Imaging for Parathyroid Surgery

14

Neelima Tummala and Lisa A. Orloff

Introduction

Preoperative parathyroid localization is the sine qua non of minimally invasive parathyroidectomy. Fortunately, there are several effective imaging modalities available today for precise localization of parathyroid disease. While the normal parathyroid gland still eludes visualization other than by open surgical identification, the enlarged parathyroid gland can be identified by noninvasive imaging techniques in the great majority of patients. Prior to the advent of these imaging modalities, bilateral cervical exploration was considered the gold standard. Ironically, some of the most ardent former critics of localizing studies, who defended routine bilateral parathyroid exploration, are the very same surgeons who currently market and practice a focused approach to parathyroidectomy that is dependent on accurate preoperative localization. Over the past several decades, with the use of imaging methods that enable mapping of disease, a minimally invasive surgical approach to treating parathyroid disease has come to represent the most common practice. Limited exploration, with a focal (single gland) or unilateral (single side) approach, is now the most frequent approach.

N. Tummala, MD • L.A. Orloff, MD (✉)
Department of Otolaryngology/Head and Neck Surgery, University of California, San Francisco, 2380 Sutter Street, Second Floor, San Francisco, CA 94115, USA
e-mail: lorloff@ohns.ucsf.edu

Approximately 83 % of patients have four parathyroid glands: two inferior glands and two superior glands. Another 13 % have more than four glands (supernumerary parathyroids), and 3 % of patients have fewer than four glands. The superior glands arise from the fourth brachial pouch, along with the thyroid gland. They descend during embryonic development into the neck alongside the thyroid gland and are rarely ectopic. They are typically located posterior to the upper-mid pole of the thyroid gland. They are more rarely located posterior to the esophagus or pharynx, in a deep, descended location.

The inferior glands arise from the third brachial pouch, along with the thymus. These glands have a longer descent and are more variable in position, with 35 % present at ectopic locations along the thymopharyngeal duct course. They are found at the inferior pole of the thyroid gland about two-thirds of the time and are at an ectopic location, anywhere from the angle of the mandible to the lower mediastinum, in the remaining cases. Due to their close proximity to the thyroid gland, the parathyroid glands may be covered by or attached to the thyroid capsule, resulting in intracapsular or intrathyroid location.

Primary hyperparathyroidism is due to idiopathic enlargement and hypersecretion of one or more parathyroid glands. The majority (about 85 %) of patients with primary hyperparathyroidism have a single adenoma, namely, a benign neoplasm of any one of the parathyroid glands. A smaller subset (about 15 %) of patients has multigland disease, including hyperplasia of all of

D.J. Terris, M.C. Singer (eds.), *Minimally Invasive and Robotic Thyroid and Parathyroid Surgery*, DOI 10.1007/978-1-4614-9011-1_14, © Springer Science+Business Media New York 2014

their parathyroid glands or hyperfunction due to two or more simultaneous parathyroid adenomas. A typical parathyroid adenoma is about 10–30 mm in length, while a normal gland usually measures about 5 × 3 × 1 mm. Hence, on imaging, a parathyroid adenoma is often identified as a round or oval mass that is well circumscribed, solid, and hypervascular. Likewise on imaging, lymph nodes, thyroid nodules, parathyroid cysts, the esophagus, and (rarely) parathyroid cancers may be mistaken for adenomas.

Preoperative localization of parathyroid disease is essential for a minimally invasive parathyroidectomy. It reduces operating room time and limits dissection while aiding in identification of multigland or ectopic disease, particularly in the mediastinum, that may not be amenable to a minimally invasive approach. Although imaging is very useful for identifying disease, it must be remembered that a positive finding on imaging does not confirm diagnosis, while a negative finding cannot rule out the existence of disease. In addition, the use of imaging modalities for parathyroid disease should be limited to patients who have a biochemical diagnosis of primary hyperparathyroidism.

There are a variety of noninvasive and invasive imaging studies that are available both for initial evaluation of patients and for patients with persistent or recurrent disease. The most common noninvasive studies include ultrasonography, nuclear scintigraphy scans that utilize sestamibi, computed tomography (CT), and magnetic resonance imaging (MRI), with variations of each type of study available. Invasive studies include fine-needle aspiration (which can be guided by ultrasound or CT), parathyroid angiography, and selective venous sampling for parathyroid hormone gradient.

Ultrasound

Ultrasonography is a highly useful tool in the preoperative evaluation of patients with parathyroid disease. It is cost effective and noninvasive, performed efficiently, does not require any preparation, and does not introduce the patient to any radiation exposure. High-frequency (7 MHz or greater), high-resolution ultrasonography provides detailed anatomic information on enlarged parathyroid glands as well as concomitant thyroid disease, if present. Ultrasonography also reveals dynamic as well as three-dimensional detail regarding parathyroid position. Ultrasonography has demonstrated sensitivities of 77–96 % and positive predictive values of 74–98 % in identifying parathyroid adenomas. Ultrasonography has been shown to be more sensitive than nuclear medicine imaging for multigland parathyroid disease, and accuracy rates for surgeon-performed ultrasonography have been some of the highest cited (up to 91 %).

On ultrasound, as with other imaging modalities, normal parathyroid glands are not visualized due to their small size and similarity to surrounding tissues. The sonographic appearance of a typical parathyroid adenoma is a solid, homogenous, hypoechoic mass, which is in distinction to the more hyperechoic thyroid tissue (Fig. 14.1). The adenoma is typically adjacent to the thyroid gland and medial to the carotid artery. It is often bean or oval shaped but can also be multilobulated, depending on its size. It is highly vascular, and if color Doppler is used, an extrathyroidal peripheral feeding vessel with a rim of vascularity around the adenoma may be visualized (Fig. 14.2).

Limitations of ultrasound include its area of coverage, as it is limited to the neck region, and the fact that it is highly operator dependent. Surgeon-performed ultrasound has been shown to be equal or superior to non-clinician-performed ultrasound for parathyroid localization, a fact that makes intuitive sense since the surgeon is ultimately responsible for the success or failure of the operation and cure of the disease. In addition, ultrasound offers real-time imaging with greater anatomic detail, as compared to scintigraphy. However, there is limited identification of retrosternal and retrotracheal disease. Another shortcoming is its use in obese patients and in patients with short necks or limited neck extension, as well as those with nodular thyroid disease, in whom it is much more difficult to obtain an adequate view to identify adenomas.

It can be difficult to distinguish small lymph nodes from diseased glands based solely on

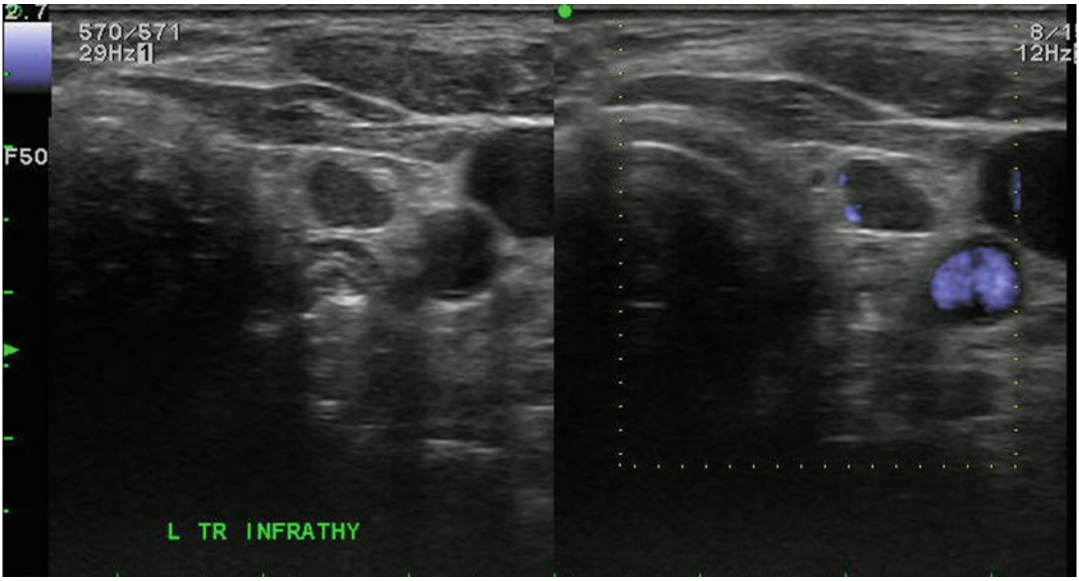

Fig. 14.1 Gray-scale ultrasound (*left*) and color Doppler ultrasound (*right*), both showing transverse view of a left inferior parathyroid adenoma, situated between the trachea and the carotid artery. A typical parathyroid adenoma is a solid, homogenous, hypoechoic mass

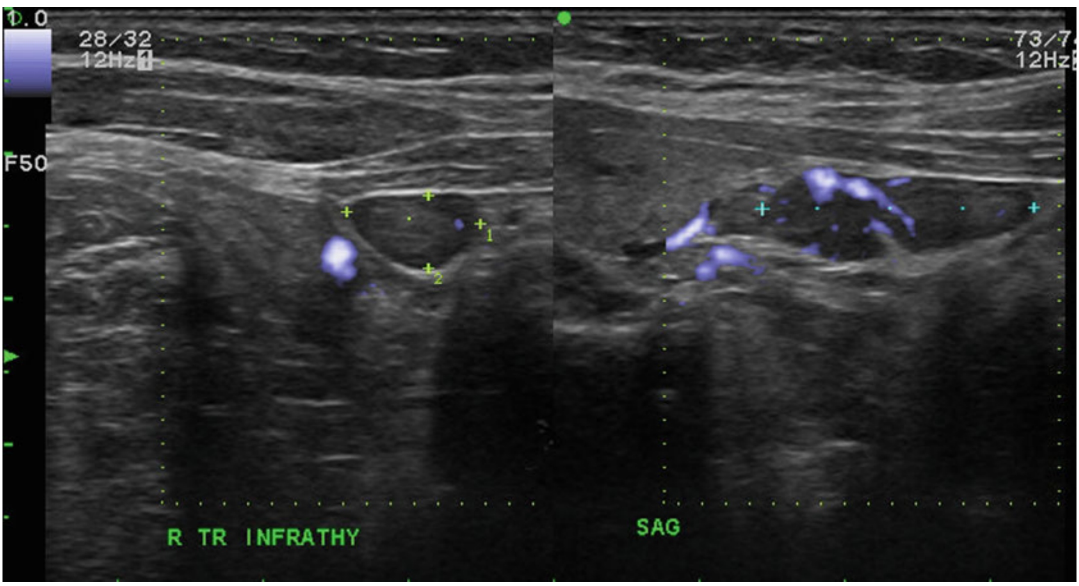

Fig. 14.2 On color Doppler ultrasound, an extrathyroidal peripheral feeding vessel and a rim of vascularity around the adenoma are typically seen (transverse and sagittal views)

ultrasound. The use of ultrasound in combination with other imaging modalities, especially the sestamibi scan, is common and in fact preferred by many surgeons. A parathyroid adenoma identified both on sestamibi scan and on ultrasound imaging is highly specific. Combining the two modalities, a false-negative rate as low as 2 % has been found, as compared to 23 % with ultrasound alone and 12 % for sestamibi alone. Ultrasound is also useful for guiding fine-needle aspiration (FNA) of a lesion, as described below.

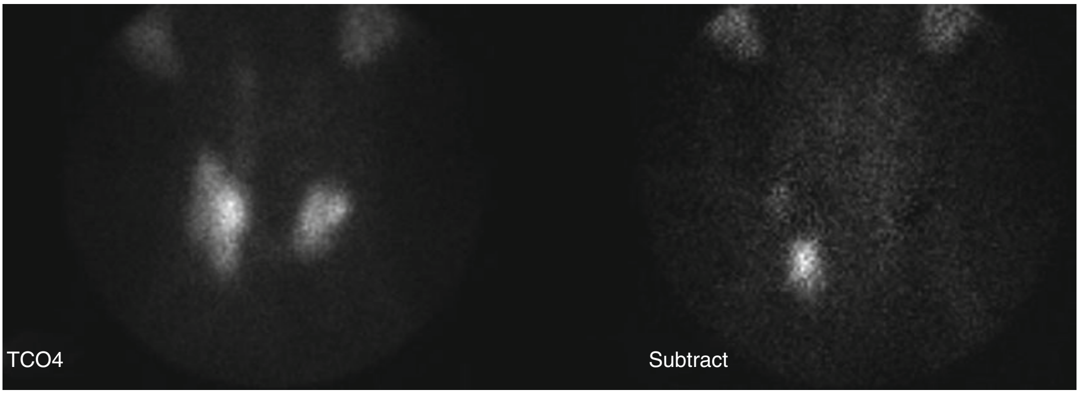

Fig. 14.3 In subtraction imaging, the image from the uptake of the thyroid-specific radionuclide (in this case, Tc-99m pertechnetate, *left*) is subtracted from the parathyroid/thyroid radionuclide (Tc-99m MIBI) image, resulting in an estimation of parathyroid tissue uptake (*right*)

Sestamibi Scan

Developed in the early 1990s, sestamibi parathyroid scanning is now widely available. This imaging modality, comprised of several different nuclear scintigraphic techniques, is the most popular procedure used for parathyroid localization and is collectively the most accurate, with a sensitivity and specificity of greater than 90 % for identifying parathyroid disease. Sestamibi scanning is particularly useful for identifying ectopic disease and has been shown to be more reliable for adenoma localization in patients with lower levels of vitamin D.

Often used in conjunction with ultrasound, this combination is highly reliable, as an ultrasound can anatomically identify a possible adenoma, while a nuclear medicine scan can differentiate it functionally from a lymph node or thyroid mass.

Tc-99m sestamibi is a lipid-soluble myocardial perfusion tracer that accumulates in the mitochondria of cells. Parathyroid adenomas are very vascular and have a high concentration of oxyphilic cells, which have increased mitochondrial content, increasing their sestamibi uptake. The sestamibi isotope, which emits gamma rays, is retained longer in the parathyroid adenoma cells than the adjacent thyroid due to this increased mitochondrial content. Thus, there is focal increased uptake on early and delayed images taken with a gamma camera in an adenoma, as compared to other surrounding tissue. The two most common techniques used are subtraction imaging and dual-phase imaging. Subtraction imaging can be especially helpful if a thyroid mass is present. Dual-phase imaging is less affected by motion artifact, making it a better option for SPECT imaging.

In subtraction imaging, both a thyroid-specific radionuclide and a thyroid- and parathyroid-specific radionuclide are administered. The most commonly used thyroid-specific radionuclides are either iodine-123 (^{123}I) or Tc-99 m sodium pertechnetate. The image from the uptake of the thyroid-specific radionuclide is subtracted from the parathyroid/thyroid radionuclide (Tc-99m sestamibi) image, resulting in an estimation of parathyroid tissue uptake (Fig. 14.3).

In the dual-phase technique, visualization of parathyroid adenomas is based on differential washout. In this process, initial images are taken 10 min after intravenous infusion, and subsequent images are taken at 2–3 h after sestamibi administration, based on the kinetics of the compound. Due to retention and delayed sestamibi washout, there should be persistent sestamibi visualization in the parathyroid adenomas in the delayed images, as compared to the initial set (Fig. 14.4). Hyperparathyroid patients with double adenomas and parathyroid hyperplasia have

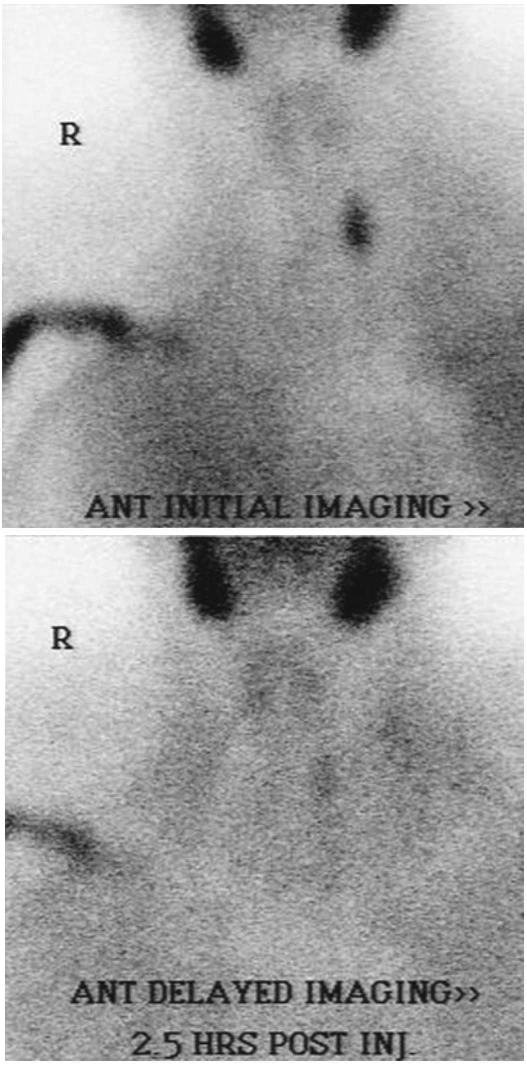

Fig. 14.4 Dual-phase technique. Early (10 min after intravenous infusion) and late (2–3 h after sestamibi infusion) show differential washout. There is typically persistent sestamibi visualization in parathyroid adenomas in the delayed images, although some adenomas, such as the one in this figure, show initial uptake and early washout

progressively less distinct or successful localization than those with single adenomas.

Sestamibi imaging was originally performed as two-dimensional (2D) planar scanning (Fig. 14.5). Such 2D scans have in some centers been replaced by SPECT (single proton emission computed tomography) scans, which provide three-dimensional (3D) reconstruction and

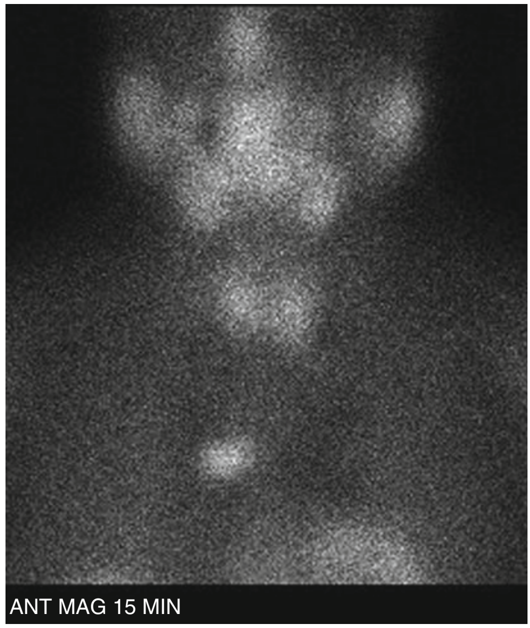

Fig. 14.5 Two-dimensional planar sestamibi scan, showing parathyroid uptake in a right inferior mediastinal adenoma

greater localizing information (Fig. 14.6). Furthermore, SPECT sestamibi scans have recently been fused with high-resolution, thin slice CT to localize disease even more precisely (Fig. 14.7). Several studies have found dual-phase SPECT/CT sestamibi imaging to be significantly superior to planar imaging in the detection of parathyroid lesions, especially when there is concomitant thyroid nodularity. However, other studies have found that SPECT/CT has no significant clinical value additional to that of conventional SPECT for parathyroid imaging except in locating ectopic parathyroid glands and that the additional time, radiation exposure, and expense do not justify the CT acquisition.

One of the main limitations of all variations of sestamibi scanning is the fact that, like ultrasound, it is highly operator dependent. It is most reliable for identifying large, solitary adenomas. False positives occur when there are other cell types that also have high mitochondrial content, such as Hurthle cell nodules in thyroid tissue.

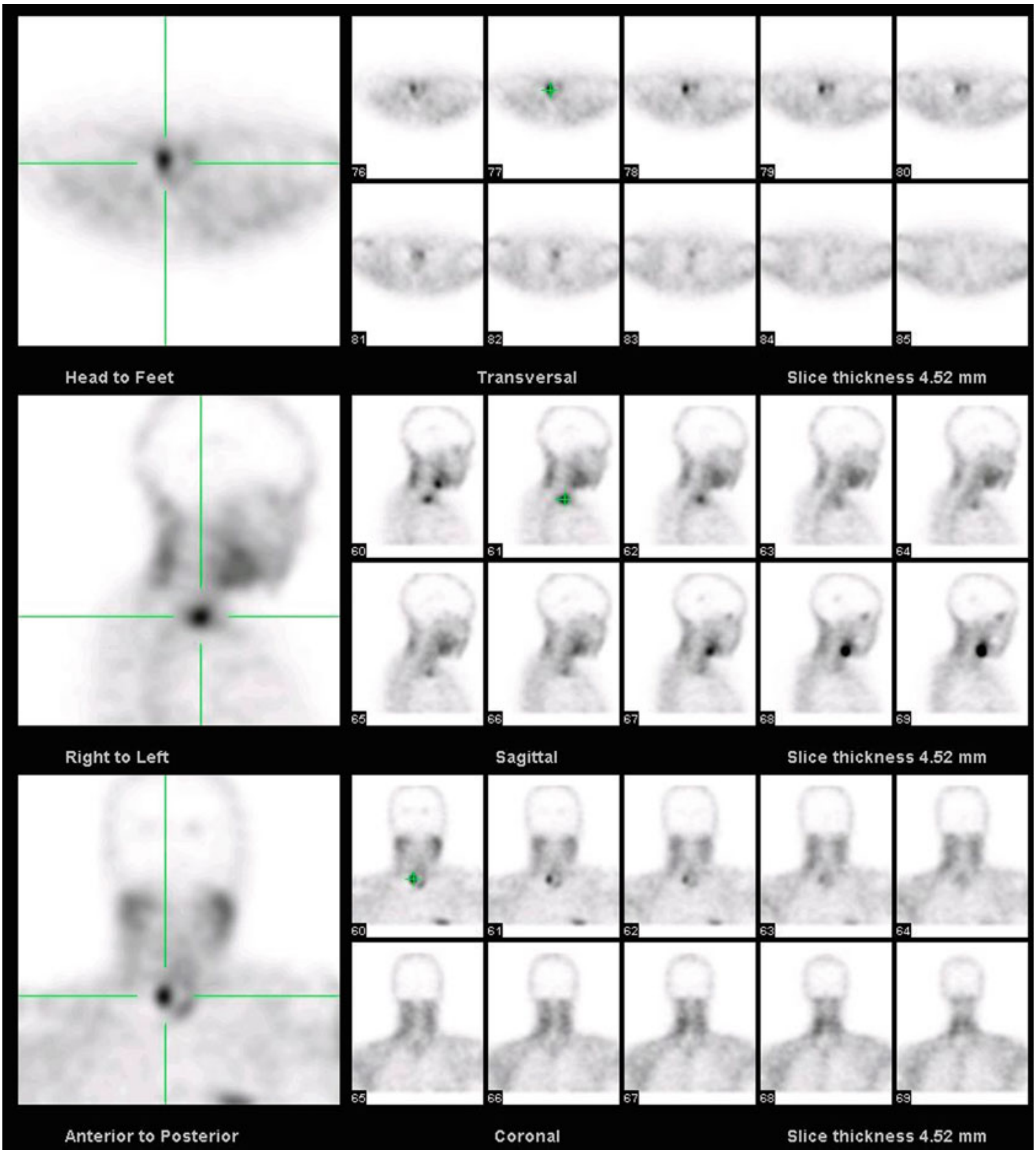

Fig. 14.6 SPECT sestamibi scan, showing axial, sagittal, and coronal 3D reconstructions and localization of a parathyroid adenoma to the right retrothyroid region

Also, brown fat, brown tumors, lymphoma, breast cancer, and thyroid carcinoma all have a propensity for increased uptake. False negatives often occur with adenomas with low oxyphilic count, which is seen in smaller adenomas and in multiglandular disease. False-negative sestamibi scanning has also been linked to patients with higher levels of vitamin D and lower levels of serum calcium, as well as patients with multigland disease (multiple adenomas or parathyroid hyperplasia.). Reviewing early, late, and subtraction pinhole images together with SPECT images maximizes parathyroid lesion detection accuracy. Also, the operating surgeon should review all sestamibi scans irrespective of what is reported, because there are often subtle findings that are pertinent but not reported on the formal interpretation.

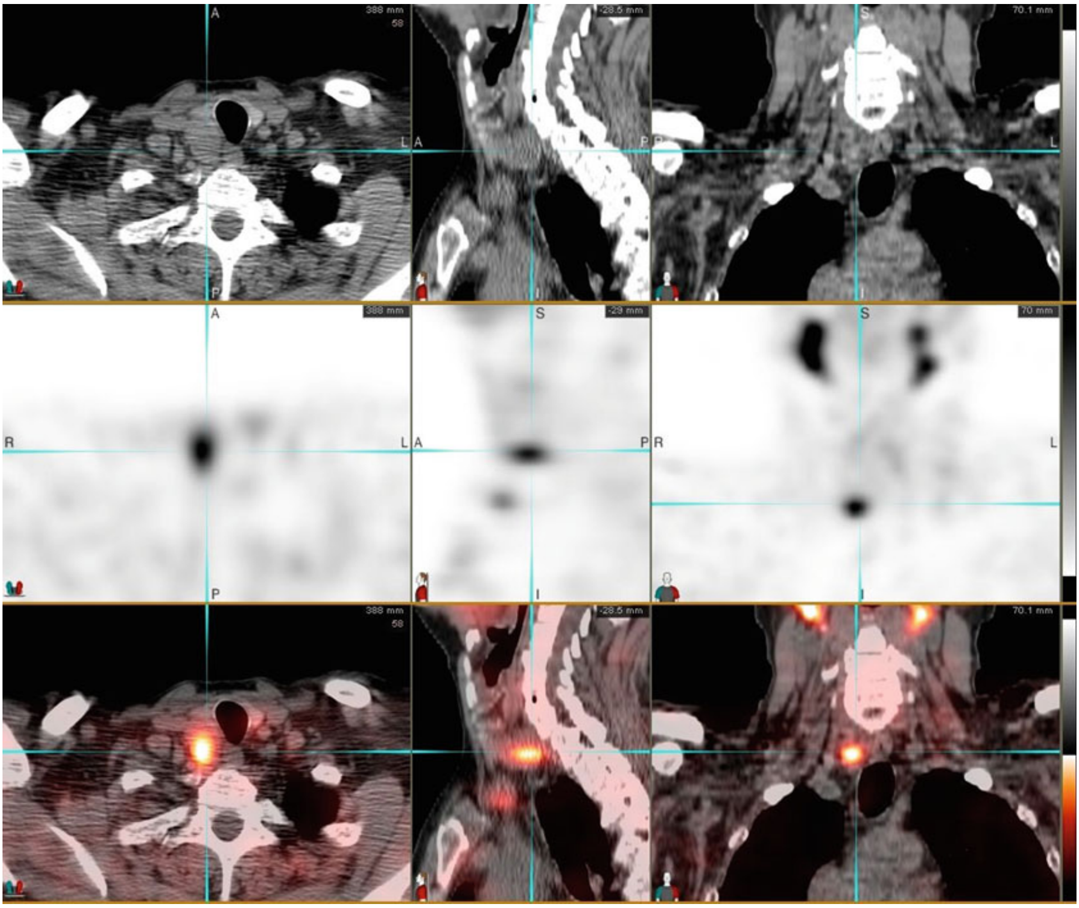

Fig. 14.7 SPECT/CT sestamibi fusion scans combine the advantages of cross-sectional imaging by CT with the functional imaging of sestamibi scintigraphy to yield a precise anatomic map such as seen for this right inferior parathyroid adenoma

Computed Tomography

Computed tomography (CT) is a second-line noninvasive imaging modality that is typically used to localize elusive parathyroid disease. Although not as sensitive as ultrasound or sestamibi scans, this imaging modality is useful for identifying ectopic disease (Fig. 14.8). It is available for use in most medical centers and can be used for guiding FNA biopsy of a lesion. In addition, it is less operator dependent than ultrasound or sestamibi imaging, and the images are easily stored in most databases.

The disadvantages of CT include its cost, exposure of the patient to radiation, and necessity for intravenous contrast. In addition, false positives

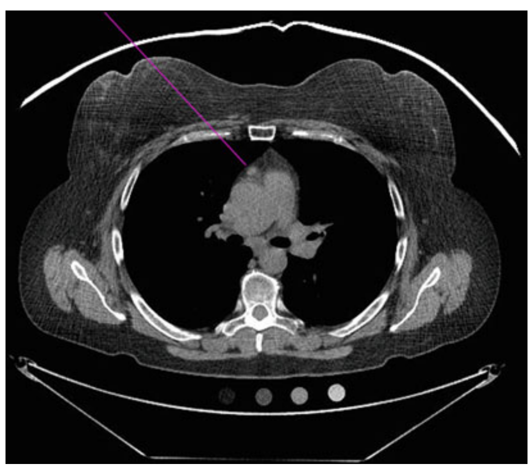

Fig. 14.8 CT can be useful for identifying ectopic disease, such as the mediastinal parathyroid adenoma located anterior to the ascending aorta in this patient (*line*)

are not uncommon, with lymph nodes most commonly mistaken for parathyroid adenomas. False negatives also result from parathyroid lesions being mistaken for lymph nodes.

The four-dimensional CT (4D-CT) imaging of the neck and upper mediastinum takes advantage of precise timing of contrast perfusion coordinated with acquisition of computed tomography data to identify the adenoma. It yields 3D multiphasic images, combined with the fourth or time dimension, to result in images at specified moments precontrast, during infusion, and 30 s after infusion. This imaging modality reveals both the anatomic location and the physiology of the lesion, by evaluating the perfusion characteristics. Parathyroid adenomas are characterized by rapid uptake of contrast with early washout of contrast. Lymph nodes are characterized by slow uptake of contrast with slow release. Thus, on the contrast-enhanced CT, a parathyroid adenoma will typically enhance earlier and more briefly than lymph nodes.

The 4D-CT has been shown in some centers to be more sensitive than ultrasound or sestamibi scan alone for precise localization of hyperfunctioning parathyroid glands, with a lateralization accuracy of 93 % and localization accuracy of 86 %. It has also been shown to be useful in localizing adenomas in the reoperative setting. The disadvantages of using this imaging modality are its cost, exposure of the patient to radiation, the necessity for contrast, and limited availability of this type of study, as compared to other imaging modalities.

MRI

The use of MRI for identification of parathyroid adenomas is mainly reserved for patients with nonlocalizing sestamibi and ultrasound studies and for previously operated patients with persistent hyperparathyroidism. MRI is also very useful for identifying ectopic disease, especially in the mediastinum (Fig. 14.9), and in cases when findings on nuclear medicine imaging and on ultrasound are discordant. Its use is limited due to its increased cost and need for expertise in interpreting the images.

On MRI, normal parathyroid glands are not seen. Adenomas are identified as soft tissue masses and are isointense to hyperintense as compared to thyroid tissue on T2-weighted images. They are isointense to hypointense on T1-weighted images as compared to thyroid tissue (Fig. 14.10). Parathyroid adenomas often enhance avidly with gadolinium on T1-weighted images. Dynamic or 4D-MRI can be performed in a manner similar to 4D-CT described above, where early uptake and subsequent washout of gadolinium from parathyroid adenomas can be detected if the scanning is timed carefully with the infusion of the contrast agent. Lymph nodes, which have similar signal intensities, can be mistaken for parathyroid adenomas on standard (nondynamic) MRI.

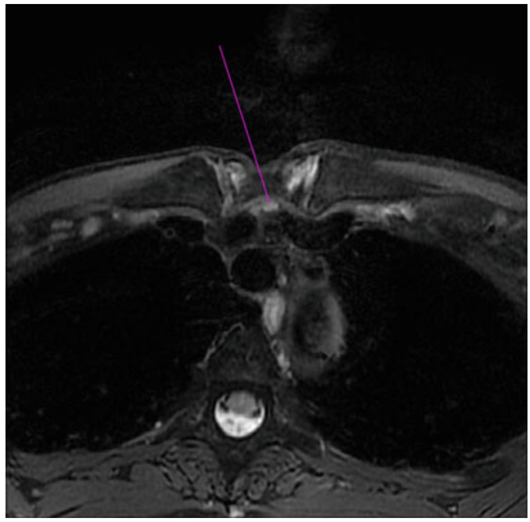

Fig. 14.9 MRI in a previously operated patient with persistent hyperparathyroidism, demonstrating ectopic disease in the retrosternal superior mediastinum (*line*)

PET/CT Scan

Like sestamibi scanning, PET/CT scanning is a functional imaging study that takes advantage of the hypermetabolic behavior of lesions, including parathyroid glands, and displays differential tracer retention and positron emission pictorially. Whereas there are case reports of the more commonly used fluorodeoxyglucose (FDG) revealing parathyroid lesions on PET scanning, more recent and larger series have described C-11 methionine (MET-PET) as highly accurate at localizing parathyroid lesions. There is limited experience to date with this type of scan, and it is significantly more costly than the alternative imaging studies.

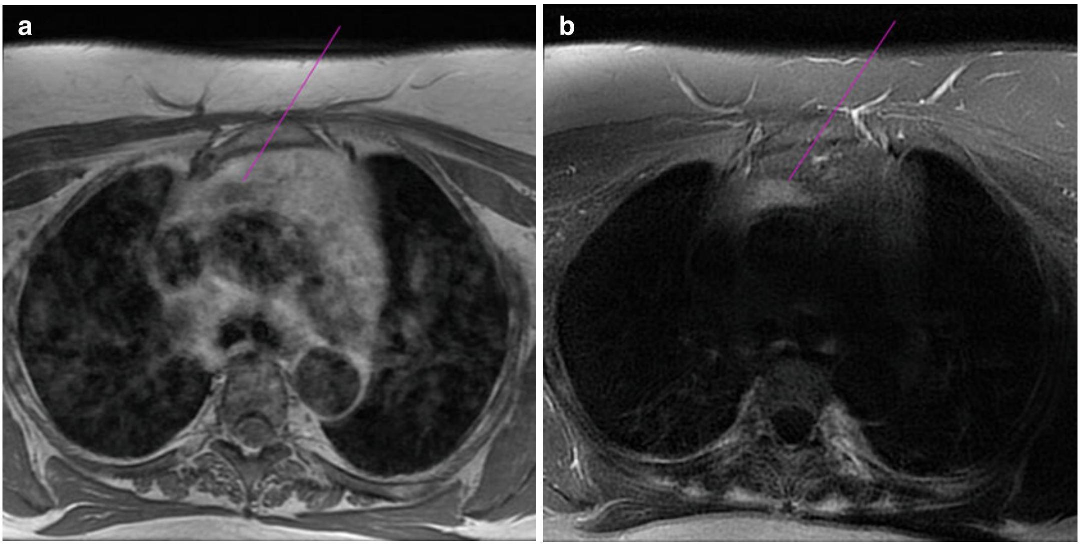

Fig. 14.10 On MRI, adenomas can be hypointense on T1-weighted images (**a**) and hyperintense on T2-weighted images (**b**), as seen in this example of a mediastinal parathyroid adenoma (*lines*)

Fine-Needle Aspiration

Fine-needle aspiration (FNA) can be guided by either ultrasound or CT (Fig. 14.11). It is very specific in distinguishing parathyroid tissue from nonparathyroid tissue, although distinction of parathyroid versus thyroid cytology can be challenging. When combined with testing for intact parathyroid hormone (PTH), FNA achieves a specificity of 95–100 %. The needle used for FNA is rinsed with saline and tested for intact PTH by the same chemical assay that is used for serum PTH. However, FNA is invasive and can lead to an inflammatory response at the biopsy site, which can have consequences for the surgical resection. There has been report of implantation of parathyroid tumor cells along the needle track, although separate literature attests to the safety of parathyroid FNA. Overall, FNA should only be considered in challenging cases.

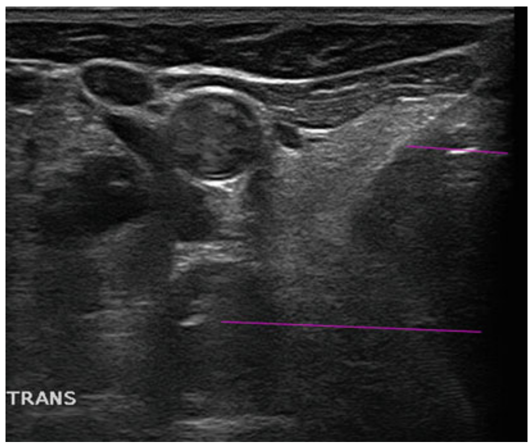

Fig. 14.11 Ultrasound-guided FNA of a deep parathyroid candidate lesion in a patient with prior unsuccessful exploration. The needle is rinsed with saline and analyzed for PTH (lines = needle tip and needle)

Selective Venous Sampling

Venous sampling for parathyroid hormone can also be used to determine the general location of a parathyroid adenoma. It is technically very challenging and success of the study is operator dependent. Blood samples are obtained from multiple bilateral sites within the venous circulation superior and inferior to the potential sites of a parathyroid tumor, and gradients in PTH are measured. It is mainly useful in complex revision operations when two or more preoperative imaging modalities have been inconclusive or unhelpful. Selective venous sampling has been shown to have a success rate of 86 % in identifying the location of a parathyroid adenoma in such patients. The use of the study is limited by its invasive nature, increased cost, need for interventional radiologist expertise, and exposure of the patient to radiation. However, recent reports of ultrasound-guided internal jugular vein sampling, even in the office setting, have renewed interest in the concept and use of PTH gradient testing for difficult cases, without the previously associated risks.

Parathyroid Arteriography

Although rarely used today due to its increased risks, this test is both specific and sensitive. Parathyroid adenomas are highly vascular, and thus angiographic imaging modalities may be utilized. Adenomas are identified as round- or oval-shaped lesions that display a vascular blush with angiographic injection. Success of the procedure is based on skill of the performing interventional radiologist. It is often utilized when other noninvasive imaging studies are equivocal. The risks of this procedure are devastating and include spinal cord injury and embolic infarction. More recently, noninvasive magnetic resonance angiography has been successfully used in the reoperative neck.

Conclusion

Accurate preoperative imaging methods have revolutionized the surgical approach to hyperparathyroidism and led to a trend toward minimally invasive, targeted procedures. While regional as well as individual surgeon preferences differ, the spectrum of choices available means that most parathyroid lesions can be localized prior to surgery. The nuclear medicine sestamibi scan, with or without SPECT/CT, is considered by most to be the optimal initial exam for localization of parathyroid adenomas. It is useful to compare this functional type of study to an anatomic study, such as an ultrasound, CT, or MRI, for precise three-dimensional targeting. Ultrasound, and increasingly surgeon-performed ultrasound, is cost effective, convenient, and highly reliable for localizing perithyroidal adenomas but has a limited role for adenomas in the mediastinum. The more expensive noninvasive imaging modalities, CT and MRI, are usually reserved for cases where nuclear medicine imaging and ultrasound are discordant or unrevealing or for revision cases. The use of invasive imaging modalities, namely, FNA, angiography, and venous sampling, is limited to cases where the noninvasive imaging modalities are nonlocalizing.

Recommended Reading

Abboud B, Sleilaty G, Rabaa L, Daher R, Abou Zeid H, Jabbour H, et al. Ultrasonography: highly accuracy technique for preoperative localization of parathyroid adenoma. Laryngoscope. 2008;118(9):1574–8.

Abraham D, Sharma PK, Bentz J, Gault PM, Neumayer L, McClain DA. Utility of ultrasound-guided fine-needle aspiration of parathyroid adenomas for localization before minimally invasive parathyroidectomy. Endocr Pract. 2007;13(4):333–7.

Adewole AD, Roman SA, Kraev AI, Kim AW. A fluorodeoxyglucose avid mediastinal parathyroid adenoma masquerading as metastatic bladder cancer. Interact Cardiovasc Thorac Surg. 2012;15(3):514–5.

Akerström G, Malmaeus J, Bergström R. Surgical anatomy of human parathyroid glands. Surgery. 1986;95(1):14–21.

Aschenbach R, Tuda S, Lamster E, Meyer A, Roediger H, Stier A, et al. Dynamic magnetic resonance angiography for localization of hyperfunctioning parathyroid glands in the reoperative neck. Eur J Radiol. 2012;81(11):3371–7.

Bancos I, Grant CS, Nadeem S. Risks and benefits of parathyroid fine-needle aspiration with parathyroid hormone washout. Endocr Pract. 2012;18(4):441–9.

Berber E, Parikh RT, Ballem N, Garner CN, Milas M, Siperstein AE. Factors contributing to negative parathyroid localization: an analysis of 1000 patients. Surgery. 2008;144(1):74–9.

Carneiro-Pla D. Effectiveness of "office"-based, ultrasound-guided differential jugular venous sampling (DJVS) of parathormone in patients with primary hyperparathyroidism. Surgery. 2009;146(6):1014–20.

Clayman GL. Targeted parathyroidectomy. In: Cohen JI, Clayman GL, editors. Atlas of head & neck surgery. Philadelphia: Elsevier; 2011. Print.

Elaraj DM, Sippel RS, Lindsay S, Sansano I, Duh QY, Clark OH, et al. Are additional localization studies and referral indicated for patients with primary hyperparathyroidism who have negative sestamibi scan results? Arch Surg. 2010;145(6):578–81.

Gayed IW, Kim EE, Broussard WF, Evans D, Lee J, Broemeling LD, et al. The value of 99mTc-sestamibi SPECT/CT over conventional SPECT in the evaluation of parathyroid adenomas or hyperplasia. J Nucl Med. 2005;46(2):248–52.

Gurney TA, Orloff LA. Otolaryngologist-head and neck surgeon-performed ultrasonography for parathyroid adenoma localization. Laryngoscope. 2008;118(2):243–6.

Haber RS, Kim CK, Inabnet WB. Ultrasonography for preoperative localization of enlarged parathyroid glands in primary hyperparathyroidism: comparison with (99m) technetium sestamibi scintigraphy. Clin Endocrinol. 2002;57(2):241–9.

Hunter GJ, Schellingerhout D, Vu TH, Perrier ND, Hamberg LM. Accuracy of four-dimensional CT for the localization of abnormal parathyroid glands in patients with primary hyperparathyroidism. Radiology. 2012;264(3):789–95.

Johnson NA, Tublin ME, Ogilvie JB. Parathyroid imaging: technique and role in the preoperative evaluation of primary hyperparathyroidism. Am J Roentgenol. 2007;188:1706–15.

Jones JJ, Brunaud L, Dowd C, Duh QY, Morita E, Clark OH. Accuracy of selective venous sampling for intact parathyroid hormone in difficult patients with recurrent or persistent hyperparathyroidism. Surgery. 2002;132(6):944–51.

Kandil E, Tufaro AP, Carson KA, Lin F, Somervell H, Farrag T, et al. Correlation of plasma 25-hydroxyvitamin D levels with severity of primary hyperparathyroidism and likelihood of parathyroid adenoma localization on sestamibi scan. Arch Otolaryngol Head Neck Surg. 2008;134:1071–5.

Kendrick ML, Charboneau JW, Curlee KJ, van Heerden JA, Farley DR. Risk of parathyromatosis after fine-needle aspiration. Am Surg. 2001;67(3):290–3.

Lau JH, Drake W, Matson M. The current role of venous sampling in the localization of endocrine disease. Cardiovasc Intervent Radiol. 2007;30(4):555–70.

Mahajan A, Starker LF, Ghita M, Udelsman R, Brink JA, Carling T. Parathyroid four-dimensional computed tomography: evaluation of radiation dose exposure during preoperative localization of parathyroid tumors in primary hyperparathyroidism. World J Surg. 2012;36(6):1335–9.

Mihai R, Gleeson F, Buley ID, Roskell DE, Sadler GP. Negative imaging studies for primary hyperparathyroidism are unavoidable: correlation of sestamibi and high-resolution ultrasound scanning with histological analysis in 150 patients. World J Surg. 2006;30(5):697–704.

Miller DL. Endocrine angiography and venous sampling. Radiol Clin North Am. 1993;31(5):1051–67.

Mitmaker J, Grogan RH, Duh QY. Guide to preoperative parathyroid localization testing. In: Randolph G, editor. Surgery of the thyroid and parathyroid glands. 2nd ed. Philadelphia: Elsevier; 2013.

Mortenson MM, Evans DB, Lee JE, Hunter GJ, Shellingerhout D, Vu T, et al. Parathyroid exploration in the reoperative neck: improved preoperative localization with 4D-computed tomography. J Am Coll Surg. 2008;206(5):888–95.

Nichols KJ, Tomas MB, Tronco GG, Rini JN, Kunjummen BD, Heller KS, et al. Preoperative parathyroid scintigraphic lesion localization: accuracy of various types of readings. Radiology. 2008;248(1):221–32.

Pata G, Casella C, Besuzio S, Mittempergher F, Salerni B. Clinical appraisal of 99m technetium-sestamibi SPECT/CT compared to conventional SPECT in patients with primary hyperparathyroidism and concomitant nodular goiter. Thyroid. 2010;20(10):1121–7.

Rodgers SE, Hunter GJ, Hamberg LM, Schellingerhout D, Doherty DB, Ayers GD, et al. Improved preoperative planning for directed parathyroidectomy with 4-dimensional computed tomography. Surgery. 2006;140(6):932–40.

Shafiei B, Hoseinzadeh S, Fotouhi F, Malek H, Azizi F, Jahed A, et al. Preoperative 99mTc-sestamibi scintigraphy in patients with primary hyperparathyroidism and concomitant nodular goiter: comparison of SPECT-CT, SPECT, and planar imaging. Nucl Med Commun. 2012;33(10):1070–6.

Shah S, Win Z, Al-Nahhas A. Multimodality imaging of the parathyroid glands in primary hyperparathyroidism. Minerva Endocrinol. 2008;33(3):193–202.

Siperstein A, Berber E, Barbosa GF, Tsinberg M, Greene AB, Mitchell J, et al. Predicting the success of limited exploration for primary hyperparathyroidism using ultrasound, sestamibi, and intraoperative parathyroid hormone: analysis of 1158 cases. Ann Surg. 2008;248(3):420–8.

Steward DL, Danielson GP, Afman CE. Parathyroid adenoma localization: surgeon-performed ultrasound versus sestamibi. Laryngoscope. 2009;116(8):1380–4.

Thomas DL, Bartel T, Menda Y, Howe J, Graham MM, Juweid ME. Single photon emission computed tomography (SPECT) should be routinely performed for the detection of parathyroid abnormalities utilizing technetium-99m sestamibi parathyroid scintigraphy. Clin Nucl Med. 2009;34(10):651–5.

Udelsman R, Pasieka JL, Sturgeon C, Young JE, Clark OH. Surgery for asymptomatic primary hyperparathyroidism: proceedings of the third international workshop. J Clin Endocrinol Metab. 2009;94(2):366–72.

Udelsman R, Lin Z, Donovan P. The superiority of minimally invasive parathyroidectomy based on 1650 consecutive patients with primary hyperparathyroidism. Ann Surg. 2011;253(3):585–91.

Untch BR, Adam MA, Scheri RP, Bennett KM, Dixit D, Webb C, et al. Surgeon-performed ultrasound is superior to 99Tc-sestamibi scanning to localize parathyroid adenomas in patients with primary hyperparathyroidism: results in 516 patients over 10 years. J Am Coll Surg. 2011;212(4):522–9.

Weber T, Maier-Funk C, Ohlhauser D, Hillenbrand A, Cammerer G, Barth TF, et al. Accurate preoperative localization of parathyroid adenomas with C-11 methionine PET/CT. Ann Surg. 2013;257:1124–8.

Yousem DM, Scheff AM. Thyroid and parathyroid gland pathology. Role of imaging. Otolaryngol Clin N Am. 1995;28(3):621–49.