OBJECTIVE ARTICLE

99mTc-Methionine Hybrid SPECT/CT for Detection of Recurrent Glioma

Comparison With 18F-FDG PET/CT and Contrast-Enhanced MRI

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OBJECTIVES: Posttherapy changes in treated glioma patients cannot be reliably differentiated from tumor recurrence. We evaluated the role of 99mTc-methionine SPECT/CT for the detection of recurrent glioma and compared the same with 18F-FDG PET/CT and contrast-enhanced MRI (CeMRI).

METHODS: Forty-four patients with histologically proven, previously treated glioma and clinical suspicion of recurrence were prospectively enrolled in the study. Of these 44 patients, 39 (28 male and 11 female subjects; age, 38.05 ± 9.7 years) underwent 99mTc-methionine SPECT/CT, 18F-FDG PET/CT, and CeMRI of the brain and were included for final analysis. Combination of repeat imaging, biopsy, and/or clinical follow-up (6-36 months) was taken as reference standard. Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were calculated. Diagnostic values among modalities were compared.

RESULTS: Positive predictive value and negative predictive value for 99mTc-methionine SPECT/CT, 18F-FDG PET/CT, and CeMRI were 95.6% and 56.2%, 92.3% and 61.5%, and 79.4% and 42.9%, respectively. Sensitivity and specificity for the 3 modalities were 75.9% and 90%, 82.8% and 80%, and 87.1% and 30%. Specificity of 99mTc-methionine SPECT/CT was significantly higher than that of CeMRI (P < 0.0001) but not of 18F-FDG PET/CT (P = 0.36). No significant difference was seen between the modalities for sensitivity and accuracy.

CONCLUSIONS: 99mTc-methionine is a promising tracer for detection of recurrent glioma. Diagnostic values of 99mTc-methionine SPECT/CT are similar to 18F-FDG, although it is more specific than CeMRI. So it may be used as a cost-effective alternative and also where PET/CT is not available.

Key Words: glioma, recurrence, 99mTc-methionine, SPECT/CT, 18F-FDG, PET/CT, MRI

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The incidence of central nervous system tumors in India ranges from 5 to 10 per 100,000 population per annum.1,2 Gliomas are the most common type of central nervous system tumors. Management of brain tumors relies heavily on imaging modalities such as CT, MRI, SPECT, and PET. Whereas CT and MRI are structure-based imaging, PET and SPECT are functional/molecular imaging methods.3 CT is generally used for initial evaluation if the patient presents with acute symptoms or is used when MRI is unavailable. Contrast-enhanced (Ce) MRI is the modality of choice for diagnosing brain tumors and planning treatment. However, in the posttreatment setting, PET/SPECT is the preferred modality.

Differentiating treatment-induced necrosis from tumor recurrence on follow-up is imperative for accurate management of posttherapy brain tumor patients. However, because of similar presentation of necrosis and recurrence, clinically as well as on MRI, reliable distinction between the two is often difficult.4 On MRI, both might show contrast enhancement with associated edema and mass effect.5 Features specific to necrosis and recurrence have been reported, but no combination of features have been established as a sufficiently reliable differentiating factor.

Among the PET tracers, 18F-fluorodeoxyglucose (18F-FDG) is most commonly used, but high physiologic uptake in normal brain tissue lowers its sensitivity. Amino acid–based PET tracers such as 11C-methionine (11C-MET), 18F-fluoroethyltyrosine, and 18F-fluorodopa have higher sensitivity, but they have limited availability. Among these, 11C-MET is the most extensively studied tracer and has shown excellent results for differentiating tumor recurrence and posttreatment necrosis. Unfortunately, because 11C has a short half-life (20 minutes), an onsite cyclotron is imperative for synthesis of 11C-methionine.6,9 99mTc-methionine (99mTc-MET) is a SPECT tracer used for imaging protein/amino acid metabolism and thus can be a possible alternative to 11C-MET PET for recurrent glioma.8,9 However, its efficacy in recurrent gliomas has not been adequately studied, as only few studies with small sample size are available in literature. No study is available comparing 99mTc-MET SPECT with the commonly used 18F-FDG PET in this regard. Furthermore, these studies have used SPECT alone, which poses problem in differentiating physiological radiotracer uptake from pathological. This problem can be overcome with use of hybrid SPECT/CT.4,10,11 Based on these findings, we hypothesized that 99mTc-MET SPECT/CT will show high diagnostic accuracy in recurrent glioma. In the present study, we have prospectively evaluated the role of 99mTc-MET SPECT/CT in suspected recurrent gliomas and compared the same with 18F-FDG PET/CT and CeMRI.

PATIENTS AND METHODS

This was a prospective study conducted at the Department of Nuclear Medicine of a tertiary-care hospital between 2012 and 2016. Ethical clearance for the study was obtained from institutional ethical committee (IEC/ NP-280/2012). The patient recruitment details including inclusion and exclusion criteria are presented in the
As per the above-mentioned criteria, 44 consecutive patients were recruited in the study and underwent 99mTc-MET SPECT/CT, 18F-FDG PET/CT, and CeMRI of the brain within a span of 2 weeks. Five of these 44 patients could not undergo all the 3 imaging studies and thus were not included for final analysis.

**Synthesis of 99mTc-MET**

Diethyl-triamine-pentaacetic acid (DTPA)-bis-methionine, as a single vial lyophilized cold kit, was synthesized and supplied by Division of Cyclotron and Radiopharmaceutical Sciences, Institute of Nuclear Medicine and Allied Sciences, Delhi, India. The synthesis of DTPA-bis-methionine, detailed radiolabeling procedure, cell-binding studies, and preclinical results have been previously reported by Hazari et al. Each vial contained 10 mg of DTPA-bis-methionine and 0.5 mg stannous chloride. It was labeled with 99mTc by adding freshly eluted 99mTc sodium pertechnetate (740–925 MBq/mL; 20–25 mCi/mL), followed by incubation at room temperature for 30 minutes. The final product was filtered using Millipore filter (0.22 μm; Durapore, Merck KGaA, Darmstadt, Germany). Labeling efficiency of the product was greater than 99%, as tested by paper chromatography using Whatman paper (stationary phase; Union Drug & Chemical Company, Mumbai, India) and methyl-ethyl ketone (mobile phase).

**99mTc-MET SPECT/CT Protocol**

Patients were injected 740 to 925 MBq (20–25 mCi) of 99mTc-MET intravenously. Two hours postinjection, SPECT/CT of the brain was acquired on a dual SPECT/CT system with 6-slice CT (Symbia T6; Siemens Medical Solutions, Erlangen, Germany). Patients were positioned supine on the scan table, and the head was immobilized using a headband. SPECT was acquired with brain contour orbits over 360-degree arc, with 90 stops (angular step 4 degrees; 25 seconds per stop; 128 × 128 matrix; 140 keV ± 20% photopeak; parallel hole, low-energy high-resolution collimator). SPECT was followed by CT examination (130 kV, 100 mAs, pitch-1, 512 × 512 matrix). SPECT emission image data were processed by use of ordered-subsets expectation maximization reconstruction software with 2 iterations and 8 subsets. CT-based attenuation correction was applied to the images. Subsequently, tomographic slices were generated and displayed transaxial, coronal, and sagittal slices. Fused emission and transmission images were visually inspected for correctness of coregistration.

**18F-FDG PET/CT Protocol**

Patients were asked to fast for at least 6 hours before the test. Blood glucose levels were below 140 mg/dL for all patients, as checked before the test. Patients were injected 296 to 370 MBq (8–10 mCi) of 18F-FDG intravenously and rested in a quiet room. Approximately 45 to 60 minutes postinjection, PET/CT of the brain was acquired on a dedicated scanner (Biograph 2; Siemens Medical Solutions) with lutetium oxyorthosilicate detectors. CT scan of the brain was acquired at 120 kV, 206 mAsEff, 3 mm slice thickness, 0.6 pitch, and 300 mm FOV. After this, 3D PET acquisition was done over 1 bed position at 15 minutes per bed scan duration, 400 × 400 matrix, and zoom 2. Image reconstruction was done with iterative reconstruction method (5 iterations; 21 subsets). CT-based attenuation correction was applied to the images. Reconstructed images were displayed and analyzed in transverse, sagittal, and coronal views.

**CeMRI**

All patients had undergone CeMRI using T1- and T2-weighted and FLAIR sequences. Slice thickness was adjusted to 1 mm. Contrast-enhanced images were obtained after intravenous administration of gadopentetate dimeglumine at a dose of 0.1 mmol/kg using standard procedures. The images of the brain were retrieved and reviewed by an experienced radiologist.

**Image Analysis**

Two experienced nuclear medicine physicians (R.K. and P.S.) independently evaluated all the images of SPECT/CT and PET/CT, whereas the MRI images were evaluated by an experienced radiologist (A.G.). In case of any discrepancy, a consensus was reached after discussion. They were blinded to clinical findings.

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**FIGURE 1.** Flowchart showing participant recruitment.

Inclusion criteria
1. Biopsy proven glioma &
2. Previous treatment for glioma &
3. Clinical/radiological suspicion of recurrence &
4. Age ≥ 18 years &
5. Written informed consent

Exclusion criteria
1. Age < 18 years &/or
2. Refusal to give written informed consent

Further exclusion
1. All three scans not done &/or
2. Failure to follow up
the basic clinical indication of suspected recurrent brain tumor) as well as to each other’s image interpretation. 99mTc-MET SPECT/CT images were interpreted first, followed by 18F-FDG PET/CT. 99mTc-MET SPECT/CT images were interpreted as positive or negative for recurrence. Abnormal focus of increased radiotracer uptake (as compared with background activity) in brain parenchyma was declared as positive for viable tumor. For quantitative analysis, region of interest was drawn surrounding the uptake area, and it was compared with the same site of the contralateral hemisphere which serve as background (T/B uptake ratio = maximum count per pixel in tumor/average count per pixel in normal brain parenchyma). 18F-FDG PET/CT images were interpreted as positive for recurrent tumor if there was a definite lesion on CT images which was hypermetabolic/isometabolic/hypometabolic on PET images or if there was an increased focal 18F-FDG uptake without any clearly discernible lesion on CT. For CeMRI, gadopentetate dimeglumine-enhancing lesions were considered positive for recurrence in MRI images. Apart from presence/absence of lesions, the number of lesions was also noted.

Reference Standard
All patients were on clinical and/or radiological follow-up for at least 6 months (range, 6–36 months). Combination of repeat imaging (CeMRI), biopsy (when available), and/or clinical follow-up was taken as reference standard. Histopathology was the reference standard in patients who underwent reoperation after diagnosis of viable tumor. Disease-related adverse events (death/neurological deterioration), progressive disease on follow-up imaging, and/or positive histopathology report were considered positive for recurrence.

Statistical Analysis
All the statistical analysis was done using MedCalc 11.3.0.0 (MedCalc Software, Acacialaan, Ostend, Belgium). Kolmogorov-Smirnov test was used to check the normality of the data. Descriptive statistics such as mean, median, range, and standard deviation were used to summarize the clinical and demographic profiles of all the patients. Sensitivity, specificity, predictive values with 95% confidence interval (CI), and accuracy was calculated for each modality. χ² test was used to compare diagnostic values. McNemar test with Yates correction was used to compare the results of 99mTc-MET SPECT/CT, 18F-FDG PET/CT, and CeMRI. Wilcoxon test was used to compare number of lesions on different modalities.

RESULTS

Patient Characteristics
Patient characteristics are summarized in Table 1. Mean age of patients was 38.0 ± 9.7 years, ranging from 18 to 58 years (95% CI 34.9–41.2). The mean duration between end of primary treatment to 99mTc-MET SPECT/CT was 11.6 months (range, 2–36 months). The mean interval between surgery (in 30 patients who underwent primary surgery) to 99mTc-MET SPECT/CT was 16.6 months (range, 4–40 months).

As per reference standard detailed previously, 29 patients were positive, and 10 patients were negative for tumor recurrence. Of the 29 positive patients, 15 had primary low-grade tumor, and 14 had primary high-grade tumor at diagnosis. Among the 21 low-grade gliomas, 15 were positive, and 6 were negative for tumor recurrence. Of the 18 high-grade gliomas, 14 were positive, and 4 were negative for recurrence.

99mTc-MET SPECT/CT Results
99mTc-MET SPECT/CT was positive in 23 patients, of whom, 22 were true positive and 1 was false positive. It was negative in 16 patients, of which, 9 true negative and 7 were false negative. Among 21 cases with low-grade gliomas, SPECT/CT was positive in 11 cases, all of which were true positives. It was negative in 9 cases, of which, 6 were true negatives and 3 were false negative. Among 18 cases with high-grade gliomas, SPECT/CT was positive in 12 cases, only one of which was false positive. It was negative in 6 cases, of which, 3 were true negative and 3 were false negative. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy in overall patient population, low-grade patients, and high-grade patients are given in Table 2 (Figs. 2–5). Twenty-six lesions were detected in 23 positive patients on MET scan. Mean tumor-to-background ratio on 99mTc-MET SPECT/CT was 6.27 (range, 2.59–27.15; 95% CI, 4.09–8.45).

18F-FDG PET/CT Results
18F-FDG PET/CT was positive in 26 patients, of which, 24 were true positive and 2 were false positive. It was negative in
TABLE 2.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>99mTc-MET SPECT/CT</th>
<th>18F-FDG PET/CT</th>
<th>CeMRI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sensitivity</strong></td>
<td>75.9% (56.6%–95.3%)</td>
<td>82.8% (64.2%–94.1%)</td>
<td>87.6% (70.2%–96.4%)</td>
</tr>
<tr>
<td><strong>Specificity</strong></td>
<td>90.4% (69.3%–97.5%)</td>
<td>80.1% (60.4%–97.5%)</td>
<td>92.8% (71.4%–99.7%)</td>
</tr>
<tr>
<td><strong>PPV</strong></td>
<td>79.5% (68.9%–90.7%)</td>
<td>62.4% (42.4%–82.0%)</td>
<td>78.3% (59.8%–94.9%)</td>
</tr>
<tr>
<td><strong>NPV</strong></td>
<td>75.9% (56.6%–95.3%)</td>
<td>87.6% (70.2%–96.4%)</td>
<td>97.5% (78.1%–99.9%)</td>
</tr>
<tr>
<td><strong>Accuracy</strong></td>
<td>79.4% (68.5%–90.3%)</td>
<td>82.0% (63.5%–97.5%)</td>
<td>91.7% (77.5%–99.8%)</td>
</tr>
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</table>

13 patients, of which, 8 were true negative and 5 were false negative. Among 21 patients with low-grade gliomas, PET/CT was positive in 14 cases, of which, 13 were true positive and 1 was false positive. It was negative in the remaining 7 cases, of which, 5 were true negative. Among 18 cases with high-grade gliomas, PET/CT was positive in 12 cases, only one of which was false positive. It was negative in 6 cases, of which, 3 were true negative and 3 were false negative. Sensitivity, specificity, PPV, NPV, and accuracy in overall patient population, low-grade patients, and high-grade patients are given in Table 2 (Figs. 2–5).

CeMRI Results

MRI was positive in 32 patients, of which, 25 were true positive and 7 were false positive. It was negative in 7 patients, of which, 3 were true negative and 4 were false negative. Among 21 cases with low-grade gliomas, CeMRI was positive in 20 cases, of which, 14 were true positive and 6 false positive. It was false negative in the remaining 1 case. Among 18 cases with high-grade gliomas, MRI was positive in 12 cases, only one of which was false positive. It was negative in 6 cases, of which, 3 were true negative and 3 were false negative. Sensitivity, specificity, PPV, NPV, and accuracy in overall patient population, low-grade patients, and high-grade patients are given in Table 2 (Figs. 2–5).

Comparison of 99mTc-MET SPECT/CT and 18F-FDG PET/CT

Overall, no significant difference was seen between sensitivity ($P = 0.64$), specificity ($P = 0.36$), and accuracy ($P = 0.99$) between 99mTc-MET SPECT/CT and 18F-FDG PET/CT. They were concordant (Figs. 2, 3, and 5) in 28 patients and discordant (Fig. 4) in the remaining 11 patients ($P = 0.55$). Sensitivity, specificity, and accuracy of 99mTc-MET SPECT/CT and 18F-FDG PET/CT were not significantly different in low-grade tumors ($P = 0.49$), $P = 0.16$, and $P = 0.72$, respectively). Among these patients, the 2 modalities were concordant in 16 patients and discordant in the remaining 5 patients ($P = 0.37$). Similarly, sensitivity, specificity, and accuracy of 99mTc-MET SPECT/CT and 18F-FDG PET/CT were not significantly different in high-grade tumors ($P = 1.00$, for all). They were concordant in 12 patients and discordant in the remaining 6 patients ($P = 1.00$).

Comparison of 99mTc-MET SPECT/CT and CeMRI

Overall, no significant difference was seen between sensitivity ($P = 0.32$) and accuracy ($P = 0.99$) between 99mTc-MET SPECT/CT and CeMRI, but the latter was more specific ($P < 0.001$). They were concordant (Fig. 2) in 22 patients and discordant (Figs. 3–5) in the remaining 17 patients ($P = 0.049$). Sensitivity and accuracy of 99mTc-MET SPECT/CT and CeMRI were not significantly different in low-grade tumors ($P = 0.18$ and $P = 0.48$, respectively), but the former was more specific ($P < 0.001$). Among these patients, they were concordant in 10 patients and discordant in the remaining 11 patients ($P = 0.01$). Similarly, sensitivity, specificity, and accuracy of 99mTc-MET SPECT/CT and CeMRI were not significantly different in high-grade tumors ($P = 1.00$, for all). They were concordant in 12 patients and discordant in the remaining 6 patients ($P = 1.00$).

Lesion-wise Comparison

99mTc-MET SPECT/CT detected 26 lesions in 23 positive patients. 18F-FDG PET/CT and CeMRI could detect 34 lesions in 26 positive patients and 40 lesions in 32 positive patients, respectively. On lesion-wise comparison, MRI detected significantly more lesions than 99mTc-MET SPECT/CT ($P = 0.01$) but not 18F-FDG PET/CT ($P = 0.14$). Also, no significance was seen between number of
lesions detected using $^{99m}$Tc-MET SPECT/CT and $^{18}$F-FDG PET/CT ($P = 0.11$).

**DISCUSSION**

Imaging of recurrent gliomas demands reliable distinction between recurrent tumor and therapy-induced necrosis. Although CeMRI and $^{18}$F-FDG PET/CT both have been used for the purpose, they have their own limitations, and therefore, newer more reliable options are being sought. $^{99m}$Tc-MET could prove to be a cost-effective and easily synthesized radiotracer for imaging recurrent brain tumor.$^{4,9}$ In the present study, methionine was easily and successfully radiolabeled with $^{99m}$Tc using indigenously developed single vial kit with high labeling efficiency (>99%). This makes it suitable for widespread use in peripheral centers as well with only gamma camera facility. The principle of using $^{99m}$Tc-MET for imaging in glioma is based on targeting upregulated amino acid transport secondary to increased amino acid demand in malignant cells. The increased uptake is attributed in part to passive diffusion that is governed by blood flow to tumor and partly to overexpression of L-type amino acid transporter 1 in glioma cells.$^{8,9,13}$

For imaging of brain tumors, $^{18}$F-FDG PET/CT has certain diagnostic drawbacks especially in lesions with uptake similar or marginally higher than the normal brain tissue, such as low-grade gliomas.$^{14–16}$ In a meta-analysis of 26 studies, the specificity and sensitivity of $^{18}$F-FDG PET in recurrent glioma ranged from 66% to 85% and 54% to 91%, respectively.$^{17}$ In the present study, the results of $^{99m}$Tc-MET SPECT/CT and $^{18}$F-FDG PET/CT were comparable with no significant difference between overall sensitivity, specificity, and accuracy. The difference was not significant in both low- and high-grade gliomas. This is important because in contrast to $^{18}$F-FDG, $^{99m}$Tc-MET has no physiological uptake in normal brain tissue. Hence, small tumors or tumors with low tracer uptake which can be masked and missed on $^{18}$F-FDG PET/CT can still be visualized with $^{99m}$Tc-MET SPECT/CT. Not to mention, the cost will be much lower as well. However, the spatial resolution of PET is better than SPECT, and this might offset some of the advantages of $^{99m}$Tc SPECT/CT, thereby giving comparable results.

When compared with CeMRI, the overall specificity of $^{99m}$Tc-MET SPECT/CT was significantly higher in the present study. This is extremely important from a clinical point of view. Because of its excellent soft tissue resolution, CeMRI is the primary
imaging modality for diagnosis and delineation of glioma. Even for previously treated patients, NPV of CeMRI is high; it is the PPV for differentiation of recurrence from radiation necrosis that is limited.\textsuperscript{18–20} So, in patients with clinical suspicion of recurrence and a positive CeMRI,\textsuperscript{9}\textsuperscript{99mTc-MET SPECT/CT can be an important problem-solving tool. More importantly, specificity of \textsuperscript{99mTc-MET was also higher in low-grade gliomas as compared with CeMRI. It is this group of patients who will respond to second line/retreatment with improved survival as recurrent high-grade gliomas have poor survival even with currently available optimum therapy. This makes high specificity of \textsuperscript{99mTc-MET SPECT/CT in low-grade glioma critical.}

Studies reporting the efficacy of \textsuperscript{99mTc-MET in recurrent glioma are scarce, and the results are quite heterogeneous. Barai et al compared \textsuperscript{99mTc-MET SPECT with contrast-enhanced CT and pathological findings in recurrent glioma. They reported \textsuperscript{99mTc-MET SPECT to be superior to contrast CT in recurrent brain tumors.\textsuperscript{5} In a recent study, Singh et al evaluated the efficacy of \textsuperscript{99mTc-MET SPECT in recurrent/remnant glioma and compared the same with CeMRI and \textsuperscript{18F-FLT PET/CT.\textsuperscript{9} They reported good agreement between results of \textsuperscript{99mTc-MET SPECT with \textsuperscript{18F-FLT PET and CeMRI. The accuracy of \textsuperscript{99mTc-MET SPECT/CT in the present study was similar to that reported by Singh et al (79.4\% versus 84.8\%).\textsuperscript{9}}

\textsuperscript{11C-MET is an excellent tracer for brain tumor imaging, especially in the setting of recurrence. However, the short half-life of \textsuperscript{11C (20 minutes) necessitates the need for an onsite medical cyclotron for use of this tracer. This makes its use costly and limited. According to available literature, sensitivity and specificity of \textsuperscript{11C-MET PET in recurrent glioma range from 75\% to 100\% and 60\% to 100\%, respectively.\textsuperscript{17,21–23 When the available results are compared with that of the present study, it seems that the diagnostic accuracy of \textsuperscript{99mTc-MET SPECT/CT and \textsuperscript{11C-MET PET in recurrent glioma is comparable. Although the results of a head-to-head comparative study of the 2 tracers would be more reliable, it seems that \textsuperscript{99mTc-MET can be a low-cost and widely available noninferior substitute for \textsuperscript{11C-MET. This is in keeping with a review by Herholz et al who reported that SPECT and PET yield similar results with amino acid tracers in brain tumors.\textsuperscript{7}}

The present study is not without limitations. First, the sample size was relatively small. Second, although histopathological examination should have been the ideal reference standard, it was not available in all patients because of ethical and technical reasons. So, clinical/radiological follow-up was used as reference standard in many patients. This might have biased the diagnostics values. Third, rather than \textsuperscript{18F-FDG PET/CT, \textsuperscript{11C-MET PET/CT should have been ideally compared with \textsuperscript{99mTc-MET SPECT/CT because

\textbf{FIGURE 4.} A 53-year-old man with anaplastic oligodendroglioma, previously treated with surgery, radiotherapy, and chemotherapy. He presented with clinical suspicion of recurrence. Transaxial contrast-enhanced T1-weighted magnetic resonance image (A) showed no definite enhancing lesion. Transaxial \textsuperscript{18F-FDG PET (B) was also negative. Transaxial \textsuperscript{99mTc-MET SPECT/CT (C) image showed intense focal tracer accumulation (arrow) in the medial occipital cortex, suspicious for recurrence. Based on reference standard, the final diagnosis was no recurrence. \textsuperscript{99mTc-MET SPECT/CT was false positive in this patient, possibly because of tracer accumulation in the posterior aspect of the sagittal sinus.

\textbf{FIGURE 5.} A 32-year-old woman with glioblastoma, previously treated with surgery, chemotherapy, and radiotherapy, presented with clinical features of recurrence. Transaxial T2-weighted MRI (A) showed an enhancing lesion in the left parieto-occipital region at postoperative site (arrow), suspicious for recurrence. Transaxial \textsuperscript{18F-FDG PET image (B) and transaxial \textsuperscript{99mTc-MET SPECT/CT (C) showed postoperative cavity (arrow) and no evidence of recurrence. Based on reference standard, the final diagnosis was recurrence with patient showing neurological progression within 6 weeks. \textsuperscript{18F-FDG PET/CT and \textsuperscript{99mTc-MET SPECT/CT were false negative in this patient.
of their similar mode of localization. Fourth, functional MRI parameters such as diffusion metrics and various perfusion parameters including cerebral blood volume have been shown to be useful in diagnosis of recurrent glioma. Unfortunately, these were not available in the present study population. Further prospective studies in larger patient population and comparing $^{99m}$Tc-MET SPECT/CT with $^{18}$F-MET PET/CT and functional MRI are warranted.

**CONCLUSIONS**

$^{99m}$Tc-MET is a promising tracer for evaluating recurrent glioma. $^{18}$F-FDG PET/CT and $^{99m}$Tc-MET SPECT/CT show similar diagnostic values in this setting. Hence, $^{99m}$Tc-MET SPECT/CT may be used as a cost-effective alternative to $^{18}$F-FDG PET/CT for recurrent glioma. Also, $^{99m}$Tc-MET SPECT/CT is more specific than CeMRI for this purpose.

**REFERENCES**