



# The utility of $^{18}\text{F}$ -FDG PET/CT in brain tumours diagnosis

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## ABSTRACT

**Background:** The purpose of the study was to discuss whether 2-deoxy-2-[ $^{18}\text{F}$ ]fluoro-D-glucose positron emission tomography/computed tomography ( $^{18}\text{F}$ -FDG PET/CT) study protocol should include brain imaging.

**Materials and methods:** Analysis of international societies recommendations compared with the original data obtained in over 1000 consecutive torso and brain  $^{18}\text{F}$ -FDG PET/CT studies collected in 2010.

**Results:** According to the international societies recommendations, the  $^{18}\text{F}$ -FDG should not be the radiotracer of choice considering the brain region PET/CT study. However, it can be performed as an additional brain imaging tool. Based on at least a 3-year follow-up, we detected 8 cases of suspicious brain findings and no primary lesion among over 1000 consecutive torso and brain  $^{18}\text{F}$ -FDG PET/CT scans performed in 2010. However, in 5 out of 8 patients, the brain lesion was the only metastasis detected, affecting further therapy.

**Conclusions:** The  $^{18}\text{F}$ -FDG PET/CT study may help detect malignant brain lesions and, therefore, including brain region imaging into the study protocol should be considered.

**Key words:** brain tumour;  $^{18}\text{F}$ -fluorodeoxyglucose; oncology

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## Introduction

The most common types of brain tumours are metastatic lesions. However, the worldwide incidence of primary brain foci seems to be increasing, especially in highly developed countries [1–5]. The role of 2-deoxy-2-[ $^{18}\text{F}$ ]fluoro-D-glucose positron emission tomography/computed tomography ( $^{18}\text{F}$ -FDG PET/CT) in brain imaging is not established due to the non-tumour specific properties of

the radiopharmaceutical  $^{18}\text{F}$ -FDG and a high physiologic glucose uptake in grey matter [6–10]. Metabolic properties of the radiotracer result in omitting the brain region scanning from the standardly performed  $^{18}\text{F}$ -FDG PET/CT scanning protocol in some of the nuclear medicine departments [11–13]. However, authors [13–15] indicate the potential usefulness of the brain and torso  $^{18}\text{F}$ -FDG PET/CT study in the primary and metastatic brain lesion evaluation.

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The  $^{18}\text{F}$ -FDG remains one of the most used PET-dedicated radiotracers. Several international societies provided recommendations regarding brain imaging using the PET/CT method. Authors [1, 6, 7, 11, 14–16] discussed the usefulness of this radio-pharmaceutical considering the limited ability of the  $^{18}\text{F}$ -FDG PET/CT method to differentiate between benign and malignant lesions within the central nervous system (CNS). In this study, we discussed the recommendations of the International Atomic Agency (IAEA) [16], the European Association of Nuclear Medicine (EANM) [14, 15, 17, 18] and the Society of Nuclear Medicine and Molecular Imaging (SNMMI) [6, 7] as valid worldwide. We compared the recommendations with our experiences in performing brain and torso  $^{18}\text{F}$ -FDG PET/CT.

Although the role of the  $^{18}\text{F}$ -FDG PET/CT in CNS has been widely described, the comparative analysis of international guidelines and the original database has not been mentioned. The study aimed to discuss whether the  $^{18}\text{F}$ -FDG PET/CT study protocol should include brain imaging.

## Materials and methods

### Bioethics

The study was designed per the principles of the Declaration of Helsinki. The study was performed based upon written informed consent received from the patients and approved by the Local Bio-ethical Committee (date of approval: 30.01.2020) as the retrospective analysis based on standardly performed unsponsored, single-institutional procedures, conducted in the year 2010.

### Literature — brain scanning recommendations

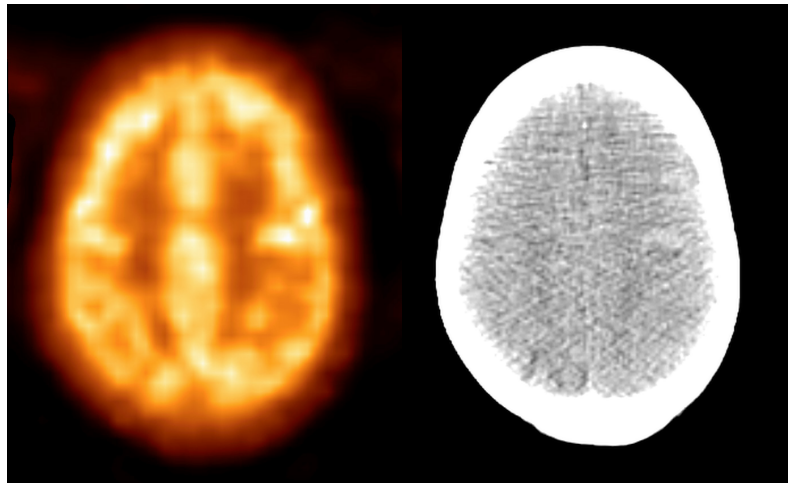
We analysed the recommendations of the most respected international societies. We have researched IAEA guidelines referring to the PET/CT procedures performance [16], EANM original and updated guidelines [14, 15, 17, 18], SNMMI recommendations [6, 7], World Health Organisation (WHO) and National Tumor Brain Society reports [1, 3] as well as other available documents (School of Medicine, Kyungpook National University) [19].

### Original data

We analysed 1083 consecutive patients examined with the torso and brain  $^{18}\text{F}$ -FDG PET/CT

study in 2010 in our institution [14]. The torso and brain  $^{18}\text{F}$ -FDG PET/CT study was performed due to the following clinical indications: suspicious finding outside the brain region, staging of the initial disease or restaging (including the recurrent disease). We excluded repeated studies of each patient, different than torso and brain scanning protocols, and patients in whom brain lesion had been reported previously. We excluded patients who were transferred for further diagnostic and therapeutic management to external hospitals. We included into the study 1002 clinical cases considering at least a 3-year follow-up and histopathologic examination availability. We included into the analysis only those subjects in whom full medical records were available.

In each patient, we performed the torso and brain  $^{18}\text{F}$ -FDG PET/CT study at 60 minutes (min) post-injection (p.i.) of the radiotracer  $^{18}\text{F}$ -FDG in mean activity up to 3.7 MBq per kilogram of body weight. We used the Philips Gemini TF16 hybrid scanner (Philips, Cleveland, Ohio, United States of America, USA) [20]. The acquisition protocol included the area from the skull-apex to mid-thigh. PET imaging preceded 16-slice CT scanning using the following parameters: mean tube current of 150 milliampereseconds (mAs; up to 244 milliamperes, mA), 120 kilovoltage peak (kVp), Pitch of 0.8, gantry rotation time of 0.5 s, slice increment of 5 mm, thickness of 5 mm [20]. The PET section scanning time was 1.5 min. The area of scanning did not exceed 1020 mm and the study duration was up to 35 minutes (min). We evaluated the patients' CT radiation exposure, using the computed tomography dose index [20] (CTDI, range: 7.0–10.1 milligrays, mGy), and the Dose — Length Product (DLP, range: 650–1000 mGy × cm). We chose the semi-automatic contouring method to evaluate lesions within the brain, using the Philips-dedicated software Fusion Viewer (Philips, Cleveland, Ohio, USA, Fig. 1) and measured the PET-dedicated metabolic parameter of the maximal Standardized Uptake Value (SUVmax). To evaluate the obtained images, we used the soft tissue CT/SUV preset (abdominal region). The SUVmax value cut-off used to evaluate the suspicious brain findings was 3.0 based on the average SUVmax value, observed within the brain lesions confirmed with the histopathologic examination.



**Figure 1.** Metastatic brain lesions evaluated in lung small cell carcinoma patient (source: original figure)

## Results

We analysed the available recommendations and guidelines describing the use of <sup>18</sup>F-FDG PET/CT study in oncology, focusing on the role of this method in primary and metastatic brain tumours diagnosis. We supported the literature evaluation results with the original data obtained in our institution.

According to IAEA, EANM and SNMMI guidelines, the standard <sup>18</sup>F-FDG PET/CT acquisition includes the area: skull-base–mid-thighs [6, 14, 16], and the brain region can be omitted in the PET/CT examination. Torso and brain protocol [14], described in the official EANM guidelines, seems to be an additional or modified protocol but not the obligatory daily PET/CT practice (Tab. 1).

According to the IAEA, EANM, and SNMMI recommendations, a high glucose utilization within grey matter [6, 7, 14–16] decreases the <sup>18</sup>F-FDG

PET/CT method’s specificity in inflammation and malignant tumours differential diagnosis. It also limits the possibility to detect small CNS lesions [6]. Literature [6, 14, 16] shows a low usefulness of the <sup>18</sup>F-FDG PET/CT technique in brain tumours detection. However, some of the authors [16] suggest that performing delayed PET/CT scanning at 240–360 min p.i. of the <sup>18</sup>F-FDG increases the tumour to background ratio, improving primary brain foci evaluation. Torso and brain <sup>18</sup>F-FDG PET/CT imaging enables the detection of brain and skull metastases. However, PET/CT brain assessment should always be followed by magnetic resonance imaging (MRI) as a method of choice in CNS diagnosis [16].

We analysed 1002 patients who underwent torso and brain <sup>18</sup>F-FDG PET/CT scanning. In this group, we found suspicious brain findings in 8 patients. Based on the patients’ medical records, we evaluated the squamous cell cancer (SCC) neck tumour,

**Table 1.** The use of <sup>18</sup>F-FDG PET/CT in brain scanning — recommendations

Society	Release [year]	Study protocol	<sup>18</sup> F-FDG utilities	<sup>18</sup> F-FDG limitations
IAEA	2013 [16]	Skull-base–mid-thigh Skull-vertex–toes <sup>a</sup>	Primary and metastatic brain tumours ev. <sup>b</sup>	High uptake in grey matter Differential diagnosis
EANM	2009 [15] 2015 [14]	Skull-base–mid-thigh	Differential diagnosis <sup>c</sup> Viable tumour tissue (i.e. recurrence) ev. Non-invasive grading	High uptake in grey matter Low specificity in brain metastases ev.
SNMMI	2006 [6] 2009 [7]	Skull-base–mid-thigh Skull-vertex–toes	Regional cerebral glucose ev. Differential diagnosis	High uptake in grey matter Limited ability to detect small lesions

IAEA — International Atomic Energy Agency; EANM — European Association of Nuclear Medicine; SNMMI — Society of Nuclear Medicine & Molecular Imaging; <sup>18</sup>F-FDG — 2-deoxy-2-[<sup>18</sup>F]fluoro-D-glucose; <sup>a</sup>for tumours with a high probability of metastases; <sup>b</sup>evaluation; <sup>c</sup>benign (i.e. inflammation) vs. malignant lesions differential diagnosis

**Table 2.** Brain lesions detected while brain and torso 2-deoxy-2-[18F]fluoro-D-glucose positron emission tomography/computed tomography (<sup>18</sup>F-FDG PET/CT) scanning: restaging (source: original database)

Initial diagnosis	<sup>18</sup> F-FDG <sup>a</sup> activity	Brain lesions	SUVmax <sup>b</sup> avg. SUVmax ± SD <sup>c</sup>	Other lesions
SCC Neck	289	1	6.4	Lymph nodes <sup>d</sup>
SCC Lung	355	1	4.2	None
SCC Lung	249	3	5.2 ± 1.7	None
Gastric ca	329	1	6.1	None
Ovarian ca	348	1	5.6	None
Colorectal ca	285	2	5.6 ± 2.1	Bone tumours
Mel. mal.	355	5	4.4 ± 0.8	None

SCC — squamous cell cancer; ca — cancer; mel. mal. — melanoma malignant; SD — standard deviation; <sup>a</sup>injection activity of 3.7 MBq/kg; <sup>b</sup>in case of 1 lesion detected; <sup>c</sup>in case of > 1 lesion detected; <sup>d</sup>cervical lymph nodes

SCC lung, gastric, ovarian, and colorectal cancer, and melanoma malignant metastatic brain foci. In one patient, we observed the unspecified benign vascular malformation (Tab. 2).

According to authors [21], the SUVmax exceeding 2.5 suggest an abnormality. We observed that the minimal SUV value within the brain found in our database was 3.3. In 5 out of 7 examined cancer patients, brain foci were the only metastatic lesions detected in PET/CT scans. The indication to perform the PET/CT was restaging. Thus, distant foci discovery was a decisive factor for continuation of the therapy or modification of treatment protocol. We did not observe tumour or tumour-like conditions in any other examined patients. According to the medical records of the remaining group of 994 studied with the torso and brain <sup>18</sup>F-FDG PET/CT cases in whom no brain lesion were found, no brain findings had been reported.

## Discussion

Primary and metastatic brain tumours are rare malignancies, causing several health ailments such as neurological, locomotory or even psychological disorders among cancer patients. Brain tumours are often lethal and, therefore, fast diagnosis is crucial [1, 2, 22, 23]. Performing brain and torso <sup>18</sup>F-FDG PET/CT may be helpful in detecting clinically silent brain lesions. In some cases, the method of choice in brain tumours therapy is the palliative approach, based on chemotherapy rather than surgery or external beam radiotherapy [4, 23]. Incidental detection of a brain tumour may significantly affect therapeutic management, especially in patients diagnosed with a cancer other than CNS primary

in which the brain lesion is one of a few or the only detected distant metastasis.

According to the international societies' recommendations, the <sup>18</sup>F-FDG PET/CT study should not be considered the method of choice in CNS malignancy diagnosis. The high <sup>18</sup>F-FDG uptake in grey matter significantly limits the specificity of the method in brain tumours detection and benign versus malignant foci differential diagnosis. However, some of the authors suggest the possibility to include brain region imaging into the <sup>18</sup>F-FDG PET/CT protocol, especially using the delayed imaging [16]. Although the MRI examination is superior to PET/CT study in CNS evaluation, including brain region imaging into standard <sup>18</sup>F-FDG PET/CT scanning may help to detect unknown brain pathologies.

Including the brain region in the daily <sup>18</sup>F-FDG PET/CT practice demands extending the acquisition duration for up to 1.5 min. The malignant brain tumours are difficult to detect and their therapy is often unsuccessful. Moreover, a high risk of post-surgical mortality among brain tumour patients often limits the possibility to perform the lesion's histopathologic assessment. Due to a high mortality rate among brain tumour patients, detecting clinically silent lesions using the diagnostic imaging method seems essential [1, 4, 23]. In our study, the number of patients in whom brain metastases were detected was statistically insignificant, which remains in line with the worldwide epidemiological data regarding the primary and distant brain tumours occurrence (brain tumours occurrence approximates at 1% of all malignancies [24]). Thus, adding up to 1.5 min to the scanning protocol duration can be considered life-saving for subjects

in whom torso and brain imaging helped to evaluate an unknown, clinically silent brain tumour.

The heterogeneity of the database may be considered the main study limitation. The consecutively obtained original database reflects the institution clinical characteristics and its versatility considering the numerous oncological diagnoses, diagnosed and treated in the institution. Moreover, we included in the analysis over 1000 consecutive patients to ensure the reliability of the study in terms of the utility of the torso and brain <sup>18</sup>F-FDG PET/CT study to detect previously unsuspected, clinically silent brain tumours.

## Conclusion

The <sup>18</sup>F-FDG PET/CT study may help detect malignant brain lesions and, therefore, including brain region imaging into the study protocol should be considered.

## Conflict of interest

None declared.

## Funding

None declared.

## Disclosure

All Authors of this manuscript have approved the whole article content.

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