Published in final edited form as:

Clin Nucl Med. 2017 March ; 42(3): 211–213. doi:10.1097/RLU.0000000000001504.

Relevant discordance between ^{68}Ga -DOTATATE and ^{68}Ga -DOTANOC in *SDHB*-related metastatic paraganglioma: is affinity to somatostatin receptor 2 the key?

Ingo Janssen, MD^{*1}, Katherine I. Wolf, BS^{*1}, Chan H Chui, MBBS, FRCS, FAMS², Corina M. Millo, MD³, and Karel Pacak, MD, PhD, DSc¹

¹Section on Medical Endocrinology, Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, 10 Center Dr., Bldg. 10, Room 1E-3140, Bethesda, MD, 20892

²Surgery Centre for Children, Mount Elizabeth Medical Centre #10-08, 3 Mount Elizabeth, Singapore

³Positron Emission Tomography Department, National Institutes of Health Clinical Center, National Institutes of Health, 10 Center Dr., Bldg. 10, Room 1C-401 and 490, Bethesda, MD, 20892

Abstract

Pheochromocytomas/paragangliomas (PPGLs) are somatostatin receptor 2 overexpressing tumors. ^{68}Ga -DOTA-peptide imaging has recently shown excellent results in the detection of metastatic lesions in these tumors. However, currently used ^{68}Ga -DOTA-peptides show different somatostatin receptor affinities. Here, we report the remarkable differences in a patient who was imaged with ^{68}Ga -DOTANOC and ^{68}Ga -DOTATATE PET/CT within a 7-month period of time. The patient presented with a nearly negative ^{68}Ga -DOTANOC PET/CT scan, while on ^{68}Ga -DOTATATE PET/CT, multiple highly positive lesions were identified.

Keywords

pheochromocytoma; paraganglioma; metastatic; positron emission tomography; ^{68}Ga -DOTATATE; ^{68}Ga -DOTANOC

Since the majority of the lesions were stable on CT (0.6 cm in the right upper compared to 0.8 cm in December 2014 and June 2015, respectively) it is very suggestive that this remarkable discordance between ^{68}Ga -DOTANOC and ^{68}Ga -DOTATATE is not related to progressive disease, but to the different affinity profiles of the different DOTA-peptides to somatostatin receptors (SSR). ^{68}Ga -DOTATATE has an approximate 9-times higher affinity to SSR2², mainly overexpressed in PGLs³, when compared to ^{68}Ga -DOTANOC, which has

Corresponding author: Karel Pacak, MD, PhD, DSc, Senior Investigator, Chief, Section on Medical Neuroendocrinology, Professor of Medicine, Eunice Kennedy Shriver NICHD, NIH, Building 10, CRC, Room 1E-3140, 10 Center Drive MSC-1109, Bethesda, MD, 20892, Phone: (301) 402-4594, Fax: (301) 402-4712, karel@mail.nih.gov.

^{*}Ingo Janssen and Katherine I. Wolf contributed equally to the production of this manuscript

Conflict of interest: The authors claim no conflicts of interest.

been shown to have a high affinity for SSR3⁴ – recently discovered to be expressed in succinate dehydrogenase-deficient PPGLs⁵. Immunohistochemical staining of the primary and lung metastases confirmed strong SSR2 expression in the lesions with negative staining of the surrounding normal tissue.

The phenomenon of additional lesions on ⁶⁸Ga-DOTATATE scans compared to ⁶⁸Ga-DOTANOC scans or vice versa for different neuroendocrine tumors or even additional findings in a post treatment scan after ¹⁷⁷Lu-DOTATATE therapy compared to the pre-treatment ⁶⁸Ga-DOTANOC scan have already been previously reported^{6–8}. However, to our best knowledge, not to this extent. These intra-individual differences in the performance of different DOTA-peptides are of important significance, since they should guide appropriate ⁶⁸Ga-DOTA-peptide functional imaging and follow-up, as well as the appropriate DOTA-peptide choice for receptor radionuclide therapy (PRRT).

Acknowledgments

Funding: This study was supported by the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, National Institutes of Health

References

1. Janssen I, Blanchet EM, Adams K, et al. Superiority of [68Ga]-DOTATATE PET/CT to other functional imaging modalities in the localization of SDHB-associated metastatic pheochromocytoma and paraganglioma. *Clin Cancer Res*. 2015; 21:3888–3895. [PubMed: 25873086]
2. Antunes P, Ginj M, Zhang H, et al. Are radiogallium-labelled DOTA-conjugated somatostatin analogues superior to those labelled with other radiometals? *Eur J Nucl Med Mol Imaging*. 2007; 34:982–993. [PubMed: 17225119]
3. Reubi JC, Waser B, Schaer JC, et al. Somatostatin receptor sst1-sst5 expression in normal and neoplastic human tissues using receptor autoradiography with subtype-selective ligands. *Eur J Nucl Med*. 2001; 28:836–846. [PubMed: 11504080]
4. Wild D, Schmitt JS, Ginj M, et al. DOTA-NOC, a high-affinity ligand of somatostatin receptor subtypes 2, 3 and 5 for labelling with various radiometals. *Eur J Nucl Med Mol Imaging*. 2003; 30:1338–1347. [PubMed: 12937948]
5. Elston MS, Meyer-Rochow GY, Conaglen HM, et al. Increased SSTR2A and SSTR3 expression in succinate dehydrogenase-deficient pheochromocytomas and paragangliomas. *Hum Pathol*. 2015; 46:390–396. [PubMed: 25554089]
6. Wild D, Bomanji JB, Benkert P, et al. Comparison of 68Ga-DOTANOC and 68Ga-DOTATATE PET/CT within patients with gastroenteropancreatic neuroendocrine tumors. *J Nucl Med*. 2013; 54:364–372. [PubMed: 23297077]
7. Kabasakal L, Demirci E, Ocak M, et al. Comparison of (6)(8)Ga-DOTATATE and (6)(8)Ga-DOTANOC PET/CT imaging in the same patient group with neuroendocrine tumours. *Eur J Nucl Med Mol Imaging*. 2012; 39:1271–1277. [PubMed: 22526963]
8. Basu S, Abhyankar A, Kand P, et al. ‘Reverse discordance’ between 68Ga-DOTA-NOC PET/CT and 177Lu-DOTA-TATE posttherapy scan: the plausible explanations and its implications for high-dose therapy with radiolabeled somatostatin receptor analogs. *Nucl Med Commun*. 2011; 32:654–658. [PubMed: 21654355]

FIGURE 1.

A ten year-old girl with a succinate dehydrogenase subunit B (*SDHB*) mutation was diagnosed with a $3.5 \times 5.2 \times 5.0$ cm upper abdominal mass in January 2014. The abdominal mass showed intense uptake on ^{68}Ga -DOTATOC positron emission tomography (PET)/computed tomography (CT) (A, B). Several sub-centimeter lung nodules were seen on CT, with two lung nodules on the right side barely ^{68}Ga -DOTATOC positive (C, D). Histopathology confirmed an abdominal PGL along with PGL-related lung metastases.

FIGURE 2.

In December of 2014, the patient underwent a ^{68}Ga -DOTANOC PET/CT scan for follow-up. The PET portion of the scan was initially read negative (A), despite the CT component showing many, apparently stable, pulmonary lesions highly suspicious for lung metastases. In our retrospectively performed review, some lung nodules appeared faintly ^{68}Ga -DOTANOC positive (B, C).

FIGURE 3.

Because of increasing normetanephrine levels suggestive for progressive disease, the patient was transferred to our institution in June 2015. After extensive discussion, and based on our experience with ^{68}Ga -DOTATATE in *SDHB* positive patients¹, the decision was made to perform a ^{68}Ga -DOTATATE PET/CT scan. Surprisingly, this scan was very positive (A), detecting several lung- and also bone lesions, with standardized maximum uptake levels (SUVmax) up to 49.6 (B), which were not, or only faintly positive, on ^{68}Ga -DOTANOC 6 months before (see Figure 2). The positive lesions on ^{68}Ga -DOTATATE PET/CT were likewise confirmed by ^{18}F -FDG PET/CT.