

The use of *O*-(2-¹⁸F-fluoroethyl)-L-tyrosine PET in the diagnosis of gliomas located in the brainstem and spinal cord

Caroline Tscherpel, Veronika Dunkl, Garry Ceccon, Gabriele Stoffels, Natalie Judov, Marion Rapp, Philipp T. Meyer, Elena Rota Kops, Johannes Ermert, Gereon R. Fink, Nadim J. Shah, Karl-Josef Langen, and Norbert Galldiks

Department of Neurology, University of Cologne, Cologne, Germany (C.T., V.D., G.C., G.R.F., N.G.); Institute of Neuroscience and Medicine, Forschungszentrum Jülich, Jülich, Germany (C.T., G.S., N.J., E.R.K., J.E., G.R.F., N.J.S., K.J.L., N.G.); Department of Neurosurgery, University of Düsseldorf, Düsseldorf, Germany (M.R.); Department of Nuclear Medicine, Medical Center–University of Freiburg, Faculty of Medicine, University of Freiburg, Germany (P.T.M.); Departments of Neurology (N.J.S.) and Nuclear Medicine (K.J.L.), University of Aachen, Aachen, Germany; Jülich-Aachen Research Alliance (JARA)–Section JARA-Brain (N.J.S., K.J.L.); Center of Integrated Oncology (CIO), Universities of Cologne and Bonn, Cologne, Germany (N.G.)

Corresponding Author: Norbert Galldiks, MD, Institute of Neuroscience and Medicine, Forschungszentrum Jülich, 52425 Jülich, Germany (n.galldiks@fz-juelich.de).

Abstract

Background. Despite an increasing number of *O*-(2-¹⁸F-fluoroethyl)-L-tyrosine (¹⁸F-FET) PET studies in supratentorial gliomas, studies regarding the usefulness of ¹⁸F-FET PET in brainstem and spinal cord gliomas to date remain scarce.

Methods. Thirty-six ¹⁸F-FET PET scans were performed in 29 patients with brainstem ($n = 29$ scans) or spinal cord glioma ($n = 7$ scans). In 32 of 36 PET scans, a dynamic acquisition was performed. Fifteen scans in 15 patients were performed to assess newly diagnosed lesions, and 21 scans were obtained during follow-up: for diagnosing tumor progression ($n = 15$ scans in 14 patients) as well as for treatment monitoring ($n = 6$ scans in 3 patients). Four patients underwent additional serial scans (range, 1–2), and 3 of these 4 patients were examined for more than one indication. Maximum and mean tumor/brain ratios ($TBR_{\max/\text{mean}}$) of ¹⁸F-FET uptake (20–40 min post injection) as well as kinetic ¹⁸F-FET uptake parameters were determined. Final diagnoses were confirmed histologically (54%) or by clinical follow-up (46%).

Results. In all newly diagnosed high-grade ($n = 3$ patients) and in 5 of 11 patients with low-grade gliomas, ¹⁸F-FET uptake was increased ($TBR_{\max} \geq 2.5$ and/or $TBR_{\text{mean}} \geq 1.9$). In 2 patients with newly diagnosed gliomas without MR contrast enhancement, ¹⁸F-FET PET nevertheless showed increased metabolism. At suspected progression, the combination of TBRs with kinetic ¹⁸F-FET parameters correctly identified presence or absence of progressive disease in 9 of 11 patients (82%).

Conclusions. This preliminary study suggests that ¹⁸F-FET PET adds valuable diagnostic information in brainstem and spinal cord glioma, particularly when the diagnostic information derived from MRI is equivocal.

Key words

amino acid PET | brainstem glioma | dynamic acquisition | FET | infratentorial

Brainstem gliomas are located in the midbrain, pons, or spinal cord. In the pediatric population, brainstem gliomas medulla oblongata. Furthermore, gliomas may occur in the account for about 20% of all brain tumors. In contrast, in

Importance of the study

The brainstem and spinal cord can be affected by various pathologies, such as gliomas, demyelination, vascular lesions, and posttherapeutic effects, some of which may overlap clinico-radiologically, thereby constituting a diagnostic challenge to date. Although conventional MRI remains the standard neuroimaging method for diagnostic purposes as well as for the planning of stereotactic biopsies or neurosurgical resection, its lack of specificity imposes problems regarding treatment planning and patient counseling. *O*-(2- ^{18}F -fluoroethyl)-L-tyrosine

(^{18}F -FET) PET may help to overcome some of the diagnostic uncertainties of conventional MRI in suspected gliomas of the brainstem and spinal cord, which are rare in adults. Our data suggest that the metabolic information derived from ^{18}F -FET PET may improve diagnostic procedures, thereby helping to avoid unnecessary invasive diagnostic procedures with the potential risk of inducing morbidity, and may thus facilitate patient counseling and treatment decisions, including the termination of potentially harmful treatments.

adults, brainstem gliomas are rare and account for less than 5% of all gliomas.^{1,2}

In 5%–10% of all spinal tumors in adults and approximately 35% in children, intramedullary spinal tumors can be diagnosed. About 90% of the tumors of the spinal cord are glial tumors, with most of these being ependymomas (~60%) or astrocytomas (~30%).^{3,4}

Evaluation of the brainstem and spinal cord with PET is, in part, hampered by spatial resolution, with compromised sensitivity for the detection of small lesions. Up-to-date PET scanners with an improved resolution may overcome this problem, which has led to the fact that brainstem and spinal PET have recently gained clinical interest.

The wealth of studies using amino acid PET in supratentorial gliomas is contrasted by the dearth of data regarding brainstem and spinal cord gliomas. In this field, most experience has been gained with the PET tracer ^{11}C -methyl-L-methionine (^{11}C -MET).^{5–12} ^{11}C -MET is an essential amino acid labeled with carbon-11, a positron-emitting isotope with a half-life of 20 minutes.¹³ This relatively short half-life limits the use of ^{11}C -MET to PET centers with a cyclotron. More recently, novel amino acid tracers labeled with positron emitters with longer half-lives have been developed, providing better clinical reach, increased efficiency, and improved cost-effectiveness. Particularly, *O*-(2- ^{18}F -fluoroethyl)-L-tyrosine (^{18}F -FET), developed in the late 1990s, has become a well-established ^{18}F -labeled amino acid for PET (half-life, 110 min) that provides logistic advantages for clinical practice compared with ^{11}C -MET,^{14,15} while clinical results in brain tumors are comparable.^{16–18} Consequently, the use of ^{18}F -FET has rapidly increased in western Europe during the last years and as the first country, Switzerland, has approved ^{18}F -FET PET as a medical drug for brain imaging in 2014.¹⁹

To date, however, experience with ^{18}F -FET and other amino acid PET tracers in patients with gliomas located in the brainstem and spinal cord remains limited and is based on single patients only.²⁰ To the best of our knowledge, dynamic ^{18}F -FET scans in a group of patients with gliomas located in the brainstem and spinal cord have not yet been reported.

Patients and Methods

Patients

Twenty-nine patients with brainstem and spinal cord glioma who had received between 2007 and 2015 dynamic ^{18}F -FET PET scans ($n = 32$) at the Forschungszentrum Jülich, Germany, or static ^{18}F -FET PET scans ($n = 4$) at the Department of Nuclear Medicine, University of Freiburg, Germany, were identified retrospectively (Supplementary Table 1). The local ethics committee approved the evaluation of retrospectively collected patient data. Patients had been referred for ^{18}F -FET PET imaging for assessment of newly diagnosed cerebral lesions ($n = 15$ scans in 15 patients) (Supplementary Table 2), and for imaging during the course of the disease ($n = 21$ scans), for instance, for diagnosing tumor progression or recurrence ($n = 15$ scans in 14 patients) or for treatment monitoring ($n = 6$ scans in 3 patients) (Supplementary Tables 3, 4). Four patients underwent serial ^{18}F -FET PET imaging (range of additional scans, 1–2), and 3 of these 4 patients were examined for more than one indication.

PET Imaging with ^{18}F -FET

The amino acid ^{18}F -FET was produced as described previously.^{15,21} According to the German guidelines for brain tumor imaging using labeled amino acid analogues, all patients fasted for at least 12 h before PET scanning.²² At the Research Center Jülich, dynamic PET studies were acquired up to 50 min after intravenous injection of 3 MBq of ^{18}F -FET/kg of body weight on an ECAT EXACT HR+ scanner (CTI/Siemens Medical Systems) in 3-D mode ($n = 22$ patients) (axial field of view, 15.5 cm; image resolution, ~6 mm) or a hybrid 3T MR-PET scanner ($n = 3$ patients). The hybrid 3T MR-PET scanner used in the present study consisted of a 3T MR imaging system (Magnetom Tim Trio; Siemens Medical Systems) and a PET insert (BrainPET; Siemens Medical Systems).^{23–25} The BrainPET is a compact cylinder that fits in the bore of the Magnetom Trio MR scanner (axial field of view, 19.2 cm; optimum image resolution in the center of the field of view, ~3 mm).

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. After correction for random and scattered coincidences as well as dead time and attenuation, PET data were iteratively reconstructed.

At the Department of Nuclear Medicine, University of Freiburg, static PET scans (20–40 min post injection) were acquired on an ECAT 922/47 scanner (CTI/Siemens Medical Systems) ($n=2$ patients) or on a PET/CT scanner (GeminiTF 64; Philips) ($n=2$ patients). Images were iteratively reconstructed.

PET Data Analysis

^{18}F -FET uptake in the tissue was expressed as standardized uptake value (SUV) by dividing the radioactivity concentration (kBq/mL) in the tissue by the radioactivity injected per gram of body weight. PET and MR images were co-registered using dedicated software (MPI tool v6.48, ATV). The fusion results were inspected and, if necessary, adapted based on anatomical landmarks. The regions of interest (ROI) analysis and the calculation of PET tumor volumes were based on the averaged PET data from 20–40 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 in an area of normal appearing supratentorial brain tissue including white and gray matter.²² The tumor area on ^{18}F -FET PET scans was determined by a 3-D auto-contouring process using a tumor–brain ratio ≥ 1.6 of ^{18}F -FET uptake as cutoff. This cutoff is based on the results of a previous biopsy-controlled study in which the best lesion-to-brain ratio for differentiating tumor from peritumoral tissue was 1.6.²⁶ When ^{18}F -FET uptake in the lesions was similar to that in the normal brain tissue, a representative irregular ROI was placed manually on the area of signal abnormality in the T1- and T2-weighted transversal MRI scan and transferred to the coregistered ^{18}F -FET PET scan in each case. Maximum and mean tumor–brain ratios (TBR_{max} , TBR_{mean}) were calculated by dividing the maximum and mean SUVs of these tumor ROIs by the mean SUV of normal brain in the PET scan.

Furthermore, time-activity curves (TACs) of ^{18}F -FET uptake in the tumor were generated by the application of a spherical volume-of-interest with a volume of 2 mL centered on maximal tumor uptake to the entire dynamic dataset.^{27,28} TAC of the brain tissue was generated by a reference ROI in the unaffected brain tissue (as described above). Time-to-peak (TTP; time in minutes from the beginning of the dynamic acquisition up to the maximum SUV of the lesion) was determined. As described previously,^{27–29} TACs of each lesion were assigned to one of the following curve patterns: (i) constantly increasing ^{18}F -FET uptake without identifiable peak uptake during data acquisition; (ii) ^{18}F -FET uptake peaking at a midway point (between 20 and 40 min) followed by a plateau; and (iii) ^{18}F -FET uptake peaking early (≤ 20 min) followed by a constant descent.

Accuracy of ^{18}F -FET PET in Newly Diagnosed Brainstem/Spinal Cord Lesions

Based on a previous study in a large series of untreated patients with suspected cerebral glioma on MR imaging,

neoplastic tissue on ^{18}F -FET PET scans was assumed when the TBR_{max} was ≥ 2.5 and/or the TBR_{mean} was ≥ 1.9 .³⁰ For the evaluation of diagnostic accuracy of ^{18}F -FET PET in newly diagnosed lesions, the histological diagnosis was used as reference. All tumors were histologically classified according to the World Health Organization (WHO) classification of tumors of the central nervous system.³¹

Accuracy of ^{18}F -FET PET for Diagnosing Tumor Progression or Recurrence

Based on a previous study investigating the potential of ^{18}F -FET PET to differentiate tumor recurrence or progression from treatment-induced changes in a large series of pretreated brain tumors,²⁸ tumor progression or recurrence as evaluated by ^{18}F -FET PET was assumed when a $\text{TBR}_{\text{max}} \geq 2.3$ or a $\text{TBR}_{\text{mean}} \geq 2.0$ in combination with a curve pattern 2 or 3 was present. For the evaluation of diagnostic accuracy of ^{18}F -FET PET for diagnosing tumor progression or recurrence, the histological diagnosis was used as reference ($n=4$ patients). If histology was not available, diagnosis was based on the follow-up (ie, clinical course and results of follow-up MRI) ($n=10$ patients). Absence of tumor progression or recurrence was assumed when the lesions showed spontaneous shrinkage or remained stable in size on contrast-enhanced MRI, and/or neurological deficits remained unchanged, ie, no new neurological symptoms occurred during follow-up (median follow-up, 11 mo; range, 8–29 mo). Presence of tumor progression or recurrence was assumed when clinical worsening prompted a change in treatment or palliative care had been initiated during follow-up/death occurred (median follow-up, 3 mo; range, 1–5 mo).

MR Imaging

All patients underwent routine MRI (1.5T or 3T) with standard coils before and after administration of a gadolinium-based contrast agent (T1- and T2-weighted and fluid attenuated inversion recovery [FLAIR] sequence). Diagnosis of tumor progression or recurrence was based on Response Assessment in Neuro-Oncology criteria.³²

Statistical Analysis

Descriptive statistics are provided as mean and standard deviation and/or median and range. 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 normally distributed. *P*-values of .05 or less were considered significant. Statistical analyses were performed using SigmaPlot software (SigmaPlot v11.0, Systat Software) and SPSS Statistics software (Release 23.0.0).

Results

Patients with Newly Diagnosed Brainstem/Spinal Cord Lesions

In the 15 patients (mean age, 34 ± 16 y; range, 9–67 y) with newly diagnosed brainstem or spinal cord lesions, a total

of 15 PET scans were performed (Supplementary Tables 1, 2). Diagnoses were distributed as follows (Supplementary Table 2): WHO grade I ganglioglioma ($n = 1$), WHO grade I pilocytic astrocytoma ($n = 1$), WHO grade II diffuse astrocytoma ($n = 6$), WHO grade III anaplastic astrocytoma ($n = 2$), WHO grade IV glioblastoma ($n = 1$), low-grade glial tumor, WHO grade histologically not specified ($n = 3$), and hyperintense MRI lesions on T2/FLAIR-weighted images without histological confirmation ($n = 1$). Histology of the latter brainstem lesion could not be obtained due to the patient's refusal (patient ID #24). In the other patients, histology was obtained by stereotactic biopsy ($n = 12$) or neurosurgical resection ($n = 2$).

^{18}F -FET Uptake and Contrast Enhancement on MRI in Newly Diagnosed Brainstem/Spinal Cord Lesions

At initial diagnosis, in 8 of 14 histologically confirmed gliomas located in the brainstem or spinal cord, an increased ^{18}F -FET uptake (57%) could be observed. All high-grade gliomas of WHO grade III ($n = 2$) (Fig. 1) and WHO grade IV ($n = 1$) as well as 5 of 11 low-grade gliomas exhibited a $\text{TBR}_{\text{max}} \geq 2.5$ and/or a $\text{TBR}_{\text{mean}} \geq 1.9$ (Supplementary Tables 1, 2). In contrast, in 3 patients with a WHO grade II diffuse

astrocytoma, in 2 patients with low-grade glial tumor in which the WHO grade could not be histologically specified, and in a patient with WHO grade I ganglioglioma, ^{18}F -FET uptake was below these thresholds. Nevertheless, 3 of these 6 tumors showed ^{18}F -FET uptake above background with a $\text{TBR}_{\text{max}} \geq 1.6$ (range TBR_{max} 1.6–2.0). The ^{18}F -FET uptake in low-grade gliomas (median TBR_{max} 2.2; range, 1.0–3.9; median TBR_{mean} 1.8; range, 0.7–2.6) was not significantly different compared with high-grade gliomas (median TBR_{max} 3.0; range, 2.4–3.5; median TBR_{mean} 1.9; range, 1.9–2.1) ($P > 0.05$). In the patient (ID #24) without histological diagnosis of the brainstem lesion, no ^{18}F -FET uptake could be observed. Static and dynamic data of ^{18}F -FET uptake of each lesion are presented in Supplementary Table 2. Furthermore, in 2 patients with newly diagnosed gliomas without contrast enhancement on MRI, ^{18}F -FET PET showed increased metabolism ($\text{TBR}_{\text{max}} \geq 2.5$ and/or a $\text{TBR}_{\text{mean}} \geq 1.9$). ^{18}F -FET uptake in non-enhancing gliomas (median TBR_{max} 2.0; range, 1.2–3.3; median TBR_{mean} 1.7; range, 0.9–2.3) showed no significant difference compared with enhancing gliomas (median TBR_{max} 2.4; range, 1.0–3.9; median TBR_{mean} 1.9; range, 0.7–2.6) ($P > 0.05$). In 2 patients with newly diagnosed glioma and contrast enhancement with a maximal diameter < 5 mm, no FET uptake could be observed (Fig. 2) (Supplementary Table 2).

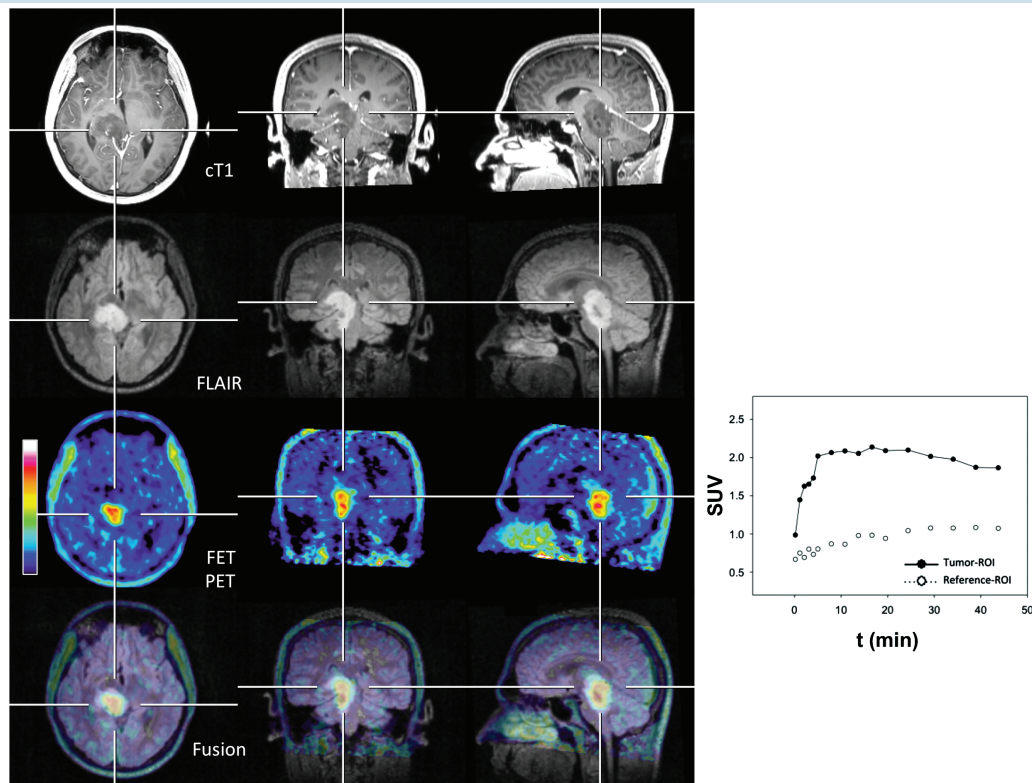


Fig. 1 Twenty-five-year-old patient (patient ID #1) with a newly diagnosed anaplastic astrocytoma (WHO grade III) of the brainstem. The MRI shows only minimal contrast enhancement, whereas the increased ^{18}F -FET uptake (TBR_{max} 3.5) is located predominantly in spatial correspondence to the alterations of the FLAIR-weighted image (second row, bottom row). The time-activity curve shows an early ^{18}F -FET uptake (17 min) followed by a constant descent.

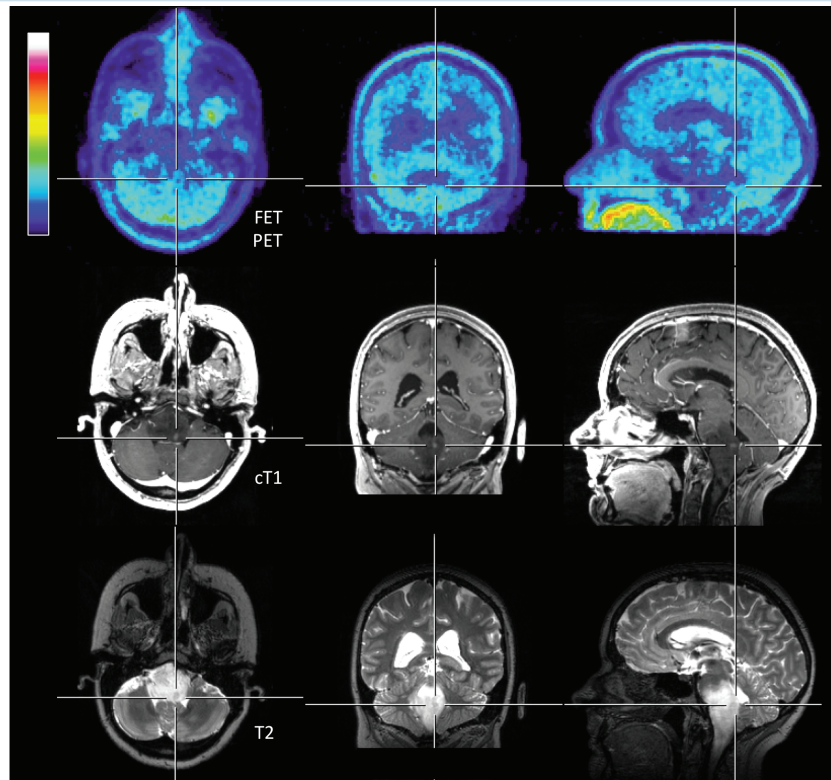


Fig. 2 Thirty-six-year-old patient (patient ID #13) with a newly diagnosed diffuse astrocytoma (WHO grade II) of the brainstem. The lesion size of contrast enhancement is small (maximal diameter <5 mm) and the T2 signal alteration is considerably larger. However, no increased ^{18}F -FET uptake can be observed.

Patients with Follow-up PET Imaging During the Course of the Disease

During follow-up, 15 patients (mean age, 46 ± 20 years; range, 7–73 years) underwent a total of 21 PET scans (Supplementary Table 3, 4). Four patients underwent serial ^{18}F -FET PET imaging (range of additional scans, 1–2), and 3 of these 4 patients were examined for more than one indication. The histologically confirmed initial diagnoses in this group of patients were distributed as follows: WHO grade I pilocytic astrocytoma ($n = 2$), WHO grade II diffuse astrocytoma ($n = 4$), WHO grade II ependymoma ($n = 1$), WHO grade III secondary anaplastic astrocytoma after malignant progression ($n = 1$), WHO grade IV secondary glioblastoma after malignant progression ($n = 3$), WHO grade IV primary glioblastoma ($n = 2$), and contrast-enhancing or hyperintense MRI lesions on T2-/FLAIR-weighted images without histological confirmation due to the patient's refusal ($n = 2$) (Fig. 3).

^{18}F -FET PET for Diagnosing Tumor Progression or Recurrence

In patients in whom histological diagnosis confirmed tumor progression or recurrence ($n = 4$ patients), all corresponding ^{18}F -FET PET scans ($n = 4$) showed increased uptake (TBR_{max} , 3.6 ± 0.8 ; range of TBR_{max} , 2.7–4.7; TBR_{mean} ,

2.7 ± 0.5 ; range of TBR_{mean} , 2.0–3.1). Furthermore, when diagnosis was based on the follow-up, TBRs were significantly higher in patients with tumor progression or recurrence ($n = 5$ PET scans in 4 patients) than in nonprogressors ($n = 4$ PET scans in 4 patients) (TBR_{max} , 2.7 ± 0.7 vs 0.4 ± 0.8 , $P = .002$; TBR_{mean} , 1.9 ± 0.5 vs 0.3 ± 0.7 , $P = .004$). However, 2 patients were lost to follow-up. Furthermore, all patients with confirmed tumor progression or recurrence showed a $\text{TBR}_{\text{max}} \geq 2.3$ or a $\text{TBR}_{\text{mean}} \geq 2.0$. Using a threshold of $\text{TBR}_{\text{max}} > 2.3$ or a $\text{TBR}_{\text{mean}} > 2.0$ in combination with presence of a curve pattern 2 or 3,²⁸ presence or absence of tumor progression or recurrence was diagnosed correctly in 82% (9 of 11 patients; sensitivity, 71%; specificity, 100%). Static and dynamic data on ^{18}F -FET uptake of each lesion are presented in Supplementary Table 3.

^{18}F -FET PET for Treatment Monitoring

In a subgroup of patients ($n = 3$), serial ^{18}F -FET PET imaging (at baseline and 2 mo later) was used to monitor chemotherapy effects of adjuvant temozolomide (5/28) in 2 patients with WHO grade IV glioblastoma³³ of the brainstem (patient ID #15, #20) and of temozolomide in combination with bevacizumab in a patient with a WHO grade II diffuse astrocytoma of the spinal cord (patient ID #19) (Supplementary Table 4). Compared with baseline PET,

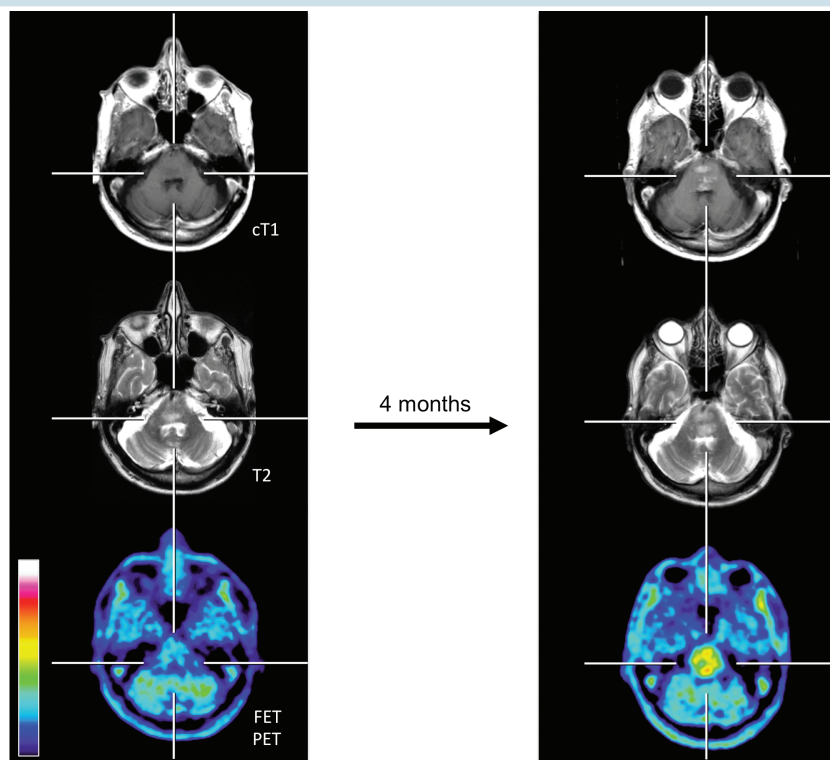


Fig. 3 Seventy-three-year-old patient (patient ID #24) with a rapid progressive tumor of the brainstem (histology of this brainstem lesion could not be obtained due to the patient's refusal). In correspondence to the clinical deterioration (ie, dysphagia, dysarthria) within 4 months, a contrast-enhancing lesion, a progression of the T2 signal, and an increase of the metabolic activity (TBR_{max} baseline, 1.6; TBR_{max} follow-up, 3.2) compared with baseline imaging (left column) are illustrated.

changes of the TBR_{max} revealed a greater variability (range of TBR_{max} changes between -11% and 26%) than the TBR_{mean} (range of TBR_{mean} changes between -4% and 5%). After treatment, no changes of the TBR_{mean} were observed,³⁴ the metabolic activity remained largely unchanged. Clinically, this finding was associated with a stable clinical course for at least 6 months.

Discussion

In contrast to numerous studies that have used amino acid PET to image supratentorial brain tumors, reports using this technique to image brainstem gliomas and tumors of the spinal cord remain scarce, particularly using the tracer ^{18}F -FET. The results of the present study suggest that ^{18}F -FET PET may be helpful to detect metabolically active tumor in both the brainstem and in the spinal cord (Fig. 1, 3, 4) and may add valuable information to standard MRI for clinical decision making both at primary diagnosis and in the further course of the disease.

Since the number of patients in this study is too small to perform a receiver-operating-characteristic curve analysis, the cutoff values to determine the sensitivity of ^{18}F -FET PET were based on threshold values determined in previous studies in larger series of brain tumors in the

entire brain.^{28,30} This approach may not be appropriate, and the sensitivity of ^{18}F -FET PET might be underestimated. Using a TBR_{max} threshold of 2.5, the sensitivity of ^{18}F -FET PET for the detection of neoplastic tissue in the brainstem and spinal cord in newly diagnosed tumors achieved a sensitivity of 57% , which is in line with previous results in brain tumors of the entire brain.³⁰ Due to the lack of nonneoplastic lesions, the calculation of specificity was not possible in the present dataset. In low-grade gliomas, only 5 of 11 tumors exceeded the TBR_{max} threshold of 2.5. In contrast, in one of the largest datasets, with 136 low-grade gliomas of the entire brain, the sensitivity of ^{18}F -FET PET was considerably higher (74%).³⁵ However, in that study ^{18}F -FET PET was evaluated only visually.³⁶

Interestingly, in 2 newly diagnosed gliomas of the brainstem without contrast enhancement on MRI, ^{18}F -FET PET showed increased metabolic activity, providing important additional diagnostic information for further clinical decision making, (ie, planning of stereotactic biopsy and definition of the target for biopsy). Accordingly, Massager and colleagues¹¹ reported in a series of adult patients with predominantly brainstem mass lesions that in some cases the biopsy target was more accurately defined using PET and ^{11}C -MET PET than MR imaging and that PET-guided stereotactic biopsy increased the diagnostic yield. Using ^{18}F -2-fluoro-2-deoxy-D-glucose

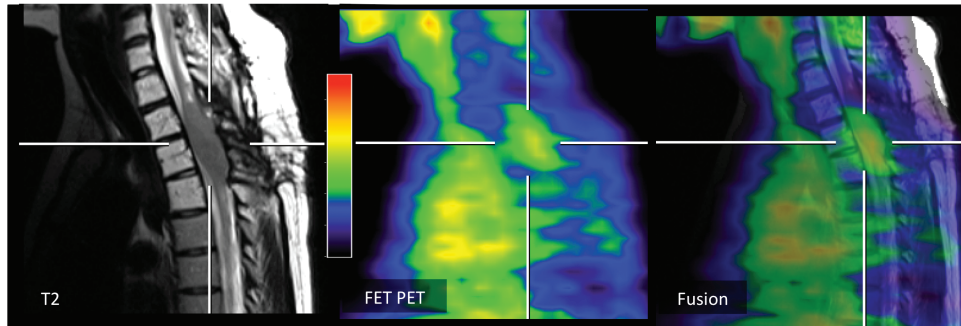


Fig. 4 Twenty-five-year-old patient (patient ID #19) with a progressive diffuse astrocytoma (WHO grade II) of the thoracic spinal cord. In spatial correspondence to the MRI signal alterations (fusion image, right), the ^{18}F -FET PET shows an increased metabolic activity ($\text{TBR}_{\text{max}}^*$ 2.7).

(^{18}F -FDG) PET as well as ^{11}C -MET PET, similar findings have been reported in children with infiltrative brainstem lesions,⁸ resulting in an improved survival.^{9,12} However, the applicability of ^{11}C -MET PET is restricted to centers with an on-site cyclotron unit, while the evaluation of ^{18}F -FDG PET uptake of the brainstem may be impaired due to high physiological uptake of other infratentorial structures, such as gray matter of the cerebellum.^{13,37}

Furthermore, our findings in pretreated patients with gliomas of the brainstem or the spinal cord suggest that static and dynamic imaging parameters derived from ^{18}F -FET PET may be helpful for the diagnosis of tumor progression or recurrence. Using TBRs in combination with curve patterns of ^{18}F -FET uptake, recurrent or progressive disease was identified correctly in 82%. Similar diagnostic performance was observed in previous studies in patients with high-grade glioma.^{27,28}

Compared with the number of reports in patients with brainstem gliomas evaluated using amino acid PET, the number of patients with spinal cord gliomas examined with this technique is rather small^{5-7,38} and thus far predominantly focused on ependymomas. Again, primarily ^{11}C -MET PET as well as ^{18}F -FDG PET as non-amino acid PET tracers were used in these reports. In these studies, both ^{18}F -FDG and ^{11}C -MET accumulated to a large degree in ependymomas as well as in astrocytic gliomas. Correspondingly, in the present study we provide initial experience with ^{18}F -FET PET in patients with both ependymoma and low-grade glioma histology of the spinal cord with a similar degree of tracer uptake.

Regarding treatment monitoring, in pretreated patients with malignant brainstem glioma, Reithmeier and coworkers²⁰ demonstrated treatment response evaluation to anti-angiogenic therapy with bevacizumab using ^{18}F -FET PET. Compared with the baseline scan, all patients of that case series ($n = 3$) revealed a decrease of metabolic activity of 25% or more. In our patients, however, no clear decrease of metabolic activity to the treatment as indicated by changes of the $\text{TBR}_{\text{mean}}^*$ ³⁴ could be observed. This finding was associated with a stable clinical course for at least 6 months, suggesting disease control without further tumor growth, but the dataset is too small to draw any conclusions.

There are limitations to the present study. It should be considered that particularly in infratentorial lesions smaller than 5 mm diameter, the evaluation of the brainstem and spinal cord with PET is likely to be compromised by the spatial resolution of the scanner. That is, sensitivity is likely to be reduced for the detection of hypermetabolic lesions smaller in size than the scanner spatial resolution, usually 5–6 mm. Furthermore, due to the retrospective study setting, only a few gliomas of the spinal cord were identified and other intramedullary tumors such as lymphomas, oligodendrogliomas, and subependymomas are not available in this series. Although this is the first study exploring the usefulness of static and dynamic ^{18}F -FET PET in a series of patients with gliomas of the brainstem or the spinal cord, the number of patients in the different subgroups is small and the results should be considered with caution. Nevertheless, this study includes to date the largest sample of patients with this tumor localization studied using static and dynamic ^{18}F -FET PET. The results are promising and further investigations in this field are recommendable.

With these caveats in mind, we recommend the use of ^{18}F -FET PET as an additional diagnostic tool in this group of patients, particularly when the diagnostic information derived from standard MR imaging is equivocal. Further investigation in a larger number of patients is warranted to determine the value of ^{18}F -FET PET in newly diagnosed infratentorial brain lesions (ie, differential diagnosis of neoplastic from nonneoplastic lesions), for diagnosing tumor progression or recurrence, and for the evaluation of treatment response.

Supplementary Material

Supplementary material is available at *Neuro-Oncology* online.

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Conflict of interest statement. The authors disclosed no potential conflicts of interest.

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