

CCK₂ Receptor–Targeted PET/CT in Medullary Thyroid Cancer Using [⁶⁸Ga]Ga-DOTA-CCK-66

Oliver Viering¹, Thomas Günther², Nadine Holzleitner², Alexander Dierks¹, Georgine Wienand¹, Christian H. Pfob¹, Ralph A. Bundschuh¹, Hans-Jürgen Wester², Johanna S. Enke¹, Malte Kircher¹, and Constantin Lapa¹

¹Nuclear Medicine, Faculty of Medicine, University of Augsburg, Augsburg, Germany; and ²Department of Chemistry, Chair of Pharmaceutical Radiochemistry, TUM School of Natural Sciences, Technical University of Munich, Garching, Germany

Medullary thyroid cancer (MTC), a neuroendocrine tumor arising from the parafollicular cells of the thyroid gland, accounts for approximately 1%–2% of all thyroid cancers (1). Only recently was cholecystikinin-2 receptor (CCK₂R) identified as a suitable target for PET/CT imaging of MTC (2,3).

We report on a 74-y-old man with a history of locally advanced MTC who had undergone tumor debulking including a hemithyroidectomy and lymph node dissection on the right side. Informed consent was obtained from the patient, and the project was approved by the institutional ethics committee of Ludwig-Maximilians-Universität München, Munich, Germany (permit 23-0627).

Postoperative [¹⁸F]F-3,4-dihydroxyphenylalanine (DOPA) PET/CT detected residual local tumor as well as cervical and upper mediastinal

lymph node metastases, prompting additional external-beam radiotherapy. After treatment, serum calcitonin levels decreased (from 5,300 to 720 pg/mL) but remained significantly elevated. Thus, another restaging with [¹⁸F]F-DOPA PET/CT (201 MBq) was performed.

To assess the possibility of CCK₂R-directed radioligand therapy, the patient additionally underwent PET/CT with [⁶⁸Ga]Ga-DOTA-CCK-66 (150 MBq; time interval between scans, 16 d), a novel CCK₂R-directed tracer. It was well tolerated and demonstrated a favorable biodistribution with only physiologic uptake in the stomach and renal tracer excretion. In concordance with [¹⁸F]F-DOPA, [⁶⁸Ga]Ga-DOTA-CCK-66 detected an identical number of MTC lesions composing the still viable local tumor (SUV_{max} of 7.4, vs. 7.0 for [¹⁸F]F-DOPA), as well as multiple

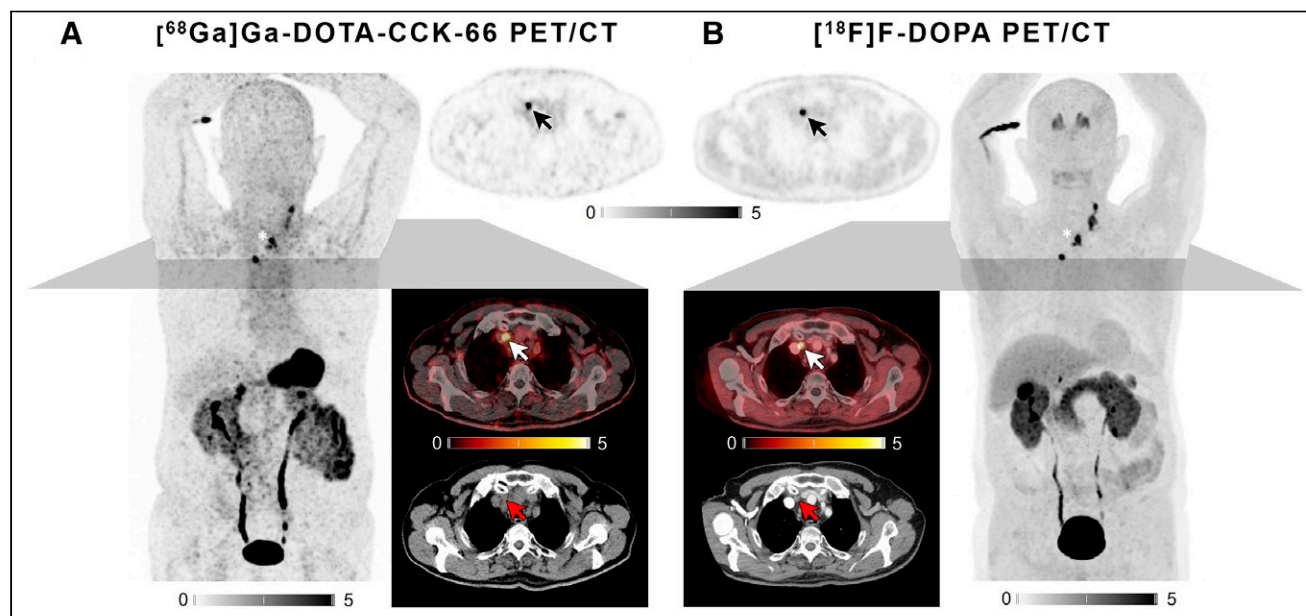


FIGURE 1. Maximum-intensity projections and axial sections of [⁶⁸Ga]Ga-DOTA-CCK-66 (A) and [¹⁸F]F-DOPA (B) PET/CT. White stars indicate local tumor in left thyroid bed. Arrows indicate lymph node metastasis in right upper mediastinum. Intensity scale bars are SUV.

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For correspondence or reprints, contact Constantin Lapa (constantin.lapa@uk-augsburg.de).
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cervical and mediastinal lymph node metastases (SUV_{max} of 9.5, vs. 8.7 for [^{18}F]F-DOPA) (Fig. 1).

CCK₂R-directed PET imaging with [^{68}Ga]Ga-DOTA-CCK-66 is feasible. Given the possibility of receptor-directed radioligand therapy using its ^{177}Lu - or ^{225}Ac -labeled analog, this new compound might prove a valuable addition to the theranostic armamentarium in MTC. Further research with a special focus on kidney doses, which have been a relevant issue for therapeutic CCK₂R ligands regarding the amount of administered activity, is warranted.

DISCLOSURE

A patent application on CCK₂R-targeted compounds was filed by Thomas Günther, Nadine Holzleitner, Hans-Jürgen Wester, and

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

REFERENCES

1. Wells SA Jr, Asa SL, Dralle H, et al. Revised American Thyroid Association guidelines for the management of medullary thyroid carcinoma. *Thyroid*. 2015; 25:567–610.
2. Reubi JC, Waser B. Unexpected high incidence of cholecystokinin-B/gastrin receptors in human medullary thyroid carcinomas. *Int J Cancer*. 1996;67:644–647.
3. von Guggenberg E, Kolenc P, Rottenburger C, Mikolajczak R, Hubalewska-Dydejczyk A. Update on preclinical development and clinical translation of cholecystokinin-2 receptor targeting radiopharmaceuticals. *Cancers (Basel)*. 2021; 13:5776.