# Imaging-Guided Use of Combined $^{177}$Lu-DOTATATE and Capecitabine Therapy in Metastatic Mediastinal Paraganglioma

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Peptide receptor radionuclide therapy targets highly expressed somatostatin receptors in well-differentiated neuroendocrine tumors, producing stability or a partial response in most patients with inoperable or metastatic disease. However, neuroendocrine tumors showing increased $^{18}$F-FDG uptake have limited treatment options and a poor outcome, and the role of peptide receptor radionuclide therapy is still unclear. Here, we present the case of a young man with mediastinal paraganglioma and extensive metastatic disease showing avidity on both somatostatin receptor imaging and $^{18}$F-FDG imaging. The patient experienced a partial response to peptide receptor chemoradionuclide therapy ($^{177}$Lu-DOTATATE and low-dose capecitabine), as well as a significantly improved quality of life. This case highlights the utility of peptide receptor chemoradionuclide therapy when there is extensive disease avid for both somatostatin receptor and $^{18}$F-FDG and a lack of other suitable treatment modalities.

**Key Words:** $^{68}$Ga-DOTANOC PET/CT; $^{177}$Lu-DOTATATE; PRCRT; neuroendocrine tumors; paraganglioma

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Somatostatin receptor (SSTR) imaging illustrates the extent and SSTR expression of well-differentiated neuroendocrine tumors. The intensity of SSTR expression at the primary and metastatic sites helps predict the grade of the tumor and its suitability for undergoing peptide receptor radionuclide therapy. Most patients with inoperable or metastatic neuroendocrine tumors treated with peptide receptor radionuclide therapy have shown disease stabilization or a partial response. However, neuroendocrine tumors showing increased $^{18}$F-FDG uptake have limited treatment options and a poor outcome, and the role of peptide receptor radionuclide therapy is still not well defined. Here, we present the case of a young man with mediastinal paraganglioma and extensive skeletal metastases avid on both SSTR imaging and $^{18}$F-FDG imaging. A partial response and significant improvement in quality of life were seen after peptide receptor chemoradionuclide therapy ($^{177}$Lu-DOTATATE and low-dose capecitabine), highlighting the utility of this treatment when other treatment modalities may not be suitable.

## CASE REPORT

A 27-y-old wheelchair-bound man who had presented with a severe left-sided low backache of 2-mo duration after a trivial injury was found to have, on radiography and pelvic MRI, a soft-tissue mass with an osteolytic lesion in the left iliac bone. Whole-body $^{18}$F-FDG PET/CT, performed with suspicion of malignancy, showed an intensely tracer-avid ($SUV_{max}$, 40) right inferior mediastinal mass (~8.0 × 5.2 × 9.4 cm), a left iliac mass ($SUV_{max}$, 47.6), and widespread lytic skeletal lesions on maximum-intensity-projection images and corresponding transaxial fused images (Fig. 1A). Histopathologic examination of the inferior mediastinal mass was suggestive of paraganglioma and positive on S-100 and chromogranin immunostaining. $^{68}$Ga-DOTANOC PET/CT, performed to assess SSTR expression and whether peptide receptor radionuclide therapy was an option, showed an intensely tracer-avid posterior mediastinal mass ($SUV_{max}$, 88) and multiple skeletal lesions (left iliac bone $SUV_{max}$, 49.5) concordant with the $^{18}$F-FDG PET/CT findings (Fig. 1B). The study protocol was approved by the Institutional Ethics Committee, and the subject gave written informed consent to participate in the study. The level of serum chromogranin-A was elevated (15,013 ng/mL; normal, <98.1 ng/mL), whereas the levels of free metanephrine and dopamine were normal. The patient received 2 cycles of $^{177}$Lu-DOTATATE infusion

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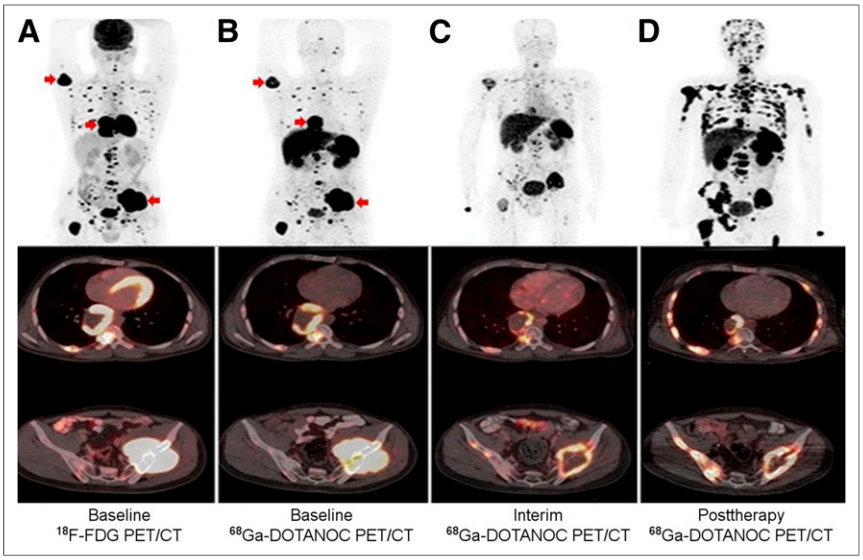


**FIGURE 1.** (A) Baseline $^{18}$F-FDG PET/CT maximum-intensity-projection and transaxial fused images showed intensely tracer-avid ($SUV_{max}$, 40) right inferior mediastinal mass (~8.0 × 5.2 × 9.4 cm), left iliac mass ($SUV_{max}$, 47.6), and widespread skeletal lesions. (B) Baseline $^{68}$Ga-DOTANOC PET/CT showed intensely tracer-avid posterior mediastinal mass ($SUV_{max}$, 88) and multiple lytic skeletal lesions (left iliac bone $SUV_{max}$, 49.5). (C) Interim $^{68}$Ga-DOTANOC PET/CT showed significant decrease in tracer avidity within lesions ($SUV_{max}$, 88–16.4 in mediastinal mass and 49.5–20.1 in left iliac bone/soft-tissue lesion) and concurrent decrease in size of lesions. (D) $^{68}$Ga-DOTANOC PET/CT 2 mo after fourth cycle of peptide receptor chemoradionuclide therapy revealed disease progression.

(7,400 MBq [200 mCi]/cycle) at 8-wk interval along with low-dose capecitabine as a radiosensitizer in divided doses (1,250 mg/m$^2$) for 14 d, starting from the first day of therapy. Positively charged amino acids (arginine and lysine) and saline were infused along with the peptide receptor chemoradionuclide therapy to prevent nephrotoxicity. $^{177}$Lu-DOTATATE scans acquired 24 h after the first treatment showed tracer uptake in the primary and metastatic lesions (Fig. 2). Interim $^{68}$Ga-DOTANOC PET/CT after 2 cycles of peptide receptor chemoradionuclide therapy showed a significant decrease in tracer avidity within the lesions ($SUV_{max}$ decreased from 88 to 16.4 in the mediastinal mass and from 49.5 to 20.1 in the left iliac bone/soft-tissue lesion) and a concurrent decrease in lesion size (according to the RECIST 1.1 criteria), suggesting a partial metabolic or morphologic response (Fig. 1C), with a fall in serum chromogranin-A level to 2,504 ng/mL. The patient's responses on the EORTC QLQ-C30 questionnaire showed a significant improvement in his quality of life, and he was able to leave his wheelchair and begin walking on his own. His Karnofsky performance score improved to 80 from 50. He received 2 more cycles of peptide receptor chemoradionuclide therapy, with a total $^{177}$Lu dose of approximately 29,600 MBq (800 mCi). Follow-up $^{68}$Ga-DOTANOC PET/CT 2 mo after the fourth cycle of peptide receptor chemoradionuclide therapy revealed disease progression (Fig. 1D). The patient finally succumbed to his disease 3 mo after receiving the last cycle of therapy.

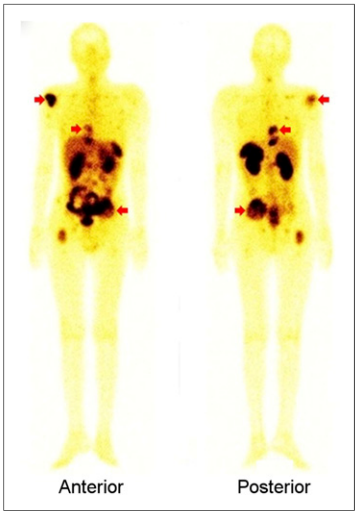


**FIGURE 2.** $^{177}$Lu-DOTATATE posttherapy whole-body scans (anterior and posterior images) acquired 24 h after first treatment showed tracer uptake in primary and metastatic lesions.

## DISCUSSION

Paragangliomas, being derived from neural crest cells, have neuroendocrine differentiation. Sympathetic chains in paraaortic and paravertebral locations can give rise to mediastinal paragangliomas, though paragangliomas are commonly seen in the head and neck region. The malignancy rate among all paragangliomas ranges from 0% to 20%. SSTR expression in paragangliomas has recently been well documented, with subtypes 2A and 3 predominating, particularly in succinate dehydrogenase–deficient pheochromocytomas and paragangliomas. Functional imaging with tracers such as $^{18}$F-FDG, $^{68}$Ga-DOTANOC, and $^{123}$I-/$^{131}$I-metaiodobenzylguanidine may be used to determine the extent of disease, the prognosis, and the therapeutic options (*1–4*). $^{18}$F-FDG–avid neuroendocrine tumors may show a transient response to combination chemotherapy, but the outcome is usually poor and the adverse effects significant. Such neuroendocrine tumors are presumed to be more radiosensitive, and their additional SSTR expression delivers the radiation dose to their proliferating cells.

In our patient, targeted internal radiotherapy in combination with capecitabine led to a favorable biochemical and imaging response without any significant toxicity, though

the patient later succumbed to the disease. A personalized approach in the form of peptide receptor chemoradionuclide therapy with acceptable toxicities is appropriate when other treatment options are limited (*5,6*).

## CONCLUSION

Peptide receptor chemoradionuclide therapy may have a role in $^{18}$F-FDG– and SSTR-avid inoperable and widespread paraganglioma when other options are either limited or ineffective.

## DISCLOSURE

No potential conflict of interest relevant to this article was reported.

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### Erratum

In the article "Comparison of Accuracy Between $^{13}$C- and $^{14}$C-Urea Breath Testing: Is an Indeterminate-Results Category Still Needed?" by Charest and Bélair (*J Nucl Med Technol.* 2017;45:87–90), the "Analysis of Negative Results" section incorrectly states that the average of 366 patients with negative $^{14}$C results was *0.0118 ± 0.0050 cps*. The correct average is *0.118 ± 0.050 cps*. The "Analysis of Positive Results" section incorrectly states that the average of 196 patients with positive $^{14}$C results was *0.300 ± 0.172 cps,* with a corresponding *5.210 ± 0.172 S/CO*. The correct average and corresponding S/CO are *2.998 ± 1.719 cps* and *9.084 ± 5.210,* respectively. In addition, the "Analysis of Positive Results" section incorrectly states that the average 20.658 ± 10.359 %Δ was determined from 119 patients with *negative* $^{13}$C results; the average was obtained from 119 patients with *positive* $^{13}$C results. The authors regret these errors.