</tbody>
</table>

h = hours; d = days; PO = oral; IV = intravenous; Ci = curies.

branchial cleft cyst. Papillary carcinoma of the thyroid may metastasize to posterior triangle, submandibular, retropharyngeal, or jugular chain lymph nodes.73,74 The nodes may enhance uniformly and dramatically or, as with cystic or calcified nodes, not at all.73,74 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.

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 to 8 weeks after administration of iodinated contrast agents.

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 carcinomas (Fig. 11).19 Lesions that have an intact and symmetric pseudocapsule are usually benign, whereas those with pseudocapsules that are penetrated or destroyed are usually cancers.19,35 Lesions that have capsules with irregular thicknesses may be malignant or benign. On MR imaging, the nodes of papillary carcinoma may be bright or dark on T1-weighted and T2-weighted scans, possibly related to the presence of intranodal hemorrhage or colloid accumulation.

Postoperatively, thyroid carcinoma recurrences are usually medium to high intensity on T2-weighted scans, whereas scar in the operative bed is usually low intensity.1 Postoperative edema, infection, or hemorrhage may simulate recurrent tumor.131I scintigrams are the best modality to evaluate the operative bed and to screen for distant metastases after thyroidectomy. MR imaging, in conjunction with 131I radioisotope scanning, has been recommended for confusing postoperative cases.4

Fine-Needle Aspiration

Intimately associated with any imaging technique is fine-needle aspiration cytology. Many palpable lesions of the thyroid gland may be aspirated without imaging, but ultrasound is the most common modality used to guide aspirations because it images in real time. Aspiration cytology in skilled hands yields outstanding results. In a series of 11,000 guided and unguided samples performed at the Mayo Clinic, the sensitivity of the technique was found to be 98% with a 99% positive predictive value for cancer.16 Nondiagnostic specimens were present in 21% of cases, however. Using fine needle aspiration with ultrasonic guidance yields results of nearly 100% sensitivity and specificities near 90%, while reducing nondiagnostic samples.16

Malignancies of the Thyroid Gland

Thyroid cancers are a mixed group of lesions. The most common histologic subtype is papillary carcinoma that accounts for 55% to 80% of thyroid malignancies.31,32,38 Although follicular elements in a papillary carcinoma are common, and this has led to a “mixed papillary-follicular” or “follicular
Figure 10. A and B, CT scans of papillary carcinoma. A, This enhanced CT scan demonstrates a mass (M), which has irregular calcification within it, in the left side of the thyroid gland. The presence of lymph nodes (arrows) is highly suggestive of papillary carcinoma. B, This cystic lesion with peripheral calcification in the wall (arrow) proved to be a degenerated adenoma.

Figure 11. A–D, Papillary carcinoma on MR scans and scintigraphy. A, Axial T1-weighted scan demonstrates a hyperintense mass (M) with peripheral hypointensity representing calcification. The wall, however, is not intact at its anterior-most border (arrows). The remainder of the gland shows diffuse enlargement with heterogeneous signal intensity compatible with goiter. The patient presented with an enlarging right-sided thyroid mass. B, Post-gadolinium-enhanced scan demonstrates minimal enhancement because it was bright on pregadolinium T1-weighted scans. No invasion of adjacent structures was identified. C, On T2-weighted scan, the border, though irregular, seems to be intact. Note that on the left side, the signal intensity of the goiterous thyroid gland is inhomogeneous. D, Scintigraphy of this mass revealed bilateral cold areas (C) within the thyroid gland with only a central area (arrows) of relatively normal uptake. Biopsy revealed papillary carcinoma of the thyroid gland. This shows how a benign appearance can be present with malignancies of the thyroid gland.
Papillary Carcinoma

The presence of psammoma bodies (laminated calcific spherules in 25–40% of cases), ground glass nuclei, and a branching pattern with a fibrovascular papillary stroma are the histologic signatures of papillary carcinoma of the thyroid gland. 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 that has the greatest likelihood of spread to lymph nodes; the nodes may be tiny, cystic, hemorrhagic, or calcified (Fig. 12). The incidence of nodal metastases during diagnosis is 50%, whereas distant metastases are reported to occur in 4% to 7%, usually to the lungs, bone, or central nervous system. Despite these features, the 20-year survival rate is reported to be as high as 90%. Approximately 10% of papillary carcinomas are bilateral.

Follicular Carcinoma

Pure follicular carcinoma is relatively uncommon when the follicular variant of papillary carcinoma is excluded. The tumor may be diffusely invasive or well encapsulated. Follicular carcinoma less frequently spreads to lymph nodes (2–10%) than does papillary carcinoma, but disseminates hematogenously more readily. The prognosis depends on the presence of hematogenous metastases or local invasiveness but is not as optimistic as that for papillary carcinoma. No distinguishing features on imaging studies suggest this diagnosis as opposed to other cancers, although, on ultrasonography, follicular carcinoma is isoechoic in 52% and hypoechoic in 44%. Compared with papillary carcinoma, follicular carcinoma rarely becomes cystic and more frequently invades vessels.

Anaplastic Carcinoma

This type of cancer is one of the most aggressive malignancies of the head and neck with prognosis marked in months rather than years. Older patients are usually affected. Anaplastic thyroid carcinomas occur within a substrate of goiters in 47% of cases and often coexist with other forms of better differentiated thyroid cancer. The outcome in mixed tumor cases is dominated by the poor prognosis of anaplastic carcinoma.

On ultrasonography, these carcinomas are most commonly hypoechoic, whereas on CT, anaplastic carcinomas show evidence of dense amorphous calcification in 58% of cases and necrosis in 74%. Metastatic lymph nodes are present in 74% to 80% of cases and show necrotic areas 50% of the time. Invasion into carotid arteries or adjacent aerodigestive structures occurs in 34% to 55% of patients, and in 25% the primary tumor extends into the mediastinum (Fig. 13). Rapid growth and obliteration of adjacent tissue planes are hallmarks of this deadly tumor with a median survival of approximately 7 months.

Medullary Carcinoma

Medullary carcinoma originates in the parafollicular or “C” cells of the thyroid gland, cells derived from neural crest tissue in the ultimobranchial bodies of the branchial pouch system. These cells normally secrete thyrocalcitonin, which decreases serum calcium. Eighty percent to 90% of medullary carcinomas express calcitonin. Functioning tumors have a better prognosis.

Medullary carcinomas are usually hypoechoic on ultrasonography, however, echogenic foci caused by deposits of calcium may be seen within these tumors and metastatic lymph nodes when present. These tumors usually do not take up iodine but may be thallium or gallium avid. Somatostatin receptor scintigraphy also may detect medullary carcinoma. The tumor is solid on CT and MR imaging and spreads to lymph nodes in more than 50% of cases (Fig. 14).

Medullary carcinoma has a familial incidence of 10% to 20%. Sipple syndrome is the association of medullary carcinoma with pheochromocytoma and parathyroid adenoma or hyperplasia. This is also known as the MEN 2A. When mucosal neuromas and marfanoid facies coexist, MEN 2B is said to be present (see Table 2). Both syndromes have been localized to an abnormal gene on the tenth chromosome.
Lymphoma

Thyroid lymphoma may present as a solitary mass (80%) or as multiple nodules (20%). An antecedent history of Hashimoto's thyroiditis in an elderly female with a rapidly enlarging, compressive, and infiltrative mass suggests lymphoma. Most are B-cell neoplasms. Response to chemotherapy and radiation is variable; some patients do very well.

Lymphomas are usually hypoechoic at sonography. Lymphoma is cold on technetium or iodine nuclear medicine studies; however, gallium scans may show increased activity. Other lymphoproliferative (leukemia) and granulomatous diseases (e.g., sarcoidosis) also may be gallium avid and are in the differential diagnosis. The tumor is hypodense on unenhanced and enhanced CT studies and shows necrosis or calcification in only 7% of cases (Fig. 15). Invasion of the carotid sheath
Figure 13. Anaplastic carcinoma on CT scan. Diffuse enlargement with irregular contrast enhancement is noted in the thyroid gland of this patient with anaplastic carcinoma. The predominant density is hypodense to the native thyroid tissue. One would expect to see marked enhancement in the normal thyroid gland due to iodine accumulation.

(19-51%) or metastases to lymph nodes (14-44%) are not uncommon. The absence of calcification and necrosis, the rarity of invasion into surrounding soft tissues, and the lower incidence of nodal dissemination help to distinguish lymphoma from anaplastic carcinoma.

Lymphoma is usually homogeneously hyperintense on T2-weighted MR scans. Although some workers have found Hashimoto's thyroiditis to be low in intensity on T2-weighted images and, therefore, distinguishable from lymphoma (which is bright), most investigators have found their signal intensities to overlap.

Metastases

Metastases to the thyroid gland are often clinically occult. Pathologically, metastases to the gland may be present in 2% to 4% of patients dying from malignant disease. The two most common primary tumors to metastasize to the thyroid gland are bronchogenic carcinoma and renal cell carcinoma. Multifocality is the norm (Fig. 16), and hemorrhage is not uncommon with renal metastases.

Benign Masses

Functioning Thyroid Adenomas

More than ninety percent of solitary hot nodules on scintigraphy are benign in etiology, usually adenomas or hyperplasias that are expressing thyroid hormone. Plummer's disease is hyperthyroidism resulting from a solitary autonomous hot nodule (Fig. 17). The difference between an autonomous and a hypertrophic functioning hot nodule depends on the response to a thyroid suppression test. After a diagnostic course of thyroid hormone administration (with confirmation of depressed thyroid stimulating hormone [TSH]), a lesion that is persistently hot on a 99mTc pertechnetate scan is considered an autonomous lesion, whereas one that becomes cold is considered hypertrophic. Other sources of hot

Figure 14. A and B, Medullary carcinoma of the thyroid gland. A. This patient has a thyroid mass (*) on the right that has invaded the tracheal wall accounting for the thickening (arrows) seen lateral to the endotracheal tube. It was medullary carcinoma. B. Note absence of right lateral tracheal wall further down.
nODULES

"Toxic" adenomas rarely cause clinically apparent hyperthyroidism until they exceed 2.5 cm in size. The patient usually presents with a slowly growing neck mass. The imaging features of toxic adenomas are nonspecific on nonscintigraphic 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 women and in men of all ages. A biopsy or aspiration is often required early in the diagnostic algorhythm. The majority of cold nodules are caused by degenerated (follicular) adenomas (Fig. 18) nodular hemorrhage, cysts, goiters, inflammatory conditions (see subsequent discussion), or amyloid deposition. Follicular adenomas occur in all age groups, in women more than in men, and are usually less than 3 cm in size. As adenomas outgrow their blood supply, they may involute or encyst. Alternatively, they may develop intralesional hemorrhage (and acutely expand), necrosis, calcification, or scarring. Malignant degeneration is not believed to occur in adenomas.

Hurthe's cell adenomas (which some investigators believe are malignant in character) are more variable in size and shape with less well-defined borders.

Occasionally, one will find a hyperplastic adenoma that is responsive to TSH in a patient with Grave's disease. This appears as a cold nodule because the hyperthyroidism of Grave's disease suppresses TSH, which in turn suppresses the adenoma on a nuclear medicine study. This entity is called Marine-Lenhart syndrome.

In one of the earliest articles on the subject of MR imaging, Gefter and colleagues identified adenomatous nodules as small as 4 mm to 5 mm in size. They noted that follicular adenomas appeared as well-circumscribed nodules with heterogeneous intensity, bright on T2-weighted images (Fig. 19).

Cysts

Most thyroid cysts actually represent degeneration of adenomas. Cysts of any kind are anechoic or echopenic on ultrasonography, show a distinct back wall, and demonstrate enhanced through-transmission. They are low density on CT unless hemorrhagic or infected. The density and intensity of the cyst may not simulate that of cerebrospinal fluid on CT and MR imaging because of the presence of hyperproteinaceous colloid within the cyst. Colloid cysts are characterized by homogeneous high signal on T1-weighted scans; however, this finding is not specific to colloid cysts because areas of hemorrhage, also bright on T1-weighted scans, can be seen in goiters, adenomas, and traumatized cysts. Even thyroglossal duct cysts (vide infra) may be hyperintense because of high protein content.

Multinodular Goiter

Another common palpable thyroid abnormality is the multinodular goiter. A goiter is simply an enlarged thyroid gland that may be seen with hyperthyroidism or hypothyroidism. In the United States, the common vernacular is to imply a non-toxic goiter when the term is used. A euthyroid or hypothyroid goiter is the most common thyroid lesion in the United States. Patients, usually older women, present because of hypothyroidism, neck masses, or tracheal-esophageal compression. In rare
instances, a previously nonfunctioning multinodular goiter evolves into one with hyperfunctioning nodules and causes hyperthyroidism. The incidence of carcinoma in a multinodular goiter is very low (below 3%) and the characteristic appearance of multiple cold areas interspersed with hot areas in a large gland usually obviates the need for aggressive biopsy of a palpable nodule (Fig. 20). A large, dominant, hard, or growing mass amidst a goiter should probably still be biopsied (see Fig. 1). 6

Nontoxic multinodular thyroid glands show minimal to moderate heterogeneity with nodularity and mildly increased signal intensity on T1-weighted MR image.18,52 Hemorrhagic foci are noted in 60% of cases and the lesions are often heterogeneous on T2-weighted scans.52 Goiters usually do not have pseudocapsules.52 On CT and ultrasonography, mixed solid and cystic zones within an enlarged, nodular thyroid gland with or without calcification is the characteristic appearance of a multinodular goiter (Fig. 21).

Teratomas

These are rare neoplasms of the thyroid gland. As in other locations in the body, thyroid teratomas may demonstrate fluid, fat, calcification, and osseous densities in various combinations. They usually occur in the midline.

Hyperthyroidism

The three most common causes of hyperthyroidism are Graves' disease (diffuse toxic goiter), toxic
multinodular goiter, and toxic adenomas. The toxic adenomas (discussed earlier) are separated into those that are TSH-responsive (hypertrophic) or TSH-independent (autonomous). Occasionally, inflammation of the thyroid gland (thyroiditis) produces a transient state of hyperthyroidism. On rare occasions, ectopic thyroid tissue (lingual or ovarian) causes hyperthyroidism.

Intenzo and colleagues have proposed a unique algorithm for evaluating a hyperthyroid patient. If thyroid function tests (TFTs) are elevated and the 24-hour radioactive iodine uptake (RAIU) is also elevated (normal, below 35%), the differential diagnosis is Graves' disease or Marine-Lenhardt disease (Graves' with coexistent TSH-dependent nodules). The latter appears on scintigraphy as a gland with diffuse increased trapping of the radiotracer with superimposed cold nodules. If the TFTs are elevated but the RAIU is normal, one should consider Plummer's disease (hyperthyroidism due to a solitary autonomous hot nodule that suppresses the remainder of the gland), Graves' disease with rapid iodine turnover, or a laboratory error. If TFTs are elevated but RAIU is depressed, the possibilities include subacute granulomatous thyroiditis, subacute lymphocytic thyroiditis, postpartum thyroiditis, and struma ovarii. With thyroiditides, thyroid hormone may escape ruptured follicles leading to transient hyperthyroidism, although the damaged gland cannot concentrate iodine so the RAIU and thyroid scans show depressed uptake.

Graves' Disease

Graves' disease is the most common cause of hyperthyroidism. This disease affects women more commonly than men and a familial tendency is present. Patients may have heat intolerance, weight loss, fatigue, insomnia, tremors, palpitations, increased thirst and hunger, and agitation. Exophthalmos may be present, although thyroid eye disease need not occur only in the setting of hyperthyroidism; it may be present post-therapy when the patient is euthyroid or even hypothyroid. Blood tests are usually able to make the diagnosis of Graves' disease because of the autoimmune phenomenon associated with the disease. Thyroid-stimulating immunoglobulins, such as long-acting thyroid stimulator, simulate the function of TSH and cause hyperthyroidism. On iodine scans, there is markedly elevated iodine uptake within a nonfocal, hot, enlarged thyroid gland.
In a patient who is hyperthyroid, scintigraphy may be useful in distinguishing Graves' disease, which shows homogeneous diffuse intense uptake (70–85%) from thyroiditides (Fig. 22). 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 subsequent discussion) 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 on 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 only 0.15% to 0.5% of patients.10

**Hypothyroidism**

Hypothyroid patients 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's thyroiditis is the most common cause of hypothyroidism in the United States (see subsequent discussion). Worldwide, iodine deficiency (endemic goiter) is another cause of hypothyroidism but is infrequently seen in developed countries. Other etiologies include the other chronic thyroiditides. Postoperative and postradiotherapy (131I or external beam irradiation) patients also account for more hypothyroid patients. It is common for patients treated with radioactive iodine for hyperthyroidism to become hypothyroid after several years.

Congenital hypothyroidism occurs more commonly in the Japanese population (1 in 3500 newborns).3 Possible causes include thyroid aplasia, hemi aplasia (the left gland is absent more commonly than the right), or ectopia (80%), dyshormonogenesis (10–15%), pituitary or hypothalamic deficiency (< 5%) and autoimmune disease (< 5%). Prompt replacement of thyroid hormone is critical because mental retardation is a possible complication of undiagnosed neonatal hypothyroidism.83 Both ultrasonography and scintigraphy are used to identify thyroid tissue in this population.

**Congenital Lesions**

*Thyroglossal Duct Cysts*

Two of the most common congenital abnormalities associated with the thyroid gland are thyroglossal duct cysts and lingual thyroid glands. 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. Any epithelial-lined tract has the potential for obstruction and a cyst may occur due to retained secretions. In thyroglossal duct cyst, a midline cystic mass is observed, which is located in an infrahyoid level in 65%, hyoid level in 15%, and suprathyroid level in 20% of cases.3 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. 23).

Because the fluid in the thyroglossal duct cyst may have a high protein content, it may appear cystic with some internal echoes on ultrasonography. It moves with swallowing or sticking the tongue out. On CT, the noninfected thyroglossal duct cyst varies in intensity from markedly hypodense (with no protein content) to slightly hyperdense (with high protein or hemorrhage within). On MR scans, the thyroglossal duct cyst may be either dark or bright on T1-weighted scans but is typically hyperintense on T2-weighted scans. 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 approximately 25% to 33% of thyroglossal duct cysts. The incidence of carcinoma within the thyroid tissue of a thyroglossal duct cyst is less than 1%. When it occurs, it is usually papillary carcinoma.

Recurrence rates of approximately 4% are observed after attempted removal of thyroglossal duct cysts. The surgery removes the entire tract of the duct including the middle one fourth of the hyoid bone and a portion of the base of the tongue that includes the foramen cecum (Sistrunk procedure). Rarely, the tract of the thyroglossal duct may serve as conduit for infection to the thyroid gland leading to acute suppurative thyroiditis.

Lingual Thyroid Glands

Lingual thyroid tissue occurs in 1 in 3000 patients who have thyroid disease and represents the most common form of functioning ectopic thyroid tissue. 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% to 80% of cases and are seen much more commonly in women. Patients often present in puberty, when the tissue may expand rapidly. Variation in size with menstruation also has been reported.

The primary role of imaging is to identify whether normal thyroid tissue is present 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 lifelong thyroid replacement therapy if the lingual thyroid gland is totally removed. A nuclear medicine study to determine whether a lingual mass represents thyroid tissue, and also to search for other (ectopic or normally located) thyroid tissue, is favored over cross-sectional imaging. The thyroidal tissue within the tongue can be identified by its high attenuation on CT (due to iodine accumulation) or its avid contrast enhancement. In a similar fashion, the MR scan demonstrates bright tissue that avidly enhances in the middle of the tongue.

A malignancy arising within a lingual thyroid gland is more common than one in a thyroglossal duct cyst. At least one report noted an incidence of 2.8%.

Aberrant Thyroid Tissue

Thyroid tissue lateral to the jugular vein unassociated with lymphadenopathy may occur due to anomalous development and is termed lateral aberrant thyroid tissue. This phrase is rarely used now, because most cases of lateral aberrant thyroid tissue actually represented thyroid carcinoma metastases to lymph nodes. Nonetheless, in rare instances, thyroid tissue may be “seeded” to this location by trauma, surgery, thyroiditis, or goiters, and must be distinguished from metastatic thyroid carcinoma.

Undescended thyroid tissue sometimes may be seen in the anterior neck superficial to the hyoid bone. Aberrant thyroid tissue also may be found in the trachea. In this site, women are affected more commonly than men, and the thyroid tissue may respond to hormonal influences.

Substernal thyroid tissue is not uncommon but usually occurs in association with a goitrous gland extending downward rather than as isolated tissue. Tracheal or esophageal compression on a chest radiograph may be the presenting finding. Imaging to distinguish a goiter from mediastinal adenopathy, thymoma, lymphoma, teratoma, carcinoma, or an
unusual bronchogenic cyst is usually pursued with CT.

Struma ovari, the presence of functioning thyroid tissue in the ovaries or in an ovarian teratoma or dermoid, is rare.

**Inflammatory Lesions**

No specific scintigraphic, sonographic, CT, or MR appearances differentiate among the various inflammatory processes involving the thyroid gland. The most useful imaging study is the nuclear medicine scan, performed with $^{99m}$Tc pertechnetate or radioactive iodine ($^{123}$I or $^{131}$I), which determines the activity of the thyroid gland. The value of the imaging studies, however, pales in comparison with that of serology for distinguishing various inflammatory lesions of the thyroid gland. On the other hand, if imaging is to be used as a map for surgical correction or resection of the thyroid gland, MR imaging and ultrasonography seem to be of particular benefit. In some instances, the administration of iodine on an enhanced CT scan might precipitate thyroid storm (acute outpouring of thyroid hormone), so CT usually is avoided.

**Suppurative Thyroiditis**

Acute suppurative thyroiditis presents with acute onset of pain and swelling in the thyroid gland associated with fever, odynophagia, and dysphagia. The role of imaging is to exclude a pyriform sinus or thyroglossal duct fistula as an etiology for the acute suppurative thyroiditis. This entity occurs sometimes in association with a fourth branchial cleft anomaly and has a left-sided predominance. Imaging may identify 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 fulminant clinical presentation.

**Hashimoto's Thyroiditis**

Most other forms of thyroiditis are subacute or chronic diseases. Hashimoto's (chronic lymphocytic thyroiditis) is the most common of the chronic thyroiditides, being five to ten times more frequent than subacute thyroiditis. It is the most common thyroiditis in children. The diagnosis is based on serology 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 FNAs may reveal a preponderance of lymphocytes, centroblasts, and Hurthle's cells. Women are affected nearly 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.

The gland with Hashimoto's thyroiditis is enlarged and shows multinodularity and heterogeneous increased or decreased uptake of radiotracers. Although early in the disease there may be increased uptake of iodine on nuclear medicine studies, the usual response is diminished or normal thyroid uptake on imaging. Patients who trap more tracer have a greater chance of returning to a euthyroid state than those who do not. Although Hashimoto's thyroiditis shows no greater risk for carcinoma, it seems to predispose to non-Hodgkin's lymphoma. Hashimoto's thyroiditis in the presence of thyroid lymphoma is seen in 25% to 67% of cases.

On ultrasonography, the thyroid gland is symmetrically enlarged and hypoechoic but may have nodules within it (Fig. 24). Calcification is seen in the chronic stages. On T2-weighted scans, MR im-

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**Figure 24.** A and B, Hashimoto's thyroiditis on ultrasonography. A, Sagittal scan through the right lobe shows an enlarged gland with some nodularity (arrows) to it. B, The transverse view also depicts a prominent irregular gland.
aging has shown increased signal intensity, sometimes with linear low intensity bands thought to represent fibrosis.\textsuperscript{18, 57}

Hashimoto's disease has been associated with other autoimmune entities, such as pernicious anemia, Sjögren's syndrome, lupus, rheumatoid arthritis, Addison's disease, and Graves' disease.

Riedel's Thyroiditis

Riedel's thyroiditis (struma thyroiditis) 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 in men. Patients present with evidence of mass effect with compression of the trachea, hoarseness, and difficulty in swallowing. The patients are usually hypothyroid. On imaging, Riedel thyroiditis is homogeneously hypoechoic on ultrasound and is usually hypodense to normal thyroid tissue on CT.\textsuperscript{20, 57} The lesion may be isodense to muscle on unenhanced CT. Riedel thyroiditis may spread to outside of the thyroid gland, infiltrating and obliterating adjacent tissue planes (Fig. 25). The characteristic finding on MR images is hypointensity on T1- and T2-weighted sequences with infiltration of adjacent structures of the neck.\textsuperscript{57} The low intensity on MR images is believed to be caused by 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's thyroiditis, which is typically increased in intensity on T2-weighted MR images.

de Quervain's Thyroiditis

de Quervain's 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.\textsuperscript{39} Pain, fever, and fatigue are common presenting symptoms. Subacute thyroiditis may present (50\% of cases) with acute toxic hyperthyroidism with subsequent return to a euthyroid state after 1 to 2 months.\textsuperscript{66} Hypothyroidism occurs approximately 2 to 4 months after onset and, typically by 6 months after the acute onset, the patient reverts to euthyroidism.\textsuperscript{58} Patients are treated medically because the prognosis is good for return of normal thyroid function. Subacute thyroiditis is hypoechoic on ultrasonography, although there may be atrophy of thyroidal tissue with time.\textsuperscript{20} Nuclear medicine studies show heterogeneous uptake that varies 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 radiating 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 hemochromatosis may affect the thyroid gland and lead to decreased signal intensity on T2-weighted MR scans. Tuberculosis, sarcoidosis, and fungal infections may cause a granulomatous inflammation of the thyroid gland but are uncommon conditions.\textsuperscript{2}

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