SPECT-CT in Neuroendocrine Tumours – a Clinical Overview

D. Piciu, Cluj-Napoca (RO)

Neuroendocrine malignant tumors (NET), defined as epithelial neoplasms with predominant neuroendocrine differentiation, arise in most organs of the body. Despite that NET are considered rare cancers, for diagnostic and treatment there is an endless effort. The system of classification and nomenclature is depending on the site of the tumor and also of the differentiation grade. These tumors might be functionally active tumors, with the symptoms due to the excessive hormone release from the tumor cells or functionally inactive tumors (expressed as mass effect). The symptoms are related to the origin of the tumors (hypoglycemia, peptic ulcer disease, diarrhea, necrotic skin rush, flush, rush, sweat, cardio-vascular effects etc.).

Imaging studies for NET are generally performed for an initial evaluation of the extent of the disease and subsequent follow-up. The goals for the initial evaluation include the identification of the primary tumor, staging and treatment planning. Subsequent follow-up imaging studies are performed for the surveillance after complete resection or during periods of stability and evaluation of response after the treatment. SPECT-CT using radiolabeled tracers has a major role in this protocol due to the specificity of the molecules used and to the systemic approach.

The primary treatment of NET is surgery with curative intent. In 80% of patients with NET for whom this is impossible, alternatives such as external beam radiation therapy or chemotherapy are suboptimal because these well-differentiated tumors are relatively unresponsive. Most of these tumors express somatostatin receptors, especially subtype 2, in high abundance, which very rapidly bind and internalize targeted peptides. Somatostatin acts through interaction with receptors expressed on the surface of cells; five subtypes have been characterized and named somatostatin receptor subtype 1-5 (SSTR1-5).

The octreotide is a somatostatin analogue. Octreotide was derivatized with diethylenetriaminepentaacetic acid (DTPA) on the amine terminus. Attaching this chelate to the peptide allowed radiolabelling of the molecule with In-111. Following that step, with the aim to find the best agent for therapy, the chelating agent, DTPA was substituted with DOTA (tetra-aza-cyclo dodecanetetraacetic acid), which enabled the radiolabelling of this conjugate with Y-90, Lu-177 or other radionuclides. The perspective of new therapies for NET using radioisotopes is an optimistic one, due to extensive researcher performed in the last decade. The goal of each treatment protocol in oncology is to be highly specific and systemic. The treatment performed by using the radiolabeled somatostatin analogues in the therapy of NET is very close to this goal.

Further readings

1. Asnacios A, Courbon F, Rochaix P et al (2008) Indium-111-pentetreotide scintigraphy and somatostatin receptor subtype 2 expression: new prognostic factors for malignant well-differentiated endocrine tumours. J Clin Oncol 26(6): 963–970.
2. Bombardieri E, Ambrosini V, Aktolun C et al (2010) 111In-pentetreotide scintigraphy: procedure guidelines for tumour imaging. Eur J Nucl Med Mol Imaging 37:1441–1448 DOI 10.1007/s00259-010-1473-6.
3. Buchmann I, Henze M, Engelbrecht S (2007) Comparison of 68Ga-DOTATOC PET and 111In-DTPAOC (Octreoscan) SPECT in patients with neuroendocrine tumours. Eur J Nucl Med Mol Imaging 34(10): 1617-1626.
4. EANM procedure guidelines for 131I-meta iodobenzylguanidine (131I-mIBG) therapy. Eur J Nucl Med Mol Imaging (2008) 35:1039–1047 DOI 10.1007/s00259-008-0715-3.
5. Forrer F Krenning EP, Kooij PP et al (2009) Bone marrow dosimetry in peptide receptor radionuclide therapy with [177Lu-DOTA(0),Tyr(3)]octreotate. Eur J Nucl Med Mol Imaging 36(7): 1138-1146.

6. Klimstra DS, Modlin IR, Coppola D et al (2010) The Pathologic Classification of Neuroendocrine Tumours: A Review of Nomenclature, Grading, and Staging Systems. DOI: 10.1097/MPA.0b013e3181ec124e.
7. Kwekkeboom DJ, Krenning EP, Scheidhauer K et al (2009) ENETS Consensus Guidelines for the Standards of Care in Neuroendocrine Tumours: somatostatin receptor imaging with (111) In-pentetreotide. Neuroendocrinology 90:184-189.
8. Modlin IM, Oberg K, Chung DC et al (2008) Gastroenteropancreatic neuroendocrine tumours. Lancet Oncol. 9(1): 61-72. Review. PubMed PMID: 18177818.
9. Nicolas G, Giovacchini G, Müller-Brand J et al (2011) Targeted radiotherapy with radiolabeled somatostatin analogs. Endocrinol Metab Clin North Am. 40(1): 187-204, Review. PubMed PMID: 21349419.
10. Vinik A, Woltering EA, Warner RRP et al (2010) NANETS Consensus Guidelines for the Diagnosis of Neuroendocrine Tumour DOI: 10.1097/MPA.0b013e3181ebaffd.
11. Virgolini I, Ambrosini V, Bomanji BJ et al (2010) Procedure Guidelines For PET/CT Tumour Imaging with 68Ga-DOTA- conjugated peptides: 68Ga-DOTA-TOC, 68Ga-DOTA-NOC, 68Ga-DOTA-TATE.
12. Wong KK, Cahill JM, Frey KA et al (2010) Incremental value of 111-In pentetreotide SPECT/CT fusion imaging of neuroendocrine tumours. Acad Radiol 17: 291–297.