Letters to the Editor

Discriminating Ability of ^{18}F-FET PET for Several Cerebral Neoplastic Lesions

TO THE EDITOR: I read with interest the paper of Rapp et al. (*1*) recently published in *The Journal of Nuclear Medicine*. The study focused on the discriminatory ability of ^{18}F-FET PET for the initial diagnosis of cerebral lesions suggestive of glioma. The data of 170 patients, excluding 4 with occult glioma, were used for the analysis. Glioblastoma and anaplastic glioma were defined as high-grade gliomas, and other gliomas including diffuse type were defined as low-grade gliomas. The numbers of high-grade gliomas, low-grade gliomas, lymphomas, and nonneoplastic lesions were 66, 77, 2, and 25, respectively.

I have concern about the authors' statistical procedures, with special emphasis on receiver-operating-characteristic (ROC) curve analysis. The authors set 3 controls—nonneoplastic lesions, low-grade gliomas, and low-grade gliomas plus nonneoplastic lesions—to differentiate neoplastic lesions, high-grade gliomas, and high-grade tumor including lymphoma, respectively. They used the Youden index for cutoff values, which, for maximum and mean tumor-to-brain ^{18}F-FET uptake ratios, were set at 2.5 and 1.9, respectively. The cutoff values were the same for differentiating neoplastic lesions, high-grade gliomas, and high-grade tumor including lymphoma. I think it would be difficult to use these cutoff values for the initial diagnosis of cerebral lesions. In general, patients with nonneoplastic lesions are set as controls, and cases of cerebral neoplastic lesions (total or specific) are determined using maximum and mean tumor-to-brain ^{18}F-FET uptake ratios. The values in Table 2 and Figures 1 and 2 of Rapp et al. indicate a trend toward an increase in maximum and mean tumor-to-brain ratios as the malignancy of glioma progressed. But I feel that the third ROC curve analysis lacks a biologic basis (*2*). In addition, each area under the ROC curve was less than 0.8, which does not have sufficient statistical significance for satisfactory diagnostic performance in differentiating gliomas using maximum and mean tumor-to-brain ^{18}F-FET uptake ratios.

Before the final conclusion of Rapp et al. on the advantage of ^{18}F-FET PET for initial diagnosis of cerebral lesions is accepted, I strongly suggest further study by adding information on the diagnostic performance of the indicators Rapp et al. used. For example, they could not compare areas under the curve of high-grade gliomas and low-grade gliomas against nonneoplastic lesions by increasing the number of nonneoplastic lesion samples (*3*). Commercially based software such as MedCalc would be useful for conducting ROC curve analysis.

REFERENCES

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REPLY: We cannot really understand the concerns of Dr. Kawada regarding our study (*1*). It appears that there is a general misunderstanding concerning the central message of our study. Our study on newly diagnosed and untreated brain lesions provides evidence that there is a wide overlap of tumor-to-brain ^{18}F-FET uptake ratios in various lesions resulting in only moderate accuracy for differential diagnosis of primary brain lesions, especially in terms of differentiation between high- and low-grade glioma.

On the basis of frequently asked clinical questions at initial diagnosis, that is, whether the diagnostic method is able to separate benign lesions from neoplastic lesions, high-grade glioma from low-grade glioma, or malignant (high-grade) lesions from low-grade glioma and nonneoplastic lesions, we divided the patient collective into corresponding groups for receiver-operating-characteristic curve analysis.

With respect to differentiation between high-grade and low-grade glioma, we stated that the diagnostic accuracy of ^{18}F-FET PET is not sufficient to decisively influence treatment decisions and that histologic confirmation by biopsy or open surgery remains necessary.

On the other hand, we observed that the tumor-to-brain ^{18}F-FET uptake ratio at initial diagnosis may provide important information for decision making. We observed that ^{18}F-FET uptake beyond a cutoff of 2.5 for maximum tumor-to-brain ratio resulted in a positive predictive value of 98% for neoplastic lesions and supports the necessity of an invasive procedure, such as biopsy or surgical resection. Furthermore, a maximum tumor-to-brain ratio of less than 2.5 yielded a negative predictive value of 84% for high-grade tumors, such as high-grade glioma or lymphomas.

Thus, the finding of low ^{18}F-FET uptake may support the clinical decision to follow a watch-and-wait strategy, especially when the clinical course and MR imaging findings additionally suggest a benign process. Therefore, our statement that ^{18}F-FET uptake ratios provide valuable additional information for both the differentiation of cerebral lesions and the grading of gliomas is justified.

With respect to ROC analysis, we used the commercially based statistical software Sigma Plot (version 11.0; Systat Software Inc.), and there is no reason that this software should lead to results different from those provided by MedCalc.

In the discussion, we pointed out that we cannot support the view of other authors that ^{18}F-FET PET provides excellent performance for diagnosing primary brain tumors (*2*). In our opinion, the value of ^{18}F-FET PET during the initial diagnosis of cerebral lesions lies especially in defining an optimal site for biopsy and determining the extent of metabolically active tumor for treatment planning rather than in making a differential diagnosis of the lesion.

REFERENCES

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