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 due to screening by automatic multi-chemistry panels. The vast majority of cases of primary hyperparathyroidism (80–85%) are due to single or multiple hyperfunctioning adenomas. Hyperplasia of several or all parathyroid glands accounts for approximately 12–15% of cases, while parathyroid carcinomas occur in only 1–3% of cases of hyperparathyroidism. In general, parathyroid adenomas larger than 500 mg can be detected scintigraphically. Recently, Tc-99m sestamibi has allowed detection of hyperplastic glands, although with less sensitivity than adenomas.

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

III. Common Indications

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

Although the use of pre-operative localizing procedures, including parathyroid scintigraphy, has been controversial, sestamibi scans have been shown to be accurate and to reduce 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 one or more surgical procedures, making re-exploration much more technically difficult. Also, ectopic tissue is much more prevalent in this population, and pre-operative 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, as preventing patient motion during the study is extremely important, particularly if using dual imaging/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 the 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.
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, MR or Ultrasound scans and other diagnostic tests.

C. Precautions
None

D. Radiopharmaceuticals
1. Thallium-201 Chloride (Tl-201)
   Tl-201 has a physical half-life of 72 hr. Its main photopeak is due to characteristic x-rays of mercury, which have an energy range of 69–83 keV. There are also gamma rays 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. Tl-201 is taken up by both abnormal parathyroid tissue and thyroid tissue in proportion to blood flow.

2. Technetium-99m Pertechnetate (Tc-99m)
   Tc-99m has a half-life of 6 hr and an energy of 140 keV. Pertechnetate is used for delineating the thyroid gland, since pertechnetate is trapped by functioning thyroid tissue. This image is subtracted from the Tl-201 or Tc-99m sestamibi image, and what remains is potentially a parathyroid adenoma. When utilizing

   TI-201, the administered radioactivity of Tc-99m pertechnetate is generally 75–150 MBq (2–4 mCi), depending on the administered radioactivity of Tl-201, and which of the two radiopharmaceuticals is administered first. When utilizing Tc-99m sestamibi, the administered radioactivity of pertechnetate is generally 185–370 MBq (5–10 mCi), since sestamibi has a higher total activity in the thyroid gland than Tl-201.

3. Technetium-99m Sestamibi (Tc-99m)
   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. Iodine-123 Sodium Iodide (I-123)
   I-123 has a half-life of 13 hr, and emits a photon with an energy of 159 keV. It has been used as a thyroid imaging agent in subtraction studies, particularly with Tc-99m 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 x 128 or larger matrix.

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Radiation Dosimetry for Adults

<table>
<thead>
<tr>
<th>Radiopharmaceutical</th>
<th>Administered Activity MBq (mCi)</th>
<th>Organ Receiving the Largest Radiation Dose ** mGy (rad)</th>
<th>Effective Dose** mSv (rem)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tl-201 chloride</td>
<td>75 – 130 i.v. (2.0 - 3.5)</td>
<td>0.54 Kidney (2.0)</td>
<td>0.23</td>
</tr>
<tr>
<td>Tc-99m pertechnetate</td>
<td>75 – 150 i.v. (2 – 4)</td>
<td>0.062 ULI† (0.23)</td>
<td>0.013</td>
</tr>
<tr>
<td>No blocking agent</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tc-99m sestamibi</td>
<td>185 – 925 i.v. (5 – 25)</td>
<td>0.039 Gallbladder (0.14)</td>
<td>0.0085</td>
</tr>
<tr>
<td>I-123</td>
<td>7.5 – 20 p.o. (0.2 – 0.5)</td>
<td>1.9 Thyroid (7.0)</td>
<td>0.075</td>
</tr>
</tbody>
</table>

*ICRP 53, page 199, 264, 373
†ICRP 62, pg. 23
‡ Per MBq (per mCi)
§ Upper Large Intestine
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 TI-201, there is not uniform agreement over which agent to administer first, since there are advantages and disadvantages for each protocol. If TI-201 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 of the patient to hold still for a longer time. The advantage of administering the Tc-99m pertechnetate first is less time for the patient to remain motionless. However, there is the disadvantage of downscatter of Tc-99m 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. Tc-99m 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 I-123 can be given first, followed by Tc-99m sestamibi, or sestamibi can be given first followed by pertechnetate. (I-123 cannot be administered following sestamibi, due to the long time needed for localization.) Overall, none of the above techniques has been shown to be superior; however, careful selection of technique on a case-by-case basis may be helpful. Disadvantages of I-123 include its high cost and long time required for localization. Using pertechnetate or I-123 as the first imaging agent, high count (10 min) images are obtained 30 min or 4 hr after radiopharmaceutical administration, respectively. Sestamibi is then injected and high count (10 min) images are obtained 10 min postinjection. 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 I-123 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 (1½–2½ hr 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 due to 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 may be 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 TI-201/Tc-99m pertechnetate studies, computer subtraction may enhance detection of parathyroid adenomas. The two images should be normalized; that is, counts per pixel in the thyroid in one image should equal that 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 severalfold 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 due to heterogeneity. An alternative method is to decrease the counts several-fold by dividing the TI-201 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 two images.

2. In Tc-99m sestamibi/I-123 or pertechnetate imaging studies, the images should be normalized similar to the technique for TI-201/Tc-99m, and the I-123 or pertechnetate image is subtracted from the Tc-99m sestamibi image.
H. Interpretation Criteria

TI-201/Tc-99m images and Tc-99m/I-123 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 appear as an area of relatively increased uptake with either TI-201 or Tc-99m sestamibi. Computer subtraction will probably be of help in cases with equivocal visual findings. If Tc-99m sestamibi is used without I-123 or pertechnetate (i.e., without computer subtraction), the two 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. However, some adenomas will show washout of tracer by 2-2½ hr. 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 one 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 post-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 I-123 and pertechnetate imaging, and will therefore compromise the use of subtraction techniques. This will not be a problem with dual phase sestamibi studies.

V. Issues Requiring Further Clarification

There is now a clear consensus that imaging with Tc-99m sestamibi is superior to Thallium-201, although Thallium-201 is still in occasional use. A few investigators have utilized Tc-99m tetrofosmin; however, it is not yet clear if this agent is as useful or accurate as Tc-99m sestamibi. There is still not yet a consensus regarding subtraction imaging versus dual phase imaging. There is a developing consensus that SPECT imaging is useful, as it improves sensitivity and anatomical localization.

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

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

VI. Concise Bibliography


VIII. Disclaimer

The Society of Nuclear Medicine has written and approved guidelines to promote the cost-effective use of high quality nuclear medicine procedures. These generic recommendations cannot be applied to all patients in all practice settings. The guidelines should not be deemed inclusive of all proper procedures or exclusive of other procedures reasonably directed to obtaining the same results. The spectrum of patients seen in a specialized practice setting may be quite different than the spectrum of patients seen in a more general practice setting. The appropriateness of a procedure will depend in part on the prevalence of disease in the patient population. In addition, the resources available to care for patients may vary greatly from one medical facility to another. For these reasons, guidelines cannot be rigidly applied.

Advances in medicine occur at a rapid rate. The date of a guideline should always be considered in determining its current applicability.