

ENETS Consensus Guidelines for the Standards of Care in Neuroendocrine Tumors: Somatostatin Receptor Imaging with ¹¹¹In-Pentetreotide

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Introduction

The purpose of this guideline is to assist nuclear medicine practitioners in performing, interpreting, and reporting the results of somatostatin receptor scintigraphy with ¹¹¹In-pentetreotide. It is not this guideline's aim to give recommendations on the use of PET tracers for somatostatin receptor imaging (SRI). The reason for this is that valid comparisons between state of the art SRI with ¹¹¹In-pentetreotide and these newer PET imaging methods are lacking, and that these newer methods have not been fully validated. Besides, because of the local production of PET radiopharmaceuticals and the diversity of peptide analogs that are applied, each with a different affinity profile and therefore potentially a different biodistribution and a different tumor detection sensitivity, it is virtually impossible to make guidelines for the application of these PET radiopharmaceuticals. The general recommendations on patient preparation and image interpretation, however, do apply. This guideline is adapted from the procedure guideline for somatostatin receptor

scintigraphy with ¹¹¹In-pentetreotide, published by the Society of Nuclear Medicine [1]. ^{99m}Tc-Depreotide (Neotect[®]) is another commercially available somatostatin analog that has been approved specifically for the detection of lung cancer in patients with pulmonary nodules [2]. Because of the relatively high abdominal background and the impossibility of performing delayed imaging due to the short half-life of the tracer, it is less suited for the detection of abdominal neuroendocrine tumors [3].

Somatostatin is a regulatory peptide widely distributed in the human body, in particular in the central and peripheral nervous system, in the endocrine glands, in the immune system as well as in the gastrointestinal tract. In all these tissues, somatostatin action is mediated through membrane-bound receptors, of which five have been cloned (sst1–sst5) [4]. They all belong to the family of G-protein-coupled receptors. Only sst2, sst5 and, to some extent, sst3 have a high affinity for the commercially available synthetic octapeptide octreotide [5]. Somatostatin receptors are expressed in several normal human tissues, including brain, pituitary, gastrointestinal

Table 1. Sensitivity of SRI using pentetretotide*High sensitivity*

Pituitary tumors [14]
GEPNETs
 Gastrinomas [15, 16]
 Nonfunctioning endocrine pancreatic tumors [17, 18]
 Functioning endocrine pancreatic tumors except insulinomas [17, 18]
 Carcinoids [19–22]
Parangliomas [23–25]
Small cell lung cancer [26–29]
Meningiomas [30, 31]
Sarcoidosis and other granulomatous diseases [12, 32]
Graves' disease and Graves' ophthalmopathy [33, 34]

Intermediate sensitivity

Insulinomas [17, 35]
Medullary thyroid carcinoma [36–38]
Differentiated thyroid carcinoma
 (including Hurthle cell carcinoma) [39–41]
Breast cancer [42]
Lymphoma (NHL, HL) [43, 44]
Pheochromocytoma [45]
Astrocytoma [31]

High sensitivity = Detection rate >75%; intermediate sensitivity = detection rate 40–75%. Sensitivity is either patient- or lesion-based. GEPNET = Gastroenteropancreatic neuroendocrine tumor; NHL = non-Hodgkin's lymphoma; HL = Hodgkin's lymphoma.

tract, pancreas, thyroid, spleen, kidney, immune cells, vessels and peripheral nervous system [6–9].

Somatostatin receptors have been identified *in vitro* in a large number of human neoplasias. A high incidence and density of somatostatin receptors are found in particular in neuroendocrine tumors, such as pituitary adenoma, pancreatic islet cell tumor, carcinoid, pheochromocytoma, paraganglioma, medullary thyroid cancer and small cell lung carcinoma [10]. Tumors of the nervous system including meningioma, neuroblastoma and medulloblastoma also very often express a high density of somatostatin receptors. But also tumors not known to classically originate from endocrine or neural cells, such as lymphoma, breast cancer, renal cell cancer, hepatocellular cancer, prostate cancer, sarcoma and gastric cancer can express somatostatin receptors. In the majority of these tumors, the sst2 receptor subtype is predominantly expressed, although low amounts of other somatostatin receptor subtypes may be concomitantly present [11]. It should also be emphasized that selected non-tumoral lesions may express somatostatin receptors. For instance,

active granulomas in sarcoidosis express somatostatin receptors on epithelioid cells [12] and inflamed joints in active rheumatoid arthritis express somatostatin receptors, preferentially located in the proliferating synovial vessels [13]. The expression of somatostatin receptor is therefore not specific for tumoral pathologies.

Imaging Results in Neuroendocrine and Other Tumors

Imaging results in tumors and other diseases are listed and subdivided according to reported sensitivity of SRI in table 1.

Normal Scintigraphic Findings and Artifacts

Normal scintigraphic features include visualization of the thyroid, spleen, liver, and kidneys, and the pituitary in some of the patients. Also, the urinary bladder and bowel are usually visualized to variable degrees. The visualization of the pituitary, thyroid, and spleen is due to receptor binding. Uptake in the kidneys is for the most part due to re-absorption of the radiolabeled peptide in the renal tubular cells after glomerular filtration. There is predominant renal clearance of the somatostatin analog, although hepatobiliary clearance into the bowel also occurs, necessitating the use of laxatives in order to facilitate the interpretation of abdominal images.

False-positive results of SRI have been reported. In virtually all cases the term 'false-positive' is a misnomer because somatostatin receptor-positive lesions that are not related to the pathology for which the investigation is performed, are present. Many of these have been reviewed by Gibril et al. [46]. The most common of these are listed in table 2 (which is not exhaustive).

Diminished uptake in the spleen due to ongoing treatment with (unlabeled) octreotide may occur, which may be accompanied by a lower liver uptake. In case of hepatic metastases, this phenomenon may be misinterpreted as a better uptake in liver metastases. During octreotide treatment, the uptake of [¹¹¹In-DTPA⁰]-octreotide in somatostatin receptor-positive tumors is also diminished. This may lead to a lower detection rate of somatostatin receptor-positive lesions, although there are also literature reports of improved tumor-to-background ratio after pretreatment with nonradioactive octreotide. A number of causes for a potential false-negative study interpretation are given in table 3.

Common Indications

- Detection and localization of a variety of neuroendocrine and other tumors and their metastases
- Staging patients with neuroendocrine tumors
- Follow-up of patients with known disease to evaluate potential recurrence
- Selection of patients with metastatic tumors for peptide receptor radionuclide therapy and prediction of the effect of peptide receptor radionuclide therapy

Procedure

Patient Preparation

- When appropriate and clinically feasible, therapy with short-acting somatostatin analogs should be discontinued for 24 h before ¹¹¹In-pentetreotide administration. Such therapy can be resumed the day after injection of the radiopharmaceutical. Long-acting preparations should preferably be stopped 5–6 weeks before the study, and patients should be switched to short-acting formulations up to 1 day before the study. In follow-up studies, it may be more convenient to plan the injection of the radiopharmaceutical just before a new administration of the long-acting formulation is due. The reader should be aware that in such a condition, tumor and spleen uptake may be diminished due to receptor occupancy
- To reduce radiation exposure, patients should be well hydrated before and for at least 1 day after injection
- Laxatives are advised, especially when the abdomen is the area of interest. A mild oral laxative 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
- There is no need for fasting prior to the investigation
- The feasibility of the investigation in patients on hemodialysis (with imaging after dialysis) should be discussed with local nephrologists and radiation protection experts

Precautions

- In patients suspected of having insulinoma, an intravenous infusion of glucose should be available because of the potential for inducing severe hypoglycemia

Table 2. Pitfalls and causes of potential misinterpretation of positive results

Radiation pneumonitis
Accessory spleen
Focal collection of stools
Surgical scar tissue
Gallbladder uptake
Nodular goiter
Ventral hernia
Bacterial pneumonia
Respiratory infections
Common cold (nasal uptake)
Cerebrovascular accident
Concomitant granulomatous disease
Diffuse breast uptake
Adrenal uptake
Urine contamination
Concomitant second primary tumor

Table 3. Causes of potential misinterpretation of negative results

Presence of unlabeled somatostatin, either because of octreotide therapy or resulting from production of somatostatin by the tumor itself, may lower tumor detectability

Different somatostatin receptor subtypes have different affinities for the radioligand; variable tumor differentiation and receptor expression also influence tumor detectability. This may be important especially in patients with insulinomas and medullary thyroid carcinomas

Liver metastases of neuroendocrine tumors may appear iso-intense because of a similar degree of tracer accumulation by the normal liver. Correlation with anatomic imaging and/or SPECT imaging may be helpful

- ¹¹¹In-pentetreotide should not be injected into intravenous lines for or together with solutions for total parenteral nutrition
- The usual precautions and considerations for nuclear medicine investigations in pregnant or breastfeeding women apply

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

Radiopharmaceutical

- ^{111}In -pentetreotide is a [^{111}In -DTPA⁰] conjugate of octreotide, a somatostatin analog (OctreoScan). The recommended administered activity is 185–222 MBq (5–6 mCi) in adults and 5 MBq/kg (0.14 mCi/kg) in children. The amount of pentetreotide injected is 10–20 μg ; this dose is not expected to have a clinically significant pharmacologic effect. ^{111}In -pentetreotide is cleared rapidly from the blood. 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
- The effective dose equivalent is 0.054 mSv/MBq. For a full patient dose of 222 MBq this is 12 mSv
- Before the administration of ^{111}In -pentetreotide, the labeling yield of the radiopharmaceutical should be tested according to the manufacturer's instructions
- The radiopharmaceutical should be used within 6 h of preparation
- ^{111}In -pentetreotide should be inspected visually before administration. Preparations containing particulate matter or color should not be administered

Image Acquisition

- Patients should void before imaging
- Images are acquired at 4 and 24 h or 24 and 48 h after injection. The 48-hour 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 the tumor-to-background ratio is lower at 4 h than at 24 and 48 h, some lesions may be missed at 4 h
- 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. For whole-body images using a dual-head camera, acquisition should be for a minimum of 30 min (head to upper femurs) and longer for the entire body (e.g., a speed of up to 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 per-

formed preferably with a multi-detector gamma camera. Early and delayed SPECT (i.e. 4 and 24 h after injection) 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 a 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

Interpretation Criteria

- When possible, images should be evaluated in conjunction or fused with relevant anatomic images (e.g., CT or MRI)
- The optimal time interval to localize tumors is 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
- 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

Reporting

- In addition to the general information to be provided in each nuclear medicine report, it is suggested that the report contain the following information
- *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)
- *Relevant medications:* For example, octreotide therapy and, when stopped, chemotherapy and/or laxatives, if given
- *Procedure description:* Timing of imaging relative to radiopharmaceutical administration; areas imaged; whether SPECT was performed and, if so, its timing and body areas included
- *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 table 2

List of Participants

List of Participants of the Consensus Conference on the ENETS Guidelines for the Standard of Care for the Diagnosis and Treatment of Neuroendocrine Tumors, Held in Palma de Mallorca (Spain), November 28 to December 1, 2007

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References

- 1 Balon HR, Goldsmith SJ, Siegel BA, Silberstein EB, Krenning EP, Lang O, Donohoe KJ: Procedure guideline for somatostatin receptor scintigraphy with ¹¹¹In-pentetreotide. *J Nucl Med* 2001;42:1134–1138.
- 2 Menda Y, Kahn D: Somatostatin receptor imaging of non-small lung cancer with ^{99m}Tc depreotide. *Semin Nucl Med* 2002;32:92–96.
- 3 Lebtahi R, Le Cloirec J, Houzard C, et al: Detection of neuroendocrine tumors: (99m)Tc-829 scintigraphy compared with (111)In-pentetreotide scintigraphy. *J Nucl Med* 2002; 43:889–895.
- 4 Patel YC, Greenwood MT, Warszynska A, Panetta R, Srikant CB: All five cloned somatostatin receptors (hSSTR1–5) are functionally coupled to adenylyl cyclase. *Biochem Biophys Res Commun* 1994;198:605–612.
- 5 Hoyer D, Epelbaum J, Feniuk W, et al: Somatostatin receptors; in Girdlestrom D (ed): *The IUPHAR Compendium of Receptor Characterization and Classification*. London, IUPHAR Media, 2000, pp 354–364.
- 6 Sreedharan SP, Kodama KT, Peterson KE, Goetzl EJ: Distinct subsets of somatostatin receptors on cultured human lymphocytes. *J Biol Chem* 1989;264:949–953.
- 7 Reubi JC, Horisberger U, Waser B, Gebbers JO, Laissue J: Preferential location of somatostatin receptors in germinal centers of human gut lymphoid tissue. *Gastroenterology* 1992;103:1207–1214.
- 8 Reubi JC, Schaefer JC, Markwalder R, Waser B, Horisberger U, Laissue JA: Distribution of somatostatin receptors in normal and neoplastic human tissues: recent advances and potential relevance. *Yale J Biol Med* 1997;70: 471–479.
- 9 Csaba Z, Dournaud P: Cellular biology of somatostatin receptors. *Neuropeptides* 2001; 35:1–23.

- 10 Reubi JC: Regulatory peptide receptors as molecular targets for cancer diagnosis and therapy. *Q J Nucl Med* 1997;41:63–70.
- 11 Reubi JC, Waser B, Schaer JC, Laissue JA: Somatostatin receptor sst1-ss5 expression in normal and neoplastic human tissues using receptor autoradiography with subtype-selective ligands. *Eur J Nucl Med* 2001;28:836–846.
- 12 Vanhagen PM, Krenning EP, Reubi JC, et al: Somatostatin analogue scintigraphy in granulomatous diseases. *Eur J Nucl Med* 1994;21:497–502.
- 13 Reubi JC, Waser B, Krenning EP, Markusse HM, Vanhagen M, Laissue JA: Vascular somatostatin receptors in synovium from patients with rheumatoid arthritis. *Eur J Pharmacol* 1994;271:371–378.
- 14 Kwekkeboom DJ, de Herder WW, Krenning EP: Receptor imaging in the diagnosis and treatment of pituitary tumors. *J Endocrinol Invest* 1999;22:80–88.
- 15 De Kerviler E, Cadiot G, Lebtahi R, Faraggi M, Le Guludec D, Mignon M: Somatostatin receptor scintigraphy in forty-eight patients with the Zollinger-Ellison syndrome. *Eur J Nucl Med* 1994;21:1191–1197.
- 16 Gibril F, Reynolds JC, Doppman JL, et al: Somatostatin receptor scintigraphy: its sensitivity compared with that of other imaging methods in detecting primary and metastatic gastrinomas. A prospective study. *Ann Intern Med* 1996;125:26–34.
- 17 Krenning EP, Kwekkeboom DJ, Bakker WH, et al: Somatostatin receptor scintigraphy with [¹¹¹In-DTPA-D-Phe¹]- and [¹²³I-Tyr³]-octreotide: the Rotterdam experience with more than 1,000 patients. *Eur J Nucl Med* 1993;20:716–731.
- 18 Lebtahi R, Cadiot G, Sarda L, et al: Clinical impact of somatostatin receptor scintigraphy in the management of patients with neuroendocrine gastroenteropancreatic tumors. *J Nucl Med* 1997;38:853–858.
- 19 Kwekkeboom DJ, Krenning EP, Bakker WH, et al: Somatostatin analogue scintigraphy in carcinoid tumors. *Eur J Nucl Med* 1993;20:283–292.
- 20 Kalkner KM, Janson ET, Nilsson S, Carlsson S, Oberg K, Westlin JE: Somatostatin receptor scintigraphy in patients with carcinoid tumors: comparison between radioligand uptake and tumor markers. *Cancer Res* 1995;55(suppl 23):5801–5804.
- 21 Westlin JE, Janson ET, Arnberg H, Ahlstrom H, Oberg K, Nilsson S: Somatostatin receptor scintigraphy of carcinoid tumours using the [¹¹¹In-DTPA-D-Phe¹]-octreotide. *Acta Oncol* 1993;32:783–786.
- 22 Ahlman H, Wängberg B, Tisell LE, Nilsson O, Fjälling M, Forssell-Aronsson E: Clinical efficacy of octreotide scintigraphy in patients with midgut carcinoid tumours and evaluation of intraoperative scintillation detection. *Br J Surg* 1994;81:1144–1149.
- 23 Kwekkeboom DJ, Van Urk H, Pauw KH, et al: Octreotide scintigraphy for the detection of paragangliomas. *J Nucl Med* 1993;34:873–878.
- 24 Telischi FF, Bustillo A, Whiteman ML, Serafini AN, Reisberg MJ, Gomez-Marin O, Civantos J, Balkany TJ: Octreotide scintigraphy for the detection of paragangliomas. *Otolaryngol Head Neck Surg* 2000;122:358–362.
- 25 Duet M, Sauvaget E, Pételle B, Rizzo N, Guichard JP, Wassef M, Le Cloirec J, Herman P, Tran Ba Huy P: Clinical impact of somatostatin receptor scintigraphy in the management of paragangliomas of the head and neck. *J Nucl Med* 2003;44:1767–1774.
- 26 Kwekkeboom DJ, Kho GS, Lamberts SW, Reubi JC, Laissue JA, Krenning EP: The value of octreotide scintigraphy in patients with lung cancer. *Eur J Nucl Med* 1994;21:1106–1113.
- 27 Bombardieri E, Crippa F, Cataldo I, et al: Somatostatin receptor imaging of small cell lung cancer (SCLC) by means of ¹¹¹In-DTPA octreotide scintigraphy. *Eur J Cancer* 1995;31A:184–188.
- 28 Reisinger I, Bohuslavitzki KH, Brenner W, et al: Somatostatin receptor scintigraphy in small-cell lung cancer: results of a multicenter study. *J Nucl Med* 1998;39:224–227.
- 29 Kirsch CM, von Pawel J, Grau I, Tatsch K: Indium-111 pentetreotide in the diagnostic work-up of patients with bronchogenic carcinoma. *Eur J Nucl Med* 1994;21:1318–1325.
- 30 Haldemann AR, Rosler H, Barth A, et al: Somatostatin receptor scintigraphy in central nervous system tumors: role of blood-brain barrier permeability. *J Nucl Med* 1995;36:403–410.
- 31 Schmidt M, Scheidhauer K, Luyken C, et al: Somatostatin receptor imaging in intracranial tumours. *Eur J Nucl Med* 1998;25:675–686.
- 32 Kwekkeboom DJ, Krenning EP, Kho GS, Breeman WAP, Van Hagen PM: Octreotide scintigraphy in patients with sarcoidosis. *Eur J Nucl Med* 1998;25:1284–1292.
- 33 Postema PTE, Krenning EP, Wijngaarde R, et al: [¹¹¹In-DTPA-D-Phe¹]-octreotide scintigraphy in thyroidal and orbital Graves' disease: a parameter for disease activity? *J Clin Endocrinol Metab* 1994;79:1845–1851.
- 34 Krassas GE, Dumas A, Pontikides N, Kaltsas T: Somatostatin receptor scintigraphy and octreotide treatment in patients with thyroid eye disease. *Clin Endocrinol (Oxf)* 1995;42:571–580.
- 35 Zimmer T, Stolzel U, Bader M, et al: Endoscopic ultrasonography and somatostatin receptor scintigraphy in the preoperative localisation of insulinomas and gastrinomas. *Gut* 1996;39:562–568.
- 36 Kwekkeboom DJ, Reubi JC, Lamberts SWJ, et al: In vivo somatostatin receptor imaging in medullary thyroid carcinoma. *J Clin Endocrinol Metab* 1993;76:1413–1417.
- 37 Tisell LE, Ahlman H, Wängberg B, et al: Somatostatin receptor scintigraphy in medullary thyroid carcinoma. *Br J Surg* 1997;84:543–547.
- 38 Adams S, Baum RP, Hertel A, Schumm-Draeger PM, Usadel KH, Hör G: Comparison of metabolic and receptor imaging in recurrent medullary thyroid carcinoma with histopathological findings. *Eur J Nucl Med* 1998;25:1277–1283.
- 39 Postema PTE, De Herder WW, Reubi JC, et al: Somatostatin receptor scintigraphy in non-medullary thyroid cancer. *Digestion* 1996;1(suppl):36–37.
- 40 Gulec SA, Serafini AN, Sridhar KS, et al: Somatostatin receptor expression in Hurthle cell cancer of the thyroid. *J Nucl Med* 1998;39:243–245.
- 41 Haslinghuis LM, Krenning EP, de Herder WW, Reijs AEM, Kwekkeboom DJ: Somatostatin receptor scintigraphy in the follow-up of patients with differentiated thyroid cancer. *J Endocrinol Invest* 2001;24:415–422.
- 42 Van Eijck CH, Krenning EP, Bootsma A, et al: Somatostatin-receptor scintigraphy in primary breast cancer. *Lancet* 1994;343:640–643.
- 43 Lugtenburg PJ, Lowenberg B, Valkema R, et al: Somatostatin receptor scintigraphy in the initial staging of low-grade non-Hodgkin's lymphomas. *J Nucl Med* 2001;42:222–229.
- 44 Lugtenburg PJ, Krenning EP, Valkema R, et al: Somatostatin receptor scintigraphy useful in stage I–II Hodgkin's disease: more extended disease identified. *Br J Haematol* 2001;112:936–944.
- 45 Van der Harst E, de Herder WW, Bruining HA, et al: [(123)I]metaiodobenzylguanidine and [(111)In]octreotide uptake in benign and malignant pheochromocytomas. *J Clin Endocrinol Metab* 2001;86:685–693.
- 46 Gibril F, Reynolds JC, Chen CC, et al: Specificity of somatostatin receptor scintigraphy: a prospective study and effects of false-positive localizations on management in patients with gastrinomas. *J Nucl Med* 1999;40:539–553.