

# Comparison of $^{18}\text{F}$ -fluoroethylo-L-tyrosine PET/CT and MR in the diagnosis of primary brain tumors referred to radiation therapy

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## Abstract

**BACKGROUND:** The diagnostic efficacy of  $^{18}\text{F}$ -FDG-PET imaging in brain tumors is markedly reduced due to high glucose metabolism in normal brain tissue. This requires further research for more sensitive and specific tracers.  $^{18}\text{F}$ -fluoroethylo-L-tyrosine ( $^{18}\text{F}$ -FET) is an interesting PET radiotracer, which shows promising results in patients with brain tumors. The aim of this study was to compare  $^{18}\text{F}$ -fluoroethylo-L-tyrosine PET/CT and MRI in the diagnosis of primary brain tumors referred to radiation therapy.

**MATERIAL AND METHODS:** Thirteen patients (5M, 8F) with mean age of  $56y \pm 13$  and histologically confirmed primary brain tumors were investigated. The MRI scans were performed on MRI 1.5T scanner with FSE, DWI method, T1, T2 and FLAIR sequence. The examination was performed using brain protocol for 35 minutes and prior to PET imaging. The PET scans were performed 20–40 min after intravenous injection of 160 MBq of  $^{18}\text{F}$ -FET. Scans were acquired on Gemini TF PET/CT scanner using 3D brain imaging protocol for 10 minutes acquisition time. The reconstructed PET images were evaluated on a dedicated EBW workstation with Time-of-Flight reconstruction algorithms. On reconstructed images, the tumor borders were drawn using dedicated software, based on various threshold values and tumor borders and volumes were calculated on each nuclear image and compared with the volume calculated on the diagnostic MRI. For statistical analysis the t-test was used.

**RESULTS:**  $^{18}\text{F}$ -FET-PET imaging in total showed more abnormal lesions than MRI; however, the difference was not significant ( $p > 0.05$ ). There were two patients with lesions detected only on the MRI study and 4 patients with abnormal tracer uptake within the brain in  $^{18}\text{F}$ -FET study with no correlation in the MRI study.  $^{18}\text{F}$ -FET-PET method showed 30 lesions in 11 patients with mean  $\text{SUV}_{\text{max}}$  value of 2.33 (range from 1.6 to 3.5). Based on 70% threshold cutoff value, the mean volume of brain focus was calculated on at  $31.15 \pm 26.89 \text{ mm}^3$  and was in concordance with mean lesion volume measured on the MRI scan  $31.51 \pm 34.97 \text{ mm}^3$ . For radiation planning purposes other-threshold values, as well as gradient based methods were evaluated on  $^{18}\text{F}$ -FET-PET imaging.

**CONCLUSION:** PET/CT imaging with  $^{18}\text{F}$ -fluoroethylo-L-tyrosine is complementary to MRI in the diagnosis of primary brain tumors referred to radiation therapy.

**KEY words:** radiotherapy, brain tumor, positron emission tomography,  $^{18}\text{F}$ -fluoroethylo-L-tyrosine, magnetic resonance

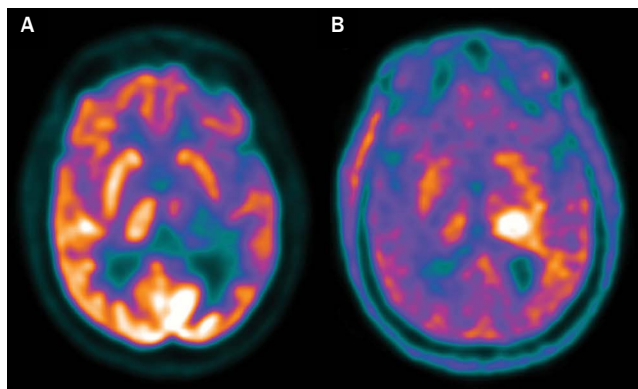
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## Introduction

The most commonly used non-invasive methods of brain imaging include computed tomography (CT) and magnetic

resonance (MR) which allow assessment of anatomical structures and are characterized by high sensitivity. The limitation in the application of these imaging methods are changes caused by the applied treatment (e.g. surgery, radiation-induced necrosis). In such cases, the nuclear medicine techniques, in particular positron emission tomography in combination with computed tomography (PET/CT) are helpful. The radiotracer most commonly used in the imaging of tumor metabolism is 2-deoxy-2-[ $^{18}\text{F}$ ]

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**Figure 1.** Differences in uptake of <sup>18</sup>F-FDG and <sup>18</sup>F-FET in primary brain tumor

fluoro-D-glucose (<sup>18</sup>F-FDG). It has been demonstrated that there is a relationship between histopathological diagnosis and <sup>18</sup>F-FDG uptake: high-grade tumors show hypermetabolism, while low-grade tumors — hypometabolism compared to gray matter. Low-grade astrocytomas had low <sup>18</sup>F-FDG uptake, while astrocytomas and glioblastoma multiforme are characterized by increased uptake [1–3]. Due to high glucose uptake in healthy brain tissue, more sensitive and specific radiotracers are used in brain tumors imaging.

<sup>18</sup>F-fluoroethylo-L-thyrosine (<sup>18</sup>F-FET) is an artificial amino acid showing increased uptake within malignant lesions and also allowing good differentiation in both high and low-differentiated tumors [4]. Differences in uptake of <sup>18</sup>F-FDG and <sup>18</sup>F-FET in primary brain tumor are shown in Figure 1.

The aim of this study was to compare <sup>18</sup>F-fluoroethylo-L-thyrosine PET/CT and MRI in the diagnosis of primary brain tumors referred to radiation therapy.

## Material and methods

Retrospective analysis was performed on a group of 13 patients (5M, 8F), with mean age of  $56 \pm 13$  y (range 35–77yrs) and histologically confirmed primary brain tumors. Eleven of these patients had craniotomies prior to the study, 2 were without any surgical intervention. The study has been approved by the Institutional Bioethical Committee and all subjects signed an informed consent form. All patients were qualified for radiotherapy treatment and tumors were located in frontal, parietal, temporal and occipital lobes.

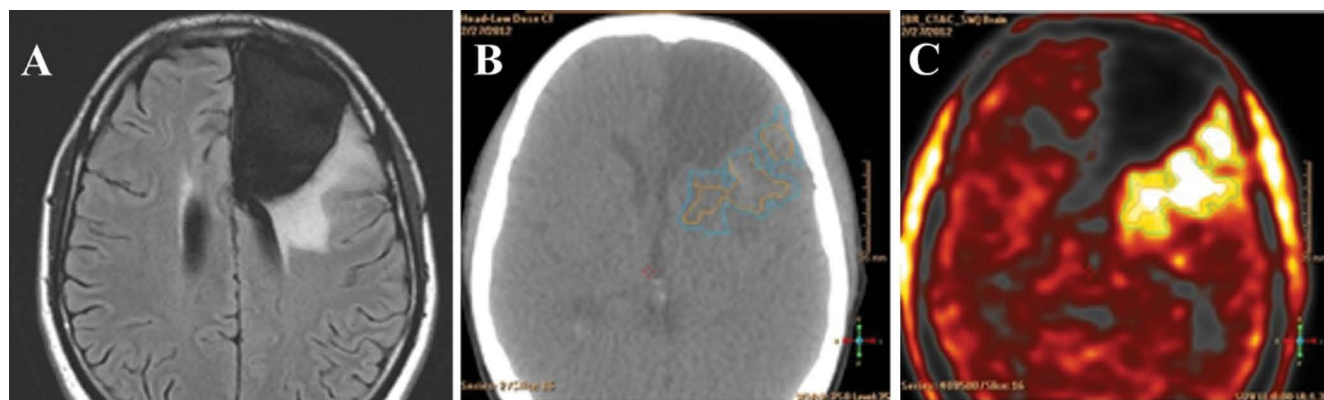
The MRI scans were performed on MRI 1.5T scanner using the brain protocol for 35 minutes, with the FSE method in transverse, sagittal and frontal planes, T1- and T2 dependent time, FLAIR sequences and DWI, with intravenous administration of the contrast agent. The PET scans were performed 20–40 min after intravenous injection of 160 MBq of <sup>18</sup>F-fluoroethylo-L-thyrosine on Gemini TF PET/CT scanner (Philips) using 3D brain imaging protocol for 10 minutes acquisition time. The reconstructed PET images were evaluated on a dedicated EBW workstation with time-of-flight (TOF) reconstruction algorithms. On reconstructed images, using semi-automatic dedicated software based on various threshold values, tumor borders and volume were calculated on each nuclear image and compared with the volume calculated on the diagnostic MRI. A 70% cutoff method was used to compare PET and MR images. All standardized uptake values (SUVs) used at work are maximum values ( $SUV_{max}$ ). For statistical analysis the T-test was used.

## Results

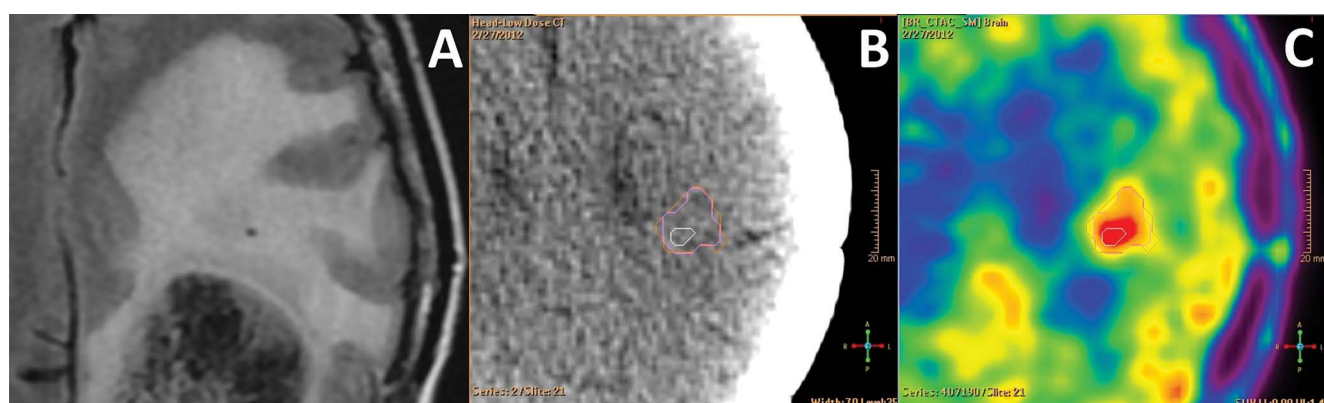
The <sup>18</sup>F-FET-PET study showed more lesions in the brain area than the MRI study; however, the difference was not statistically significant ( $p > 0.05$ ). There were two patients whose lesions were detected only in MRI, and 4 patients in whom PET imaging with tyrosine showed increased radiotracer uptake without reference to MRI (Tab. 1).

**Table 1.** Sensitivity of MRI and <sup>18</sup>F-FET-PET imaging

No.	Diagnosis	MRI		18F-FET-PET		
		N	Scan results (positive/negative)	N	Scan results (positive/negative)	SUVmax.
1	Glioblastoma multiforme	1	+	0	-	-
2	Glioblastoma multiforme	1	+	1	+	1.7
3	Glioblastoma multiforme	4	+	4	+	1.9
4	Oligoastrocytoma Grade II	4	+	1	+	2.8
5	Astrocytoma Grade II	1	+	2	+	2.5
6	Oligoastrocytoma Grade II	0	-	1	+	1.6
7	Glioma Grade II	0	-	5	+	1.9
8	Astrocytoma Grade II	5	+	0	-	-
9	Astrocytoma Grade III	1	+	1	+	1.9
10	Glioblastoma multiforme	4	+	4	+	3.5
11	Oligoastrocytoma Grade II	0	-	3	+	2.7
12	Astrocytoma Grade III	4	+	4	+	2.8
13	Astrocytoma Grade III	0	-	4	+	2.3



**Figure 2.** Patient after left-sided craniotomy. (A) MRI images, (B) CT images, (C)  $^{18}\text{F}$ -FET-PET images



**Figure 3.** Patient after left-sided occipital craniotomy. (A) MRI images, (B) CT images, (C)  $^{18}\text{F}$ -FET-PET images

$^{18}\text{F}$ -FET-PET showed 30 lesions in 11 patients with an average  $\text{SUV}_{\text{max}}$  of 2.33 (range 1.6–3.5), while the MRI examination showed 25 lesions in 9 patients.

Based on 70% cutoff, the mean volume in the  $^{18}\text{F}$ -FET-PET study was  $31.15 \pm 26.89 \text{ mm}^3$  and was comparable to the volume of changes measured in the MRI  $31.51 \pm 34.97 \text{ mm}^3$ .

An example of a patient who underwent left-sided frontal craniotomy is shown in Figure 2. In MRI images, after intravenous administration of contrast medium on the back contour of the post-surgical cavity, 4 fine-grained regions of up to 10 mm<sup>3</sup> were found, which corresponded to the resumption of the malignant process. In the  $^{18}\text{F}$ -FET-PET study, the area of non-uniformly increased  $^{18}\text{F}$ -FET accumulation along the side and rear walls of the post-surgical cavity. The most active focal points are visible at the rear wall and at the side wall. The image suggests an active proliferative process in the left frontal lobe. As another example, a patient after left-sided occipital craniotomy with increased  $^{18}\text{F}$ -FET uptake in the lateral part of the post-surgical cavity. In MRI hyperintensive area in T2-weighted images caused by previous treatment which make some difficulties in interpretation of the study (Fig. 3).

An important aspect is the size of the observed lesions in this two studies. In both methods, the formula for the volume of the ellipse was used to assess the volume ( $V = 4/3 \cdot \pi \cdot a \cdot b \cdot c$ ). In the case of 7 lesions, the volumes in MRI were higher than in  $^{18}\text{F}$ -FET-PET,

while in 9 lesions volumes were higher in  $^{18}\text{F}$ -FET-PET than MRI. The mean of all lesions detected in the MRI (25) was 44.70 mm<sup>3</sup> while in the  $^{18}\text{F}$ -FET-PET (30) study it was 25.28 mm<sup>3</sup>. However, the differences were not statistically significant ( $p > 0.05$ ).

## Discussion

Many authors point to the difficulty in differentiating the recurrence of the tumor from postoperative edema, occurring in the area of the post-surgical cavity. Using the PET imaging with  $^{18}\text{F}$ -fluoroethylo-L-thyrosine does not cause such a problem, because this radiotracer accumulates only in the areas of active proliferative process. This makes it easier to distinguish a tumor from healthy brain tissue, changes occurs postoperatively or under the influence of radiotherapy. Studies have shown that the  $^{18}\text{F}$ -fluoroethylo-L-thyrosine PET defines biological tumor volume (BTV) and reflects brain tumor tissue more accurately than MRI [5,6]. Other studies on a small group of patients, suggest that the post-operative  $^{18}\text{F}$ -FET-PET is a prognostic factor before radiotherapy [7–10]. This study on PET imaging with  $^{18}\text{F}$ -fluoroethylo-L-thyrosine showed more lesions than MRI. The difference in the number of foci between  $^{18}\text{F}$ -FET-PET and MRI may result from the difficulty in differentiating MRI lesions caused by the recurrence of the tumor, from edema occurring after the surgical treatment. Similar

studies were conducted by Grosu et al. where they compared <sup>18</sup>F-fluoroethyl-L-tyrosine-based biological tumor volume for radiotherapy planning in high-grade glioma with conventional MRI-based gross tumor volume. They found that biological tumor volume and gross tumor volume were different in size and localization in two thirds of the patients [11].

Because of specificity of <sup>18</sup>F-fluoroethyl-L-tyrosine which does not accumulate in inflammatory and reactive tissues, imaging with this agent is more accurate in detection of tumor recurrence and gives a better definition of target volumes prior to radiotherapy [12–13]. Kläsner et al. performed a study on a group of 25 patients where they investigated the value of early post-operative <sup>18</sup>F-FET-PET to assess the resection status in comparison to intra-operative findings, as well as MRI. They reported complete resection in 12 out of 25 (48%), in 6 out of 25 cases (24%) incomplete resection and in 7 patients <sup>18</sup>F-FET-PET showed discordant findings [14]. In our limited study, in 85% PET showed positive scans results, while MRI only in 70%.

The major limitation of this study is a small group of patients and because of that the statistical analysis for sensitivity and specificity was not performed. However even in spite of this, the study showed a comparable value of <sup>18</sup>F-FET-PET/CT and MRI in the assessment of primary brain tumors. As a consequence of these observations <sup>18</sup>F-FET-PET/MR should be considered as a method which provides better disease status evaluation of primary brain tumor. Another important limitation of this study is that not all lesions detected in both methods were verified by histopathological examination, so false positive findings could not be excluded.

## Conclusions

<sup>18</sup>F-FET-PET/CT and MRI play complementary roles in the diagnosis of primary brain tumors referred to radiation therapy.

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