American College of Radiology
ACR Appropriateness Criteria®
Parathyroid Adenoma

Variant: 1 Adult or child. Primary hyperparathyroidism. Initial imaging.

Procedure	Appropriateness Category	Relative Radiation Level
US parathyroid	Usually Appropriate	O
Sestamibi scan and pertechnetate thyroid scan	Usually Appropriate	
CT neck without and with IV contrast	Usually Appropriate	☢☢☢
Sestamibi dual-phase scan neck	Usually Appropriate	☢☢☢
Sestamibi dual-phase scan with SPECT or SPECT/CT neck	Usually Appropriate	☢☢☢
Sestamibi scan and I-123 thyroid scan	Usually Appropriate	☢☢☢
Sestamibi scan and I-123 thyroid scan with SPECT or SPECT/CT neck	Usually Appropriate	☢☢☢
Sestamibi scan and pertechnetate thyroid scan with SPECT or SPECT/CT neck	Usually Appropriate	☢☢☢
MRI neck with IV contrast	May Be Appropriate	O
MRI neck without and with IV contrast	May Be Appropriate	O
CT neck with IV contrast	May Be Appropriate	☢☢☢
Venous sampling parathyroid	Usually Not Appropriate	Varies
MRI neck without IV contrast	Usually Not Appropriate	O
CT neck without IV contrast	Usually Not Appropriate	☢☢☢

Variant: 2 Adult or child. Primary hyperparathyroidism, recurrent or persistent after parathyroid surgery. Initial imaging.

Procedure	Appropriateness Category	Relative Radiation Level
US parathyroid	Usually Appropriate	O
Sestamibi scan and pertechnetate thyroid scan	Usually Appropriate	
CT neck without and with IV contrast	Usually Appropriate	☢☢☢
Sestamibi dual-phase scan neck	Usually Appropriate	☢☢☢
Sestamibi dual-phase scan with SPECT or SPECT/CT neck	Usually Appropriate	☢☢☢
Sestamibi scan and I-123 thyroid scan	Usually Appropriate	☢☢☢
Sestamibi scan and I-123 thyroid scan with SPECT or SPECT/CT neck	Usually Appropriate	☢☢☢
Sestamibi scan and pertechnetate thyroid scan with SPECT or SPECT/CT neck	Usually Appropriate	☢☢☢
Venous sampling parathyroid	May Be Appropriate	Varies
MRI neck with IV contrast	May Be Appropriate	O
MRI neck without and with IV contrast	May Be Appropriate	O
CT neck with IV contrast	May Be Appropriate	☢☢☢
MRI neck without IV contrast	Usually Not Appropriate	O
CT neck without IV contrast	Usually Not Appropriate	☢☢☢

Variant: 3 Adult or child. Secondary hyperparathyroidism. Initial imaging.

Procedure	Appropriateness Category	Relative Radiation

		Level
US parathyroid	Usually Appropriate	O
CT neck without and with IV contrast	Usually Appropriate	☢☢☢
Sestamibi dual-phase scan neck	Usually Appropriate	☢☢☢
Sestamibi dual-phase scan with SPECT or SPECT/CT neck	Usually Appropriate	☢☢☢
Sestamibi scan and I-123 thyroid scan with SPECT or SPECT/CT neck	Usually Appropriate	☢☢☢
Sestamibi scan and pertechnetate thyroid scan with SPECT or SPECT/CT neck	Usually Appropriate	☢☢☢
Sestamibi scan and pertechnetate thyroid scan	May Be Appropriate (Disagreement)	
MRI neck with IV contrast	May Be Appropriate	O
MRI neck without and with IV contrast	May Be Appropriate	O
CT neck with IV contrast	May Be Appropriate	☢☢☢
Sestamibi scan and I-123 thyroid scan	May Be Appropriate (Disagreement)	☢☢☢
Venous sampling parathyroid	Usually Not Appropriate	Varies
MRI neck without IV contrast	Usually Not Appropriate	O
CT neck without IV contrast	Usually Not Appropriate	☢☢☢

Variant: 4 Adult or child. Tertiary hyperparathyroidism. Initial imaging.

Procedure	Appropriateness Category	Relative Radiation Level
US parathyroid	Usually Appropriate	O
Sestamibi scan and pertechnetate thyroid scan	Usually Appropriate	
CT neck without and with IV contrast	Usually Appropriate	☢☢☢
Sestamibi dual-phase scan neck	Usually Appropriate	☢☢☢
Sestamibi dual-phase scan with SPECT or SPECT/CT neck	Usually Appropriate	☢☢☢
Sestamibi scan and I-123 thyroid scan with SPECT or SPECT/CT neck	Usually Appropriate	☢☢☢
Sestamibi scan and pertechnetate thyroid scan with SPECT or SPECT/CT neck	Usually Appropriate	☢☢☢
MRI neck with IV contrast	May Be Appropriate	O
MRI neck without and with IV contrast	May Be Appropriate	O
CT neck with IV contrast	May Be Appropriate	☢☢☢
Sestamibi scan and I-123 thyroid scan	May Be Appropriate (Disagreement)	☢☢☢
Venous sampling parathyroid	Usually Not Appropriate	Varies
MRI neck without IV contrast	Usually Not Appropriate	O
CT neck without IV contrast	Usually Not Appropriate	☢☢☢

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Summary of Literature Review

Introduction/Background

Hyperparathyroidism is defined as excessive parathyroid hormone (PTH) production. The most common form, primary hyperparathyroidism (PHPT), occurs when ≥1 parathyroid glands autonomously overproduce PTH, typically resulting in hypercalcemia [1]. PHPT is diagnosed by biochemical testing, specifically serum calcium and serum PTH. Usually due to a single parathyroid adenoma (80%), PHPT can also occur from multiple adenomas, parathyroid hyperplasia, or, rarely, parathyroid carcinoma (<1%). Multigland disease (MGD), defined as multiple adenomas or multiple gland hyperplasia, affects approximately 15% to 20% of patients with PHPT [1,2]. PHPT is more common in women, with an incidence of 66 per 100,000 person-years, and 25 per 100,000 person-years in men; the prevalence appears to be increasing significantly [3]. Most cases are sporadic, although hereditary causes exist, including multiple endocrine neoplasia types 1 and 2A as well as familial hyperparathyroidism. In countries where biochemical screening is routine, such as the United States, Canada, and most of Europe, PHPT predominately presents as an asymptomatic disorder. Conversely, in countries where routine biochemical screening is not commonplace, such as China or India, PHPT predominately presents with symptoms related to target organ involvement including: bone demineralization, fractures, nephrolithiasis, nephrocalcinosis, muscle weakness, or neurocognitive disorders [1]. Treatment of PHPT is surgical excision of the abnormally functioning parathyroid tissue and is typically indicated even when asymptomatic, given potential negative effects of long-term hypercalcemia [1,2].

There are 2 accepted curative operative strategies for PHPT: bilateral neck exploration (BNE) and minimally invasive parathyroidectomy (MIP). BNE refers to a bilateral operation in which all parathyroid glands are identified and examined by the surgeon, who resections the diseased glands. MIP is defined variably in the literature—for this document—MIP refers to a unilateral operation utilizing limited dissection for targeted removal of only the affected gland. MIP is therefore less invasive than BNE. BNE has traditionally been the standard surgical method of parathyroidectomy and remains the necessary method in cases of discordant or nonlocalizing preoperative imaging or when there is high suspicion for MGD [2]. However, because most patients with PHPT have a single adenoma [2], directed MIP is often performed as it conveys the benefits of shorter operating times, faster recovery, and decreased perioperative costs [4-8]. MIP requires confident and precise preoperative localization of a single parathyroid adenoma to guide the surgical approach; intraoperative PTH monitoring is used to confirm removal of the hyperfunctioning gland [2,9]. Therefore, the role of imaging in PHPT is to localize the abnormally functioning gland or glands with high accuracy and high confidence to facilitate targeted curative surgery. Importantly, imaging has no utility in confirming or excluding the diagnosis of PHPT [2,8].

Persistent PHPT is defined as failure to achieve normocalcemia within 6 months of initial parathyroidectomy, whereas recurrent PHPT is defined as hypercalcemia occurring after a normocalcemic interval of 6 months or more after parathyroidectomy [2,10]. Parathyroid reoperations are surgically challenging, with lower cure rates than first-time surgery and higher complication rates. As such, recent international guidelines state that preoperative imaging is essential in the reoperative setting to localize a target parathyroid lesion (or lesions) and to identify postoperative changes from previous parathyroid explorations that can impact a subsequent

surgery [10].

Secondary hyperparathyroidism (SHPT) is a failure of calcium homeostasis whereby increased PTH production in response to hypocalcemia (and/or hyperphosphatemia) is unable to correct plasma calcium because of organ failure or reduced calcium availability. This is most commonly due to chronic kidney disease but can also be a result of malabsorption or vitamin D deficiency, among other causes [11]. Rarely, tertiary hyperparathyroidism (THPT) can occur in patients with longstanding SHPT and is characterized by a lack of PTH suppression despite rising serum calcium levels, manifesting as hypercalcemic hyperparathyroidism. This is most commonly encountered following kidney transplantation in patients with longstanding chronic kidney disease [11]. Surgical excision is recommended for medically refractory cases of SHPT and THPT. As these are typically disorders of MGD (ie, parathyroid hyperplasia), the goal of imaging is to identify all eutopic and potential ectopic or supernumerary glands in an attempt to guide the surgical approach [10,12-14]. There is no universally accepted algorithm for parathyroid imaging. As detailed in the following variants, there is much variability in the reported sensitivities for imaging modalities, with no single technique shown to be clearly superior in localizing parathyroid lesions in all patients. The selection of an initial imaging study should be made with consideration for surgeon and radiologist preference, regional expertise, and characteristics unique to each patient's presentation (eg, suspicion for MGD, underlying hereditary cause, concomitant thyroid disease, etc). Multiple imaging modalities may be utilized in combination during the initial imaging evaluation in an attempt to maximize the accuracy and confidence of parathyroid localization via concordant imaging results [2,8,10,15]. This is supported by various studies in the literature showing improved sensitivity and positive predictive value (PPV) in parathyroid lesion localization with a combination of examinations over each examination in isolation [12,16-25].

Initial Imaging Definition

Initial imaging is defined as imaging at the beginning of the care episode for the medical condition defined by the variant. More than one procedure can be considered usually appropriate in the initial imaging evaluation when:

- There are procedures that are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care)

OR

- There are complementary procedures (ie, more than one procedure is ordered as a set or simultaneously wherein each procedure provides unique clinical information to effectively manage the patient's care).

Special Imaging Considerations

For the purposes of parathyroid imaging, CT neck without and with intravenous (IV) contrast is understood to represent a "4-D parathyroid CT." Originally described in 2006 [26], this multiphase technique leverages the unique perfusion characteristics of parathyroid adenomas to differentiate them from mimics such as exophytic thyroid nodules and lymph nodes. Variations on the original 4-phase 4-D parathyroid CT technique have since been described, including 2- [27] and 3-phase [28-33] protocols. The optimal number of postcontrast phases is undetermined; however, the most

commonly performed method consists of 3 phases: noncontrast, arterial, and venous [34].

Discussion of Procedures by Variant

Variant 1: Adult or child. Primary hyperparathyroidism. Initial imaging.

All patients undergoing imaging in the setting of PHPT should have biochemically proven disease, as imaging has no role in confirming or excluding the diagnosis [2]. As such, assessing the imaging test specificity and negative predictive value is not clinically relevant. Rather, the role of initial imaging in PHPT is to aid in selecting appropriate patients for MIP by accurately identifying and localizing a single parathyroid adenoma; accordingly, these criteria focus on imaging test sensitivity and PPV. Patients with negative or inconclusive imaging results typically remain surgical candidates but will likely require BNE; inconclusive findings on imaging should not preclude surgical referral [2].

Multiple imaging modalities may be utilized in combination during the initial imaging evaluation of PHPT in an attempt to maximize the accuracy and confidence of parathyroid localization via concordant imaging results [2,8,15]. This is supported by multiple studies in the literature showing improved sensitivity and PPV in parathyroid lesion localization with a combination of examinations over each examination in isolation [16-23,25].

Variant 1: Adult or child. Primary hyperparathyroidism. Initial imaging.
A. CT neck

Neck CT for preoperative localization of PHPT is most commonly performed without and with IV contrast (4-D parathyroid CT) [34]. As such, most published data relate to the performance of CT neck without and with IV contrast; however, there are also some data on the performance of CT neck with IV contrast. There is no relevant literature regarding the use of CT neck without IV contrast in the evaluation of PHPT.

As the initial imaging study, retrospective studies report the overall sensitivity of CT neck without and with IV contrast to range between 62% and 88% [35,36] and the overall PPV to range between 84% and 90% [32,37]. The largest retrospective study (400 patients) reports an overall sensitivity of 79% and PPV of 90% [32]. For single-gland disease, reported sensitivities and PPVs range from 92% to 94% [30,38] and 88% to 92% [38,39], respectively. For MGD, reported sensitivities and PPVs range from 43% to 67% [39,40] and 89% to 100%, respectively [32,39].

A data-driven rationale for the noncontrast CT phase has been provided (eg, differentiation of parathyroid from thyroid tissue): 22% of parathyroid lesions have an enhancement pattern similar to thyroid on arterial and venous phases and therefore may be missed if the noncontrast phase were excluded [30]. However, a few retrospective reports suggest that eliminating the noncontrast CT phase may not adversely affect test performance [41-43]. The largest retrospective study (278 patients) of CT neck with IV contrast (without the noncontrast phase) reports sensitivity of 55% and PPV of 57% among patients with single-gland disease, and sensitivity of 23% and PPV of 19% among patients with MGD [44].

Several studies have directly compared the performance of neck CT without and with IV contrast to ultrasound (US) and to nuclear medicine scans within the same patient population. Most of these studies found the performance of neck CT without and with IV contrast to be superior [29,31,38,40]; however, a prospective study of 91 patients found neck CT without and with IV

contrast (58% sensitivity, 88% PPV) to be inferior to dual isotope (sestamibi and I-123) pinhole subtraction scintigraphy (93% sensitivity, 98% PPV) [45].

Variant 1: Adult or child. Primary hyperparathyroidism. Initial imaging.
B. MRI neck

MRI neck is an emerging technique for PHPT preoperative localization and may be performed without IV contrast, with IV contrast, or without and with IV contrast. Most studies evaluating the performance of MRI neck for preoperative localization in the setting of PHPT are retrospective and include fewer than 50 patients.

As the initial imaging study, the sensitivity of MRI neck without and with IV contrast performed at 1.5T has been reported to be between 64% and 79% [46-48]. In 2 prospective studies performed at 3.0T, the sensitivity of MRI neck without and with IV contrast ranged between 64% and 98%, and the PPV ranged between 67% and 95% [49,50]. A third prospective study of MRI without and with IV contrast performed at 3.0T reported accurate localization of parathyroid adenomas in 92% (34/37) of patients with single-gland disease and 74% (35/47) of patients with MGD [51]. For MRI without IV contrast, the reported sensitivity was 67% at 1.5T [52]. There is no relevant literature regarding the use of 3.0T MRI without IV contrast in the initial imaging evaluation of PHPT.

Variant 1: Adult or child. Primary hyperparathyroidism. Initial imaging.
C. Sestamibi dual-phase scan neck

Dual-phase Tc-99m sestamibi planar parathyroid scintigraphy is an accepted and traditionally widely utilized method for parathyroid adenoma localization in PHPT. The sensitivity of this method (typically reported as localization to the correct quadrant or to an ectopic location) varies widely in the literature, ranging from 41% to 96% [45,52-63]. A larger retrospective study of 180 patients reported a sensitivity of 79% [58]. A systematic review of 11 studies reported a pooled sensitivity of 76% [17]. Some variability in these results may arise from varied technical parameters of these scans (eg, timing of early and delayed scans, use of pinhole versus parallel collimators, addition of oblique acquisitions, etc).

There is no clear consensus regarding the superiority between sestamibi dual-phase and dual-tracer subtraction planar imaging. One recent study of 63 patients showed greater sensitivity with dual-phase sestamibi (79%) over both dual-tracer (sestamibi and pertechnetate) (69%) and a combined dual-tracer/dual-phase technique (65%) [59]. However, other studies report similar or improved sensitivity of dual-tracer methods (either pertechnetate or I-123, plus sestamibi) over dual-phase sestamibi when utilizing a planar technique [45,54,64,65]. There is a growing consensus that the addition of single-photon emission CT (SPECT) without or with a coregistered CT (SPECT/CT) improves localization of parathyroid adenomas over a planar dual-phase sestamibi method [59,61,62].

The sensitivity of sestamibi imaging is decreased in the setting of MGD [55,58], concomitant nodular thyroid disease [56,66], small adenomas [53], and mild hypercalcemia [58].

Literature regarding the pediatric population is limited. A retrospective review of 29 patients reported that sestamibi was useful only in older children with a single adenoma in the setting of sporadic PHPT, and added minimal additional information compared with US, with otherwise no utility for sestamibi in neonates or familial PHPT [67].

Variant 1: Adult or child. Primary hyperparathyroidism. Initial imaging.

D. Sestamibi dual-phase scan with SPECT or SPECT/CT neck

The addition of SPECT or SPECT/CT to a dual-phase sestamibi scan is more commonly utilized than planar imaging alone. Although there are a number of variations in the timing of the SPECT or SPECT/CT acquisition (ie, early, delayed, or both), it is generally accepted that the improved contrast resolution of SPECT or SPECT/CT over planar imaging provides more precise anatomic localization of parathyroid adenomas [68,69].

Reported sensitivities of sestamibi dual-phase scan with SPECT or SPECT/CT range from 67% to 86%.

- Thomas et al: In a study of patients with parathyroid adenomas and parathyroid hyperplasia, direct comparison of dual-phase sestamibi planar imaging to dual-phase sestamibi with SPECT showed improved sensitivities from 42% to 67%, respectively; this includes detection of parathyroid hyperplasia by SPECT, which was missed by planar imaging [61].
- Cheung et al: A meta-analysis of 7 studies found a pooled sensitivity of 79% and a pooled PPV of 91% for dual-phase sestamibi with SPECT [70].
- Wong et al: A meta-analysis of 24 studies found a pooled sensitivity of 86% for dual-phase sestamibi with SPECT/CT compared with 74% for sestamibi with SPECT and 70% for sestamibi planar alone [62].
- Yeh et al: A study of 400 patients reported a sensitivity of 58% and PPV of 96% for sestamibi with SPECT/CT. A combined method of sestamibi with SPECT/CT plus 4-D parathyroid CT yielded a sensitivity of 80%, which was not substantially different than 4-D parathyroid CT alone at 79% [32].

The sensitivity of dual-phase sestamibi with SPECT or SPECT/CT is decreased by MGD, uptake masked by retained radionuclide in adjacent thyroid or submandibular gland tissue, and smaller size of the adenoma (within these subsets, sensitivity ranges from 24% to 66%) [71-73].

Variant 1: Adult or child. Primary hyperparathyroidism. Initial imaging.
E. Sestamibi scan and I-123 thyroid scan

Subtraction scintigraphy of parathyroid glands using a combination of sestamibi and I-123 sodium iodide is a commonly utilized alternative or adjunct to the dual-phase sestamibi technique. The 2009 European Association of Nuclear Medicine parathyroid guidelines expressed a preference for the dual-tracer sestamibi and I-123 technique, citing improved sensitivity for MGD and improved likelihood of distinguishing sestamibi-avid thyroid nodules from parathyroid lesions [15]. A major technical advantage of using I-123 for a subtraction technique is that thyroid and parathyroid images can be acquired simultaneously in a dual-energy window.

Reported sensitivity for dual-tracer sestamibi and I-123 subtraction scintigraphy ranges from 75% to 94% [54,74-76], including a retrospective review of 2,681 patients revealing a sensitivity of 87% and PPV of 92% [77]. The latter study showed that negative or inconclusive results had a higher association with MGD and lower serum calcium levels.

There is no clear consensus regarding the superiority between dual-tracer subtraction and sestamibi dual-phase planar imaging. One recent study of 63 patients showed greater sensitivity with dual-phase sestamibi (79%) over both dual-tracer (sestamibi and pertechnetate) (69%) and a combined dual-tracer/dual-phase (65%) technique [59]. However, other studies report similar or improved sensitivity of dual-tracer methods (either pertechnetate or I-123, plus sestamibi) over dual-phase sestamibi when utilizing a planar technique [45,54,64,65].

Variant 1: Adult or child. Primary hyperparathyroidism. Initial imaging.
F. Sestamibi scan and I-123 thyroid scan with SPECT or SPECT/CT neck

Although there are a number of variations in the timing of the SPECT or SPECT/CT acquisition (ie, early, delayed, or both), it is generally accepted that the improved contrast resolution of SPECT or SPECT/CT over planar imaging provides more precise anatomic localization of parathyroid adenomas [68,69]. However, there are conflicting data in the literature as to what extent the addition of SPECT or SPECT/CT changes the sensitivity of the examination. For example, Bhatt et al [74] evaluated a pinhole protocol, SPECT/CT alone, and a combination of pinhole/SPECT/CT, revealing sensitivities of 88%, 69%, and 81%, respectively. Other studies have shown superior performance of the combined sestamibi/I-123 plus SPECT/CT protocol with sensitivities ranging from 86% to 95% and PPV from 86% to 100% [45,75,78,79].

The sensitivity and PPV of a sestamibi/I-123 subtraction technique are least negatively impacted by concomitant thyroid disease when SPECT/CT is included in the protocol [75].

Variant 1: Adult or child. Primary hyperparathyroidism. Initial imaging.
G. Sestamibi scan and pertechnetate thyroid scan

Subtraction scintigraphy of parathyroid glands using a combination of sestamibi and Tc-99m pertechnetate is a commonly utilized alternative or adjunct to the dual-phase sestamibi technique. Unlike the dual-tracer method with I-123, the pertechnetate method requires 2 separate acquisitions, which prolongs the overall examination time. Although techniques based solely on planar imaging have largely been supplanted by methods with SPECT or SPECT/CT, there are some noteworthy applications of a planar sestamibi and pertechnetate subtraction in recent literature with reported sensitivities ranging from 69% to 79% [59,80]. A meta-analysis including 5 studies utilizing a dual-tracer technique reported sensitivities ranging from 47% to 87%; however, it is unclear which studies relied purely on a subtracted dual-tracer (sestamibi and pertechnetate) planar method and which were performed in combination with a dual-phase sestamibi scan [17]. In a study of 116 patients with PHPT, the addition of pertechnetate subtraction to a dual-phase sestamibi scan increased reader confidence in adenoma localization and changed the final interpretation in 15% of patients from the dual-phase study [81].

MGD decreases the sensitivity of the subtraction sestamibi and pertechnetate scan from 71% to 64% [82].

There is no clear consensus regarding the superiority between dual-tracer subtraction and sestamibi dual-phase planar imaging. One recent study of 63 patients showed greater sensitivity with dual-phase sestamibi (79%) over both dual-tracer (sestamibi and pertechnetate) (69%) and a combined dual-tracer/dual-phase technique (65%) [59]. However, other studies report similar or improved sensitivity of dual-tracer methods (either pertechnetate or I-123, plus sestamibi) over dual-phase sestamibi when utilizing a planar technique [45,54,64,65].

Variant 1: Adult or child. Primary hyperparathyroidism. Initial imaging.
H. Sestamibi scan and pertechnetate thyroid scan with SPECT or SPECT/CT neck

Although there are a number of variations in the timing of the SPECT or SPECT/CT acquisition (ie, early, delayed, or both), it is generally accepted that the greater contrast resolution of SPECT or SPECT/CT over planar imaging provides more precise anatomic localization of parathyroid adenomas [68,69]. The addition of a pertechnetate thyroid scan may further improve localization: in a study of 268 patients, planar pertechnetate subtraction in combination with a dual-phase sestamibi scan with SPECT/CT outperformed the dual-phase sestamibi SPECT/CT alone, increasing sensitivity to 93% and PPV to 96% compared with 88% and 92%, respectively [83].

In patients with concomitant thyroid disease, the addition of CT to a dual-tracer sestamibi and pertechnetate SPECT scan increases sensitivity from 80% to 94% [84].

Variant 1: Adult or child. Primary hyperparathyroidism. Initial imaging.
I. US parathyroid

US of the parathyroid glands is widely utilized as the initial imaging study in PHPT. Both the American Head and Neck Society Endocrine Surgery Section and the American Association of Endocrine Surgeons deem US to be the preferred initial localization study in patients with PHPT, noting the advantage of concomitant thyroid evaluation [2,8]. A 2012 meta-analysis of 19 studies evaluating US in patients with PHPT revealed a pooled sensitivity of 76% and PPV of 93% [70]. A subsequent 2017 meta-analysis of 12 studies (with few studies also included from the 2012 meta-analysis) revealed a pooled sensitivity of 80% [85]. However, the range of sensitivities reported in the literature varies widely. For example, a study of 604 patients comparing US, scintigraphy, and 4-D CT reported a sensitivity of 59% for US [31], with other smaller studies reporting US sensitivities ranging from 44% to 97% [18,20,58,86-90].

Nonlocalizable adenomas by US are most often due to ectopic or far posterior location, MGD, small adenoma size, and concomitant thyroid disease [58,86,91].

The literature in the pediatric population is limited. In a retrospective review of 29 patients, Alagaratnam et al [67] reported that US in 2 neonates resulted in false-negatives; sensitivity improved in older children to 93%. In a separate study of 16 children, sensitivity of US was 60% [7].

Variant 1: Adult or child. Primary hyperparathyroidism. Initial imaging.
J. Venous sampling parathyroid

Parathyroid glands tend to drain ipsilaterally and inferiorly relative to their anatomic location. As such, sampling of PTH levels during selective transvenous catheterization of multiple neck and mediastinal veins can be used to infer the laterality and regional location of parathyroid lesions [8,92,93]. Direct differential jugular venous sampling of PTH to infer laterality of an adenoma in patients with PHPT has also been described in the literature but is beyond the scope of this document [94,95]. Because of its invasive technique, selective parathyroid venous sampling is typically reserved for reoperative surgical candidates with recurrent or persistent PHPT after noninvasive examinations (eg, US, sestamibi, CT, etc) yield nonlocalizing, equivocal, or discordant results [96]. Otherwise, there are limited data regarding the use of selective venous sampling for parathyroid localization as the initial examination for PHPT in the surgically naïve patient. Hader et al [92] in a study of 23 patients from Germany underwent parathyroidectomy for hyperparathyroidism, 8 of which as their initial surgery, and results of selective parathyroid venous sampling were retrospectively reviewed. Across the entire cohort, the reported sensitivity was 94% and PPV was 89%.

Variant 2: Adult or child. Primary hyperparathyroidism, recurrent or persistent after parathyroid surgery. Initial imaging.

All patients undergoing imaging in the setting of recurrent or persistent PHPT should have biochemically proven disease, as imaging has no role in confirming or excluding the diagnosis [2,10]. As such, assessing the imaging test specificity and negative predictive value is not clinically relevant. Rather, the role of initial imaging in recurrent or persistent PHPT is to accurately identify and localize a parathyroid lesion (or lesions) and identify postoperative changes from previous

parathyroid explorations which can impact a subsequent surgery. Accordingly, these criteria focus on imaging test sensitivity and PPV.

Multiple imaging modalities may be utilized in combination during the initial imaging evaluation of recurrent or persistent PHPT after prior surgery in an attempt to maximize the accuracy and confidence of parathyroid localization via concordant imaging results [10,15].

Variant 2: Adult or child. Primary hyperparathyroidism, recurrent or persistent after parathyroid surgery. Initial imaging.
A. CT neck

Neck CT in the evaluation of recurrent or persistent PHPT after prior surgery is most commonly performed without and with IV contrast (4-D parathyroid CT) [34], which is reflected in the published data regarding the performance of neck CT for parathyroid localization in the setting of prior failed surgery. There is no literature regarding the use of CT neck with IV contrast specifically limited to patients with recurrent or persistent PHPT. Additionally, there is no relevant literature regarding the use of CT neck without IV contrast in the evaluation of PHPT.

In the setting of recurrent or persistent PHPT, retrospective studies report the sensitivity of CT neck without and with IV contrast to range between 50% and 91% and the PPV to range between 69% and 100% [29,36,40,97].

Variant 2: Adult or child. Primary hyperparathyroidism, recurrent or persistent after parathyroid surgery. Initial imaging.
B. MRI neck

Neck MRI is an emerging technique in the evaluation of recurrent or persistent PHPT after prior surgery. There are limited data regarding the use of MRI neck without and with IV contrast in the setting of prior surgery:

- Aschenbach et al: 30 patients from Germany underwent reoperative parathyroidectomy for PHPT, and results of MRI performed prior to reoperation were retrospectively reviewed. Using only conventional MRI sequences (without and with IV contrast), the sensitivity was 63%, and the PPV was 100%. With the addition of dynamic sequences, the sensitivity was 93%, and the PPV was 100% [98].
- Kluijfhout et al: 84 patients from California underwent reoperative parathyroidectomy for persistent PHPT, and results of MRI performed prior to reoperation were retrospectively reviewed. The sensitivity of MRI neck without and with IV contrast was 82%, and the PPV was 85%. The sensitivity and PPV of dynamic sequences were both 90% [48].

There is no relevant literature regarding the use of MRI without IV contrast in the evaluation of recurrent or persistent PHPT.

Variant 2: Adult or child. Primary hyperparathyroidism, recurrent or persistent after parathyroid surgery. Initial imaging.
C. Sestamibi dual-phase scan neck

There is no relevant literature regarding the use of planar sestamibi dual-phase scans in the evaluation of recurrent or persistent PHPT after prior surgery.

Variant 2: Adult or child. Primary hyperparathyroidism, recurrent or persistent after parathyroid surgery. Initial imaging.

D. Sestamibi dual-phase scan with SPECT or SPECT/CT neck

There are limited data regarding the use of sestamibi dual-phase scans with SPECT or SPECT/CT in the setting of prior surgery:

- Kluijfhout et al: 84 patients from California underwent reoperative parathyroidectomy for persistent PHPT, and results of sestamibi scans with SPECT/CT performed prior to reoperation were retrospectively reviewed. The reported sensitivity was 74%, and the PPV was 86% [48].
- Witteveen et al: 19 patients from The Netherlands underwent reoperative parathyroidectomy for persistent PHPT. Results of sestamibi scans with SPECT performed prior to reoperation were retrospectively reviewed and compared with a 23-patient cohort undergoing the same preoperative imaging for surgically naïve sporadic PHPT. For patients with persistent PHPT, the sensitivity for localizing parathyroid glands on a per-lesion basis was 33% as compared with 61% for the cohort imaged prior to their initial surgery [99].

Variant 2: Adult or child. Primary hyperparathyroidism, recurrent or persistent after parathyroid surgery. Initial imaging.
E. Sestamibi scan and I-123 thyroid scan

There is no relevant literature regarding the use of planar sestamibi and I-123 scans in the evaluation of recurrent or persistent PHPT after prior surgery.

Variant 2: Adult or child. Primary hyperparathyroidism, recurrent or persistent after parathyroid surgery. Initial imaging.
F. Sestamibi scan and I-123 thyroid scan with SPECT or SPECT/CT neck

There are limited data regarding the use of sestamibi and I-123 scans with SPECT or SPECT/CT in the setting of recurrent or persistent PHPT after prior surgery:

- Shin et al: 176 patients from Ohio underwent reoperative parathyroidectomy for recurrent or persistent hyperparathyroidism, including patients with PHPT, SHPT, and THPT. Results of sestamibi and I-123 scans with SPECT (103 patients) and sestamibi and I-123 scans with SPECT/CT (73 patients) performed prior to reoperation were retrospectively reviewed. Reported sensitivities were 74% and 86%, respectively [100].

Variant 2: Adult or child. Primary hyperparathyroidism, recurrent or persistent after parathyroid surgery. Initial imaging.
G. Sestamibi scan and pertechnetate thyroid scan

There is no relevant literature regarding the use of planar sestamibi and pertechnetate scans in the evaluation of recurrent or persistent PHPT after prior surgery.

Variant 2: Adult or child. Primary hyperparathyroidism, recurrent or persistent after parathyroid surgery. Initial imaging.
H. Sestamibi scan and pertechnetate thyroid scan with SPECT or SPECT/CT neck

There is no relevant literature regarding the use of sestamibi and pertechnetate scans with SPECT or SPECT/CT in the evaluation of recurrent or persistent PHPT after prior surgery.

Variant 2: Adult or child. Primary hyperparathyroidism, recurrent or persistent after parathyroid surgery. Initial imaging.
I. US parathyroid

A 2017 joint consensus statement of the American Head and Neck Society and the British Association of Endocrine and Thyroid Surgeons recommends US as a first-line imaging examination in the reoperative setting, citing the added advantage of revealing nodular thyroid disease, lymphadenopathy, and postoperative changes from the previous parathyroid exploration [10]. Otherwise, there are limited data within the last 10 years regarding the use of US in the setting of recurrent or persistent hyperparathyroidism after prior surgery:

- Hamidi et al: 58 patients from Massachusetts underwent reoperative parathyroidectomy for recurrent or persistent PHPT and results of US performed prior to reoperation were retrospectively reviewed. An examination was considered a true-positive if it identified the correct laterality (compared to quadrant or region). The reported sensitivity on a per-lesion basis (62 lesions) was 46% [101].
- Kluijfhout et al: 84 patients from California underwent reoperative parathyroidectomy for persistent PHPT, and the results of US performed prior to reoperation were retrospectively reviewed. The reported sensitivity was 54%, and the PPV was 71% [48].
- Shin et al: 176 patients from Ohio underwent reoperative parathyroidectomy for recurrent or persistent hyperparathyroidism, including patients with PHPT, SHPT, and THPT. Results of US performed prior to reoperation were retrospectively reviewed, with reported sensitivity of 69% [100].

Variant 2: Adult or child. Primary hyperparathyroidism, recurrent or persistent after parathyroid surgery. Initial imaging.
J. Venous sampling parathyroid

Parathyroid glands tend to drain ipsilaterally and inferiorly relative to their anatomic location. As such, sampling of PTH levels during selective transvenous catheterization of multiple neck and mediastinal veins can be used to infer the laterality and regional location of parathyroid lesions [8,92,93]. Because of its invasive technique, selective parathyroid venous sampling is typically reserved for reoperative surgical candidates with recurrent or persistent PHPT after noninvasive examinations (eg, US, sestamibi, CT, etc) yield nonlocalizing, equivocal, or discordant results [96,102].

Although parathyroid venous sampling has been in use since the 1990s [102], there are few pertinent studies within the last 10 years, and nearly all evaluate patients who have had prior nonlocalizing examinations, as this is the subset of patients for whom this examination is typically reserved. These studies are retrospective and each evaluated fewer than 40 patients, reporting sensitivities ranging from 40% to 93% [92,93,97,103-105].

There is a potential for false regionalization and/or lateralization of parathyroid lesions due to congenitally variant venous anatomy or alteration of regional venous drainage secondary to previous surgical interventions [93]. As with many invasive vascular procedures, venous sampling is potentially associated with serious but uncommon complications [10].

Variant 3: Adult or child. Secondary hyperparathyroidism. Initial imaging.

All patients undergoing imaging in the setting of SHPT should have biochemically proven disease, as imaging has no role in confirming or excluding the diagnosis [11]. As such, assessing the imaging test specificity and negative predictive value is not clinically relevant. Rather, as SHPT is typically a disorder of MGD and is therefore treated with BNE, the role of initial imaging is to accurately identify all eutopic and potential ectopic or supernumerary glands in an attempt to

decrease surgical failure rates [12-14]; accordingly, these criteria focus on imaging test sensitivity and PPV.

It is possible that multiple imaging modalities may be utilized in combination during the initial imaging evaluation of SHPT in an attempt to maximize the accuracy and confidence of parathyroid localization via concordant imaging results. This is supported by limited literature specific to SHPT [12] and otherwise inferred from data regarding PHPT [16-23] showing improved sensitivity and PPV in parathyroid lesion localization with a combination of examinations over each examination in isolation.

Variant 3: Adult or child. Secondary hyperparathyroidism. Initial imaging.
A. CT neck

There are limited data regarding the use of CT neck for localization in SHPT:

- Lee et al: 109 patients from Korea underwent parathyroidectomy for refractory SHPT, and results of preoperative localization studies were retrospectively reviewed. The reported sensitivity of CT neck was 85%, although details related to the CT acquisition (ie, without IV contrast, with IV contrast, or without and with IV contrast) are not provided; furthermore, the overall incidence of reported ectopic glands was much lower than typical at 1%, with all ectopic glands missed by CT [106].
- Hiramitsu et al: 291 patients from Japan underwent parathyroidectomy for SHPT, and results of preoperative localization studies were retrospectively reviewed. The reported sensitivity of CT neck was 60%, and the PPV was 100%. Details related to the CT acquisition are not provided [107].

Variant 3: Adult or child. Secondary hyperparathyroidism. Initial imaging.
B. MRI neck

There is no relevant literature regarding the use of MRI neck performed without IV contrast, with IV contrast, or without and with IV contrast in the evaluation of SHPT.

Variant 3: Adult or child. Secondary hyperparathyroidism. Initial imaging.
C. Sestamibi dual-phase scan neck

There are limited data regarding the use of planar sestamibi dual-phase scans in the evaluation of SHPT:

- Vulpio et al: 21 patients from Italy underwent parathyroidectomy for SHPT, and the results of preoperative sestamibi scans were retrospectively reviewed. The reported sensitivity on a per-lesion basis was 62% [12].

Variant 3: Adult or child. Secondary hyperparathyroidism. Initial imaging.
D. Sestamibi dual-phase scan with SPECT or SPECT/CT neck

There are limited data regarding the use of sestamibi dual-phase scans with SPECT or SPECT/CT in the evaluation of SHPT:

- Yang et al: 80 patients from China with SHPT on hemodialysis underwent parathyroidectomy and results of preoperative sestamibi scans with SPECT/CT were retrospectively reviewed. The reported sensitivity was 85% on a per-patient basis [108].
- Li et al: 50 patients from China with SHPT underwent parathyroidectomy and results of

preoperative sestamibi scans with SPECT/CT were retrospectively reviewed. The reported sensitivity was 59% on a per-lesion basis (out of 183 hyperplastic parathyroid glands) [109].

- Karipineni et al: This is the largest and most comprehensive study, a retrospective review of 2,975 patients from Maryland from 2004 to 2015. The aim of the study was to evaluate whether preoperative imaging could reliably identify ectopic glands in patients expected to have MGD. As such, the study was not limited to patients with SHPT but also included patients with THPT, lithium-induced PHPT, and PHPT due to multiple endocrine neoplasia; patients with SHPT comprised 55% of the cohort. On a per-lesion basis, the reported sensitivity of sestamibi dual-phase scans with SPECT in detecting ectopic glands was 29% [110].

Variant 3: Adult or child. Secondary hyperparathyroidism. Initial imaging.
E. Sestamibi scan and I-123 thyroid scan

There is no relevant literature regarding the use of planar sestamibi scan and I-123 thyroid scan in the evaluation of SHPT.

Variant 3: Adult or child. Secondary hyperparathyroidism. Initial imaging.
F. Sestamibi scan and I-123 thyroid scan with SPECT or SPECT/CT neck

There are limited data regarding the use of sestamibi scan and I-123 thyroid scan with SPECT or SPECT/CT in the evaluation of SHPT:

- Alkhalili et al: 103 patients from the United States with either SHPT or THPT underwent parathyroidectomy and results of preoperative localization were retrospectively reviewed. The reported sensitivity for ectopic glands on a per-lesion basis by sestamibi and I-123 scan with SPECT was 36% [14].

Variant 3: Adult or child. Secondary hyperparathyroidism. Initial imaging.
G. Sestamibi scan and pertechnetate thyroid scan

There is no relevant literature regarding the use of planar sestamibi scan and pertechnetate thyroid scan in the evaluation of SHPT.

Variant 3: Adult or child. Secondary hyperparathyroidism. Initial imaging.
H. Sestamibi scan and pertechnetate thyroid scan with SPECT or SPECT/CT neck

There is no relevant literature regarding the use of sestamibi scan and pertechnetate thyroid scan with SPECT or SPECT/CT in the evaluation of SHPT.

Variant 3: Adult or child. Secondary hyperparathyroidism. Initial imaging.
I. US parathyroid

When utilized as an initial imaging study in SHPT, US conveys additional benefits of concomitant evaluation of the thyroid gland. Studies evaluating the use of US in patients with SHPT vary in their design. Those studies evaluating the sensitivity of US on a per-lesion basis, inclusive of both eutopic and ectopic locations, report sensitivities ranging from 46% to 94% [12,85,111,112]. Although localization of eutopic glands is useful, the identification and localization of ectopic and supernumerary glands is paramount to decreasing failure rates of BNE:

- Alkhalili et al: 103 patients from New Mexico with either SHPT (34%) or THPT (66%) underwent parathyroidectomy and results of preoperative localization were retrospectively reviewed. The reported sensitivity for ectopic glands on a per-lesion basis by US was 32%

[14].

- Andrade et al: 166 patients from Brazil with either SHPT (27%) or THPT (73%) underwent parathyroidectomy and results of preoperative localization were retrospectively reviewed. The reported sensitivity for ectopic glands on a per-lesion basis by US was 20% [13].
- Karipineni et al: This is the largest and most comprehensive study, a retrospective review of 2,975 patients from Maryland from 2004 to 2015. The aim of the study was to evaluate whether preoperative imaging could reliably identify ectopic glands in patients expected to have MGD. As such, the study was not limited to patients with SHPT but also included patients with THPT, lithium-induced PHPT, and PHPT due to multiple endocrine neoplasia; patients with SHPT comprised 55% of the cohort. On a per-lesion basis, exclusive of ectopic glands in the mediastinum (which were not included due to the assumption that US could not adequately image the mediastinum), the reported sensitivity of US in detecting ectopic glands was 7% [110].

Variant 3: Adult or child. Secondary hyperparathyroidism. Initial imaging.
J. Venous sampling parathyroid

There is no relevant literature regarding the use of venous sampling in the evaluation of SHPT.

Variant 4: Adult or child. Tertiary hyperparathyroidism. Initial imaging.

All patients undergoing imaging in the setting of THPT should have biochemically proven disease, as imaging has no role in confirming or excluding the diagnosis [11]. As such, assessing the imaging test specificity and negative predictive value is not clinically relevant. THPT is typically a disorder of MGD in which the role of initial imaging is to accurately identify all eutopic and potential ectopic or supernumerary glands in an attempt to guide the surgical approach [12-14]; accordingly, these criteria focus on imaging test sensitivity and PPV.

It is possible that multiple imaging modalities may be utilized in combination during the initial imaging evaluation of THPT in an attempt to maximize the accuracy and confidence of parathyroid via concordant imaging results. This is inferred from data regarding PHPT [16-23] and SHPT [12] showing improved sensitivity and PPV in parathyroid lesion localization with a combination of examinations over each examination in isolation.

Variant 4: Adult or child. Tertiary hyperparathyroidism. Initial imaging.
A. CT neck

There is no relevant literature regarding the use of CT neck in the evaluation of THPT.

Variant 4: Adult or child. Tertiary hyperparathyroidism. Initial imaging.
B. MRI neck

There is no relevant literature regarding the use of MRI neck performed without IV contrast, with IV contrast, or without and with IV contrast in the evaluation of THPT.

Variant 4: Adult or child. Tertiary hyperparathyroidism. Initial imaging.
C. Sestamibi dual-phase scan neck

There is no relevant literature regarding the use of planar sestamibi dual-phase scan neck in the evaluation of THPT.

Variant 4: Adult or child. Tertiary hyperparathyroidism. Initial imaging.
D. Sestamibi dual-phase scan with SPECT or SPECT/CT neck

There are limited data regarding the use of sestamibi dual-phase scans with SPECT or SPECT/CT in the evaluation of THPT:

- Karipineni et al: This is the largest and most comprehensive study, a retrospective review of 2,975 patients from Maryland from 2004 to 2015. The aim of the study was to evaluate whether preoperative imaging could reliably identify ectopic glands in patients expected to have MGD. As such, the study was not limited to patients with THPT but also included patients with SHPT, lithium-induced PHPT, and PHPT due to multiple endocrine neoplasia; patients with THPT comprised 21% of the cohort. On a per-lesion basis, the reported sensitivity of sestamibi dual-phase scans with SPECT in detecting ectopic glands was 29% [110].

Variant 4: Adult or child. Tertiary hyperparathyroidism. Initial imaging.
E. Sestamibi scan and I-123 thyroid scan

There is no relevant literature regarding the use of planar sestamibi scan and I-123 thyroid scan in the evaluation of THPT.

Variant 4: Adult or child. Tertiary hyperparathyroidism. Initial imaging.
F. Sestamibi scan and I-123 thyroid scan with SPECT or SPECT/CT neck

There is no relevant literature regarding the use of sestamibi scan and I-123 thyroid scan with SPECT or SPECT/CT in the evaluation of THPT.

Variant 4: Adult or child. Tertiary hyperparathyroidism. Initial imaging.
G. Sestamibi scan and pertechnetate thyroid scan

There is no relevant literature regarding the use of planar sestamibi scan and pertechnetate thyroid scan in the evaluation of THPT.

Variant 4: Adult or child. Tertiary hyperparathyroidism. Initial imaging.
H. Sestamibi scan and pertechnetate thyroid scan with SPECT or SPECT/CT neck

There is no relevant literature regarding the use of sestamibi scan and pertechnetate thyroid scan with SPECT or SPECT/CT in the evaluation of THPT.

Variant 4: Adult or child. Tertiary hyperparathyroidism. Initial imaging.
I. US parathyroid

When utilized as an initial imaging study in THPT, US conveys additional benefits of concomitant evaluation of the thyroid gland. There are limited data regarding the use of US in the evaluation of THPT:

- Alkhalili et al: 103 patients from New Mexico with either SHPT (34%) or THPT (66%) underwent parathyroidectomy and results of preoperative localization were retrospectively reviewed. The reported sensitivity for ectopic glands on a per-lesion basis by US was 32% [14].
- Andrade et al: 166 patients from Brazil with either SHPT (27%) or THPT (73%) underwent parathyroidectomy and results of preoperative localization were retrospectively reviewed. The reported sensitivity for ectopic glands on a per-lesion basis by US was 20% [13].
- Karipineni et al: This is the largest and most comprehensive study, a retrospective review of 2,975 patients from Maryland from 2004 to 2015. The aim of the study was to evaluate whether preoperative imaging could reliably identify ectopic glands in patients expected to have MGD. As such, the study was not limited to patients with SHPT but also included

patients with THPT, lithium-induced PHPT, and PHPT due to multiple endocrine neoplasia; patients with SHPT comprised 55% of the cohort. On a per-lesion basis, exclusive of ectopic glands in the mediastinum (which were not included because of the assumption that US could not adequately image the mediastinum), the reported sensitivity of US in detecting ectopic glands was 7% [110].

Variant 4: Adult or child. Tertiary hyperparathyroidism. Initial imaging.
J. Venous sampling parathyroid

Because of its invasive technique, selective parathyroid venous sampling is typically reserved for reoperative surgical candidates with recurrent or persistent PHPT after noninvasive examinations (eg, US, sestamibi, CT, etc) yield nonlocalizing, equivocal, or discordant results [96]. Otherwise, there are limited data regarding the use of selective venous sampling in the initial evaluation of THPT:

- Witteveen et al: 20 patients from The Netherlands underwent parathyroidectomy for hyperparathyroidism, including 8 patients with THPT, and results of selective parathyroid venous sampling were retrospectively reviewed. Across the entire cohort, the reported sensitivity was 75% [93].

Summary of Highlights

- **Variant 1**: US parathyroid or CT neck without and with IV contrast or sestamibi dual-phase scan neck or sestamibi dual-phase scan with SPECT or SPECT/CT neck or sestamibi scan and I-123 thyroid scan or sestamibi scan and I-123 thyroid scan with SPECT or SPECT/CT neck or sestamibi scan and pertechnetate thyroid scan or sestamibi scan and pertechnetate thyroid scan with SPECT or SPECT/CT neck is usually appropriate as the initial imaging of all patients with PHPT. These procedures are typically equivalent alternatives (ie, only 1 procedure will be ordered to provide the clinical information to effectively manage the patient's care), although they may be used in a complementary manner to maximize the accuracy and confidence of parathyroid localization via concordant imaging results.
- **Variant 2**: US parathyroid or CT neck without and with IV contrast or sestamibi dual-phase scan neck or sestamibi dual-phase scan with SPECT or SPECT/CT neck or sestamibi scan and I-123 thyroid scan or sestamibi scan and I-123 thyroid scan with SPECT or SPECT/CT neck or sestamibi scan and pertechnetate thyroid scan or sestamibi scan and pertechnetate thyroid scan with SPECT or SPECT/CT neck is usually appropriate as the initial imaging of all patients with recurrent or persistent PHPT after parathyroid surgery. These procedures are typically equivalent alternatives (ie, only 1 procedure will be ordered to provide the clinical information to effectively manage the patient's care), although they may be used in a complementary manner to maximize the accuracy and confidence of parathyroid localization via concordant imaging results.
- **Variant 3**: US parathyroid or CT neck without and with IV contrast or sestamibi dual-phase scan neck or sestamibi dual-phase scan with SPECT or SPECT/CT neck or sestamibi scan and I-123 thyroid scan with SPECT or SPECT/CT neck or sestamibi scan and pertechnetate thyroid scan with SPECT or SPECT/CT neck is usually appropriate as the initial imaging of all patients with secondary hyperparathyroidism. These procedures are typically equivalent alternatives (ie, only 1 procedure will be ordered to provide the clinical information to effectively manage

the patient's care), although they may be used in a complementary manner to maximize the accuracy and confidence of parathyroid localization via concordant imaging results. The panel did not agree on recommending sestamibi scan and pertechnetate thyroid scan or sestamibi scan and I-123 thyroid scan for this clinical scenario. There is insufficient medical literature to conclude whether or not these patients would benefit from sestamibi scan and pertechnetate thyroid scan or sestamibi scan and I-123 thyroid scan. These procedures in this patient population are controversial but may be appropriate.

- **Variant 4**: US parathyroid or CT neck without and with IV contrast or sestamibi dual-phase scan neck or sestamibi dual-phase scan with SPECT or SPECT/CT neck or sestamibi scan and I-123 thyroid scan with SPECT or SPECT/CT neck or sestamibi scan and pertechnetate thyroid scan or sestamibi scan and pertechnetate thyroid scan with SPECT or SPECT/CT neck is usually appropriate as the initial imaging of all patients with THPT. These procedures are equivalent alternatives (ie, only 1 procedure will be ordered to provide the clinical information to effectively manage the patient's care), although they may be used in a complementary manner to maximize the accuracy and confidence of parathyroid localization via concordant imaging results. The panel did not agree on recommending sestamibi scan and I-123 thyroid scan for this clinical scenario. There is insufficient medical literature to conclude whether or not these patients would benefit from sestamibi scan and I-123 thyroid scan. This procedure in this patient population is controversial but may be appropriate.

Supporting Documents

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

For additional information on the Appropriateness Criteria methodology and other supporting documents, please go to the ACR website at https://www.acr.org/Clinical-Resources/Clinical-Tools-and-Reference/Appropriateness-Criteria.

Appropriateness Category Names and Definitions

Appropriateness Category Name	Appropriateness Rating	Appropriateness Category Definition
Usually Appropriate	7, 8, or 9	The imaging procedure or treatment is indicated in the specified clinical scenarios at a favorable risk-benefit ratio for patients.
May Be Appropriate	4, 5, or 6	The imaging procedure or treatment may be indicated in the specified clinical scenarios as an alternative to imaging procedures or treatments with a more favorable risk-benefit ratio, or the risk-benefit ratio for patients is equivocal.
May Be Appropriate (Disagreement)	5	The individual ratings are too dispersed from the panel median. The different label provides transparency regarding the panel's recommendation. "May be appropriate" is the rating category and a rating of 5 is assigned.

Usually Not Appropriate	1, 2, or 3	The imaging procedure or treatment is unlikely to be indicated in the specified clinical scenarios, or the risk-benefit ratio for patients is likely to be unfavorable.

Relative Radiation Level Information

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

Relative Radiation Level Designations

Relative Radiation Level*	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range
O	0 mSv	0 mSv
☢	<0.1 mSv	<0.03 mSv
☢☢	0.1-1 mSv	0.03-0.3 mSv
☢☢☢	1-10 mSv	0.3-3 mSv
☢☢☢☢	10-30 mSv	3-10 mSv
☢☢☢☢☢	30-100 mSv	10-30 mSv

*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (e.g., region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as “Varies.”

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

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