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EDITORIAL

Gallium-68 somatostatin receptor PET/CT: Is it time to replace ^{111}Indium DTPA octreotide for patients with neuroendocrine tumors?

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In the era of theranostics which tries to integrate some form of diagnostic testing to determine the presence of molecular targets for which a specific compound is intended, molecular imaging serves these diagnostic functions and provides powerful means for non-invasively detected disease. The reason for the tremendous excitement of theranostics is its revolutionary approach that promises improved therapy selection on the bases of specific molecular features of disease, greater predictive power for adverse effects, and new ways to objectively monitor therapy response [1]. A unique feature of neuroendocrine tumors (NETs) is the expression of different receptors on the tumor cells for peptide hormones such as somatostatin receptors as well cholecystokinin (CCK) and gastrin releasing peptide (GRP) receptors [2]. These receptors can be targeted with radiolabeled peptides for imaging and treatment. Somatostatin receptors are G-protein coupled membrane glycoproteins and at the moment five subtypes of human somatostatin receptors have been cloned (sstr 1–5). The expression of somatostatin receptor type 2 is present in 70–90 % of NETs [3]. Therefore, radioactive-labeled somatostatin analogs allow the visualization and staging of these tumors. The gold standard for detection and staging of most NETs is ^{111}Indium-DTPA-octreotide (Octreoscan®) (SRS) recently performed by co-registration with computerized tomography [4]. Nowadays, SPECT images are obtained using a triple-headed camera. ^{111}In-DTPA-octreotide can be used to visualize receptor-bearing tumors efficiently after 24 and 48 h, by which times interfering background radioactivity has been reduced by renal clearance. The sensitivity of SRS varies for different subtypes of NETs to be somewhere between 50 and 95 % [4]. There are of course limitations for lower sensitivity in some tumor types not only due to low expression of somatostatin type 2 receptors but also the size of the tumor. In clinical practice, tumors less than 1 cm in size are not detected by SRS.

The ability to tag somatostatin analogs with Gallium-68 has significantly improved the diagnosis and staging of patients with NETs [5]. Positron emission tomography is a non-invasive technique for measurement of regional accumulation and quantification of radioactive substances. The most recent PET-scanners provide 2.5-mm slices with a resolution of approximately 5 mm. Several studies have shown that Gallium-68 PET/CT or PET scanning using different radio pharmaceuticals, such as Gallium-68 DOTANOC, Gallium-68 DOTATOC, and Gallium-68 DOTATATE, are accurate methods imaging methods in the diagnosis of NETs [6–9]. In the current paper by Treglia and co-workers entitled Diagnostic performance of Gallium-68 somatostatin receptor PET and PET/CT in patients with thoracic and gastroenteropancreatic neuroendocrine tumors, a meta-analysis reports on the high specificity and sensitivity for this method [10]. A comprehensive computer literature search of studies published in Pub/Med/MEDLINE, Scopus, and Embase databases through October 2011 were analyzed to get information about the diagnostic accuracy of Gallium-68 somatostatin receptor positron emission tomography and PET/CT. Sixteen studies comprising 567 patients were included in this meta-analysis. The pooled sensitivity and specificity in detecting NETs were 93 % (95 % confidence interval:

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91–95 %) and 91 % (95 % confidence interval: 82–97 %) respectively, on a per patient-based analysis. The area under the ROC curve was 0.96. The study clearly demonstrates high sensitivity and specificity for this method. Therefore, this technique might be the gold standard and considered as first line diagnostic imaging method in patients with suspected thoracic or gastroenteropancreatic NETs. However, we are still lacking prospective randomised trials between traditional somatostatin receptor scintigraphy and Gallium-68 PET/CT scans. It must however be pointed out that there are several advantages with the Gallium-68 PET/CT technique as it is a one-stop procedure, the patient does not have to come back for scanning the next day. The isotope is produced by a generator not a cyclotron and therefore less expensive to produce. The technique can also be used to semi-calculate the number of somatostatin receptors before decision on peptide radio receptor treatment (PRRT) with ^{177}Lutetium-DOTATATE or ^{90}Yttrium-DOTATOC. The cost for Gallium-68 PET/CT will probably be less than for SRS. The current problem is that the technique is not available everywhere, but in a couple of years it will probably replace traditional somatostatin receptor scintigraphy in most centres dealing with patients suffering from NETs.

Somatostatin receptor PET/CT using Gallium-68-labeled somatostatin analogs is the most comprehensive diagnostic molecular imaging technique for neuroendocrine tumors.

References

1. D.Y. Lee, K.C. Li, Molecular theranostics: a primer for the imaging professional. AJR Am. J. Roentgenol. **197**, 318–324 (2011)
2. J.C. Reubi, B. Waser, Concomitant expression of several peptide receptors in neuroendocrine tumours: molecular basis for in vivo multireceptor tumour targeting. Eur. J. Nucl. Med. Mol. Imaging **30**, 781–793 (2003)
3. I.M. Modlin, K. Oberg, D.C. Chung, R.T. Jensen, W.W. de Herder, R.V. Thakker, M. Caplin, G. Delle Fave, G.A. Kaltsas, E.P. Krenning, S.F. Moss, O. Nilsson, G. Rindi, R. Salazar, P. Ruszniewski, A. Sundin, Gastroenteropancreatic neuroendocrine tumours. Lancet Oncol. **9**, 61–72 (2008)
4. E.P. Krenning, D.J. Kwekkeboom, W.H. Bakker, W.A. Breeman, P.P. Kooij, H.Y. Oei, M. van Hagen, P.T. Postema, M. de Jong, J.C. Reubi 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. **20**, 716–731 (1993)
5. P. Antunes, M. Ginj, H. Zhang, B. Waser, R.P. Baum, J.C. Reubi, H. Maecke, Are radiogallium-labelled DOTA-conjugated somatostatin analogues superior to those labelled with other radiometals? Eur. J. Nucl. Med. Mol. Imaging **34**, 982–993 (2007)
6. R.P. Baum, V. Prasad, Molecular imaging of neuroendocrine tumors using Ga-68 DOTA-NOC receptor PET/CT semiquantitative analyses after 1,257 studies (EPOS). In European Congress of Radiology, Edition Vienna, Austria, (2007)
7. S. Koukouraki, L.G. Strauss, V. Georgoulias, J. Schuhmacher, U. Haberkorn, N. Karkavitsas, A. Dimitrakopoulou-Strauss, Evaluation of the pharmacokinetics of 68 Ga-DOTATOC in patients with metastatic neuroendocrine tumours scheduled for 90Y-DOTATOC therapy. Eur. J. Nucl. Med. Mol. Imaging **33**, 460–466 (2006)
8. J. Kowalski, M. Henze, J. Schuhmacher, H.R. Macke, M. Hofmann, U. Haberkorn, Evaluation of positron emission tomography imaging using [68 Ga]-DOTA-D Phe(1)-Tyr(3)-octreotide in comparison to [111In]-DTPAOC SPECT. First results in patients with neuroendocrine tumors. Mol. Imaging Biol. **5**, 42–48 (2003)
9. M. Gabriel, C. Decristoforo, D. Kendler, G. Dobrozemsky, D. Heute, C. Uprimny, P. Kovacs, E. Von Guggenberg, R. Bale, I.J. Virgolini, 68 Ga-DOTA-Tyr3-octreotide PET in neuroendocrine tumors: comparison with somatostatin receptor scintigraphy and CT. J. Nucl. Med. **48**, 508–518 (2007)
10. G. Treglia, P. Castaldi, G. Rindi, A. Giordano, V. Rufini, Diagnostic performance of Gallium-68 somatostatin receptor PET and PET/CT in patients with thoracic and gastroenteropancreatic neuroendocrine tumours: a meta-analysis, Endocrine (2012)