Procedure Guideline for Somatostatin Receptor Scintigraphy with ^{111}In-Pentetreotide

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PART I: PURPOSE

The purpose of this guideline is to assist nuclear medicine practitioners in recommending, performing, interpreting, and reporting the results of somatostatin receptor scintigraphy with ^{111}In-pentetreotide.

PART II: BACKGROUND INFORMATION AND DEFINITIONS

^{111}In-pentetreotide is a [^{111}In-DTPA-D-Phe-] conjugate of octreotide, a somatostatin analog that binds to somatostatin receptors (predominantly somatostatin receptor subtypes sst2 and sst5). This octapeptide concentrates in neuroendocrine and some nonneuroendrocrine tumors containing somatostatin receptors. Tumors that may be detected by somatostatin receptor scintigraphy with ^{111}In-pentetreotide include, but are not limited to, the following:

- Adrenal medullary tumors (pheochromocytoma, neuroblastoma, and ganglioneuroma).
- Gastroenteropancreatic tumors (e.g., gastrinoma, insulinoma, glucagonoma, vasoactive intestinal polypeptide secreting tumor [VIPoma], and nonfunctioning gastroenteropancreatic tumors).
- Carcinoid tumors.
- Medullary thyroid carcinoma.
- Melanoma.
- Merkel cell tumor of the skin.
- Paraganglioma.
- Pituitary adenomas.
- Small cell lung carcinoma.

Other tumors and disease processes may also be detected by ^{111}In-pentetreotide scintigraphy and knowledge of the patient's history is thus important. These disorders may include, but are not limited to, the following:

- Astrocytomas.
- Benign and malignant bone tumors.
- Breast carcinoma.
- Differentiated thyroid carcinoma (papillary, follicular, and Hürthle cell).
- Lymphoma (Hodgkin's and non-Hodgkin's).
- Meningioma.
- Non–small cell lung carcinoma.
- Prostate carcinoma.
- Renal cell carcinoma.
- Sarcomas.
- Autoimmune diseases (e.g., rheumatoid arthritis, Graves' disease, and Graves' ophthalmopathy).
- Bacterial pneumonia.
- Cerebrovascular accident.
- Fibrous dysplasia.
- Granulomas (e.g., tuberculosis and sarcoid).
- Radiation pneumonitis.

In addition to these tumors, healthy organs, such as the pituitary, thyroid, spleen, liver, and renal parenchyma, also show avidity for this tracer. The gallbladder, bowel, renal collecting systems, ureters, and urinary bladder are seen as a result of clearance of ^{111}In-pentetreotide.

PART III: COMMON INDICATIONS

A. Detection and localization of a variety of suspected neuroendocrine and some non-neuroendocrine tumors and their metastases (see Interpretation Criteria, Section IV.H).

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B. Staging patients with neuroendocrine tumors.
C. Determination of somatostatin receptor status (patients with somatostatin receptor–positive tumors may be more likely to respond to octreotide therapy).
D. Follow-up of patients with known disease to evaluate potential recurrence.
E. Selection of patients with metastatic tumors for peptide receptor radionuclide therapy and prediction of the effect of peptide receptor radionuclide therapy, where available.

PART IV: PROCEDURE

A. Patient Preparation
   1. When appropriate, consideration should be given to discontinuing octreotide therapy for 24 h before ^{111}In-pentetreotide administration, as the patient is monitored for signs of withdrawal. See also Section IV.K.2.a.
   2. To reduce the radiation exposure, patients should be well hydrated before and for at least 1 d after injection.
   3. The use of laxatives should be considered, especially when the abdomen is the area of interest. A mild oral laxative (e.g., bisacodyl or lactulose) may be administered in the evening before injection and in the evening after injection. The need for bowel preparation should be assessed on an individual basis and laxatives should not be used in patients with active diarrhea.

B. Information Pertinent to Performing the Procedure

A relevant history of the type of suspected or known primary tumor, its hormonal activity, the results of other imaging studies (CT or MRI), laboratory results (tumor markers), history of recent surgery, chemotherapy, radiation therapy, and octreotide therapy should be obtained. History of cholecystectomy should also be noted.

C. Precautions
   1. In patients suspected of having insulinoma, an intravenous infusion of glucose should be available because of the potential for inducing severe hypoglycemia.
   2. ^{111}In-pentetreotide should not be injected into intravenous lines for, or together with solutions for total parenteral nutrition.

D. Radiopharmaceutical (see Table 1)

^{111}In-pentetreotide is a [^{111}In-DTPA-D-Phe-] conjugate of octreotide, a long-acting somatostatin analog (OctreoScan). The recommended administered activity is 222 MBq (6 mCi) in adults and 5 MBq/kg (0.14 mCi/kg) in children. The amount of pentetreotide injected is 10–20 μg; that dose is not expected to have a clinically significant pharmacologic effect (see Section IV.C.1). ^{111}In-pentetreotide is cleared rapidly from the blood (one third of the injected dose remains in the blood pool at 10 min, 1% at 20 h after injection). Excretion is almost entirely through the kidneys (50% of the injected dose is recovered in the urine by 6 h, 85% within 24 h). Hepatobiliary excretion is only about 2% of the administered dose. It is not known whether ^{111}In-pentetreotide is removed by dialysis.

TABLE 1
Radiation Dosimetry for Adults

Radiopharmaceutical	Administered activity MBq (mCi)	Organ receiving the largest dose mGy/MBq (rad/mCi)	Effective dose equivalent mSv/MBq (rem/mCi)
^{111}In-pentetreotide		spleen	
	222	0.665	0.117
	(6)	(2.46)	(0.433)

Data adapted from (*11*).

E. Image Acquisition
   1. Patients should void before imaging.
   2. Images are acquired at 4 and 24 h or 24 and 48 h after injection. The 48 h images may be needed when there is significant bowel activity at 24 h, which may potentially obscure lesions. Four-hour images may be obtained to enable evaluation before appearance of activity in the gut, but since tumor-to-background ratio is lower at 4 h than at 24 and 48 h, some lesions may be missed at 4 h.
   3. Planar images are acquired using a large-field-of-view gamma camera fitted with a medium-energy collimator. Symmetrical 20% energy windows are centered over both photopeaks of ^{111}In (173 and 247 keV) and the data from both windows are added. Planar localized images of the head, chest, abdomen, pelvis, and, if needed, the extremities can be acquired for 10–15 min/image, using a 512 × 512 word matrix or 256 × 256 word matrix. Occasionally, images may be required in areas with low tracer activity. If this is the case, images should be acquired in a suitable byte mode acquisition matrix. For whole-body images using a dual-head camera, it is suggested that anterior and posterior images be acquired into a 1024 × 512 word matrix or 1024 × 256 word matrix for a minimum of 30 min (head to upper femurs) and longer for the entire body (e.g., a speed of 3 cm/min has been suggested) in a single pass. Since cervical lymph node metastases may be missed on the whole-body images, additional planar localized images of the head and neck, including lateral views, are suggested.

SPECT imaging of the appropriate regions, as indicated based on the clinical history, should be performed preferably with a multi-detector gamma

camera. Early and delayed SPECT may be helpful in distinguishing bowel activity from pathological lesions. If only one SPECT acquisition is obtained, acquisition at 24 h is preferred because of higher target-to-background ratio.

Although imaging systems may vary, an example of potentially useful acquisition parameters for a multi-detector system are the following: 3° angular sampling, 128 × 128 matrix, 360° rotation, 20–30 s/stop.

For more information see the *Society of Nuclear Medicine Procedure Guideline for General Imaging*.

F. Interventions

None

G. Processing

See the *Society of Nuclear Medicine Procedure Guideline for General Imaging.*

In general, SPECT raw data are prefiltered using an appropriate low-pass filter, with the order and frequency set according to local preferences and software manufacturer recommendations. The data are then reconstructed using a ramp filter and attenuation correction. Newer systems may include iterative reconstruction algorithms, which may eliminate some of the artifacts seen with filtered backprojection in areas adjacent to intense tracer activity.

H. Interpretation Criteria

1. When possible, images should be evaluated in conjunction or fused with relevant anatomic images (e.g., CT or MRI).
2. The optimal time interval to localize tumors is at 24 h after injection or later. At 4 h the background activity may be high. Nevertheless, early images may be important for comparison and evaluation of abdominal activity imaged at 24 h.
3. Images are best viewed at the computer display with individualized physician-directed optimization of intensity and contrast. Three-dimensional rendering of the SPECT data and its review in cinematic display is encouraged.
4. Knowledge of normal tissue accumulation of ^{111}In-pentetreotide is important for study interpretation. This radiotracer is seen in the pituitary, thyroid, liver, spleen, kidneys, bladder, and occasionally the gallbladder. Intestinal activity is usually not present at 4 h, but may be present at 24 h; images at 48 h may be necessary to clarify abdominal activity.
5. *Islet cell tumors:* Peptide hormone-producing endocrine tumors of the pancreas and gastrointestinal tract and their metastases, including gastrinomas, insulinomas, vasoactive intestinal polypeptide-secreting tumors, and glucagonomas, as well as nonfunctioning islet cell tumors, may be imaged with ^{111}In-pentetreotide. The sensitivity for these lesions is 75%–100% except for insulinoma, where it may be as low as 50%–60%, because of the presence of different somatostatin receptor subtypes on this tumor.
6. *Pheochromocytomas, neuroblastomas, and paragangliomas:* The advantage of somatostatin receptor scintigraphy with ^{111}In-pentetreotide is the ability to detect primary lesions and metastases in unexpected (extra-adrenal) sites not investigated by CT or MRI. Tumors in the adrenal glands may be difficult to detect because of high renal activity; imaging with ^{131}I- or ^{123}I-metaiodobenzylguanidine may be preferable for tumor localization in the adrenal area. The sensitivity of ^{111}In-pentetreotide for these tumors is over 85%.
7. *Medullary thyroid carcinoma:* The sensitivity of ^{111}In-pentetreotide scintigraphy may be lower than for other tumors (65%–70%). Comparison with ^{99m}Tc sulfur colloid scintigraphy for liver metastases or with ^{123}I scintigraphy for intrathyroidal tumors may increase the rate of lesion detection, especially when the uptake of ^{111}In-pentetreotide in these organs is homogeneous.
8. *Carcinoid:* The overall sensitivity of ^{111}In-pentetreotide scintigraphy is approximately 86%–95%. For extrahepatic lesions, sensitivity for lesions over 1 cm in diameter may exceed 90%; however, hepatic lesions may be isointense. SPECT imaging of the liver is recommended even if the planar images appear normal.
9. *Intracranial tumors:* Meningiomas are rich in somatostatin receptors and are therefore highly detectable. ^{111}In-pentetreotide scintigraphy may be used for postoperative follow-up of this tumor. Grade I and II astrocytomas are also somatostatin receptor–positive, grade III astrocytomas may or may not be, whereas grade IV (glioblastoma multiforme) is typically somatostatin receptor–negative. Localization of ^{111}In-pentetreotide in an astrocytoma also requires that the blood–brain barrier be impaired.
10. *Lung carcinoma:* The sensitivity for primary sites of disease is reported to be 80%–100% for small cell lung cancer, and it may be lower for non–small cell lung cancer.

I. Reporting

In addition to the general information to be provided in each Nuclear Medicine report as recommended in the *Society of Nuclear Medicine Guideline on General Imaging* (Section VI.D), it is suggested that the report contain the following information:

1. *Indication:* Results of laboratory tests (e.g., neuroendocrine tumor markers if applicable), or results of other imaging studies as well as other relevant history (known tumor and its type, recent radiation therapy, and chemotherapy).

2. *Relevant medications:* For example, octreotide therapy and, when stopped, chemotherapy and/or laxatives, if given.
3. *Procedure description:* Timing of imaging relative to radiopharmaceutical administration; areas imaged; whether SPECT was performed and, if so, its timing and body areas included.
4. *Study limitations:* The referring physician may be reminded that some tumors may lack somatostatin receptors or the appropriate receptor subtypes and, therefore, may not be detected. The differential diagnosis should consider the many potential causes for a false-positive study, as listed in Section IV.K.1.

J. Quality Control
1. Before the administration of ^{111}In-pentetreotide, the labeling yield of the radiopharmaceutical should be tested according to the manufacturer's instructions. The product should not be used if radiochemical purity is less than 90%.
2. The radiopharmaceutical should be used within 6 h of preparation.
3. ^{111}In-pentetreotide should be inspected visually before administration. Preparations containing particulate matter or color should not be administered.

K. Sources of Error
1. Potential causes for a false-positive interpretation:
   a. Accumulation of ^{111}In-pentetreotide in the nasal and pulmonary hilar areas can be seen with respiratory infections.
   b. Diffuse pulmonary or pleural accumulation of ^{111}In-pentetreotide can be observed after radiation therapy to the lung or bleomycin therapy.
   c. The tracer may accumulate at recent surgical and colostomy sites.
   d. Accumulation of the tracer in normal structures (pituitary, thyroid, liver, spleen, kidneys, bowel, gallbladder, ureters, bladder, or stimulated adrenal glands) and in multiple disorders (some listed in Section II) must be kept in mind. Caution must be used to avoid interpreting physiologic gallbladder activity as hepatic metastasis.
2. Potential causes for a false-negative interpretation:
   a. Presence of unlabeled somatostatin, either as a result of octreotide therapy or because production of somatostatin by the tumor itself may lower tumor detectability; however, there are also literature reports of improved tumor-to-background ratio after pretreatment with nonradioactive octreotide.
   b. Different somatostatin receptor subtypes have different affinities for the radioligand; variable tumor differentiation/receptor expression also influences tumor detectability. This is a consideration, especially with insulinomas and medullary thyroid carcinomas.
   c. Liver metastases of neuroendocrine tumors may appear isointense because of a similar degree of tracer accumulation by the normal liver. Correlation with anatomic imaging or subtraction scintigraphy with sulfur colloid may be considered.

PART V: ISSUES REQUIRING FURTHER CLARIFICATION

1. Because ^{111}In-pentetreotide elimination in patients with impaired renal function has not been studied, possible dosage adjustment in these patients needs to be clarified.
2. The role of ^{111}In-pentetreotide scintigraphy in breast carcinoma, renal cell carcinoma, Hodgkin's and non-Hodgkin's lymphoma, and other tumors (see Section II), as well as in the evaluation and management of some granulomatous and autoimmune processes (e.g., activity of sarcoidosis, response of Graves' ophthalmopathy to steroids, etc.) is yet to be determined.
3. This procedure guideline only covers imaging with ^{111}In-pentetreotide. Imaging with other somatostatin analogs (e.g., ^{99m}Tc-depreotide) is not a subject of this guideline.

PART VI: CONCISE BIBLIOGRAPHY

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PART VII: 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.

PART VIII: LAST HOUSE OF DELEGATES APPROVAL DATE

February 11, 2001

PART IX: NEXT ANTICIPATED APPROVAL DATE

2004–2005

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