

Society of Nuclear Medicine Procedure Guideline for Scintigraphy for Differentiated Papillary and Follicular Thyroid Cancer

Authors: Edward B. Silberstein, MD, Chair (University of Cincinnati Medical Center, Cincinnati, OH); Abass Alavi, MD (Hospital of the University of Pennsylvania, Philadelphia, PA); Helena R. Balon, MD (William Beaumont Hospital, Royal Oak, MI); David Becker, MD (Weill Cornell Medical School, New York, NY); N. David Charkes, MD (Temple University Hospital, Philadelphia, PA); Susan E.M. Clarke, MD (Guy's and St. Thomas NHS Foundation Trust, School of Medicine, King's College, London); Chaitanya R. Divgi, MD (Hospital of the University of Pennsylvania, Philadelphia, PA); Kevin J. Donohoe, MD (Beth Israel Deaconess Medical Center, Boston, MA); Dominique Delbeke, M.D, PhD (Vanderbilt University Medical Center, Nashville, TN); Stanley J. Goldsmith, MD (Weill Cornell Medical Center, New York, NY); Donald A. Meier, MD (William Beaumont Hospital, Royal Oak, MI); Salil D. Sarkar, MD (Jacobi Medical Center, North Bronx Healthcare Network, Bronx, NY); Alan D. Waxman, MD (Cedars Sinai Medical Center, Los Angeles, CA)

I. Purpose

The purpose of this guideline is to assist nuclear medicine practitioners in recommending, performing, interpreting, and reporting the results of extended scintigraphy for differentiated thyroid cancer.

II. Background Information and Definitions

Scintigraphy for detection of thyroid metastasis and/or residual functioning thyroid tissue consists of obtaining images of the body, 1–3 d following the oral ingestion of ^{131}I , or 6–48 h after ^{123}I (recognizing that the longer time period will require higher dosages of ^{123}I). ^{18}F -FDG PET may be helpful for patients with a rising serum thyroglobulin and negative or minimal iodine uptake. Other radiopharmaceuticals such as ^{201}Tl and $^{99\text{m}}\text{Tc}$ sestamibi may also provide useful information.

III. Examples of Clinical or Research Applications

To determine the presence and extent of residual functioning thyroid tissue shortly post-thyroidectomy and, after ^{131}I ablation, to detect the presence and location of functioning thyroid cancer, recurrences and/or metastases.

IV. Procedure

The patient should be seen by the nuclear medicine physician sufficiently early to ensure the appropriate diagnosis has been made, the patient is suitable for scintigraphy, the necessary laboratory studies have been obtained, and low-iodine diet instructions have been given. This initial appointment is important for establishing the doctor/patient relationship.

The Society of Nuclear Medicine (SNM) has written and approved these guidelines as an educational tool designed to promote the cost-effective use of high-quality nuclear medicine procedures or in the conduct of research and to assist practitioners in providing appropriate care for patients. The guidelines should not be deemed inclusive of all proper procedures nor exclusive of other procedures reasonably directed to obtaining the same results. They are neither inflexible rules nor requirements of practice and are not intended nor should they be used to establish a legal standard of care. For these reasons, SNM cautions against the use of these guidelines in litigation in which the clinical decisions of a practitioner are called into question.

The ultimate judgment about the propriety of any specific procedure or course of action must be made by the physician when considering the circumstances presented. Thus, an approach that differs from the guidelines is not necessarily below the standard of care. A conscientious practitioner may responsibly adopt a course of action different from that set forth in the guidelines when, in his or her reasonable judgment, such course of action is indicated by the condition of the patient, limitations on available resources, or advances in knowledge or technology subsequent to publication of the guidelines.

All that should be expected is that the practitioner will follow a reasonable course of action based on current knowledge, available resources, and the needs of the patient to deliver effective and safe medical care. The sole purpose of these guidelines is to assist practitioners in achieving this objective.

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

A. Patient Preparation

1. Avoidance of interfering materials
The concentration of radioiodine in functioning thyroid tissue is affected by many factors such as:
 - a. Medications, especially thyroid hormones.
 - b. Iodine-containing food (eg, kelp) and medications (eg, iodinated contrast, amiodarone, betadine). Imaging should be delayed for a period long enough to eliminate the effects of these interfering factors. A low-iodine diet is followed for 7–14 d before the radioiodine is given, as it significantly increases the uptake of radioiodine by functioning thyroid tissue. The goal is a 24-h urine iodine output of about 50 mcg, but this measurement is not felt to be necessary in most cases.
2. The sensitivity of whole-body scintigraphy for detection of functioning metastases can be optimized at TSH levels of 30 mIU/L or more. This is achieved by the administration of recombinant human TSH (rhTSH, Thyrogen[®], given as two injections of 0.9 mg intramuscularly on each of two consecutive days, with 4 mCi of ¹³¹I given the next day, TSH and serum tg obtained 2 d after the oral ¹³¹I), or, in the near athyreotic patient, by withdrawing replacement thyroid hormone therapy for 3–4 weeks. The patient should be informed of the potential side effects of rhTSH injection, and of hypothyroidism, if this latter course is taken. In order to avoid severely symptomatic, prolonged hypothyroidism, patients may be maintained on triiodothyronine (T3) until 10–14 d prior to administration of the radioiodine. rhTSH will be required if the patient cannot be prepared by near-total thyroidectomy, in the presence of sufficient functioning tumor to suppress endogenous TSH, or with pituitary insufficiency or isolated TSH deficiency.
3. Serum TSH level should be measured 1–3 d prior to radioiodine administration. The TSH level should be greater than about 30 mIU/L, unless there is significant residual functioning thyroid tissue that will prevent an endogenous TSH elevation. Concomitant serum thyroglobulin and anti-thyroglobulin antibody assays should be obtained.

4. The sensitivity of whole-body scintigraphy can be improved if the patient follows a strict low-iodine diet starting 7–14 d prior to administration of the radioiodine tracer and continuing throughout the period of imaging (and for a day or so after treatment).

B. Information Pertinent to Performing the Procedure

1. Compliance with a low-iodine diet
2. TSH level
3. History of thyroid hormone withdrawal or utilization of rhTSH.
4. Serum thyroglobulin and anti-thyroglobulin antibody levels.
5. Description of operative procedure (extent of thyroidectomy) and detailed pathologic findings
6. Tumor histology, including presence or absence of capsular and/or vascular invasion and lymph node involvement
7. Results of other imaging procedures
8. Physical examination findings
9. History of prior ¹³¹I treatment
10. Results of prior radioiodine scintigraphy
11. History of prior administration of iodinated contrast (especially as part of a CT examination) or iodine-containing drugs (eg, amiodarone)
12. Menstrual history/pregnancy test
13. Nursing/lactation history
14. Surgeon performing the thyroidectomy has sufficient and ongoing expertise in performing this procedure.

C. Precautions

Patients receiving more than about 5–7 mCi of ¹³¹I should follow the same precautions as patients treated with ¹³¹I for hyperthyroidism.

D. Radiopharmaceuticals

1. Oral ¹³¹I is administered in activities of 1–5 mCi or less, with many preferring a range of 1–2 mCi because of data suggesting that stunning (decreased uptake of the therapy dose of ¹³¹I by residual functioning thyroid tissue or tumor due to cell death or dysfunction caused by the activity administered for diagnostic imaging) is less likely at the lower activity range. However, stunning may not influence the outcome of treatment. With higher dosages, detection of more iodine concentrating tissue has been reported.
2. Oral ¹²³I may be administered at a dosage typically between 0.4–5.0 mCi, which may avoid stunning.

3. Positron emission tomography with ^{18}F -FDG may be used to identify tumors that are not visualized with radioiodine. While these tumors are less likely to respond to ^{131}I treatment, they may be amenable to surgical resection, external radiation or embolization. Tumors that are radioiodine-negative and FDG-positive are associated with a less favorable prognosis. Imaging with FDG is more sensitive when the serum TSH level is elevated, which can be achieved with rhTSH or, less quickly, with thyroid hormone withdrawal. $^{99\text{m}}\text{Tc}$ -sestamibi, preferably with SPECT, may be used to image radioiodine-negative metastases if FDG-PET is not available. ^{201}Tl is uncommonly used for this purpose today.

E. Image Acquisition

1. Instrumentation

For ^{131}I , a large-field-of-view camera and a high-energy parallel hole collimator is used. For ^{123}I , ^{201}Tl and $^{99\text{m}}\text{Tc}$, a low-energy collimator and a large-field-of-view camera are preferred. PET/CT scanning will provide the optimal imaging when ^{18}F -FDG is employed. If PET/CT is performed, refrain from using oral or intravenous iodinated contrast agents, as this will impact potential ^{131}I treatment.
2. Patient positioning

Lying supine on an imaging table.
3. Imaging protocols
 - a. Post-thyroidectomy, pre-ablation choices:

Radiation Dosimetry for Adults

Radiopharmaceuticals	Administered Activity	Organ Receiving the Largest Radiation Dose	Effective Dose
	MBq (mCi)	mGy/MBq (rad/mCi)	mSv/MBq (rem/mCi)
^{18}F -fluorodeoxyglucose ^a	370–740	0.16 bladder wall	0.019
	(10–20)	(0.59)	(0.07)
Na ^{123}I iodide ^b (0% thyroid uptake)	14.8–185 po	0.09 bladder wall	0.013
	(0.4–5.0) ^c	(0.33)	(0.048)
Na ^{131}I iodide ^b (0% thyroid uptake)	37–185	0.81 bladder wall	0.11
	(1–5) ^c	(3.0)	(0.41)
^{201}Tl chloride ^b	110–185 iv	0.46 kidney	0.16
	(3–5)	(1.70)	(0.60)
$^{99\text{m}}\text{Tc}$ sestamibi ^b	370–740 iv	0.050 upper large intestine	0.015
	(10–20)	(0.185)	(0.056)

a. Delbeke D, Coleman RE, Guiberteau MJ, et al. Procedure guideline for tumor imaging with ^{18}F -FDG PET/CT 1.0. *J Nucl Med* 2006;47:885–895.

b. International Commission on Radiological Protection. *Radiation Doses to Patients from Radiopharmaceuticals*. Oxford: Pergamon Press, 1988.

c. In general the larger activity of radioiodine one administers, the higher the scan sensitivity for metastatic thyroid cancer. This must be balanced with the apparent “stunning” effect described for both ^{123}I and ^{131}I at higher dosages, although the effect this stunning has on eventual outcome is unclear and may be minimal. The ranges for diagnostic dosages of radioiodine given in the table are wide, but all have been used successfully by thyroid cancer consultants. 4 mCi of ^{131}I are recommended by the manufacturer if rhTSH is employed.

- i. rhTSH may be used to elevate the serum TSH for post-operative pre-ablative scanning with either ^{125}I or ^{131}I (dosages in table above) prior to ^{131}I therapeutic ablation. This is an “off-label” indication for rhTSH (not in the FDA package insert), but employed by a number of consultants.
 - ii. Using endogenous TSH stimulation, the patient may be allowed to become hypothyroid, minimizing symptoms by checking the patient’s blood as early as three weeks post-thyroidectomy for the desired TSH level (>30 mIU/L) to optimize scan sensitivity.
 - iii. The American Thyroid Association Guideline suggests not imaging before ^{131}I therapy. Nuclear medicine consultants are divided as to the need for thyroid imaging *before* ^{131}I ablation, but one must recognize the low but finite frequency of significant clinical problems such scanning can uncover, including the following:
 - (a) About 1% of the time the thyroidectomy is truly total, and, if there are no remnants to be ablated, then giving ^{131}I would achieve no purpose, although in high-risk patients treatment of occult metastases may be warranted.
 - (b) If too large a thyroid remnant remains post-operatively, and one is unaware of this, then the usual ablative dose, ranging from about 75–150 mCi of ^{131}I , might uncommonly cause radiation thyroiditis with clinically significant neck pain and swelling.
 - (c) Distant metastases in the brain or spinal cord might require pre-radiation corticosteroids to avoid complications caused by radiation-induced swelling.
 - (d) At some institutions, large thyroid remnants, especially in high risk patients, are removed with a second thyroidectomy before high dosage ^{131}I can be given, as lower dosages of ^{131}I may fail to ablate large remnants.
 - (e) Larger dosages of radioiodine are usually given at the time of ablation if regional or distant metastases are detected on the pre-ablation scan.
 - iv. Post- ^{131}I ablation scintigraphy is recommended 4–10 d after administering the ablative dosage, as this provides enhanced sensitivity over all the pre-ablative imaging procedures noted above. SPECT or SPECT/CT may improve tissue/tumor localization.
 - b. Post-thyroidectomy, post-ablation imaging for restaging 6–12 months (and later) post-ablation.
 - i. 1–5 mCi of ^{131}I with scanning at 1–3 d (daily scanning required if quantitative dosimetry is employed).
 - ii. rhTSH protocol if likelihood of ^{131}I therapy is low or intermediate.
 - iii. Endogenous TSH stimulation if probability of ^{131}I therapy is high; some consultants are now employing rhTSH “off label” successfully for this therapeutic purpose.
 - c. ^{18}F -FDG
 - i. Indication: rising serum thyroglobulin with one post- ^{131}I therapy scan negative.
 - (a) When there is a suspicion that the ^{131}I scan will be negative or have low sensitivity, some consultants recommend simultaneously performing a ^{18}F -FDG scan (the sensitivity of which is higher when the serum TSH is elevated) after rhTSH stimulation, on the Wednesday (day 3) following rhTSH injections on days 1 and 2, then the ^{131}I scan on day 5, Friday. This saves the cost and inconvenience of two sets of rhTSH injections. Simultaneous ^{18}F -FDG and ^{131}I imaging are also possible after thyroid hormone withdrawal with resultant TSH elevation.
 - ii. Patient preparation requires 2 d of rhTSH injection to optimize sensitivity.
- #### 4. Timing of the Images
- a. For ^{131}I , images are obtained 1–3 d after the radiopharmaceutical administration. Later images, when background is diminished, often provide better definition of low-activity lesions. Imaging 4–10 d

after a therapeutic dose of ^{131}I can be helpful in demonstrating small or functioning metastases not visible with the low scanning dose.

- b. For ^{123}I , images are obtained 6–48 h following the administration of the radiopharmaceutical, recognizing that higher dosages will be necessary for the longer time period.
 - c. For ^{18}F -FDG, images are begun 60–90 min following injection.
 - d. For $^{99\text{m}}\text{Tc}$ sestamibi and ^{201}Tl , images are obtained 15 min after administration of the radiopharmaceutical. SPECT may be more accurate for localization of abnormalities.
5. Image Acquisition (all tracers)
- a. Anterior and posterior images from the top of the skull through the femurs are obtained. Spot images should be obtained for approximately 10–15 min per view. Longer imaging times may be helpful for images obtained more than 3 d after administration of the radioiodine.
 - b. If images are obtained with a whole-body scanner, the scan speed should be adjusted so that whole body imaging takes approximately 40 min per pass or 4–5 cm/min for a dosage of 4 mCi ^{131}I , using a high-energy collimator.
 - c. Pinhole images of the neck for single photon emitters, in combination with adequate anatomic markers and careful palpation, may be effective in differentiating between normal residual thyroid tissue, salivary gland uptake, residual thyroid cancer, and lymph node metastasis, but this is often a difficult determination. SPECT/CT with ^{131}I may occasionally be helpful in this distinction.
 - d. 24-h neck iodine uptake measurements are often helpful in determining the mass of remaining thyroid tissue or tumor.
 - e. SPECT or SPECT/CT may be helpful to improve tissue localization

F. Interventions

Giving the patient an apple or crackers to chew and swallow is more useful than a drink of water to eliminate common artifacts from mouth and esophageal activity.

G. Processing

None

H. Interpretation Criteria

An adequate physical examination and history should be obtained. The presence of palpable tissue in the neck should be defined for correlation with the scintigraphic findings.

Special attention should be paid to the precise placement of markers on anatomical landmarks. For appropriate interpretation of anterior thyroid bed findings, it is necessary to be certain of the location of the nose and/or mouth, thyroid cartilage and sternal notch in the neck. For whole-body imaging, other landmarks may be important such as costal margins, xyphoid process, pubic symphysis, and iliac crests. Posteriorly, the location of the spine, iliac crests, etc, can be identified and transferred to the film. In addition to the scintigraphic images with markers, duplicate images should be obtained without the markers to avoid interference with areas of uptake adjacent to the markers.

I. Reporting

The report should include a qualitative estimate of the size, activity and location of any areas of uptake that correspond to any functioning normal or abnormal thyroid tissue. Particular attention should be paid to activity in the thyroid bed. Scan images cannot differentiate residual normal thyroid tissue (ie, thyroid remnants) from tumor there. Comparison with prior scans can often be useful in defining the significance of localized neck activity. Lateral and oblique views may be useful in separating thyroid bed activity from neighboring lymph node activity.

Results of recent thyroglobulin assays may be useful, especially in interpreting negative scintigraphic finding, recognizing that about 20% of patients with thyroid cancer have antibodies to thyroglobulin, which invalidate the serum thyroglobulin measurement.

J. Quality Control

See Society of Nuclear Medicine Guideline on General Imaging.

K. Sources of Error

1. Local contamination (clothing, skin, hair, collimator, imaging table)
2. Esophageal activity
3. Asymmetric salivary gland uptake
4. Breast uptake
5. Thymus uptake

V. Issues Requiring Further Clarification

- A. What is the best dose of ^{131}I for whole-body imaging that would provide the most diagnostic information with minimal stunning (see section IV.D.1. above) both in the initial work-up and to detect recurrences?
- B. What are the detrimental long term affects, if any, of thyroidal stunning?
- C. What is the role, and adequate minimal dosage, of ^{123}I in whole-body surveys post-thyroidectomy and pre-ablation, and possibly for metastatic disease, compared to ^{131}I ?
- D. Does lithium administration promote retention of radioiodine in metastatic foci sufficiently to be of therapeutic value?
- E. What is the role of radioiodine scanning after surgery and before ablation?
- F. What is the role of somatostatin receptor agents in detecting thyroid cancer when the serum thyroglobulin is elevated but the ^{131}I and ^{18}F -FDG scans are negative?
- G. Does the sensitive serum thyroglobulin assay allow the nuclear medicine physician to use only 1–2 mCi of ^{131}I for the detection of thyroid cancer, rather than higher, potentially stunning dosages, since sensitivity of this dosage is lower than one would see using 5 mCi?
- H. What is the value of administering ablative dosages of ^{131}I when the post-thyroidectomy scan and serum thyroglobulin are negative in a high-risk patient?

VI. Concise Bibliography

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