

# Incidental finding of a breast carcinoma on Ga-68-DOTA-1-Nal3-octreotide positron emission tomography/computed tomography performed for the evaluation of a pancreatic neuroendocrine tumor

## A case report

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### Abstract

**Rationale:** Functional imaging using radiolabeled somatostatin analogues plays an important role in the management of patients with neuroendocrine tumors, and it is a promising tool in the new era of theragnosis and personalized medicine.

**Patients Concerns:** The authors present the case of a 63-year-old woman referred for evaluation of a suspected pancreatic neuroendocrine tumor by Ga-68-DOTA-1-Nal3-octreotide positron emission tomography/computed tomography (Ga-68-DOTA-NOC PET/CT).

**Diagnoses:** PET/CT confirmed increased uptake of Ga-68-DOTA-NOC in a pancreatic lesion compatible with hyperexpression of somatostatin receptors in a neuroendocrine tumor. Furthermore, PET/CT revealed increased uptake in a breast lesion and in lymphadenomegalies (less intense than in the pancreatic tumor), which conducted to the incidental diagnosis of a breast carcinoma with lymph node metastases.

**Interventions:** For the breast cancer, the patient underwentneoadjuvant chemotherapy and anti-HER2 monoclonal antibody, after which she was submitted to surgery. Regarding thepancreatic neuroendocrine tumor, it was decided to maintain it under surveillance.

**Outcomes:** Breast carcinomas are known to express somatostatin receptors and this is the first report of Ga-68-DOTA-NOC uptake in a breast tumor.

**Lessons:** Ga-68-DOTA-NOC PET/CT could be useful for the management of breast cancer patients in the new era of theragnosis and personalized medicine.

**Abbreviations:** Ga-68-DOTA-NOC PET/CT = Ga-68-DOTA-1-Nal3-octreotide positron emission tomography/computed tomography, Ga-68-DOTA-TOC = Ga-68-DOTA-D-Phe1-Tyr3-Octreotide, Ga-68-TATE = Ga-68-DOTA-Tyr3-Thr8-octreotide, F-18-FDG = 2-deoxy-2-(F-18)fluoro-D-glucose, SUV<sub>max</sub> = maximum standardized uptake value.

**Keywords:** breast carcinoma, Ga-68-DOTA-NOC PET/CT, incidental finding, neuroendocrine tumor

## 1. Introduction

Functional imaging using radiolabeled somatostatin analogues plays an important role in the management of patients with

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neuroendocrine tumors, and it is a promising tool in the new era of theragnosis and personalized medicine.<sup>[1,2]</sup>

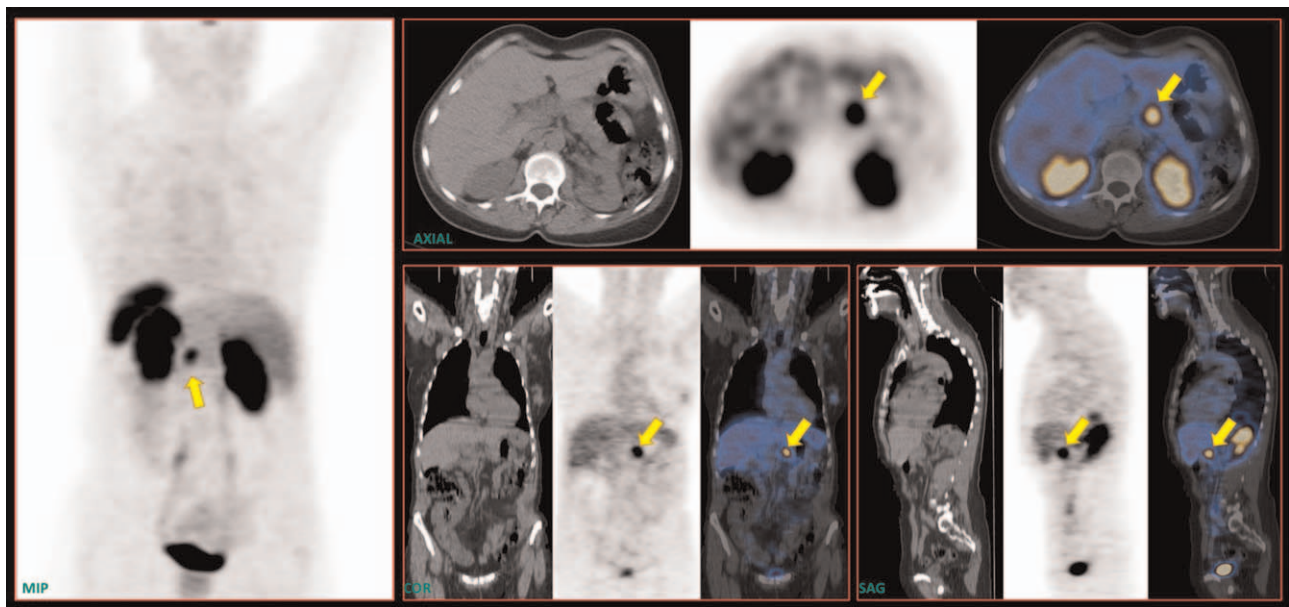
Somatostatin receptor imaging for the evaluation of other than neuroendocrine tumors has been studied.<sup>[3]</sup>

The use of positron emission tomography/computed tomography (PET/CT) for the analysis of somatostatin receptor status of neoplastic lesions is a rapidly evolving field<sup>[4]</sup> and the wider receptor-binding profile of Ga-68-DOTA-1-Nal3-octreotide (Ga-68-DOTA-NOC) compared to other PET tracers such as Ga-68-DOTA-D-Phe1-Tyr3-Octreotide (Ga-68-DOTA-TOC) and Ga-68-DOTA-Tyr3-Thr8-octreotide (Ga-68-DOTA-TATE) may be advantageous for imaging.<sup>[5]</sup>

The incidental finding of breast cancers in patients with neuroendocrine tumors was previously reported using Ga-68-DOTA-TOC<sup>[6]</sup> and Ga-68-DOTA-TATE<sup>[7]</sup> PET, but as to the authors knowledge, there is no case in the literature of an incidentally detected breast cancer while performing Ga-68-DOTA-NOC, which we report here for the first time.

## 2. Case report

Informed consent was obtained from the patient for publication.



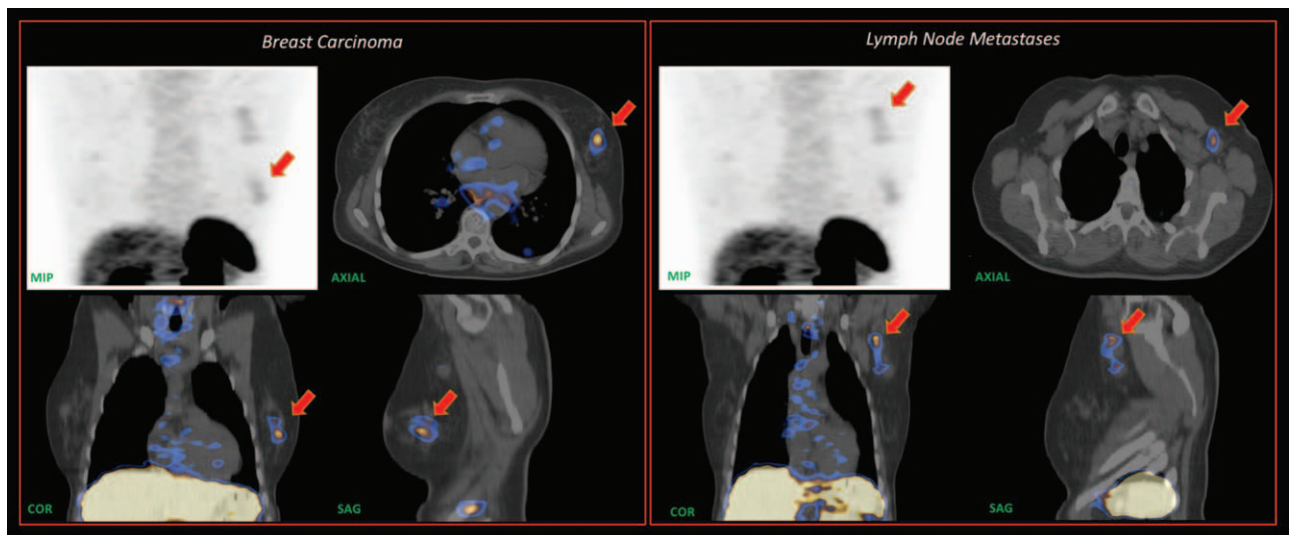
**Figure 1.** Maximum intensity projection image and selected axial, sagittal, and coronal Ga-68-DOTA-1-NaI<sub>3</sub>-octreotide slices showing intense uptake (SUVmax=16.3) in the lesion located in the body of the pancreas, compatible with a neuroendocrine tumor.

We report the case of a 63-year-old woman who performed Ga-68-DOTA-NOC PET/CT for the diagnosis of a pancreatic lesion suspected to be a neuroendocrine tumor. PET/CT revealed intense uptake of Ga-68-DOTA-NOC (SUVmax=16.3) in the lesion located in the body of the pancreas, compatible with a neuroendocrine tumor (Fig. 1).

PET/CT also showed increased uptake in a lesion in the left mammary gland (SUVmax=3.3) and foci of increased uptake (SUVmax=2.8) in enlarged left axillary lymph nodes (Fig. 2).

Anatomopathology confirmed the breast lesion as a grade 3 no special type (NST) invasive carcinoma, as well as metastatic axillary lymphadenopathies of breast cancer. Immunohistochem-

istry showed the breast cancer to be estrogen-receptor-positive (5%), progesterone-receptor-negative, HER2-positive (3+), mammaglobin focally positive, and to have a high Ki-67 level (~ 60%). For the breast cancer, the patient underwent neoadjuvant chemotherapy and anti-HER2 monoclonal antibody, after which she was submitted to surgery. Regarding the pancreatic neuroendocrine tumor, it was decided to maintain it under surveillance, as it was a small 1-cm lesion, confirmed as a well differentiated neuroendocrine tumor (G1) by an endoscopic ultrasound-guided fine needle biopsy. After 14 months of clinical, biochemical, and morphological imaging follow-up, the patient shows no signs of breast cancer recurrence and the pancreatic neuroendocrine tumor remains stable.



**Figure 2.** Maximum intensity projection image and selected axial, sagittal and coronal Ga-68-DOTA-1-NaI<sub>3</sub>-octreotide slices showing intense uptake in a lesion in the left mammary gland (SUVmax=3.3) and foci of increased uptake (SUVmax=2.8) in enlarged axillary lymph nodes.

### 3. Discussion

As to the authors knowledge, this is the first case reported in the literature of an incidental finding of a breast carcinoma on Ga-68-DOTA-NOC PET/CT performed for the evaluation of a neuroendocrine tumor.

A previous research reported the incidental finding of breast lesions with increased uptake of Ga-68-DOTA-TOC in 4 of 33 consecutive patients who performed PET for the evaluation of neuroendocrine tumors, and 2 of these breast lesions were primary breast cancers.<sup>[6]</sup> Additionally, a recent pictorial essay showed an incidentally detected breast carcinoma in a woman with liver neuroendocrine tumor metastases performing Ga-68-DOTA-TATE for investigation of unknown primary site.<sup>[7]</sup>

Somatostatin receptor expression is higher in estrogen-receptor-positive breast cancer.<sup>[8]</sup> Importantly, all 5 somatostatin receptor subtypes have been identified and are variably expressed in primary NST breast tumors, and there seems to exist receptor-specific correlations with histological markers as well as estrogen-receptor and progesterone-receptor levels.<sup>[9]</sup>

PET with 2-deoxy-2-(F-18)fluoro-D-glucose (F-18-FDG), a glucose analog, is recommended for staging in locally advanced breast cancer.<sup>[10]</sup> However, regarding breast cancer diagnosis, the lesion detectability of F-18-FDG PET was shown to be affected by the tumor size and the histological type and grade of the tumoral cells.<sup>[11]</sup>

Meanwhile, new hardware and software developments in PET imaging, such as dedicated PET scanners,<sup>[11]</sup> time-of-flight technology,<sup>[12]</sup> and Bayesian penalized likelihood reconstruction algorithms,<sup>[13]</sup> are improving the detectability of small lesions, which could impact the detection of infracentimetric breast cancers with Ga-68-DOTA-NOC PET, while also significantly reducing the radiation dose to the patients.

On the other hand, as it happens with the variable glycolytic metabolism of diverse malignant breast lesions noticed while performing F-18-FDG PET, the variable quantity of somatostatin receptors in breast cancers can affect the sensitivity of Ga-68-DOTA-peptides PET. Indeed, a recent research suggested the utilization of Ga-68-DOTA-TOC for the imaging of low-grade breast carcinomas not detected with F-18-FDG.<sup>[14]</sup>

An ingenious strategy that could be used to increase the sensitivity of PET imaging for breast cancer was previously proposed for the evaluation of neuroendocrine tumors and consisted in the administration of a double tracer combination of Ga-68-DOTA-peptides and F-18-FDG to improve the diagnostic accuracy over single tracer-PET.<sup>[15]</sup>

Moreover, radiomics, a new and emerging method extracting a large amount of quantification image features, can potentially improve the diagnostic accuracy of imaging techniques like PET, as well as the characterization of tumors.<sup>[16]</sup> This, combined with the unique molecular information obtained from Ga-68-DOTA-NOC might further assist on prognostication and therapeutic decisions for personalized clinical management in breast cancer patients.

Our case reinforces the importance of being aware that other than neuroendocrine tumors, namely breast carcinoma, express somatostatin receptors and can be found on PET with somatostatin analogues.

In the new era of personalized medicine, PET with Ga-68-DOTA-NOC could become a useful tool for diagnosis and

staging, as well as to predict and monitor the response to anti-hormonal therapy in patients with breast cancer.

### Author contributions

**Conceptualization:** Tiago Sampaio Vieira.

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**Resources:** Diogo Borges Faria.

**Supervision:** Tiago Sampaio Vieira, José Pereira de Oliveira.

**Validation:** Tiago Sampaio Vieira, Conceição Souto Moura, Elsa Francisco, Sérgio Barroso, José Pereira de Oliveira.

**Visualization:** Tiago Sampaio Vieira, Diogo Borges Faria.

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**Writing – review & editing:** Tiago Sampaio Vieira, Diogo Borges Faria, Conceição Souto Moura, Elsa Francisco, Sérgio Barroso, José Pereira de Oliveira.

### References

- [1] Deroose CM, Hindié E, Kebebew E, et al. Molecular imaging of gastroenteropancreatic neuroendocrine tumors: current status and future directions. *J Nucl Med* 2016;57:1949–56.
- [2] Kwekkeboom DJ, Kam BL, van Essen M, et al. Somatostatin receptor-based imaging and therapy of gastroenteropancreatic neuroendocrine tumors. *Endocr Relat Cancer* 2010;17:R53–73.
- [3] Sollini M, Erba PA, Fraternali A, et al. PET and PET/CT with 68gallium-labeled somatostatin analogues in non GEP-NETs tumors. *Sci World J* 2014;2014:19.
- [4] Johnbeck CB, Knigge U, Kjaer A. PET tracers for somatostatin receptor imaging of neuroendocrine tumors: current status and review of the literature. *Future Oncol* 2014;10:2259–77.
- [5] Wild D, Bomanji JB, Benkert P, et al. Comparison of 68Ga-DOTANOC and 68Ga-DOTATATE PET/CT within patients with gastroenteropancreatic neuroendocrine tumors. *Journal of Nuclear Medicine* 2013;54:364–72.
- [6] Elgeti F, Amthauer H, Denecke T, et al. Incidental detection of breast cancer by 68Ga-DOTATOC-PET/CT in women suffering from neuroendocrine tumours. *Nuklearmedizin* 2008;47:261–5.
- [7] Yamaga LYI, Wagner J, Funari MBG. 68Ga-DOTATATE PET/CT in nonneuroendocrine tumors: a pictorial essay. *Clin Nucl Med* 2017;42:e313–6.
- [8] Dalm US, Verzijlbergen FJ, De Jong M. Review: receptor targeted nuclear imaging of breast cancer. *Int J Mol Sci* 2017;18:2.
- [9] Kumar U, Grigorakis SI, Watt HL, et al. Somatostatin receptors in primary human breast cancer: quantitative analysis of mRNA for subtypes 1-5 and correlation with receptor protein expression and tumor pathology. *Breast Cancer Res Treat* 2005;92:175–86.
- [10] Caresia Aroztegui AP, García Vicente AM, Alvarez Ruiz S, et al. 18F-FDG PET/CT in breast cancer: evidence-based recommendations in initial staging. *Tumour Biol* 2017;39:10.
- [11] Fowler AM. A molecular approach to breast imaging. *J Nucl Med* 2014;55:177–80.
- [12] Surti S. Update on time-of-flight PET imaging. *J Nucl Med* 2015;56:98–105.
- [13] Teoh EJ, McGowan DR, Macpherson RE, et al. Phantom and clinical evaluation of the Bayesian penalized likelihood reconstruction algorithm Q.Clear on an LYSO PET/CT system. *J Nucl Med* 2015;56:1447–52.
- [14] Chereau E, Durand L, Frati A, et al. Correlation of immunohistochemical expression of somatostatin receptor-2 in breast cancer and tumor detection with 68Ga-DOTATOC and 18F-FDG PET imaging in an animal model. *Anticancer Res* 2013;33:3015–9.
- [15] Pellicciari M, Ortolani S, Grego E, et al. Double tracer PET/CT: what is it and what does it mean? *J Cancer Metastasis Treat* 2016;2:321–8.
- [16] Lambin P, Leijenaar RTH, Deist TM, et al. Radiomics: the bridge between medical imaging and personalized medicine. *Nat Rev Clin Oncol* 2017;14:749–62.