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Letter to the Editor: "^{18}F-FDOPA PET for the Noninvasive Prediction of Glioma Molecular Parameters: A Radiomics Study"

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To the Editor,

We have read with interest the paper by Zaragori et al. about the role of PET using 6-^{18}F-fluoro-L-DOPA (^{18}F-FDOPA) in the prediction of molecular parameters by radiomics [1]. We agree that radiomics is a promising approach to improve the accuracy of amino acid PET [2]. This has been demonstrated for example for the differentiation of recurrent tumor from treatment related changes [3, 4].

Zaragori et al. report that radiomics features of static and dynamic ^{18}F-FDOPA data in patients with a neuropathologic diagnosis of grade II, III, or IV glioma were able to predict IDH mutations and the 1p/19q codeletion with an area under the curve of 0.831 and 0.724, respectively. They conclude that ^{18}F-FDOPA PET using a full set of radiomics features is an effective tool for the noninvasive prediction of IDH mutations as well as for prediction of the 1p/19q codeletion in routine practice.

Although we have no doubt about the quality of the study, we would like to point out a problem with the pre-selection of patients. For the study, 74 patients with grade II - IV gliomas were retrospectively selected from a larger collective. The authors assume that the results of this study are valid for the non-invasive prediction of molecular parameters in patients with suspected glioma, i.e. in the situation of preoperative diagnostics in which, apart from clinical and radiological parameters, no information is available about the histology of the tumors.

Previous studies investigating the final diagnosis of patients referred for amino acid PET with suspected brain tumour, however, report a proportion of benign lesions or non-glial tumours of 20 - 40 % (inflammation, ischemia, lymphoma etc.) [5-7]. The radiomic features of these lesions were not considered in the present analysis and could significantly affect the results of the study. Therefore, the validity of the study for non-invasive prediction of molecular parameter in the situation of preoperative diagnostics is at least doubtful.

A similar misconduct can also be observed in another recently published study [8], which investigated the prediction of TERTp mutation status in IDH-wildtype (IDHwt) high-grade gliomas using pre-treatment dynamic ^{18}F-FET PET radiomics. In that study patients with IDHwt tumors were selected from a mixed population of patients and the authors report that radiomics based on time-to-peak images extracted from dynamic O-(2-^{18}F- fluoroethyl)-L-tyrosine (^{18}F-FET) PET could predict the TERTp mutation status of IDH-wildtype diffuse astrocytic high-grade gliomas with high accuracy preoperatively. Since the IDH mutation status in the preoperative population is not known, the analysis is considerably affected by the IDH negative gliomas and benign lesions and the validity also of this study in the situation of preoperative diagnostics has to be seen very cautiously.

Summarizing, we would like to point out that image analysis methods aiming at non-invasive prediction of molecular parameters have to be based on a representative preoperative population. Pre-selection of such populations based on postoperative histological data is leading to an erroneous and not clinically useful conclusion.

We conclude that the results of such studies can only be considered as hypotheses and have no relevance for clinical practice.

Competing Interests

The authors declare that they have no competing interests.

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