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The use of dynamic *O*-(2-^{18}F-fluoroethyl)-L-tyrosine PET in the diagnosis of patients with progressive and recurrent glioma

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Background. We evaluated the diagnostic value of static and dynamic *O*-(2-[^{18}F]fluoroethyl)-L-tyrosine (^{18}F-FET) PET parameters in patients with progressive or recurrent glioma.

Methods. We retrospectively analyzed 132 dynamic ^{18}F-FET PET and conventional MRI scans of 124 glioma patients (primary World Health Organization grade II, $n = 55$; grade III, $n = 19$; grade IV, $n = 50$; mean age, 52 ± 14 y). Patients had been referred for PET assessment with clinical signs and/or MRI findings suggestive of tumor progression or recurrence based on Response Assessment in Neuro-Oncology criteria. Maximum and mean tumor/brain ratios of ^{18}F-FET uptake were determined (20–40 min post-injection) as well as tracer uptake kinetics (ie, time to peak and patterns of the time–activity curves). Diagnoses were confirmed histologically (95%) or by clinical follow-up (5%). Diagnostic accuracies of PET and MR parameters for the detection of tumor progression or recurrence were evaluated by receiver operating characteristic analyses/chi-square test.

Results. Tumor progression or recurrence could be diagnosed in 121 of 132 cases (92%). MRI and ^{18}F-FET PET findings were concordant in 84% and discordant in 16%. Compared with the diagnostic accuracy of conventional MRI to diagnose tumor progression or recurrence (85%), a higher accuracy (93%) was achieved by ^{18}F-FET PET when a mean tumor/brain ratio ≥ 2.0 or time to peak <45 min was present (sensitivity, 93%; specificity, 100%; accuracy, 93%; positive predictive value, 100%; $P < .001$).

Conclusion. Static and dynamic ^{18}F-FET PET parameters differentiate progressive or recurrent glioma from treatment-related non-neoplastic changes with higher accuracy than conventional MRI.

Keywords: FET PET, malignant glioma, progressive disease, tumor recurrence.

Conventional MRI with a gadolinium contrast agent is the method of choice for the diagnosis and follow-up of cerebral gliomas. Tumor relapse typically presents as newly occurring or increasing contrast-enhancing lesion. However, a frequent and highly relevant clinical problem in glioma patients is that transient treatment-related blood–brain barrier alterations with consecutive contrast enhancement on conventional MRI can mimic tumor recurrence or progression.[1,2] These treatment-induced changes in glioma patients typically occur either early—within the first 3 months of radio(chemo)therapy (ie, pseudoprogression)[3,4]—or later on, even up to several years after treatment.[5] Such findings may interfere with the reliable and early diagnosis of tumor recurrence or progression. This constitutes the risk that a potentially effective treatment might be erroneously terminated, which may have a negative consequence for subsequent survival. To date, the differentiation of glioma recurrence or progression from treatment-induced effects is a diagnostic challenge, particularly for contrast-enhanced conventional MRI.[5–7]

Amino acid PET is a promising molecular neuroimaging technique that provides information on tumor metabolism,

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thereby complementing structural imaging using MRI.[8] Several studies have evaluated the role of amino acid PET using different tracers, such as *O*-(2-[^{18}F]fluoroethyl)-L-tyrosine (^{18}F-FET), ^{11}C-methyl-L-methionine (^{11}C-Met), and *L*-3,4-dihydroxy-6-^{18}F-fluoro-phenylalanine (^{18}F-FDOPA), for differential diagnoses of suspected glioma recurrence or progression.[8] However, in most studies, either the sample size was relatively small or histological confirmation of diagnosis was unavailable in a large fraction of patients, which limits the validity of the results. ^{18}F-FET especially is an amino acid tracer, the use of which has rapidly increased in western Europe due to the longer half-life of the ^{18}F-label and efficient synthesis. To date, the diagnostic accuracy of ^{18}F-FET PET for differentiating tumor recurrence or progression and treatment-related changes has been assessed in a few studies only. Although promising data have been reported,[9–12] further validation is needed. The aim of the current study was to identify the ^{18}F-FET PET imaging parameters that most accurately differentiate tumor recurrence or progression from treatment-induced changes.

Materials and Methods

Patients

One hundred twenty-four glioma patients (males, 81; females, 43; mean age, 52 ± 14 y) with suspected tumor recurrence or progression between 2006 and 2013 were included in this retrospective study. The primary World Health Organization (WHO) glioma grading was distributed as follows: grade II, $n = 55$; grade III, $n = 19$; grade IV, $n = 50$. Patients were consecutively referred for PET assessment with clinical signs and/or MRI findings suggestive of tumor progression or recurrence based on Response Assessment in Neuro-Oncology (RANO) criteria. The study was approved by both the local ethics committee and the federal authorities, and all patients gave written informed consent before each ^{18}F-FET PET investigation. Further details of the patient cohort are presented in Table 1.

Table 1. Patient population

Patients, *N*	124
^{18}F-FET PET scans, *N*	132
Sex	
Female, *n* (%)	43 (35)
Male, *n* (%)	81 (65)
Mean age at recurrence or progression	52 ± 14 y
Histology at initial diagnosis, *n* patients (%)	
Diffuse astrocytoma, grade II	36 (29)
Oligoastrocytoma, grade II	14 (11)
Oligodendroglioma, grade II	5 (4)
Anaplastic astrocytoma, grade III	15 (12)
Anaplastic oligoastrocytoma, grade III	4 (3)
Anaplastic oligodendroglioma, grade III	0 (0)
Glioblastoma, grade IV	49 (40)
Gliosarcoma, grade IV	1 (1)
[a]Cases at first tumor recurrence or progression, *n* (%)	84 (64)
[a]Cases at second tumor recurrence or progression, *n* (%)	35 (26)
Cases at ≥3rd tumor recurrence or progression, *n* (%)	13 (10)
Patients with malignant progression during the course of disease, *n* (%)	48 (38)
Grade II to grade III	36 (29)
Grade II to grade IV	7 (5)
Grade III to grade IV	5 (4)

[a]Note that in 8 patients, imaging and treatment were performed at both first and second recurrence/progression.

PET Imaging With ^{18}F-FET

The amino acid ^{18}F-FET was produced as described previously.[13,14] According to the German guidelines for brain tumor imaging using labeled amino acid analogues, all patients fasted for at least 12 hours before PET scanning.[15] Dynamic PET studies were acquired up to 50 min after intravenous injection of approximately 200 MBq ^{18}F-FET on an ECAT EXACT HR+ scanner (Siemens Medical Systems) in 3-dimensional mode (32 rings; axial field of view, 15.5 cm). The emission recording consisted of 16 time frames (time frames 1–5: 1 min; 6–10: 3 min; and 11–16: 5 min) covering the period up to 50 min post-injection. For attenuation correction, transmission was measured with 3 ^{68}Ge/^{68}Ga rotating line sources. After correction for random and scattered coincidences as well as dead time, 63 image planes were iteratively reconstructed (ordered subset expectation maximization: 6 iterations, 16 subsets) using the ECAT 7.2 software. The reconstructed image resolution was approximately 5.5 mm.

PET Data Analysis

Uptake of ^{18}F-FET in the tissue was expressed as standardized uptake value (SUV) by dividing the radioactivity (kBq/mL) in the tissue by the radioactivity injected per gram of body weight. PET and MR images were coregistered using dedicated software (MPI tool v6.48; ATV). The fusion results were inspected and, if necessary, adapted based on anatomical landmarks. Region-of-interest (ROI) analysis was based on the summed PET data from 20 to 40 min post-injection. The transaxial slices showing the highest tracer accumulation in the tumors were chosen for ROI analyses. The uptake in the unaffected brain tissue was determined by a larger ROI placed on the contralateral hemisphere in an area of normal-appearing brain tissue including white and gray matter.[15] Mean amino acid uptake in the tumor was determined by a 2-dimensional autocontouring process using a tumor-to-brain ratio (TBR) of 1.6 as described previously[16]; for maximal amino acid uptake a circular ROI with a diameter of 1.6 cm was centered on maximal tumor uptake. Maximum and mean TBRs (TBR_{max}, TBR_{mean}) were calculated by dividing the mean SUV of these tumor ROIs by the mean SUV of normal brain in the PET scan.

Furthermore, time–activity curves (TACs) of mean SUV of ^{18}F-FET uptake in the tumor and in the brain were generated by application of a spherical volume of interest of 2 mL centered on maximal tumor uptake and of a reference ROI in the unaffected brain tissue (as described above) to the entire dynamic data set. We determined time to peak (TTP), in minutes from the beginning of the dynamic acquisition up to the maximum SUV of the lesion. Furthermore, as previously described,[17,18] the TACs of each lesion were assigned to one of the following curve patterns: constantly increasing ^{18}F-FET uptake without identifiable peak uptake (pattern I); ^{18}F-FET

uptake peaking at a midway point (>20–40 min) followed by a plateau or a small descent (pattern II); and ^{18}F-FET uptake peaking early (≤20 min) followed by a constant descent (pattern III). The assignment of TACs to the various curve patterns was performed by 3 experienced raters (N.G., K.-J.L., and G.S.).

MR Imaging

All patients underwent routine MRI (1.5 T Sonata or 3 T Magnetom Trio MR; Siemens) with a standard head coil before and after administration of a gadolinium-based contrast agent (T1- and T2-weighted and fluid attenuated inversion recovery sequence). Axial T1-weighted images were obtained from the second cervical vertebral body to the vertex. Diagnosis of tumor progression or recurrence was based on RANO criteria.[2]

Histological Confirmation

In 126 of 132 cases (95%) suspicious for tumor recurrence or progression, ^{18}F-FET PET and MRI findings were confirmed histologically either by stereotactic biopsy (in 28 cases; 22%) or tumor resection (in 98 cases; 78%). If no histological confirmation was available (6 cases; 5%), the diagnosis of tumor recurrence or progression was based on the clinical course. The median follow-up time was 9 months (range, 7–14 mo).

Statistical Analysis

Descriptive statistics are provided as mean and standard deviation. To compare 2 different groups, the Student *t*-test for independent samples was used. The Mann–Whitney rank sum test was used when variables were not distributed normally. $P < .05$ was considered significant.

The diagnostic performance of ^{18}F-FET uptake as determined by TBR_{max} and TBR_{mean} to identify tumor recurrence or progression was assessed by analyses of receiver operating characteristic (ROC) curves using the histological confirmation or clinical course as reference. Decision cutoff was considered optimal when the product of paired values for sensitivity and specificity reached its maximum. In addition, the area under the ROC curve (AUC), its standard error, and level of significance were determined as a measure of diagnostic quality. The diagnostic performance of RANO criteria, ^{18}F-FET TAC patterns alone and in combination with the corresponding TBRs, was evaluated by chi-square or Fisher exact tests for 2×2 contingency tables.

After the assignment of TACs of ^{18}F-FET uptake to the 3 curve patterns, Cohen's κ-test was used to measure the degree of interrater agreement (N.G., K.-J.L., G.S.); κ values of 0–0.20 were considered to indicate a positive but slight correlation, 0.21–0.40 a fair correlation, 0.41–0.60 a good correlation, 0.61–0.80 a very good correlation, and >0.80 an excellent correlation.

P-values of .05 or less were considered significant. Statistical analyses were performed using SigmaPlot software (SigmaPlot v11.0, Systat Software) and PASW Statistics software (release 22.0.0, SPSS).

Results

Pretreatment

At the time point of suspicion of tumor recurrence or progression, 110 of 124 patients (89%) had been pretreated. In the remaining 14 patients, diagnostic biopsies had been performed only and the patients were followed by a "watch and wait" approach. In 88 of 110 pretreated patients (80%), at least one neurosurgical tumor resection (median number of resections, 1; range, 1–4) had been performed. Due to tumor localization in eloquent brain regions, in 22 of 110 pretreated patients (20%) a tumor resection had not been performed. Furthermore, during the course of disease, the majority of patients received radiotherapy and/or chemotherapy (94 of 110 patients; 86%). A detailed overview of the patients' pretreatment is provided in Table 2.

Diagnoses at the Time Point of Suspected Tumor Recurrence or Progression

Tumor progression or recurrence could be diagnosed in 121 of 132 cases (92%). In the remaining 11 cases (8%), diagnosis was consistent with nonneoplastic changes (reactive tissue changes, 10; abscess, 1).

Diagnostic Performance of Static and Kinetic ^{18}F-FET PET Parameters

ROC analysis yielded a TBR_{max} of 2.3 as an optimal cutoff to identify tumor recurrence or progression (sensitivity, 68%; specificity, 100%; accuracy, 71%; AUC, 0.85 ± 0.04; $P < .001$). The corresponding cutoff for the TBR_{mean} to identify tumor recurrence or progression was 2.0 (sensitivity, 74%; specificity, 91%; accuracy, 75%; AUC, 0.91 ± 0.03; $P < .001$). For TTP, ROC analysis yielded <45 min as an optimal cutoff to identify tumor recurrence or progression (sensitivity, 82%; specificity, 73%; accuracy, 81%; AUC, 0.81 ± 0.06; $P < .001$). The evaluation of the interrater agreement for the assignment of TACs to the 3 curve patterns yielded very good agreement, with a mean κ value of 0.77 ± 0.10 (range, 0.67–0.87). Presence of a curve pattern II or III alone identified tumor recurrence or progression with a sensitivity of 78%, a specificity of 73%, and an accuracy of 77% ($P = .001$). The combined analysis of $TBR_{max}/TBR_{mean} \geq 2.3/2.0$ and/or a kinetic pattern II or III identified tumor recurrence or progression with a sensitivity of 93%, a specificity of 73%, and an accuracy of 91% ($P < .001$). The combined analysis of $TBR_{mean} \geq 2.0$ and/or TTP < 45 min yielded the best result to identify tumor recurrence or progression, with a sensitivity of 93%, a specificity of 100%, and an accuracy of 93% ($P < .001$) (Table 3).

Congruence of MR and PET Findings in Relation to Histology

MRI data were available in 128 of 132 cases. RANO criteria for tumor recurrence or progression were fulfilled in 118 cases. In these cases, tumor recurrence or progression could be confirmed in 108 cases, while 10 cases were false positive (reactive tissue changes, 9; abscess, 1). In contrast, in 9 of 10 cases with false positive MRI findings, PET showed low ^{18}F-FET uptake

Table 2. Overview of pretreatment

	Treatment	WHO Grade II Glioma	WHO Grade III Glioma	WHO Grade IV Glioma
Cases at first tumor recurrence or progression ($n = 84$; 64%)	"Watch and wait"	14	—	—
	Resection alone	11	—	—
	RTx alone	2	1	—
	CTx alone	1	1	—
	Resection and RTx	4	—	—
	Resection and CTx	2	3	2
	RTx and CTx	1	5	1
	Resection, RTx, and CTx	1	2	33
Cases at second tumor recurrence or progression ($n = 35$; 26%)	CTx alone	3	—	—
	RTx and CTx	—	1	—
	Resection and CTx	1	—	—
	Resection and RTx	1	—	—
	Resection, RTx, and CTx	2	4	4
	Two resections alone	3	—	1
	Two resections and CTx	1	1	—
	Two resections, RTx, and CTx	3	1	9
Cases at ≥3rd tumor recurrence or progression ($n = 13$; 10%)	RTx and CTx	1	—	—
	Resection, RTx, and CTx	1	—	—
	Two or more resections alone	1	—	—
	Two or more resections and CTx	—	1	—
	Two or more resections and RTx	2	—	—
	Two or more resections, RTx, and CTx	3	1	3

Abbreviations: RTx, radiotherapy; CTx, chemotherapy.

($TBR_{max} < 2.3$) (Fig. 1). In the remaining 10 of 128 cases, MRI was suspect for tumor recurrence or progression, but RANO criteria were not fulfilled. In these cases, tumor recurrence or progression could be histologically diagnosed in 9 of 10 cases, while in one case reactive tissue changes were determined. In these cases, in which RANO criteria for tumor recurrence or progression were not fulfilled, ^{18}F-FET PET showed increased uptake ($TBR_{max} \geq 2.3$) in 6 of 10 cases with tumor recurrence or progression. The diagnostic performance of conventional MRI to detect tumor recurrence or progression based on RANO criteria as assessed by chi-square analysis for 2×2 contingency tables resulted in a high sensitivity of 92%, but a low specificity of 9% (accuracy, 85%; $P = .673$).

Discussion

In the present retrospective study we evaluated the diagnostic value of ^{18}F-FET PET for assessing recurrent or progressive gliomas after pretreatment. We observed that the combination of static and kinetic ^{18}F-FET PET parameters reached a higher diagnostic accuracy in distinguishing recurrent or progressive disease from treatment-related changes than did conventional MRI (Figs 1 and 2). To the best of our knowledge, this is currently the largest study to evaluate static and kinetic ^{18}F-FET PET parameters in pretreated patients with glioma recurrence or progression. In nearly all of the cases (95%), imaging findings could be confirmed histologically. Thus, our findings indicate that ^{18}F-FET PET is a useful method in this clinically challenging situation, especially when conventional MRI is inconclusive. The detection of tumor recurrence or progression with high accuracy is essential to optimize patient counseling as well as the treatment strategy for each patient.

In principle, our study confirms the high diagnostic accuracy of ^{18}F-FET PET for differentiating recurrent glioma and nonspecific posttherapeutic changes as reported in previous studies.[9–12] At the same time our results extend previous studies, which were based on smaller collectives and where histological confirmation was lacking in a large fraction of the patients. Furthermore, in the mentioned previous studies the high diagnostic accuracy of ^{18}F-FET PET was grounded exclusively on the analysis of the tumor-to-brain contrast. Importantly, the high accuracy of that approach could not be confirmed in the current study; that is, the diagnostic accuracy in our study was 75% for the TBR_{mean} and 71% for the TBR_{max} compared with 86%–100% accuracy reported in previous studies.[9–12]

The results concerning the diagnostic accuracy of the TBR for differentiating recurrent glioma and nonspecific posttherapeutic changes in the present study are, however, in line with the results of PET studies using other amino acid tracers. A meta-analysis of 5 ^{11}C-Met PET studies[19–23] by Nihashi and colleagues[24] revealed a cumulative sensitivity of 70% and a cumulative specificity of 93% for the correct diagnosis of glioma recurrence or progression. A retrospective study by Herrmann et al[25] analyzed data obtained with ^{18}F-FDOPA PET for the detection of glioblastoma recurrence in a group of 110 patients. In that study, the diagnostic accuracy for the correct diagnosis using tumor-to-striatum ratios and visual evaluation was 78%. Taken together, these

Table 3. Results of diagnostic performance of imaging parameters to diagnose tumor recurrence or progression

Identification of Tumor Recurrence or Progression	TBR_{max}	TBR_{mean}	TTP	Curve Pattern	Combined Analysis TBR_{max} and Curve Pattern	Combined Analysis TBR_{mean} and Curve Pattern	Combined Analysis of TBR_{max} and TTP	Combined Analysis of TBR_{mean} and TTP	MRI
Best threshold	2.3	2.0	<45 min	[a]	[b]	[c]	[d]	[e]	RANO criteria
Sensitivity (%)	68	74	82	78	93	93	92	93	92
Specificity (%)	100	91	73	73	73	73	73	100	9
Accuracy (%)	71	75	81	77	91	91	90	93	85
Positive predictive value (%)	100	99	97	97	97	97	97	100	92
AUC ± standard error	0.85 ± 0.04	0.91 ± 0.03	0.81 ± 0.06	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
P-value	<.001	<.001	.001	.001	<.001	<.001	<.001	<.001	.673

n.a., not available.
[a]Presence of kinetic pattern II or III.
[b]$TBR_{max} \geq 2.3$ and/or presence of curve pattern II or III.
[c]$TBR_{mean} \geq 2.0$ and/or presence of curve pattern II or III.
[d]$TBR_{max} \geq 2.3$ or TTP < 45 s.
[e]$TBR_{mean} \geq 2.0$ or TTP < 45 s.

results suggest that the accuracy of TBR of amino acid uptake is within the range of 70%–80% and thus lower than that reported previously for ^{18}F-FET PET.[9–12]

A number of studies have indicated that the TAC of ^{18}F-FET uptake contains additional biological information that may be helpful for differential diagnosis. For example, it has been reported that high-grade gliomas are characterized by an early peak around 10–15 min after injection followed by a decrease of ^{18}F-FET uptake, while low-grade gliomas typically exhibit delayed and steadily increasing tracer uptake.[17,18,26–28] These patterns were observed for primary as well as recurrent tumors[18,27,29] and appear to be a special characteristic of ^{18}F-FET, since they were not observed for other amino acid tracers such as ^{11}C-Met and ^{18}F-FDOPA.[30,31] In one study evaluating ^{18}F-FET kinetics in recurrent gliomas, some patients were included with treatment-related changes that exhibited an increasing ^{18}F-FET uptake curve similar to that observed in low-grade glioma.[27] A recent study assessed the diagnostic value of ^{18}F-FET PET uptake ratios as well as ^{18}F-FET uptake kinetics for differentiation of pseudoprogression and early tumor progression after radiochemotherapy of glioblastoma.[3] In that study, ^{18}F-FET uptake TBRs provided valuable information for differential diagnosis, but the analysis of kinetic ^{18}F-FET uptake yielded no further improvement in diagnostic accuracy. In contrast, another study investigated the diagnostic value of dynamic ^{18}F-FET PET to differentiate recurrent brain metastases and treatment-related changes and reported that the accuracy increased from 78% when using the TBR_{max} alone to 93% when using a combined analysis of TBR and tracer kinetics.[32]

In the present study we evaluated for the first time the additional value of ^{18}F-FET kinetics for differential diagnosis in a larger series of patients with suspected recurrent or progressive gliomas. Taken alone, kinetic parameters such as TTP and curve pattern analysis yielded accuracies of 81% and 77%, respectively, which were not better than TBR alone. However, when using a combination of TBR and kinetic parameters, accuracy could be improved to more than 90%. Data suggest that the combination of the TBR and dynamic parameters is more effective for evaluation of suspected tumor recurrence than TBR alone. It should be noted that in clinical routine, dynamic ^{18}F-FET PET imaging has several constraints, which should be considered. This technique requires longer acquisition times (50–60 min compared with 10–20 min for a static scan), which reduces the number of patients who can be investigated with one synthesis or delivery of ^{18}F-FET. This increases the costs of the investigation in routine clinical practice. Furthermore, the shorter acquisition time is more comfortable for patients and reduces motion artifacts. However, despite this constraint, the extra effort appears to be justified given the high relevance of this clinical issue. Furthermore, our study suggests that ^{18}F-FET may be the preferable amino acid tracer for evaluation of brain tumor recurrence, since tracer kinetics of other amino acids, such as ^{11}C-Met and ^{18}F-FDOPA, do not provide additional diagnostic information.[30,31]

Nevertheless, some limitations of the current study need to be discussed. The current study is based on retrospective data and the results need to be confirmed in a prospective study. Additionally, as patients were selected based predominantly on MRI findings suggestive of recurrent or progressive disease, a selection bias may have influenced our results. Furthermore,

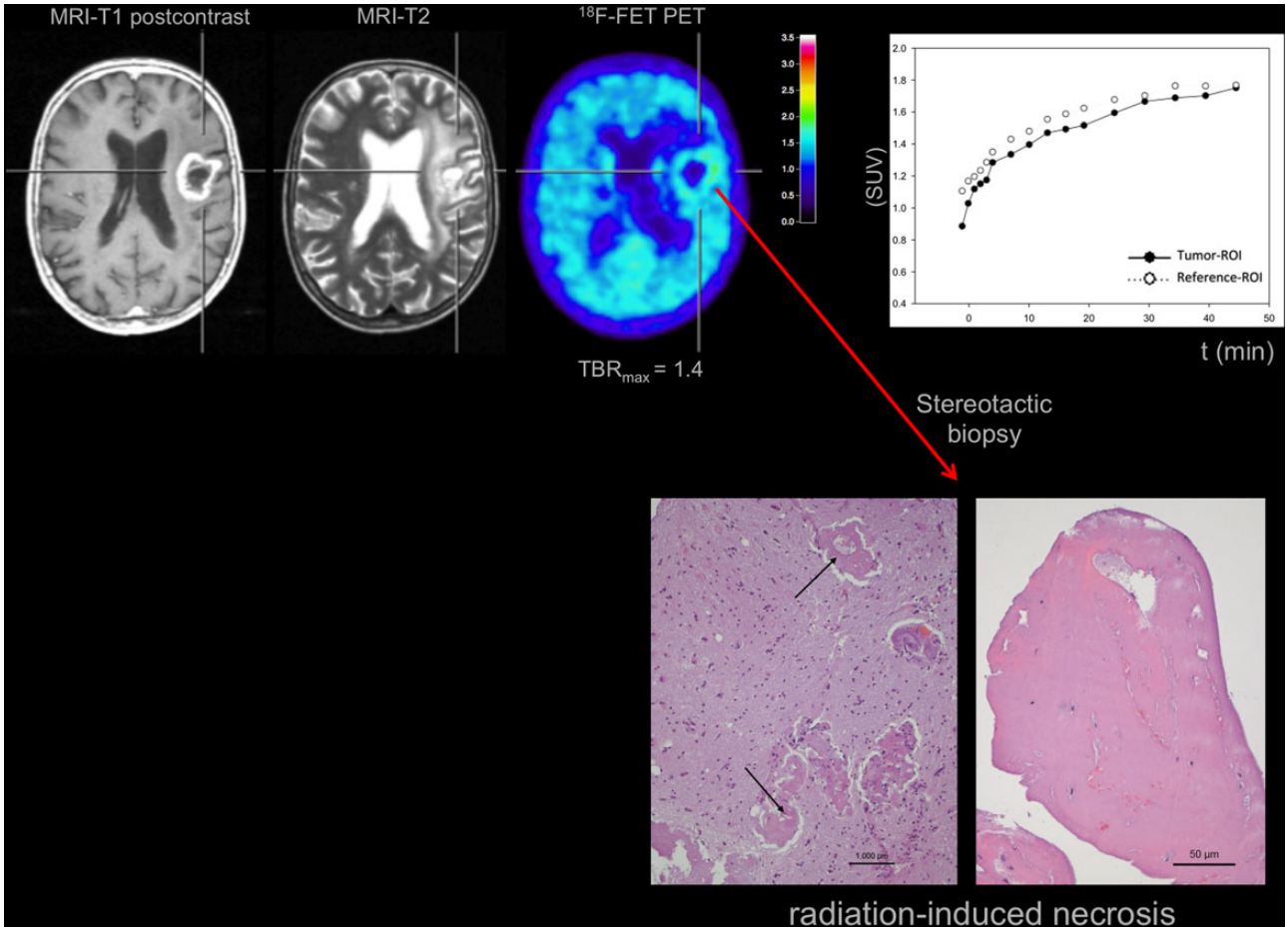

Fig. 1. A 70-year-old patient with an anaplastic astrocytoma (WHO grade III). (Top row, left) Contrast-enhanced MRI 31 months after radiation therapy suggests tumor progression. (Top row, middle) In contrast, ^{18}F-FET shows only slight metabolic activity (TBR_{max}, 1.4), and (top row, right) the time–activity curve shows a constantly increasing ^{18}F-FET uptake, consistent with treatment-related changes. (Bottom row, right) After a stereotactic-guided biopsy, histological examination yielded signs of radiation-induced necrosis (hematoxylin and eosin [H&E] staining, original magnification ×200; scale bar, 50 µm). (Bottom row, left) Brain parenchyma shows reactive changes and blood vessels with thickened hyalinized walls (arrows; H&E staining, original magnification ×100; scale bar, 1.000 µm).

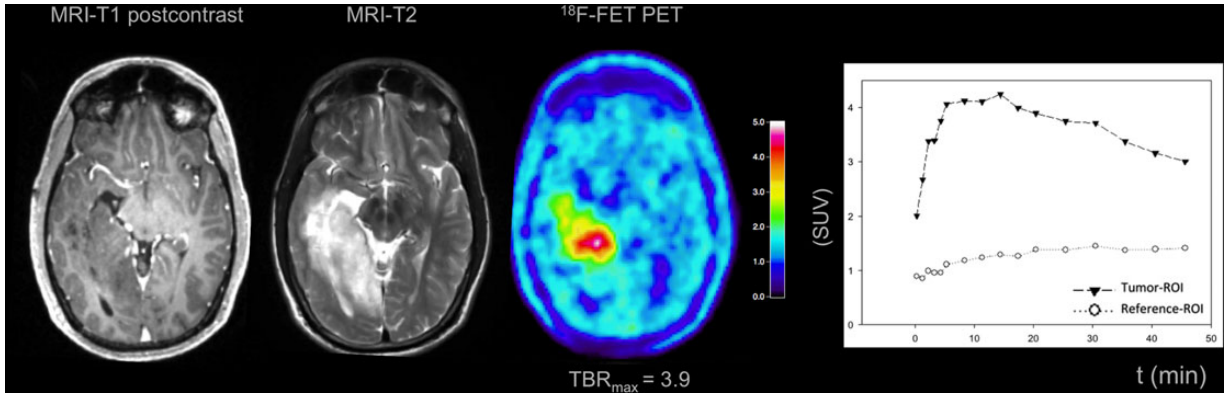

Fig. 2. A 35-year-old patient with initial diagnosis of a diffuse astrocytoma (WHO grade II). Follow-up MRI 86 months after initial diagnosis shows a slight progression of the hyperintensity in the T2-weighted MRI, but no clear contrast enhancement in the right temporal. In contrast, ^{18}F-FET shows highly increased metabolic activity (TBR_{max}, 3.9) in the right temporal, and the time–activity curve shows an early ^{18}F-FET uptake (<20 min) followed by a descent (pattern III), consistent with tumor recurrence. After a stereotactic-guided biopsy of the metabolically active tumor, histological examination was consistent with a malignant progression to an anaplastic oligoastrocytoma (WHO grade III).

one might argue that the group included patients with gliomas of different histologies and that the evaluation should focus on selected subgroups based on their histology. In our view, however, the composition of the group of patients reflects the typical pattern of referral in clinical practice and is therefore well suited to address the clinical problem of suspected tumor recurrence or progression.

In summary, static and dynamic ^{18}F-FET PET parameters are helpful for differentiating progressive or recurrent glioma from treatment-related nonneoplastic changes with a high diagnostic accuracy. Our results need to be confirmed in a prospective study, but data suggest that ^{18}F-FET PET provides useful information in this clinically challenging situation, especially when conventional MRI is inconclusive.

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Conflict of interest statement. The authors declare that they have no conflict of interest.

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