Photopenic defects in gliomas with amino-acid PET and relative prognostic value: a multicentric ^{11}C-Methionine and ^{18}F-FDOPA PET experience

Timothée Zaragori[1, 2], Angelo Castello[3], Eric Guedj[4, 5], Antoine Girard[6], Norbert Galldiks[7, 8, 9], Nathalie L. Albert[10], Egesta Lopci[3]*, Antoine Verger[1, 2]*

* *The two last authors equally contributed to this work*

[1]Université de Lorraine, Department of Nuclear Medicine and Nancyclotep Imaging Platform, F-54000 Nancy, France

[2]Université de Lorraine, IADI, INSERM U1254, F-54000 Nancy, France

[3]Nuclear Medicine Department, Humanitas Clinical and Research Hospital – IRCCS, Via Manzoni 56, Rozzano (MI), Italy

[4]APHM, Timone Hospital, Nuclear Medicine Department, Marseille, France

[5]Aix Marseille Univ, CNRS, Ecole Centrale Marseille, UMR 7249, Institut Fresnel, CERIMED, Marseille, France

[6]Department of Nuclear Medicine, Eugène Marquis Center, Rennes 1 University, Rennes, France

[7]Dept. of Neurology, Faculty of Medicine and University Hospital Cologne, University of Cologne, Germany

[8]Inst. of Neuroscience and Medicine (INM-3), Research Center Juelich, Juelich, Germany

[9]Center of Integrated Oncology (CIO), Universities of Aachen, Bonn, Cologne, and Duesseldorf, Germany

[10]Department of Nuclear Medicine, University Hospital, LMU Munich, Munich, Germany

Corresponding author:

Timothée Zaragori

timothee.zaragori@univ-lorraine.fr

Médecine Nucléaire, Hôpital de Brabois, CHRU-Nancy, Allée du Morvan, 54500 Vandoeuvre-les-Nancy, France.

Tel: (+33) 3 83 15 39 09; Fax: (+33) 3 83 15 38 39

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ABSTRACT

The aim is to explore the concept of photopenic defects in newly-diagnosed glioma patients with the two widely-used ^{11}C-MET and ^{18}F-FDOPA PET amino-acid tracers. Thirty-two ^{11}C-MET and twenty-six ^{18}F-FDOPA PET scans with amino-acid PET-negative gliomas were selected in this European multicentric study. Out of these gliomas, 16 ^{11}C-MET and 10 ^{18}F-FDOPA PET scans with photopenic defects were identified, exhibiting lower TBR_{mean} as compared to isometabolic gliomas ($p<0.001$). Gliomas with photopenic defects had not different progression-free-survival (PFS) than isometabolic gliomas in the whole-population ($p=0.40$), but shorter PFS in the subgroup of WHO grade II IDH-mutant astrocytomas (35 vs. 68 months; $p=0.047$).

Key-words: glioma; ^{11}C-MET; ^{18}F-FDOPA; photopenic; prognosis

FIGURE

	^{11}C-MET	^{18}F-FDOPA	Total	p-value
WHO grade *n (%)*				0.22
II	25 (78)	18 (69)	43 (74)	
III	7 (22)	8 (31)	15 (26)	
WHO 2016 classification *n (%)*				0.05*
IDH-mutant astrocytoma	17 (53)	18 (69)	35 (60)	
IDH-wildtype astrocytoma	4 (13)	6 (23)	10 (17)	
IDH-mutant and 1p/19q co-deleted oligodendroglioma	11 (34)	2 (8)	13 (22)	
Photopenic defects *n (%)*	16 (50)	10 (38)	26 (45)	0.38

IDH: Isocitrate dehydrogenase; WHO: World Health Organization

**p<0.05 for comparison between ^{11}C-MET and ^{18}F-FDOPA*

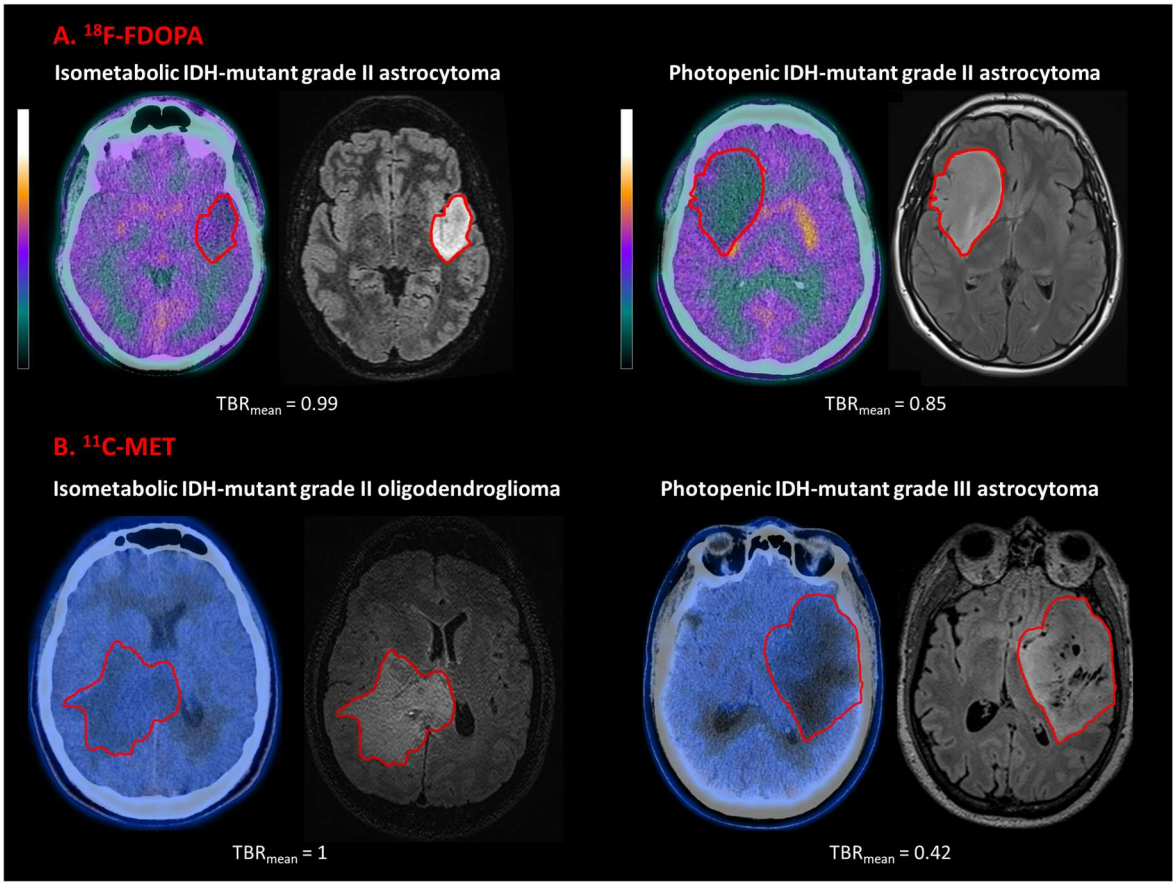

FIGURE LEGEND

In a recent publication, Galldiks and colleagues stated that gliomas with photopenic defects in a series of negative ^{18}F-FET PET scans may have a more aggressive clinical course as compared to isometabolic gliomas [1]. Since the exact comparability of diagnostic and prognostic information provided by each amino-acid radiotracer remains to be specified [2], we wanted to explore whether the knowledge on photopenic defects in newly-diagnosed glioma patients could be extended to ^{11}C-MET and ^{18}F-FDOPA PET scans, involving two other widely used amino-acid tracer [3–5]. Glioma patient characteristics of this multicentric study are presented in the upper part of the Figure. ^{18}F-FDOPA PET scans were collected in Nancy, Rennes and Marseille centers (France) while ^{11}C-methionine PET scans were collected in Milan center (Italy). Informed consent was obtained from all individual procedures included in the study. The proportions of visually negatives gliomas (17% for ^{11}C-MET, 13% for ^{18}F-FDOPA) and among them, photopenic defects gliomas (50% for ^{11}C-MET, 38% for ^{18}F-FDOPA) were similar with those reported for ^{18}F-FET (around 10% of negative gliomas and among them 40% with photopenic defects [1]). Representative examples of isometabolic and photopenic defects astrocytomas are shown in the lower part of the Figure with axial slices of amino acid PET scans (^{18}F-FDOPA (A.) and ^{11}C-methionine (B.)) and their respective tumor regions based on the signal alteration on fluid attenuated inversion recovery MR images (red contours). The semi-quantitative analysis comparison of isometabolic and photopenic defects gliomas confirmed that the latter had a significantly lower mean tumor-to-background ratios ($p<0.001$ for the whole-population and both radiotracers). This lower uptake might be related to a lower expression of L-type amino acid transporters which is consider as the main mechanism of ^{11}C-MET and ^{18}F-FDOPA amino-acid radiotracers uptake [6,7]. Regarding survival in the 58 patients, photopenic defects gliomas on ^{11}C-MET or ^{18}F-FDOPA PET reached no statistically significant difference in

progression-free-survival (PFS) compared to isometabolic gliomas (p=0.40). On the other hand, a subgroup analysis of WHO grade II IDH-mutant astrocytomas revealed that photopenic defects glioma patients (n=13) had a significantly shorter PFS than isometabolic gliomas (n=9) (35 vs. 68 months; p=0.047) which is in line with the results of Galldiks et al. for ^{18}F-FET PET [1]. The photopenic gliomas might represent a transient state before the impeding transformation of the tumor [8] as observed in the follow-up of gliomas having beneficiated from a ^{18}F-FET PET: a significant increased ^{18}F-FET uptake, likely corresponding to a glioma transformation, happened earlier in photopenic in comparison to isometabolic WHO grade II IDH-mutant astrocytomas [9]. Overall, the presented results suggest that the concept of photopenic defects in glioma patients can be expanded to the ^{11}C-MET and ^{18}F-FDOPA amino-acid tracers. Although occurring in apparently less aggressive gliomas, photopenic defects seem capable to delineate subgroups of patients with poorer outcome. A particular attention should be paid on patients with WHO grade II IDH-mutant astrocytomas exhibiting a photopenic defect since they appear to have a more aggressive clinical course.

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