Update on Clinical Evaluation of 3-[^{18}F]fluoro-*p*-hydroxyphenethylguanidine ([^{18}F]3F-PHPG) for Localization of Paraganglioma and Pheochromocytoma using Positron Emission Tomography (PET)

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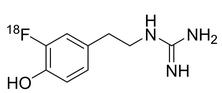
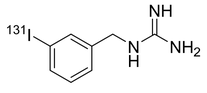
OBJECTIVE

We previously reported our initial results with the new PET tracer 3-[^{18}F]fluoro-*para*-hydroxyphenethylguanidine ([^{18}F]3F-PHPG) in six paraganglioma (PGL) and pheochromocytoma (PCC) patients.[1] Like [^{123}I]metaiodobenzylguanidine ([^{123}I]mIBG), [^{18}F]3F-PHPG is a substrate of the norepinephrine transporter (NET) and the two vesicular monoamine transporter isoforms, VMAT1 and VMAT2. This update provides further examples from the *n* = 16 new PGL and PCC patients studied over the last year.



[^{18}F]3F-PHPG



[^{123}I]mIBG

RADIOCHEMISTRY AND IMAGING

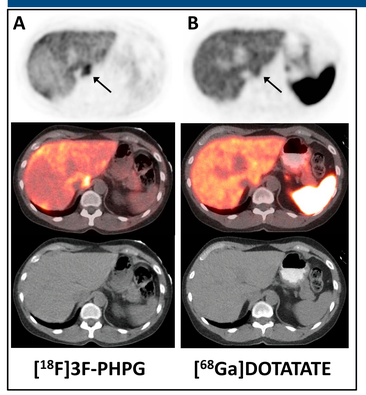
[^{18}F]3F-PHPG was prepared using a new iodonium ylide precursor, providing 75 to 185 mCi with >99% radiochemical purity. Whole-body scans were acquired on a Siemens Biograph TruePoint TrueV PET/CT scanner starting 90 min after i.v. injection of 8.2 to 12.7 mCi of tracer. Standardized uptake values (SUV_{max} or SUV_{mean}) of [^{18}F]3F-PHPG retention in tumors and organs were measured.

NEW SUBJECTS

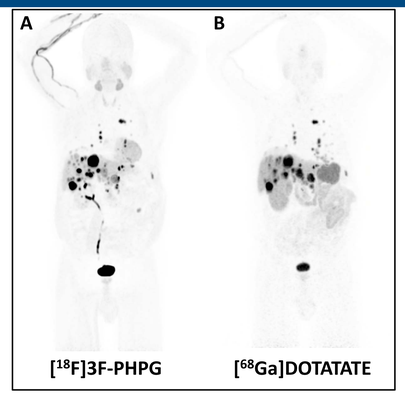
Table 1. New patient demographics and diagnosis.

Subject #	Sex	Age (y)	Diagnosis	Genetic Predisposition
7	F	53	Right paraadrenal PGL	sporadic
8	M	60	Right PCC	sporadic
9	M	72	Metastatic PGL	sporadic
10	F	24	Head & Neck PGL Left glomus jugulare PGL	SDHD
11	F	50	Head & Neck PGL Left glomus jugulare PGL	SDHB
12	F	49	Head & Neck PGL Right carotid body mass	SDHB
13	M	68	Metastatic PGL & PCC (Prior Lutathera PRRT)	sporadic
14	F	73	Head & Neck PGL Left carotid body mass	SDHD
15	M	56	Right paraadrenal PCC	sporadic
16	M	31	Pancreatic NET and Left PCC	Von-Hippel Lindau
17	M	47	Metastatic prostate PGL	sporadic
18	F	37	Left PCC	sporadic
19	F	47	Cardiac PGL	SDHB
20	M	58	Right PCC	sporadic
21	F	50	Left PCC	sporadic
22	F	63	Left abdominal PGL	sporadic

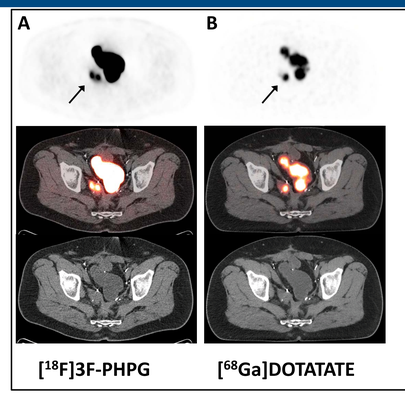
PARAGANGLIOMA PATIENTS



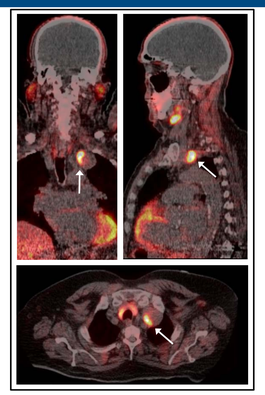
Subject 7. [^{18}F]3F-PHPG (**A**) detected the mass with good tumor-to-liver contrast and SUV_{max} = 7.1, compared to 8.5 for [^{68}Ga]DOTATATE (**B**).



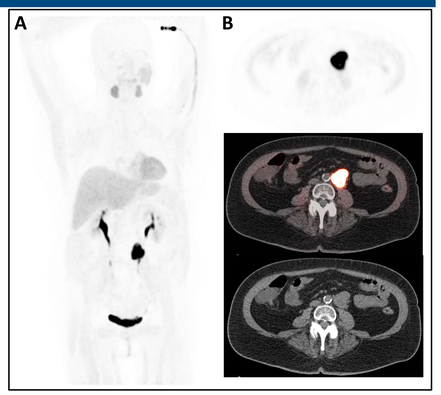
Subject 9. Highly concordant lesion detection between [^{18}F]3F-PHPG (**A**) and [^{68}Ga]DOTATATE (**B**) in a metastatic PGL, with comparable SUV_{max} values.



Subject 17. [^{18}F]3F-PHPG detected the two lesions near the bladder with SUV_{max} = 23.8, compared to 51.3 for [^{68}Ga]DOTATATE (**B**) taken two years earlier.

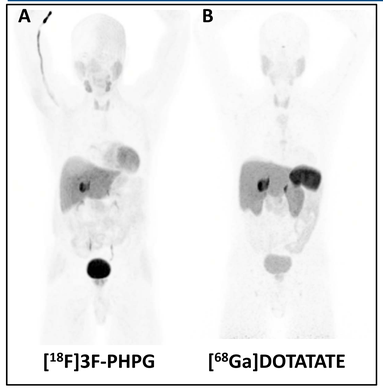


Subject 13. [^{18}F]3F-PHPG lit up only one metastatic site, showing a partial response to prior PRRT.



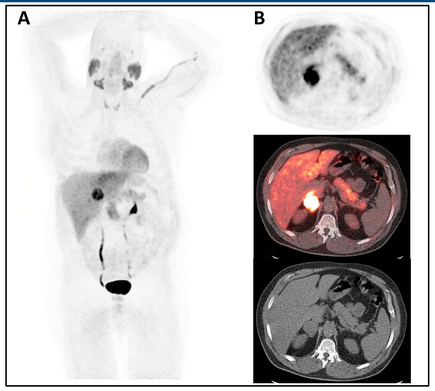
Subject 22. [^{18}F]3F-PHPG exhibited high uptake in the left abdominal PGL, with SUV_{max} = 46.2 (**A**, **B**). No metastatic sites were observed.

PHEOCHROMOCYTOMA PATIENTS

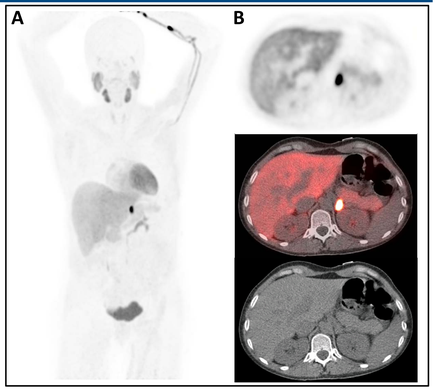


Subject 8. [^{18}F]3F-PHPG detected the right adrenal PCC with SUV_{max} = 24.1 (**A**), compared to 37.2 in a [^{68}Ga]DOTATATE scan taken 3 months prior (**B**).

Subject 15. Comparison of PET scans in a recently diagnosed patient with a large right PCC. SUV_{max} values in the baseball-sized tumor were 16.1 for [^{18}F]3F-PHPG (**A**), 29.7 for [^{68}Ga]DOTATATE (**B**), and 10.8 for [^{18}F]FDG (**C**).

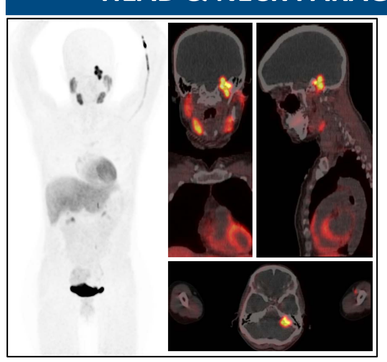


Subject 20. [^{18}F]3F-PHPG identified the right adrenal PCC, with SUV_{max} = 16.3 (**A**, **B**). Size = 4.5 × 4.3 × 4.2 cm. No metastatic sites were detected.

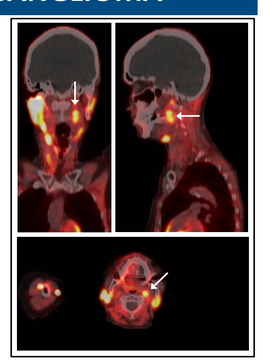


Subject 21. [^{18}F]3F-PHPG localized in the small left PCC, with SUV_{max} = 28.0 (**A**, **B**). Size = 1.8 cm. No metastatic sites were observed.

HEAD & NECK PARAGANGLIOMA



Subject 11. [^{18}F]3F-PHPG had high uptake in the left jugular foramen mass (SUV_{max} = 20.1). A prior [^{68}Ga]DOTATATE scan 5 y prior had SUV_{max} = 3.3.



Subject 14. [^{18}F]3F-PHPG uptake was moderate in the left carotid body tumor (SUV_{max} = 6.6).

OTHER RESULTS

Subject 10. [^{18}F]3F-PHPG uptake in the left glomus jugulare was mild, SUV_{max} = 2.2, compared to 8.0 for [^{18}F]FDG. The absence of brain uptake of [^{18}F]3F-PHPG and its high specificity for adrenergic pathways may be advantages of this tracer over [^{18}F]FDG in HNPGL.

Subject 12. [^{18}F]3F-PHPG uptake in the right carotid body tumor was mild (SUV_{max} = 2.2), but the lesion was detectable.

Subject 16. [^{18}F]3F-PHPG uptake in the left adrenal nodule in this VHL patient with PCC was moderate, with SUV_{max} = 4.6.

Subject 18. [^{18}F]3F-PHPG uptake in the left adrenal PCC mass was moderate with SUV_{max} = 13.3, compared to 54 for [^{68}Ga]DOTATATE.

Subject 19. [^{18}F]3F-PHPG had mild uptake in the cardiac mass, with SUV_{max} = 3.3, compared to 14.4 in a [^{68}Ga]DOTATATE scan 2 y earlier.

CONCLUSION

PET with [^{18}F]3F-PHPG appears to provide diagnostic performance comparable to [^{68}Ga]DOTATATE in most PGL and PCC patients. Compared with [^{123}I]mIBG, [^{18}F]3F-PHPG offers the advantages of same-day imaging, higher lesion contrast, and higher spatial resolution for improved lesion detection in PGL and PCC.

REFERENCES

1. Wong KK, Else T, Viglianti BL, Brooks AF, Frey KA, Raffel DM. *Eur J Nucl Med Mol Imaging* 49(6): 2098-2099, 2022.

ACKNOWLEDGMENTS & CONTACT

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