The role of ^{11}C-methionine PET in patients with newly diagnosed WHO grade 2 or 3 gliomas

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Editorial

To be submitted to *Neuro-Oncology*

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Declaration

The text is the sole product of the authors and that no third party had input or gave support to its writing. Related to the present work, the authors disclosed no potential conflicts of interest.

EDITORIAL

Amino acid PET is a well-established method for brain cancer diagnostics and recommended by the RANO group in all stages of the treatment of glioma patients [1,2]. The longest-established amino acid tracer for brain tumor imaging is [^{11}C]-methyl-L-methionine (^{11}C-MET), but its application remains restricted to centers with an onsite cyclotron due to the short half-life of ^{11}C (20 minutes). Although amino acids labeled with ^{18}F (half-life, 110 minutes) such as O-(2-[^{18}F]-fluoroethyl)-L-tyrosine (^{18}F-FET) or 3,4-dihydroxy-6-[^{18}F]-fluoro-L-phenylalanine (^{18}F-FDOPA) have replaced ^{11}C-MET in many neurooncological centers, ^{11}C-MET PET still constitutes an important diagnostic method [3].

In patients with newly diagnosed WHO grade 2 or 3 gliomas, the number of studies concerning the use of amino acid PET is limited and further studies are urgently needed. In this edition of Neuro-Oncology, Ninatti and colleagues evaluated the role of ^{11}C-MET PET in 153 patients with newly diagnosed glioma [4], which were histomolecularly characterized as grade 2 or grade 3 gliomas according to the latest WHO classification [5] representing the largest study in this field to date.

The study by Ninatti et al. confirmed the observation of previous studies that ^{11}C-MET PET is of considerable value for the preoperative assessment of the glioma type and

grade. Increased ^{11}C-MET uptake was more prevalent in WHO grade 3 than in grade 2 gliomas, and WHO grade 3 tumors had higher tracer uptake than grade 2 tumors. In particular, the majority of oligodendrogliomas (87%) showed considerably increased ^{11}C-MET uptake, i.e., low ^{11}C-MET uptake makes the diagnosis of an oligodendroglioma unlikely. Patients with IDH-mutant astrocytoma showed the lowest tracer uptake and represented 71% of all negative lesions, i.e., lack of ^{11}C-MET uptake should raise the suspicion of an IDH-mutant glioma. Furthermore, 25% of patients showed areas with pathological increased ^{11}C-MET uptake outside of regions with FLAIR hyperintensities, further supporting the additional role of amino acid PET in tumor delineation. Moreover, in patients with IDH-mutant astrocytoma, the extent of resection and maximum tumor-to-background ratios of ^{11}C-MET uptake showed an independent prognostic value in multivariate analysis.

Interestingly, 42 of 111 tumors (27%) showed no increased ^{11}C-MET uptake, and 10 of these tumors (6%) were even hypometabolic. A previous study using ^{18}F-FET PET has demonstrated that these photopenic gliomas seem to have an unfavorable outcome and should be managed more aggressively [6]. Another study with a smaller number of patients reported the phenomenon of hypometabolic gliomas also for ^{18}F-FDOPA (n=16 gliomas) and ^{11}C-MET PET (n=10 gliomas) [7]. Apparently, photopenic gliomas are rare, and the number of ^{11}C-MET photopenic lesions in the study by Ninatti et al. was too small to draw general conclusions. The value of ^{11}C-MET PET to predict an unfavorable outcome in patients with photopenic glioma should be further evaluated.

In conclusion, the results of the study by Ninatti et al. demonstrate that a routine implementation ^{11}C-MET PET may optimize the management of patients with newly

diagnosed WHO grade 2 or grade 3 gliomas. These results should be reproduced by more widely available amino acid tracers such as ^{18}F-FET, ^{18}F-FDOPA, or the synthetic amino acid analog anti-1-amino-3-[^{18}F]fluorocyclobutane-1-carboxylic acid (Fluciclovine) [8].

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