EDITORIAL - ENDOCRINE TUMORS

## Beta Probe for Radioguided Surgery in Gastrointestinal Neuroendocrine Tumors: A Move in the Right Direction

## Electron Kebebew, MD<sup>D</sup>

Division of General Surgery, Department of Surgery, Stanford University, School of Medicine, Stanford, CA

There have been significant advances in the management of patients with gastrointestinal neuroendocrine tumors due to more accurate imaging modalities and new therapeutic agents. Complete surgical resection remains the most optimal treatment in patients with gastrointestinal neuroendocrine tumors. Preoperative imaging with DOTA peptides in patients with well-differentiated grade I and II neuroendocrine tumors is most accurate for detecting all sites of disease and has been shown to impact the selection of the most optimal treatment based on more accurate staging.<sup>1</sup> In some patients, DOTA peptide-based positron emission tomography (PET) imaging may show disease that is small and could be difficult to localize at the time of the operation.

Radioguided surgery in patients with neuroendocrine tumors has been evaluated with the use of intraoperative DOTA peptides labeled with 68-Gallium, given its short half-life and minimal radiation exposure. The goal of radioguided surgery in patients with gastrointestinal neuroendocrine tumors is to ensure resection of all sites of disease, while possibly reducing the need for more extensive resection (e.g. extended mesenteric lymphadenectomy for small and large intestine neuroendocrine tumors). To date, a gamma probe has been used for radioguided surgery with 68-Gallium DOTA peptides to help detect tumor sites and to determine optimal tumor-to-background (TBR) ratios when

This article refers to: Bertani E, Mattana F, Collamati F, et al. Radio-guided surgery with a new generation  $\beta$ -probe for radiolabelled somatostatin analogue, in patients with smallintestinal neuroendocrine tumors. Annals Surgical Oncology. Epub 23 Apr 2024. https://doi.org/10.1245/s10434-024-15277-x.

© Society of Surgical Oncology 2024

First Received: 23 April 2024 Accepted: 24 April 2024

E. Kebebew, MD e-mail: kebebew@stanford.edu evaluating a lesion as being involved with or without tumor. While these studies have shown that it is feasible, safe, and beneficial, variable TBR cut-offs and detection rates have been reported.<sup>2–4</sup>

68-Gallium induces both gamma-ray and  $\beta$ -particle emissions. More recently, the direct detection of  $\beta$ + particle emissions has been studied using a less cumbersome beta probe for radioguided surgery using both open and minimally invasive techniques.<sup>5</sup> In this issue of Annals of Surgical Oncology, Bertani and colleagues report on their prospective study evaluating radioguided surgery using a beta probe in patients with gastrointestinal neuroendocrine tumors.<sup>6</sup> Patients were given 1.1 MBq/Kg of 68-Gallium DOTA-TOC 10 min prior to surgery. Bertani et al. found a TBR cut-off of 1.35 had a sensitivity of 89.3% and specificity of 86.4% using histopathology as the gold standard in 134 tissue samples (primary tumors and lymph node metastases) removed from 20 patients undergoing an operation (18 open and 2 minimally invasive procedures). Using adjacent tissue for background measurement as compared with the omentum had better accuracy based on area under the curve analyses. In two patients, lesions that were not detected on preoperative imaging were detected with the beta probe. The study results are promising and suggest that radioguided surgery using a beta probe with 68-Gallium DOTA peptides may be a helpful adjunct and may have a superior detection rate than a gamma probe due to reduced interference from background radioactivity. It would have been interesting if the authors measured ex vivo levels with the beta probe as a way of confirming successful resection, as frozen sections are often done in these types of procedures. Regardless, this is an important study that shows the feasibility, safety, and the TBR threshold cut-off that could be used in patients with gastrointestinal neuroendocrine tumors undergoing beta probe radioguided surgery with 68-Gallium-DOTA-TOC. I look forward to the results of their planned multicenter study to determine whether (1) the technique and TBR cut-off



established are transportable to other medical centers and surgeons; and (2) their findings are generalizable and could lead to a personalized surgical intervention in patients with gastrointestinal neuroendocrine tumors.

**DISCLOSURE** Electron Kebebew declares no conflicts of interest in relation to this manuscript.

## REFERENCES

- Sadowski SM, Neychev V, Millo C, et al. Prospective study of 68Ga-DOTATATE positron emission tomography/computed tomography for detecting gastro-entero-pancreatic neuroendocrine tumors and unknown primary sites. J Clin Oncol. 2016;34(6):588–96. https://doi.org/10.1200/JCO.2015.64.0987.
- Cockburn KC, Toumi Z, Mackie A, Julyan P. Radioguided surgery for gastroenteropancreatic neuroendocrine tumours: a systematic literature review. *J Gastrointest Surg.* 2021;25(12):3244– 57. https://doi.org/10.1007/s11605-021-05115-w.

- El Lakis M, Gianakou A, Nockel P, et al. Radioguided surgery with gallium 68 dotatate for patients with neuroendocrine tumors. *JAMA Surg.* 2019;154(1):40–5. https://doi.org/10.1001/ jamasurg.2018.3475.
- Sadowski SM, Millo C, Neychev V, et al. Feasibility of radioguided surgery with (68)gallium-DOTATATE in patients with gastro-entero-pancreatic neuroendocrine tumors. *Ann Surg Oncol.* 2015;22(Suppl 3):S676–82. https://doi.org/10.1245/ s10434-015-4857-9.
- Collamati F, Morganti S, van Oosterom MN, et al. First-inhuman validation of a DROP-IN beta-probe for robotic radioguided surgery: defining optimal signal-to-background discrimination algorithm. *Eur J Nucl Med Mol Imaging*. 2024. https://doi. org/10.1007/s00259-024-06653-6.
- 6. Bertani E, Mattana F, Collamati F, et al. Radio-guided surgery with a new generation  $\beta$ -probe for radiolabelled somatostatin analogue, in patients with small-intestinal neuroendocrine tumors. *Ann Surg Oncol.* 2024. https://doi.org/10.1245/ s10434-024-15277-x.

**Publisher's Note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.