Novel Functional Imaging of Neuroendocrine Tumors

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KEYWORDS

• ^{68}Ga-Dota-toc • ^{68}Ga-Dota-tate • ^{68}Ga-Dota-noc, ^{18}FDG • ^{18}F-Dopa
• ^{11}C-5-hydroxy-tryptophan

KEY POINTS

- ^{68}Ga-DOTA-somatostatin analogue-PET/computed tomography constitutes an integral part in neuroendocrine tumor visualization and is especially advantageous to detect metastases to lymph nodes, bone, liver, peritoneum, and brain.
- PET/computed tomography should be performed together with diagnostic intravenous contrast-enhanced computed tomography to take full advantage of the technique.
- Similarly, MRI with PET/MRI should use dynamic intravenous contrast enhancement of the liver and pancreas and whole-body diffusion-weighted imaging.
- MRI is superior to computed tomography for neuroendocrine tumor imaging of liver, pancreas, brain, and bone, but may miss small lung metastases, which are best visualized by computed tomography.

INTRODUCTION

Imaging of neuroendocrine tumors (NETs) is based on the combination of morphologic (radiologic) and functional (nuclear medicine) techniques because they provide complementary information (**Box 1**). Functional imaging with modern scanners can currently be performed as hybrid imaging procedures, whereby PET and single photon emission computed tomography (SPECT) are performed together with computed tomography (CT) scan as PET/CT scan and SPECT/CT scanning, and in recent years also PET/MRI. Hybrid procedures generally achieve a better imaging yield, as compared with separate interpretation of morphologic and functional imaging, and additionally improve reader confidence. Because conventional radiologic cross-sectional methods (CT scanning and MRI) constitute the basis for NET imaging and because the quality of both components is crucial for the result of hybrid imaging (PET/CT scanning and PET/MRI), this article concentrates on the functional

Disclosure: The author has nothing to disclose.
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Endocrinol Metab Clin N Am ■ (2018) ■–■
https://doi.org/10.1016/j.ecl.2018.04.003 **endo.theclinics.com**

Box 1
Points of interest

- NET imaging should always use a combination of morphologic and functional whole-body imaging.
- In low grade NETs, somatostatin receptor imaging with ^{68}Ga-DOTA-somatostatin analogue-PET/CT is preferred to scintigraphy because of the vastly superior performance of PET/CT.
- In high-grade NETs, somatostatin receptor expression is usually low or absent and metabolic imaging with ^{18}FDG-PET/CT is, therefore, preferred.
- Above a suggested approximate 15% KI-67 cutoff, metabolic imaging with ^{18}FDG-PET/CT is usually preferred rather than ^{68}Ga-DOTA-somatostatin analogue-PET/CT because of the risk of low or absent somatostatin receptor expression in the NET lesions.
- A combination of ^{68}Ga-DOTA-somatostatin analogue-PET/CT and ^{18}FDG-PET/CT is advantageous because high-grade NETs may show somatostatin receptor expression sufficient for PRRT and low-grade NETs may be ^{18}FDG-avid, which is a negative prognostic indication, although this policy is usually not possible because of financial constraints.
- The most commonly used ^{68}Ga-DOTA-somatostatin analogue preparations are ^{68}Ga-DOTA-TOC (tyrosine octreotide), ^{68}Ga-DOTA-TATE (octreotate) and ^{68}Ga-DOTA-NOC (1-NaI3-octreotide), with no convincingly reported differences in imaging capacity.
- ^{18}F-DOPA is an alternative PET tracer for lesion detection available in some countries.
- ^{11}C-5-hydroxy-tryptophan is yet another PET tracer; however, it has limited availability, which can be used when ^{68}Ga-DOTA-somatostatin analogue-PET/CT fails.
- For CT together with PET/CT, a fully diagnostic examination protocol should be used, including IV contrast-enhanced CT of the liver and pancreas in the late arterial phase and of the whole body in the venous phase.
- Small (<5 mm) NET lesions may be missed by PET because of its limited spatial resolution and concomitant IV contrast-enhanced CT may pick up these lesions.
- Because of the better tissue contrast, MRI is better than CT for imaging of the liver, pancreas, bone and brain, and can be considered in addition to PET/CT.
- Diffusion-weighted imaging and dynamic IV gadolinium contrast-enhanced MRI should be included for optimal NET imaging of the liver and pancreas.
- For MRI of the liver, hepatocyte-specific contrast media are available.
- PET/MRI is so far available for clinical NET imaging in merely a few centers and should use fully diagnostic whole-body MRI protocols.
- The recent development of somatostatin receptor antagonists for clinical applications hold interesting potentials for future NET hybrid imaging.

Abbreviations: CT, computed tomography; IV, intravenous; NET, neuroendocrine tumor; PRRT, peptide receptor radiotherapy.

techniques and comments on relevant details related to the concomitant morphologic imaging procedures.

Depending on how the NET patient presents with the disease, the requirements for imaging are very varying. A functioning pancreatic NET may produce pronounced hormonal symptoms and yet be very small, and for its preoperative localization several morphologic and functional imaging techniques and also endoscopy may be required. The other end of the spectrum may be represented by a patient presenting with a disseminated small intestinal NET (SI-NET) and bulky liver metastases for whom the imaging workup by comparison is straightforward and will comprise tumor staging