tumor cells, in order to detect tumors and validate the treatment response [Table 1].

Hypometabolism on FDG PET in brain lesions and stability over a period is indicative of nonmalignancy.[24] When it is difficult to differentiate preoperatively a primary brain tumor from metastasis,[25] FDG PET may be helpful in depicting areas of systemic involvement,[26] or localizing the primary cancer site.[27,28] Occasionally, patients may present with brain lesions, radiologically compatible with brain metastases that after biopsy are proven to be multifocal gliomas.[29,30] In such cases, FDG PET may aid in pinpointing the area of stereotactic biopsy,[31,32] assist in tumor delineation during radiotherapy planning[33] and assessment of treatment response.[34]

In a study of 81 recurrent glioma patients studied by FDG PET, it was found that the higher the FDG uptake by the tumor it was associated with worse survival.[35] In addition, pretreatment uptake of FDG in 25 patients with recurrent gliomas subsequently

Table 1: Representative studies on utility of FDG PET and comparison with other tracers in patients with primary brain tumors

Study	No. of patients	Reason for the exam	Results (%)	Study conclusion
Colavolpe *et al.*[12]	25 patients with recurrent glioma	To assess utility of FDG PET/CT in patients receiving bevacizumab and irinotecan therapy	FDG uptake was the most powerful predictor of both PFS and OS using the RANO criteria	Pretreatment FDG PET predicts survival in recurrent glioma patients following anti-angiogenic therapy
Santra *et al.*[13]	90 patients with possible recurrent glioma	To compare FDG PET/CT with contrast MRI	PET sensitivity: 70 Specificity: 97 MRI sensitivity: 95 Specificity: 23	FDG PET/CT was an accurate modality to detect glioma recurrence
Borbely *et al.*[14]	59 patients with primary and recurrent brain gliomas (50 had MET PET; 33 had FDG PET)	To compare FDG PET with MET PET for *in vivo* grading of malignant gliomas	FDG PET superior to MET PET for grading of gliomas	FDG PET recommended for grading but MET PET may be used for assessing the extent of the tumor
Singhal *et al.*[15]	102 patients with confirmed gliomas were followed for an average of 34.6 months after PET	To compare FDG PET with MET PET and MRI	MET PET superior to FDG PET and MRI in predicting survival in low-grade gliomas	For low grade gliomas MET PET preferred to FDG PET
Yamaguchi *et al.*[16]	26 patients with untreated or recurrent adult gliomas had preoperative FDG (n = 25) and/or MET (n = 22) PET	To compare FDG PET with MET PET	FDG better for tumor grade MET better for delineating the extent of the tumor	Both tracers complement each other to plan the extend of tumor resection
Tripathi *et al.*[17]	15 patients with untreated or recurrent low grade gliomas	To compare FDG PET with FDOPA PET and FLT PET	FDOPA PET superior to both FDG and FLT PET for detection of low grade gliomas	FDOPA PET should be the radiotracer of choice for low grade glioma
Chen *et al.*[18]	25 patients with with untreated or recurrent adult gliomas	To compare FDG PET with FLT PET	FLT PET better to image recurrent high-grade tumors, to correlate with Ki-67 values, and predict tumor progression and survival	FLT a promising tracer of proliferation in high-grade gliomas
Enslow *et al.*[19]	15 recurrent glioma patients	To compare FDG PET with FLT PET	Both FDG PET and FLT PET could differentiate between tumor recurrence and radiation necrosis	FLT PET offers no advantage over FDG PET
Karunanithi *et al.*[20]	28 patients with recurrent gliomas	To compare FDG PET with FDOPA PET for diagnosis of recurrence	FDG sensitivity: 47.6 FDG specificity: 100 FDOPA sensitivity: 100 FDOPA specificity: 85.7	The difference between FDOPA and FDG PET was significant for low grade glioma but not for high grade tumors
Tripathi *et al.*[21]	35 patients with recurrent glioma	To compare FDG PET with MET PET	FDG sensitivity: 81.2 FDG specificity: 88.9 MET sensitivity: 94.7 MET specificity: 88.9	MET should be the radiotracer of choice for recurrent gliomas
Potzi *et al.*[22]	28 patients with recurrent GBM	To evaluate FDG and MET PET for recurrent glioma		FDG PET of limited value; MET PET not superior to conventional imaging
Nihashi *et al.*[23]	Meta-analysis of 26 heterogenous studies	To evaluate the diagnostic accuracy of PET and compare it with conventional imaging modalities	FDG PET and MET PET with acceptable accuracy for diagnosing recurrent glioma	Prospective studies with direct comparisons between various imaging modalities required

PET: Positron emission tomography; CT: Computed tomography; MRI: Magnetic resonance imaging; RANO: Response assessment in neuro-oncology; FDG: (18)F-flurodeoxyglucose; FET: O-(2-(18)F-fluoroethyl)-l-tyrosine; GBM: Glioblastomamultiforme; MET: (11)C-methionine; FDOPA: (18)F-FDOPA; FLT: 3'-Fluoro-3' deoxythymidine; PFS: Progression-free survival; OS: Overall survival; HGG: WHO grades III or IV; LGG: WHO grades I or II

treatment with bevacizumab and irinotecan predicted response to the treatment and correlated with overall survival.[12] Similar predictive value of FDG-PET was reported with other therapies in glioma patients.[36] FDG PET compared to MRI scans with and without contrast enhancement had much higher specificity (97% *vs*. 23%) for detection of recurrence in 90 glioma patients clinically suspicious of tumor growth.[13]

OTHER POSITRON EMISSION TOMOGRAPHY TRACERS AND COMPARISON WITH (18)F-FLURODEOXYGLUCOSE

During the last several years, new PET tracers have been developed for a wide range of biological targets [Table 2].[37]

PET of amino acid transport and metabolism could be a reliable method in assessing a metabolic response after treatment of a tumor or in establishing a treatment-related effect, depending on the rate of the tracer uptake by tumor. Employment of imaging amino acid transport may prove to have an important clinical role in the management of brain tumor patients since it may result in changes in therapeutic management.[62]

For example, application of O-(2-(18)F-fluoroethyl)-L-tyrosine (FET) PET/CT in newly diagnosed brain tumors could predict their biologic behavior in most of the cases.[48,52,63] FET represents an artificial amino acid not incorporates into proteins but transports into active glioma cells.[46] FET-PET may be more accurate than FDG-PET for differentiation of malignant gliomas from low-grade gliomas,[64,65] by their low FET uptake on PET in the low-grade tumors.[66,67] Thus, in a study of 88 patients with an intracerebral lesion observed by MRI, FET PET was performed, followed by biopsy in 60 patients. The sensitivity of FET PET for high-grade tumors (WHO III-IV) was reported 94% and for low-grade tumors (WHO I-II) 68%. However, there were

Table 2: Other PET tracers for patients with gliomas

Tracer	Mechanism	No. of studies	Untreated or recurrent glioma	Advantages	Disadvantages
AMT[38]	Amino acid PET tracer not incorporated into proteins but transported into gliomas via the kynurenine pathway	1	Recurrent	AMT PET could differentiate between tumor and XRT necrosis	False positive results can occur in cortical dysplasia with epileptic focus[39]
MET PET[40]	MET is transported by the LAT1 amino acid transporter into glioma and is incorporated into proteins[41]	5	Upfront[15] Recurrent[41-44]	MET uptake correlated with prognosis[15] MET PET could differentiate between tumor and XRT necrosis[40,42] Correlate with OS and outcome[43,44]	Short half-life (20 min) requiring on site production; MET may accumulate in brain abscesses or inflammation[45]
FET PET	FET is an artificial amino acid transported into active glioma cells but incorporated into proteins[46]	5	Upfront[47,48] Recurrent[49-51]	FET PET could differentiate glioma from nonneoplastic tissue FET PET distinguished active tumor from radiation necrosis;[50,51] dynamic FET uptake could differentiate between high and low grade tumors[49]	Rare false positive in granulomatous conditions and reactive astogliosis[52] or false negative cases[53]
FDOPA PET: (18)F-FDOPA	l-DOPA is the precursor of dopamine and is transported physiologically into the brain and abnormally into the brain tumors[54]	2	Upfront[55] Recurrent[55,56]	Correlation of FDOPA uptake, tumor proliferation and grade Diagnostic accuracy of recurrence similar to MRI[56]	Diagnostic usefulness mostly in upfront gliomas; limited data
FLT PET[57,58]	FLT is an analog of deoxythymidine, which is composed of deoxyribose and the pyrimidine base thymine and phosphorylated by thymidine kinase 1 during DNA synthesis[59]	2	Upfront[57] Recurrent[58]	FLT PET could differentiate between high and low grade tumors FLT-PET responses correlated with OS	FLT may accumulate in benign lesions with BBB disruption[45]
CHO: (18)F-fluoromethylcholine	During glioma cell proliferation choline is trapped into the cells to produce phosphatidylcholine, a necessary constituent of the plasma membrane[60]	1	Various brain lesions (tumors or nontumors)	Higher uptake in malignant tumors	It may also accumulate in various inflammatory processes[61]

PET: Positron emission tomography; MRI: Magnetic resonance imaging; XRT: Radiation therapy; BBB: Blood brain barrier; MET: (11)C-methionine; AMT: Alpha-(11)C-methyl-l-tryptophan; FDG: (18)F-flurodeoxyglucose; FET: O-(2-(18)F-fluoroethyl)-l-tyrosine; FDOPA: (18)F-FDOPA; FLT: 3'-fluoro-3' deoxythymidine; PFS: Progression-free survival; OS: Overall survival

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