

Combined PET/MRI in brain glioma imaging

ABSTRACT

Gliomas are the most common primary brain tumours in children and adults, consisting of a heterogeneous group of neoplastic diseases arise from the supporting cells of the CNS (glial cells). Their histopathological and molecular characteristics vary considerably as do their management and prognosis. Conventional gadolinium-enhanced magnetic resonance imaging (MRI) is considered the primary imaging modality for initial work up and follow up of patients with gliomas, although it has some limitations, especially in differentiating high from low grade tumours and in distinguishing disease recurrence from post-therapy changes. Hybrid positron emission tomography (PET)/MRI is a relatively novel tool that combines MRI sequences with metabolic information from PET, and therefore different PET radiotracers, in a single scan. This article discusses the main advantages and disadvantages of combined PET/MRI compared to other conventional or more widely available imaging tools, such as MRI or combined positron emission tomography-computed tomography. The main uses of PET/MRI and the most commonly used PET radiotracers in providing diagnostic, prognostic and predictive information in patients with glioma are covered.

Primary brain neoplastic diseases arise from different cells in the CNS and have very diverse histopathological and molecular characteristics. Based on their histological and molecular features, the 2016 World Health Organization classification of CNS tumours includes more than 120 types of primary CNS tumours which have different prognoses (Komori, 2017).

In children, primary nervous system tumours are the most common solid cancers accounting for around 26% of all childhood cancers (American Cancer Society, 2016). Around half of paediatric brain tumours arise from CNS supportive glial cells (gliomas) with 40% being the astrocytoma subtype (Children with Cancer UK, 2019).

In adults, glioma of astrocytoma subtype is the most common type. The World Health Organization classification defines four grades: grade I (pilocytic astrocytomas) and II (diffuse astrocytoma) are usually called low grade tumours, while grade III and IV are high grade tumours. Grade IV

astrocytoma, also known as glioblastoma multiforme, is the most common and aggressive primary brain malignancy, with 5-year survival of around 4% (Davis, 2016). Grade III astrocytoma (anaplastic astrocytoma) also carries a poor prognosis (Komori, 2017). Although the diffuse astrocytomas (grade II) are considered low grade gliomas they usually progress to a higher grade (anaplastic or secondary glioblastoma multiforme) (Gerges et al, 2013). Differentiating among these subtypes is very important, as it affects management strategy and prognosis.

Combined positron emission tomography–magnetic resonance imaging: an overview

Hybrid positron emission tomography–magnetic resonance imaging (PET/MRI) combines the high contrast and morphological resolution of MRI with the metabolic and physiological information from the integrated PET scan, by using different PET radiopharmaceutical tracers. This advanced technology is a product of many years of research and development to overcome technical difficulties. One major technical problem in combining both modalities in the same device was the interference of the strong magnetic field produced by the MRI with the PET components. This was solved by using rings of magnetic field-insensitive PET detectors inside a 3T MRI gantry (Tudisca et al, 2015).

The first successful combined PET/MRI was developed by Siemens (Biograph mMR System), and approved for clinical use in 2011. It allowed whole body acquisition of MRI and PET data, lowering the scanning time from 60–90 minutes (for two sequential acquisitions) to approximately 30 minutes (Koktysh, 2017). Combined PET/MRI is currently used for clinical and research purposes for diagnosis, treatment planning and following up various oncological and non-oncological disorders of different body systems.

PET radiopharmaceuticals

It is important to have a basic understanding about some of the PET radiotracers that are used for imaging brain tumours, in research or clinical practice. Different PET radiopharmaceuticals target different metabolic processes or receptors and can provide valuable information about a tumour's physiological activities.

18F-fluodeoxyglucose

18F-fluodeoxyglucose (¹⁸F-FDG) is well known and the most widely available PET tracer. It is an indicator of glucose uptake and metabolism. One application of FDG-PET is to assess the tumour grade. High grade gliomas

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show higher tracer uptake than low grade tumours, and CNS lymphoma usually shows significantly higher FDG uptake than high and low grade gliomas (Figure 1) (Das et al, 2011). Another important use of FDG is to optimize the biopsy site, if it is taken from the most avid part of the tumour, which represents the viable, and usually the more aggressive, part of the tumour (Spence et al, 2007), although physiological FDG uptake by normal brain tissue causes poor tumour margin delineation, so this information is less useful for radiotherapy or surgery planning than other PET radiopharmaceuticals (amino acid and choline labelled radiotracers). Another drawback is its non-specific uptake (increases with inflammation) which might affect its ability to differentiate tumour recurrence from post-therapy inflammation (Figure 2), although it has been used for this purpose with relatively moderate sensitivity and specificity (around 77%) (Nihashi et al, 2013).

Radiolabelled amino acid PET tracers

Transport and consumption of amino acids is increased in malignant cells. Radiolabelled amino acids, such as ^{18}F -deoxyphenylalanine, ^{18}F -fluoro-ethyl-tyrosine (^{18}F -FET), ^{11}C -methionine (^{11}C -MET) and ^{18}F -fluoro-L-3,4-dihydroxyphenylalanine (^{18}F -FDOPA), can be used as markers of amino acid uptake and protein synthesis by tumour cells. Generally amino acid radiotracer uptake is low in the normal brain tissue, allowing better tumour delineation compared to FDG, making these tracers more reliable for surgery and radiotherapy planning (Ciarmiello and Mansi, 2016) (Figure 3). However, they have limited ability to differentiate low from high grade gliomas in pre-treatment assessment (Ciarmiello and Mansi, 2016). Other studies showed that ^{11}C -MET PET (Kato et al, 2008) and ^{18}F -FET PET (Kunz et al, 2011) are able

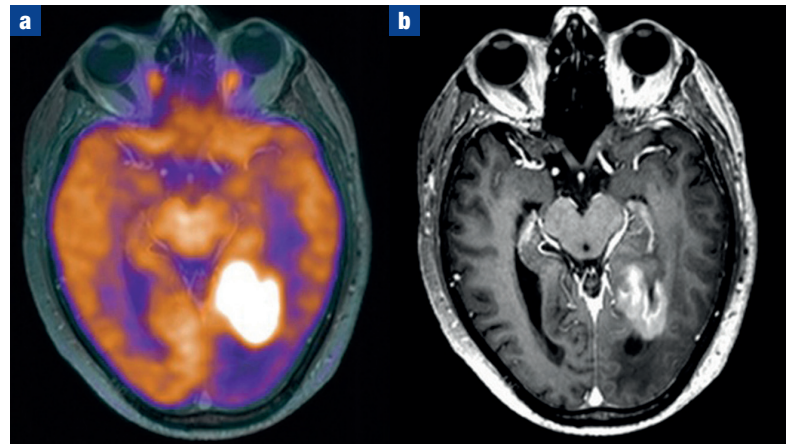


Figure 1. Primary CNS lymphoma. **a.** Fused ^{18}F -fluodeoxyglucose PET/MRI and **(b)** gadolinium-enhanced T1 MRI images. There is intense fluodeoxyglucose uptake in the enhanced left parieto-occipital lesion. Notice the high physiological fluodeoxyglucose uptake by normal brain tissue.

to differentiate low from high grade gliomas with high sensitivity and specificity. Kunz et al (2011) studied 55 patients with suspected grade II gliomas (based on MRI findings) to assess the correlation between the hot spots on dynamic ^{18}F -FET PET and the higher grade tumour parts, and whether this PET tracer is able to change tumour grading. Histopathologically, 44% of the gliomas originally considered grade II harboured high grade components (grade III or IV). Examination of 373 biopsy samples indicated a strong correlation with the analyses of the ^{18}F -FET-PET uptake kinetics ($P < 0.0001$), and anaplastic foci can be accurately identified by using ^{18}F -FET PET mapping (Kunz et al, 2011).

Another important advantage of these tracers is that they are less influenced by inflammation, although they are not absolutely tumour specific. Amino acid PET tracers are more reliable than FDG in differentiating tumour recurrence from inflammation and necrosis in post-therapy assessment (Ciarmiello and Mansi, 2016).

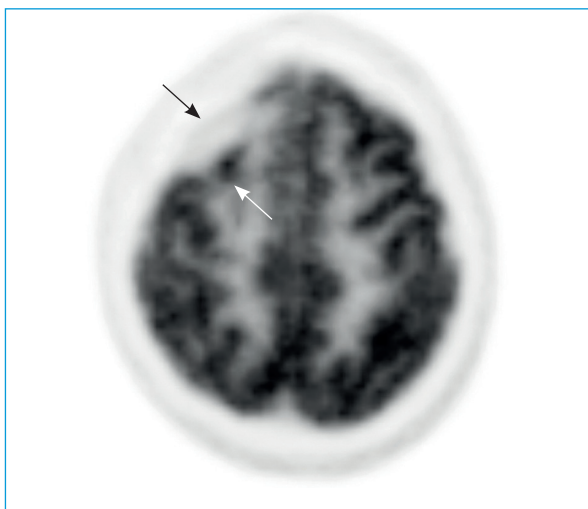


Figure 2. Axial ^{18}F -fluodeoxyglucose-PET scan in a patient with resected high grade glioma in the right frontal lobe. The ^{18}F -fluodeoxyglucose uptake (white arrow) in the area adjacent to the resected tumour (photopenic area, black arrow) could represent physiological cerebral uptake, inflammatory uptake or a residual tumour.

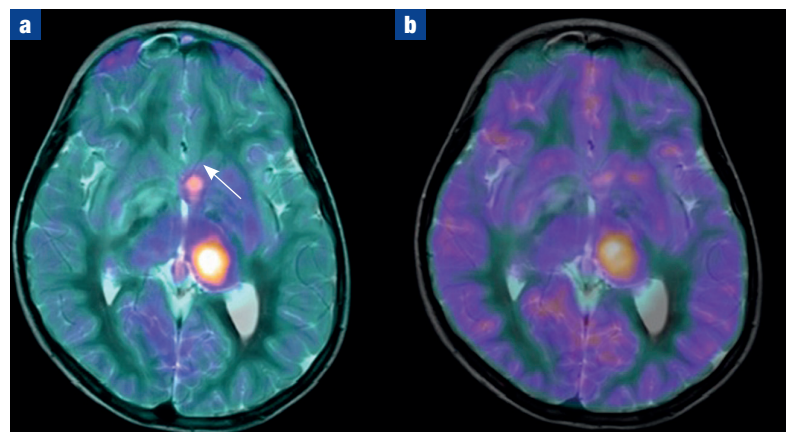


Figure 3. Comparison of **(a)** ^{11}C -methionine MRI and **(b)** ^{18}F -fluodeoxyglucose MRI in a patient with high-grade glioma. Notice the low normal brain tissue uptake of ^{11}C -methionine compared to ^{18}F -fluodeoxyglucose, which allowed the identification of a further spot of focal uptake in the right anterior commissure (arrow).

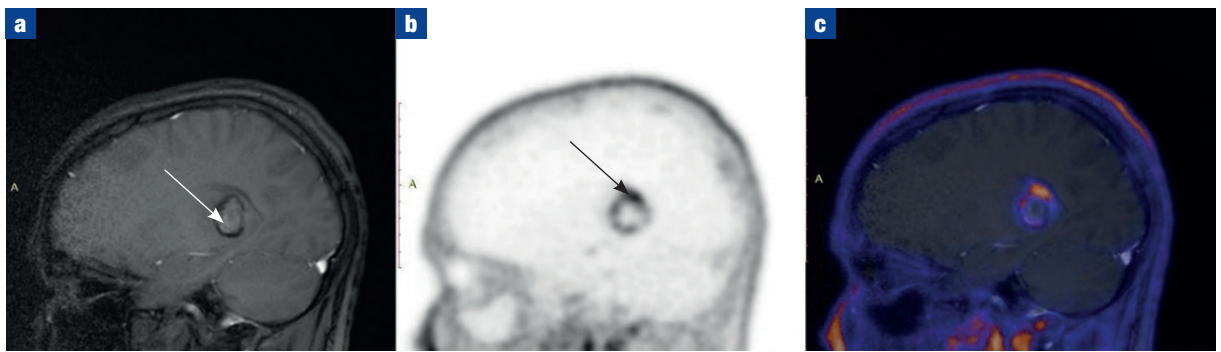


Figure 4. **a.** Sagittal T1 MRI with a post-biopsy haemorrhagic core (white arrow), **(b)** F-choline PET and **(c)** fused PET/MRI images in a patient with high grade glioma. Notice the high F-choline uptake especially in the superior part of the tumour (black arrow) with the negligible uptake by the normal brain tissue.

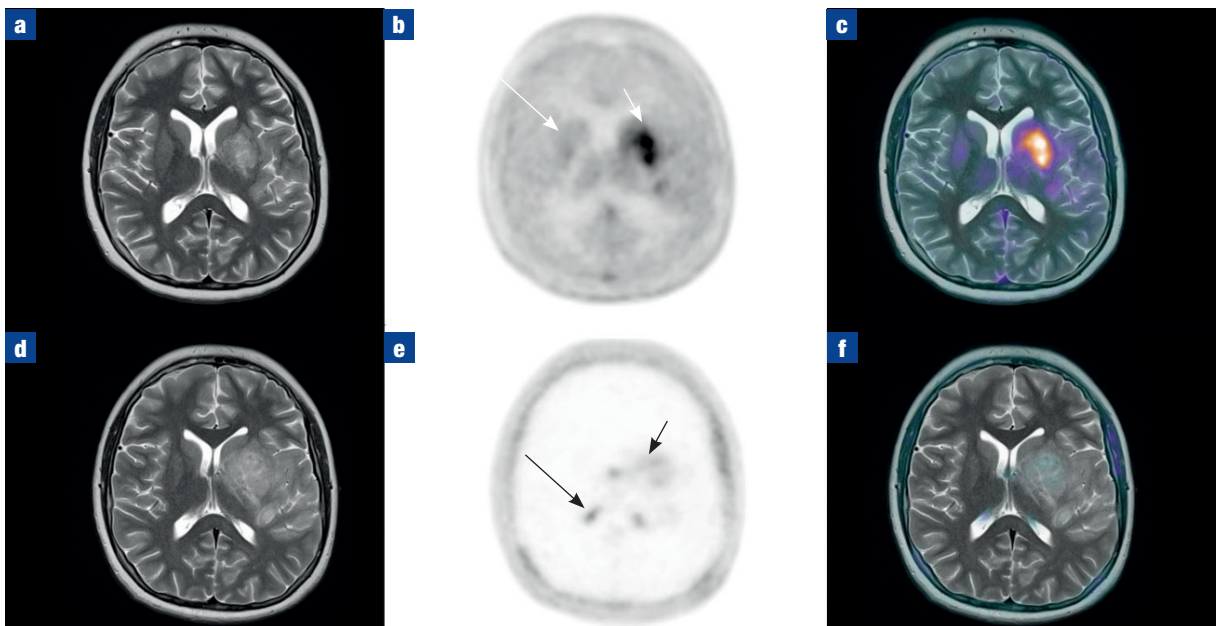


Figure 5. **a–c.** ^{18}F -dihydroxyphenylalanine (F-DOPA) and **(d–f)** F-choline in a patient with World Health Organization grade III anaplastic astrocytoma. The uptake in the lesion is more consistent with F-DOPA (white arrowhead) than with F-choline tracer (black arrowhead). Notice the physiological uptake of F-DOPA in the basal ganglia (white arrow) and F-choline in the choroid plexus (black arrow).

Choline-labelled PET tracers

^{18}F -fluorocholine and ^{11}C -choline are markers of cell membrane turnover (lipid metabolism) which also increases in malignant tumours. One advantage of using labelled choline tracers is the significantly low uptake by the normal brain tissue compared to other tracers, allowing superior tumour delineation (Figure 4).

Figure 5 compares F-DOPA and F-choline in a patient with World Health Organization grade III anaplastic astrocytoma.

The advantages, disadvantages and potential uses of some PET radiotracers in brain glioma imaging are summarized in Table 1.

Combined PET/MRI in pre-treatment brain glioma imaging

In the pre-treatment assessment, it is particularly important to evaluate the extent of the tumour, the probable grade of

tumour and the possibility of malignant transformation of low grade glioma, as well as assessing the best site to biopsy. PET tracers can provide valuable information regarding this.

Current guidelines do not support using PET/MRI (or positron emission tomography-computed tomography; PET/CT) for primary diagnostic work up of a suspected primary brain tumour. However, they suggest using PET imaging in pre-treatment work up as this may correlate with tumour grade or indicate the optimal area for biopsy (National Comprehensive Cancer Network, 2018). Gadolinium-enhanced MRI is the modality of choice. However, MRI still has limitations in differentiating low from high grade gliomas. On gadolinium-enhanced MRI, around 10% of glioblastoma multiforme and 30% of anaplastic astrocytomas show no enhancement, while low grade gliomas sometimes show enhancement (Knopp et al, 1999; Scott et al, 2002).

Table 1. Mechanism of uptake, advantages, disadvantages and uses of some PET radiotracers in brain glioma imaging

PET radiopharmaceutical	Mechanism of uptake or indicator of:	Advantages	Disadvantages
¹⁸ F-fluorodeoxyglucose	Glucose uptake and metabolism	<ul style="list-style-type: none"> ■ Readily available ■ Relatively less expensive ■ Can differentiate low from high grade gliomas and helps in guiding biopsy (Spence et al, 2007) ■ Longer half-life of ¹⁸F (110 minutes) 	<ul style="list-style-type: none"> ■ High physiological tracer uptake by normal brain tissue ■ Low specificity (uptake by inflammation or infection) ■ Less reliable in post-therapy assessment compared to amino acid and choline-PET radiotracers
¹¹ C-choline ¹⁸ F-fluorocholine	Lipid metabolism (plasma membrane synthesis)	<ul style="list-style-type: none"> ■ Better tumour delineation (very low normal brain tissue uptake) ■ Differentiating low from high grade gliomas and guiding biopsy (Hara et al, 2003) ■ Better than fluoroxyglucose and conventional magnetic resonance imaging in differentiating tumour recurrence from post-therapy changes (Tan et al, 2011) 	<ul style="list-style-type: none"> ■ Logistical problems regarding the short half-life of ¹¹C (20 minutes) which requires an on-site cyclotron were overcome with ¹⁸F-labelled choline ■ Physiological uptake in choroid plexus, venous sinuses and pituitary gland could affect its accuracy ■ Uptake in some CNS inflammatory, granulomas and demyelinating diseases
¹¹ C-methionine	Amino acid uptake and protein synthesis	<ul style="list-style-type: none"> ■ More specific and sensitive than fluoroxyglucose in differentiating recurrence from necrosis in post-therapy scenarios ■ Less affected by inflammation ■ Low normal brain tissue uptake, allowing better tumour delineation ■ Carbon is a building block of all organic compounds, so can be substituted with radioisotope ¹¹C without disturbing their basic physiological functions 	<ul style="list-style-type: none"> ■ Shorter half-life of ¹¹C (20 minutes) ■ Might be less reliable in differentiating high from low grade gliomas
¹⁸ F-FET ¹⁸ F-FDOPA	Amino acid uptake (transport)	<ul style="list-style-type: none"> ■ Extra advantage of the longer half-life of ¹⁸F compared to ¹¹C 	<ul style="list-style-type: none"> ■ Physiological uptake of ¹⁸F-FDOPA in the basal ganglia potentially affects its accuracy in assessing lesions close to these areas

¹⁸F-FDOPA = ¹⁸F-fluoro-L-3,4-dihydroxyphenylalanine; ¹⁸F-FET = ¹⁸F-fluoroethyltyrosine.

Some studies showed discrepancy between MRI and PET findings, so combining both modalities provides a better approach to reach a more accurate diagnosis. In one study, ¹¹C-MET PET/MRI identified the most aggressive part of the tumour which was not always related to areas of high cell membrane proliferation seen with magnetic resonance spectroscopy (Bisdas et al, 2013).

Filss et al (2014) compared the information which is obtained from ¹⁸F-FET PET with the perfusion-weighted MRI regional cerebral blood volume in patients with gliomas ($n=56$). They concluded that the two modalities displayed different information, and ¹⁸F-FET PET showed larger tumour volumes than regional cerebral blood volume maps, with poor spatial congruence between them, i.e. the locations of the local hot spots vary considerably. Therefore, PET data add metabolic and physiological information to MRI and increases its diagnostic power. Possible applications of PET imaging in the pre-treatment assessment of brain gliomas are summarized in *Table 2*.

Combined PET/MRI in post-therapy glioma evaluation

PET/MRI is used to assess brain tumours during post-therapy follow up to differentiate possible tumour residual, recurrence or progression from tumour necrosis or scarring (*Figures 6 and 7*).

Radiolabelled amino acid PET tracers showed better accuracy than contrast-enhanced MRI in differentiating between pseudoprogression and progression in patients with glioblastoma multiforme after radiochemotherapy treatment. Galdiks et al (2015) conducted a study on 22 patients who had recently completed radiochemotherapy for glioblastoma. All lesions showed >25% enhancement on gadolinium-enhanced MRI. They found that pseudoprogression had significantly less ¹⁸F-FET uptake than the early progression (¹⁸F-FET maximum tumour:brain ratio was 1.9 ± 0.4 vs 2.8 ± 0.5 respectively, $P < 0.001$).

Regarding the diagnostic accuracy of ¹¹C-MET, ¹¹C-choline and ¹⁸F-FDG in distinguishing glioma recurrence from radiation necrosis, Takenaka et al (2014)

Table 2. Possible applications of some PET radiotracers in pre-therapy assessment of brain gliomas

Pre-therapy application	PET radiotracers used	Notes
Better delineation of the tumour; helps in surgical and radiotherapy planning	Amino acid (Ciarmiello and Mansi, 2016) and choline (DeGrado et al, 2001)	Fludeoxyglucose-positron emission tomography (FDG-PET) might be applied in high-grade gliomas with marked intratumoural heterogeneity, where the hot spots could be targets with a higher radiation dose (Ciarmiello and Mansi, 2016)
Tumour grading	¹⁸ F-fludeoxyglucose (Delbeke et al, 1995) and choline (Kato et al, 2008)	There is controversy over whether amino acid tracers are suitable for grading tumours (Kato et al, 2008; Kunz et al, 2011) or not (Chen et al, 2006)
Guiding biopsy	¹⁸ F-fludeoxyglucose (Spence et al, 2007), choline (Hara et al, 2003) and amino acids (Kunz et al, 2011)	Directing the stereotactic biopsy to the most avid part increases the yield
Prognosis	¹⁸ F-fludeoxyglucose and amino acid (Kim et al, 2005)	Increased uptake correlated with worse prognosis. Kim et al (2005) found that ¹¹ C-methionine is better than ¹⁸ F-fludeoxyglucose for this purpose

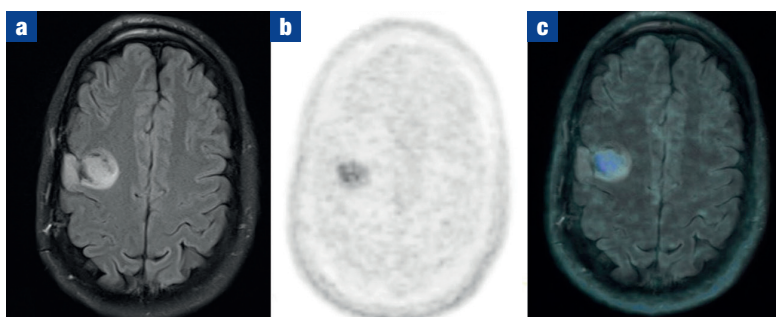


Figure 6. a. Axial flair MRI, **(b)** ¹⁸F-dihydroxyphenylalanine (F-DOPA) PET and **(c)** fused PET/MRI in a patient with previously de-bulked glioma in the right frontal lobe showing focal F-DOPA uptake indicating recurrent tumour.

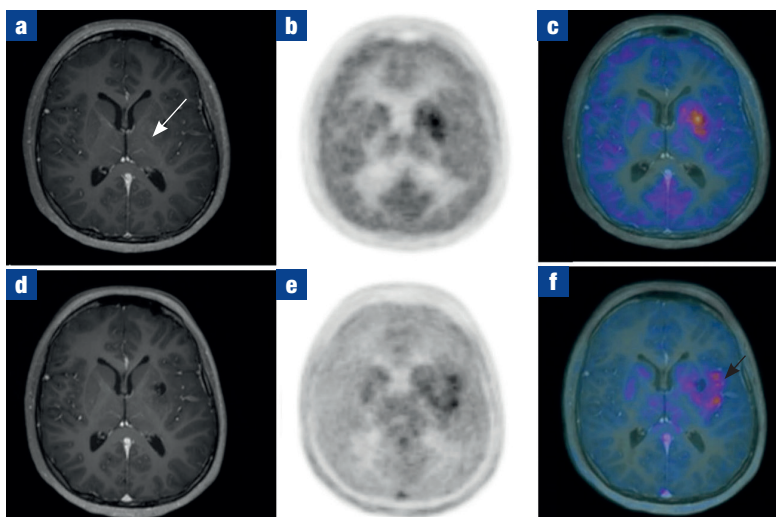


Figure 7. Two ¹⁸F-dihydroxyphenylalanine (F-DOPA) PET/MRI studies for a patient with anaplastic astrocytoma treated with chemoradiation. a–c. The first study showed avid tumour in and around the left basal ganglia, with minimal gadolinium enhancement (white arrow). **d–f.** The second scan was taken 6 months later and showed lateral disease extension to the left insula (black arrow) indicating disease progression, with no significant radiological changes on MRI.

compared the results from patients with suggestive glioma recurrent on MRI scans (*n*=50). They found that ¹¹C-MET had superior diagnostic accuracy compared to ¹¹C-choline and ¹⁸F-FDG in distinguishing recurrence from radiation

necrosis, and that ¹¹C-MET lesion:normal brain uptake ratio >2.51 showed the best sensitivity and specificity for diagnosing glioma recurrence (around 91% and 87% respectively).

Once more, combining PET and MRI data increases the accuracy of the test, especially when advanced MRI sequences are included. To distinguish recurrence from radiation necrosis, Jena et al (2016) conducted a study on previously treated glioma patients (*n*=26) using simultaneous ¹⁸F-FET PET/MRI, measurement of choline/ creatine (Cho/Cr) ratio (magnetic resonance spectroscopy) and normalised mean relative cerebral blood volume. The combined results from these different modalities yielded higher diagnostic accuracy. Combined ¹⁸F-FET maximum tumour:brain ratio (or mean tumour:brain ratio) and Cho/Cr ratio accuracy was 97%, and combined ¹⁸F-FET mean tumour:brain ratio, regional cerebral blood volume and Cho/Cr ratio produced the maximum area under the curve. In a more recent study by Hojjati et al (2018) to differentiate glioblastoma multiforme recurrence from post-radiation necrosis, combining data from FDG-PET/MRI with the perfusion MRI resulted in an area under the curve of 1.0, indicating the highest sensitivity and specificity.

Advantages of combined PET/MRI

Combined PET/MRI vs combined PET/CT

One of the main advantages of PET/MRI over PET/CT is the elimination of the ionizing radiation of the CT component. As brain tumours are the most common solid malignancy in children and multiple follow-up scans are needed, this advantage is more significant in these scenarios.

MRI has superior soft tissue resolution which allows more detailed imaging than a CT scan (Figure 8). It excels in imaging brain pathologies, and allows better diagnostic images of the tumour structures.

Combined PET/MRI vs MRI scan alone

Additional metabolic information from different PET tracers will be added to the morphological and molecular

information from the MRI, which allows more accurate diagnosis. Targeting the most avid part of the tumour increases the yield of the stereotactic biopsy.

Post-therapy changes can be more confidently differentiated from tumour residual or recurrence when PET information is added to MRI.

The combination of PET and MRI allows more accurate detection of malignant transformation of low grade gliomas.

Combined PET/MRI vs sequential PET and MRI acquisitions

Simultaneous acquisition of PET and MRI data allows shorter scanning time which alleviates the patient's stress and the staff's workload and improves workflow. It eliminates the need for two administrations of general anaesthesia, which can be an advantage for young children or for claustrophobic patients.

Combined PET/MRI allows acquisition of data simultaneously in space and time, minimizing the chance of image misregistration, and eliminating interval changes that could happen in between the two scans.

Disadvantages of combined PET/MRI

The high price of the hybrid PET/MRI system along with the cost of device maintenance has affected its availability. The PET/MRI system costs 3–4 times more than a PET/CT system – the combined PET/MRI machine costs from \$4–5 million, with an additional 10% per year for maintenance and operation (Koktysh, 2017).

Another factor that affects the spread of the combined PET/MRI scan is the presence of the PET/CT scan, which is already established as a valuable imaging modality with lower cost and faster performance, and is supported by a large amount of evidence-based data and guidelines. Combined PET/MRI, on the other hand, is a relatively newer technology with limited spread, and this makes it harder to conduct large, multicentre studies and establish standardized protocols among specialists and centres.

Another issue with combined PET/MRI is related to the attenuation correction. In combined PET/CT, the CT component is used for attenuation correction and anatomical localization. However, in PET/MRI, the MRI signal is not directly correlated to the tissue density, for example, cortical bone and air have poor or no signal, but cause the highest and lowest attenuation in PET respectively, so MRI cannot be directly used for attenuation correction (Wagenknecht et al, 2013). Methods for MRI-based attenuation correction, such as Dixon, ultra-short echo or zero echo time are fast techniques, but they are subjective to image noise and artefacts (Chen and An, 2017).

Other limitations are related to the absolute and relative contraindications of the MRI itself, such as patients with cochlear implant, sensitive heart pacemaker, metallic foreign body in the eye and others.

KEY POINTS

- Hybrid positron emission tomography–magnetic resonance imaging (PET/MRI) is a relatively new technology that combines the high contrast and morphological resolution of the MRI with the physiological information from the integrated PET scan.
- The complexity of brain structures and the subtlety of the neuropathologies makes hybrid PET/MRI an ideal tool for imaging primary brain tumours.
- Hybrid PET/MRI eliminates the ionizing radiation of computed tomography, and allows shorter scanning time which alleviates the patient's stress, reduces the staff's workload and improves workflow.
- Nonetheless, the widespread use and lower cost of positron emission tomography–computed tomography along with its well-established guidelines and consensus, negatively impact the spread of PET/MRI.

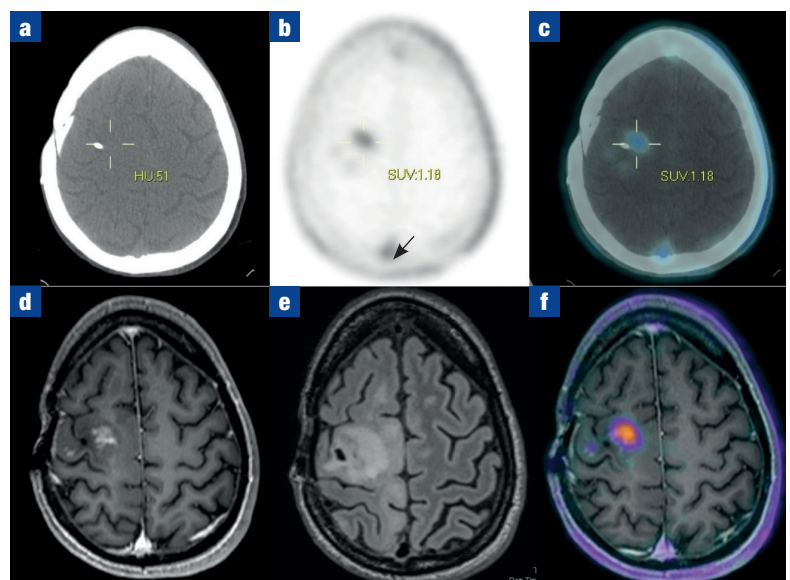


Figure 8. Comparison between ^{18}F -choline PET/CT and PET/MRI in a patient with recurrent glioblastoma multiforme. **a–c.** Axial F-choline PET/CT and **(d–f)** axial F-choline PET/MRI show disease recurrence at the site of previously resected glioblastoma multiforme. Notice the superior details of the tumour extension on the MRI images compared to the CT scan. There is physiological uptake of F-choline in the sagittal sinus (arrow).

Conclusions

Combined PET/MRI is a valuable tool for imaging brain gliomas and can provide morphological and physiological information about the tumour after a single scan. It is superior to conventional MRI in differentiating low from high grade gliomas and detecting malignant transformation of low grade gliomas. It also can support radiotherapy and surgery planning, provide prognostic information, and differentiate tumour recurrence from benign post-therapy changes more accurately than the MRI scan alone. Nevertheless, the higher cost of the combined PET/MRI and the presence of other alternatives, such as PET/CT, restrict its availability. **BJHM**

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- American Cancer Society. 2016. Cancers that Develop in Children. (accessed 25 October 2018) <https://www.cancer.org/cancer/cancer-in-children/types-of-childhood-cancers.html>
- Bisdas S, Ritz R, Bender B et al. Metabolic mapping of gliomas using hybrid MR-PET imaging: feasibility of the method and spatial distribution of metabolic changes. *Invest Radiol.* 2013 May;48(5):295–301. <https://doi.org/10.1097/RLI.0b013e31827188d6>
- Chen W, Silverman DH, Delaloye S et al. 18F-FDOPA PET imaging of brain tumors: comparison study with 18F-FDG PET and evaluation of diagnostic accuracy. *J Nucl Med.* 2006 Jun;47(6):904–911.
- Chen Y, An H. Attenuation correction of PET/MR imaging. *Magn Reson Imaging Clin N Am.* 2017 May;25(2):245–255. <https://doi.org/10.1016/j.mric.2016.12.001>
- Children with Cancer UK. 2019. Brain and Spinal Tumours. (accessed 11 June 2019) <https://www.childrenwithcancer.org.uk/childhood-cancer-info/cancer-types/brain-spinal-tumours/>
- Ciarniello A, Mansi L. 2016. PET-CT and PET-MRI in Neurology: SWOT Analysis Applied to Hybrid Imaging. Springer Nature: Switzerland. <https://doi.org/10.1007/978-3-319-31614-7>
- Das K, Mittal BR, Vasistha RK, Singh P, Mathuriya SN. Role of (18)F-fluorodeoxyglucose positron emission tomography scan in differentiating enhancing brain tumors. *Indian J Nucl Med.* 2011 Oct;26(4):171–176. <https://doi.org/10.4103/0972-3919.106698>
- Davis M. Glioblastoma: overview of disease and treatment. *Clin J Oncol Nurs.* 2016 Oct 1;20(5) Suppl:S2–S8. <https://doi.org/10.1188/16.CJON.S1.2-8>
- DeGrado TR, Baldwin SW, Wang S et al. Synthesis and evaluation of (18)F-labeled choline analogs as oncologic PET tracers. *J Nucl Med.* 2001 Dec;42(12):1805–1814.
- Delbeke D, Meyerowitz C, Lapidus RL, Maciunas RJ, Jennings MT, Moots PL, Kessler RM. Optimal cutoff levels of F-18 fluorodeoxyglucose uptake in the differentiation of low-grade from high-grade brain tumors with PET. *Radiology.* 1995 Apr;195(1):47–52. <https://doi.org/10.1148/radiology.195.1.7892494>
- Filss CP, Galldiks N, Stoffels G et al. Comparison of 18F-FET PET and perfusion-weighted MR imaging: a PET/MR imaging hybrid study in patients with brain tumors. *J Nucl Med.* 2014 Apr 01;55(4):540–545. <https://doi.org/10.2967/jnumed.113.129007>
- Galldiks N, Dunkl V, Stoffels G et al. Diagnosis of pseudoprogression in patients with glioblastoma using O-(2-[18F]fluoroethyl)-l-tyrosine PET. *Eur J Nucl Med Mol Imaging.* 2015 Apr;42(5):685–695. <https://doi.org/10.1007/s00259-014-2959-4>
- Gerges N, Fontebasso AM, Albrecht S, Faury D, Jabado N. Pediatric high-grade astrocytomas: a distinct neuro-oncological paradigm. *Genome Med.* 2013;5(7):66. <https://doi.org/10.1186/gm470>
- Hara T, Kondo T, Hara T, Kosaka N. Use of 18F-choline and 11C-choline as contrast agents in positron emission tomography imaging—guided stereotactic biopsy sampling of gliomas. *J Neurosurg.* 2003 Sep;99(3):474–479. <https://doi.org/10.3171/jns.2003.99.3.0474>
- Hojjati M, Badve C, Garg V et al. Role of FDG-PET/MRI, FDG-PET/CT, and dynamic susceptibility contrast perfusion MRI in differentiating radiation necrosis from tumor recurrence in glioblastomas. *J Neuroimaging.* 2018 Jan;28(1):118–125. <https://doi.org/10.1111/jon.12460>
- Jena A, Taneja S, Gambhir A et al. Glioma recurrence versus radiation necrosis. *Clin Nucl Med.* 2016 May;41(5):e228–e236. <https://doi.org/10.1097/RLU.0000000000001152>
- Kato T, Shinoda J, Nakayama N et al. Metabolic assessment of gliomas using 11C-methionine, [18F] fluorodeoxyglucose, and 11C-choline positron-emission tomography. *AJNR Am J Neuroradiol.* 2008 Jun;29(6):1176–1182. <https://doi.org/10.3174/ajnr.A1008>
- Kim S, Chung JK, Im SH et al. 11C-methionine PET as a prognostic marker in patients with glioma: comparison with 18F-FDG PET. *Eur J Nucl Med Mol Imaging.* 2005 Jan;32(1):52–59. <https://doi.org/10.1007/s00259-004-1598-6>
- Knopp EA, Cha S, Johnson G et al. Glial neoplasms: dynamic contrast-enhanced T2*-weighted MR imaging. *Radiology.* 1999 Jun;211(3):791–798. <https://doi.org/10.1148/radiology.211.3.r99jn46791>
- Koktysh L. 2017. The Past, Present and Future of PET/MRI Scanners. (accessed 20 October 2018) <https://www.itnonline.com/article/past-present-and-future-petmri-scanners>
- Komori T. The 2016 WHO classification of tumours of the central nervous system: the major points of revision. *Neurol Med Chir (Tokyo).* 2017;57(7):301–311. <https://doi.org/10.2176/nmc.ra.2017-0010>
- Kunz M, Thon N, Eigenbrod S et al. Hot spots in dynamic (18)F-FET-PET delineate malignant tumor parts within suspected WHO grade II gliomas. *Neuro Oncol.* 2011 Mar;13(3):307–316. <https://doi.org/10.1093/neuonc/noq196>
- National Comprehensive Cancer Network. 2018. Central Nervous System Cancers (Version 1.2017). (accessed 2 February 2019). https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf
- Nihashi T, Dahabreh IJ, Terasawa T. Diagnostic accuracy of PET for recurrent glioma diagnosis: a meta-analysis. *AJNR Am J Neuroradiol.* 2013 May;34(5):944–950, S1–S11. <https://doi.org/10.3174/ajnr.A3324>
- Scott JN, Brasher PM, Sevick RJ, Rewcastle NB, Forsyth PA. How often are nonenhancing supratentorial gliomas malignant? A population study. *Neurology.* 2002 Sep 24;59(6):947949. <https://doi.org/10.1212/wnl.59.6.947>
- Spence AM, Mankoff DA, Muzi M. 2007. The role of PET in the management of brain tumors. (accessed 1 March 2019). <https://appliedradiology.com/articles/the-role-of-pet-in-the-management-of-brain-tumors>
- Takenaka S, Asano Y, Shinoda J et al. Comparison of (11)C-methionine, (11)C-choline, and (18)F-fluorodeoxyglucose-PET for distinguishing glioma recurrence from radiation necrosis. *Neurol Med Chir (Tokyo).* 2014;54(4):280–289. <https://doi.org/10.2176/nmc.0a2013-0117>
- Tan H, Chen L, Guan Y, Lin X. Comparison of MRI, F-18 FDG, and 11C-choline PET/CT for their potentials in differentiating brain tumor recurrence from brain tumor necrosis following radiotherapy. *Clin Nucl Med.* 2011 Nov;36(11):978–981. <https://doi.org/10.1097/RLU.0b013e31822f68a6>
- Tudisca C, Nasoodi A, Fraioli F. PET-MRI: clinical application of the new hybrid technology. *Nucl Med Commun.* 2015;36(7):666–678. <https://doi.org/10.1097/MNM.0000000000000312>
- Wagenknecht G, Kaiser HJ, Mottaghy FM et al. MRI for attenuation correction in PET: methods and challenges. *Magn Reson Mater Phys.* 2013 26:99. <https://doi.org/10.1007/s10334-012-0353-4>

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