The Society of Nuclear Medicine Procedure Guideline For Parathyroid Scintigraphy

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I. Purpose

The purpose of this guideline is to assist nuclear medicine practitioners in recommending, performing, interpreting, and reporting the results of parathyroid imaging.

II. Background Information and Definitions

Primary hyperparathyroidism is characterized by increased synthesis and release of parathyroid hormone, which produces an elevated serum calcium level and a decline in serum inorganic phosphates. Asymptomatic patients are frequently diagnosed as a result of screening by automatic multichemistry panels. The vast majority of cases of primary hyperparathyroidism (80%–85%) are the result of single or multiple hyperfunctioning adenomas. Hyperplasia of several or all parathyroid glands accounts for approximately 12%–15% of cases, whereas parathyroid carcinomas occur in only 1%–3% of cases of hyperparathyroidism. In general, parathyroid adenomas larger than 500 mg can be detected scintigraphically. ^{99m}Tc-sestamibi allows detection of hyperplastic glands, although with less sensitivity than adenomas.

Dual-phase or double-phase imaging refers to utilizing ^{99m}Tc-sestamibi and acquiring early and delayed images. Dual-isotope or subtraction studies refer to protocols using 2 different radiopharmaceuticals for imaging acquisition.

III. Examples of Clinical or Research Applications

A. To localize hyperfunctioning parathyroid tissue (adenomas or hyperplasia) in primary hyperparathyroidism. This may be useful before surgery to help the surgeon find the lesion, thus shortening the time of the procedure.

Although the use of preoperative localizing procedures, including parathyroid scintigraphy, has been controversial, sestamibi scans have been shown to be accurate and to reduce the time and, therefore, the cost of an initial operation for hyperparathyroidism. Selected high-surgical-risk patients and those with life-threatening adenomas are especially likely to benefit from parathyroid scintigraphy. An unequivocally positive study will aid the surgeon in streamlining the surgical procedure.

B. To localize hyperfunctioning parathyroid tissue (usually adenomas) in patients with persistent or recurrent disease. Many of these patients will already have had 1 or more surgical procedures, making reexploration much more technically difficult. Also, ectopic tissue is much more prevalent in this population, and preoperative localization will likely increase surgical success, in part by sometimes helping to direct the surgical approach.

IV. Procedure

A. Patient Preparation

No special patient preparation is necessary.

The procedure should be explained to the patient, because preventing patient motion during the study is extremely important, particularly if using dual-tracer/subtraction techniques. Patients who are unable or unwilling to remain completely immobilized during the study may require sedation.

B. Information Pertinent to Performing the Procedure

1. Documentation of an elevated serum calcium and parathyroid hormone. Documented increased urinary excretion of calcium is also advised when other laboratory abnormalities are mild.
2. Results of physical examination, especially palpation of the neck.
3. Presence of concurrent thyroid disease, especially nodular thyroid disease. History of prior thyroid or parathyroid surgery.
4. Recent administration of iodine-containing preparations, such as for radiographic studies (i.e., CT scans, intravenous urography), or thyroid hormone, when the technique utilizing thyroid imaging and subsequent subtraction will be employed.
5. Results of CT, MRI, or ultrasound scans and other diagnostic tests.

C. Precautions

None

D. Radiopharmaceuticals

1. ^{201}Tl-Chloride

^{201}Tl has a physical half-life of 72 h. Its main photopeak is due to characteristic x-rays of mercury, which have an energy range of 69–83 keV. In addition, gamma rays are produced at 167 keV (8% abundance) and 135 keV (2% abundance). The administered radioactivity is 75–130 MBq (2–3.5 mCi) and is given intravenously. ^{201}Tl is taken up by both abnormal parathyroid tissue and thyroid tissue in proportion to blood flow.

Radiation Dosimetry: Adults

Radiopharmaceuticals	Administered activity MBq (mCi)	Organ receiving the largest radiation dose* mGy/MBq (rad/mCi)	Effective dose * mSv/MBq (rem/mCi)
^{201}Tl-chloride	75–130 iv (2.0–3.5)	0.54 Kidney (2.0)	0.23 (0.85)
^{99m}Tc-pertechnetate No blocking agent	75–150 iv (2–4)	0.062 Upper large intestine (0.23)	0.013 (0.048)
^{99m}Tc-sestamibi	185–925 iv (5–25)	0.039 Gallbladder (0.14)	0.0085 (0.031)
^{123}I 15% uptake	7.5–20 po (0.2–0.5)	1.9 Thyroid (7.0)	0.075 (0.28)

* International Commission on Radiological Protection. *Radiation Dose to Patients from Radiopharmaceuticals.* ICRP Publication 53. London, UK: ICRP; 1988:199,264,373. International Commission on Radiological Protection. *Radiation Protection in Biomedical Research.* ICRP Publication 62. New York, NY: Pergamon Press; 1993:23.

2. 99mTc-Pertechnetate
   ^{99m}Tc has a half-life of 6 h and an energy of 140 keV. Pertechnetate is used for delineating the thyroid gland, because pertechnetate is trapped by functioning thyroid tissue. This image is subtracted from the ^{201}Tl or ^{99m}Tc-sestamibi image, and what remains is potentially a parathyroid adenoma. When utilizing ^{201}Tl, the administered radioactivity of ^{99m}Tc-pertechnetate is generally 75–150 MBq (2–4 mCi), depending on the administered radioactivity of ^{201}Tl and which of the 2 radiopharmaceuticals is administered first. When utilizing ^{99m}Tc-sestamibi, the administered radioactivity of pertechnetate is generally 185–370 MBq (5–10 mCi), because sestamibi has a higher total activity in the thyroid gland than ^{201}Tl.
3. ^{99m}Tc-Sestamibi
   The range of intravenously administered radioactivity is 185–925 MBq (5–25 mCi); the typical dosage is 740 MBq (20 mCi). This radiopharmaceutical localizes in both parathyroid tissue and functioning thyroid tissue but usually washes out of normal thyroid tissue more rapidly than out of abnormal parathyroid tissue. (Hyperplastic parathyroid glands generally show faster washout than most adenomas.)
4. ^{123}I-Sodium Iodide
   ^{123}I has a half-life of 13 h and emits a photon with an energy of 159 keV. It has been used as a thyroid imaging agent in subtraction studies, particularly with ^{99m}Tc-sestamibi. The administered radioactivity, given orally, ranges from 7.5–20 MBq (200–550 µCi).

E. Image Acquisition

Digital data should be acquired in a 128 × 128 or larger matrix.

1. Planar images of the neck and mediastinum can be obtained with a gamma camera fitted with a high-resolution collimator. Images of the mediastinum should be obtained in all cases. Although the yield is low, the positive predictive value is quite high. Mediastinal images are most helpful in cases of residual or recurrent disease, where there is a much higher likelihood of ectopic tissue. Additional pinhole or converging collimator images of the neck may be useful.

   When utilizing ^{201}Tl, there is not uniform agreement over which agent to administer first, because there are advantages and disadvantages for each protocol. If ^{201}Tl is given first, there is the advantage of administering the lower energy radionuclide first and avoiding problems with technetium scatter. There is also the advantage of being able to image the mediastinum. However, the disadvantage is the requirement for the patient to hold still for a longer time. The advantage of administering the ^{99m}Tc-pertechnetate first is less time for the patient to remain motionless. However, there is the disadvantage of downscatter of ^{99m}Tc into the thallium window, as well as not being able to image the mediastinum. These studies should be acquired and stored digitally so that image manipulation can be performed. Acquiring a dual-isotope image may avoid registration problems.
2. ^{99m}Tc-sestamibi studies may be performed using either the dual-phase and/or the subtraction techniques. If the subtraction technique is used, the procedure is similar to thallium subtraction imaging. Either pertechnetate or ^{123}I can be given first, followed by ^{99m}Tc-sestamibi, or sestamibi can be given first, followed by pertechnetate. (^{123}I cannot be administered after sestamibi, because of the long time needed for localization.) Overall, none of the techniques discussed here has been shown to be superior; however, careful selection of technique on a case-by-case basis may be helpful. Disadvantages of ^{123}I include its high cost and long time required for localization. Using pertechnetate or ^{123}I as the first imaging agent, high count (10-min) images are obtained 30 min or 4 h after radiopharmaceutical administration, respectively. Sestamibi is then injected, and high-count (10-min) images are obtained 10 min after injection. If pertechnetate is injected after sestamibi images are obtained, the patient should be immobilized for 15–30 min after the pertechnetate injection, and then a 10-min image is acquired. In all cases, both sets of images are normalized to total thyroid counts and computer subtraction of ^{123}I or pertechnetate images from the sestamibi images is obtained.

   If a dual-phase study is performed, then a high-resolution parallel-hole collimator or a pinhole or converging collimator can be used. Early (10-min postinjection) and delayed (1.5–2.5-h postinjection) high-count images are obtained.

   It has now become clear that SPECT imaging is useful. SPECT imaging in conjunction with planar imaging provides increased sensitivity and more precise anatomical localization. This is particularly true in detecting both primary and recurrent hyperparathyroidism resulting from ectopic adenomas. In the mediastinum, accurate localization may assist in directing the surgical approach, such as median sternotomy versus left or right thoracotomy. Cine of volume-rendered images is often helpful. With large-field-of-view gamma cameras, magnification may be of help.

F. Interventions

None.

G. Processing

Processing with computer subtraction is only necessary with dual radiopharmaceutical studies.

1. In ^{201}Tl/^{99m}Tc-pertechnetate studies, computer subtraction may enhance detection of parathyroid adenomas. The 2 images should be normalized; that is, counts per pixel in the thyroid in 1 image should equal those in the other image. There are usually more counts in the pertechnetate image than the thallium image, and it may be necessary to decrease counts several fold by dividing the pertechnetate image by a constant. The pertechnetate image is then subtracted from the thallium image. However, normalization by this method can be difficult as a result of heterogeneity. An alternative method is to decrease the counts several fold by dividing the ^{201}Tl image by a constant and then using successive subtractions until the body of the thyroid disappears. Image shifting can be used to ensure optimal registration of the 2 images.
2. In ^{99m}Tc-sestamibi/^{123}I or pertechnetate imaging studies, the images should be normalized similar to the technique for ^{201}Tl/^{99m}Tc, and the ^{123}I or pertechnetate image is subtracted from the ^{99m}Tc-sestamibi image.

H. Interpretation Criteria

^{201}Tl/^{99m}Tc images and ^{99m}Tc/^{123}I images should be inspected visually as well as evaluated with computer subtraction and/or with rapid alternating display of images (cine). Abnormal parathyroid tissue will most likely appear as an area of relatively increased uptake with either ^{201}Tl or ^{99m}Tc-sestamibi. Computer subtraction will probably be of help in cases with equivocal visual findings. If ^{99m}Tc-sestamibi is used without ^{123}I or pertechnetate (i.e., without computer subtraction), the 2 sets of images (early and delayed) are inspected visually. Abnormal parathyroid tissue will usually appear as an area of increased uptake and should become more prominent on the delayed images. Occasionally, parathyroid adenomas may not show increased activity and may only appear as tissue fullness behind the thyroid. Some adenomas will show washout of tracer by 2–2.5 h and therefore may not be obvious on the delayed images. Washout of tracer from adenomas may be variable. Many hyperplastic glands will show rapid washout. SPECT images may reveal lesions not seen on planar images, especially if they are small.

I. Reporting

In addition to patient demographics, the report should include the following information:

1. Indication for the study
2. Procedure
   a. Radiopharmaceutical(s)
      i. Dosage and route of administration
      ii. If more than 1 radiopharmaceutical is used, the order in which they are administered and the timing of those administrations should be stated.
   b. Acquisition and Display
      i. Timing of acquisition of images.
      ii. Planar and/or SPECT.
      For planar images, list projections acquired (e.g., anterior) and region imaged (neck, mediastinum). For SPECT, list timing of acquisition after injection and region imaged (neck or mediastinum).
3. Findings
   a. Time of detection of lesion (early or late images).
   b. Location (thyroid bed [upper or lower pole, and which side] or mediastinum).
4. Study limitations, confounding factors (e.g., patient motion).
5. Interpretation.

J. Quality Control

Gamma camera quality control will vary from camera to camera. Multiple spatial and energy window registration should be checked periodically if dual-isotope studies are performed. For further guidance in gamma camera quality control, refer to the Society of Nuclear Medicine Procedure Guideline for General Imaging for routine quality control procedures for gamma cameras.

K. Sources of Error

1. Patient motion.
2. Image misregistration.
3. Adenomas or hyperplastic glands less than 500 mg in size are often difficult to detect.
4. Ectopic adenomas can be difficult to detect; the entire neck as well as the upper and mid mediastinum to the heart should be imaged.
5. Lesions of the thyroid, such as adenomas and carcinomas, may be indistinguishable from parathyroid adenomas.
6. Parathyroid carcinomas are also indistinguishable from parathyroid adenomas.
7. Recently administered radiographic contrast material or thyroid hormone (within the previous 3–4 wk) will interfere with ^{123}I and pertechnetate imaging and, therefore, will

compromise the use of subtraction techniques. This will not be a problem with dual-phase sestamibi studies.

Some parathyroid adenomas wash out rapidly.

V. Issues Requiring Further Clarification

There is now a clear consensus that imaging with ^{99m}Tc-sestamibi is superior to ^{201}Tl, although ^{201}Tl is still in occasional use. A few investigators have utilized ^{99m}Tc-tetrofosmin; however, it is not yet clear if this agent is as useful or accurate as ^{99m}Tc-sestamibi. There is still no consensus regarding subtraction imaging versus dual-phase imaging. There is a developing consensus that SPECT imaging is useful, because it improves sensitivity and anatomical localization.

There is still controversy regarding the utility of this study as a preoperative evaluation in primary hyperthyroidism in patients who have not had prior surgery. However, there are now some data that suggest that these studies may shorten the operative time and reduce cost. In cases of residual or recurrent disease, these studies are clearly helpful.

There are now some data emerging suggesting that PET imaging may be useful in imaging parathyroid adenomas.

VI. Concise Bibliography

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