



Flip-flop phenomenon on dual SSTR PET and amino acid PET in a case of recurrent meningioma with malignant transformation

Adrien Holzgreve^{1,2} · Patrick N. Harter^{3,4,5} · Robert Forbrig⁶ · Stefanie Quach⁷ · Niklas Thon^{4,7} · Christian Schichor^{4,7} · Joerg-Christian Tonn^{4,5,7} · Maximilian Niyazi^{8,9,10,11} · Matthias Brendel^{1,4,5,12,13} · Louisa von Baumgarten^{4,5,7} · Nathalie L. Albert^{1,4,5}

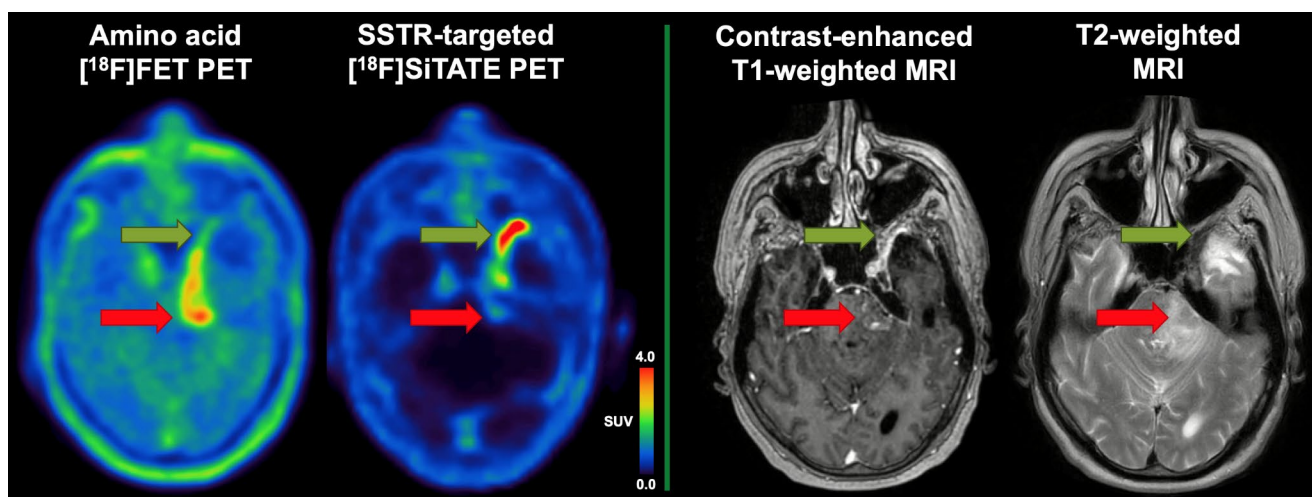
Received: 20 September 2024 / Accepted: 15 November 2024
© The Author(s) 2024

Keywords [¹⁸F]FET · [¹⁸F]SiTATE · Somatostatin receptor · PET imaging · Differential diagnosis · Dedifferentiation

✉ Adrien Holzgreve
Adrien.Holzgreve@med.lmu.de

- ¹ Department of Nuclear Medicine, LMU University Hospital, LMU Munich, Marchioninistr. 15, 81377, Munich, Germany
- ² Ahmanson Translational Theranostics Division, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA
- ³ Institute of Neuropathology, Faculty of Medicine, LMU Munich, Munich, Germany
- ⁴ German Cancer Consortium (DKTK), partner site Munich, a partnership between DKFZ and Ludwig-Maximilians-Universität München (LMU), Munich, Germany
- ⁵ Bayerisches Zentrum für Krebsforschung (BZKF), partner site Munich, Munich, Germany
- ⁶ Institute of Neuroradiology, LMU University Hospital, LMU Munich, Munich, Germany
- ⁷ Department of Neurosurgery, LMU University Hospital, LMU Munich, Munich, Germany
- ⁸ Department of Radiation Oncology, University Hospital Tübingen, Tübingen, Germany
- ⁹ Department of Radiation Oncology, LMU University Hospital, LMU Munich, Munich, Germany
- ¹⁰ Center for Neuro-Oncology, Comprehensive Cancer Center Tübingen-Stuttgart, University Hospital Tübingen, Tübingen, Germany
- ¹¹ German Cancer Consortium (DKTK), partner site Tübingen, a partnership between DKFZ and University Hospital Tübingen, Tübingen, Germany
- ¹² DZNE– German Center for Neurodegenerative Diseases, Munich, Germany
- ¹³ Munich Cluster for Systems Neurology (SyNergy), University of Munich, Munich, Germany

Amino acid PET is used for glioma imaging but has no established role in meningioma [1, 2]. We present a “flip-flop” constellation on SSTR and amino acid PET in meningioma that enabled to detect unrecognized malignant tumor tissue. A 65-year-old patient in continuous clinical follow-up presented with a new contrast-enhancing lesion on MRI in the left cerebral peduncle (red arrows), 5 years after radiotherapy of a left temporal suspected low-grade meningioma, and 1 year after its resection (revealing atypical meningioma CNS WHO grade 2). The patient received ongoing everolimus/octreotide for dural tumor remnants (green arrows). MRI findings were suggestive of reactive changes but could not exclude vital tumor. SSTR-targeted PET/CT with 187 MBq [¹⁸F]SiTATE showed markedly increased SSTR-expression at the known residue, whereas the adjacent new lesion only showed low tracer uptake, suggesting radiation necrosis [3]. Due to uncommon late-onset after radiotherapy, additional amino acid PET with 173 MBq [¹⁸F]FET was performed. In contrast to SSTR-PET, [¹⁸F]FET-PET displayed only minor uptake in the known meningioma residue; and while the time-activity curves were continuously increasing in the dynamic analysis, the new lesion showed markedly increased [¹⁸F]FET uptake, typical for malignant tumor tissue. Taken together, the findings were suggestive for meningioma recurrence with signs of dedifferentiation and malignant transformation. Stereotactic biopsy revealed malignant tumor tissue but was inconclusive regarding the tumor type. Eventually, surgical resection of the new lesion revealed malignant meningioma, now classified as CNS WHO grade 3, including homozygote CDKN2A/B deletion in the DNA-methylation profile [4], which was not present in the initial CNS WHO grade 2 tumor. Additional amino acid PET imaging in meningioma may help to identify



metabolically active dedifferentiated tumor tissue in cases with equivocal previous imaging findings.

Acknowledgements Parts of this work have been presented as an Oral Presentation at the Annual Meeting of the European Association of Nuclear Medicine (EANM) in 2023.

Author contributions Adrien Holzgreve: Writing— original draft, Visualization, Validation, Project administration, Methodology, Funding acquisition, Conceptualization. Patrick N. Harter: Writing— review & editing, Investigation. Robert Forbrig: Writing— review & editing, Investigation. Stefanie Quach: Writing— review & editing. Niklas Thon: Writing— review & editing. Christian Schichor: Writing— review & editing. Joerg-Christian Tonn: Writing— review & editing. Maximilian Niyazi: Writing— review & editing. Matthias Brendel: Writing— review & editing. Louisa von Baumgarten: Writing— review & editing. Nathalie L. Albert: Writing— review & editing, Supervision, Resources, Methodology, Funding acquisition, Conceptualization.

Funding Adrien Holzgreve received funding by the Bayerisches Zentrum für Krebsforschung (BZKF, Bavarian Cancer Research Center) and is currently funded by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation)— 545058105. Matthias Brendel was funded by the Deutsche Forschungsgemeinschaft (DFG) under Germany's Excellence Strategy within the framework of the Munich Cluster for Systems Neurology (EXC 2145 SyNergy— ID 390857198). Open Access funding enabled and organized by Projekt DEAL.

Data availability The datasets used and/or analyzed during the current study are presented in the manuscript.

Declarations

Ethics approval The analysis was performed in compliance with the principles of the Declaration of Helsinki. No identifiable patient data is included in the manuscript, in this respect the right to informational self-determination is not affected. The patient provided written informed consent for the imaging studies within clinical routine. In accordance with the ethics committee of the Ludwig-Maximilians-University of Munich this work is not subject to review.

Competing interests AH reports compensation for scientific consulting by ABX advanced biochemical compounds. JCT reports travel cost reimbursement from Servier. MB received consulting/speaker honoraria from Life Molecular Imaging, GE healthcare, and Roche, and reader honoraria from Life Molecular Imaging. NLA has received honoraria for consultation or advisory board participation from Novartis, Advanced Accelerator Applications, Servier, and Telex Pharmaceuticals; and has received research funding from Novocure. The remaining authors have no relevant financial or non-financial interests to disclose.

Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>.

References

1. Albert NL, Preusser M, Traub-Weidinger T, Tolboom N, Law I, Palmer JD, et al. Joint EANM/EANO/RANO/SNMMI practice guideline/procedure standards for diagnostics and therapy (theranostics) of meningiomas using radiolabeled somatostatin receptor ligands: version 1.0. *Eur J Nucl Med Mol Imaging*. 2024. <https://doi.org/10.1007/s00259-024-06783-x>.
2. Holzgreve A, Albert NL, Galldiks N, Suchorska B. Use of PET Imaging in Neuro-Oncological surgery. *Cancers (Basel)*. 2021;13. <https://doi.org/10.3390/cancers13092093>.
3. Müller KJ, Biczok A, Schichor C, von Baumgarten L, Albert NL. The value of [(18)F]FET PET and somatostatin receptor imaging for differentiating pseudoprogression in residual meningioma. *Eur J Nucl Med Mol Imaging*. 2024;51:1194–6. <https://doi.org/10.1007/s00259-023-06479-8>.

4. Sahm F, Aldape KD, Brastianos PK, Brat DJ, Dahiya S, von Deimling A, et al. cIMPACT-NOW update 8: clarifications on molecular risk parameters and recommendations for WHO grading of meningiomas. *Neuro Oncol.* 2024. <https://doi.org/10.1093/neuonc/noae170>.

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